AZN Earnings Call Transcript

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Operator: Good afternoon, and welcome to AstraZeneca's 9 months and Q3 2025 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 carefully review the forward-looking statements disclaimer in the slide deck that accompanies this presentation and webcast. There will be an opportunity to ask questions after today's presentation. [Operator Instructions] And with that, I'd now like to hand the conference over to the Head of Investor Relations at AstraZeneca, Andy Barnett.

Andrew Barnett: A very warm welcome to AstraZeneca's Year-to-Date and Third Quarter 2025 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'd like to cover some important housekeeping items. Firstly, all of the materials presented today are already available on our AstraZeneca Investor Relations website. Next slide, please. This slide contains our cautionary statements regarding forward-looking statements, including the safe harbor provision, which I'd encourage you to take the time to read carefully. 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 as usual, contained within our results announcement. All numbers quoted are in millions of U.S. dollars unless otherwise stated. And next slide, please. This slide shows the agenda for today's call. And following our prepared remarks, we'll open the line for questions. As usual, we will try and cover as many questions as we can during the allotted time, although please limit the number of questions that you asked to allow others a fair chance to participate in the Q&A.; And with that, please advance to the next slide, and I will hand over to Pascal.

Pascal Soriot: Thank you, Andy, and welcome, everyone. I'm pleased to report that our strong growth momentum and pipeline delivery have continued through the first 9 months of 2025. Total revenue grew by 11%, driven by continued demand for our innovative medicines and core EPS increased by 15%. Since our full year results in February, we've achieved 31 regulatory approvals across key regions and the pace at which we are bringing new medicines to patients continues to accelerate. Importantly, we've announced positive results from 16 Phase III trials and 6 of our data sets were presented in plenary sessions at major conferences, a clear reflection of the importance of this data to the medical community. Please advance to the next slide. Combined, our global reach and diverse sources of revenue have a significant strength, ensuring low concentration risk and resilience to regional disruptions. We have continued to deliver strong growth across therapy areas and geographies. In the first 9 months, our oncology franchise grew by 16%, reflecting the ongoing demand for our medicines across the globe. Our Biopharmaceuticals and Rare Disease franchises were also up 8% and 6%,

respectively, with strong growth from our newer medicines more than offsetting the loss of exclusivity of a limited number of mature brands, including Brilinta, Pulmicort and Soliris. Importantly, we continue to see robust growth across all key geographies, particularly in the U.S. and the emerging markets outside of China, where revenues were up 11% and 21%, respectively. Please move to the next slide. We are in a unique catalyst rich period, one that I'm excited to say, look set to continue well beyond 2026. Shown here are the high-value positive studies we've announced in 2025. And as you can see, we are delivering success across all of our key therapy areas. Since our last quarterly update, we've announced four additional positive Phase III study readouts. DESTINY-Breast05 together with DESTINY-Breast11 that read out earlier this year marks an important advance for patients with early HER2-positive breast cancer that could potentially benefit from a HER2. TROPION-Breast02 has the potential to establish Datroway as a new standard of care in triple-negative breast cancer. The Bax24 trial results reinforce the best-in-class profile of baxdrostat in treatment-resistant hypertension. And finally, TULIP-Subcu will enable us to bring a more convenient subcutaneous administration of Saphnelo to SLE patients. All these positive Phase III readouts continue to give us confidence towards our $80 billion 2030 ambition. Next slide, please. I'd like to address recent developments for AstraZeneca in the United States. The U.S. remains our largest market and is projected to account for around 50% of our total revenue by 2030. We announced a landmark agreement with the U.S. government which provides greater clarity around pricing and a 3-year exemption from tariffs. The agreement will lower the cost of many prescription medicines for American patients, while safeguarding Americas cutting-edge Biophamaceutical innovation. With the administration support, we are now working with others to deliver price equalization across wealthier markets, an approach that offers a more sustainable future for governments, industry and patients. In addition, we continue to focus on clinical trial diversity and further enhancing our clinical trial footprint in the U.S. To support our growth ambitions, we've been steadily expanding our global manufacturing capacity including broadening our U.S. footprint over the last several years. Last month, I was pleased to break ground on our new Virginia facility joined by Senator, Lutnick; Governor, Youngkin; and Dr. Ross. And lastly, I'm grateful for our shareholders to voting through our proposal to harmonize our listing structure in London, Stockholm and New York. AstraZeneca ordinary shares will be listed on the New York Stock Exchange from February next year. This new listing structure will offer flexibility to access the broadest available pool of capital, including in the U.S. and enable more shareholders to participate in AstraZeneca's exciting future. And with that, please advance to the next slide, and I will hand over to Aradhana.

Aradhana Sarin: Thank you, Pascal, and good morning, good afternoon, everyone. As usual, I will start with the reported P&L.; Next slide, please. Total revenue increased by 11% in the first 9 months. Product sales grew by 9% with strong growth seen across the business in key regions. Alliance revenue increased by 41%, driven by continued growth for both Enhertu and Tezspire in regions where our partners book product sales. Next slide, please. This is our core P&L.; Our core gross margin in the first 9 months was 83%. We continue to anticipate a slight decrease in the core gross margin for the full year versus 2024, due to the Medicare Part D reform, Brilinta LOE, Soliris biosimilars and increased profit sharing from partnered products. Similar to prior years, we anticipate the core gross margin in the fourth quarter to be lower than in the third quarter, driven by the usual seasonal pattern with more sales from lower-margin products like FluMist and Beyfortus. R&D; expenses increased by 16% in the first 9 months, driven by sustained high activity, including many clinical trials having enrolled ahead of plan. We've also made significant investments in high-value pipeline opportunities, such as our I/O bispecifics, weight management and cell therapy portfolios. As a percentage of total revenue, core R&D; costs accounted for 23.3%, and we continue to expect R&D; to land at the upper end of the low 20s percentage range for the full year. We have continued to make progress towards our 2026 margin goal and remain on track, as you can see from our 9-month results with core operating margin at 33.3%. Operating leverage continues to remain a focus internally. And again, as you can see from the first 9 months, product revenue grew at 11% and SG&A; grew at 3%. Core EPS of $7.04 represents CER growth of 15%. Next slide, please. We have seen strong cash flow inflow from operating activities in the year-to-date, up by 37% versus the prior year to $12.2 billion, driven by robust underlying business momentum. In the year-to-date, we saw CapEx of $2.1 billion. And as previously stated, we anticipate an increase of around 50% for the full year versus 2024, which implies a step-up in the fourth

quarter which also is normal as in prior years. Our capital allocation priorities remain unchanged. We currently have interest-bearing debt of close to $33 billion, which is a level we're comfortable with as we plan to continue making investments to support future growth, build our supply chain globally and further strengthen our R&D; pipeline. Our net debt-to-EBITDA ratio currently stands at 1.2x. Turning to guidance. Today, we are reiterating our full year guidance with total revenue and core EPS anticipated to increase by high single-digit and low double-digit percentage, respectively, at constant exchange rates. We expect our strong revenue momentum in growth brands to continue. I would like to remind you that in the fourth quarter of 2024, we booked more than $800 million in sales-based milestones under collaboration revenue. This year, we do not anticipate any significant milestone revenue in the fourth quarter, which will affect the year-over-year growth rate comparisons for the fourth quarter. In addition, in China, while growth has been strong throughout the year, fourth quarter revenues are anticipated to be affected by VBP-associated stock compensation costs for Farxiga, Lynparza and Roxadustat and the usual year-end hospital budget capping, in addition to tender order variability in emerging markets. Similar to prior years, we also anticipate a sequential step-up in both R&D; and SG&A; expenses in the fourth quarter versus the third quarter. With that, please advance to the next slide, and I will hand over to Dave, who will take you through the incredible performance of our oncology and hematology business.

David Fredrickson: Thank you, Aradhana. Next slide, please. Oncology total revenue grew 16% in the first 9 months to $18.6 billion with broad-based double-digit growth across U.S., Europe and emerging markets. The U.S., in particular, continued to report strong year-over-year growth of 19%, highlighting robust demand for our medicines, which substantially outpaced the increased liabilities resulting from Medicare Part D redesign. Emerging markets also delivered impressive performance with 20% growth during the period. Focusing on third quarter performance, we achieved robust 18% growth for the second quarter in a row. Tagrisso delivered sales of $1.9 billion in the third quarter, representing 10% growth on the prior year. Widespread demand across all major regions reinforces Tagrisso's role as the backbone of care for EGFR-mutated lung cancer. The first-line lung cancer combination market continues to expand with FLAURA2, the clear leader, in terms of new patient starts and total scripts. The compelling overall survival results presented at the World Congress of Lung Cancer and subsequently published in the New England Journal of Medicine will drive further leadership. Calquence remains the leading BTK inhibitor in first-line CLL across major markets, with total revenues increasing by 11% to $916 million in the third quarter. In the U.S., we continue to see increased demand more than offset the impact of Part D redesign with improved market share versus the same period last year. We're seeing positive early signs of adoption for AMPLIFY in Europe and expect this trajectory to continue through the remainder of the year with the U.S. launch anticipated in the first half of 2026. Lynparza, which remains the leading PARP inhibitor globally delivered revenues of $837 million in the third quarter, up 5% year-on-year with consistent growth across key regions. Truqap total revenues of $193 million in the third quarter represented 54% growth versus Q3 last year. With the AKT/PTEN biomarker altered population almost fully penetrated, growth is now primarily driven by increased uptake of the PIK3CA population and ongoing launches in developed and emerging markets. This was another outstanding quarter for our I/O franchise with growth of Imfinzi and Imjudo of 31% and 14%, respectively. We see continued enthusiasm for Imfinzi in the new lung indications, ADRIATIC and AEGEAN and in bladder cancer with NIAGARA, alongside further expansion in our more established indications such as HIMALAYA and CASPIAN. We are also starting to see early signs of adoption of MATTERHORN in the U.S. following its Category 1 NCCN guideline inclusion and eagerly await regulatory decisions. Enhertu total revenues grew 39% in the third quarter with ongoing launches of the DESTINY-Breast06 indication, further strengthening our leadership position in HER2-low metastatic breast cancer. The strong initial uptake in China following NRDL enlistment has persisted through Q3 as we achieve even broader coverage and continue to drive adoption. Positive readouts across HER2-positive breast cancer at ASCO and ESMO are anticipated to further drive growth with data now spanning across the spectrum of HER2-positive disease. And finally, Datroway continues to make inroads in hormone receptor positive breast cancer across the U.S. and Europe. And this quarter, we have started to see encouraging early signals of uptake in the previously treated EGFR-mutated lung cancer space following U.S. approval and NCCN guideline inclusion. We are confident in carrying our

strong performance from the first 9 months through to year-end as we continue to expand the reach of our innovative medicines. With that, please advance to the next slide, and I'll pass over to Susan to cover key R&D; highlights from the quarter.

Susan Galbraith: Thank you, Dave. Just over 2 weeks ago at the European Society of Medical Oncology, AstraZeneca delivered multiple pivotal data sets with the potential to reshape clinical practice, including two featured in presidential sessions. This underscores the quality and breadth of our science and reinforces AstraZeneca's leadership in bringing new advances to patients worldwide. DESTINY-Breast11 and 05 advanced Enhertu into the early treatment setting for HER2-positive breast cancer, highlighting its potential to become a foundational therapy in early disease and ultimately increasing the likelihood that more patients could be cured of breast cancer. In DESTINY-Breast11, treatment with Enhertu followed by THP prior to surgery resulted in a pathologic complete response rate of 67% in patients with high-risk HER2-positive early-stage breast cancer, the highest ever reported rate in the Phase III registrational trial in this setting. We also saw an early trend towards an event-free survival benefit with Enhertu followed by THP. Importantly, this regimen demonstrated a favorable safety profile versus the 5-drug AC-THP regimen with lower rates of Grade 3 or higher adverse events, serious adverse events and treatment interruptions. This makes DESTINY-Breast11 the first regimen in over a decade to significantly improve outcomes in the earliest treatment setting for HER2-positive breast cancer, and these data are now under FDA review. In DESTINY-Breast05, Enhertu reduced the risk of disease recurrence or death by 53% compared to T-DM1 in patients with high-risk HER2-positive early breast cancer following neoadjuvant therapy, with over 92% of patients treated with Enhertu free of invasive disease at 3 years. This data set offers a critical second opportunity to reduce recurrence risk in this patient population. Taken together, DESTINY-Breast11 and 05 have the potential to transform early-stage HER2-positive breast cancer by reducing metastatic recurrence and bringing patients closer to cure. And this represents a blockbuster opportunity across the alliance. We also shared data from the TROPION-Breast02 trial, which evaluated Datroway versus chemotherapy as a first-line treatment for patients with locally recurrent inoperable or metastatic triple-negative breast cancer for whom immunotherapy is not an option. These patients typically have poor outcomes with the current standard of care and 5-year overall survival rates of just 15%. TB02 included those with the poorest prognosis often excluded from clinical trials, such as patients with a short disease-free interval and those presenting with brain metastases at baseline. In TB02, Datroway delivered an unprecedented 5-month improvement in median overall survival versus chemotherapy, along with a statistically significant and clinically meaningful 43% reduction in the risk of disease progression or death. In addition, almost 2/3 of patients experienced a complete or partial response to Datroway, double the rate seen with chemotherapy, alongside a manageable safety profile, low rates of discontinuation and no treatment-related deaths. These data clearly differentiate Datroway and together with its convenient 3-weekly dosing, position it to reshape the TNBC landscape for the 70% of first-line patients who are not suitable for immune checkpoint inhibitors. Our other key Phase III readout at ESMO was POTOMAC. This trial moves Imfinzi into earlier-stage bladder cancer, demonstrating that adding 1 year of Imfinzi to BCG induction and maintenance therapy delivers both early and sustained disease-free survival benefits with a 32% reduction in risk of recurrence or death compared to BCG alone in high-risk non-muscle invasive bladder cancer. With this Imfinzi regimen, 87% of patients remained alive and disease-free at 2 years, highlighting its potential to change the trajectory for these patients and further building on Imfinzi's impact in muscle-invasive disease as shown in NIAGARA. These results reinforce the strength of our bladder program, and we very much look forward to data from the VOLGA trial in cisplatin-ineligible muscle invasive bladder cancer, which is now expected in the first half of next year. In addition, we presented Phase III data from CAPItello-281 for Truqap in combination with abiraterone and androgen deprivation therapy in PTEN-deficient metastatic hormone-sensitive prostate cancer. Taken together, these pivotal data sets strongly support our strategy to advance novel therapies into earlier-stage disease, where they have the greatest potential to improve patients' lives. We also presented significant new data at ESMO across our early programs, including first-in-human results for our folate receptor alpha ADC, AZD5335 or torvusam, in platinum-resistant relapsed ovarian cancer. New data for our PARP1 selective inhibitor, saruparib, in combination with androgen receptor pathway inhibitors in metastatic prostate cancer, updated findings

for rilvegostomig in checkpoint inhibitor naive lung cancer, which compares favorably to current PD-1-based therapies and encouraging new results for the combination of rilvegostomig and Datroway in bladder cancer. All these results build our confidence in the long-term strength of our pipeline, positioning us to deliver innovation well beyond 2030. Before closing, I want to highlight the upcoming American Society of Hematology Meeting in December, where we will present updates of our CD19/CD3 T-cell engager, surovatamig, and our CD19 BCMA dual CAR-T AZD0120. These pipeline assets both have $5 billion-plus non-risk-adjusted peak year revenue potential, and we will build our position in hematologic malignancies with the opportunity to set new standards across this space. 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 a strong performance in the year-to-date with total revenue reaching $17.1 billion, reflecting growth of 8%. Starting with R&I;, we saw growth of 40% in the quarter, driven by strong performances across our inhaled and biologic portfolio. The growth medicines now constitute over 60% of the therapy area's revenue and have grown at an impressive rate of 30% year-to-date. Our products now make up half the new-to-brand prescriptions for the severe asthma biologics segment in several markets. Fasenra continues to lead in eosinophilic asthma. We were pleased to see growth accelerating to 20% in the quarter with Fasenra's product profile being strengthened by uptake in EGPA and our first revenues from China. Tezspire continued its rapid market share gains in severe asthma with 47% growth in the quarter. Its growth potential has been further enhanced by recent approvals in the United States and the EU for chronic rhinosinusitis with nasal polyps based on the WAYPOINT trial, which demonstrated a significant reduction in nasal polyp size and nearly eliminated the need for surgery. Breztri grew at 20%, driven by market share gains in the growing triple class. All revenues today come from COPD patients, and we have now filed regulatory submissions for asthma in all major regions following the positive readouts from the KALOS and LOGOS trials. We are pleased to receive a positive CHMP recommendation for our next-generation propellant, which has 99.9% lower global warming potential, a key milestone towards our company's sustainability goals. Breztri will be the first of our inhaled medicines to transition to the next-generation propellant. Saphnelo, our biologic medicine for SLE, continues to win share in the intravenous segment of the market and grew at 44% in the quarter. In September, we announced positive high-level results based on the interim analysis from the TULIP subcutaneous study, which paves the way for Saphnelo to reach SLE patients who prefer a subcutaneous option. TULIP-SC recently received a positive CHMP recommendation in the EU. Total revenue from the CVRM therapy area was flat in the quarter, reflecting the loss of exclusivity for Brilinta, which saw a revenue decline of 56%. Farxiga delivered 8% growth despite a slight decline in Europe due to the earlier-than-expected entry of generic competition in the United Kingdom. Lokelma grew 30%, maintaining its leading share in the potassium binder class for chronic kidney disease and heart failure patients. In anticipation of further growth for Lokelma, we were excited to have recently opened an expanded manufacturing facility in Texas. In addition to the strong product performances in the year-to-date, I'm also particularly excited to see the number of high-value biopharma trials due to readout in 2026. And with that, I will now hand over to Sharon to discuss the latest developments for baxdrostat, the next NME we anticipate to launch in biopharma with more than $5 billion peak year revenue potential.

Sharon Barr: Thank you, Ruud. Next slide, please. At AstraZeneca, our ambition is to transform care across interconnected cardiorenal and metabolic diseases where multiple risk drivers and organ systems overlap. Hypertension is a key part of this challenge. And in the past 20 years, there has been very limited innovation. For example, around half of patients currently treated in the U.S. remain uncontrolled while on multiple medicines. Baxdrostat is designed precisely for these patients. As a reminder, baxdrostat is a once-daily, highly selective and potent aldosterone synthase inhibitor, targeting the aldosterone pathway at its source. Excess aldosterone is well established as a driver of hypertension and broader cardiorenal disease. By limiting aldosterone production, baxdrostat provides a clean targeted mechanism that has the potential to enable more patients to reach their treatment goals, particularly those with uncontrolled or resistant hypertension. In the third quarter, we presented the first Phase III data for baxdrostat monotherapy with the BaxHTN trial at the European Society of

Cardiology. We were also delighted to report the positive high-level results for the Phase III Bax24 trial. Collectively, these readouts reinforce our confidence in baxdrostat's more than $5 billion potential as a franchise. In the BaxHTN trial for patients with uncontrolled and treatment-resistant hypertension on maximally tolerated background therapy, baxdrostat delivered the largest systolic blood pressure reduction reported in a primary analysis to date. At 12 weeks, placebo-adjusted reductions were 8.7 and 9.8 millimeters of mercury on the 1 and 2 milligram doses, respectively. Responses were highly consistent across prespecified subgroups, and we saw a powerful target engagement with a 60% to 65% reduction in serum aldosterone at week 12. Importantly, this reduction was sustained over time. Furthermore, in the randomized withdrawal period, patients continuing baxdrostat saw further reductions in blood pressure out to 32 weeks. Baxdrostat also demonstrated a favorable tolerability profile. Adverse events were mostly mild with no off-target hormonal effects and no clinically relevant drug-drug interactions observed. Confirmed hyperkalemia above 6 millimole per liter was 1.1% in both dose arms, and we saw low discontinuation rates of 0.8% and 1.5% for the 1- and 2-milligram doses, respectively. 24-hour control of hypertension matters clinically. Early morning blood pressure variability is strongly correlated to the risk of cardiovascular events. So sustained control of blood pressure between doses is important. Baxdrostat's long half-life is a key differentiator. In an ambulatory sub-study of BaxHTN, we saw substantial reductions in 24-hour average and night-time systolic blood pressure. Building on this, we recently reported positive high-level results from the Phase III Bax24 trial, which was conducted in the most difficult-to-treat patients, those with resistant hypertension. In Bax24, baxdrostat demonstrated a statistically significant and highly clinically meaningful reduction in ambulatory 24-hour average systolic blood pressure. Efficacy was observed across the entire 24-hour period, including early morning. We look forward to sharing you exciting data with the medical community at the American Heart Association this coming weekend. These results solidify baxdrostat's potential as a first and best-in-class option for patients with uncontrolled and resistant hypertension, offering convenient once-a-day dosing with sustained blood pressure control around the clock. We are advancing our regulatory filings and rapidly progressing our robust clinical development program for baxdrostat, both as a monotherapy and in combination with dapagliflozin. And with that, please proceed to the next slide, and I'll pass over to Marc to cover Rare Disease.

Marc Dunoyer: Thank you, Sharon. Can I get the next slide, please? Rare Disease medicine grew 6% to $6.8 billion in the first 9 months of the year, driven by growth in neurology indications, increased patient demand and continued global expansion. In the third quarter, Ultomiris grew 17%, driven by patient demand growth across indication, including the competitive MG and PNH markets. Soliris revenues continues to decline due to the successful conversion to Ultomiris as well as biosimilar pressure in Europe. Strensiq grew 28% and Koselugo grew by 79%, respectively, due to strong underlying demand for these medicines. Koselugo's growth also benefited from some tender orders in emerging markets. We continue to see great momentum across the rare disease portfolio with recent approval for Koselugo and Ultomiris that further our geographic reach for this medicine. Please advance to the next slide. We presented data from our Phase III PREVAIL trial, investigating gefurulimab on our dual branding nanobody targeting C5 in patients with generalised myasthenia gravis. Gefurulimab demonstrated 1.6 point improvement from baseline, placebo adjusted in myasthenia gravis activities of the living total score at week 26. The MG-ADL total score change from baseline reached 4.2 points at week 26 in the gefurulimab-treated patients. A clinically meaningful improvement in MG-ADL total score was observed as early as week 1 and was sustained through week 26. Gefurulimab demonstrated rapid, complete and sustained complement inhibition. Gefurulimab also met all secondary endpoints, including quantitative myasthenia gravis total score, where gefurulimab demonstrated a 2.1 point improvement at week 26 compared to placebo. A pre-specified measurement at week 4 also made statistical significance, again demonstrating the rapid onset of action of gefurulimab in patient with gMG. The PREVAIL trial was conducted in a broader gMG patient population compared with prior trials of C5-targeted therapies. Gefurulimab is a convenient, self-administered subcutaneous once-a-week treatment with the potential for two delivery option, a pre-filled syringe and auto-injector, which would be the first in gMG. We believe that the strength of this data and convenient administration, gefurulimab has a potential to become a new first-line therapy following immunosuppressive therapies. I also wanted to update on other important Phase III data we

had this year. Analysis of the 52 weeks results on the CALYPSO trial to further characterize eneboparatide are ongoing. We will continue monitoring these patients in the open-label extension. For anselamimab, we have shared clinical results from the Phase III CARES program with regulatory authorities. Following further discussion, we plan to submit for the pre-specified patient subgroup in which anselamimab demonstrated a highly significant improvement in both time-to-all-cause mortality and frequency of cardiovascular hospitalization compared to placebo. And finally, efzimfotase alfa, we expect to announce results from all Phase III studies, HICKORY, CHESTNUT and MULBERRY in the first half of next year. Together, these three trials cover patients across pediatric, adolescent and adult hypophosphatasia population. And with that, please advance to the next slide, and I will hand over to Pascal.

Pascal Soriot: Thank you, Marc. Next slide, please. As I mentioned at the start of this call, we are in the midst of an unprecedented catalyst switch period, one which is anticipated to extend through 2026 and beyond. We look forward to exciting readouts in each of our key therapy areas in 2026, which on a combined basis represent a risk -- sorry, risk-adjusted peak year revenue opportunity of more than $10 billion. Our exceptional performance for the first 9 months so has delivered a core operating margin of 33.3%. This is a clear demonstration that despite the opportunities to invest in this rich pipeline, we remain committed to driving operating leverage and we remain on track for both our 2026 margin target of mid-30s and our $80 billion 2030 revenue ambition. Next slide, please. In closing, I'm very pleased to report that we are making exciting progress across our transformative technologies, which have the potential to drive AstraZeneca's growth well beyond 2030. We are moving at pace with our oral PCSK9 inhibitor, laroprovstat. And now we have three Phase III trials ongoing, and we are looking forward to the results from our Phase II trials across our weight management portfolio next year. We're driving forward with our ADC and our radioconjugate portfolio with the first Phase III of our wholly owned ADC sone-vedo reading in the first half of next year. Supporting our ambition to replace current immune checkpoint inhibitors with next generation bispecifics, we now have 14 Phase III trials underway for rilvegostomig and volrustomig. And we are continuing to strengthen our hematology portfolio with our first Phase III trial already underway for our CD19 CD3 T-cell engager surovatamig, and we are planning to advance CD9, BCMA, CAR-T, AZD0120 into Phase III next year. And lastly, our first gene therapy is now entering the clinic. And with that, please advance to the next slide, and we will move to the Q&A.;

Pascal Soriot: As Andy mentioned at the start of the call, please limit the number of questions you ask to allow others a fair chance to participate. For those online, please use the raise hand function on Zoom, and with that, let's move to the first question. Our first question is from Michael Leuchten at Jefferies. Over to you, Michael.

Michael Leuchten: Two questions for you, please. One, thank you for the comments around the environment in Washington. Just wondering if you could comment on what is the risk of residual activity coming from the administration? How confident are you that the deal that AstraZeneca has managed to secure removes enough of the overhang? So, we don't have to look over our shoulders constantly as we think about R&D; productivity and the cost of innovation. And the second question for you, Pascal, the $10 billion number that you just mentioned in terms of the catalyst potential coming out of the '27/'28 period, is that part of the $80 billion? Or is that incremental potential already on top of that?

Pascal Soriot: So, the first question, what I would say about this is that we have addressed the four points in the President's letter. And the four points, as you know, they covered Medicaid, they cover prospective equalization, direct to consumer and also returning to the U.S. government, some of the potential price increases for existing products. And so, we've covered all of this. So, now our expectation is that essentially, we have an agreement with the U.S. government, and we don't expect anything more to come. But of course, we are not the government, so we cannot guarantee anything. We can only say that our expectation from the discussions we've had, our expectation is that this agreement is delivering what the President was looking to achieve. On the $10 billion, this is part of our $80 billion. This is, by the way, not a 2030 number. It's a peak year revenue number. It's a risk adjusted $10 billion. But certainly, it will contribute to achieving our 2030 ambition. There is more to come. We have a number of readouts next year and we expect from the readouts to expect another $10 billion -- actually $11 billion of risk-adjusted sales to come out of these readouts, assuming, of course, they are

positive, we could get even more. So, as I said before, it is quite unprecedented for us as a company to have such a rich series of readout across not only oncology but also hematology, cardiovascular disease, respiratory disease, immunology, rare disease. So really, I would say, the company is firing from all engines in terms of our ability to innovate and come up with new products. So with this, I'll move to Sarita Kapila at Morgan Stanley. Sarita, over to you.

Sarita Kapila: Thanks for taking my questions and the comments on 2026 margins. Perhaps you could indicate your level of comfort on where 2026 consensus sits at the low end at 34% and talk about the step-up to get there? And then more broadly, could you speak about the pushes and pulls, please, on 2026 margin? And then secondly, there's been a lot of investor focus on the Roche persevERA trial coming in Q1 '26, which is looking at duradestrant in all-comer breast cancer. Could you talk about the potential read across to camizestrant? Are there any notable differences between the molecules or any differences in the trial design that could increase chances of SERENA for success versus persevERA and why it may not be a good read?

Pascal Soriot: Thank you, Sarita. So, it's really three great questions. The first two, Aradhana, can you cover, and Susan with -- can you pick up the persevERA question and Ruud to camizestrant?

Aradhana Sarin: Sure. Thanks, Sarita. Though as you've seen, we've had very strong momentum in all our growth brands. And with this momentum going into the year-end, we hope it continues and expect it to continue in all markets and all brands. The key headwind in 2026 will really be the loss of Farxiga in both U.S. as well as China. And that's something that we had anticipated and are obviously planning around. We're right now going through our budget process, and we'll take all these different pushes and pulls as well as the recent agreement with the U.S. government and all those impacts into account. As we set our budget, we will continue to invest behind growth brands and plan for new launches such as baxdrostat, cami and dato. And given all the portfolio, I think we'll continue to invest in R&D; towards the high end of the 20% given all the progress in the ADC and the cardiovascular and weight management portfolio. So, those are some of the pushes and pulls. And you've seen the performance and the continuous margin progression as well as the SG&A;, which we have maintained very strong leverage over and R&D;, obviously, is where we always find great opportunities. So, while we remain disciplined, we're going to continue investing behind that.

Pascal Soriot: Just before Susan covers the next point. I think, Aradhana covered really very well. Our view of 2026 one, maybe a piece I wanted to add is that, some people may be wondering about the impact of the agreement with the U.S. government. What I would say on this is that, Aradhana covered it, we have a very broad portfolio geographically and also a broad portfolio of new products, new launches, and we think we can absorb the impact of this agreement. We're confident we can absorb it in '26 and beyond and really doesn't affect our 2030 ambition and doesn't affect our midterm ambition. So, over to you, Susan with persevERA.

Susan Galbraith: Thanks, Pascal. So just as a reminder, camizestrant with the data that we showed in both the SERENA-2 study and then with the recent SERENA-6 study in first-line, has really shown the best profile of all of the oral SERDs that have reported so far. We've had the best hazard ratio versus fulvestrant in both the ESR mutant as well as in the wild type. But the fundamental point is, as you move from second line to first line, there's an increase in the endocrine sensitive part of the population. So, for those wild-type patients, they can still be expected to benefit because what you're doing is, you're inhibiting both the transcriptional signal downstream of the estrogen receptor regardless of whether it's wild type or mutated. And you're also reducing the amount of that receptor through degradation to very low levels, and we showed that in the SERENA-3 study. So, both those mechanisms of action are expected to be superior to the aromatase inhibitor component of current first-line backbone therapy. In terms of cost comparisons, I would point out that the SERENA-4 study is a larger study than persevERA. And we've designed it to enrich for patients that have got endocrine sensitive profile based on the clinical inclusion/exclusion criteria. So, we've designed it taking into account what we've previously learned and including from trials such as persevERA, et cetera, to optimize for the opportunity for success in that first-line setting.

Pascal Soriot: Thank you, Susan. So the next question is Justin Smith at Bernstein. Over to you, Justin.

Justin Smith: Just a couple on Wainua for Sharon or Ruud. Just firstly on CARDIO-TTRansform. Just your thoughts on whether that could meaningfully reshape treatment guidelines long term? And then

also just your thoughts on whether any new simpler diagnostic tests are coming soon to potentially expand the cardiomyopathy population?
Pascal Soriot: So Sharon, do you want to cover and Ruud if you have anything to add please jump in.
Sharon Barr: Sure. So, we look forward to the readout of the Phase III CARDIO-TTRansform study in 2026. Do we have the potential to meaningfully transform that treatment algorithm for patients? I think what we're able to demonstrate with the CARDIO-TTRansform study is both the role of silencers in adequately treating disease and in a planned subset, key secondary endpoint readout will be looking at the effect of eplontersen in patients who have tafamidis. And so that will give us the opportunity to be able to address that key question for patients comparing the effect of silencer plus stabilizer versus silencer, which I think will be very important in guiding patient treatment decisions. And then finally, AstraZeneca is in a unique position in developing new therapies for patients living with ATTR amyloidosis and that we also have Alexion 2220, the amyloidosis depleter in our portfolio. And we continue to work towards creating a combination approach of a depleter and a silencer, which we think could be truly pivotal for patients living with ATTR amyloidosis. Now with regards to diagnosis, we know that's a key part of the patient journey. And we know that this is not simply a hereditary disease. The hereditary variants are rare, but the disease is not. This is also a disease of the aging. So, being able to screen for and detect patients earlier in their disease progression will be really fundamental to offering patients improved outcomes. So to that end, we are exploring a number of different opportunities to be able to more accurately and earlier diagnose ATTR amyloidosis. And those include AI-informed models that allow us to identify patients on screening with echocardiogram or potentially EKG as well as developing new biomarker assays to be able to detect soluble amyloid. So, we continue to work on all fronts to be able to drive both earlier detection and earlier treatment.
Pascal Soriot: Thanks, Sharon. Ruud, anything you wanted to add or?
Ruud Dobber: No. Just like everyone, everyone is eagerly waiting for the results. What hasn't mentioned yet by Sharon is that, this is the largest CM trial so far in ATTR cardiomyopathy. And if successful, hopefully, we will see a CV mortality benefit, which, of course, is extremely important for treating cardiologists. Now on top of that, we are very pleased to see, let's say, the progress we are making in the first indication, the PN indication. So we can only hope for patients and also for the company and other interested that the ATTR-CM trial will be positive, and we will know that in the course of 2026.
Pascal Soriot: Sachin Jain, Bank of America.
Sachin Jain: I've got one each for Sharon and Susan on Phase III starts you've each referenced. So for Sharon, I wonder if you could just remind us of the obesity portfolio, the oral and amylin as we look for Phase II data next year. How are you thinking about your target competitive profile given the competitive landscape has rapidly changed? Obviously, with oral, we've seen the ortho data since you last presented. And with amylin, we've had the Lilly data out today. And then for Susan, I think you referenced the Phase III start for the BCMA CAR-T, where we see data at ASH and $5 billion peak. Just looking at the abstract, it looks like you've got 100% MRD negativity in almost fourth-line patients. So just wondering how you're thinking about the fastest route to market for that and beyond efficacy, how you're seeing differentiation on safety and administration.
Pascal Soriot: Thank you. Sharon, do you want to start? And then Susan?
Sharon Barr: Sure. So Sachin, as you know, we are moving forward with multiple molecules in our weight management portfolio. That is AZD5004 that's currently in Phase II for patients with obesity and type 2 diabetes. AZD6234, that's our long-acting amylin peptide, subcutaneous injectable that is also in Phase II for the same patient populations. And ACD9550, and that's our dual GLP-1 glucagon receptor agonist, also subcutaneous injectable also in Phase II. As we move all three of these forward at pace, of course, we're looking to have highly competitive molecules that give us reason to believe that these could be valuable treatment options for patients. As we move forward, we're also thinking about the potential for market segmentation, and we know that there will be room for multiple mechanisms. And the bar is high. We've seen the very interesting data from Eloralintide today. And so that gives us more reason to believe that a selective amylin receptor agonist similar to 6234 has the potential for efficacy in terms of weight loss and better sugar control for patients with type 2 diabetes. So, we have seen no red flags to date and continue to move forward at pace and expect to enter Phase III pending competitive

data and we will be making those decisions in 2026.
Susan Galbraith: So, in terms of the 0120, which is the CD19 BCMA dual CAR, thanks for the question, Sachin. We will be presenting data in the later-line patient population at ASH. This includes patients who are triple-class refractory and a substantial proportion that have had prior BCMA CAR-T therapy. So, what the data show is that, we do have a really impressive response rates and complete response rates in evaluable patients that are also progressing, and they tend to evolve over time. There's a relatively small number of patients that are currently MRD evaluable, but you rightly point out in that small number in the abstract, all of them have achieved MRD negativity. The overall profile of this cell is as dosed is attractive. We have no Grade 3 CRS and no ICANS in the dataset that we've presented in the abstract. And I think the -- both the efficacy and the safety profile is related in part to the FasTCAR manufacturing, which Gracell had developed, which is helping to deliver this predictable CRS profile and deep and early responses. So, we're very excited about the prospects for this. And we want to reiterate that we're going to start Phase III trials for this next year. And again, we'll be taking this forward in multiple settings, in multiple myeloma.
Pascal Soriot: Thank you, Susan. The next question is from Richard Vosser at JPM.
Richard Vosser: Two questions, please. Firstly, one, just following up on the TB02 Datroway data at ESMO. Maybe you could talk about the read across. From the better tolerability you showed relative to competing products there, both to your Datroway trials, but also more importantly, across the other ADC programs, what can we learn from that? And then secondly, maybe a more commercial rollout question. Just the Imfinzi or Imfinzi sales were very, very strong this quarter. I wonder if you could give a little bit more color on the rollouts. You highlighted bladder and lung, but how should we think about the runway of growth from here for Imfinzi?
Pascal Soriot: Susan, do you want to cover the first one? And David, the Imfinzi rollouts question?
Susan Galbraith: Sure. Thanks for the question. So yes, we're delighted with the TROPION-Breast02 data that was presented at ESMO. And I think this does speak to the actual design of this ADC, which similar to the Enhertu design, is based on linker stability. So it's really important to have linker stability so that you're actually delivering a higher proportion of the payload actually to the tumor cells and less exposure in the peripheral circulation. That drives the difference in terms of the bone marrow toxicity profile that you see with Datroway compared to some other TROP2-based ADCs. And I think that also speaks to the fact that we then delivered a higher response rate, longer progression-free survival and this 5-month improvement in overall survival, which I think is a differentiated profile. So that -- first of all, within the breast cancer space, it increases the confidence in the early-stage studies, the TROPION-Breast03, which is in the post neoadjuvant setting, a little bit analogous to the DESTINY-Breast05 setting. And that's in combination, of course, with Imfinzi, the TROPION-Breast04 setting, which is in the neoadjuvant treatment of PD-L1 negative breast cancer and then TROPION-Breast05, which takes that double-up combination of Datroway and Imfinzi also into the first-line setting. So with those studies, plus, of course, the lung cancer studies, the AVANZAR studies, I think the profile that we've got is one that we're confident about, and we look forward to having the future readouts in the coming months and years.
David Fredrickson: Thanks, Susan. With respect to the Imfinzi growth drivers in '25 and outlook moving forward, I think it has really been a great example of delivery against multiple new life cycle expansion opportunities. The primary growth drivers have been with Adriatic and small cell, AEGEAN in early lung cancer and then also NIAGARA has also been an important area of growth. All three of those represent opportunities for us to continue to see full year benefits across the globe as we launch those. Now, there is competitive pressures that we face on all of those. With that said, our differentiation, I think, is strong and our first-mover advantage is clear. I would also just point out that very importantly, we've got positive studies with MATTERHORN, with strong overall survival that was presented at ESMO. We've got POTOMAC. Those are both studies that we are looking forward to hopefully achieving regulatory approvals across the globe. And there will be further readouts as well that we have coming forward from here. So, the Imfinzi trajectory is one that has been both strong and I anticipate will be sustained.
Pascal Soriot: Thank you, Dave. Next question is from Peter Verdult at Exane.
Peter Verdult: Peter Verdult here, BNP. Apologies for any background noise. Two questions for you, Pascal. I thought it was noteworthy at the investor event, the ESMO cancer event. You called out

baxdrostat in your opening remarks. KOLs that we're speaking to, say, they see sort of placebo-adjusted blood pressure lowering in sort of 11, 12, 13 range. Their excitement around this asset is going to be cranked up. So, I know you can't talk to the data. We're going to have to wait until Sunday. But when you look at consensus expectations down at $2 billion, would you expect that expectations for this asset materially increase post the Bax24 data? And then secondly, we've talked about the political environment in the U.S. I mean, the industry wants to and has to invest more in the U.S., wants to invest more in China. Where is that leaving Europe? I mean Europe, what's the political environment in Europe? Are the politicians waking up to the direction of travel. Do you think that the innovation debate can be genuinely had in Europe? Or are you more, you say, sanguine about the outlook of -- regarding innovation being paid for in Europe?

Pascal Soriot: Thank you, Peter. So, let me start with baxdrostat and then maybe I'm sure, Ruud, who is very excited about this product, will want to add some more. I'm personally very excited about this product, because not only because hypertension -- uncontrolled hypertension is a big problem. A lot of people are on three drugs and still uncontrolled. That drives kidney disease, heart disease, cardiovascular events. So that's a big unmet need, much, much bigger than people understand really. The second reason is the effect on aldosterone, the 60%, 65% reduction that Sharon mentioned a bit earlier, I think will prove over time a massive benefit. Because aldosterone has not only effect on blood pressure, but also a deleterious effect on the organ. It still has to be proven, but I think there's good reason to believe it is actually the case because it docks on not only aldosterone receptor, but also the other aldosterone receptors and are not blocked by traditional MRIs. And if you have too much aldosterone in your body, it drives organ damage over time. So, I think this is going to prove really a big deal. And then you will see the data we have over 24 hours. This is really important because you need to control blood pressure at night in particular, the early morning. Sharon mentioned it. That's when people tend to have cardiovascular events, strokes, MIs. So again, this long-lasting effect over 24 hours is important. And I can tell you, you won't be disappointed with the blood pressure reduction, you would see. Ruud, anything you want to add in terms of the question about peak sales and the potential for this agent?

Ruud Dobber: Yes. No, of course. And we are very excited, and hopefully, on Sunday, you will see why. I'm not going to speculate whether it is more than the peak $5 billion peak year sales we've articulated. The only thing I can say, Peter, is that we have, in total, seven studies on this program as we speak. And there are a few studies also in the fixed dose combination with dapagliflozin. And Pascal was alluding to that. Yes, blood pressure in itself is important to control that. But it has a quite devastating effects on the kidney, and we truly believe that the combination of a well-known product like dapagliflozin plus the potential effect -- the positive effect of baxdrostat will be a very substantial driver whether it is $5 billion or perhaps even $10 billion. Time well tell. But there is an enormous amount of excitement, not only in the company, but more importantly, among physicians for these products. And let's not forget, that's my last remark that if a 10-millimeter mercury increases your risk of a MACE event with 30%. So I think you will see a renaissance of the treatment of hypertension with a product like baxdrostat. So very exciting.

Pascal Soriot: Thank you, Ruud. The the U.S. political environment, I mean, we've talked a lot about it. And this issue has been long coming in my opinion. Because, if you go back 20 years or so, there was limited difference in pricing between the U.S. and Europe. Let's talk about Europe for a second, really. And over time, what has happened is, there's been a growing difference mostly because in Europe, we've been facing price cut, clawbacks, a whole cottage industry of price reductions and control of access. And if you look at healthcare costs today, well, 20 years ago, I guess, healthcare, 20%, 30%, 15% of healthcare costs were dedicated to pharmaceuticals, innovative pharmaceuticals in particular. Today, you are at 7%, 8%, 9%. And one of the lowest is the U.K. with 7% of healthcare costs dedicated to innovative pharmaceuticals. And you got to ask yourself, I mean, what can you do with 7%? Not much. It creates limited room for innovation and innovation that can save lives, but also reduce healthcare costs by delaying or delaying things like dialysis, saving patients' lives and in cancer, et cetera, et cetera. So, I think there has to be a rebalancing. Because the U.S. for the last number of years has been really paying for the cost and the risk associated with innovation. We should never forget the risk. Everybody talks about the cost, but there's a massive risk. I mean, we have a portfolio

committee. And very often, we spend several hundred million dollars in one meeting. And if those studies fail, it's a lot of money in the rubbish bin. We've been lucky. This year, we've had almost 90% success rate with our Phase III, but it's -- that's not the norm, right? So, people have to realize innovation is expensive, but it's also very risky. So, I think there has to be a rebalancing, and Europe has to cover a little bit more of this innovation by increasing budgets allocated to innovative pharmaceuticals. And finally, I would say that if you look at innovation, it's happening in the U.S., very rapidly now it's happening in China, and there's not so much in Europe. So, it would be great for everybody, starting with patients. If Europe was also innovating a lot in our industry, it will also attract investment from companies and drive economic growth. Now whether we are able to show the benefit of these investments to governments in Europe is still to be seen, but there's clearly benefits to patients, of course, but it also benefits to healthcare cost as innovation can drive healthcare costs down. And there is also economic benefit as the Life Sciences sector can drive economic growth like we see in the U.S., we see now in China. So, whether we succeed or not, I don't know, but the danger for Europe is that a lot of these new technologies that we are talking about, they need new capacity, new manufacturing capabilities. And right now, this is going to happen in the U.S. And so, the risk is in 15, 20 years, Europe realized that they have lost control of their supply chain for some of those most important innovative technologies, because they are manufactured in the U.S. and in China. So more to come, and of course, a lot of convincing to try to achieve, but we'll see whether we are able to do that or not. So, we see. I'll move to the next question, Mattias Häggblom at Handelsbanken.

Mattias Häggblom: Mattias Häggblom, Handelsbanken. Two questions, please. Firstly on Farxiga, following the validation of the pattern in U.K. and subsequent generic launch, remind me why this loss would not encourage generic companies to explore similar challenges elsewhere in Europe prior to pattern exploration in '28. And why the situation in the U.K. was unique? And then secondly, for Sharon, Marc will present Phase III data for its oral PCSK9 inhibitor this weekend. Once we get the detailed data, what in particular will your team be studying to better understand its clinical profile and how it compares with your own small molecule PCSK9 inhibitor currently in Phase III?

Pascal Soriot: And the first one I can quickly cover for -- in the interest of time, Mattias, it's a very specific U.K. law. We can cover the details separately with you if you want offline. But just for everybody's interest, it's a very specific U.K. law that doesn't apply to other countries. And the PCSK9 question, Sharon, do you want to cover that?

Sharon Barr: Sure. I'd love to. So as you know, our own laroprovstat is a true small molecule inhibitor of PCSK9 currently in Phase III. We have shared the Phase II data. They're very encouraging. And we note that because our PCSK9 is a true small molecule, it does not require solubility enhancers, and it doesn't require fasting. And so, it offers a target patient profile that we think is very attractive for both monotherapy and combination approaches. And in fact, we're exploring combination approaches with a small molecule Lp(a) that is in our portfolio in Phase I, and it also allows us to easily combine with statins, which is standard of care. We were thrilled to see that with combinations, we were able to bring 80% of patients on study to their LDL-C lowering goals. And so, we think that we're in a very solid place in the competitive landscape. Now of course, we'll be watching Merck's data to understand how we can continue to meaningfully differentiate ourselves in this landscape as we continue to work on our go-forward plans. We remain very positive about the potential for laroprovstat in this environment and for the potential to really meaningfully change patients' lives because dyslipidemia is not yet solved. We know the majority of patients aren't reaching their LDL-C lowering goals. And so, there's still a major unmet medical need in the marketplace.

Pascal Soriot: Thank you, Sharon. So, we still have quite a number of questions. So, can I suggest that we go one question per person, and we on our side will try to be short in our responses. So the next one is Seamus Fernandez. Over to you, Seamus.

Seamus Fernandez: So my one question is on the competitive developments and the evolution of the treatment of asthma and COPD. Just hoping, Ruud, if you could comment on your, I guess, primary competitors outside of Dupixent, but GSK specifically making moves to advance long-acting agents both depemokimab and their potential long-acting CSLP program. Can you just help us with your thoughts specifically on the value of having long-acting agents in that marketplace? And how your own -- whether it be pipeline pursuits or separately, your own existing portfolio is built to defend against

that?
Ruud Dobber: Yes. Thank you so much for your question. And let me first emphasize that, where we are as a company with both Fasenra and Tezspire, is very pleasing. We have for the second quarter -- consecutive quarter, sales of above $0.5 billion for Fasenra. So, the product is now annualizing of more than $2 billion a year. And the reason I'm mentioning it is that, in all the market research and our own experience in the last few years across all geographies, clearly, efficacy is the #1 reason to prescribe products. And I think that's very important in the choice of physicians. Having said that, there's always room for further other modalities. And AstraZeneca is putting a lot of effort in order to generate the first inhaled T-slip molecule, which is quite exciting in order to broaden the patient access for severe uncontrolled asthmatics. We think there's a high unmet medical need. For the simple reason that still too many patients are suffering from severe asthma and are not eligible for injectable. So, moving earlier in the treatment paradigm with an inhaled T-slip if it is working, of course, and we will know that in the course of 2026, I think will be a huge advantage for so many patients still suffering. But all in all, it's clear that there are great products. We are in a very good position. We're the market leader in new-to-brand prescriptions, as I mentioned in my prepared remarks, but there's still an enormous opportunity to further accelerate the bio penetration. And last but not least, we are a verge in order to launch Fasenra in China, which is another very important growth driver for us as a company.
Pascal Soriot: The next question is from Matthew Weston at UBS.
Matthew Weston: Thank you, Pascal. I think it's probably a question for Dave, but you flagged in your comments that '25 has been or seen a very significant benefit from new patients due to lower Part D co-pays. Of course, that's allowed companies to bring free drug patients into paid coverage. As we think about '26, do we need to consider a significant slowdown in the underlying growth of some of your assets as that free drug warehouse bolus runs out? And if yes, which product should we be most aware of?
Pascal Soriot: Dave, do you want to cover this?
David Fredrickson: Yes, Please. Thanks, Matthew, for the question. So, I think just to take a small step back, if we compare what we'll expect to see in Q2 -- excuse me, Q1 '26 versus '25. First, we'll have a good, if you will, apples-to-apples comparison because both quarters will include the impact of the Part D liability. Secondly, I think also we will continue to see benefit of patients staying on commercial medicine who had switched over this year or were otherwise abandoning. So, I think that one of the things that is really important here is that if you take a look at the oral medicines Tagrisso and Calquence in particular, although it's also true of Lynparza. They have fairly long durations of therapy, CLL with treat to progression, Tagrisso in terms of the early settings but also indeed what we see with FLAURA2. So, I would expect that patients who've come over to commercial medicine as opposed to being on free drug that we'll continue to see the benefit of those patients and the TRxs come into 2026. The bolus patients who would have been your prevalent pool who came on as the co-pay cap went from the mid-300s down into the 2,000s. We may not see that repeat. But I really do think we're going to see demand coming forward from new patients, new indications. And I think that we'll see good oral growth moving forward on our assets.
Pascal Soriot: Thanks, Dave. Maybe I could add that, a year ago, you may remember a number of people were worried about the impact of the part D liability on our growth rate. And you can see we've been able to manage that as we said we would, and Dave and his team have been doing an amazing job driving usage and growing our share and growing the volume, to compensate for this part D liability that we've had to absorb in 2025. The next question is from Steve Scala at Cowen. Steve, over to you.
Steve Scala: Actually, a question on Calquence. Is the upper end of the peak sales guidance of $3 billion to $5 billion is still achievable given the positive data from competitors Calquence's 2027 IRA negotiated price, which you presumably have by now and IMBRUVICA's IRA negotiated price. And related to all this, was the Calquence IRA price in line with your expectations?
Pascal Soriot: Dave, I think it's for you again.
David Fredrickson: Steve, thanks for the question. On your last piece, we will share the IRA negotiated price on Calquence once that's public, which will be happening later this quarter. What I do want to comment on, though, with respect to your peak year sales question, recall that when we put forth the ambition for 2030 in 2024, we had visibility at that time into the fact that we anticipated that the

Calquence would be an IPA. So that's absolutely consistent with the expectations that we had. We expected that we would get positive data from AMPLIFY. That's come through and been part of what we've seen. And I think that we've seen really even better than we expected volume growth of Calquence, particularly within the United States. So, in terms of the assumptions that went into the projections that we put forth or the ambition that we put forth in 2024, I think it's been positive news, against that and good momentum against those figures. I'm happy that we've seen good share growth in the United States this year on the work that we're doing. We're seeing AMPLIFY in Europe with good initial uptake and we look forward to the AMPLIFY opportunity in the U.S. I do want to note that remember that there are no BTK/BCL-2 combinations for finite that are approved in the U.S. in frontline CLL. There's a large number of patients that are receiving a finite treatment that don't involve BTK at all, and we see this as an important opportunity for the asset going forward.

Pascal Soriot: Thanks, Dave. So, still lots of growth coming from those approved or soon to be approved indications. And -- we also have escalate in DLBCL that is still to come. Next question is Rajan Sharma, Goldman Sachs.

Rajan Sharma: I just wanted to get your thoughts on Enhertu's trajectory from here, given that we now have the DB09 and the DB11 data and PDUFA next year, which have been seen historically as two of the largest opportunities. Some of our KOL feedback has suggested that initial uptake may be a little bit tentative to begin with. So yes, we'll just be keen to get your thoughts on that. And do you expect those potential approvals during the first half to drive an immediate step-up in Enhertu's growth in '26 and '27? And then just thinking further out, do you think you'll be reaching peak penetration in breast cancer as you approach your 2030 target?

Pascal Soriot: Thank you. So question, we'll switch up to David, go ahead.

David Fredrickson: All right. We'll do. So first of all, I think as we take a look at 09 and the combination of both 05 and 11, let's take those in two separate parts. DESTINY-Breast09 is clearly a very important opportunity to move Enhertu from the later line metastatic setting or the second-line plus metastatic setting that we're in today into a frontline setting. The reason that, that is important is, first and foremost, many more patients will have the opportunity to benefit from an Enhertu. Because unfortunately, the number of patients that are able to receive a second-line therapy goes down just as patients unfortunately either pass away or they're unable to receive further treatment. So, opening up that population is going to be really important. Secondly, the duration of therapies that we see because of the long PFSs within DB09 are really important. And that's as a result of this treat to progression, new paradigm that's being established. And I think that on this, it's important to note that one of the things that's been really well received by the clinical community is the lack of cumulative toxicity that is associated with Enhertu and what we're seeing within these studies. That cumulative toxicity is in large part why there's been discontinuation of the taxanes in some of the other metastatic settings. And so, we're really looking for this to be an opportunity to make sure that we're driving to the way that DB09 was designed, which is treat to progression. DB05 and DB11 in early stage, they represent a blockbuster opportunity together. This is a great opportunity to bring Enhertu into early settings. And I think that in terms of when will we expect uptake, certainly, the clinical community does follow guidelines. DB09, we anticipate coming into guidelines sometime soon, we would hope. Remember that the New England Journal of Medicine publication just came through just very, very recently. And we'll obviously look forward to making sure that the progress that we've made on the early studies gets published as well.

Pascal Soriot: So, we'll try the last four questions in the time that remains. Let's go with one question per person and be short in our responses. Luisa at Berenberg. Over to you.

Luisa Hector: Thank you, Pascal. I wanted to return to the 2030 ambition. Because you've talked about and we've seen there's unprecedented success rate this year. So is the $80 billion now conservative? Can you comment at all on the mix that you're seeing with the success and what that means for profitability? And although the ex U.S., you're sticking at 50% ex U.S. contribution, are there any changes in timing of launches or the mix of the ex U.S. in light of that U.S. deal?

Pascal Soriot: Thank you, Luisa. Not long ago, people were thinking the $80 billion was not achievable. Now it's going to be a soft goal. It remains an ambitious goal. And of course, we are very excited with all this new positive readouts. But it's a risky business. That's what I said not long, a few minutes ago. So,

we have to remain cautious with the readouts that are coming next year. We don't know. I hope to God, we continue to have a high positive success readout -- in our readouts, but we can't be sure. So, let's stick to the $80 billion. It's an ambitious goal. And if we can overachieve of course, we'll do our very best to overachieve. Now in the second question with the profitability, we want to be a growth company until 2030, but also beyond 2030. So certainly, we can assume -- we can assume profitability increases, but you also have to understand we will want to continue investing in R&D.; We have tremendous technologies in our hands, cell therapy, T-cell engagers, radioligands, which we haven't talked about today, all of those are making good progress. So, we certainly would want to invest in those from an R&D; perspective, but also from a commercial perspective. And beyond oncology, we have a lot to do also in biopharma and rare disease. So, we're not going to commit to any profitability target or improvement beyond what we've already said in the past. Aradhana, anything you wanted to add to this?

Aradhana Sarin: No, not at all. It's a long answer, obviously, with all moving parts. So, maybe another time to reach out.

Pascal Soriot: Good. so, the next question is from Gonzalo Artiach at Danske Bank.

Gonzalo Artiach Castanon: Gonzalo Artiach at Danske Bank. I have one for Marc on gefurulimab and the data has been recently presented. It seems that the efficacy and safety signals have come fairly in line with Ultomiris in MG. How should we understand the dynamics between these two products in MG? And also I wanted to ask if you have any plans ahead for gefurulimab in other indications where Ultomiris is now approved. Thank you very much.

Marc Dunoyer: First of all, thank you very much for the question on the rare disease. So, if you remember what the trial of gefurulimab was done in patients earlier than the trials we have done historically with Ultomiris. You will remember that Alexion was a pioneer company to obtain the first approval with modern medicine in myasthenia gravis. And subsequently, we -- after Soliris, we developed Ultomiris and now we go one step earlier. The other important factor of gefurulimab is a mode of administration, a subcut weekly provided in either prefilled syringe or an auto-injector that can be injected in 15 seconds. So, it's a very patient convenient, patient easy type of administration. And the speed of onset has been demonstrated in the study and also the sustainability is as good as it was for Ultomiris. So, that's what I can say about gefurulimab.

Pascal Soriot: Thank you, Marc. And the last question is from Simon Baker at Redburn. Over to you, Simon.

Simon Baker: Just changing the subject slightly. We don't ask many questions on. But one for Susan, could you give us an update on your confidence in sone vedotin as we come up to the gastric Phase III data in H1 '26? And also some thoughts on the broader scope of Claudin18 beyond gastric?

Susan Galbraith: Thanks for the question. So, sone vedotin is a Claudin18.2 ADC with an MMAE tubulin-based payload. And we've seen encouraging response rate data in late-line patient populations. We are investigating this versus current standard of care, but we're also looking within the potential to take it into earlier line settings, including in combinations. And you all have seen, of course, that there are exciting opportunities for MMAE-based ADCs in combination with I/O therapy. So, that represents a significant opportunity to sone v. Claudin18.2 is expressed in a high proportion of gastric cancer more than 50% of patients. So it's a much bigger opportunity than the HER2 high group, if you want to compare with what we've seen with HER2. And I think, it's also expressed in pancreatic cancer. And we are looking at the data in pancreatic cancer as well. I mean, of course, there the bar is high. So, what we've done is go forward with the gastric cancer opportunity first, and we'll continue to explore the opportunity for this and also a topo-based ADC with a Claudin18.2 targeting also in pancreatic cancer, just to see which payload works best.

Pascal Soriot: Thank you, Susan. So in closing, maybe a few words back to Luisa's question. I realized I didn't totally answer Luisa's question. As the pipeline develops, you can see we'll have a lot of Specialty Care products moving forward. And of course, those tend to drive higher profitability as we know. But we also have products that will address conditions like weight loss, metabolic conditions, metabolic disease and those, of course, require more investment. So, I think overall, you can suddenly assume improvement of profitability from a commercial viewpoint. The R&D;, we want to continue spending at the -- in the low 20s, as we've done in the past. But as I said before, we will not commit to

any direction of travel of our profitability, because we need to see how the pipeline develops, and that's what we've said in the past. And more frankly, we've been good and lucky. We have had a very high success rate, and I hope it continues. And if it does, then we have to support all these products. So with this, thank you so much for your great questions and your interest, and I wish you a good rest of the day.