GSK plc

GSK plc - Q4 2024 Earnings Call

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Event Participants

Executives 6

Emma Walmsley, Luke Miels, David Redfern, Julie Brown, Tony Wood, Unknown Executive

Analysts 8

Emily Field, Richard Parkes, Peter Welford, Steve Scala, Rajan Sharma, Justin Steven Smith, Graham Parry, James Gordon

Operator Operator

Hello, everyone. Welcome to today's call and webcast. The presentation was sent to our distribution list by e-mail, and you can also find it on gsk.com.

Please turn to Slide 2. This is the usual safe harbor statement. We will comment on our performance using constant exchange rates or CER and excluding COVID solutions, unless stated otherwise.

Please turn to Slide 3. Today's call will last approximately 1 hour and 15 minutes. With the presentation taking around 40 minutes and the remaining time for your questions. Our speakers today are Emma Walmsley, Luke Miels, Julie Brown and David Redfern, who will be covering HIV in the absence of Deborah Waterhouse, who's recovering from a successful medical procedure. And Tony Wood will be joining us for Q&A.

Please ask only one to two questions so that everyone has a chance to participate. Turning to Slide 4. I will now hand the call to Emma.

Emma Walmsley Executive

Thank you, Jeff, and welcome to everyone joining us today. Today, we are reporting our 2024 results and providing you with updates on our growth outlooks, investment plans and focus on improving shareholder returns. Please turn to the next slide. 2025 will mark 3 years since the demerger and the creation of GSK as a new dedicated biopharma company for patients and for shareholders. The demerger enabled a fundamental restructure of GSK and its balance sheet, bringing new capacity to invest in growth and to deliver returns to shareholders.

Three years on, I'm pleased to say that we've seized this opportunity and made significant progress, building a strong track record of performance delivery. Specialty medicines and

vaccines now dominate our reshaped portfolio and pipeline. Our long-term outlooks have consistently improved alongside the quality of our innovation. And we've delivered sustained year-on-year sharper operational performance, underpinned by a stronger balance sheet. This all points to GSK having the platform to deliver sustained profit growth and returns in the short, medium and long term.

Next slide, please. Our 2024 performance demonstrates the transformation of the business. sales grew 8% to over GBP 31 billion, with strong growth and increasing contribution from Specialty medicines more than offsetting headwinds in vaccines. Core operating profit was up 13% and core EPS was up 12%. This level of performance delivered two upgrades to guidance in 2024 and supports the increased dividend of 61p per share announced today.

I'm also pleased to report that we maintained good progress in our six priority areas to build trust, not least retaining a leadership position in the Access to Medicine Index, but we've been placed first or second in the industry since its inception in 2008. And of course, during the year, we also resolved the Zantac litigation, prioritizing shareholder interests.

Next slide, please. Operational delivery in 2024 reflected strong growth in accelerating momentum of specialty medicines with double-digit growth in all therapy areas and sales of Oncology nearly doubling to more than GBP 1.4 billion for the year. Vaccine sales reflects the challenges we've seen from external pressures in the U.S. and China for Arexvy and Shingrix. Going forward, we expect these to continue in 2025, but equally remain confident that Arexvy, Shingrix and our vaccines pipeline will contribute meaningfully in the medium and long term.

Importantly, 2025 will see further additions to GSK's portfolio with five new product approvals expected this year. At the forefront, our potential step changes in treatment with Blenrep, our novel ADC treatment for multiple myeloma and depemokimab, our new long-acting IL-5 medicine for the treatment of severe asthma. Of these two, Blenrep will be the first to launch with an expected FDA PDUFA in July.

Next slide, please. Last year, GSK had 13 positive Phase III readouts, a record achievement for our R&D organization. I'm also pleased with the confirmed development and strengthening of our mid- and early-stage pipeline with positive clinical progress and the addition of several promising new assets in the areas of Oncology and Respiratory Immunology and Inflammation or RI&I.

Next slide, please. So with all this progress to date, R&D is now heavily focused on the clinical development of 14 scale opportunities with PK sales potential above GBP 2 billion, and expected launches before 2031 and the majority in Specialty Medicines. In RI&I, we're prioritizing depemokimab, Nucala COPD, camlipixant and long-acting IL-33, IL-5 and TSLP medicines. The aim here being to leverage GSK's deep expertise in inflammatory mechanisms to lead in COPD and to target new options to treat fibrotic lung, liver and kidney diseases. In Oncology, we're prioritizing resources to Blenrep and to the acceleration of our very promising ADCs targeting B7-H3 and B7-H4 antigens as well as continuing life cycle innovation for Jemperli.

In HIV, our plans for long-acting and ultra-long-acting treatment and PrEP options for 4 and 6

months are all progressing very well. And infectious disease, we're prioritizing development of bepirovirsen, or potential functional cure for hep B and of course, our high potential new mRNA and MAPS vaccines. Alongside these, and as Tony starts to outline in December, we're also prosecuting the early-stage pipeline with a further 40 assets or so in Phase 1 and 2. Lastly, we continue to add new opportunities through targeted business development, the recent agreement to acquire IDRx being a great example of what we want to do here.

Next slide, please. Looking at GSK's launch portfolio over the next 5 years, we expect it to offer scale opportunity for growth, together with an attractive risk profile. By 2031, we're increasing our outlook again and now expect risk-adjusted sales to be more than GBP 40 billion. This increase reflects the inclusion of BLENREP, our significant Phase III progress since last year and multiple launch opportunities in the 26 to 31 period. With almost 90% of our 2031 sales ambition coming from products already approved or planned for launch in the next 3 years, we're confident that our portfolio will deliver against this guidance.

In terms of contribution, we now expect Specialty medicines to be more than 50% of sales by 2031, with this area being the key growth driver for GSK over the next few years too, reflecting the high number of opportunities we have in the maturing late-stage pipeline for specialty products, particularly in our RI&I and Oncology.

For vaccines, while we've adjusted expectations to accommodate for new sales growth trajectories of Arexvy and Shingrix over this period, as you can see here, we continue to expect this part of GSK's business to remain a key source of future growth. General Medicines will also remain an important and relatively stable contributor to sales over the period. As before, we have further upside from our early-stage pipeline, including notably Q6 month, HIV and prospective BD, where we will continue to pursue smart opportunities at the same kind of scale and pace seen in recent years. And as you can see from the two bars here, there is significant potential for upside with successful clinical outcomes.

Next slide, please. Overall then, we continue to set out positive outlook for growth in the short, medium and long term, and we are all strongly committed to maintaining our track record of delivering this together. We expect 2025 will be another year of profitable growth led by specialty medicines. And with our recent progress, we're now even more confident in our ability to deliver not only our '26 but also our new 2031 outlooks. All of this while retaining the flexibility we need to invest competitively in growth and to deliver improving returns to shareholders.

Next slide, please. We remain extremely focused on disciplined allocation of capital. Our first priority for capital remains to invest in growth and in R&D. With the pipeline opportunities we now have, we are deliberately prioritizing investment to accelerate development of key assets in RI&I and Oncology alongside long-acting HIV medicines and existing core vaccines opportunities. In addition to growth, we also remain focused on delivering improving returns for shareholders.

Our primary mechanism for this remains via delivery of a progressive dividend. For 2024, we've declared 61p, and we expect to pay 64p in 2025.

And as we've previously said, we also look to deliver returns using other mechanisms when

circumstances and opportunities allow. And today, we are announcing our intention to buy back up to GBP 2 billion of shares over the next 18 months. We believe this offers a very attractive return for shareholders at current share price levels. Very importantly, and to reconfirm, we will maintain planned increased levels of investment in R&D, new launches and targeted business development alongside the share buybacks. So let me now hand over to Luke to start to take you through more detail on our 2024 performance and the prospects we see for some of our near-term growth drivers.

Luke Miels Executive

Thanks, Emma. Please turn to the next slide. As Emma highlighted, overall sales for the year were up 8%, with strong growth from Specialty and General medicines, more than offsetting short-term headwinds, primarily in the U.S. to our vaccines business. Next slide, please.

Specialty medicines continues to show excellent momentum and pipeline progress. And as Emma said, it's now expected to be over half our business by 2031. In 2024, Specialty grew 19%, with strong performances across all therapy areas. Respiratory Immunology products were up 13% in the year. Nucala, our anti-IL-5 biologic treatment grew 12%, driven by strong performances in Europe and international.

Benlysta, our treatment for lupus was up 14% in the year, with strong demand across all regions.

In Oncology, sales almost doubled in the year. Zejula grew 17% with strong growth across all regions, driven by sustained increases in patient demand. Jemperli sales more than triple in 2024, benefiting from increased patient uptake in the U.S. following FDA all-comers approval for primary, advanced or recurrent endometrial cancer, and we received EMEA all-comers approval in January this year.

Ojjaara sales increased more than 10x in the year, largely driven by continued strong uptake in the U.S. Contributions from Europe and International are also increasing following launches in the U.K., Germany and Japan, and we expect further launches in 2025. David will cover HIV shortly, we expect the excellent momentum in our Specialty Medicines portfolio to continue in 2025 with sales growth of low double-digit percent, while absorbing the IRA impact.

Next slide, please. looking at what's next in specialty, in RI&I, we are targeting a major new indication for Nucala to treat COPD following positive headline results from our Phase III MATINEE trial. COPD affects more than 300 million people globally and is the third leading cause of death worldwide, excluding COVID, an FDA decision is expected ahead of the seventh of May PDUFA date and launch preparations are fully underway.

We plan to publish the full MATINEE results at this year's ATS meeting. Depemokimab, our new long-acting anti-IL5 medicine has now been filed in all major markets for dual approval in severe asthma and chronic rhinitis with nasal polyps. Depomokimab has the potential to be the first approved ultra-long-acting biologic with 6-month dosing, offering physicians and patients the reassurance of prolonged efficacy through sustained suppression of inflammation and could improve compliance and adherence for patients with severe asthma. We expect more Phase III readouts over the next 18 months for other eosinophil-driven indications. And also plan to start a Phase III trial in COPD this year.

And we have camlipixant, a highly selective P2X3 antagonist with the potential to be a best-in-class medicine for treatment of refractory chronic cough and disease with significant unmet need.

First Data from the Phase III CALM development program are expected this year with more early next year. In oncology, we're working to realize the full potential of our existing medicines as well as to expand our portfolio in areas of high unmet need. We have significant potential assets to drive growth for GSK and I am very optimistic about what we, as GSK can deliver here. We're building a portfolio of novel pipeline ADCs with the ability to target tumor cells while sparing healthy ones. GSK 227 targets B7-H3, an antigen, which is overexpressed in a wide range of solid tumors.

Early data showed promising clinical activity and we expect to share updated small cell lung osteosarcoma and additional data from our clinical development programs at the ASCO and ESMO conferences this year.

Pivotal studies for 227 are expected to start before the end of the year. GSK 584 targets B7-H4, which is also overexpressed across a number of solid tumors. And our initial focus here is for the treatment of ovarian and endometrial cancers. Again, we expect to share more data on 584 at the conferences of this year. As you may have seen, we started 2025 with the announcement to acquire IDRx.

This gives us access to IDRX-42, a very promising and highly selective KIT tyrosine kinase inhibitor designed to treat gastrointestinal stromal tumors. This adds to our GI cancer portfolio, and we plan to accelerate development of this exciting asset. Lastly, as a reminder, we also expect initial results from our AZUR-1 and AZUR-2 trials, exploring Jemperli in rectal and colon cancer in 2026 and 2027 respectively, and the Phase III JADE study to read out in 2028. All this highlights the very strong progress GSK is making in oncology. 2025 will be another key year with the launch of Blenrep.

Next slide, please. Blenrep is at the forefront of our ADC portfolio. In December, we presented overall survival data from the DREAMM-7 second-line multiple myeloma study at ASH, and the data demonstrated a statistically significant and clinically meaningful 42% reduction in the risk of death when comparing Blenrep to the depemokimab-based standard of care. Median overall survival has not yet been reached in DREAMM-7, but the projected difference is 33 months. For context, that's almost an additional 3 years of survival versus the current standard of care.

If approved, unlike a number of alternative second-line treatments, Blenrep would be an off-the-shelf treatment option delivered by a 30-minute infusion in a community setting with no requirements for pre-infusion protocols, hospital admission or post-infusion monitoring. This could be important for the 70% of patients treated in the community. In the newly diagnosed or first-line setting, we're encouraged by the second-line trial readouts, but also by the [Indiscernible] trial, which demonstrated 100% response rates. Our pivotal trial for Blenrep in the first line, DREAMM-10 started recruitment at the end of 2024, and we anticipate headline results towards the end of 2027.

Next slide, please. I remain very ambitious for Blenrep, which I believe will become an

important new growth driver for GSK. We have gained extensive experience of treating patients with Blenrep and have a better understanding of how to mitigate eye-related side effects. Around 1/3 of patients in Blenrep studies have reported blurred vision as an adverse event. But for the vast majority of these patients, this was manageable, transient and reversible and data suggests did not impact patients' quality of life.

Eye-related side effects in DREAMM-7 were generally managed by dose modification, for example, by extending the interval between doses.

Data recently presented at ASH showed that when dosing intervals were extended from 8 to 12 weeks, the incidence of ocular events declined and critically, the efficacy of Blenrep was maintained. We've completed a number of regulatory filings and have an FDA PDUFA date of July 23. As we prepare for Blenrep's launch, market research tells us intent to prescribe has significantly improved. With the overall survival data, a strong motivator. However, ACIPs are mindful of eye-related side effects and therefore, educating them in the appropriate dosing will be key.

As a result, in the initial phase, we expect a staged ramp-up as we build physician experience for the medium to longer term. I'll now hand over to David to talk through HIV before I cover vaccines and general medicines.

David Redfern Executive

Thank you, Luke. HIV sales continued to deliver strong growth, up 13% for the full year, with Q4 delivering our ninth consecutive quarter of double-digit growth. Growth in 2024 was driven by strong patient demand for our oral 2-drug regimen, Dovato, up 27% and long-acting injectables Cabenuva and Apretude, which reached GBP 1.3 billion of sales and contributed more than 50% of total growth. This resulted in a 2 percentage point increase in global market share compared to the prior period. Cabenuva, the first and only approved complete long-acting injectable regimen for the treatment of HIV grew 47% to over GBP 1 billion of sales in 2024.

Growth was driven by strong patient demand across the U.S. and Europe of 70,000 people living with HIV now benefiting from this transformative medicine globally.

In January, we announced European Commission approval for use in adolescents. This marks an important step in bringing this medicine to younger people in line with our commitment to leave no person living with HIV behind. Apretude, the first and only approved long-acting option for HIV prevention delivered sales of nearly GBP 300 million in 2024, continuing its strong growth trajectory at 93%. With 99% effectiveness, we are confident in its strong efficacy, safety and overall tolerability. In 2024, of the 13% growth, 10% was volume with the remainder favorable in-year pricing dynamics.

In 2025, we anticipate sales growing by mid-single-digit percentage, supported by ongoing growth in volume, partly offset by pricing headwinds with the introduction of the inflation Reduction Act which we expect to be GBP 150 million to GBP 200 million impact. The potential for the long-acting market remains significant with the market today for treatment and PrEP together worth more than GBP 22 billion, with treatment accounting for around 90% of this, and we believe treatment will continue to be the much larger market going forward.

Next slide, please. Our pipeline is founded on Integrase inhibitors or INSTIs, the gold standard of HIV treatment and prevention due to their potency, long-term tolerability and high barrier to resistance. We have a clear road map to deliver more long-acting innovation with three new INSTIs in development and five planned launches by the end of the decade. In December, our registrational study for cabotegravir 4 monthly long-acting injectable prep began, and we are on track to start our registrational study for every 4-month long-acting injectable treatment this year. Early data on assets with the potential for 6 monthly dosing will be available in 2025, including selected presentations at the CROI Congress in San Francisco in March.

We are on track to confirm in 2026, the assets that will deliver sixth monthly dosing. For PrEP, this will be one of three long-acting INSTIs and for treatment one of those INSTIs in combination with our bNAb N6LS, or our capsid inhibitor. As pioneers in long acting injectables, we are confident we have a strong and innovative pipeline to secure and deliver future competitive performance. With that, I will hand back to Luke.

Luke Miels Executive

Thanks, David. Turning to vaccines. Total sales were GBP 9 billion, down 3% in the year, largely due to lower sales of Arexvy in the U.S. Overall, Arexvy continues to be the market leader in the U.S. with around 10 million adults now protected.

However, demand for the vaccine was lower in 2024, following new ACIP recommendations, a late RSV season and an unfavorable comparison to launch stocking in 2023. Going forward, we continue to assume no revaccination or expansion of age cohorts in 2025, but we do expect both in time, given the protection Arexvy can offer against RSV. Outside of the U.S., Arexvy is now launched in 36 markets, and we are seeing good momentum in uptake with national recommendations in 17 markets and national reimbursement programs in 6, and we expect more this year.

Moving to Shingrix. Sales grew 1% in the year, with growth in Europe and international offsetting lower sales in the U.S., whereas anticipated, the pace of penetration is slowing. The U.S. immunization rate at the end of the third quarter was 40%, up 5 percentage points in line with our expectations for around 3 to 5 percentage points per year. Ex U.S.

growth was driven by higher uptake across European countries and a national immunization program in Australia. Shingrix is now launched in 52 countries, and the average immunization rate across the top 10 markets outside the U.S. is now around 7%.

In meningitis, our portfolio achieved another year of double-digit growth with sales up 18%. Bexsero reached blockbuster status with sales up 23%, aided by CDC purchasing and positive recommendation in Germany. Menveo grew 5%, impacted by comparison to stockpile replenishments in 2023. And in February, we anticipate U.S. FDA approval of our new pentavalent MenABCWY vaccine, combining the antigen components of Bexsero and Menveo.

In time, we expect this to simplify immunization schedules, increasing coverage and protection against a serious life-threatening illness. Medium and long term, we expect vaccines to remain a key source of future growth. In the short term, given the challenging

China macro environment and the potential for changes to U.S. vaccination policies and uptake in the next 12 to 18 months, we're expecting vaccine sales to decrease low single-digit percent in 2025.

Next slide, please. General Medicine sales grew 6% in the year, and this was largely driven by Trelegy, up 27% with strong demand across all regions, strengthening its position as the top-selling brand in asthma and COPD. In 2024, increased use of authorized generic versions of Advair and Flovent fully offset the headwind from the removal of the AMCAP on Medicaid drug prices. This year, we are excited to launch gepotidacin, the first completely new antibiotic to treat complicated urinary tract infections in more than 20 years. And we expect to see demand increase from 2026 once payers have completed their review process and put gepotidacin on formally.

Overall, looking across the General Medicines portfolio, while we expect volume growth across key brands to continue, we expect that to be broadly offset by pricing and genericization pressures and so I anticipate sales to be broadly flat in 2025. I'll now hand over to Julie.

Julie Brown Executive

Thank you, Luke, and good morning, everyone. Next slide, please. Building on the comments made by Luke and David, this slide shows a significant growth contribution from specialty medicines. Having delivered more than 80% of the growth this year by building scale and momentum in our respiratory immunology and oncology business as well as ongoing growth in our HIV portfolio.

Next slide, please. Moving to the income statement for the full year with growth rates stated at CER and ex-COVID. Sales increased 8% and core operating profit 13%, despite a 6% headwind from the loss of Gardasil royalties. Within this, gross margin grew 80 basis points, benefiting from the positive mix from specialty medicines and the supply chain efficiencies. Despite incorporating GBP 150 million charge to drive future supply chain productivity.

SG&A increased 2% year-on-year, benefiting from our returns focused, disciplined approach to investments, supporting global market expansion for key assets, including Jemperli, Nucala, long-acting HIV, Arexvy and Shingrix as well as a one-off credit from the Zejula royalty dispute in quarter 1. R&D grew 7%, broadly in line with sales as we invested in Phase III trials, particularly in RI&I and Oncology.

Core EPS grew 12%, slightly below operating profit, as anticipated due to an expected increase in the core tax rate. And turning to the total results, operating profit decreased materially year-on-year to GBP 4 billion. The reduction reflected a GBP 1.8 billion charge relating to the resolution of the Zantac litigation and a higher CCL charge driven by the improved long-term outlook for our HIV business.

Next slide, please. Core operating margin improved to 29.2% up 130 basis points year-on-year at CER and ex-COVID, notwithstanding the absorption of 140 basis points due to the loss of Gardasil royalties. This marked improvement demonstrates productivity, efficiency and optimized resource allocation to the key commercial and R&D assets in the business. The gross margin benefited from the outperformance of specialty medicines, positive channel

mix and supply chain productivity.

Next slide, please. Turning to cash. Cash generated from operations was GBP 7.9 billion, impacted by settlement payments relating to the resolution of Zantac. Excluding this impact, we continued our track record of improving cash every year with CGFO up GBP 0.4 billion, totaling GBP 8.5 billion. This improvement primarily reflected the increase in core operating profit together with favorable working capital largely due to lower receivables and lower pension contributions.

These benefits were partly offset by lower other payables due to the reduced rebates and returns from AMCAP. Free cash flow improved to GBP 3.5 billion, excluding the Zantac payments, notwithstanding increased investment of GBP 0.4 billion in BD intangibles.

Next slide, please. This slide demonstrates how we have deployed our cash in line with the capital allocation framework. Free cash generation, pre capital expenditure and excluding Zantac was strong at over GBP 6 billion. Our first priority is to invest for growth. And in 2024, we deployed GBP 3.6 billion on CapEx and BD.

Our second priority is returns to shareholders. And today, we have declared a dividend of 61p, an increase of 5% year-on-year and ahead of guidance, reflecting the strong outperformance of our 2024 results compared with our original position. In 2025, we anticipate paying a dividend of 64p, a further 5% increase year-on-year. And finally, we had two one-off factors. The monetization of Haleon, which generated GBP 2.3 billion and the resolution of the Zantac litigation.

At December 2024, net debt reduced to GBP 13 billion, driven by strong free cash generation and the Haleon proceeds. As we've previously said, we will look to deliver incremental returns when business needs have been fulfilled and the balance sheet allows. And given the significant transformation since the demerger, we now have a strong balance sheet, which gives us a high level of flexibility to the acceleration of organic investments and further business development, whilst also enabling a step-up in shareholder returns. As Emma said, we will augment our dividend with a GBP 2 billion share buyback program to be completed over the next 18 months. So to summarize, our focus is on investing for growth, and there is no change to our capital allocation priorities, and we remain fully committed to maintaining a balance sheet with a strong investment-grade credit rating.

Next slide, please. Now turning to guidance at constant rates. I'll cover 2025 and phasing and then move to the outlook for '21 to '26. So first for 2025, we expect another year of good profitable growth for GSK. Sales are expected to increase between 3% and 5%.

Core operating profit and EPS to increase between 6% and 8%, with EPS impacted by higher interest charges and the tax rate rising to around 17.5%, offset by up to a 1% benefit from the share buyback. Some points to note for modeling purposes. Firstly, we expect our sales growth to be driven by specialty medicines in 2025, which also benefit gross margin.

Secondly, in terms of OpEx, we expect SG&A to grow at a low single-digit percentage with strong investments behind product launches whilst focusing on competitive precision analytics and an AI-enabled approach driving increased ROI. R&D is expected to grow broadly in line with sales as we prioritize investment in key pipeline assets, including our I&I oncology

and next-generation vaccines. And finally, we expect royalty income to be in the range of GBP 650 million to GBP 700 million. As previously stated, at Q3, our guidance incorporates a 400 million to 500 million revenue headwind from the introduction of the IRA.

Next slide, please. In terms of phasing, we anticipate growth in 2025 to be second half weighted, largely due to a significant sales comp base effect, particularly in vaccines, as well as benefits last year that will not repeat, namely Zejula in Q1 and return a rebate adjustments in Q2.

Next slide, please. Emma has covered the overall outlook. And therefore, I would just like to give more color on the change in the product mix outlook from '21 to '26. The contribution from Specialty Medicines has increased significantly, with growth accelerating due to strong RI&I, Oncology and HIV performances. This performance momentum means we now expect a low to mid-teens 2026 CAGR, ahead of the previous guidance, and for HIV specifically to grow high single digits across this period.

The vaccines, the recent performance has been volatile.

And whilst we continue to expect material contributions from vaccines in the medium and long term. In the near term, we have reduced our expectations for the 2026 CAGR to a mid- to high single digits. Where we ultimately land in the range will depend on a number of factors, most notably the overall U.S. environment for vaccination ACIP recommendations, disease incidents and the China macro backdrop and its implications for Shingrix uptake. General Medicines has also outperformed, which means we expect a low single-digit contribution to our 26% CAGR.

Alongside sales, we continue to focus on margin improvement with no change to our guidance of more than 31% margin by 2026 and more than 500 basis point improvement over the 5 years. And we continue to expect a broadly stable operating margin through the dolutegravir patent expiry.

Next slide, please. Turning to our IR road map. We have made significant progress this year in our pipeline and execution and the deployment of capital to support growth. Next slide, please. And turning to '25, '26, as mentioned, we expect five major approvals this year, including Blenrep and depemokimab.

Over the coming 24 months, we also anticipate Phase III readouts for camlipixant for refractory chronic cough, and bepirovirsen for hepatitis B as well as pivotal Phase IIs for our 4 monthly HIV PrEP and Jemperli rectal for cancer.

Next slide, please. Before I finish, I just wanted to take a minute to reflect on the progress we've delivered over the last few years, which demonstrates a marked improvement in capital management, operational efficiency and our commitment to improving outlooks. Firstly, operating margin improved 360 basis points, and we have moderated the growth of SG&A as we leverage investments and take a disciplined returns-based approach together with supply chain efficiencies and mix benefits. Importantly, over the period, our investment into R&D has increased at a 10% CAGR. And going forward, R&D growth is expected to be broadly in line or ahead of sales.

Secondly, cash generated from operations has been growing to about GBP 8 billion per year since 2021, with 2024 being a record year adjusting for the one-off impact of Zantac.

We anticipate this rising further to more than GBP 10 billion by 2026. This strong cash generation has allowed us to commit to a progressive dividend policy, with more than 5% growth over the last 3 years alone. And it has allowed us to announce the GBP 2 billion share buyback program today. Including this, we will have returned in excess of GBP 8 billion of cash to shareholders over the 3-year period to 2025. Our balance sheet is now very strong, with net debt to EBITDA at just 1.2x, allowing us significant firepower for future BD and shareholder returns.

We will continue to benchmark all future deals against stringent criteria to ensure capital is deployed optimally. And ultimately, you will only see us investing in opportunities that are strategically aligned to our main therapeutic areas. And with that, I'd now like to hand back to Emma for her closing remarks.

Emma Walmsley Executive

Thanks Julie. So in summary, GSK is powering forward. This comes on the back of a strong track record of operational delivery and accelerating progress in innovation and pipeline development, where, of course, there is always more to do. Our portfolio is demonstrating both growth and resilience built around high-quality specialty medicines and vaccines with more to come in key areas of therapeutic strength for GSK. As we head into 2025, we expect another year of profitable growth, and we have further improved our long-term outlook to sales of now more than GBP 40 billion by 2031.

Our outperformance and stronger balance sheet support our future investment plans, including for more investments in R&D, more business development as well as providing us with the opportunity to deliver enhanced shareholder returns. All of this underscores GSK's opportunity to deliver scale, health impact to patients through this decade and beyond. Combining science, technology and the talent of our people to get ahead of disease together. Thank you very much, and I will now open up the call for Q&A with the team.

Operator Operator

Okay. Thank you. For the Q&A portion of our call, [Operator Instructions]. For our first question, we will go to Emily Field from Barclays. Emily.

Can you please ask your question?

Emily Field Analyst

I'll ask two, hopefully quick ones. Firstly, I know you mentioned impact from sort of the China macro on Shingrix. Obviously, with the Merck announcement yesterday on Gardasil, a lot of concern that this has -- the deterioration in this outlook has accelerated. So I was just wondering if you could provide a little bit more granularity on your expectations for Shingrix in China in 2025. And then secondly, within the mid-single-digit growth for HIV for 2025, are you assuming much of a competitive impact from the launch of Lenacapavir in the second half of this year?

Emma Walmsley Executive

Thanks. We'll come to David in a minute on HIV and our confidence there. Let's go to Luke first on China. I just would flag this is something that we addressed last year with the repositioning of our deal with our trusted partner, [Indiscernible] and I think still remain ambitious, although the short-term pressures were acknowledged both through '24, and of course, in the guidance that we've given to '25, but none of that takes away from our longer-term ambition. Luke, do you want to comment on China?

Luke Miels Executive

Thanks, Emily. I mean, as Emma said, look, there's not much more to add than what I covered on the Q3 call. I mean our market share is around 70%, and that's our target population there. We're very happy with the partnership with [Indiscernible], but the intent to extend it out to 2034 was to address exactly what we're seeing right now, which is just to navigate the short-term headwinds. Our focus operationally is partnering on the ground with [Indiscernible] to expand in those high-tier cities and initial signs are encouraging.

But again, I wouldn't expect too much in 2025. This is a mid- to longer-term play here.

David Redfern Executive

Yes. No. Thanks, Emily. [Indiscernible] very pleased, obviously, with the continued strong growth momentum in HIV in Q4, contributing almost GBP 2 billion of sales. I think on your specific question, look, we certainly expect Apretude to continue to grow this year.

First and foremost, the PrEP market in the U.S. is actually significantly underdeveloped. CDC estimates, I think, about 1.2 million Americans could benefit from PrEP and stay only about 1/3 of those are getting any form of PrEP treatment. And we also know that the PrEP market is very well suited to long-acting options. And I think Apretude and now the competitor product have very similar strong efficacy, probably -- or definitely better than the orals, mainly due to compliance.

So I think with the second long-acting entrant coming into the market this year, it should help grow the market for all of us. And then secondly, the competitive product definitely won't be for everyone. We now know that there's quite a high frequency of nodules that people experience in their abdomen, where the two injections are given. I think in the pivotal study is about 63% of participants experiencing nodules with a mean duration of about 6 months and 7 cases of ulceration.

I expect we'll learn a lot more as the year goes on through more data and more real-world evidence of exactly what type of patients and the size of these nodules and so forth. But for potential PrEP users who are body image conscious, which will be quite a proportion of them, I think that potentially is an issue. And then I would also flag that the competitive product has quite a high number of drug-drug interactions made 14 classes of commonly prescribed prescription medicines, corticosteroids, erectile dysfunction meds and so forth. And also DDIs are recreational and [Indiscernible] drugs, opioids, fentanyls and so forth, and these DDIs can be serious in very extreme cases, potentially cause fatal respiratory depression. So again, for PrEP users or potential PrEP users who are taking these meds, it may not be for

them.

So we'll see how this unfolds, but I think we expect to grow in a growing market.

Emma Walmsley Executive

Thanks, David. And just to underpin, we welcome the opportunities to grow the market. But even if this market triples in size and we get to the 100% participation to the part of the market that the CDC said could be treatment is still where most of the businesses. And here, we obviously lead the way. So next question, please.

Operator Operator

Great. The next question will be from Richard Parkes at BNPP Exane. Richard?

Richard Parkes Analyst

So I've got a couple of questions on vaccines and the targets. So on Arexvy, obviously, you saw a rapid penetration of the U.S. market, but there's still a large international opportunity. Can you discuss how prepared you are to access that in 2025 and what the key factors are in driving that limiting your ability to access the opportunities. And then again, vaccines.

Obviously, you talked about moderating expectations for Arexvy, Shingrix. Can you talk about what's assumed for peak sales of both those products now? Because I think the market is quite skeptical about your prior peak sales targets given the current headwinds? And just wondering what the offsets are to raising your 2031 targets? I know Blenrep obviously been included, but it sounds like there's some other offsets there where you're more optimistic.

So helping understand those moving parts would be helpful.

Emma Walmsley Executive

Thanks, Richard. And I'll come to Luke to add a bit more color on how we see the opportunities for growth over time on Arexvy because we really are in the foothills of this vaccine, which, as you know, we've really filled with the data that's come through on its efficacy and a high burden of disease area. Explicitly, there's no change to our ambitions for our assets, be that our existing ones or some exciting pipeline that's coming through later in the decade. The real question is actually the area under the curve. And obviously, last year, you saw us re-calibrate our expectations in '24.

We did say in Q3, we expected to recalibrate those -- or sorry, to maintain that the -- and acknowledge the short-term pressures on vaccines in '25, duly flagged then that we expected the mix to change has been more explicit today. We've been more explicit today on how that mix changes. And obviously, that has flowed through to our updated 2031 outlooks.

Alongside, as you suggest, Richard, the impact of 13 positive Phase III, the momentum in our specialty business more broadly. And as Julie said, we've upgraded whilst acknowledging the pressures on vaccines, we've upgraded our '26 outlooks for total specialty for HIV, also for Gen Meds, these have rolled through and we've added in Blenrep as I outlined in my introduction, this doesn't yet include our intent to invest in progressing the early-stage pipeline or our intent to pursue further BD like the kind of assets that you right at the

beginning of January, IBRX isn't yet in there.

So I think the key takeaway on this is the strength of our broader portfolio, the progress we're making in the broader pipeline means we can digest these what we think are short-term pressures in both the U.S. and in China, and we remain optimistic about our broader vaccines pipeline and lots more to come particularly in oncology and RI&I, be it Blenrep or ADCs or the other pipeline that's coming through. So with that, I think that's come back explicitly to Arexvy, Luke, and how you see the international opportunity, whatever the weather in the U.S. is at the moment.

Luke Miels Executive

Sure. Thanks Emma, and thanks, Richard. I mean you know last year, we had about 15% of revenue was ex U.S. I'm very encouraged by what we're seeing. It's early days, but we know what we're doing in this context.

I think with these national immunization program, which I said earlier, we've got six, that's in the U.K., Greece, the one in Czech, Saudi, strong tender there, as well as critical success with [Indiscernible] in Germany, in addition to the U.S., I think it's an encouraging start. I think what also is important as these systems will differentiate based on clinical data. and the market research that we have in these key markets is certainly very encouraging in terms of the perception of Arexvy, the efficacy of high-risk groups as well as the durability and cost effectiveness of the vaccine. So I look forward to updating you more this year. But so far, it's a good start.

Operator Operator

Great. The next question, we will go to Steve Scala from TD Cowen.

Emma Walmsley Executive

Hi, Steve, thanks for joining us early.

Operator Operator

All right. Steve will come back to you. And instead, let's go to Peter Welford at Jefferies. Peter?

Peter Welford Analyst

Two questions. Firstly, just sticking with Arexvy at this time in the U.S. I wonder if you could talk a little bit about the commercial environment there, if you can. Because I guess in the last -- particularly the last part of the season that we can see the prescription data for, it looks as though Pfizer is beginning to claw back quite a bit of share compared to what we've seen in the past. Can you just talk a little bit about contracting that you're seeing, I guess, for this year and perhaps also reluctance, I guess, on that from pharmacies and buyers, I guess, to engage given what I imagine from their part must be pretty uncertain demand going into the next season, which I appreciate are still month and months away.

And then secondly, just on the buyback, I mean it clearly reflects your confidence in the longer-term pipeline that you already have, I'm guessing, internally relative to how the market

perceives the R&D and what you have for new launches. So I guess -- could you talk a little about how -- I guess, how much of -- when we look at that chart, how much of it do you think is reflecting also things like long-acting HIV. And maybe you can put a number on how big do you think the HIV long acting business could be beyond the sort of LOE expiries that we're seeing. And I guess trying to just sort of build some [Indiscernible] what is it in the market is missing, do you think, in terms of the sort of resilience perhaps of the base business that gives you the confidence to do to allocate capital to a buyback today.

Emma Walmsley Executive

Yes. Well, lots of questions in that, Peter, I'll come back in a minute to look on the U.S. commercial, environment and vaccines. Obviously, lots of external commentary and speculation on that for 2025, which also depends where we see the sort of pressured external environment, but Luke can add further comment on the commercial side. Look, buyback is completely consistent with the capital allocation framework that we've laid out.

And the first priority continues to be, as both Julie and I said, to invest in the future growth of the company, to invest in the pipeline, to invest competitively, and these exciting new launches that we've got coming through, be that the five approvals we hope to have this year or hopefully, as they progress, the 14 key assets that R&D with commercial partners working together on bringing forward. We also want to continue to supplement and plan to continue to supplement that with further business development.

The point is that alongside that priority, we also continue to demonstrate our focus on improving shareholder returns. And obviously, considering the momentum in the business, the progress in the business, the strengthening of the balance sheet. We are very confident that we have both the circumstances and the opportunity to deliver really compelling returns to shareholders with this announcement that we've made today. Now I am not going to guide by individual product forecast in terms of what we will deliver in 2030. We've given, I think, a reasonable schematic that we've presented to you that showed most importantly.

And this is really the key thing I think people should take away from today is our biggest business -- 19% in 2024 with every single therapy area growing at double digits.

It's still a nascent business, but the progress we're making in oncology is very exciting, and we have a potentially really material contribution to make. Even if the launch is staged. And it's really about the contribution to '26 to '31, certainly not to '25, but we're very excited about Blenrep coming through. And remember, that doesn't yet include first line, but we were pleased to start the study. Let's see.

But the data we have on overall survival is, we think, game changing as well as life changing. And so very excited to see what comes there and what could be added with ADCs and further progress we want to make.

Explicitly on HIV, the 6 monthly drugs are not yet included in this outlook. So that's also worth bearing in mind. So I think that's where people should focus. No one should doubt for 1 second, our commitment to our vaccine portfolio, really is the shift in the mix, which as Julie also said, secures the profitability of the business and the gross margin too. So with that, maybe, Luke, you can comment specifically on the commercial world in...

Luke Miels Executive

Yes. Thanks, Peter. Look, I mean, I think when I said -- came out with its surprising decision in June. I mean, we call a spade a spade, and we said it was going to be tough. And I think the evidence has indicated that, that was correct.

If you look at penetration rates in the U.S., the most recent data we have is in November, if we contrast that with December of 2023, and I mean what I said signal has clearly happened, people follow ACIP. If you look at penetration, the 75-plus population at the end of '23, it's about 17% that only increased up to 26% over 2024. And if you look at high-risk individuals in the 60 to 74 population, it went from 11% to 18%. And in the generally healthy population where ACIP was steering people away, it just increased from 9.4% to around 14%. So there is a shift here in terms of demand.

If we look at market research and profile, physicians still prefer Arexvy. But -- and I've said this a couple of times, for me, the key element here is to navigate what we think is going to be a transition from a three vaccine market to a two vaccine market. There is a huge amount of pressure -- competitive pressure in the market through the contracting cycle last year. I think we've navigated that quite well. Our focus remains on retail.

And what I would strongly stress is we need to compare apples with apples when we're talking market shares. So you need to adjust the market shares from internal volumes where we don't have the label. So if you do that, the end of 2024, we had about a 58% market share. So about 4.1 doses out of 7 million were with Arexvy. I think we're happy with that.

The key thing is to preserve value and position ourselves for the future. When we do think ACIP ultimately will move to expand this population. Based on the evidence, there will be a revax at some point, and we want to be positioned to compete with Pfizer very actively at that point.

Emma Walmsley Executive

And David, I think you want to add something on 6 monthly.

David Redfern Executive

Just on 6 monthly, Peter. I mean, as Emma said, it's not in our forecast, but I certainly agree with you that it could be a potential upside. This year will actually be an important year for 6 monthly. We will have proof of concept data on 184 and also the two options that we could put with either 184 or one of the other entities. So N6LS the EMBRACE study at 6 months, I think we'll have a CROI and also our capsid.

So the aim is to look at that data this year and then make a regimen selection of treatment and also choose our INSTIs for PrEP next year and potentially run -- start running the pivotal studies in 2027. So as we go into next year in '27, that's probably the time when we think about formalizing the forecasts.

Emma Walmsley Executive

And let's remember, it was only 4 years ago that we said we were expecting more than GBP

33 billion in 2031. Today, it's more than GBP 40 million. And you can see we're already close to that number in the near term. So yes, we are confident in our prospects. And yes, we know we've always got more to do.

Next question, please.

Operator Operator

Great. Let's go back to Steve Scala from TD Cowen and Steve, see if you can ask a question now.

Steve Scala Analyst

That was my mistake. I have two questions. For Nucala, is the exacerbation data competitive with Dupixent and have you shown an FEV benefit I mean, if not, your statements that you will lead in COPD might seem less secure. And secondly, you noted that GSK expects changes to U.S. vaccine policy.

This contrasts with what another major vaccine company said just last week when they reported that company expects no changes. So in practical on the ground everyday terms, what exactly do you expect to happen and to which vaccines? Or is this more of kind of a big concern?

Emma Walmsley Executive

Well, thanks, Steve. I'll come to Tony in a second on Nucala. The only point I would make is our ambition in COPD is across a portfolio of pipeline that Tony did share in December. So as well as Nucala, I'm sure he wants to comment on that. Nucala is just the first foray into biologics for us there.

And then in terms of changes to U.S., I think our point was we noted a significant speculation and let's face it. There's been a lot of it over the last few months around what kind of changes there might be to U.S. vaccine policy. And that is definitely one of the contributors to our view around the short-term pressures on the environment in the U.S. We also, as Luke reemphasize are still living with the decisions that were made by ACIP last year.

And the key assumption is from us in that context is that there will be no further indications or cohort expansion assumed on RSV this year, although we do, over time, expect them to be added, as Luke said, revax as well. I think the only point I would add without wishing to predict exactly what's going to happen is it was good to hear through the nomination process RFK reiterate his recognition of the value of vaccines. His own children have been vaccinated and also, obviously, over the weekend, to hear that in the discussions with Senator Cassidy, the CDC vaccine guidance is -- and the ACIP should remain unchanged. So let's see how this plays out, although we all know a lot more through 2025 and look forward to some of the speculation being settled here. Tony, do you want to...

Tony Wood Executive

Yes, let me start with Steve. The first thing I'd say is that we're looking forward to being able to share that the total Nucala data set with you soon. I'm obviously not going to get into the

details of that ahead of publication. But perhaps I might just stress a few aspects of this in particular in the context of exacerbations and the patient population. So if approved, Nucala is going to be the first monthly biologic proven to reduce exacerbations across the full spectrum of COPD disease.

And in particular, that includes individuals with emphysema who are the most difficult to treat. You'll recall from the data that we've previously published around the two prior Phase III studies across that population, an exacerbation reduction risk in the order around about 20% is typical in the broader population.

I'd also stress that we went to great lengths to ensure that we removed comorbid asthma patients from that study as well. And so I don't think it's difficult to compare side by side. However, we have a broader population, about 1/3 of the COPD population of emphysema. And I'd like to ask just to comment on that. But one final thing, again, if you look back in our data similar populations and we've published similar sort of headline efficacy on exacerbations, but it's important not to compare across headline data because it's a very different patient characteristics from the two studies.

Luke Miels Executive

Yes. Thanks, Steve. I mean Tony and I spent a lot of time talking about this. I think you just need to look at it practically on the ground. Tony mentioned about 1/3 of those patients have emphysema alone, about 1/3 of them have bronchitis, but also 1/3 of them have mixed and can be difficult to separate those.

So just practically, also, when you look at the Dupixent population, they were not sick. They have a GOLD 2 to 3, so moderate to severe, whereas we were 2 to 4, which included very severe. And I think if you look at what the GOLD report, which just came out last year, said it's pretty much positioning Dupixent in that bronchitis subset. So again, I don't want to preempt our data, but I think we have a broader argument here.

And also the important thing is to focus on hospitalizations because when people go into a hospital, obviously, many of them don't come out, and it sits off a cascade here. So in summary, we've got efficacy in tougher to treat patients, a broader population. And yes, let's see what the publication and the reception from the community says, but we intend to compete. There was a request for Dupixent for more competition, and we intend to provide it.

Emma Walmsley Executive

[Indiscernible] is the opportunity to grow biologics on the back of, by the way, are fantastic Trelegy business in COPD. And I am really excited to see what long-acting drugs are going to bring here. So good to see that we're going into COPD study for decade. We've also got the ILs and TSLP as well that Tony laid out. So I think this is the beginning of some exciting prospects and biologics that will get much stronger through the end of the decade, too, in a disease that is the third leading cause of death.

And so when you're talking about scale opportunities to address health, and I feel that we really know what we're talking about, this is a good one.

Operator Operator

Question. Next question is from Rajan Sharma from Goldman Sachs. Rajan, you're up.

Rajan Sharma Analyst

Just first one was on HIV. Could you just discuss the dynamics driving that positive impact from channel mix? Is that implying that there's a low proportion of Medicaid patients? And do you expect that to continue into '25 and '26. And then the second question is just on the 2031 guidance update.

So you've taken up guidance by GBP 2 billion in revenue, which includes Blenrep, which you've previously talked there is a GBP 3 billion peak sales opportunity. So just to be clear, should we read that as kind of a GBP 1 billion reduction in the guidance, excluding Blenrep or are you not expecting Blenrep to reach its peak until after that. And then just related -- there's obviously quite a bit of a difference between where consensus is right now. Is there anything particularly that you'd call out as where that delta is? .

Emma Walmsley Executive

Yes. I mean, Julie, you might want to comment in a minute on consensus as much as you wish to, and I'll come to David on HIV. But first of all, to be clear, the outlook for '31 is a more than GBP 40 billion. And we're pleased to have moved that up, as I've said, which is a combination of rolling forward the mix shift in '26, progress in our Phase III results and across the portfolio and the inclusion of the Blenrep second line launch as well. There is no change to our ambition for Blenrep to be more than GBP 3 billion peak year sales.

There was no time put on that and we're looking forward to the contribution of the five approvals that we flagged and more to come, really contributing to that '26 to '31 outlook. So David, do you want to comment on the HIV?

David Redfern Executive

Right. I think the main channel mix evolution we expect this year is just the ongoing rise of 340B, which is somewhat of a headwind, but not huge. Other than that, I think it's going to be more of the same in the Medicaid and the related programs like Ryan White, ADAP and so forth are about 40% of the U.S. HIV book of business. Medicare is about 20%, but is steadily increasing over time.

Obviously, as patients get older, and the rest is private insurance. So very much apart from 340B, I think pretty much the same trends continuing.

Emma Walmsley Executive

Thanks. So Julia.

Julie Brown Executive

So in terms of the difference with consensus in terms of our outlook, which is more than GBP 40 billion, the two main therapeutic areas where we've got a difference, our oncology and respiratory immunology and inflammation. And within the oncology category, the two biggest

ones are Blenrep. And obviously, people are probably waiting for the launch and then also Jemperli. So we've got life cycle indication. And you've seen the track record we've got on Jemperli, already with some important readouts coming up.

So those are two big differences. And then within the respiratory immunology and inflammation area, we've got camlipixant, where obviously people are waiting for the readout that's coming in about a year. And then also depemokimab, interestingly, even though we've now got successful filing. Clearly, we've got the approval expected towards the end of the year and the launch at the beginning of '26. So those are the main areas of difference, which we have got with consensus.

Emma Walmsley Executive

Let's remember, I think it's 72% of reductions in exacerbations that cause hospitalization on depe. So even if that's really a '26 launch totally with an approval at the end of this year, just considering the burden of disease, cost of hospitalization, the enthusiasm and [Louis] presented this research before from HCPs as well as patients for this that's definitely one to watch.

Operator Operator

Next question will be from Justin Smith at Bernstein. Justin?

Justin Steven Smith Analyst

Yes. Many. It's just one on Blenrep. I'm sorry if this is a slightly ignorant question, but with regards to that DREAMM-10 Phase III first line, the MRD endpoint. Just could you share a few thoughts how that endpoint resonates with payers and community docs, particularly those outside the U.S.?

Unknown Executive Executive

Let me just start with the dynamics and data plan associated with MRD and remind you of what we've already seen with molecular measures in DREAMM-7 and DREAMM-8 and then Luke perhaps I can hand over to you in terms of the resonance with key docs. So we were expecting. And again, a reminder that an ODAC approval or the use of MRD as an end point was only just last year or a recommendation of the use of MRD's endpoint. We started the studies Emma mentioned in December, we're expecting the first readout on MRD data in '27. What needs to occur over the intervening period and others will be driving this based on their own first-line studies is a relationship between an understanding of MRD and a more established regulatory endpoint like PFS.

What we know from our own analysis in DREAMM-7, DREAMM-8 and indeed, other first-line service for Blenrep is when we look at the characteristic on details of MRD readouts. And we see a similarly improved outcome for Blenrep relative to competitive assets. But Luke, you might want to comment on?

Luke Miels Executive

Yes. I mean, thanks, Justin. And just to build on Tony's point, I mean the market research we

get is exactly what the FDA is signaling, which is MRD is a practical response to very long durations and clinical trial feasibility in first line. What it is not is a replacement for survival in second line. And I think that's absolutely critical when you see that.

So -- and as we've covered earlier, we've got very strong data in second line and look forward to talking more about it over the year.

Operator Operator

Next question will be from Graham Parry at Bank of America.

Graham Parry Analyst

So first question is just on the guide mix for 2025. So relative to consensus, it looks like the guide is a little bit worse than consensus is looking on vaccines, but Gen Med is better and stable. I think most were looking for a decline there. So could you give us some little bit more color behind the outlook on Gen Med, especially because I think there was some rebate adjustment benefits to Trelegy in 2Q last year. So you're actually looking for underlying growth.

So what gives the confidence in that holding flat in the year and maybe the durability of that beyond 2025. And then secondly, on the buyback and free cash flow allocation, just perhaps give us a little bit of a sense of where you see free cash flow in 2025. If you're generating around GBP 3 billion in '24, you're moving to a GBP 2 billion share buyback and you -- but you highlighted low leverage. Are you now assuming you're going to increase leverage through the year as you see opportunistic -- to fund opportunistic BDL to make sure you're still funding the pipeline?

Emma Walmsley Executive

Well, two brief questions. But Julie, so over to you. .

Graham Parry Analyst

Thanks, Graham. So in terms of the RAR adjustment we had last year in the second quarter, it was largely, there was -- there's a high level, obviously, Trelegy was performing extremely well, and that attracts high levels of RAR. We had a true-up in the second quarter simply because when the claims were coming in, they were at a lower level than expected when the people were moving into the catastrophic coverage quicker, and that was causing that. Obviously, we don't know, but it was a benefit in the second quarter of last year. In terms of the leverage point, obviously, we've ended the year really well.

We've got leverage of 1.2x net debt to EBITDA. We'd expect to run the buyback, as we've mentioned over a period of within 18 months. Obviously, the weighting will be more towards 2025. So the leverage will move up during the course of the year. In terms of cash flow expectations, the '25, obviously, slightly below 2024.

We've got the Zantac settlement going through, which is expected in the second quarter. And then we will have an upside from obviously, operating profit growth RAR likely and trade payables.

Emma Walmsley Executive

Okay. Great. Next question, please. That's the last question?

Operator Operator

Yes. So let's go with one final question from James Gordon. James?

James Gordon Analyst

Two quick ones, please. One was just capital allocation building on one of the earlier questions. So where is the ceiling in terms of how levered the company would now be? I think you'll now be about 1.6x, could you go much above that and so you could still do multibillion pipeline deals? Or is that optionality off the table really?

That's the first question. And the second question is just camlipixant is mentioned. So I think we're going to get one of the Phase III end of this year and one early next year. But Merck [indiscernible], which is also P2X3, that had maybe similar efficacy to you in Phase II and obviously didn't come to market. So what is the latest thinking and what you actually need to show in camlipixant.

And how confident are you because this is going to be a blockbuster product in GSK.

Emma Walmsley Executive

Thanks. Well, I'll come to Tony to answer on that and the two studies that we've got coming. And Luke, you might want to add also a reminder on why we wanted to do this deal and what the patient opportunity is. In terms of capital allocation and business development, I'm just going to repeat what we've said, which is our #1 priority is to invest in growth. We do want to do more BD.

I'm really pleased with the discipline that has gone into the kind of business development that we've been doing, the bolt-ons in our core areas, some with -- that might be a risk, but very high return and really nice tuck-ins, including the IDRx one that we just announced. You should expect, James, the kind of BD we've been doing at the kind of scale and pace and with the focus and with the discipline that we've been doing. Obviously, we want to underpin all of that capital allocation with a strong balance sheet. And Julie, I don't know if there's a sense as what you want to say on leverage, but...

Julie Brown Executive

Now I think in terms of the ceiling, you questioned about the ceiling. Obviously, we want to retain the strong investment-grade rating. Clearly, rating agency is getting a period of leeway with regard to that. So we're not going to set a number because it's not a scientific number, but we're basically very comfortable with where the balance sheet is. As Emma mentioned, very clear priorities about capital allocation.

They haven't changed. It's just the robustness of the balance sheet that allows us to do the buyback complemented with what we're already doing in BD.

Emma Walmsley Executive

And all supported by the strong momentum in the delivery of the business, which we're running to maintain. So -- camlipixant...

Tony Wood Executive

And just quickly then, James, I think it's really important when you look at this area in P2X3, not just to think about efficacy, but in particular to think about therapeutic index. If you remember, camlipixant has a far improved therapeutic index, particularly with regards to taste disturbance. We have less than 6.5% adverse events in our study so far, compare that was Gefapixant, which had a nearly 70% taste disturbance. So it makes it hard to run a study when you're unblinding your treatment group. I think we have just to keep short, far superior asset on a clinical trial program, which has been designed to take account of the aspects of frequency of cough.

And as I mentioned, we will not be unblinded functionally by the taste disturbance in the way Gefapixant was.

Luke Miels Executive

Yes. I mean just to build on Tony's point, I mean, the smooth Phase IIb, we saw around 34% cost reduction. I think Tony's team is doing an excellent job in terms of execution of that study. Merck's molecule was basically a product, right? Validated the target, but had flaws in its selectivity and there were some challenges in study design around count.

These have all been incorporated into our program. When we talk to pulmonologist, they still express high enthusiasm. The numbers are quite big. If we model out to 2030, we expect around just under 3 million patients in the U.S. who have had chronic cough for more than a year, and actually over that number in Europe.

So we're talking large numbers of patients sitting in primary care and also pulmonologist, respiratory physicians' offices and there are limited options for those people at this point.

Emma Walmsley Executive

They're really high dissatisfaction with current standard of care options. So thanks, everybody. Again, after a strong '24, we really are looking forward to another year of profitable growth and pipeline progress, and we're really pleased to be upgrading together our 2031 outlook again, with prospects of 50% of our business by then more than 50% being in specialty medicines. And this continued performance and a stronger balance sheet are really underpinning our plans to continue to increase investment in the 14 key assets that we're focused on in the pipeline, in BD and in the successful launches ahead, and of course, staying focused on improving our direct returns to shareholders. Thanks to everyone.

We look forward to catching up with you in coming days.