Q3 2021 Earnings Call

Company Participants

- Anat Ashkenazi, Senior Vice President and Chief Financial Officer
- Anne E. White, Senior Vice President and President, Lilly Neuroscience
- Daniel M. Skovronsky, Senior Vice President and Chief Scientific and Medical Officer
- David A. Ricks, Chairman and Chief Executive Officer
- Jacob Van Naarden, Senior Vice President, CEO of Loxo Oncology at Lilly and President, Lilly Oncology
- Kevin Hern, Investor Relations
- Michael B. Mason, Senior Vice President and President, Lilly Diabetes
- Patrik Jonsson, Senior Vice President President, Lilly Immunology President, Lilly USA and Chief Customer Officer

Other Participants

- Aaron Gal
- Andrew Baum
- Carter Lewis Gould
- Christopher Schott
- Geoffrey Meacham
- Kerry Ann Holford
- Louise Chen
- Matthew Kelsey Harrison
- Seamus Fernandez
- Stephen Michael Scala
- Timothy Anderson
- Umer Raffat
- Vamil Kishore Divan

Presentation

Operator

Ladies and gentlemen, thank you for standing by, and welcome to the Lilly's Quarter 3 2021 Earnings Call. At this time, all participants are in a listen-only mode. Later we will conduct a question-and-answer session and instructions will be given at that time. (Operator Instructions) As a reminder, today's conference is being recorded.

I would now like to turn the conference over to your host, Vice President of Investor Relations, Kevin Hern. Please go ahead.

Kevin Hern {BIO 20557573 <GO>}

Good morning. Thank you for joining us for Eli Lilly and Company's Q3 2021 earnings call. I'm Kevin Hern, VP of Investor Relations. Joining me on today's call are Dave Ricks, Lilly's Chairman and CEO; Anat Ashkenazi, Chief Financial Officer; Dr.Dan Skovronsky, Chief Scientific and Medical Officer; Anne White, President of Lilly Neuroscience; Jake Van Naarden, CEO of Loxo Oncology at Lilly and President of Lilly Oncology; Patrik Jonsson, President of Lilly Immunology and Lilly USA; and Mike Mason, President of Lilly Diabetes. We're also joined by Lauren Zierke, Kento Ueha and Sara Smith of the Investor Relations team.

During this conference call, we anticipate making projections and forward-looking statements based on our current expectations. Our actual results could differ materially due to a number of factors including those listed on slide 3. Additional information concerning factors that could cause actual results to differ materially is contained in our latest Forms 10-K and subsequent Forms 10-Q and 8-K filed with the Securities and Exchange Commission. The information we provide about our products and pipeline is for the benefit of the investment community. It is not intended to be promotional and is not sufficient for prescribing decisions. As we transition to our prepared remarks, a reminder that our commentary will focus on non-GAAP financial measures.

Now, I'll turn the call over to Dave for a summary of our third quarter results.

David A. Ricks {BIO 16504838 <GO>}

Thanks, Kevin. Once again, Lilly had a very strong quarter, growing our newest medicines around the world and continuing to advance significant potential new medicines in the late-stage development, while also building long-term opportunities through early-stage investments in technology and progress in early-stage programs. Q3 2021 was also a period where the resilience of our company, our people and collaborators were tested by the pandemic. And again, they rose to the challenge. I want to personally recognize and thank my Lilly teammates for delivering such a strong overall performance, innovating to maintain pipeline velocity, running our plans to meet the rapidly growing demand of medicines and continuing to serve our customers whether it be in person or online.

Turning to our strategic deliverables on Slide 4, Q3 revenue grew 18% compared to Q3 2020, or 17% in constant currency. This performance was driven entirely by volume. Volume growth was 17 percentage points. When excluding COVID-19 therapies, which includes revenue from COVID-19 antibodies and sales of Olumiant for the treatment of COVID-19, revenue grew an estimated 11% for the quarter and year to date. Revenue attributable to our newer medicines grew over 35% and now represents nearly 60% of our core business this quarter, an important indicator for our long-term growth potential.

Our non-GAAP gross margin was 79% in Q3, or 79.3% excluding for the impact of foreign exchange on international inventories sold. Excluding this FX impact, our gross margin

decreased by approximately 60 basis points compared to last year. Our non-GAAP operating margin was 30.5%, representing an improvement of over 400 basis points compared to Q3 of last year, and over 100 basis points of sequential improvement from Q2 of this year.

We had a number of significant pipeline milestones since our last earnings call in August, including the FDA approvals for Verzenio in certain people with high risk early breast cancer and for Jardiance in collaboration with Boehringer Ingelheim in heart failure with reduced ejection fraction. Regulatory submissions for tirzepatide for type 2 diabetes in the U.S., to which we applied a priority review voucher, as well as the EU, and Jardiance in heart failure with preserved ejection fraction.

We initiated a rolling submission in the U.S. for donanemab in early Alzheimer's disease and have positive Phase 3 readouts from lebrikizumab in atopic dermatitis. We also continue to augment our pipeline with business development opportunities, as we continue to leverage external innovation to build our discovery capabilities with a focus on new modalities at Lilly.

In Q3, we announced a research collaboration and licensing agreement with Lycia Therapeutics to utilize their proprietary protein degradation technology. Finally, on financials, we distributed nearly $800 million to shareholders via the dividend this quarter.

Moving to Slide 5 and Slide 6, you'll see a list of key events since our Q2 earnings call, including issuing the company's first sustainability bond with proceeds allocated toward environmental projects, including pollution prevention, energy efficiency, and renewable energy, as well as social projects to increase access to essential services and socio-economic advancement and empowerment.

We announced a series of leadership and organizational changes this quarter. Recent positive data readouts this year led us to the natural decision to increase our focus on immunology and neuroscience, and to unify the Loxo Oncology and Lilly Oncology organizations. We believe these changes enhance our ability to execute on a broad range of exciting commercial and pipeline opportunities.

I'd like to welcome Jake Van Naarden to Lilly's Executive Committee and look forward to Anne, Patrik and Jake continuing their leadership in their new roles. They'll be focused on increasing our competitiveness in their therapeutic areas and growing our existing medicines while also launching our late-stage pipeline of new medicines, which could benefit patients across a diverse set of medical conditions. Similarly, I'm grateful for Ilya's continued leadership and look forward to him leading our growing International Business.

Finally, I'd like to thank Chito Zulueta for his impact on our company across more than three decades of his commitment to patients, to development of our industry-leading commercial capabilities and his relentless focus on execution and mentorship of countless Lilly leaders. Chito, thank you for your service to our company.

We have a deep leadership bench here at Lilly. They're smart, they're energetic and experienced, and I know they are as excited as I am to take Lilly to another level in the decade ahead.

Now, I'll turn the call over to Anat to review our Q3 results and provide an update on our financial guidance for 2021.

Anat Ashkenazi {BIO 19888043 <GO>}

Thanks, Dave. Slide 7 and 8 summarize financial performance in the third quarter and year-to-date. I'll focus my comments on non-GAAP performance. Revenue increased 18% this quarter compared to Q3 2020, or 11% excluding the items Dave mentioned earlier, representing strong momentum for core business despite the impact of Alimta's OUS patent expiry.

We continue to be pleased with the strong volume growth across key brands like Trulicity, Taltz, Verzenio and Jardiance as our key growth products made up nearly 60% of our core business during the quarter. Gross margin as a percent of revenue declined 10 basis points to 79% in Q3. Favorable product mix, excluding COVID-19 therapies and a favorable impact from foreign exchange rates on international inventory sold, were more than offset by lower gross margin on COVID-19 therapies.

Total operating expenses grew 8% this quarter compared to the same quarter last year. Marketing, selling and administrative expenses increased 1% while R&D expenses increased 17%, driven by significant investments in exciting late-stage pipeline opportunities, including donanemab, pirtobrutinib and tirzepatide. We also invested approximately $50 million in research and development for COVID-19 therapies in Q3, bringing our total COVID-19 R&D investment to approximately $350 million year-to-date.

Operating income increased 37% compared to Q3 2020. And operating income as a percent of revenue was 30.5% for the quarter, an increase of 420 basis points compared to the prior year, with sequential growth for second straight quarter. This increase was driven by revenue growth, outpeace and expense growth and we expect continued margin expansion in the fourth quarter. Other income and expense was expense of $7 million for this quarter compared to income of $10 million in Q3 2020.

Our effective tax rate was 14.3%, a decrease of 70 basis points compared with the same quarter last year. The lower effective tax rate in the third quarter of 2021 was driven by a mix of earnings in lower tax jurisdictions, partially offset by a decrease in net discrete tax benefit compared to the same period in 2020. At the bottom line, we delivered strong growth as earnings per share increased 38% in Q3 2021.

On Slide 9, we quantify the effect of price, rate and volume on revenue growth, and we're encouraged by the growth seen across the world. This quarter, U.S. revenue grew 26% compared to the third quarter of 2020. Adjusting for revenue from COVID-19 therapies, revenue grew 14% in the U.S. This increase, driven largely by volume was led by Trulicity, Taltz, Jardiance and Verzenio.

The higher net realized price in the U.S. this quarter was driven by a lower utilization in the 340B segment, unfavorable changes to estimates for rebates and discounts for Trulicity in the third quarter of 2020, and modest list price increases, partially offset by increased rebates to maintain broad patient access for our medicine. Our year-to-date U.S. net price decrease of 1% is in line with the low-to-mid single digit guidance we gave last December and our full-year outlook is consistent with those expectations. Our 340B Limited Distribution Program began September 2020, and so the fourth quarter of 2021 will be the first full quarter where its impact will also be included in the base period when calculating year-over-year price changes in the U.S. Given the increase in variability in payer mix, we continue to expect quarterly variability in reported U.S. net price changes across our business.

Moving to Europe, revenue grew 3% in constant currency. Excluding the impact of the first full quarter of loss of exclusivity for Alimta, revenue grew 16% in constant currency, driven primarily by volume growth for Trulicity, Taltz and Verzenio. We are pleased with the momentum of our business in Europe and expect continued growth, excluding Alimta.

In Japan, revenue decreased 6% in constant currency, driven primarily by the decline of post-patent products. Revenue in Japan continues to be negatively impacted by decreased demand for several products that have lost market exclusivity, now including Alimta, as well as by the COVID-19 pandemic. Importantly, our key growth products grew 12% in Q3 in Japan. We expect improved revenue growth in Japan moving forward based on the uptake of these newer products.

In China, revenue grew 30% in constant currency, primarily driven by continued uptake of Tyvyt and Trulicity. We're excited by the significant growth we're seeing in China with sales of new medicine continuing to drive growth there. Revenue in the rest of the world increased 16% in constant currency, driven primarily by our key growth products.

At the bottom of the slide is the price rate and volume effect on revenue for our September year-to-date results, which shows double-digit growth across all major geographies except Japan.

As shown on Slide 10, our key growth products continue to drive strong worldwide volume growth. These products drove 15 percentage point of growth this quarter and continue to drive our overall performance and outlook.

Slide 11 highlights the contributions of our key growth products. In total, these brands generated nearly $3.9 billion in revenue this quarter and made up 58% of our core business revenue. We're encouraged by the strength of our key growth products in Q3, collectively up over 35% compared to the same period in prior year. Trulicity, Verzenio and Jardiance all continued to outgrow their respective classes and we're pleased with Taltz growth driven by increased access.

On Slide 12, we provide an update on capital allocation. In the first nine months of 2021, we invested $7 billion to drive our future growth through a combination of R&D expenditures, business development outlays and capital investments. In addition, we

returned over $2.3 billion to shareholders in dividends and have repurchased $500 million in stock. We will continue to fund the growth of our key products and recent launches, invest in our pipeline, seek external innovation to augment our future growth prospects and return capital to shareholders.

Turning to our 2021 financial guidance on Slide 13, we're updating our GAAP and non-GAAP guidance. We're increasing the full-year revenue outlook by $200 million at the top end of the range and $400 million at the lower end of the range to reflect additional COVID-19 antibody revenue and the outlook for our core business. COVID-19 antibody revenue expectations are roughly $1.3 billion based on the existing U.S. government purchase agreement for additional doses of etesevimab in Q3 and Q4. The net impact of these changes is an updated revenue range of $27.2 billion to $27.6 billion, up from the previous range of $26.8 billion to $27.4 billion. Our outlook for GAAP and non-GAAP gross margin percent remains unchanged.

For research and development and SG&A, our guidance ranges remain unchanged. As we noted last quarter, investments in promising R&D opportunities and exciting potential launches are expected to push us to the top end of our guidance range for operating expenses.

Our reported and non-GAAP operating margin guidance is unchanged. Excluding the impact of COVID-19 antibodies, non-GAAP operating margin remains approximately 31%. Our non-GAAP ranges for other income and expense and our expected tax rate remains unchanged as well.

On a reported basis, other income and expense is now expected to be expense in the range of $250 million -- $250 million, reflecting the impact of the charges associated with a repurchase of debt and net mark-to-market losses on investments in equity securities in the third quarter of 2021. The 2021 effective tax rate is now expected to be approximately 11% on a reported basis, reflecting the tax impact of the charges associated with the repurchase of debt and acquired IPR&D, as well as unfavorable mark-to-market adjustments on investments in equity securities in the third quarter of 2021. Finally, the non-GAAP range for earnings per share has been raised to $7.95 to $8.05, while the GAAP EPS is expected to be in the range of $6.38 to $6.48.

At our Investors Day in December, we will share our initial 2022 guidance. Today, before I turn the call over to Dan for the R&D update, I'd like to provide a few reminders on the pushes and pulls across the P&L as we begin thinking about next year.

In Q3, we saw the initial impact of Alimta's OUS patent expiry in Europe and Japan. Next year, we will see its full-year impact as well as the U.S. patent expiry with limited launches from a single generic company in Q1 before the full launch of generic entrants starting in Q2.

As for revenue from COVID-19 therapies, we intend to reflect in guidance our expectations related to signed purchase agreements for COVID-19 antibodies. Currently, we expect minimal revenue from COVID-19 therapies in 2022, leading to more difficult year-over-year

comparisons. As we do this year, we will provide commentary on our financials, excluding the impact of revenue and certain expenses from COVID-19 therapies to enable a more helpful year-over-year comparison of the performance of our core business. Absent major U.S. drugs pricing reform, our 2022 and mid-term outlook continues to be mid-single digit net price erosion in the U.S. and globally if the impact of lower utilization of 340B segments moved into the base space period as we enter Q4 2021.

We continue to invest in our bright future as we advance promising R&D opportunities and scale up to support exciting potential launches from our late-stage pipeline. While these investments may pressure operating margin in the near term, they are critical to maximizing pipeline opportunities to help sustain top-tier revenue growth and operating margin expansion over the mid to long-term.

Now, I will turn over the call to Dan to provide an update on our pipeline.

Daniel M. Skovronsky {BIO 15349505 <GO>}

Thanks Anat. Like 2020 before it, 2021 continues to be a very productive year for R&D at Lilly. Before I get into the broader portfolio update, I'll highlight several updates from our late-stage pipeline. Starting with tirzepatide, we shared detailed results from tirzepatide's SURPASS-4 study at EASD this quarter. SURPASS-4 is the largest and longest SURPASS trial completed to-date, and we were encouraged by the continued hemoglobin A1C and weight control, which participants experienced even past the initial 52 week treatment period and continuing up to two years.

Looking at Slide 14, this shows the change from baseline in hemoglobin A1C over time during the study. A1C reduction plateaued by roughly 24 weeks and was maintained at 52 weeks, and thereafter to 104 weeks across all three tirzepatide doses. While in the insulin glargine comparator arm, A1C began to increase after 52 weeks. Durability of A1C control is a challenge for type 2 diabetes treatments. While the 104 week data isn't a definitive answer as to whether tirzepatide could potentially offer even longer term durable blood glucose control. These data certainly are encouraging.

Moving to Slide 15, as you can see, weight loss plateaued at approximately 52 weeks and was maintained thereafter such that at two years, weight difference at the highest dose was approximately 15% compared to insulin glargine. We've seen in previous incretin therapy trials conducted with GLP-1s, a further increased impact on weight reduction in participants with obesity without type 2 diabetes compared to studies in participants who do have type 2 diabetes such as this one. It will be interesting to see if this trend also extends to the dual agonism of tirzepatide, which has demonstrated weight reductions in type 2 diabetes trials beyond what has been shown by GLP-1's to-date. We clearly are excited about the weight loss potential here and we believe the data to-date bode well for upcoming readouts in obesity, starting with SURMOUNT-1, which reads-out next year. Tirzepatide represents a new class of medicines and we're focused on continuing our significant investment for patients with type 2 diabetes, obesity and related metabolic disorders, who may benefit from tirzepatide.

Moving to Slide 16, today we announced the U.S. submission tirzepatide in type 2 diabetes and that we used a priority review voucher with the intention of bringing this investigational treatment to patients as quickly as possible. We're delighted that the continued progress for this novel dual agonist incretin and hope to obtain approval in the U.S. by the middle of next year.

Moving to donanemab, we have several important updates for this program. First, in the U.S., we initiated a rolling BLA submission to the FDA for accelerated approval in early Alzheimer's disease. We intend to complete the submission in the next few months and expect regulatory action in the second half of 2022. We've also completed the original planned enrollment of 1500 participants for TRAILBLAZER-ALZ 2 and based on the pre-specified 18 month primary endpoint, expect to have top-line results by the middle of 2023. We've added a separate single arm addendum for safety exposures to TRAILBLAZER-ALZ 2, which has already enrolled more than 300 patients and is continuing to enroll rapidly. This addendum will provide us with additional safety data to support the rolling submission.

Moving to TRAILBLAZER-ALZ 3, this is a prevention study for cognitively unimpaired individuals who already have Alzheimer's brain pathology, but don't yet have clinical symptoms. We're excited to report that we have already initiated screening. This pioneering trial has multiple novel elements to reduce research subject burden, including the use of our phospho-tau217 blood assay currently in development to help detect Alzheimer's disease pathology in the patient's screening process, video call technology for assessing cognitive function in the subject's home and a large network of infusion centers that allow subjects to select the site most convenient to them in a decentralized clinical trial paradigm.

We also announced today our plans to conduct a head-to-head Phase 3 study, comparing donanemab to aducanumab to assess superiority of brain amyloid plaque clearance in early symptomatic Alzheimer's disease. The co-primary endpoints will evaluate complete amyloid plaque clearance as measured by florbetapir F-18 PET scan. And we'll assess superiority on brain amyloid plaque clearance in the total population, and also the intermediate tau sub-population. This study, TRAILBLAZER-ALZ 4 is expected to begin enrollment this year and we expect to share primary endpoint data in the second half of 2022.

We're encouraged with the progress we've made with donanemab and with its potential to positively impact patients with high unmet medical need. We have, of course, followed progress in the Alzheimer's disease landscape since our last call and are watching closely as CMS's National Coverage Determination process plays out. We're committed to facing the challenges of effectively communicating donanemab's clinical data and value proposition, and to ensuring that the diagnostic and patient management ecosystems are adequately well prepared. Given the current environment, we think it's reasonable to have modest expectations for the scale of patient impact for anti-amyloid therapies available under accelerated approval prior to the readout of their definitive Phase 3 data. Assuming potential accelerated approval for donanemab in the second half of 2022, our expected TRAILBLAZER-ALZ 2 Phase 3 readout by mid-2023 would follow quickly, meaning the window of accelerated approval without definitive Phase 3 data is likely to be brief.

Assuming positive Phase 3 results, we should be confident in the mid and long-term opportunity for donanemab if approved.

Moving on to Verzenio, in line with the expectations I outlined last quarter, we were pleased with Verzenio's recent FDA approval as the first and only CDK4/6 inhibitor in combination with endocrine therapy for adult patients with HR+, HER2-, node positive early breast cancer, who are at high risk of recurrence with the Ki-67 index of greater than equal to 20% as detected by an FDA approved test. This approval in the adjuvant setting represents the first new addition to endocrine therapy in adjuvant treatment of HR+, HER2- breast cancer in nearly two decades. We're delighted to bring this important new treatment option to patients.

Also, we recently shared updated data from the entire monarchE study at the ESMO Virtual Plenary meeting and co-published these data in Annals of Oncology. These data which reflect additional follow-ups since our last public presentation, highlight the robustness and the effect size we're seeing for Verzenio in the adjuvant setting. Notably, with a median follow-up of 27 months, we were pleased to see both IDFS and DRFS benefit extend beyond the two-year study treatment period. These data are not only important for patients, but also to help dispel concerns that the curves would come back together over time. We're clearly observing -- we clearly observed continued separation of the curves if not expanding separation. Since the adjuvant approval two weeks ago, there have been questions regarding why the FDA approval applied only to a subset of the study population.

As previously communicated, overall survival was a secondary outcome measure for the monarchE study, an important component of the FDA's review. While we do not typically publish immature overall survival data, we feel it's valuable to address these important questions about the difference between the enrolled study population and the approved indication. As a result, while the overall survival data remain immature, we do plan to publish the OS data from the additional follow-up analysis with cutoff of April 1, 2021, in a medical journal in the coming days. These data will show, what we observed thus far for overall survival trends in the ITT population compared to the approved population. We'll continue to follow patients in the ITT population for more mature overall survival data. If a positive OS trend emerges in the ITT population, we plan to work with regulators to expand our adjuvant indication.

Importantly, the collective results from Verzenio's clinical development program have demonstrated a differentiated CDK4/6 inhibitor profile and we look forward to continued investment in Verzenio for breast and prostate cancer, and are excited about the opportunity to serve more patients.

Slide 17 shows select pipeline opportunities as of October 22, and Slide 18 shows potential key events for the year. There have been several important developments since our last earnings call and I'll cover these by therapeutic area.

In oncology, in addition to the exciting news for Verzenio, we continue our investment in Pirtobrutinib's Phase 3 program with an additional study starting chronic lymphocytic

leukemia, including fixed duration Pirtobrutinib plus Venetoclax and Rituximab in relapsed or refractory patients. We plan to start the study in first-line treatment compared to bendamustine plus rituximab before year-end. We prioritize this first-line study rather than the head-to-head study evaluating superiority compared to brutinib, as we think this first-line study could provide a faster pathway to bring Pirtobrutinib to patients in the first-line setting. We expect the head-to-head brutinib CLL study to start in the first half of 2022. We look forward to sharing an updated data set from the Phase 1/2 BRUIN study at a medical meeting later this year. We plan to provide a regulatory update for Pirtobrutinib at our Investor Day in December.

Imlunestrant, our oral SERD, also moved into Phase 3 with the start of its monotherapy study compared to exemestane or fulvestrant.

Finally, we also publicly identified and presented pre-clinical characterization for two new agents at the Molecular Targets meeting this month. LOXO-783, which is a highly mutant selective allosteric PI3K alpha inhibitor and LOXO-435, which is a highly isoform selective FGFR3 inhibitor. We look forward to filing INDs for both programs in 2022 and subsequently moving them into the clinic.

In diabetes, in addition to the tirzepatide update, we obtained U.S. approval for Jardiance and HFrEF, presented detailed results from the EMPEROR-Preserved study at the European Society of Cardiology and submitted for HFpEF in the U.S. and Europe. We're excited about the opportunity Jardiance has to improve outcomes for patients across type 2 diabetes, heart failure and chronic kidney disease. We also started Phase 2 studies for our GLP-1 non-peptide agonist in collaboration with Chugai in type 2 diabetes and in obesity, and look forward to sharing some Phase 1 data from this molecule in December.

In Immunology, we were delighted to have multiple positive Phase 3 readouts for lebrikizumab in atopic dermatitis and look forward to the readout of the maintenance data from the ADvocate1 and 2 studies in the first half of next year, ahead of global submissions expected by the end of 2022. We're pleased with our progress in Immunology this year with positive Phase 3 readouts from mirikizumab and lebrikizumab and look forward to sharing more about our next generation of early phase Immunology assets in December.

In Neurodegeneration, our anti-tau antibody zagotenemab recently concluded its Phase 2 study in early symptomatic Alzheimer's. Zagotenemab failed to meet the primary endpoint and was unable to modulate tau spread in the brain. The placebo population progressed as expected. While this negative outcome was disappointing and we're discontinuing development for zagotenemab, we remain committed to tau as a high conviction target in Alzheimer's disease and plan to continue studying tau biology, including inhibition of tau aggregation with a small molecule OGA inhibitor currently in the clinic.

In the pain therapeutic area, in collaboration with Pfizer, we discontinued the global clinical development program for tanezumab, following receipt of a Complete Response Letter from the FDA for the tanezumab in osteoarthritis pain and a negative opinion adopted by the CHMP.

And finally, the FDA expanded the emergency use authorization for bamlanivimab and etesevimab; administered together to include post-exposure prophylaxis in certain individuals for the prevention of SARS-CoV-2 infection.

To recap, Q3 was another positive quarter for R&D at Lilly, continuing the positive momentum we've seen with a steady stream of significant pipeline advancements over the last couple of years, as we move closer towards our goal of delivering more first or best-in-class treatment options for patients in areas of unmet need.

Now, I'll turn the call back to Dave for some closing remarks.

David A. Ricks {BIO 16504838 <GO>}

Okay. Thanks, Dan. Before we go to Q&A, let me sum up the progress we've made during the quarter.

We have seen continued strength in our core business through the first nine months of the year with double-digit volume driven revenue growth, net of COVID-19 therapies and strong performance across key brands. We're pleased to see sequential and year-over-year operating margin expansion as well as strong non-GAAP earnings growth. We have made significant progress developing new medicines, and Q3 was another important quarter for our pipeline as we announced the submission of tirzepatide in type 2 diabetes. The initiation of a rolling submission for donanemab in the U.S. for early Alzheimer's disease, key lifecycle approvals, and submissions for Verzenio and Jardiance, and positive Phase 3 readouts for lebrikizumab. We returned nearly $800 million to shareholders through dividends in Q3, reflecting confidence in the ongoing strength of our business.

As we move toward the close of 2021, we are confident in our long-term growth prospects. While the past year has seen tremendous advances in our late-stage pipeline, at our Investor Day in December, we look forward to sharing information with you regarding the next generation of assets that we believe will enable us to sustain the flow of innovative medicines to patients and augment our future growth prospects.

Now, I'll turn the call over to Kevin to moderate the Q&A session.

Kevin Hern {BIO 20557573 <GO>}

Thanks, Dave. We'd like to take questions from as many callers as possible. So we ask that you limit your questions to two per caller. Luis, please provide the instructions for the Q&A session and then we're ready for the first caller.

Questions And Answers

Operator

(Question And Answer)

Thank you. (Operator Instructions) And our first question is from the line of Chris Schott. Please go ahead.

Q - Christopher Schott {BIO 6299911 <GO>}

Great. Thanks so much for the questions. I guess the first one for me is just on some of the 2022 comments. I know you're not giving formal guidance yet. But should we be thinking about margin expansion next year from the, I guess, roughly 30% or so margins that are implied in this year's guidance? I'm just trying to get my hands around how meaningful of a step up in OpEx we should be thinking about supporting these major new launches coming next year.

And the second one was just one related to BIIB's roll-out of ADUHELM. It's obviously been a challenging launch. Are there learnings here or just changes about how you're thinking about your go-to-market strategy for donanemab? And I know, Dan, you made some of those comments in the remarks. But should we be thinking about much in the way of revenue at all for donanemab? And, I guess, in that window between when it's approved and prior to TRAILBLAZER-2? I'm just trying to get a sense of, again, just as you look at what's happened there, has there been surprises or changes in your thinking on the market. Thanks so much.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Chris. We'll go to Anat for the first question on 2022 margin expansion and then to Anne on thoughts about the uptake and outlook for donanemab.

A - Anat Ashkenazi {BIO 19888043 <GO>}

Great. Thanks. So for 2022, we will provide further details and guidance in December. So not too far from now, and we'll provide additional clarity on how we view the year and what investments and pushes and pulls we have going into next year.

As you think about our margin expansion, the goals we've set out and we've communicated in terms of getting to mid to high-30s in terms of margin expansion, we still have a clear line of sight to get there and that's still our goal. They'll be -- but it's not a linear growth. So there will be years, there are going to be stronger years that we're going to be making specific targeted investments. And as you've seen us do this year with donanemab, when we have strong convictions in a pipeline asset or when we're preparing to launch very promising opportunities and products, we will invest behind them. So think about this as still growing to mid to high-30s, but not necessarily in a linear fashion, but in line with investments we would need to make.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Anat. Anne?

A - Anne E. White {BIO 20764375 <GO>}

Well, as Dan stated and as our competitor has shared, they've experienced, there clearly is work to do to ensure that the diagnostic and the patient ecosystems are prepared for

these medicines. And until there is definitive Phase 3 data, we do believe that we should really expect modest use of these medicines.

Now fortunately, as Dan said for donanemab, this confirmatory data comes quickly in mid-'23 for TRAILBLAZER-ALZ 42. And so, this will be the opportunity to really help patients on a more significant scale. Now some of the opportunities here, certainly pursuing accelerated approval is really important, both to provide early access, but also to let us begin addressing some of these infrastructure challenges ahead of the Phase 3 data. We need to build out the diagnostic ecosystem, particularly PET scans and blood tests. We need to make sure that there's adequate infusion capacity. And then very importantly, we need to ensure that there's reimbursement, so that the appropriate patients can have access to donanemab.

So these are going to be our areas of focus now through our Phase 3 window. We're confident in our ability to address these infrastructure challenges over time. And I would say by clearing plaque faster and deeper, we believe that as well as identifying the right patients, we've optimized the chances for showing compelling benefits in the Phase 3 which, as we said, is what was going to show significant uptake in the class. We continue to see the same opportunity for donanemab in the mid to long-term once these challenges are addressed and the confirmatory data is available.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Ann. Chris, thanks for your questions. Next caller, please.

Operator

The next caller is Geoff Meacham from Bank of America. Please go ahead.

Q - Geoffrey Meacham {BIO 21252662 <GO>}

Hey, guys. Good morning, and thanks for the question. I had two on Alzheimer's probably for Dan. For donanemab, would you expect completion of the rolling submission by the end of this year? And is there a regulatory threshold you need to hit in terms of the safety exposure? I'm just trying to think of the number of patients that you have to get exposed to? And then for zagotenemab, what are the next steps here? Is it moving to another anti-tau asset altogether? Or do you want to optimize monotherapy zagotenemab or maybe even move forward in combination with donanemab? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Geoff. Dan?

A - Daniel M. Skovronsky {BIO 15349505 <GO>}

Great. Thanks, Geoff, for two good questions. The first is just on the timing of the completion of the donanemab rolling submission. I think you can assume, we chose our words carefully here in the call prepared remarks on the timing. You're sort of driving out like what's the regulatory hurdle with respect to safety exposures. You're right, that's the key gating factor on timing. You've heard we've enrolled a lot of patients in the clinical

trials, including patients in a safety addendum. So, we're extremely confident we'll reach that safety exposure hurdle.

I guess, looking forward, there's probably two risks or question marks. One is just around the timing of exactly when do databases get locked and data get cleaned and submitted to the FDA. So that's why we're a little vague on timing here. I think the second one, of course that we don't know and won't know until all that data is in is what does the safety data actually show. And so the assumption here, of course, is that they continue to be consistent with what we've seen in Phase 2. So if those things work out, then 0I think that will be the opportunity to talk a little more specifically about the data.

With respect to zagotenemab, look, I think we have here a very potent anti-tau antibody designed against what we believe is an important species of aggregated tau delivered at relatively high doses for any monoclonal antibody, and we were unable to slow the spread of tau progression in the brain. So at present, I don't see a path forward for this antibody, and I would be reluctant to invest in really any anti-tau antibody given what we've seen here. Tau is still a great target. It's just hard to hit it with a monoclonal antibody, I think, given that most of the tau that we care about is inside of cells.

Q - Geoffrey Meacham {BIO 21252662 <GO>}

Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dan. Geoff, thanks for your question. Next caller please.

Operator

And the next caller is Louise Chen from Cantor. Please go ahead.

Q - Louise Chen {BIO 6990156 <GO>}

Hi. Thanks for taking my questions here. So my first question is, how are you preparing for the launch of donanemab in tirzepatide next year? And how should we think about the costs associated with that launch? And then second question I had for you is, do you think it's the national coverage determination or the price of ADUHELM that is keeping doctors on the sidelines? Thanks.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks. We'll go to Anat for the question on just launch prep and the overall costs for both tirzepatide and donanemab, how we think about that going into next year. And then we'll go to Anne for the question around the NCD and ADUHELM.

A - Anat Ashkenazi {BIO 19888043 <GO>}

Sure. So as we're preparing to launch both these medicines, obviously, one is in an area where we have significant commercial footprint, manufacturing scale-up capabilities. And the other one is an area we're currently building. So we're investing in advancing both of these efforts forward, preparing for a potential launch of tirzepatide mid-next year and

then a regulatory decision on donanemab at the second half of next year. Those will be factored into the guidance that we will provide on December 15 as we go into next year. But rest assured, we're building the commercial footprint that we needed to launch these effectively and leveraging the existing footprint we have as well.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Anat. Anne?

A - Anne E. White {BIO 20764375 <GO>}

Well, it's a good question that you've asked, and I do think there's a number of things that are a challenge here. I think as you look at donanemab, what's incredibly important is that we had a positive Phase 2 study that clearly met its primary endpoint showing cognitive benefits for donanemab. As well, we were able to share that we had limited duration dosing to plaque clearance. And so, we believe that this is going to be important for the decisions that physicians and payers make.

So I believe that the donanemab data is incredibly strong. And then as I said, following quickly the Phase 3 confirmatory data, which I think is important. And all of this published in the New England Journal of Medicine. So as we're talking to thought leaders and physicians, I do believe that they see the strength of the data that we brought forward into donanemab. And I think that's been a challenge that they've had with some of the competitive space. So I do think that data is one thing on their minds.

I think as well the NCD is playing a role. Obviously, that will be resolved before we launch. And we'll be ready for any of the potential outcomes there, and have been working closely with them along the way to make sure that they understand the donanemab data, particularly the rapid clearing of plaques as well as the limited duration dosing that offers, we think, benefit to them as well.

So it's been a good conversation with them so far. We really look forward to seeing what they have to say, CMS has to say in January and then launching with this strong data set, as Dan said, in the second half of next year.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Anne. Louise, thanks for your question. Next caller please.

Operator

The next caller is Tim Anderson from Wolfe Research. Please go ahead.

Q - Timothy Anderson {BIO 3271630 <GO>}

Hi. Thank you. I have a couple of questions on the pending NCD by CMS. So two questions. First, it's commonly said that this upcoming decision will pertain to the whole ABA class. I've struggled to see how that can realistically be the case, because that decision will be made on only one company's mixed Phase 3 data. And there's still other really important informative Phase 3 data sets that are on the come. So wouldn't the NCD,

whatever it is initially, potentially be revised later as CMS has more information from these additional trials?

And then second, if this is indeed a decision that pertains to the whole class, then presumably Lilly has a view on what will happen in January. So do you expect CMS will say that ADUHELM and the class more broadly should be covered in a way that will be commercially meaningful? One can envision that there could be lots of restrictions that might, in fact, limit their commercial market opportunities.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Tim. We'll go to Anne for those questions on the NCD process.

A - Anne E. White {BIO 20764375 <GO>}

Well, thanks. Good questions on the process with the NCD. So CMS has been clear that the NCD as they're running the process is to cover the class. Now as I said, we are actively participating in the process, including we provided oral comments in July and additional written comments in August. And we, and I'm sure others as well, have been meeting with CMS throughout the process to share our specific data and ensure that the differences in these medicines are understood. And so, we've asked them really to evaluate each drug based on their own data.

And this is, I think, as I said, particularly important considering that there are some differences between these. We share the data later in the year subsequent to the original readout that the degree of donanemab plaque clearance relates to clinical benefit, which I know is very important to CMS in this decision as well as the limited duration dosing. So, we really look forward to seeing what they have to say in January and what that readout will look like. We do acknowledge there's a lot of skepticism in the national discussion.

And so, we do really hope and will continue to influence that we think each drug should be evaluated by CMS by payers and prescribers on their own data. It is possible that NCD -- the NCD will narrow for the patients most likely to benefit. That's a possibility out of this. But that's really aligned with the goals that we've had in our clinical trial designs, which has long been to use the diagnostic tools to make sure that the right patients are getting treatment. So we'll look forward to the readout in January. We'll continue to stay very engaged in this. And yes, I believe as additional data comes out, our data and others in the class that this will continue to influence the process.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Anne. Tim, thanks for your questions. Next caller please.

Operator

The next question comes from Andrew Baum from Citi. Please go ahead.

Q - Andrew Baum {BIO 22142111 <GO>}

Noise coming out of Washington suggests that Peter's bill [ph], some of the components of that are gaining traction and some of the more worrying components of price negotiations seem to be more and more limited. I just wonder if you could share any thoughts on what you think just take the Peter's proposal on out-of-pocket caps could mean to Lilly and the pharma in terms of increased volume without catastrophic coverage changes? And then second, could you comment on whether you're seeing neutralization of donanemab by the antibody drug antibodies that you see with prolonged usage? And is this one of the factors which is contributing to the finite treatment duration? Or is neutralization simply not a concern here?

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Andrew. We'll go to Dave for the first question and Dan for the second.

A - David A. Ricks {BIO 16504838 <GO>}

Yes. Thanks, Andrew, for the question. Obviously, there's a lot of talking and discussing going on in Washington about how to make medicines more affordable. I think we've been pretty consistent in our view that both as Lilly, and I can -- I think I can speak for the industry here, we are for progress. We are not for the status quo. And the centerpiece of almost every part of legislation being discussed, which is, I think, good news for seniors is some reform to the Part D benefit. That is certainly highlighted in representative Peter's bill. It's in HR19. It was in the grassy-widen effort. It's, I'm sure, in the Senate Finance effort now. And I think that's good news.

The contours of that are all kind of different. But the general idea is that industry would pay additional costs into the system that that would reduce monthly out-of-pocket cost, both below and above the catastrophic phase. Catastrophic costs as well as eliminate the donut hole. I think we're basically for all those things, and we think that's a good set of initiatives.

Where the debate sort of kicks in is around how to pay for that or whether paid for from the industry should go to other healthcare priorities. And of course, we have clear positions on that. One piece of Peter's bill we don't like is the retroactive CPI cap. I think that's punitive and unfair. It also is disproportionate on some types of medicines versus others. So, I think the industry is aligned, we don't care for that. Although in general, the idea of a CPI regulator on forward price increases is something people have gotten used to talking about.

And then the thing we do put our foot down and firmly opposed and why we're so against HR3 and other efforts, is taking money out of the pharmaceutical industry for other priorities. Isn't drug pricing a big enough problem? Why don't we take the money out of the pharmaceutical industry and give it to patients who want to buy our medicines. And that's a position we've had for a long time. I think it's been a busy week into next week probably negotiating out this package. But we're hopeful that some of these messages are resonating, and we could land with a Part D reform and modest impact on the industry, so we can keep innovating for the future.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dave. Dan?

A - Daniel M. Skovronsky {BIO 15349505 <GO>}

Thanks, Andrew, for the question on antidrug antibodies or ADAs. We do see ADAs with donanemab. They arise pretty early in treatment. There is no connection though with ADAs and our decision on fixed duration dosing. The reason for that is because the doses that we're using are so much higher than the level of antidrug antibodies that we don't see an effect in our clinical trials at these doses of the ADAs on PK or importantly on PD, which is the plaque clearance effect of donanemab. So no connection there.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dan. Andrew, thanks for your question. Next caller please.

Operator

The next caller is Seamus Fernandez from Guggenheim Securities. Please go ahead.

Q - Seamus Fernandez {BIO 7525186 <GO>}

Thanks for the question. So maybe first on the performance of Verzenio in the quarter, and then your conviction that this market can accelerate moving forward now with the Ki-67 approval. We're hearing good things from physicians, but it just doesn't seem to be reflected in the opportunity that I think we all see ahead for Verzenio. And then as a separate question, I'm sure Mike Mason is tracking the opportunity in obesity very closely. Just wondering what feedback is on the types of patients that are going on to Wegovy at this point? And how Lilly is thinking about the opportunity in obesity given the attempted acceleration of the launch of tirzepatide with the PRB. And obviously, that's in diabetes, but just wondering when we might see a full launch in obesity given all the trials. Thanks.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Seamus. We'll go to Jake for the question on Verzenio and then Mike for the question on tirzepatide.

A - Jacob Van Naarden {BIO 18103115 <GO>}

Thanks, Seamus. So just starting with Verzenio's performance in the quarter, as you probably remember, we had some stocking that happened in the channel in the second quarter. And so, part of what happened this quarter is just a modest work down of that inventory. I think the fundamentals of where we stand in the metastatic setting continue to look really strong. I like where we are in terms of NBRx share hovering around 30% and hopefully we can continue to grow that. I think that we still haven't seen the entire class of CDK4/6 inhibitors return to pre-COVID levels of prescriptions. And so that's obviously an important lever for growth going forward. Probably levered to things like mammogram volumes and other types of preventative care measures that get patients diagnosed and into doctors' offices. But we continue to grow our share of NBRx within the market.

Turning to adjuvant. Obviously, we're very excited about launching this medicine for men and women with early breast cancer, specifically Ki-67 high patients. It's a real opportunity.

As I think you've probably heard us say before, it's about 8,000 to 10,000 patients. It's obviously a smaller opportunity than the entire study population that we enrolled in monarchE. And as you know, we'll be looking, again, next year will be the next analysis of survival to potentially expand to that broader population should OS trend in the direction that we and FDA want to see to do that. But we have a great opportunity ahead of us. I think certainly, it's growth from where we stand today. It's a brand-new indication of real size in terms of both patient numbers and duration.

In many ways, realizing that is also linked to the prior comments I made about patients returning to the doctor for preventative care to get diagnosed at levels hopefully that return to pre-COVID and we don't need that, obviously, to make headway going into next year. But I think for the long term, it's important for patients to make sure they get into the physician's office to get diagnosed.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Jake. Mike?

A - Michael B. Mason {BIO 18347681 <GO>}

Hi, Seamus. First of all, you're 100% right. We're looking very closely at the obesity opportunity for tirzepatide. We're very excited about just the weight loss that we saw in the Type 2 diabetes patients up to 14% weight loss and the potential of that being even higher in the obesity population. Obviously, just a massive unmet need, 110 million Americans live with obesity. Only about 3% of them are treated with some type of anti-obesity medication. So we think the opportunity is huge to really help people who live with chronic weight management issues.

Now with our program, we have four trials in our SURMOUNT obesity registration program. Our first obesity trial will read out next year, our SURMOUNT-1. We're very excited to see that. That should happen in mid next year. And then SURMOUNT-2, 3 and 4, we'll get the data of those trials are on track to wrap up in '23. And then so when you look at our obesity submission and approval, it looks like our approval in 2024 is most likely outcome if everything goes well as we expect in our SURMOUNT program. So very excited about Wegovy's launch. I think they've done a nice job. I think not a surprise to us. We thought that what was holding back the current market was just the current products in the marketplace just didn't have clinically meaningful enough weight loss. We thought if we had products on the marketplace that had a clinically meaningful weight loss, and those products were able to show good clinical outcomes, overall medical outcomes for those live with obesity, that physicians would write it and payers would provide access for it. So it's not going to develop overnight, but we're very encouraged by the early launch of Wegovy. And just very excited about tirzepatide's opportunity.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Mike. Seamus, thanks for your question.

Operator

The next caller is Umer Raffat from Evercore. Please go ahead.

Q - Umer Raffat {BIO 16743519 <GO>}

Hi. Thanks so much for taking my question. Dan, I was very intrigued by the donanemab versus aducanumab head-to-head trial. And my question really was, I understand the primary endpoints on amyloid plaque. But will the trial be able to gauge clinical efficacy on endpoints like CDR, some of the boxes? I asked because my understanding is an open-label trial. And then secondly, I feel like there's been a fair amount of investor debate and perhaps confusion on what exactly is Lilly messaging on the Innovent PD-1 launch in U.S. and the sort of debate rages anywhere from Lilly will be a dominant player or not so much? So just so we're all on the same page, I guess what are you guys expecting? And do you expect it to be a meaningful PD-1 in the U.S. market? And if you could speak to your thoughts on whether data generated in Chinese patients would be a relevant commercial consideration for U.S. oncologists or not?

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Umer. We'll go to Dan for the first question and Jake for the second.

A - Daniel M. Skovronsky {BIO 15349505 <GO>}

Thanks, Umer. Your question is whether the donanemab versus aducanumab trial -- head-to-head trial will be powered to measure clinical efficacy outcomes. They will not be. It is a small and a shorter trial. So, we won't be able to draw conclusions about that. But I'd point out that if we believe that plaque lowering is the appropriate surrogate and that question will certainly be answered in the next year to 18 months as we get data from a number of Phase 3 plaque lowering drug. So if it turns out that plaque lowering is an appropriate surrogate for predicting clinical efficacy. Then I think that the degree and speed of plaque lowering could be the basis of comparison across different Alzheimer's drugs in the same way that surrogates in oncology are used to compare different drugs in a class, knowing that the long-term outcome trials would have to be extremely large and long duration powered for clinical outcomes.

I also sort of point out that we're expecting here to have in the scenario where we're really excited about this, we're expecting to have a positive Phase 3 trial for donanemab, which in itself is a differentiator, I think, from current competitors. So head-to-head on efficacy against adu may not actually be relevant.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dan. Jake?

A - Jacob Van Naarden {BIO 18103115 <GO>}

Hey Umer, thanks for the question. So sintilimab, the PD-1 inhibitor from Innovent, we brought into the company in terms of ex-China rights, explicitly with the intent to use pricing as a lever to disrupt the U.S. market starting with the United States and potentially moving to Europe as well. And as we've said publicly, over the past couple of months, the intent there is really through price predominantly versus other mechanisms such as rebating, et cetera. There are certain customers out there, certain practices and care models for which this is going to be an attractive -- this is going to be an attractive tool for lowering costs to their system. And unfortunately, for the way the system is designed

today, there are going to be many channels for which a lower-priced option actually isn't appealing.

And so, as you -- your question is about whether or not we intend to be a dominant player, it's hard for me to say that with any degree of assertion today. We will be focusing initially on the segments for which this is an attractive option given the way that their payer dynamics work. And today, that's not a majority by any stretch. But that will be our focus out of the gate should sintilimab be approved.

On to your second question about whether or not the data package that's been generated for the agent will have issues with prescribers in the United States. Our market research to-date suggests this won't be an issue. But obviously, we haven't launched the product yet. We haven't gotten approved yet. So I can't say that with certainty, but our market research suggests it won't be an issue. But really in front of us initially is just getting the drug approved. And I think as you know, that's something we hope for in the early part of next year. But the drug will be subject to an advisory committee, and we await the details of what that will cover.

Q - Umer Raffat {BIO 16743519 <GO>}

Super helpful. Thank you so much.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Jake. Umer, thanks for your question. Next caller please.

Operator

The next caller is Ronny Gal from Bernstein. Please go ahead.

Q - Aaron Gal {BIO 15022045 <GO>}

Hi. Good morning and thank you for taking my question. Two of those, first, staying with Umer's points around sintilimab in the U.S. Essentially two-part on this one. First, any comments about FDA change in policy in using China-only patient population as a basis of permission in the United States? We've heard some things in conferences that suggest there might be some change there.

And second, on the same point, you've kind of talked about price as the dominant note here. I guess the question is more around your thinking process. Pharma has struggled for a long time in commercializing low-cost products and innovative products to the same company. If PD-1 should have a low-cost option, why not tau, why not lebrikizumab? Why should those not follow a deep discounting strategy given the clinical profile versus other products in the same class?

And second question, given the recent impact of interchangeable Lantus, can you discuss a little bit how the insulin -- the fast-acting insulin market is different, assuming we will see interchangeable products there, how are the features of the market differ? And would that also be a market which is more amenable to adopting any interchangeable insulin?

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Ronny. We'll go to Dave for the first couple of questions around low-cost entrants and FDA policy. And then we'll go to Mike for the question on the interchangeability of Lantus and how that can potentially read through the fast-acting insulin.

A - David A. Ricks {BIO 16504838 <GO>}

Sure. Happy to. Maybe before we go to me on the FDA, Jake, do you have any comments on the -- FDA comments on China data?

A - Jacob Van Naarden {BIO 18103115 <GO>}

Yes, I think it's a good observation. We've observed the same thing. The tone from D.C. does seem to have changed a bit over the past 18 months on this topic. So I think we're hearing and reading in some ways, probably the same things that you guys are. We don't have a lot more information than that. And so we await again the regulatory decision from FDA as to the acceptability of the package.

A - David A. Ricks {BIO 16504838 <GO>}

As it relates, Ronny, to the broader question about why not more sort of like everyday low price kind of strategies in the main and pharmaceuticals. I mean, I think a couple of things come to mind here. First, I think in oncology, in particular, it is infeasible quite often to run comparative studies. And so once an incumbent is established, it's very difficult to displace that incumbent. Maybe the one narrow exception might be what Jake highlighted with sintilimab, where you could have a more price-sensitive segment. And here, we have analogous data from a different country that was conducted in a time gap that was prior to other PD-1s being approved in that setting.

And so, that presents an opportunistic play. We have, of course, also pursued this in insulin, and Mike can comment on that in a second. But basically, our launch to the 30% discount to the other insulin glargine. We've pursued our own low-cost authorized generic of Humalog, now reducing the price to effectively 70% off the original brand. But here again, it illustrates the point Jake was making is that even in the retail side, it's not universally adopted. Today, the half-price form of Humalog and the third half-price of insulin glargine that we provide have a minority market shares. And that's a little bit counterintuitive, but of course, we all know the incentives of the supply chain, which do tend to favor higher list price products. And that's, I think, where that shows up.

Finally, you asked, why don't we pursue this for our whole portfolio. Well, I think the overriding thought for our portfolio is often to create differentiated data sets. And one thing different from sintilimab, different from Basaglar and authorized generic Humalog that those aren't differentiated datasets. So they're more or less interchangeable. So, when we create a new medicine, we're seeking to create something better. And in the main, that's how the system is set up and that favors typically, an introductory price that's similar to other innovative competitors and then rebating and discounting to the channel to get formulary access and use, and that remains our main strategy.

Of course, if there was some big policy shift that flattened gross to net or reduced somehow the incentives of the intermediaries, we'd take a look at that. And I think our goal would be to deliver lower cost points to consumers if we could. Right now, mostly the system rewards something else, and that's how we are forward planning for the portfolio that Dan was talking about. Maybe Mike has any final comments on insulin and interchangeability.

A - Michael B. Mason {BIO 18347681 <GO>}

Yes. Thanks, Dave. First of all, when we look at Semglee, it's only interchangeable with the reference product, which is Lantus, not Basaglar. So we do think it's going to have a more of an impact on Lantus versus Basaglar. I mean, you look at the mealtime segments, that first reference product will be insulin aspart, not Lispro. Now I think you also have to take a look at kind of the Semglee's interchangeable biosimilar. I think many stakeholders in Washington believe that Semglee's interchangeable insulin would launch at a significant discounted price. Now that hasn't been the case. The net impact of Semglee's interchangeable launch is actually the introduction of a higher price presentation, not a lower price presentation. The new presentation is priced at $269 a vial versus $99 a vial the original Semglee, which is a 273% increase.

So I think what you're not going to see, at least what we haven't seen in the insulin biosimilar space is that Semglee interchangeable will really disrupt the basal insulin market. Rather, what it'll do is allow it to compete in kind of the traditional healthcare system that we know have gaps, which we talked about earlier, and which we've been trying to fill with our insulin value program and the senior savings model.

When you look at and kind of pivot to the mealtime insulin market, mealtime insulins are a bit more complicated. They require more presentations than what you see with a basal insulin. So premixes, our human insulins are also included on the contracting. So I think the mealtime insulin is a little bit different than what you see on the basal insulin. But what we've seen to-date is that given Semglee's our price point on interchangeability, we don't think it's going to be really disruptive to the system, but more work within the current system, which we feel that we can strongly defend. At the end of the day, I think to reiterate Dave's point, I think it's better when we're focused on improvements. And with our Connected Care launch with BIIF, with our weekly basal insulin, I think we're focused on really driving innovation and better patient outcomes.

Q - Aaron Gal {BIO 15022045 <GO>}

Thanks, Mike.

A - Kevin Hern {BIO 20557573 <GO>}

Ronny, thanks for your question. Next caller please.

Operator

The next caller is Kerry Holford from Berenberg. Please go ahead.

Q - Kerry Ann Holford {BIO 21698599 <GO>}

Hi. Thank you. Two questions for me on the generic, please. Firstly, on price. The increase in demand this quarter, we said we partially offset by lower realized prices. Now going to (inaudible) in Q2, where you detailed higher realized price. So maybe you can just talk a bit more about the dynamics and whether that's related in any way to the upcoming adjuvant launch?

And then secondly, on the adjuvant situation, Novartis commented on their call earlier today the FDA has stated to them submission based on IDFS (inaudible) will be submission as long as there's no debt effect on OS. And now I think (inaudible) going to ask your experience, perhaps there'd be more relaxed approach in the FDA boots [ph] that has been set out. So I'm just curious as to why you think there might be any feedback you can give there? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Great. Kerry, you're kind of breaking in and out. But I think these are for Jake. And the first question, Jake, if you didn't catch it, was about quarter-on-quarter revenue and whether that was affected by pricing in the CDK4/6 market or rather the stocking point you made earlier. And then I think the second point was about IDFS versus OS in the FDA's sort of policy. I don't know if you call all that.

A - Jacob Van Naarden {BIO 18103115 <GO>}

Yes. Thanks. On the first point, yes, I mean, the sequential quarters was really mostly related to the inventory stocking and destocking point that I made earlier. We haven't seen a ton of fluctuation in price. On your comment about adjuvant, I can't comment on the back and forth that Novartis had with FDA. I just I'm obviously not privy to that. Though from what -- the framing of your question that actually doesn't sound particularly different than the conversation that we've had with the agency.

As Dan mentioned in his prepared remarks, we've, of course, as you can imagine, gotten a fair number of questions from folks around the nature of the approval in the subgroup versus the enrolled population among, and we'll be publishing in the coming days the actual OS or overall survival data that were part of the regulatory submission. You'll see what those trends look like in both the intent-to-treat population as well as the approved subset. And again, trends in one direction or another, that you'll be able to interpret for yourself. But I don't -- from what I can hear, I don't think the Novartis feedback from the agency is all that different from what we've received.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks Jake. Kerry, thanks for your question. Next caller please.

Operator

The next question is from Vamil Divan from Mizuho Securities. Please go ahead.

Q - Vamil Kishore Divan {BIO 15748296 <GO>}

Thanks for taking my question. Maybe just a couple of other topics that haven't been discussed as much. So one on Emgality. It feels like the CGRP sort of market has been impacted by COVID more than some others. Maybe if you could just sort of give us a sense of the dynamics you're seeing there. And have you seen any impact from the oral CGRPs that have entered or prevention. Is that at any role on Emgality or on the class in the last few months? And then the second one just on the JAK side. Obviously, a lot of focus on the FDA sort of updates on that space. I'm curious if you have any updated timing around when you expect a new kind of final update label for Olumiant in RA and/or a decision on the atopic dermatitis applications? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Vamil. I'll go to Anne for the question on Emgality and Patrik for the question on Olumiant.

A - Anne E. White {BIO 20764375 <GO>}

Great. Well, thanks for the question on Emgality. So at present, what we've seen is the total migraine prescription market has seen growth, but it's driven primarily by the total new acute new patient starts and additional concomitant use. With the injectable class, I do think that we're still experiencing headwinds from the pandemic, and increased competition in the prevention space overall. We do see some variability of this across the market. Some OUS markets are returning really to pre-COVID growth levels.

And while we've seen improvement in the volume of new patient starts, the CGRP MAb class in the U.S. is still about 13% below where we were with the start of the pandemic. So with the new competition and then appropriate treatment for acute and prevention, we're seeing that the market should continue to grow as patients reengage in the system. And on your question on oral impact, I think it's still a bit early to -- early days in the launches to see how this has impacted the space in this way. So, we'll watch that carefully.

I think our belief is that with so many patients and so much unmet need, the opportunity for these medicines, particularly the MAbs, remains significant. And obviously, in the end, it comes down to what's best for that patient and how we get them to their migraine-free days. And that's one place that we think we believe Emgality has an advantage. So we'll continue to watch this space. We continue to believe in the efficacy that Emgality brings to the market. And so, you'll see us continue to push forward in supporting the product.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Anne. Patrik?

A - Patrik Jonsson {BIO 21139959 <GO>}

Well, thank you very much. In terms of the question related to rheumatoid arthritis, the FDA has requested changes to the box warning for all JAK inhibitors to include serious heart-related events, cancer, blood clots and death. And we believe in light of that, it's most likely that the JAKs will be placed after the biologics, also the treatment of rheumatoid arthritis. And that's pretty much where Olumiant is currently placed in the U.S. So we don't see any major impact on Olumiant driven by this change.

When we move to atopic dermatitis, we know that the FDA meets the PDUFA due to the ongoing assessment of JAK inhibitors. And we believe also here it's most likely that the JAK inhibitors will end up being placed after the biologics. Despite that, we also recognize that atopic dermatitis is a very heterogeneous disease, and our clinicians have a use for more tools in the toolbox, but that's what we believe is most likely moving forward. And we would expect some regulatory actions prior to the end of this year.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Patrik. Vamil, thanks for your questions. Next caller, please.

Operator

The next caller is Carter Gould from Barclays. Please go ahead.

Q - Carter Lewis Gould {BIO 21330584 <GO>}

Good morning. Thanks for taking the questions. Maybe first for Dan, just coming back to the head-to-head study. I don't think I've heard you say yet kind of the time period in which you're going to be measuring these reductions in amyloid. I believe you did give up the sort of second half '22 kind of timeline for reading out that result. But should we be thinking about that as like a three-month or six-month time point or just sort of the number of patients that get to below the lower limit of detection over some period? And then maybe for Jake on the SERD class. I know you guys have expressed some cautiousness on kind of the role of SERD in the treatment paradigm in the past. We started to see some of the later-stage data sort of roll out from some of your competitors, wanted to get your latest thoughts there. And if we might start to see some of the -- your SERD combination data from the original EMBER study before year-end. Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Carter. We'll go to Dan for the first question on donanemab head to head and then Jake for SERD.

A - Daniel M. Skovronsky {BIO 15349505 <GO>}

Yes. Thanks for your question, Carter. I think you're appropriately pointing out that actually both things matter in terms of plaque clearance, how fast you clear the plaques and also how deep you clear the plaques. I think in the fullness of time, when we have Phase 3 readouts for multiple drugs that look at efficacy, I predict those will be two important predictive factors in how well a drug helps patients is how quickly and how deeply it clears plaques. I think we have significant advantages there in both aspects with donanemab. So you can be sure we'll be looking at both of those things and reporting that out, as I said, in the back half of next year.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dan. Jake?

A - Jacob Van Naarden {BIO 18103115 <GO>}

Yes. Thanks for the questions about the oral SERD program. We're looking forward to seeing the Radius Menarini data at San Antonio, I'm sure you are. That study is a little interesting, and that is very heavily enriched for ESR1 mutated tumors. And so, we're interested in seeing the degree to which the effect size observed in the study was really driven by that enriched subgroup, where you would expect an outsized effect size versus a drug like fulvestrant versus in the non-ESR1-mutant patients. I think that that question has meaningful read-through as to the overall value of the class. If it's really just limited or driven by the ESR1 mutants, I think that's a very different proposition than a true all-comer effect size. As it relates to the combination data of ours, those are data we'll probably present next year.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Jake. Carter, thanks for your questions. Next caller please.

Operator

The next question is from Steve Scala from Cowen. Please go ahead.

Q - Stephen Michael Scala {BIO 22139067 <GO>}

Thank you. I have a couple of questions. First, is it not possible for Lilly to file tirzepatide for obesity in 2022? On just the SURMOUNT-1 trial with supporting weight loss data from the diabetes trials, other follow-on indications for other drugs have been approved on one study and SURMOUNT-1 is a trial of 2,400 patients. So it's a big trial. Second question, are you planning to use blood-based biomarkers such as P-tau217 as companion diagnostics with the -- or within the donanemab filing? I think you have used the Quanterix diagnostic in the TRAILBLAZER trial. So wondering if that's part of the filing. Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Steve. We'll go to Mike for the question on tirzepatide and then Dan for the question on the P-tau217 assay and submission of donanemab. Mike?

A - Michael B. Mason {BIO 18347681 <GO>}

Yes, Steve, good question. In our discussions with the FDA, we've agreed upon four trials for the SURMOUNT program that make up our submission for the obesity indication for tirzepatide. As I said earlier, those will read out -- SURMOUNT-1 will readout next year. SURMOUNT-2, 3 and 4 readout in '23, and we'll submit and expect approval in '24. Based on conversations with the FDA, when we set our development program, that's the current plan.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Mike. Dan?

A - Daniel M. Skovronsky {BIO 15349505 <GO>}

Thanks, Steve. Good question on sort of companion diagnostics and their role in FDA approval of Alzheimer's drugs. I think based on what we've seen with Adu, our sort of

base case expectation here is that the FDA is operating under an assumption that standard of care now for Alzheimer's disease, if you are diagnosing a patient for Alzheimer's should include biomarker confirmation of disease. So for that reason, my guess is that they won't be -- biomarkers won't be included in prescribing information as companion diagnostics.

I would take the opposite position probably with payers where I think they are likely to be required for reimbursement for these medicines, but that has to be worked out. So those assumptions I just laid out sort of underlie our thinking about how P-tau or Amyvid or any other biomarker CSF Abeta will be incorporated into labels probably not and into practice, probably yes. And so, we're proceeding accordingly to make sure that P-tau217 as well as other biomarkers can be widely available around the same time as we launched donanemab, so that it can be incorporated into standards of clinical practice as a biomarker for detecting Alzheimer's pathology and triaging patients to therapy.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dan. Steve, thanks for your questions. Next caller please.

Operator

The next caller is from Matthew Harrison from Morgan Stanley. Please go ahead.

Q - Matthew Kelsey Harrison {BIO 17603148 <GO>}

Okay. Great. Thanks. I was just wondering if you could comment on lebrikizumab and your sort of views on the AD market. And in particular, now that you've seen the OX40 data from Amgen-KK, if that has any impact on how you think about the longer-term potential of that market? Thanks.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks. Matthew, we'll go to Patrik for the question on lebrikizumab.

A - Patrik Jonsson {BIO 21139959 <GO>}

Well, thank you very much for the question. We are very encouraged by the induction that of lebrikizumab, where we saw more than 50% of patients treated with lebrikizumab achieving an EASI 75. And we also met all the key secondary endpoints. And we actually believe that we have an opportunity here to launch a best-in-class IL-13. And currently, we are looking forward to the 52 weeks data during the first half of 2022, and a potential submission in the second half of next year.

When it comes to the Amgen data, it doesn't change our outlook for lebri. As I said, we believe we have a best-in-class IL-13. And we also believe that we have a very competitive asset with the market leader. And this in a market that we know there is a big unmet need, and the biologic penetration is still very low. And we know that there is a need for many more medications and particularly with the heterogeneous need in the marketplace.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Patrik. Matthew, thanks for your question. We'll wrap up our Q&A. Go to Dave for a close.

A - David A. Ricks {BIO 16504838 <GO>}

Great. Thanks, Kevin. We appreciate your participation in today's earnings call and your interest in our company. We continue to grow our broad commercial portfolio with strong momentum in our core business, supported by many key brands and accelerating classes. This is complemented by a compelling pipeline with industry-leading opportunities, and we remain focused on bringing new medicines to patients and creating value for all of our stakeholders. Thanks again for dialing in. And please follow up with Investor Relations if you have any questions we did not address on the call, and hope you have a great day.

Operator

Thank you. And ladies and gentlemen, that does conclude our conference for today. Thank you for your participation and for using AT&T Teleconference service. You may now disconnect.