Q2 2021 Earnings Call

Company Participants

- Anne White, President of Lilly Oncology
- David A. Ricks, Chairman, Chief Executive Officer & President
- Dr.Daniel M. Skovronsky, Senior Vice President, Chief Scientific Officer & Pres of Lilly Research Labs
- Ilya Yuffa, President of Lilly Bio-Medicines
- Jake Van Naarden, Chief Executive Officer, Loxo Oncology
- Kevin Hern, Vice President of Investor Relations
- Mike Mason, President of Lilly Diabetes
- Ms.Anat Ashkenazi, Senior Vice President & Chief Financial Officer

Other Participants

- Andrew Baum
- Carter Gould
- Chris Schott
- Geoff Meacham
- Louise Chen
- Matthew Harrison
- Ronny Gal
- Seamus Fernandez
- Steve Scala
- Terence Flynn
- Tim Anderson
- Umer Raffat
- Vamil Divan

Presentation

Operator

Ladies and gentlemen, thank you for standing by, and welcome to Lilly's Q2 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 Q2 2021 earnings call. I'm Kevin Hern, Vice President of Investor Relations.

And 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 Oncology; Ilya Yuffa, President of Lilly Bio-Medicines; Mike Mason, President of Lilly Diabetes; and Jake Van Naarden, CEO of Loxo Oncology at Lilly. We're also joined by Lauren Zierke, (inaudible) 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 second quarter results.

David A. Ricks {BIO 16504838 <GO>}

Thank you, Kevin. Q2 of last year was the peak of the pandemic's negative impact to our business. And one year later, I'm proud of the innovation and resilience displayed by my Lilly colleagues to deliver against our objectives in new ways, while also mobilizing to develop treatments to help combat COVID-19.

Looking at Q2 2021, we were encouraged by the increasing worldwide vaccination rates, as well as the underlying environment in most of our major markets. COVID-19 related stocking in Q1 followed by destocking in Q2 of last year complicates quarterly performance comparisons. Therefore, looking at revenue growth in the first half of 2021, better reflects the underlying trends in our business.

On today's call, we will provide year-over-year comparisons for both Q2 and the first half of the year. In the first half of 2021, we delivered 11% growth in our core business. This excludes COVID-19 antibody revenue, this is buoyed by strong volume-driven growth across key brands in major geographies, including the U.S., Europe and China.

Turning specifically to Q2. Revenue grew 23% compared to Q2 2020 or 20% in constant currency. This performance was driven entirely by volume growth of 22 percentage points. As previously highlighted in Q2 2020, we saw a reversal of the $250 million pandemic-related products stocking, which occurred in Q1 2020.

When excluding COVID-19 antibody revenue, the Q2 2020 COVID-19-related destocking and the sale of Cialis in China, our core business grew 12% for the quarter, up from 7% in Q1 on the same basis.

We were pleased to see sequential top-line growth in the core business this quarter, signaling that healthcare systems continued recovery from the pandemic and the strength of our underlying business.

Key growth products continue to drive our revenue growth and represent 54% of our core business this quarter. Our non-GAAP gross margin was 79.3% in Q2 or 79.7% excluding impact of foreign exchange on international inventory sold. Excluding the FX impact, our gross margin increased by approximately 60 basis points compared to last year. Our non-GAAP operating margin was 29.4%, representing an improvement of nearly 140 basis points. We are pleased to see operating margin expand year-over-year and we expect continued expansion in the second half of this year.

On the pipeline front, we achieved multiple milestones since our earnings call in April, including receiving Breakthrough Therapy designation for donanemab and announcing our plan to submit to the FDA under the accelerated approval pathway.

Announcing positive Phase 3 results for tirzepatide SURPASS-4 trial, with planned global submissions of the SURPASS program for tirzepatide in Type 2 diabetes by the end of 2021. Obtaining approval for Jardiance in partnership with Boehringer Ingelheim for HFrEF in Europe, and announcing positive Phase 3 results from the EMPEROR-Preserved trial for Jardiance in HFpEF, the first and only successful trial for this patient population. And initiating Phase 3 trial results for pirtobrutinib in mantle cell lymphoma, tirzepatide in HFpEF and Verzenio in HR+ HER2+ early breast cancer and now prostate cancer.

We also continue to augment our pipeline with business development deals and announced the acquisition of Protomer Technologies. We welcome the Protomer team to Lilly and are excited to bring this technology to our diabetes pipeline. As we believe, glucose sensing insulin may become the next-generation for insulin treatment to improve the quality of life for people living with diabetes.

Lastly, on financials, we've returned approximately $1.3 billion to shareholders via the dividend and share repurchases in the quarter and authorized the repurchase of up to $5 billion in stock, in addition to the $500 million authorization remaining under our 2018 share repurchase program.

Moving on to Slides 5 and 6. You'll see a list of key events since our Q1 earnings call, including a May webcast, which highlighted our updated environmental, social and governance strategy, and our sustainability efforts as well as the launch of a new ESG website to serve as a comprehensive resource to provide increased transparency regarding the company's ESG goals and progress.

Further as part of our goal to become carbon neutral in our own operations at our manufacturing plant in Kinsale, we recently inaugurated a new solar field, which is now the

largest in Ireland. We also announced donations of COVID-19 therapies at no cost to low-income and lower middle income countries heavily impacted by the pandemic. And are proud of the impact we're having around the world as we work to combat COVID-19.

Now, I'll turn the call over to Anat to review our Q2 results and to provide an update on our financial guidance for 2021.

Ms.Anat Ashkenazi

Thanks, Dave. Slide 7 and 8 summarize financial performance in the second quarter and year-to-date. I'll focus my comments on non-GAAP performance. Revenue increased 23% this quarter compared to Q2 2020 or 12% excluding the items, Dave mentioned earlier, representing strong momentum for our core business.

Given the COVID-19-related stocking and destocking in between Q1 and Q2 2020, our first half performance of 11% revenue growth or 8% in constant currency excluding COVID-19 antibody revenue is a more accurate reflection of underlying performance and the sequential quarter-over-quarter revenue growth better represent the strength in our core business.

Sequential revenue growth from Q1 to Q2 for core business, increase in vaccination rates in many major markets and the majority of our sales reps now being back in the field, suggests a recovery from the pandemic was in line with our expectation for the quarter.

We're particularly pleased with the strong volume growth across key brands like Trulicity, Taltz, Verzenio and Jardiance. Verzenio in the U.S. grew nearly 6 percentage points and share total prescription exiting June compared to the prior year. While Trulicity, Taltz and Jardiance increase their leading market share in the same period while class growth accelerated. These products along with other key growth products represented 54% of revenue in the core business this quarter.

Gross margin as a percent of revenue declined 30 basis points to 79.3% in Q2. The decrease in gross margin percent was driven primarily by unfavorable effect of foreign exchange rates on international inventory sold.

Excluding this FX impact, gross margin as a percent of revenue grew 60 points this quarter. Total operating expenses grew 18% this quarter compared to the same quarter last year. Marketing, selling and administrative expenses increased 16% as the base period in Q2 2020 included a meaningful reduction in direct-to-consumer marketing and customer-facing expenses as healthcare system closed. R&D expenses increased 20%, driven by investment exciting late-stage pipeline opportunities, including pirtobrutinib, tirzepatide, donanemab and lebrikizumab.

In Q2, we also invested approximately $85 million in COVID therapies R&D, bringing our cost of total COVID-19 R&D investment to approximately $300 million year-to-date. Net of COVID-19 R&D investment operating expense growth was 18% compared to Q2 of 2020, and 10% for the first half of the year.

Operating income increased 29% compared to Q2 of 2020 and operating income as a percent of revenue was 29.4% for the quarter, an increase of 140 basis point compared to the prior year. This increase was driven by revenue growth outpacing expense growth and we expect continued margin expansion in the second half of 2021.

Other income and expense was income of $5 million this quarter compared to expensive $57 million in Q2 2020, driven by income from European patent settlements for ALIMTA. Our effective tax rate was 14.4%, an increase of 350 basis point compared with the same quarter last year.

The effective tax rate for both periods were reduced by net discrete tax benefits with the lower net discrete tax benefit reflected in the second quarter of 2021. At the bottom line, net income and earnings per share increased 29% in Q2 and 22% year-to-date, or 30% and 24% respectively in constant currency.

On Slide 9, we quantify the effect of price, rate and volume on revenue growth across the world and we are encouraged by the growth seen across most of our major geographies.

This quarter, U.S. revenue grew 18% compared to the second quarter of 2020. Adjusting for COVID-19 antibody revenue and the Q2 2020 COVID-19-related destocking, the core business grew 8% in the U.S. up from 5% in Q1 on that same basis. These results were driven entirely by volume, laid by Trulicity, Taltz, Verzenio and Jardiance.

Pricing was a 1% drag on U.S. revenue growth this quarter with increased rebates to maintain excellent access and higher growth in lower net price segment, largely offset by lower utilization in the 340B segment, changes for estimates to rebates and discounts, and to a lesser extent, modest list price increases.

The year-to-date price decline of 3% in the U.S. is in line with our net price expectations for the full-year. Specific to Taltz in the U.S., performance for the quarter was in line with the expectation we described on the Q1 earnings call and we are pleased to see a return to net sales growth this quarter as volume gains more than offset price declines.

Taltz's Q2 performance benefited from a favorable change to par estimates for rebates and discounts. And COVID-19 related inventory destocking last year, excluding these items, Taltz still return to double-digit growth in the second quarter.

We believe the net price decline for Taltz in the first half of 2021 represents the underlying full price trend and that continued volume growth will drive net sales acceleration in the second half of the year. While midterm price trends are currently stable, given increasing variability and payer mix, we continue to expect quarterly variability in reported U.S. net price changes across our business.

Moving to Europe. Revenue grew 27% in constant currency. Excluding COVID-19 antibody revenue and the negative impact of Q2 2020 COVID-19-related customer buying patterns, revenue grew 14% in constant currency, driven entirely by volume growth, primarily for

Trulicity, Taltz, Alimta and Olumiant. We continue to be pleased with the momentum of our business in Europe and expect continued growth in the second half of this year, excluding the expected impact from the loss of exclusivity for Alimta.

In Japan, revenue grew 2% in constant currency, driven primarily by the launches of Olumiant and Emgality. Revenue growth in Japan continues to be negatively impacted by the decreased demand for several products that have lost market exclusivity. But our key growth products grew 21% in Q2 in Japan and represented approximately 50% of the business there.

Recent surges of COVID-19 cases continue to negatively impact recovery in Japan. So we currently expect improved revenue growth in the second half of the year, based on the uptake of newer products.

In China, revenue grew 106% in constant currency, primarily driven by the divestiture of Cialis and the launches of Tyvyt and Trulicity. Excluding the impact from the Cialis transaction, our revenue in China grew 35% in constant currency. We are excited about the continued momentum in China, as sales of new medicines have accelerated significantly in the past three quarters. Revenue in the rest of the world increased 5% in constant currency, driven primarily by our key growth products.

At the bottom of the slide is the price rate volume effect on revenue for our June 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 nearly 17 percentage points of growth this quarter and continue to drive our overall performance and outlook.

Slide 11 highlight the contributions of our key growth products. In total, these brands generated over $3.5 billion in revenue this quarter and made up 54% of our core business revenue in Q2. We're encouraged by the strength of our key products in Q2, collectively up over 34% compared to the same period last year.

Trulicity, Taltz, Verzenio and Jardiance, all continue to outgrow their respective classes. We are now tracking above pre-COVID-19 new to brand prescription baseline in the U.S. across all major therapeutic areas with the exception of oncology and the CGRP antibody class, which we expect will continue to recover in the second half of the year.

On Slide 12, we provide an update on capital allocation. In the first half of 2021, we invested $5 billion to drive our future growth through a combination of after-tax investments in R&D, business development and capital investments. In addition, we return over 1.5 billion to shareholders in dividends and share repurchase. As we look ahead to the second half of the year, we will continue to fund our growth of our key products in recent launches, investor pipeline and seek external innovation to augment our future prospects, as well as returning capital to shareholders.

Turning to our 2021 financial guidance on Slide 13. We are updating our GAAP and non-GAAP guidance. Well, the COVID-19 pandemic is still impacting countries around the world, the pace of recovery from the pandemic was in line with our expectations in Q2.

New to brands, scripts and most of the classes in which we compete with are tracking above pre-COVID baseline in the U.S. And healthcare systems, in most major markets are largely returning to normal as we enter the second half of 2021. We are increasing our full-year revenue outlook for the core business by $200 million to reflect the strong performance and favorable impact from foreign exchange. We are however lowering the top end of the range for COVID-19 antibody revenue by $400 million and confirming the bottom end of that range.

Moving forward, we expect COVID-19 antibody revenues to be less of a factor as demonstrated by Q2 revenue declining to $150 million from $810 million in Q1. As variants are growing, we recognize the situations across the globe can evolve quickly and we plan to adapt as required.

The net impact of these changes is an updated revenue range of $26.8 billion to $27.4 billion. Our outlook for non-GAAP gross margin percent remains unchanged at approximately 79%. On a reported basis, we've lowered guidance for gross margin percent to approximately 75% to reflect the impact of COVID-19 antibodies excess inventory charge due to the combination of changes to current and forecasted demand from the U.S. and international government and near-term expiry of COVID-19 antibodies inventory.

For research and development and SG&A, our guidance ranges remain unchanged. However, investment in promising R&D opportunities and exciting potential launches could push us towards the top end of our guidance range for both R&D and SG&A. Our non-GAAP operating margin guidance is now expected to be approximately 30% driven by lower COVID-19 antibody revenue.

However, it remains approximately 31% excluding COVID-19 antibodies. Our GAAP operating margin is not expected to be approximately 24%. We are increasing our non-GAAP range for OID to an expense of zero to $100 million, to reflect the Alimta patent settlements in Europe, I noted earlier. And our GAAP range is now income of $375 million to $475 million, which also reflects the impact of equity investment gains in the first half of the year.

On a non-GAAP basis, our expected tax rate remains unchanged and on a reported basis, we've lowered our expected tax rate to approximately 12%. Finally, the non-GAAP range for earnings per share remains unchanged at $7.80 to $8.00, while GAAP EPS is expected to be in the range of $6.73 to $6.93, primarily driven by the impact of the COVID-19 antibody inventory charge, the impact of equity investment gains and the Alimta patent settlements in Europe.

We are confident in our ability to achieve our 2021 revenue goals for the core business while delivering mid-teens EPS growth. As we look at the underlying volume and shared

trends across our key growth products, we're confident in our full-year outlook for the core business. And the pipeline successes in the first half of this year, strengthen our conviction in our mid-term and long-term outlook for continued top-tier revenue growth and operating margin expansion.

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

Dr.Daniel M. Skovronsky

Thanks, Anat. 2021 has clearly been a productive year for R&D at Lilly, with continued strong progress in our pipeline and more potential catalysts on the way.

Before I get into the broader portfolio update, I'll spend a few minutes highlighting several updates for our late-stage pipeline. I'll start with the donanemab. In Q2, the first amyloid lung agent for the treatment of Alzheimer's disease was approved under the FDA's accelerated approval pathway, based on plaque lowering, which we believe reflects a shift in policy and sets a new path for Alzheimer's drug approval in the U.S.

Lilly has long been an advocate for using biomarkers for amyloid plaque and neurofibrillary tangles to identify patients for treatment and to monitor the response to therapy. We were pleased to see the FDA's conclusion that improvements in brain pathology are appropriate surrogates for clinical efficacy of Alzheimer's drugs.

Based on data we've seen to date, we believe donanemab clears plaque faster and deeper than previously seen with other therapies and achieved complete plaque clearance in a majority of patients in TRAILBLAZER-ALZ after only limited duration of dosing.

On the basis of the clinical evidence for donanemab, we were pleased to have received Breakthrough Therapy designation from the FDA. At the Alzheimer's Association International Conference last week, we shared additional important analyses from donanemab TRAILBLAZER-ALZ. Briefly, I'll highlight several findings. First, we shared detailed exploratory statistical analyses, comparing a variety of methods beyond MMRM and DPM as summarized on Slide 14.

We are pleased to see that these new analyses showed consistency of effects on primary and secondary outcomes across all statistical methods. Notably, all of the new analyses conducted showed good separation of treatment from placebo with statistical significance achieved foremost endpoints at nearly all relevant time points measured.

The robustness of the treatment efficacy across analytical methods increases our confidence in the potential clinical benefit of donanemab. While all statistical methods evaluated should similar results. We note that the Bayesian disease progression model, DPM, closely reflected the raw observed data with the smallest standard error of any method. These results reinforce our hypothesis that DPM is a preferred analytical method for Alzheimer's trials.

Additionally, we shared new data showing a relationship of amyloid plaque reduction and slowing of cognitive decline as shown on Slide 15. To our knowledge, this is the first time such results have been available. When we initially reported the results of TRAILBLAZER-ALZ, we commented that at a group level, patients treated with the donanemab showed both statistically better plaque reduction and statistically better slowing of cognitive decline at 18 months. But patient level correlations between degree of plaque reduction and magnitude of slowing a cognitive decline were not significant.

Now using a more sophisticated PK iADRS exploratory analysis that uses all of the available time course data. We showed a highly significant relationship between degree of amyloid plaque reduction and slowing of cognitive decline with P less than 0.001.

The Conrado model shown here was published in 2014 and is the result of efforts from the Coalition Against Major Diseases, CAMD, which collected placebo data from 15 randomized trials, including almost 4,500 participants.

We introduced a treatment arm and incorporated percent amyloid plaque removal into this model to generate these results. And we believe this is important support for the use of amyloid plaque reduction as a surrogate for clinical efficacy.

Notably, these data suggests that full clearance of amyloid plaque is required for highest efficacy as model results predict that patients achieving a 100% clearance of amyloid plaque, could have more than 40% slowing of disease progression.

Moving to Slide 16, we show an exploratory analysis, looking at the effect of donanemab's plaque clearance on development of tau pathology. Tau pathology is an exciting biomarker. Since measures of Alzheimer's disease tau, unlike measures of amyloid plaque, have been correlated with clinical measures of cognitive and functional decline as noted here.

Importantly, we had previously shown that donanemab treated patients had slower accumulation of regional brain tau pathology than placebo-treated patients. This is an important finding because the amount of brain tau pathology is an excellent predictor of subsequent cognitive decline. At finding we observed the solanezumab, an Expedition 3 and reproduced once again in TRAILBLAZER-ALZ.

Now, we've extended these results to show that the donanemab treated patients who achieved complete clearance of amyloid plaque by six months, had the most marked slowing of tau spread with nearly complete abrogation of progression the frontal lobe.

This reinforces our hypothesis that both deep and rapid amyloid plaque clearance are required for optimal drug efficacy. With this new data, we presented last week, we have now linked degree of amyloid plaque reduction with degree of clinical benefit, as well as degree of amyloid plaque reduction with degree of benefit on brain tau pathology, which is itself linked to clinical benefit.

As displayed on Slide 17. We've just recently obtained data with our plasma tau biomarker, phospho-tau217. These new data demonstrate that amyloid plaque clearance with donanemab also resulted in reversal of the typical increases of phosphorylated tau seen in the blood, with decreases from baseline of more than 24% and a change from the untreated arm with a p-value of less than 0.0001.

This highly significant effect was seen as early as three months, following initiation of treatment and could reflect a combination of less tau spread in the brain as well as less neuronal damage, which could account for tau leakage into the periphery.

You can see on the right side of the slide that the effect on plasma tau is also correlated to degree of plaque reduction, with nearly every patient on treatment, who achieved substantial plaque clearance showing flat or declining plasma phospho-tau. We are delighted to see the potential utility of P-tau217, not just for diagnosing disease, but also for monitoring treatment efficacy. We believe this could be another important contribution to the Alzheimer's field.

Finally, on Slide 18, the significant relationship between plasma P-tau217 reduction and the slowing of cognitive decline is shown. This additional biomarker for efficacy links the donanemab mechanism of amyloid plaque clearance with positive effects on both clinical outcomes in tau pathology. These data suggest that patients who achieved a 30% decrease in P-tau217 from baseline showed more than 40% slowing of disease progression.

The three main findings I just discussed. One, the consistency of clinical benefit across statistical methods. Two, the correlation of plaque lowering the clinical benefit, with patients who achieved the greatest plaque clearance, I mean, the greatest opportunity for benefit. And three, the correlation between achieving complete plaque clearance and beneficial effects on tau pathology seen in the brain and measured in the periphery, which themselves are predictors for clinical benefit, strongly support the efficacy of donanemab and give us confidence that the remarkable levels of amyloid plaque clearance achieved by donanemab, could translate into a meaningful breakthrough for patients.

Moving to Slide 19. Accordingly, we've announced that we plan to submit to the FDA under the accelerated approval pathway before the end of this year. Based on data from completed studies, supplemented by additional safety data from the ongoing TRAILBLAZER-ALZ 2 study.

We've remain focused on enrolling TRAILBLAZER 2 with the aim to replicate the positive results of TRAILBLAZER 1. Replication is important to overcome skepticism in the field. We hope the TRAILBLAZER-ALZ 2 will generate important confirmatory data for patients, physicians and payers, and help us understand how to make sure the right patient, gets the right duration of therapy, at the right stage of disease.

We are pleased to announce today that we have closed screening for TRAILBLAZER-ALZ 2, with an adequate number of subjects, now in the trials screening process to fully enrolled to study. Given that conducting and processing an imaging study is used during screening

takes several weeks to complete. We expect that the final subject to complete screening procedures and receive their first dose of donanemab or placebo by the end of the third quarter and the study will complete 18 months later.

Given this progress in enrollment, we are confident that we will achieve the number and duration of drug exposures needed to appropriately characterize the safety profile of donanemab, allowing for regulatory submission by the end of this year. Discussions with the FDA are consistent with our prior statement, supporting a submission before the end of 2021.

I also want to provide a few comments in how we believe the national coverage determination opened for monoclonal antibody therapies targeting amyloid by the centers for Medicare and Medicaid services may impact the Lilly and donanemab. We believe this NCD is a clear opportunity to focus treatment on the patients most likely to benefit from amyloid plaque reducing therapies. This would align with our goals, which have long been to use advanced diagnostic tools to identify the right patients that can benefit the most from amyloid reducing therapies. We're particularly encouraged that our progress with the plasma P-tau217 assay could open up a broader access to diagnostic tools.

Still, despite the advances in diagnostics and the promise of donanemab, we acknowledge the current skepticism in the national discussion, and we hope that each drug will be evaluated by payers and prescribers based on its own data. This could be particularly important, given the data I've shared today, which suggests that the degree of donanemab's amyloid plaque clearance relates to clinical benefit.

In summary, we look forward to submitting donanemab to the FDA later this year with the potential to bring a robust amyloid plaque clearing agent with limited treatment duration to market for early symptomatic Alzheimer's patients in 2022, with potential replicated clinical efficacy results expected in 2023.

Transitioning now to Verzenio. On the last earnings call, we commented that FDA had asked to see an overall survival trend in favor of Verzenio in the monarchE trial and adjuvant breast cancer. We also noted that the OS data set is quite immature in the overall population, which makes interpretation challenging.

We have now provided to the FDA additional data from the monarchE study and we were encouraged to see continued strengthening of the primary endpoint of invasive disease-free survival, IDFS, as well as consistent benefit in the key secondary endpoint of distant recurrence-free survival, DRFS.

Of note, with this continued follow-up, we can now confirm this benefit extend beyond the two-year Verzenio treatment period. We look forward to disclosing this new analysis at the medical meeting this fall.

Our discussions with the FDA have focused on the pre-specified sub-population of patients with high Ki-67 index. A marker of increased cell proliferation. These patients have

more aggressive disease and higher risk of relapse and thus, are more mature for overall survival analysis. This group, which makes up approximately half of the monarchE population are demonstrating an overall survival trend that favors the treatment arm and based on FDA feedback, we expect an initial approval in adjuvant breast cancer in this population before the end of the year, in line with the current review cycle.

Importantly, since the IDFS and DRFS hazard ratio is favoring Verzenio are similar in patients with high and low Ki-67 index. We expect that the OS trend first seen in the Ki-67 high population will in time be replicated in the broader study population.

We hope to expand the label to the entire world population in the future once we see more overall survival events in the broader population. To-date, regulators outside the U.S. have not raised the same questions on overall survival.

Finally, moving to Olumiant, we shared in July that the FDA will not meet the PDUFA action date for the supplemental new drug application for atopic dermatitis. This delay is related to the FDA's ongoing assessment of JAK inhibitors.

Patient safety is critical to Lilly and we continue to further evaluate their safety profile with ongoing randomized and observational safety studies. We're confident to the efficacy and safety data for baricitinib support a favorable benefit risk profile for the treatment of atopic dermatitis. And we look forward to continuing to work with the FDA during the remainder of the review process.

We do not have additional information on timing or specific action date from the FDA, but we see potential for regulatory action for atopic dermatitis in the U.S. later this year. We're committed to bringing Olumiant to market in the U.S. to help meet the needs for people living with atopic dermatitis.

Slide 20 shows select pipeline opportunities as of July 30 and Slide 21 shows potential key events for the year. There have been several additional major development since our last earnings call and I'll cover these by therapeutic area.

In May, we share the positive results for tirzepatide in SURPASS-4 and announce that the SURPASS program met regulatory submission requirements for evaluating cardiovascular risk and confirmed our intention to submit a registration package for tirzepatide in Type 2 diabetes to global regulatory authorities by the end of 2021.

At ADA in June, tirzepatide was our large focus, as we shared detailed data for the first four studies from the tirzepatide SURPASS program for the treatment of Type 2 diabetes. These results support our belief that tirzepatide may represent a substantial improvement in the treatment of patients with Type 2 diabetes with early and unsurpassed improvements in A1C and body weight reduction across doses.

We remain on track for global regulatory submissions before the end of this year. We are also excited about tirzepatide's opportunity across multiple indications, including

cardiovascular outcomes, Obesity, NASH and heart failure. In Q2, we initiated SUMMIT, our planned Phase 3 study for tirzepatide in heart failure.

In July, we achieved an important milestone with Jardiance, as the first and only medicine to achieve a primary endpoint for heart failure with preserved ejection fraction or HFpEF. The EMPEROR-Preserved Phase 3 trial met its primary endpoint and demonstrate significant risk reduction with Jardiance for the composite of cardiovascular death or hospitalization for heart failure in adults with HFpEF. This is a significant breakthrough for patients and we're proud of what we've achieved here in partnership with Boehringer Ingelheim.

We look forward to presenting detailed results from this study at the European Society of Cardiology on August 27, and we expect to submit this indication to regulators later this year.

We also received approval in the EU for Jardiance HFrEF in June and expect regulatory action in the U.S. and Japan later this year for this indication. Additionally, we've advanced our GGG TriAgonist into Phase 2 for diabetes based on the promising data we shared at ADA, which supports the potential for differentiated efficacy from tirzepatide with respect to body weight, while maintaining glycemic control. We also started two Phase 1 studies for diabetes and cardiovascular disease. Lastly, we removed one of our oral GLP/GIP Phase 1 molecules from our pipeline.

In oncology, we also continue to make important progress. Starting with Verzenio. We've initiated two Phase 3 studies since our last update. As planned, we've initiated an adjuvant study for HR positive HER2 breast cancer. And we are announcing today that a result -- as a result of a favorable blinded interim analysis for our Phase 2 trial in metastatic castration resistant prostate cancer, we've also initiated the Phase 3 portion of this adaptive study.

This action was based on a recommendation from the independent data monitoring committee or IDMC. The IDMC reviewed interim efficacy and safety data, and concluded that the results met the pre-specified expansion criteria based on Radiographic Progression Free Survival and recommended advancing the study to the registrational Phase 3 stage.

While Lilly remains blinded to the study, we are obviously very pleased with this development and have already begun dosing patients in the Phase 3 portion of this trial. Given that the expansion of Phase 3 includes the cohort of patients who were in the Phase 2 study, these data remain blinded and we will not be disclosing this at medical meeting.

On the development front in oncology, we also made progress with pirtobrutinib and our oral SERD. We've initiated the Phase 3 study for pirtobrutinib and relapsed/refractory MCL monotherapy executing on our commitment to robust Phase 3 program for this molecule.

Regarding oral SERD, we announced our plans to begin a Phase 3 study later in 2021 based on the Phase 1 results we shared at ASCO in June, that showed an efficacy and

safety profile in line with our expectations. In addition, we've now achieved the first human dose for our next generation KRAS G12C inhibitor.

Lastly, in oncology, we announced that the FDA has accepted our submission of solanezumab for non-small cell lung cancer. This submission is an encouraging start for our collaborative efforts within events to make solanezumab available in countries beyond China.

In neurodegeneration, in addition to the donanemab news I just shared, we anticipate a Phase 2 readout for zagotenemab later this year and note that our GPA 1 gene therapy asset from Prevail started a Phase 2 study in Type 2 Gaucher Disease.

For immunology, we do not have additional significant updates in Q2, but we're looking forward to the Phase 3 readouts of lebrikizumab in atopic dermatitis and baricitinib for lupus later this year. We also submitted baricitinib for alopecia areata in Japan.

Lastly, we're moving our COVID-19 antibody therapy LY-CoV1404, now known as BEBTELOVIMAB into Phase 2 to address viral variance as part of our ongoing commitment to help combat COVID-19 if needed.

To recap, Q2 was another positive quarter for R&D at Lilly and we're excited about a number of further readouts and important milestones coming later this year, reflecting continued advances on behalf of patients suffering from disease.

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

David A. Ricks {BIO 16504838 <GO>}

Thanks a lot, Dan, appreciate that. Before we go to Q&A, let me sum up the progress we've made during this quarter. We've seen strength in our core business in the first half of this year and increased momentum in Q2. This is driven by strong volume driven growth across key brands and most major geographies.

We're pleased to see sequential top-line growth this quarter as well as year-over-year margin expansion. We made significant progress developing new medicines. And Q2 was another positive quarter for our pipeline as we announced plans to submit to your tirzepatide in Type 2 diabetes, and donanemab Alzheimer's disease later this year.

As well as an approval for Jardiance in HFrEF, and as Dan outlined, positive results in HFpEF. We returned nearly $800 million to shareholders through dividends and completed $500 million in share repurchases, reflecting confidence in the ongoing strength of our business. As we look forward to the rest of the year, we are quite confident in our long-term prospects.

Before we move on to Q&A, I would like to share -- also like to share that we will hold a live investor meeting this December to highlight our R&D pipeline and progress for investors. We will also provide our initial 2022 guidance at this meeting.

Given the limited physical space available, this event will have an accompanying webcast. We're hopeful that we can host this event in person, but are watching the evolution of the pandemic closely and we'll adjust accordingly to a virtual event, if needed. Our IR team will be in contact in the coming weeks to issue invitations and provide more logistical details on this meeting.

Now let me turn it over to Kevin to moderate our 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.

Lois, can you 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 Terence Flynn from Goldman Sachs. Please go ahead.

Q - Terence Flynn {BIO 15030404 <GO>}

Hi. Thanks for taking the question. Maybe, Dan, I was just wondering if you could elaborate at all on your comments regarding your discussions with the FDA on donanemab. It sounds like they're consistent with your expectations but any more color you can provide if they've actually signed off fully on your plans to file the BLA? And then how much additional safety data would they want to see from the ongoing TRAILBLAZER 2 study? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Terence. Dan?

A - Dr.Daniel M. Skovronsky

Yeah, sure, Terence. Thanks for that question on donanemab and FDA and safety. In June when we got the Breakthrough Therapy designation, we announced our expectations to file the BLA by the end of the year. That was based on our current understanding of the situation. Since then things have progressed and I would say, I'm even more confident now, than I was then. That we should have an adequate package to support a complete submission, by the end of this year, that includes of course our confidence that we have enough safety data to support a full evaluation of the benefit risk of this drug. I think given limited duration of dosing, that helps as well as given the near completion now of enrollment in TRAILBLAZER 2. So it's our intent, then to use combined safety data from the

completed Phase 1 and Phase 2 studies as well as an early look at safety data from that ongoing Phase 3 study to support the package now. Of course, with any ongoing study, there's always risk we don't know what that safety data is going to show, if it's consistent with safety data we've collected prior to the study, then I think we should also be confident that, that would support a positive benefit risk assessment and put us on track to launch next year as we said.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

And the next question is from Ronny Gal with Bernstein. Please go ahead.

Q - Ronny Gal {BIO 15022045 <GO>}

Good morning and thank you for taking my question. Two. The first one I'll stay with the donanemab. You have kind of suggested in your comments there that there will be a good chance to use some of the biomarkers that you are developing in the early commercial use of donanemab. Can you talk a little bit about what markets do you expect, you have proved, by when? And how do you see, the essentially, the entire patient passage through the use of the donanemab going forward? And how does it differ from other amyloid data? And second Basaglar, seems to have a bit of a price drop this quarter. Can you discuss a little bit, what you're seeing here, what you're expecting with the approval of the first interchangeable biosimilar? Any impact there and as we go forward how should we think about that franchise?

A - Kevin Hern {BIO 20557573 <GO>}

Thanks Ronny. We'll go to Dan for the questions on donanemab, and then Mike Mason for the questions on biosimilar.

A - Dr.Daniel M. Skovronsky

Thanks Ronny for the question on biomarkers in the commercial use. Of course, this has been an area of great progress and great investment by Lilly. We continue to put a lot of emphasis here. I think objectively you wouldn't have had the progress that we're seeing now in Alzheimer's disease, had it not been for the ability to select patients for treatment and follow their response treatment with biomarkers. We don't see that as a research-only application, that should be available those kinds of tools to patients in the clinical, who are being clinically treated for Alzheimer's disease in the future. So, the status of the tools right now is both of the pet agents, the tau PET imaging, TAUVID that we used in that amyloid PET imaging, the name of it, those are both of course FDA approved. And availability is somewhat limited right now, particularly for TAUVID but could quickly be scaled with launch of donanemab in the future.

The third agent, which is probably the one that will be the most accessible to patients is the phospho-tau217 assay. Just as we continue to work on that assay, we're more and more impressed with its performance, its ability to identify patients and even as I showed today track their progression. So this could be an answer for patients in the near term. We'll work

hard to make that available, the bars often lower for in vitro diagnostics and in vivo diagnostics and I think there's good potential there. You asked about the patient flow, once all these things are approved and available and presumably that happens around the time of the genetic donanemab launched up before. I think it would make sense if it with medical practice, if screening starts with some sort of simple cognitive exams by physician to assess the patients' eligibilities, early Alzheimer's, then they would move on to probably a blood-based tests like phospho-tau217 if that's positive, that could either be a basis for treatment depending on if data support that or that could triage patients to PET scans for further evaluation.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dan. Now to Mike for the questions around Basaglar Q2 performance and Semglee interchangeability.

A - Mike Mason {BIO 18347681 <GO>}

Yes. Thanks for the question. and Basaglar. The performance that you're seeing in the second quarter '21 has primarily been driven by pricing pressure and volume pressure in the medicaid segment for Basaglar. And let me give you a little bit of color on how the medicaid segment works. There is really two different types of states those that have one signal unified preferred drug lists across managed medicaid and fee-for-service, and then others that have two different kind of unique preferred drug lists across fee-for-service and a different one for managed medicaid. What we've seen with Basaglar is when states decide to transition from having two preferred drug list to a unified preferred drug list. The economics for the state tends to favor the long-standing brands like Lantus and so at that point, you see if we have one state for an managed medicaid, you'll see the transition back to Lantus. So, that's what you've seen driving our Q2 performance. Also, in the managed medicaid space, we have seen some pricing pressure there from Semglee that's required us to put more rebates on the -- in order to preserve volume for that.

Now, let me turn to kind of -- well, first of all, before turning to Semglee now that the trends for Basaglar are fully baked into our guidance for the remaining part of the 2021.

Now let me let me turn to Semglee, first of all understand that Semglee has gained interchangeability just with Lantus not with Basaglar, so we don't anticipate any immediate impact on Basaglar. If you look at Semglee performance to date, they've captured about 2% share of market on the TRx, and about 1% percent of new treatment starts and the vast majority of that is coming from medicare part A, which is hospitals and the medicaid segment. If you look at the price point for Semglee, it's currently at $99 per vial and about $150 for five pack of pens and, with the moved interchangeability, we really support any actions that help patients with diabetes, more affordable out-of-pocket experience, which is why anyone regardless of insurance status is eligible to buy their monthly prescriptions of Lilly insulin for $35 or less through our Insulin Value Program. The Insulin Value Program has helped lower the average pocket -- out-of-pocket costs for a monthly prescription of Lilly insulin, which often requires or includes multiple vials, our insulin pen packs to $28.05 in the face of raising health insurance deductibles. So it's great that people living with diabetes has access to many options to lower their out-of-pocket costs. Thanks for the question.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks Mike. Thanks Ronny for your questions. Next caller please.

Operator

Thank you. And the next question is from Tim Anderson from Wolfe Research. Please go ahead.

Q - Tim Anderson {BIO 3271630 <GO>}

Well, thank you. A couple of questions. Just your general thoughts on subcu dosing with antibodies to plaque, does that offer meaningful differentiation at a high level, the benefits would seem quite obvious to being able to dose drug at home. But some argue that it falls outside of a medicare Part-B framework, so maybe docks would be more inclined to stick with an infusion. And I believe you originally did not pursue subcu because you're worried you wouldn't get enough drug across the blood-brain barrier. Roche has shown us that they can achieve that, so can we expect Lilly might also pursue a subcu and would this require a formal Phase 3 study looking at plaque reduction as primary end point? And then last quick question, why wouldn't something like P-tau217 become a separate meaningful revenue stream in its own right for Lilly?

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Tim. We'll go to Dan for all those questions.

A - Dr.Daniel M. Skovronsky

Okay. Thanks. It's a good question and line of questions here on subcu dosing for anti-amyloid therapies. Probably two factors that we have taken to account in addition to the ones, you mentioned. First and most important is efficacy for patients and I think all of the data that we have so far suggests and support the notion that deep and rapid clearance is key here. And so, if you're going to go to subcu dosing, it's important to make sure you do get enough drug in, so that you can quickly get patients to clear. That's not going to always be possible with every drug. I think the second consideration with subcu dosing is the duration of therapy. So if it's limited duration of therapy, the difference between IV and subcu, if it's once a month for six months, that's not a big difference between IV and subcu, whereas, if it's for the rest of your life, maybe that is a bigger difference.

Finally, with respect to our plans for subcu. I do think it's an important option to offer patients. Notwithstanding the previous comments, even for a limited duration therapy some patients may prefer it. Assuming you can get the same kind of efficacy. I think with donanemab that's unlike would be possible and we're not pursuing it given the doses we need and the formulation we have. However, we have a second-generation antibody here that we call N3PG 4, which I think is quite likely to be viable in a subcutaneous presentation and that is our focus of development around N3PG 4. My expectation around that is that it should be able to show comparable amyloid plaque lowering with subcutaneous dosing, as donanemab does with IV dosing. If so given the similarities between the drugs, we would seek accelerated approval pathway for that drug in the future as a sort of a subcutaneous version of donanemab, although it is a new enemy.

Your second question was around the phospho-tau assay and whether that's a significant revenue stream, it's certainly conceivable and we haven't sort of thought through all of our commercial plans around that. But really for Lily and it may be significant for some companies. I think for Lilly though, our focus is on removing barriers for treatment to patients. And so as we think about how we positioned diagnostics and therapeutics in the marketplace, our focus will be on really making sure the most patients possible can get treated appropriately.

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

And maybe just to comment. Thanks, Dan and Tim. On the access and payment environment, I think our priority at Lilly is always going to be how to make it easier for patients to get to a therapy and then we solve for value on the back end. There are clearly benefits in a short-duration treatment like Dan said, with donanemab in Part B. They're going to be watched closely by their physicians initially. Anyway, there are real and important side effects, which require imaging analysis for this class of drugs. And so it's intensively managed disease. But through time, as we've seen with other classes as comfort level will rise in primary care and particular in using therapeutic antibodies to treat Alzheimer's. A more convenient form available at a local pharmacy perhaps for self-injection or injection by a caregiver would be preferred. So our plans line-up with in pursuing both those channels, although in early days, probably the intensive nature of the treatment and specialist nature will favor the infusion. But we're committed to both and we're solving for patient convenient at the end of the day.

Q - Tim Anderson {BIO 3271630 <GO>}

Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks Dave and Dan. Tim, thanks for your questions. Next caller please.

Operator

The next question is from Chris Schott from JPMorgan. Please go ahead.

Q - Chris Schott {BIO 6299911 <GO>}

Great. Thanks very much for the questions. Just one on donanemab and then one on Verzenio. Just -- I guess my bigger question on donanemab is, how you're thinking about the role of A-beta antibodies may be prior to definitive Cognition data being available? So I guess, do you see Cognition data significantly expanding the market opportunity for these products? Or do you anticipate we are seeing broad usage, even in the event well let's just say, the additional Cognitive readouts you see on donanemab where less definitive than what we saw in the Phase 2? I'm trying to see do you think the whole market at this point is going to move to plaque regression or reduction or at least Cognition still very important, I think in terms of the commercial opportunity?

My second question was on the Verzenio update. Just two part here just, when do you think you'll have that incremental OS data for the other 50% of the population? And how

hard is it to identify these higher risk patients as we think about maybe the initial commercial opportunity in action? Thanks so much.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Chris. Over to Dan for donanemab and then Anne for the questions on Verzenio.

A - Dr.Daniel M. Skovronsky

Yeah. So your question is, may I break it in two parts. The first part is like, how important is, in the near term to have additional cognitive benefit data for a amyloid plaque drugs, and then in longer term, what happens, if the confirmatory studies give a negative surprise? So, in the short term I just clarify that, we have compelling clinical efficacy data for donanemab, the only trial of its kind to be successful, positive Phase 2 study and its primary endpoint, showing cognitive benefits for donanemab. That's different unique and exciting published in the New England Journal, that's exciting. And I think that will be helpful even before we have the confirmatory data being in that unique position. There will be some physicians I'm sure as are today who still say I don't want to use a drug until I have cognitive data fine. For those physicians who are willing to make that link between the surrogate efficacy data and the Phase 2 data in donanemab. If you believe that lowering amyloid plaque is a good thing to do, you're going to want the drug that lowers amyloid plaque the most. And I think that's an exciting aspect of donanemab as well. But then we come to the confirmatory studies, I think surely everyone have to acknowledge if for multiple sponsors, multiple drugs are all clearly negative that would be a bad thing and we would retreat and say that this was a wrong way of thinking. I think that's scenario is extremely unlikely. I think the most likely scenario is probably a mixed picture. Some drugs will be better than others. Some trials will reach significance, others might not. You've heard me speak about the confidence in our trial, but we have to see the data. I think in that scenario, that will strengthen, that would be good enough to reinforce the notion that amyloid is an important surrogate in reducing amyloid is a good idea.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dan. Anne on Verzenio.

A - Anne White {BIO 20764375 <GO>}

Yeah. Chris, thanks for the question. And as Dan shared, we are incredibly pleased with what we're seeing out of Verzenio and monarchE data and as we shared key endpoints, such as IDFS have continued to strengthen with further follow-up. And now we have two years of median follow-up. And so very pleased with that and as we shared, we remain very confident. There will be an OS trend, favoring Verzenio in the broader population. So we would work with the FDA to expand our label to include these patients in the future. So obviously, this is event driven and so, the timing of this will be determined by the event rate. So our next planned analysis is in the second half of '22 and this analysis will help us really further inform the timing of that final analysis.

So as you commented the overall survival data in the broader population is still immature. We still have less than 50% of the events needed to do that final OS analysis. But with what we're seeing and again, strong performance in both the high and low Ki67, we remain confident to see this trend in OS favoring Verzenio to replicate. As far as Ki67, good

news here is that, this is really a familiar concept to physicians. It is already accepted as a prognostic factor in breast cancer and it has really easily performed through an IHC assay, so very simple assay. And these are broadly available in the pathology labs. And the assay and the methodology that we used on monarchE is straightforward and proven to be accurate, and really highly reproducible. So our belief is that oncologist will move to quickly adopt this in practice and really this clarity in patients with the highest risk. I think will help to accelerate uptake in this setting. So we look forward to launching in this setting.

A - Kevin Hern {BIO 20557573 <GO>}

Thank you, Anne. Chris, thanks for your questions. Next caller, please.

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 questions. I surprisingly also want to talk about Alzheimer's today. Dan I have three sub parts. First, are you expecting to use interim data from your ongoing Phase 3 as part of the regulatory filing or during the review? Secondly, once the plaque is clear and I think 60% of patients have clearance by 12 months. What rate of onset of new amyloid plaque do you expect subsequently? I'm just trying to understand your expectation on finite duration of dosing versus Biogen's opinion on continued dosing.

And then finally, I'm also trying to reconcile the slide you showed on the nonlinear model, the Conrado model, suggesting a relationship between plaque decrease and a slowing in clinical progression. Are you seeing there's a relationship or you're seeing there's a causality because you might recall, the New England Journal paper on your Phase 2 mentioned, there was no association between plaque and clinical benefit at patients level and Biogen's data suggested similar. Thank you very much.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Umer. Dan?

A - Dr.Daniel M. Skovronsky

Okay. Three great questions, Umer, thanks. So the first question you actively use interim data, I commented that we'll take a safety cut of data in the right way to support that submission. We don't plan to support that submission or do we see the need to support that submission with any looks at efficacy data. We have adequate efficacy data supporting the plaque lowering, which would be the basis for submission of approval under accelerated approval.

Your second question is, once plaque clears how long does it take to come back? We have some data on that, that was also presented at AAIC, I didn't highlight it this morning, but what we found is that off therapy there is very slow negligible really re-growth of

plaque. I think, if you sort of extrapolate it out, it might take 14 or 15 years, like that to re-grow amyloid plaque, average age of patients in this trial is 75. And remember we haven't fully halted progression of disease. So that doesn't feel like a near-term thinking on re-dosing, we necessary keep them clear. But we'll have the ability to follow patients for many years and confirm that.

Finally, I think you've correctly summarized the situation which is that in our initial analysis, we didn't see a correlation and now we are reporting that we do see a correlation. Why is that? And of course, correlation can't prove correlation, so it is just a correlation. So why do we see it now? I think what we learned was quite interesting and that's that the amount of plaque remove depends a lot on how much plaque you have to start with. So if you only have 50 centerlines [ph] of plaque, there's always so much you can remove. If you have 100 centerlines of plaque, based on, you can remove a lot more. So that turns out to be a pretty important confound in these kinds of correlations. The people who are have the more severe disease perhaps longer duration, lower cognitive performance, older age; they might have more plaque at baseline. You can remove more, but they still might be the worst progressors than people who have lower plaque and you remove less. So I think our thinking initially and maybe the field's thinking was a little bit backwards on this, to look for straight correlation between changed, unchanged without adjusting for all of those important of baseline co-variance.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

And our next question is from the line of Andrew Baum. One moment. Please go ahead.

Q - Andrew Baum {BIO 1540495 <GO>}

Thank you. Got two questions, please. Just going back to interim analysis, with TRAILBLAZER out to not so much as user support accelerated that. To accelerate the readout for the full standard regulatory review, you're using a data in disease progression model. Given that you're getting such a rapid clearance of Alzheimer's and that's linked to cognition in those patients who have that. Do we have to assume that the follow-up is going to go out to the full 72 weeks, so is there possibility of early underlying being driven by efficacy in those patients? And then second, perhaps you could comment on the manufacturing capacity for donanemab, as well as the regulatory outlook for P-tau assay, assuming that you attain regulatory approval, on the accelerated? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Andrew. Dan, over to you for those questions.

A - Dr.Daniel M. Skovronsky

Yeah. So Andrew, you've asked a follow-up question here. Important one on the potential, even in the phase of an accelerated review for the accelerated approval rather for plaque lowering, whether we'd still be keen to get that cognitive data bit earlier by pulling forward in the interim on TRAILBLAZER 2. We haven't ruled that out, we also don't have

plans at this moment in time. I think we just need to see, where we are and where the field is but really the maintaining a pristine Phase 3 trial would probably be a pretty high priority particularly if accelerated approval gives the path for patients have access to the medicine, then it becomes less urgent to get that data faster. So that's our current thinking. We've been working hard to make sure we have manufacturing capacity. I feel good about where we are to support launch and growth of donanemab, and hopefully someday N3PG 4 even to follow that. With response, with respect to the commercialization of the P-tau diagnostic, there are different paths forward for in vitro diagnostic, including a lab-developed tester or LDT, which can be done in a centralized location for example under CLIA. And that's a pretty fast path and that's one of the options that we consider.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

Thank you. And next question comes from Louise Chen from Cantor. Please go ahead.

Q - Louise Chen {BIO 6990156 <GO>}

Hi. Thanks for taking my questions. So, first question I have for you is, how do you think about a potential outcome for the national coverage determination of monoclonal antibodies treat [ph] Alzheimer's disease? And then second question is, how would you think about pricing donanemab if it is approved? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Louise. Dan?

A - Dr.Daniel M. Skovronsky

Okay. Thanks two sort of commercially focused questions on donanemab. I mean the first one on the national coverage decision, determination, of course that's important. When -- I think it was widely said that when the first approval came, it was quite broad indication and then subsequently the FDA working with the sponsor focused the patient population. I think there could still be opportunity for further focusing here. And that's one direction the experts at CMS may take, in that case, it could be requiring patients to have evidence of Alzheimer's pathology in the form of amyloid plaques or even tau pathology. As I said before, I think that matches our goals and what we think is right. It'll take some time for that to play out probably over the next nine months or so. And surely we'll be part of some of those discussions and share our data and thinking in the right way. And then on pricing. I think I simply say it's too early to comment on that, we have some time yet.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dan. Thanks for your questions Louise. Next caller please.

Operator

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

Q - Geoff Meacham {BIO 21252662 <GO>}

Morning, everyone. Thanks so much for the questions. Dan you're popular today. So just have a couple more for you. On donanemab, is there a hurdle that FDA has provided in terms of number of patients for safety either for the filing or during the review? And then as the data from TRAILBLAZER matures, what is your estimate on, what the duration of therapy benefit could ultimately be? And then, real quick on tirzepatide, just wanted know, as you guys complete the filing, at this point what's the gating factor as you look at the different geographies and you prepare? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks. Jeff. We'll go to Dan for the donanemab questions and then Mike Mason on tirzepatide.

A - Dr.Daniel M. Skovronsky

Yeah. So with respect to the safety hurdle for donanemab or for any drug really is having adequate exposures and duration of exposures in a broad population to be able to fully assess the benefit risk of a given drug. Now that's not a number, that depends on the particulars of the drug, the population of course that you hope to treat the duration of therapy, of course. But also the particular surround the safety data and the efficacy data that you collect. So it would be nice and easy, I think for sponsors and the FDA, if there was a particular line in the sand that could be drawn, but as I said, it needs to be tailored for each drug based on our current thinking and analysis and discussions. As I said, I think we'll be there comfortably at the end of this year.

Your second question was about I think it was about the duration of benefit as the TRAILBLAZER data mature. I commented on the duration of plaque lowering, which appears to be sustained. But I think Jeff you're getting at the duration of the cognitive benefit. We see a slowing of decline on average, which means that patients are still declining. You could ask are the lines coming together going apart, I think, on some of the cuts of the initial data there might have been a perception that the lines were not diverging at the later time points. I think, as I showed the additional statistical methods and even as we look at the raw data, we're pretty comfortable here that we have lines that diverge over time. And therefore, I would expect that benefit of slowing would continue over time but too soon to have real data on that.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks Dan. Mike, on tirzepatide.

A - Mike Mason {BIO 18347681 <GO>}

Yeah, thanks for the question. In our Phase 3 SURPASS program for type 2 diabetes is done and completed, so the only gaining factor here is how quickly we can summarize the data and submit to the regulators which we plan to do by the end of the year to major global regulators. Thanks.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Mike. Jeff, thanks for your questions. Next caller please.

Operator

Thank you. And the next caller is Carter Gould from Barclays. Please go ahead.

Q - Carter Gould {BIO 20035589 <GO>}

Great. Good morning. Maybe I guess, I'll try to take another stab at the pricing question. I appreciate it's early, but it is sort of the elephant in the room and just maybe if Dave and team could comment, just on the appropriateness of the pricing benchmarks in the space already today in Alzheimer's as you think about it. And then obviously, 3Q has tripped you in the past around Trulicity dynamics. So, just hoping if you could just be offer a little bit more clarity there on as you think about pricing headwinds into 3Q specifically. Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Carter. So we'll go to Dave for the question on pricing for donanemab then Mike on Trulicity pricing dynamics.

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

Yeah. Appreciate the question and we totally get the curiosity, as you understand probably, lot of limitations in what we would say at this stage. One of the reasons for the limitation is, really the ultimate label we have and the value we can demonstrate a customer, is a key input at Lilly for pricing. And we have unfortunately the only study in the space that hit its pre-specified endpoint for disease reduction or disease progression reduction and those are key, as we demonstrated at AAIC, we continue to cut that data. I think there was an earlier question about how we might differentiate an NCD process, but that's one of them as we have this completed study with exquisite biomarker profiles of the product and can continue to elucidate, what donanemab does in the brain of Alzheimer's patients in ways that perhaps others could not and those are inputs as well.

Finally, Lilly has been a leader in value-based concepts and really partnerships to make sure that the appropriate patients can easily access a little out-of-pocket costs, our medicines and we're applying that thinking to this problem as well in the U.S. as well as outside. Our goal isn't to just get an approval, but to make sure that all of the people, millions in the US who could qualify for it, could access it on day one. So, those are all inputs into that process and without throwing out a number here, which wouldn't be appropriate till we get an approval, that's how we think about it. Hopefully, that gives you some color behind the scenes.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dave. And then to Mike on Trulicity for pricing dynamics, pricing trends.

A - Mike Mason {BIO 18347681 <GO>}

Yeah. Thanks for the question. Really, nothing new to report on Trulicity pricing at the beginning of the year we gave guidance that when you take a look at the impact of increased rates in market, second mix and offset by lower utilization 340B, and modest list price increases that for the year we would see low single digit price decline for Trulicity that's what we're experiencing, so really not the new to update at this point in the year.

A - Anne White {BIO 20764375 <GO>}

Yeah, let me just add more general comment on pricing movement through the year and I know we've had numerous conversations also on this and it does there's does tend to be some volatility throughout the year. We do tend to see us patient flow through the healthcare system. More pronounced impact from the coverage gap in the second and third quarter of the year. So you see that dynamic throughout every -- really every year, as Mike said, and we've built those assumptions into our full-year guidance in terms of pricing dynamics for the year and obviously as we have more color and insight we'll provide that. But right now, as we look at the full-year estimate for U.S. pricing dynamic, it's consistent with what we previously discussed in terms of overall erosion, you saw 3% for the first half of the year which is what you should expect for the full-year.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

The next question is from Seamus Fernandez from Guggenheim. Please go ahead.

Q - Seamus Fernandez {BIO 7525186 <GO>}

Great. Thanks for the question. So I really wanted to kind of focus on the palbociclib and prostate cancer and the update that was provided. I think in abstract published at AACR, some of the details were provided with regard to the sort of threshold for moving forward as it relates to the hazard ratio and it's like the hazard ratio 0.64, 80% power, so that with a P-value of 0.1 to I think continued advancing into the next stage of CYCLONE 2. So just wanted to clarify if that information is consistent and driving force for moving forward, that would seem like a robust piece of information to have as we head into that.

And then as incremental to that, just wanted to get a sense of the magnitude of the opportunity that really believes this would represent for Verzenio going forward. And if there are, let's say RB, so the retinoblastoma-related requirements for enrollment or any other biomarker requirements that could limit the size of the patient population.

And then just as a follow-up in terms of the NCD determination. Just wanted to clarify if the pricing of the initially priced product would have any impact on Lilly's ability to independently price its own product and if that's part of the reason why Lilly has argued for the products being treated independently as part of the NCD rather than as a class? Thanks.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Seamus. We're going toss it to Dan first to start on Verzenio and then Anne will follow around that out and then we'll go back to Dan for the NCD question.

A - Dr.Daniel M. Skovronsky

Yeah. You're asking Seamus very smartly about the criteria to expand the study from Phase 2 study to Phase 3 study. I don't think we want to get into the very precise details on what that was. But you're correct that it was a very robust threshold. So we're excited to see that happen. We take Phase 3 start very seriously at Lilly; we don't want Phase 3 failures. So when we have studies like this one in any therapeutic area where we move from Phase 2 to Phase 3 without ever seeing the data. We set aggressive bars that data really have to match to move forward to Phase 3. So you can expect that's what we did here. Anne for more detail.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dan. And for more details thee and also the magnitude of the opportunity we see in prostate.

A - Anne White {BIO 20764375 <GO>}

Yeah. I mean, as Dan said, we were incredibly pleased with this outcome and the recommendation by the DNC and we set very aggressive threshold on this adaptive design and we're impressed that it met that threshold and I think it just continues to be another example of how Verzenio differentiates from the competition. So Phase 3 is open, it's already enrolling patients, we anticipate the results of the analysis in 2024.

And the question on market side, so CYCLONE 2 is, it's a metastatic cancer resistant prostate cancer trial that really targets patients who have not yet received prior novel hormone agent so in earlier settings. So our initial research shows that the addressable market could be in the range of 25% to 50% of metastatic CRPC. So it's depending really a bit on how the market evolves with the use of NHS in that earlier setting. So in the U.S. for example, based on that we currently estimate between 7,000 and 14,000 patients would match that inclusion criteria for CYCLONE 2 and exciting in this space is that, there always being a high unmet need in a large patient population. There's also a long length of anticipated treatment duration. So this could be treatment duration of up to two years or longer. So that's why we're particularly excited about this opportunity as what it delivers there. There is no RB or other biomarker requirements in the study.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Anne. Dan on NCD.

A - Dr.Daniel M. Skovronsky

Last question was on NCD and why did I say that, we think each drug should be evaluated on its own merits, is that a illusion of pricing or something like that, no, my primary focus here is on the patient and the outcomes that a drug could deliver, which even within the same class could be different. Our theory in AAIC's presented data, support that theory is that the amount of amyloid you remove and how quickly you do that is important for predicting outcomes. If that's the case, you can easily imagine different drugs even with

the same class, having different benefits for patients and some of those benefits may be above a threshold for coverage and others may not that's conceivable. Not what I anticipate as the most likely scenario, but we want to be prepared for all scenarios here.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

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

Q - Vamil Divan {BIO 15748296 <GO>}

Great. Thanks for taking my questions, and thanks for all the updates on the pipeline. So maybe a couple sort of separate topics from that have been covered more on the call, so for one on lebrikizumab, actually that one maybe get under-appreciated a little, we got Phase 3 data coming up. Can you just set the sort of expectations and what you're hoping to see; you have a dosing advantage potentially with that product. But obviously you do have pretty formidable competitor over there so. Can you sort of frame what you're hoping to see?

And then tirzepatide, just one quick follow-up, I know you mentioned you started that and you said the SURPASS study for that product. Are you looking at that or have progressed as well? I just, I don't remember you mention that, if not I'm just curious why, why you wouldn't pursue that?

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Vamil. We'll go to Ilya for the question on lebrikizumab and then Mike for tirzepatide.

A - Ilya Yuffa {BIO 21952737 <GO>}

Great. Thank you for the question on lebrikizumab. We're excited for the second half of the year to see the data related to our induction phase for the lebrikizumab across a number of trials. And so what we're hoping to see and expect to see is replicating some of the positive signals we saw in Phase 2 where we have strong efficacy in skin itch, and we believe have a very good safety profile. And so we anticipate that lebrikizumab will have a very competitive profile versus dupixent in a growing, and a significant unmet need and we see lebrikizumab being an important asset for us as we think about not only atopic dermatitis, but our overall presence and strength in dermatology and our growing immunology franchise.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Ilya. Mike?

A - Mike Mason {BIO 18347681 <GO>}

Okay. Thanks for the question. Yes, we have only announced a half study for tirzepatide and that's currently all we're planning on announcing at this point. I think, we're very confident in the opportunity of tirzepatide and have path when you look at patients that have path. There's a large segment that also are obese and obesity, as HFpEF phenotype within this patient population. So I think we feel good about our results we've seen. And our Phase 2 studies that give us confidence that we'll be successful and have path and so right now, our efforts are focused on have path. Thanks.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

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

Q - Steve Scala {BIO 1505201 <GO>}

Thank you. Two questions, first on the Q1 earnings call Lilly said in monarchE, there had been 76 events, 39 on abemaciclib, 37 on control. Can you provide an update with numbers on a like-for-like basis? And then secondly, on your oral SERD, did Lilly see potential for differentiation in the ASCO data? And if so, what differentiation did it see particularly as competitor data and news flow of evolves? Lilly has previously said, it would not pursue a need to SERD. So I'm wondering what is different about yours. Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Steve. We'll go to an for the first question on Verzenio and then Jake for the question on oral SERD differentiation.

A - Anne White {BIO 20764375 <GO>}

Well, thanks Steve. And as Dan shared, we're going to be presenting data from this recent analysis in a medical meeting later this year. So we won't be able to share further details and then obviously due to the embargo. But as you can tell, we are very pleased to see the data continue to strengthen in this latest analysis with more than two years of follow-up. As we said previously, the overall survival data remains immature. So, at this point, what I can share is we have less than half of the events needed, so less than 50% of the events needed for the pre-specified OS analysis, so the data remains immature. Again, we were really pleased even with that majority, see that the patients with highest risk already had this favorable trend. But thanks for the question and look forward to sharing more at meeting later on.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks Anne. Jake?

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

Sure, happy to take a question on SERD. We're pleased with how the drug is performing clinically it's doing everything that we expected it to do from a pharmacology safety and efficacy perspective. I think the data package that we presented at ASCO and that which

we continue to see in the trial subsequent to ASCO place the drug in a vacuum on par with the best agents in development from our peers. But this is not a class of medicine that stands on its own period. This is really a development program and I think as it relates to ME2 is, what I would say is that we're not interested in pursuing a ME2 development program and we stand by that statement and frankly our leadership position in breast cancer in particular with emerging Verzenio data as we've been talking about today, I think put us in a unique position as it relates to this class of medicines. That all having been said, I also think we are a bit more cautious about the long-term role of SERD in this landscape and we're looking forward to some randomized data for the first time from some of our competitors later this year that I think will shed some light on where these drugs ought to fit in the overall treatment paradigm.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

And that comes to Matthew Harrison from Morgan Stanley. Please go ahead.

Q - Matthew Harrison {BIO 17603148 <GO>}

Great. Thanks for fitting me. And I guess two for me. So first, just a follow-up, two parts on the Conrado model. One, do you know regulators view of this model? And then secondly, maybe you can just explain what we're seeing in a little bit more detail looks like you're seeing about 40% regression slowing, at a 100% clearance. I assume this is over 18 months, would you expect that to continue to compound, I'm just wondering why only sort of 40% slowing, when you've cleared all the plaque? And then just a second, follow-up on SERD, any plans to look at that in combination with CDK4/6 or other combinations? Thanks.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks. Matthew. We'll go to Dan for the questions on the Conrado model and then Jake on SERD.

A - Dr.Daniel M. Skovronsky

Yeah, thanks Matthew for the question there. I know we don't have a regulator' view on the Conrado model, but we're encouraged that this model was built as I said earlier, by the Can-D by -- data from the Can D Consortium and it's been around for a while and used for various applications. What we're doing here though, to be clearer, is checking a patient's progression against what we predict their progression would be. So knowing all of their baseline factors, how much would they predicted to have progressed, had they not been on drugs versus how much that they actually progressed. And so that's essentially what you're seeing in the graph. You're right, even with full plaque clearance, there's still some progression. There's only a 40% decrease. Now, that's as bigger, the fact that anyone ever has talked about in Alzheimer's disease. But surely over time, we're going to need additional therapeutics for Alzheimer's beyond just clearing the plaque at least in this stage of disease. And I think that's probably where tau therapeutics come into play. So, that's how we think about. I think earlier, in the disease course it could be quite different

perhaps, if you get it early enough, you could have a 100% disease, slowing progression and in essence to Alzheimer's but that is yet to be proven.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks Dan. Going to Jake for the question on SERD.

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

Yes. The question on SERD, of course, we plan to explore combining overall SERD with CDK4/6 in particular with abemaciclib and we're doing that right now in the context of an expansion cohort of the Phase 1/2 trial. The same trial for which we presented data at ASCO has expansion cohorts that contemplate rational combinations including with abemaciclib.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Jake. Matthew, thanks for your questions. And we've exhausted queue. Back to Dave for the close.

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

Thanks Kevin. Thanks to Dan for answering all those questions. We appreciate your participation in today's call and your interest in the company of course. We continue to see growth with our broad commercial portfolio and we have strong momentum across our core business and supported by a breadth of brands and accelerating classes and robust growth across U.S., Europe, and China.

In addition as you heard today, we believe we have a compelling pipeline with industry-leading opportunities and we remain focused on bringing new medicines to patients and creating value for all our stakeholders.

Thanks again for dialing in. Please follow up with Investor Relations team if you have any questions we have not addressed today, and hope you have a great day. Thanks.

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.