Q1 2021 Earnings Call

Company Participants

- Anat Ashkenazi, Senior Vice President and Chief Financial Officer
- Anne E. White, Senior Vice President and President, Lilly Oncology
- Daniel M. Skovronsky, Senior Vice President and Chief Scientific Officer
- David A. Ricks, Chairman and Chief Executive Officer
- Ilya Yuffa, Senior Vice President and President, Lilly Bio-Medicines
- Jacob Van Naarden, Chief Executive Officer at Loxo Oncology Inc.
- Kevin Hern, Vice President of Investor Relations
- Michael B. Mason, Senior Vice President and President, Lilly Diabetes

Other Participants

- Andrew Baum, Analyst
- Carter Gould, Analyst
- Chris Schott, Analyst
- Geoff Meacham, Analyst
- Gregg Gilbert, Analyst
- Kerry Holford, Analyst
- Louise Chen, Analyst
- Ronny Gal, Analyst
- Seamus Fernandez, Analyst
- Steve Scala, Analyst
- Terence Flynn, Analyst
- Tim Anderson, Analyst
- Umer Raffat, Analyst
- Vamil Divan, Analyst

Presentation

Operator

Ladies and gentlemen, thank you for standing by, and welcome to the Lilly Q1 2021 Earnings Conference Call. (Operator Instructions)

I would now like to turn the conference over to our host, Mr. Kevin Hern. Please go ahead.

Kevin Hern {BIO 20557573 <GO>}

Good morning. Thank you for joining us for Eli Lilly and Company's Q1 2021 Earnings Call. I'm Kevin Hern, Vice President of Investor Relations. Joining me on today's call are Dave Ricks, Lilly's Chairman and CEO; Anat Ashkenazi, Chief Financial Officer; Dan Skovronsky, Chief Scientific Officer; Anne White, President of Lilly Oncology; Ilya Yuffa, President of Lilly Bio-Medicines; Mike Mason, President of Lilly Diabetes; and we'd also like to welcome Jake Van Naarden, CEO of Loxo Oncology at Lilly, who will be joining us today and moving forward to answer your questions about discovery and early-stage oncology efforts he's leading. Now, I'll turn the call over to Dave -- sorry. We're also joined by Sara Smith and Lauren Zierke 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 Form 10-K and subsequent forms 10-Q and 8-K filed with the Security 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 results from the first quarter of 2021.

David A. Ricks {BIO 16504838 <GO>}

Okay. Thanks, Kevin. Lilly entered 2021 focused on expanding our reach to over 45 million patients by scaling our key growth brands around the world; continuing the advancement of our pipeline, following a very successful 2020; and increasing productivity in the SG&A line, while investing in research for sustainable long-term growth. We are pleased with the progress we've made on these objectives in our first quarter, while also delivering hundreds of thousands of doses of our COVID-19 antibodies to patients to help the continued fight against COVID-19.

As we unpack this quarter's results, we will attempt to give you a clear picture of the underlying trends in our core business. We recognize this quarter was noisy, catching the increased consumer stock-in from the Q1 2020 in our quarterly compare and increase COVID-19 therapy R&D spend in 2021. These items, coupled with the FX rate movement and a number of changes to US government purchase agreements for COVID-19 antibodies throughout the quarter, make for a longer earnings call and press release, and we realized for those keeping score on sell-side model accuracy, perhaps some disappointment.

Nonetheless, underneath all that is a strong and growing core business for Lilly and a significant number of positive, even compelling pipeline readouts in the quarter, to support long-term growth across all of our core therapy areas. And we continue to expect topline growth and margin expansion to accelerate throughout this year.

This quarter, revenue grew 16% compared to Q1 2020 or 13% in constant currency. This performance was driven entirely by volume, which grew 17 percentage points. As previously highlighted in Q1 2020, we had roughly a $250 million COVID-19 related inventory build, that is impacting the year-over-year comparison. When excluding COVID-19 antibody revenue and the Q1 2020 stocking benefit, our core business grew 7% for the quarter. Key growth products continue to drive volume and revenue growth, and now represent 52% of our core business in Q1 2021.

Our non-GAAP gross margin was 75.4% in Q1 and 78% excluding the impact of foreign exchange on international inventories sold. Our non-GAAP operating margin was 27.5% for the quarter and 30.1% excluding the FX impact. While foreign exchange on international inventories sold has a modest effect on our Q1 -- on our results in 2019 and 2020, in the first quarter of 2021, we experienced over a 250 basis point of negative impact on our gross margin and operating margin. Recall that is purely a non-cash accounting item.

On the pipeline front, we achieved multiple milestones since our Q4 earnings call, including the Phase 3 initiation of pirtobrutinib, formerly known as LOXO-305 and for additional obesity studies in tirzepatide's SURMOUNT program. The FDA granted Emergency Use Authorization for the administration of bamlanivimab and etesevimab together as a treatment for COVID-19. Positive Phase 3 results from tirzepatide SURPASS 2, 3 and 5 trials in type 2 diabetes and positive Phase 3 results for mirikizumab in ulcerative colitis and baricitinib in alopecia areata.

About a decade ago Lilly made the decision to enter into and invest in immunology with the Phase 3 initiation of ixekizumab, now known as Taltz. Since then, we have added Olumiant in rheumatoid arthritis in several new indications with first or best in category data for Taltz and Olumiant in rheumatology and dermatology. This year, we see further expansion of our immunology strategy with the successful completion of Phase 3 studies of mirikizumab in ulcerative colitis; the first IL-23p19 antibody medicine to demonstrate results in this setting.

We are also excited about lebrikizumab's potential to differentiate from Dupixent on itch, sleep and safety primarily in conjunctivitis, in what is an increasingly large and growing class with meaningful unmet medical need. And we anticipate multiple Phase 3 readouts for lebrikizumab later this year in monotherapy and in combination with corticosteroids. We look forward to potentially reaching increasing numbers of patients in difficult-to-treat immunology conditions in the coming years.

We also entered into several business development deals including the in-licensing of a RIPK1 inhibitor from Rigel Pharmaceuticals and the divestiture of QBREXZA, which along with lebrikizumab was part of the Dermira acquisition last year. We also distributed nearly $800 million in dividends this quarter, with the share -- dividend per share increasing 15% versus last year.

Moving on to slides 5 and 6, you'll see a list of key events since our last earnings call. We announced plans to host a webinar to provide an overview of the Company's commitment

in the areas of environmental, social and governance for the investment community for media and the general public on May 4th, 2021.

Additionally, we announced two planned retirements of long-tenured executives and several additions to our leadership team. I'd like to thank Myles O'Neill, President of Lilly Manufacturing; and Melissa Barnes, our Chief Ethics and Compliance Officer for their leadership and service to our Company. We also extend a warm welcome to Edgardo Hernandez, who will be succeeding Myles; to Alonzo Weems, who will succeed Melissa; and to Diogo Rau, who will be joining Lilly next month as Chief Information and Digital Officer succeeding Aarti Shah, whose retirement was announced last fall.

Finally, we announced the appointment of Anat Ashkenazi, our CFO. Anat has a deep experience having been the CFO of every part of our value chain. For the last four years, Anat has a large -- has led a large portion of our finance organization with all of our divisional CFOs reporting to him, as well as our accounting and financial reporting team, our corporate strategy group and our business transformation office. During this time, Anat worked closely with me, our Executive Committee and our Board of Directors to develop and implement our annual business and long-term strategic plans. I have no doubt that Anat will perform extremely well as CFO of Lilly and expect no changes in our priorities, our strategy or execution given her significant involvement in all those areas.

Anat, welcome to our leadership team and I'll turn the call over to you for our Q1 results.

Anat Ashkenazi {BIO 19888043 <GO>}

Thanks, Dave. Slide 7 summarize our non-GAAP financial performance in the first quarter. As Dave mentioned, revenue increased 16% this quarter compared to Q1 2020 or 7% when excluding the COVID-19 antibody revenue in the Q1 2020 COVID-related stocking benefit representing a good momentum for our core business.

Last year, with the health and safety of our employees, patients and providers in mind, we shifted from in-person interactions to primarily virtual interactions, and began 2021 with few sales reps in the field in the US. We feel good about our capabilities to work with providers virtually and are encouraged as we exited Q1 2021 with the majority of US reps back in the field. As we navigate the early stages of the recovery, we're focused on operational excellence in both virtual and in-personal environment, and are pleased with the volume and share growth in key brands, despite continued pandemic-related headwinds for several classes.

As we look at gross margin, gross margin as a percent of revenue declined 490 basis points to 75.4%. Excluding the impact of foreign exchange on international inventories sold, gross margin as a percent of revenue was 78%, a decrease of 260 basis points, primarily due to the unfavorable product mix driven largely by sales of COVID-19 antibodies and to a lesser extent by lower realized prices on revenue.

Moving down to P&L. Operating expenses grew 11% compared to the same quarter last year. Marketing, selling and administrative expenses increased 2%, while R&D expenses increased 21%, driven primarily by $220 million of investments in COVID-19 therapies. Net

of the COVID-19 expenses, R&D increased 5% driven by continued investments in our late-stage pipeline. Total operating expense growth was less than 3% compared to Q1 2020 when excluding the investments in COVID-19 therapies.

Operating income increased 6% compared to Q1 of 2020. And operating income as a percent of revenue was 27.5% for the quarter, a decline of 250 basis points compared to prior year. This decline was driven entirely by the impact of foreign exchange on international inventories sold.

Other income and expense was income of $35 million this quarter compared to expense of $73 million in Q1 of 2020, driven primarily by a benefit related to favorable European patent settlement for Alimta.

As we noted previously, beginning in 2021, we are excluding the gains or losses due to equity investments from our non-GAAP measures and have provided revised figures for 2020 in our investor workbook to enable year-over-year comparison on that same basis.

Our effective tax rate was 10.8%, a decrease of 210 basis points compared with the same quarter last year. The effective tax rate for both periods was reduced by net discrete tax benefits with the larger net discrete benefit reflected in the first quarter of 2021. At the bottom line, net income and earnings per share increased 16%.

On Slide 8, we quantify the effect of price, rate and volume on revenue growth across the world. US revenue grew 18% compared to the first quarter 2020, while revenue decreased slightly excluding COVID-19 antibodies. Adjusting for the Q1 2020 stocking benefit, the core business grew 5% in the US. These results were driven entirely by volume led by Trulicity and Taltz, partially offset by a mid single-digit price decline. Pricing was a 6% drag on US revenue growth this quarter, driven primarily by Taltz improved access and corresponding higher contracted rates, partially offset by a modest list price increase. Excluding the impact of Taltz win at ESI, we experienced low-single digit net price decline in the US in the first quarter of 2021.

We noted on previous calls that we expected Taltz would experience price headwind in Q1 beyond general rate pressure with improved access position. There were two pieces of the ESI impact. The first, existing patients already covered through medical exceptions were moved to the newly contracted rates, a one-time step down in prices as we move through 2021. In addition, we were pleased with the uptake for new patient at ESI, at the contracted rate and we expect that that population will grow meaningfully over time.

There is always a near-term impact when we have a step -- a significant step-up in access, and this win nearly doubled our commercial access. We're encouraged by the volume growth we saw in the first quarter and believe Taltz will return to net sales growth in the second quarter, which should continue to accelerate as we move through the year as the volume growth from the major access upgrades outpaces the related pricing headwinds.

Beyond Taltz, segment that was not a major of US price performance in the first quarter has increased utilization in the more highly rebated government segments was offset by

lower utilization in the 340B segment primarily for diabetes portfolio. While mid-term trends are stable at present, given the increase in variability and payer mix, we continue to expect quarterly variability in reported net price changes. We also expect Taltz price impact to moderate as we move through the year and overall low-to-mid single digit total net price decline in the US for the full year.

Moving to Europe. Revenue grew 15% in constant currency. Excluding COVID-19 antibody revenue and the impact of Q1 2020 COVID-related stocking, revenue grew 5% in constant currency. Despite lockdowns in number of European countries and driven primarily entirely by volume growth for Alimta, Trulicity and Taltz. We're pleased with the momentum of our business in Europe and are looking forward to continued strong growth in 2021.

In Japan, revenue decreased 8% in constant currency driven entirely by decreased volume for Cialis and Forteo. Net of the impact for those post-patent expiry products, Japan grew 5% in constant currency driven by Verzenio, Jardiance in collaboration with BI and Olumiant.

In China, revenue grew 26% in constant currency, driven by 32% volume growth, primarily from Tyvyt and to a lesser extent our diabetes portfolio. We are excited about the momentum in China as our business accelerated significantly the past two quarters. Tyvyt continues its strong growth. Trulicity and Olumiant are now in the NRDL, and we look forward to launch uptake for Verzenio.

Revenue in the rest of the world decreased 1% in constant currency, driven primarily by continued erosion of Cialis.

As shown on Slide 9, our key growth products continue to drive impressive volume growth. Despite the Q1 2020 COVID-related stocking benefit impacting year-over-year growth, these newer medicines delivered over 9 percentage point of growth this quarter, with COVID antibodies also contributing roughly 14 percentage points of growth. The strong volume growth was partially offset by post-LOE products, as well as insulin. This volume growth was also meaningfully impacted by the Q1 2020 stocking benefits.

Slide 10 highlights the contribution of our key growth products. In total, these brands generated approximately $3.1 billion in revenue this quarter and made up 52% of core business revenue.

We are particularly encouraged by Trulicity's performance. Three years ago Trulicity was the number two injectable GLP-1 in the US market at roughly 40% share of market. Weekly scripts for the class were approximately 180,000, and a new weekly injectable entrant had just launched. Since that time, Trulicity has become the most prescribed GLP-1 in the US with the 48% share of the injectable market in a class that is now twice the size at roughly 360,000 weekly scripts.

Trulicity continues to have the highest insurance of any diabetes medication oral or injectable with the additional dose of 3 milligram and 4.5 milligram providing the

potential for Trulicity to both extend the time of therapy for existing patients and compete for new patients as demonstrated by the new to brand share of market have increased more than 4 points since the launch of these additional doses in September 2020.

As we start 2021, we are pleased with Trulicity's ability to outgrow the injectable class and establish all-time highs in new therapy starts, as well as total market share. We see meaningful opportunity for continued robust class growth for GLP-1s, as they are still less than one in 10 Diabetes script. And have significant opportunity for further penetration in the first injectable space as well. With more positive readouts from the tirzepatide in type 2 diabetes this quarter, we remain focused on sustaining Trulicity leadership position, accelerating class growth and providing continued innovation in the incretin space.

On Slide 11, we provide an update on capital allocation. In Q1, we invested nearly $3 billion to drive our future growth through a combination of business development, capital expenditures and after tax investments in R&D. In addition, we returned nearly $800 million to shareholders via dividend. We are focused on utilizing our cash flow, our strong cash flow to develop the next wave of new medicines through both internal and external sources as highlighted by the recently completed in-licensing of the RIP kinase 1 inhibitor from Rigel Pharmaceuticals. We will remain active in assessing the in-licensing opportunities, as well as bolt-on acquisitions, where we believe we can create shareholders value and enhance our future growth prospects.

Turning to our 2021 financial guidance on Slide 12. We are updating our GAAP and non-GAAP guidance. We continue to support healthcare professionals navigating the ongoing pandemic and driving broad vaccination to enable return to normalcy for healthcare systems in the second half of the year. Despite some therapeutic class still at or below pre-COVID baselines for new therapy starts and the highlighted inventory impact on year-over-year growth, we are confident with the performance of our core business.

We are increasing our full-year revenue outlook by $100 million to reflect the FX benefit realized on the topline in the first quarter. We are however narrowing the range for COVID-19 antibody revenue from approximately $1 billion to $2 billion, to $1 billion to $1.5 billion for the year based on the rollout of the vaccine across major markets, current antibody utilization rates, existing US government bamlanivimab supply and the transition to only supply bamlanivimab and etesevimab administered together in the US. We believe this update range contemplates a variety of potential scenarios. We recognize that situations across the globe can evolve quickly and we'll plan to adapt as required moving forward. The net impact of these changes is an updated revenue range of $26.6 billion to $27.6 billion.

Our outlook for gross margin percent remains unchanged with the impact of COVID-19 antibodies diluting our total gross margin percent by approximately 100 basis points. For research and development, we're increasing our range from $6.5 billion to $7.7 billion, to $6.9 billion to $7.1 billion. This reflects an increase of $100 million in COVID-19 antibody expense to support the advancement of a third antibody LY-1404 as we continue to address the COVID-19 pandemic; and approximately $300 million on the core business driven by investments in donanemab for the expansion of the Phase 3 TRAILBLAZER 2

study and the initiation of the new Phase 3 study TRAILBLAZER-ALZ 3 in asymptomatic Alzheimer's patients.

Our investments in donanemab is consistent with our R&D strategy to continue to bolster our pipeline to ensure long-term growth. And based on the strength of the data, invest meaningfully in innovative molecules that we believe have the potential to deliver practice changing data that could significantly improve patient outcomes in areas of high unmet need. We're increasing our non-GAAP range for OID to an expense of $100 million to $200 million to reflect the Alimta patent settlement in Europe, I noted earlier, while our GAAP range is now income of $150 million to $250 million, which reflects the impact of equity investment gains in the first quarter. We are lowering our effective tax rate to approximately 13% to reflect higher discrete tax items in the first quarter and the lower base rates.

We're lowering our non-GAAP operating margin guidance to approximately 31%. The decrease in operating margin is driven entirely by the decreased investments in Alzheimer's for donanemab. Our longer term margin expansion remains unchanged as we expect continued operating margin expansion to mid-to-high 30s. Our GAAP operating margin is expected to be approximately 26%.

Finally, the non-GAAP range for earnings per share is now $7.80 to $8. The increase on the lower end of the range reflects the net benefit for the core business related to the changes to OID and tax rate, as well as increased revenue, offset by increased R&D for investments in donanemab. The reduction in the upper end of the range reflects the narrow revenue range and increased R&D expense for COVID-19 therapies.

Our GAAP EPS is expected to be in the range of $7.03 to $7.23, which reflects an increase to acquired IPR&D related to completed business development transactions, other specified item related primarily to asset impairment, COVID-19 inventory charges and acquisitions integration costs, as well as the benefit from net gain on investments in equity securities. We're confident in our ability to achieve our 2021 revenue goals for the core business, while also delivering operating margin expansion and mid-teens EPS growth.

As we move forward, I would encourage you to look at trends in our core business for the first half of the year given the significant variability we saw across the period in 2020. As a reminder, revenue performance in the second quarter of 2020 was impacted by the reversal of largely all the $250 million COVID-related stocking benefit from Q1 of 2012, as well as an additional $250 million due to the significant decline in new patients prescription as healthcare utilization decreased and systems temporarily closed down the phase of a surge in pandemic.

As we look at underlying volume and share trends across our key products, we are confident in our full year outlook for the core business. And the pipeline successes in the first quarter only furthers our conviction and our mid-term and long-term outlook for continued revenue growth and operating margin expansion.

Now, I will turn the call over to Dan to highlight progress in R&D.

Daniel M. Skovronsky {BIO 15349505 <GO>}

Thanks, Anat. 2021 is clearly off to a very positive start for R&D at Lilly with strong pipeline progress already and more potential catalysts on the way.

Before I get into the broader portfolio update, I'll spend a few minutes highlighting results from tirzepatide's first four topline readouts from the Phase 3 SURPASS program, including the strong results from SURPASS 2, the head-to-head trial with semaglutide 1 milligram. This program is aptly named, as we've seen tirzepatide surpass our expectations through these initial readouts, displaying significantly greater hemoglobin A1C reduction, weight loss and percent of patients reaching normal glucose levels than any GLP-1 on the market.

On Slide 13, you can see impressive performance in the efficacy estimate analysis in glycemic control for tirzepatide, with each dose demonstrating superiority in each trial across a range of patient populations, comparators and background medications. A clear highlight is the impressive A1C reduction of the 5 milligram dose across each of these three -- each of these different patient populations, while the higher doses provide additional glucose control up to and surpassing 2.5% A1C reductions.

Moving to Slide 14. You can see how tirzepatide performed across all three doses in terms of patients achieving HbA1c below 5.7%, a normal glycemic level seen in people without type 2 diabetes. We believe this is an exciting finding that may reset expectations for the impact diabetes medications could have for patients. Using the efficacy estimate analysis across SURPASS 1, 2 and 3, we see about half of the patients on the 15 milligram dose of tirzepatide achieved this remarkable level of HbA1c control.

In SURPASS 5, which focused on patients on background insulin glargine, 62% of patients on 15 milligram tirzepatide achieved this level of A1c, compared to only 3% of patients in the placebo group. Remember, this is a patient population on background basal insulin with an average duration of diabetes of over 13 years. Achieving this level of glucose control in such a population is something that prior to GIP GLP-1 agonist like tirzepatide, we did not even contemplate as possible.

On Slide 15, we show the efficacy estimate analysis for weight reduction across the four studies. Here again we see levels of efficacy that previously were thought unobtainable with the incretin therapy in type 2 diabetes patients. As we and others have discussed, studies like AVORDO-11 [ph] and SUSTAIN FORTE have begun to show the limit of what fully hitting the GLP-1 mechanism can accomplish for weight loss and A1c. There appear to be diminishing returns as doses of GLP-1 alone fully saturate the GLP-1 receptor-mediated mechanism and a flattening of the dose response curve occurs.

And then you look at this Slide, including importantly SURPASS-2 and you can see quite clearly that there's something different going on here. As the dual GIP GLP-1 receptor agonist is beyond the flattening of the dose response curve of GLP-1 performance, which we believe evidences the power of adding in the GIP mechanisms. Highlights from these studies include the 15 milligram dose, delivering 14% weight reduction in SURPASS-3, noting here a weight gain of 3% on insulin degludec comparator. The 15 milligram dose

nearly doubling the weight reduction of semaglutide 1 milligram in SURPASS-2, and strong performance from the 5 milligram and 10 milligram doses with statistically superior weight loss, even as high as 11% on the 10 milligram dose versus placebo or active comparators.

We are encouraged that in these 40-week and 52-week studies, we haven't yet seen the weight loss curves plateau on the higher doses. It's really exciting to think about how tirzepatide could potentially perform with the longer duration of treatment that we'll see in future studies. We had a lot of confidence in the efficacy data coming out of Phase II, but there was a lot we didn't yet know about safety and tolerability. Recall, for example, that the primary Phase 2 trial had only about 200 patients on therapy and patients were only on therapy for 26 weeks.

As we look at Slide 16, we've been pleased to see through these four SURPASS readouts that the overall safety profile was similar to the well-established GLP-1 receptor agonist class and the most commonly reported adverse events were GI related and mild-to-moderate in severity. We're particularly encouraged by the potential impact of the optimized dose escalation scheme; and accordingly, by the tolerability profile observed in the Phase 3 program, which improved greatly in comparison to Phase 2, including the lower rates of nausea, diarrhea and vomiting that we've seen, consistent with what we saw in Phase 3 studies for other well-tolerated and highly used incretin therapies, including our own Trulicity. In addition, we're pleased with the discontinuation rates due to adverse events, which have ranged from 3% to 11% across doses in these studies.

Stepping back from the data a bit, we're excited about the safety and efficacy results across all doses, but perhaps especially so for the efficacy of the 5 milligram dose, which is performed well in each study including showing superiority to semaglutide 1 milligram in SURPASS 2 on both A1c reduction and weight loss. I think these data show that the 5 milligram dose could be a great first incretin that can potentially deliver best-in-class efficacy with tolerability that is as good or better than other leading incretins. So we have the low maintenance dose of 5 milligrams that, if approved, could potentially be appropriate for many patients with physicians, knowing they could have higher doses available as they continue management of disease.

Tirzepatide could provide patients with the opportunity to set treatment goals that might surpass what was previously thought possible in type 2 diabetes, both in terms of getting patients to normal glucose control, which has never been contemplated as a potential treatment goal, as well as for impressive weight loss, with the highest dose of tirzepatide having roughly doubled the weight loss of semaglutide 1 milligram in SURPASS-2.

Today, type 2 diabetes is largely a treat-to-fail disease. With these results, tirzepatide, if approved, could potentially provide doctors options to enable early control of glucose and weight. This has the potential to translate to improved levels of end organ protection and a more meaningful reduction in disease complications that has yet been seen. We'll be testing this potential for tirzepatide in ongoing and planned studies in diabetes, obesity, heart failure and NASH. Accordingly we've now initiated SURMOUNT 2, 3 and 4 for tirzepatide in obesity and topline results from SURMOUNT 1 are expected next year.

Moving back to diabetes. The topline readout for SURPASS-4, which is in a high cardiovascular risk population and we believe will provide an important contribution to our CV safety assessment, is the gating trial for global submissions in type 2 diabetes. Completion of this trial has always been contingent on accruing a pre-specified number of CV events. We've achieved the necessary events, which triggers bringing patients in for final treatment and safety visits before moving the trial to completion. Based on this update, we anticipate a topline readout by the middle of this year.

We look forward to disclosing the results of SURPASS 1, 2, 3 and 5 at the ADA 2021 Virtual Meeting, which will include a 90-minute ADA symposium featuring these results the morning of June 29th. While we're excited with the progress of tirzepatide, we think innovation in the incretin space is not over. At ADA, we'll also be discussing preclinical and Phase 1 data for our glucagon GLP GIP tri-agonist, also known as GGG, which we're pleased to announce will be moving into Phase 2 later this quarter.

We've previously commented that in this space we have a high bar for progressing molecules in development, one that has been raised recently by tirzepatide. While it's still early, we're advancing GGG to Phase 2 based on our belief that it could exceed the benefits seen with tirzepatide. With our GGG molecule, we expect to see even more weight loss than what can be achieved with tirzepatide, while preserving glucose lowering efficacy.

In addition, due to glucagon's direct action on the liver, we'd also hope to see benefits in NASH. Consequently, our ambitious Phase 2 program is designed to evaluate GGG for obesity, type 2 diabetes and NASH. In addition to our next-generation incretins, we're also very excited by our novel weekly insulin basal insulin FC. Thanks to Lilly's work on Trulicity, weekly incretin therapy is now the standard of care in the GLP-1 space. And together with tirzepatide, we hope incretin-based therapies will become the standard of care in the first injectable space for people with type 2 diabetes.

For those people who need basal insulin therapy in addition to their incretin therapy, we'd like to make weekly insulin therapy possible, ultimately avoiding daily injections completely. We'll give an update at ADA on our novel weekly basal insulin. We plan to have an investor call on the morning of July 1st to discuss the data releases at ADA for tirzepatide, GGG and weekly basal insulin.

While the progress in our diabetes portfolio is compelling, Lilly has continued to advance the rest of our pipeline this quarter. Slide 17 shows select pipeline opportunities as a April 23rd, and Slide 18 shows potential key events for the year. In addition to the progress on tirzepatide I just discussed, major developments since our last earnings call include progress with donanemab on multiple fronts.

In terms of data, we presented detailed results at ADPD showing the donanemab met its primary endpoint significantly slowing cognitive decline compared to placebo on the integrated Alzheimer's Disease Rating Scale, a composite measure of cognition and daily function in patients with early symptomatic Alzheimer's disease. The data from secondary analyses showed donanemab consistently slowed cognitive and functional decline with

ranges between 20% and 40% in all secondary endpoints with nominal statistical significance at multiple time points compared to placebo.

On the clinical front, as we discussed in detail on our call last month, we expanded TRAILBLAZER-ALZ 2 to be a Phase 3 study, and it's now enrolling quickly. And today, we're announcing that we will start a new Phase 3 study TRAILBLAZER-ALZ 3 in asymptomatic Alzheimer's disease. This trial is anticipated to begin enrollment later this year. Our goal here is to enroll patients who already have Alzheimer's brain pathology, but don't yet have any clinical symptoms. The study will have development and progression of Alzheimer's disease symptoms as the primary endpoint. And we anticipate it will take approximately three years from completion of enrollment to reach a sufficient number of events. We'll be testing if a short course of donanemab treatment at the start of the trial can prevent progression in a substantial fraction of patients over the subsequent several years. These types of trials are extremely challenging to enroll and conduct. But here we are buoyed by our expertise and biomarkers including both PET scans and importantly our plasma P-tau217 assay.

On the regulatory front, based on feedback from the FDA, we currently do not see a path forward for near-term submission and approval based on the first TRAILBLAZER-ALZ study alone. As you know, the unmet need in Alzheimer's disease is significant. So while we remain focused on speeding up enrollment and completion of our second pivotal study TRAILBLAZER-ALZ 2, we are continuing to actively engage with the FDA and are fully exploring any opportunities for early submission.

Another highlight this quarter was the initiation of pirtobrutinib's Phase 3 program with study start in chronic lymphocytic leukemia as monotherapy. We're also proud of the continuation of our work against COVID-19, including a planned transition from bamlanivimab alone to the administration of bamlanivimab and etesevimab together for the treatment of COVID-19 in the US, accomplished by first gaining Emergency Use Authorization for bamlanivimab and etesevimab administered together in February and then a request for ratification of the EUA for bamlanivimab alone, which FDA subsequently granted.

We also submitted bamlanivimab and etesevimab administered together for regulatory review in Europe and we initiated the evaluation of bamlanivimab with VIR-7831 in collaboration with VIR and GSK, as well as started trials with the new potentially broadly neutralizing antibody LY-1404 in collaboration with AbCellera, in case new combinations are needed to fight variance.

We announced topline Phase 3 results evaluating baricitinib on top of standard of care, which did not meet statistical significance on the primary endpoint for treatment of COVID-19, but did result in a significant reduction of death from any cause by 38% by day 28. And baricitinib received regulatory approval in conjunction with the remdesivir as a treatment for COVID-19 in Japan. Our work on tirzepatide, donanemab and pirtobrutinib brings great potential for patients in the long-term and is highly prioritized at Lilly.

Our work on COVID-19 is another clear highlight where we moved quickly to help address an unmet medical need in the midst of a pandemic. We're optimistic though that this need will wane in the coming years. Beyond these significant efforts, there has been progress across many other commercial stage and clinical stage assets. Starting in oncology, we're pleased with the approval of selpercatinib for non-small cell lung cancer and thyroid cancer in Europe.

We're also pleased that the results of monarchE, our adjuvant breast cancer study are now submitted in Japan along with Europe, China and the US. As you know, the primary endpoint for the study was invasive disease-free survival, which we hit at the interim analysis. As anticipated, this hazard ratio continues to strengthen over time as more events have accrued. Important secondary endpoints of the study include distant relapse-free survival and overall survival.

For the US submission, the FDA has noted and we agreed that the OS data are immature and thus unreliable as we shared in the JCL publication last year. FDA therefore asked us to see an updated OS analysis during the review cycle to determine that OS is trending in favor of Verzenio. Given the robust distant relapse-free survival data, we're highly confident that the overall survival data will eventually reflect and reinforce the survival benefit, but it takes time for these events to accrue, especially in the adjuvant setting.

In immunology, we have positive Phase 3 readouts for baricitinib and alopecia areata, a disease with significant unmet medical need and we look forward to regulatory submission starting in the second half of this year. We also announced that the FDA extended the review period for baricitinib for atopic dermatitis by three months, another disease where we think JAK inhibition could potentially alleviate important unmet medical needs.

With mirikizumab, we reported positive Phase 3 results in ulcerative colitis in the 12-week induction study, hitting the primary endpoint and all key secondary endpoints. And we look forward to seeing the maintenance data early next year. We also have updates of the mirikizumab psoriasis program. While the Oasis program generated positive results with safety and efficacy similar to other IL-23p19s, we believe the psoriasis market is well served with highly effective treatment options, including Taltz.

Lilly's immunology strategy is to focus our new molecules in indications on areas where patients have significant unmet needs, not merely adding new options or leveraging commercial presence to create a space where effective solutions like Taltz already exist for patients. Therefore, we will not pursue submission in mirikizumab in psoriasis, but instead, we'll focus our efforts on the ulcerative colitis and Crohn's disease indications where unmet medical need is higher and where we believe the potential of the IL-23p19 mechanism to create a new standard of care is greater.

In addition to late-stage progress, our early stage portfolio continues to advance, with the introduction of five new Phase 1 assets in the attrition of two. In addition to the progress we've made in just the first few months of the year, we anticipate important developments for the remainder of 2021, including the final readout for tirzepatide's Phase 3 type 2

diabetes program SURPASS 4, noted earlier, Phase 3 results for Jardiance in HFpEF and for lebrikizumab in atopic dermatitis. Regulatory actions for Jardiance for HFrEF, Verzenio in the adjuvant setting for ER-positive breast cancer, baricitinib for atopic dermatitis and tanezumab for osteoarthritis pain, where we previously noted, our disappointment in the outcome of the tanezumab advisory committee.

The presentation of Phase 1 data for our oral SERD, the initiation of Phase 1 for Bcl-2 inhibitor and for KRAS G12C inhibitor, along with the filing of an IND for a next-generation RET inhibitor later this year, as we announced at AACR and the Phase 2 readout for zagotenemab, our anti-tau antibody for early Alzheimer's disease. We believe our continued pipeline success drives increasing visibility to meaningful long-term growth and we look forward to continued progress across our portfolio in the coming quarters.

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

David A. Ricks {BIO 16504838 <GO>}

Thanks, Dan. Before we go to Q&A, let me briefly sum up the progress we've made to start the year. Amidst several moving pieces and a challenging healthcare environment, we are excited by the momentum we are seeing. our business grew 16% in the first quarter with the core business growing 7% adjusted for COVID-19 antibody revenue and last year's COVID-19 related inventory stocking benefit. Our topline growth continues to be strong, driven strongly by volume across our key growth products which account for more than half of our core business.

Net of the significant impact from foreign exchange on international inventories sold, our operating margin was in line with our expectations as we continue to expect operating margin expansion throughout the year and further expansion in years to come. We made significant progress developing new medicines with many more data readouts expected this year. Advances for tirzepatide, donanemab, pirtobrutinib, Verzenio, mirikizumab, Retevmo and Olumiant serve as a reminder of the breadth and depth of opportunities we have to sustain robust long-term growth. We returned nearly $800 million to shareholders being an increased dividend reflecting confidence in the ongoing strength of our business.

I want to say thank you to my Lilly teammates, whose commitment to excellence and dedication to our purpose of bringing innovative new medicines to patients is inspiring, and drove these accomplishments amidst ongoing pandemic headwinds. While our people, healthcare providers and patients continue to face near-term challenges associated with COVID-19, our long-term outlook is as bright as ever.

This concludes our prepared remarks. And 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. Tony, can you please provide the instructions for

the Q&A session, and then we're ready for the first caller.

Questions And Answers

Operator

Thank you. (Operator Instructions) Our first question comes from the line of Chris Schott with J.P. Morgan. Please go ahead.

Q - Chris Schott {BIO 6299911 <GO>}

Great. Thanks so much and appreciate all the color on today's call. I'm just going to two on the pipeline. I guess, first one Verzenio, did I hear that you mentioned FDA is looking for updated OS data as part of the review? So I just wondering when you have that data and does that push out approval timelines any meaningful way that we need to think about.

And then the second one I had was on tirzepatide. I guess, in light of the data you've seen from the SURPASS studies, does that -- has that changed how you think about what patient populations you'll focus on from a commercial standpoint or your go-to-market strategy and I guess as part of that as we think about tirzepatide coming to market, do you expect substantial switches from Trulicity or is tirzepatide growth more about the new patient starts and kind of expanding the market? Thanks so much.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Chris. We'll go to Anne for the Verzenio question and then Mike on fro tirzepatide.

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

Well, thanks, Chris, for the question on Verzenio. And so we will be delivering this dataset to the FDA without delaying our standard review timing. We can't really comment on what the FDA will do with the data or the application, but these discussions are progressing as planned. Important to note as the data matures, I think, as Dan said, given the strength of the DOFF hazard ratio remember with 0.6, 0.7 hazard ratio with a very strong p-value, we are highly confident that the OS will trend in favor of Verzenio.

So really what we believe we're discussing is when that will occur. So, obviously, as I said, we can't comment on the discussion with FDA, but we do look forward to working with them on bringing this medicine to patients. And maybe just a comment to reference how immature this data is, at the time of the interim analysis that we published in JCO late last year, there were 39 deaths in the edema arm and 37 in the control arm. So that makes it really challenging to interpret this data when there's over 5,000 patients in the study. Thanks for the question.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Anne. Mike?

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

Chris, thanks for the question. No, the tirzepatide results have not changed the way we want to position tirzepatide in the marketplace. We're obviously very pleased with those results. We're also just really blessed to have both Trulicity and tirzepatide. Our goal will be to maximize our entire incretin portfolio. Trulicity has established a strong market position. And I think the best data to support that is just how we've been able to grow share of market in the face of (inaudible). So it has a strong position in the marketplace and that will remain.

But now, as we think about tirzepatide, the dual incretin mechanism that GIP component is really a game changer. Dan went through the results, but we just haven't seen the ability to return someone living with type 2 diabetes whether they are late or early someone with type 2 diabetes progression back to normally one seeing effect we were able to get 50% to 60% people back is really incredible. Also weight loss at the highest dose up to 14%.

So when you just take a look at that and you take a look at the fact that 90% of people who live with type 2 diabetes are overweight or obese, they can really benefit from early treatment with type 2 diabetes. So the real question is, why would you want to put them on something else early on and why we do want to wait for them to have those benefits. So we see tirzepatide has the potential to really transform the market, driving earlier use of incretins in particular tirzepatide dual mechanism and really expand the incretin market. So I think tirzepatide will clearly win some new patients that would have went on to Trulicity, you have some people who were may be not performing well or not -- are needed more efficacy that will go on to tirzepatide. But clearly, our focus will be to profoundly change and disrupt the type 2 diabetes marketplace by driving an earlier use of incretins with tirzepatide.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

Yes, our next question comes from the line of Geoff Meacham with Bank of America. Please go ahead.

Q - Geoff Meacham {BIO 21252662 <GO>}

Good morning, guys. Thanks for taking the question. Also I have two pipeline ones. Just wanted to get your perspective on mirikizumab, the decision to focus on just IBD. You have good head-to-head data in psoriasis. So, is it more of a commercial focus or is it that you want to focus more on Taltz in psoriasis? And then in Alzheimer's, you have zagotenemab data in the second half of this year. How are you thinking about the opportunity to combine potentially with donanemab? I wasn't sure what steps need to happen prior to thinking about that type of trial and maybe from a regulatory perspective, what do you think would be a gating factor? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Geoff. We'll go to Ilya for the first question, and Dan for the question on Alzheimer's.

A - Ilya Yuffa {BIO 21952737 <GO>}

Great. Geoff, thank you for the question. On mirikizumab, really we see the greatest opportunity for unmet need for patients and we've said all along we believe that mirikizumab has the greatest opportunity in GI in IBD and ulcerative colitis and Crohn's disease. We were pleased with the LUCENT-1 results. And so, we're looking forward to seeing the maintenance data at the early part of next year.

In terms of psoriasis, as we take a look at the market and unmet need, we do continue to believe that Taltz is the gold standard and best in disease. And I believe that really is a market well served. And so the decision from a portfolio standpoint is to focus our efforts in places where we believe we can have a greatest unmet need and GI is where we're focused for mirikizumab.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Ilya. Dan?

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

Yeah. Thanks, Geoff, for the question on zagotenemab, our anti-tau antibody. Before I come to combinations, maybe I just handicap this Phase 2 trial quickly. The pro here in favor of tau is clearly a genetic validation and pathologic validation of the target, it's a great target for Alzheimer's disease. The cons here that we have to acknowledge is data from other companies, tau antibodies which hasn't been particularly promising and the difficulty in hitting the tau target in the brain. We have a differentiated antibody here that binds just aggregated tau, so perhaps there is reason to think we could get different results.

We're certainly eagerly awaiting those data in the second half of the year. And you're exactly right, if we see efficacy, combination would be an important consideration here. For sure, the general theme of combining an anti-amyloid drug with an anti-tau drug is a good one, particularly when you have a drug like donanemab where you can completely clear amyloid plaques with a limited duration of therapy and then perhaps at that moment intervene with a anti-tau drug. I do think that's the future something we're actively considering pending, of course, the data on the tau antibody.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

Thank you. Our next question comes from Vamil Divan with Mizuho Securities. Please go ahead.

Q - Vamil Divan {BIO 15748296 <GO>}

Great. Thanks so much for taking the questions. Maybe one on Taltz, maybe just a little more clarity or color on the pricing dynamics there. You mentioned kind of picking return to net sales growth in the second quarter in an accelerating. I'm just trying to think about as we think about full year dynamic, sort of, I know get product level guidance, how you think about sort of the kind of full year comparison 2021 to 2020. I assume you're expecting growth year as a whole. But if you could just clarify is that contract with ESI, not sure is that a full year contractor, does that go beyond one year I'm just trying to get a sense of sort of pricing dynamics in 2022 and 2023 and if we should expect another step down?

And then one quick follow-up just on the comments around TRAILBLAZER-3. I don't know if you could maybe just share a little more in terms of the number of patients you're looking to enroll on that trial, just looking to get a sense of how long the enrollment might actually take. Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Vamil. We'll go to Ilya for the question on Taltz and kind of the full-year picture and then Dan on TRAILBLAZER-3.

A - Ilya Yuffa {BIO 21952737 <GO>}

Sure. So on Taltz, (inaudible) we're really pleased about the progress we're making on Taltz and the growth that we're seeing with the step-up in access, upgrades, ESI and beyond. And so, as we take a look even though that we've had some price impact in Q1, there are some elements there where we have a number of patients that were on medical exception that are now in the rebated contract that we have with the ESI. Of course, we're also seeing an increase in overall volumes with ESI. What's encouraging is that we're not only seeing improvements in overall volume based off of switches, we're also seeing significant improvement in our new therapy starts. And so, we're in dermatology now the leading share in dermatology with over 19% share. And then in rheumatology, we're almost doubling our share from previous year.

And so as we think about the year in terms of growth, we do believe we'll get to net sales growth in Q2 and we'll continue to accelerate that volume growth throughout the year. The contracting that we have for Taltz is -- it goes beyond one year. And so, we're encouraged about the volume growth of over 20% now, and we continue to see encouraging signs in the market.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Ilya. Dan?

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

Yeah. Thanks, Vamil, for the question on a TRAILBLAZER-3 and our enrollment goals here. We probably don't get into too many details here, but we are, of course, expecting this to be a large trial involving thousands of individuals. But yet, we also set very ambitious enrollment goals. And while we don't have all the details planned out on how to achieve this, our goal is that we should be able to enroll this trial in about a year. That's pretty exciting to contemplate.

And Alzheimer's prevention trial is something that makes great sense given the science and the biology here, and what we know about the onset of Alzheimer's disease and its relation to years of having amyloid plaque in the brain. But there have been two major drawbacks that have not made these trials really very practical. First is finding the patients that has gone from impossible before our introduction of amyloid PET scan to possible, but really hard with amyloid PET scans as we experienced firsthand in A4 trial to now something that's eminently feasible with our advent of the plasma tau217 assay, that's a huge advance that just unlocks this trial.

The second is, if you think about this population, which is not experiencing symptoms is a bit younger than Alzheimer's population and introducing a therapy that is likely an infusion that they take for the rest of their lives, that's also a pretty significant hurdle. Again, we've I think aggregated that risk with donanemab and a limited treatment duration to give lasting plaque clearance. So excited about the TRAILBLAZER-3 trial.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

Thank you. Our next question comes from Seamus Fernandez with Guggenheim. Please go ahead.

Q - Seamus Fernandez {BIO 7525186 <GO>}

Great. Thanks so much for the question. So just first off, a question for Dave. Dave, as you think about some of the various proposals that are in Congress currently, could you just give us your thoughts on the tax proposal? And maybe Anat could give a little bit of the potential implications for Lilly. And then, separately, there is obviously a lot of controversy swirling on drug pricing. Just wanted to get your sense of the proposals that are out there currently. And if the industry is poised to or ready to step-up with a with a more reasonable proposal.

And then just the second question is on the JAK inhibitor space and Lilly's opportunity with lebrikizumab, particularly in atopic dermatitis, there's a bit of a compare and contrast. Only Lilly, I think, has both potential opportunities in this space. I think there is a lot of speculation that there is going to be a safety update from the FDA, if not a full safety panel. I'm hoping, Dan, that you could give us a little bit of your thoughts in that regard. Thanks so much.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Seamus. Lot to unpack there. We'll start with Dave on some of the policy and maybe Anat on the tax piece of that, and then we'll go to Ilya on kind of what he sees from JAK and lebrikizumab standpoint.

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

Yeah. Hi, Seamus. Look, on tax, there's a lot of discussion, of course, because of the presence introduced a number of ideas on corporate tax changes. I guess we join a growing chorus of large companies who oppose. That means to raise revenue, especially, when the stated policy goal, the infrastructure plan is to build back the economy. Of course, private money and corporate actions make up the vast majority of the investment that could or would occur and taxing that seems like a bad idea, maybe the opposite idea from the bill itself.

Within the bill, maybe just a couple of general comments, and we can follow-up if we need to. There is the nominal rate discussion, which of course when we say moving from '21 to '28 is moving toward the middle of the pack is not true, because of course in the US we have state level income tax. It would really put the US at the highest developed economy in terms of corporate tax rate. Additionally, we're the only major economy that taxes overseas earnings of its domiciled companies. And changing the so-called GILTI tax foreign minimum tax, really is punitive to our home companies in multiple ways, and is something that would have a disproportionate effect on pharmaceutical companies. And so both these actions don't make a lot of sense to us and we oppose. We would favor things like looking at funding the IRS, so they can collect taxes from all the people that don't pay including businesses and other items that could be paid for us. We certainly support the infrastructure in many ways.

On drug pricing, this has been pushed out a little bit. I wouldn't be surprised if we see H.R. 3 being debated soon, but as you may have read, apparently, it won't be part of the second package from the White House. That's good, because H.R. 3 and those concepts are really set to take a huge piece out of the industry, do nothing for patient out of pocket affordability and really derail the innovation machine that is the only reason we're escaping from the COVID-19 pandemic. So we will oppose that with every ounce of our being at pharma.

That said, we are all for changes to the system to make out-of-pocket costs go down for patients. There are a lot of ways to do this within the system that the industry is willing to pay for us on the table. This is much more around the contours and maybe what we saw with Senate Finance or the reported proposals made in the 11th hour of the last administration. We will table those ideas, we are tabling those ideas. And I think probably in the second-half you'll hear more about that. And we think there's a great opportunity to improve affordability and strengthen the healthcare system and really address healthcare in equities as well that occur, because people who are of lower economic means, people of color, women are disproportionately affected by bad insurance design and bad benefit design. We can shore those up and make the healthcare system work better for everyone.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dave. Ilya?

A - Ilya Yuffa {BIO 21952737 <GO>}

Yeah. Seamus, so thank you for the question. As you noted, and what we said on the call, that we are quite excited about our progress in immunology as a whole. And if we think about the growth opportunities within immunology, atopic dermatitis is one catalyst for the Company, both in what we believe in Olumiant success, but also the lebrikizumab.

In terms of the question around JAK and FDA decision, I won't speculate on any decision the FDA may make, but it's safe to say that the delay across all JAKs in atopic dermatitis and other indications suggest that there is a broader review on JAK safety. We feel that Olumiant has a robust safety profile. And with dermatology being more safety conscious, we do believe that Olumiant has a very good prospect to compete in this space, especially, after a topical failure and then lebrikizumab is one to watch out for for the second half of the year as we get more data. What we feel like we can compete and differentiate versus Dupixent. And so long-term prospect in catalyst for growth are very good for having both mechanisms and we also see catalyst for growth in alopecia areata, a very -- to be first in disease with Olumiant. And so we feel very good about our chances to not only compete, but also to have a significant growth and have meaningful outcomes for patients.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

Thank you. Our next question comes from the line of Louise Chen with Cantor. Please go ahead.

Q - Louise Chen {BIO 6990156 <GO>}

Hi. Thanks for taking my questions here. So, first question I had for you was on lebrikizumab. What do you think will differentiate your product from others that are already approved and those in development? And do you plan to pursue lebrikizumab for any other indications?

And then second question is on LOXO-305 plus LOXO-338. What do you think your competitive advantages are here versus others that are trying to do the same thing? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Great. Thanks, Louise. We'll go to Ilya for the first question and Jake for the second.

A - Ilya Yuffa {BIO 21952737 <GO>}

Yeah, Louise, thank you for the question about lebrikizumab. In terms of area differentiation, the focus for lebrikizumab is not only to look at the efficacy on skin, but also one of the lower impactful symptoms related to atopic dermatitis is itch. And so, we believe we may have the opportunity to differentiate on itch, which also has impact on sleep. And we believe that lebrikizumab may have a better safety profile. And so that's where we believe we can differentiate and so we're excited to get the results for lebrikizumab at the back half of the year. In terms of new indications, I think it's early to take a look at any new indications. We're obviously evaluating opportunities to grow lebrikizumab, but our full focus right now is making sure we have success in atopic dermatitis.

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

Ilya, just to jump in on top of that, of course, there will be a dosing convenience and dosing certainty benefit with lebri as well.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks. Jake?

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

Thanks for the question, Louise, about pirtobrutinib LOXO-305 and LOXO-338, the Bcl-2 inhibitor. I think, as it relates to differentiation, I point out a few things. First off, obviously, as I think, you and others know, pirtobrutinib itself is a differentiated BTK inhibitor that we believe afford certain advantages in combination. Obviously, we need to prove that clinically, but that's our hypothesis right now. So that sort of stands on its own.

The LOXO-338 program, the Bcl-2 inhibitor, we're putting into the clinic this year and obviously important that drug needs its human pharmacology goals, so that we know that it itself is on track as a drug. Should that prove to be the case, which we expected to, we will then look to combine these two agents. I think when you look out at others that are combining BTK and Bcl-2, the latter largely being venetoclax, I think what you see is a very fragmented landscape of asset ownership across companies.

And as a result of that some oftentimes perverse incentives about how to combine those drugs and where. We think it's important that if you have a new and differentiated BTK inhibitor like we believe we do with pirtobrutinib, we thought it was strategically important to own our own Bcl-2 inhibitor. And so we think we'll be the really the only player in the field who owns both agents outright. So that to us is a key differentiating feature downstream. But still a bunch of hoops we have to jump through to enable that combination.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

Thank you. Next we go to the line of Carter Gould with Barclays. Please go ahead.

Q - Carter Gould {BIO 21330584 <GO>}

All right. Good morning, guys. Thanks for the comprehensive updates and for taking the question. I guess, first for Dan or Mike, you guys put the details of the SUMMIT study of tirzepatide and (inaudible) recently. And I think the design, size and timeline were all surprising relative to expectations. I guess getting to a readout much, much faster than some have had expected. Can you maybe just walk through some of those key design choices in the extent regulators have bought in and also confirm that single study would be sufficient for approval in that setting. And then also historically Lilly has done a, I think, done a better job of franchise building and in certain areas and some of its peers. Now

with sort of mirikizumab derisking data, can you talk around how you're thinking about building around the GI portfolio? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Carter. We'll go to Mike for the question on tirzepatide and Ilya for the question on miri.

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

Yeah, thanks for the question on the SUMMIT trial. We're bullish on the opportunity for tirzepatide in HFpEF. When you look at that, it's a really a large unmet need with nearly 4 million people living with HFpEF heart failure, leading cause of hospitalization in the US. When you look at scientifically, you do see that there is a BC related HFpEF phenotype that we believe that tirzepatide could play a large role in helping out. And so, that's what really drove our investment in SUMMIT. And I think the team has done a nice job of coming up with creative approach that will provide, I think, robust data for payors and clinicians to make that decision. So I think we're very confident in this -- in both our clinical trial design, as well as the commercial opportunity.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Mike. We'll go to Ilya for the next answer.

A - Ilya Yuffa {BIO 21952737 <GO>}

Yeah, Carter, as you noted, in terms of building franchises across immunology, we've built up our scale in dermatology and excited about increasing number of treatments there; the same with the rheumatology in the hope for finding a lupus as well. And then in GI, mirikizumab will be our first entrant into GI with ulcerative colitis and Crohn's disease. And then we do have a pretty robust pipeline in both Phase 1 and proof-of-concept studies in particular to conjugate that we're studying for ulcerative colitis as well, and we look forward to bringing our new treatments across all three of those areas in the coming years.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

Thank you. Our next question comes from Tim Anderson with Wolfe Research. Please go ahead.

Q - Tim Anderson {BIO 3271630 <GO>}

Thank you. Couple of questions. On Verzenio and the CDK class more broadly, can you talk about what you're seeing in the US in terms of rebating for this oral oncology category? My understanding is that the level of rebates maybe stepping up. And I'm not sure which company or companies are driving that maybe it's Pfizer driving that as they try to hang on to market share. But what's the outlook for gross to net price trends in this category?

And then on Tyvyt your PD-1 from Innovent, a Chinese company, you note that you will file for approval in non-small cell lung in the US this year. It's really hard for me to see how you gain any share with this product, given what would be a limited label and given payor and prescriber dynamics where and things like Part B, you can't really compete on price. So what's realistic to expect with this product from a commercial perspective not only US, but in other western markets like Europe?

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Tim. We'll go to Anne White for both of those.

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

Well, thanks, Tim, for the question on Verzenio. So, I think, as you're mentioning, it's incredibly competitive market with the CDK4/6s. And so, we and others continue to do we need to do to make sure that patients get access to the right medicines. So, we have a, I would say, a strong strategy there. I can't comment on the specifics. But we do see competition in -- really what we're seeing -- I think, you're seeing in Verzenio, what we're seeing is incredibly nice trend growing in Q1. As you thought, we had positive momentum with the US strong share growth in March and we saw TRx of over 17% and NBRx of over 28%. So, and this is despite as you've noticed a modest year-on-year TRx market decline.

So I think what we're seeing is both from a payor strategy, but also very much from a data strategy, we're seeing that Verzenio is growing its share nicely. And so I like how all of our different programs are coming together. And obviously, the data in breast cancer reinforced growing awareness of these medicines are different, but what really has been the focus for our execution has been capitalizing on positive OS data, and making sure that people are aware of that. And we're seeing more trial, more adoption as we go through that. So very pleased how all of our strategies with Verzenio are coming together.

On Tyvyt, yes, I mean, as you've mentioned, it's a competitive space, obviously. And while I can't really comment on our commercial strategy prior to approval,

You can be reassured that we're looking at ways to differentiate and really add value to this innovative class of medicines. So obviously we know that there is certain commercial approaches was to take to capture share is really a late entrant in the field. But we see opportunity here and obviously this deal made sense with the partnership that we've had with Innovent and we're committed to the US submission this year, and so more to come as we look to launch the product and share that strategy and how we intend to make an opportunity here. But as you said, I wouldn't assess this as a large opportunity for Lilly, but an opportunistic one that we think makes sense, makes sense for patients globally at driving value for them.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Anne. Tim, thanks for your questions. We'll move to the lightning round. So we can try to get everyone in. Our answers will be brief and we'll actually ask each of you to only have one question for us. The next caller please.

Operator

Thank you. Next we have Andrew Baum with Citi. Please go ahead.

Q - Andrew Baum {BIO 1540495 <GO>}

Yeah, questions to Dan on Verzenio and the monarchE filing. As you outlined, the survival data is thankfully going to take a long time to mature. If the answer that the FDA is looking for more about further maturation and progression-free survival or -- sorry, disease-free survival, just given the historic presence into the PENELOPE-B data with palbociclib, where you had separation that then coming together. Isn't that really what the FDA wants given if you're waiting for survival you could be waiting for very long time indeed.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Andrew. Dan?

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

I'll just take it quickly. No, Andrew, it's -- the focus here is on the overall survival. On the distant free survival, as we commented, the curves are not coming together, they are actually separating more, it's improving as we get more advanced. So I'm not aware of any concerns around that.

Q - Andrew Baum {BIO 1540495 <GO>}

Got it. Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

Thank you. Next we go to the line of Steve Scala with Cowen. Please go ahead.

Q - Steve Scala {BIO 1505201 <GO>}

Thank you. I think, it was stated that the number of CV events in SURPASS-4 has been reached, if I heard that correctly. If that's correct, then it looks like the study is going to achieve its endpoint earlier than expected. So my question is, is that either confidence building or concerning? Are you worried COVID-19 cardiovascular effects may have impacted the accrual of events? And if tirzepatide trends worse than insulin glargine, can you still file? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Steve. We'll go to Mike on that.

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

Yeah, thanks for the question. No, we have no concerns. We will -- we have reached the number we needed to complete the trial. We're getting patients back in. We'll have that data should start to see topline in May and will release that information before the end of the quarter. We're very excited about tirzepatide and very confident in its CV profile and looking forward to see in the SURPASS-4 data.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Mike. Steve, thanks for your question. Next caller please.

Operator

Thank you. Next we go to the line of Terence Flynn with Goldman Sachs. Please go ahead.

Q - Terence Flynn {BIO 15030404 <GO>}

Hi. Thanks for taking the questions. I was just wondering on monarchE, if there is any possibility of an NCCN listing before the FDA action. And then, can you give us an update on the Retevmo launch dynamics this quarter? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Terence. We'll go to Anne for the question on Verzenio and Retevmo.

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

Thanks for the question. So on monarchE and NCCN, I really can't comment for them. So obviously, we feel that this data is incredibly impactful. I think one of our thought leaders call it the most notable development in HER-2 positive breast cancer in the last two decades. But we'll just have to wait and see what NCCN decides to do.

And then on Retevmo, the launch is going well. So we get a virtual launch in May. We finished 2020 with $37 million in sales and we see positive momentum in Q1. So we've had a great engagement with customers unaided brand awareness is strong. So we're quite pleased. And this is incredibly important medicine as you know, some patients over an 80% response rate. So a great response from the customers, very enthusiast with what we're seeing so far.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

Thank you. Our next question comes from Ronny Gal with Bernstein. Please go ahead.

Q - Ronny Gal {BIO 15022045 <GO>}

Good morning and thank you for making the time. So we are seeing you adopting cost conscious strategies on both Taltz and mirikizumab. And I was kind of wondering, if you're going to look forward five years, where do you see immunology pricing band goes in

terms of dollars per unit. It's right now in the low-to-mid 30s the way we can see it. Five years from now we're going to be in the mid-20s under-20, 30-plus, what do you see the bandwidth price looking like?

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Ronny. We'll go to Ilya for questions on immunology pricing trends.

A - Ilya Yuffa {BIO 21952737 <GO>}

Yeah. Ronny, thanks for the question on immunology. In terms of our focus, it's lesser cost conscious is more related to looking at opportunities for growth. We have a long runway for Taltz, and so we do believe that Taltz is kind of at the foundation of our immunology strategy. We have numerous head-to-head studies and real-world evidence suggest that Taltz is a best-in-disease treatment. And as part of our growth strategy, looking at mirikizumab in GI, we do believe that within the next five to 10 years, we can across multiple mechanisms in those three specialized groups: dermatology, rheumatology and GI have significant growth and become a top tier immunology company. In terms of pricing, I think, they're all very competitive field and so our goal is to have great evidence and create access opportunities for patients that need these treatments.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Ilya. Ronny, thanks for your question. Next caller please.

Operator

Thank you. Next we go to the line of Kerry Holford with Berenberg. Please go ahead.

Q - Kerry Holford {BIO 21698599 <GO>}

Thank you. Just on the COVID antibodies, I wonder if you can just discuss the disconnect between your lower 2021 sales guidance here in the higher associated R&D spend. And with that context, do you have a budget cap in mind for your ongoing COVID investments? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Kerry. We'll go to Anat for that.

A - Anat Ashkenazi {BIO 19888043 <GO>}

Sure. Thanks, Kerry. Let me start with the budget. So we did increase our guidance for the COVID antibody investments from $300 million to $400 million, to $400 million to $500 million. And the investments that we've announced this morning is really to address the growth in variance that we see globally and looking at additional antibody that could address that. The lowering on the high end of the range really relates to the changes you've seen here in the US government, as well as what we see global in terms of progression of the disease. And this is one I know that is more challenging to forecast given that there is not a lot of TRx data or data for you to look at and we'll continue to update obviously with every quarter.

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

And maybe just add as a mindset thing, we didn't get into this because we were thinking about margins or business profile was to be useful during the pandemic, which is still going on, obviously raging in other parts of the world. One other driver for the topline is that increasingly it will be selling our products into lower-priced markets are giving it away, because that's where the disease is. And when the pandemic period ends, I think, we can then take a different look at this and during business, but we're not there yet. So we're making the investments we need to, to be useful and selling the product where it's needed at the price structure we had previously announced, which is heavily discounted in low GDP markets.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dave and Anat. Kerry, thanks for your question. Next caller please.

Operator

Thank you. Next we go to the line of Umer Raffat with Evercore. Please go ahead.

Q - Umer Raffat {BIO 16743519 <GO>}

Hi. Thanks for taking my question. Dan, last we spoke in March, it seems like you haven't had a lot of regulatory discussions on donanemab, but it does feel like you've had them now. So I'm curious FDA feedback on the new endpoint IDRS, as well as the Bayesian analysis. And also very briefly on CD-73, there is an interesting emerging signal in some of the other CD-73s in pancreatic setting. I noticed you guys discontinued. Would love to find out any additional color.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Umer. Dan?

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

Yeah, sure. So, FDA feedback has been continuing, I should say, we had some, and it continues to come. I think, our view here is unchanged. We previously said that the FDA has concerns around ADAs [ph] because it combines cognition and function and there's always a risk that you could have a positive signal on ADAs driven by cognition with no benefit on function or function going the other way or vice versa and that wouldn't be acceptable for approval of a new drug. So that's the risk there. On CD-73 Phase 1 termination, I don't have additional comments.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

And last question comes from Gilbert with Truist Securities. Please go ahead.

Q - Gregg Gilbert {BIO 3565226 <GO>}

Thanks. Dan, on tanezumab, is the outlook anymore hopeful than the optics of the AdCom vote and can you comment on where pain fits into your overall R&D priority list at this point? Thanks.

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

Sure. Gregg, thanks for the question. Pain is still a really important unmet medical need. Clearly, the regulatory bar is high here in terms of safety, and we saw that from tanezumab Advisory Committee meeting, which was a pretty decisive outcome there and one that we were disappointed in.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dan. Gregg, thanks for your question. Back to Dave for the close.

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

Okay. Thanks, Kevin. We appreciate your participation in today's call and your interest in Eli Lilly and Company. 2021 has been -- has begun with a good momentum in our underlying business. We remain focused on executing our innovation-based strategy to bring new medicines to patients and create value for all our stakeholders. As we continue to scale our diverse commercial portfolio, complemented by a pipeline of industry-leading opportunities, we believe Lilly continues to be a compelling investment. Thanks again for dialing in today. Please follow up with our IR team, if you have any questions we have not addressed on today's call. Hope everyone has a great day.

Operator

Thank you, ladies and gentlemen. That does conclude our conference for today. We thank you for your participation and for using AT&T Event Conferencing Service. You may now disconnect.