Q1 2022 Earnings Call

Company Participants

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

Other Participants

- Alice Nettleton, Analyst
- Andrew Baum, Analyst
- Chris Schott, Analyst
- Chris Shibutani, Analyst
- Evan Seigerman, Analyst
- Geoff Meacham, Analyst
- Justin Burns, Analyst
- Kerry Holford, Analyst
- Louise Chen, Analyst
- Robyn Karnauskas, Analyst
- Seamus Fernandez, Analyst
- Steve Scala, Analyst
- Terence Flynn, Analyst
- Umer Raffat, Analyst
- Vamil Divan, Analyst

Presentation

Operator

Ladies and gentlemen, thank you for standing by and welcome to the Lilly Q1 2022 Earnings Call. At this time, all participants are in a listen-only mode. Later we will conduct a question-and-answer session, instructions will be given at that time. (Operator Instructions) And as a reminder, your conference is being recorded.

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

Kevin Hern {BIO 20557573 <GO>}

Good morning. Thank you for joining us for Eli Lilly and Company's Q1 2022 earnings call. I'm Kevin Hern, Vice President of Investor Relations. Joining me on today's call are Dave Ricks, Lilly's Chair and CEO; Anat Ashkenazi, Chief Financial Officer; Dr. Dan Skovronsky, Chief Scientific and Medical Officer; Anne White, President of Lilly Neuroscience; Ilya Yuffa, President of Lilly International; Jake Van Naarden, CEO of Loxo Oncology at Lilly and president of Lilly Oncology; Mike Mason, President of Lilly Diabetes; and Patrik Jonsson, President of Lilly Immunology and Lilly USA. We're also joined by Sara Smith, Kento Ueha, 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 several 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 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, please note that our commentary will focus on non-GAAP financial measures.

Now I'll turn the call over to Dave.

David A. Ricks {BIO 16504838 <GO>}

Thanks, Kevin. 2022 is off to a strong start with solid volume-driven revenue growth led by our key products and the new tirzepatide obesity data we announced this morning. We are focused on driving adoption of our newer medicines, preparing for key product launches, delivering several global submissions for potential new medicines, all the while advancing our pipeline to power the next wave of growth.

We are pleased with the progress we saw in the first quarter. Before I get to our results, I'd like to take a moment to address the tragic loss of life and the hardships we are seeing in Ukraine. Our Ukraine office is currently closed and operations are suspended. The safety of our employees and their families continues to be our top priority. We are working through logistical challenges in order to ensure supply of our medicines to those in need in Ukraine. Earlier this month, an initial shipment of medicines donated by Lilly including insulin arrived in Ukraine, thanks to the tremendous efforts of our partners, project HOPE, and direct relief. Few of our clinical trial participants are in Ukraine. So while we're doing everything we can to ensure continuity of their medical care, there is minimal impact to our global trials.

With regard to Russia, we have suspended investments, our promotional activities and new clinical trials there. Our Russian operations are now only focused on ensuring people suffering from diseases like cancer and diabetes continue to get the Lilly medicines they need. Should we generate any profits from our sales in Russia, we will donate them to organizations dedicated to humanitarian relief. Our revenue in Russia and Ukraine account for less than 1% of our total company sales in 2021.

Moving to our results. You can see on Slide 4 the progress we've made on our strategic deliverables so far this year. Q1 revenue grew 15% or 17% on a constant currency basis and was driven by volume growth of 20%. When excluding revenue from COVID-19 antibodies and Alimta due to loss of exclusivity, revenue grew 10% for the quarter. This volume-driven performance in Q1 is attributable to our key growth products, which grew 24% and now account for 61% of our core business. With long IP runways for many of these products and less than 10% of our 2022 revenue exposed to patent expiry in the next five years, along with the potential launch of five new medicines over the next 18 months, the durability of our growth outlook is quite strong.

Our non-GAAP gross margin was 76.1% in Q1, an increase of approximately 70 basis points, excluding revenue from COVID antibodies, gross margin was approximately 80% for the quarter. Our non-GAAP operating margin was 33.4%, an increase of roughly 1,000 basis points, primarily driven by both higher gross margin and lower R&D expenses for COVID antibodies.

In our pipeline, we have several important updates since our Q4 earnings call, including the U.S. and EU approval for Jardiance in heart failure with preserved ejection fraction, as well as a recommendation from the Independent Data Monitoring Committee for an early start to the Phase 3 trial studying Jardiance for chronic kidney disease due to clear positive efficacy; the U.S. Emergency Use Authorization for bebtelovimab for the treatment of mild to moderate COVID-19; the recent U.S. submission of Mirikizumab for the treatment of adults with moderately to severely active ulcerative colitis; and a positive Phase 3 topline readout for SURMOUNT-1, the first of four global studies to evaluate tirzepatide for adults living with obesity or overweight.

Dan will talk in more detail later, but we are very excited with the results of the Phase 3 SURMOUNT-1 top-line readout. We believe there is significant potential for tirzepatide to build off the impressive results we saw from our clinical program in Type 2 diabetes and help people with obesity, a disease impacting over 110 million people in United States and approximately 650 million people worldwide. Obesity is a chronic and progressive disease that causes over 2.8 million deaths globally each year. The economic impact associated with obesity is more than one trillion dollars in the U.S. alone. We believe addressing obesity could make a difference in millions of people's lives, have a significant impact on public health, and reduce healthcare costs. We're hopeful that we are entering a new era of obesity care where people have medicines that can help treat their obesity and this is our first proof point on that journey.

We continue to rapidly advance nucleic acid innovation at Lilly, building on our growing portfolio with the launch of the Lilly Institute for Genetic Medicines, a $700 million facility in Boston. We will develop novel RNA and DNA-based medicines as well as push the boundaries of delivery technology to unlock difficult to treat targets in key strategic areas for us like neurodegeneration, diabetes, and obesity.

Finally, we distributed nearly $900 million in dividends in the quarter and completed $1.5 billion in share repurchases. On Slide 5 and 6, you'll see a list of key events since our Q4 earnings call including several important regulatory, clinical, and COVID-19 antibody updates we are discussing today.

Now I'll turn the call over to Anat to review the Q1 results.

Anat Ashkenazi {BIO 19888043 <GO>}

Thanks, Dave. Before I review the financial results for Q1, it is important to note that beginning this quarter, following directions from the SEC, presentation of non-GAAP measures will not include upfront charges and development milestones related to acquired in-process R&D and development. While this has no bearing on how we conduct our business, it will have an impact on how we represent our non-GAAP measures. This change in presentation of financial results will have the effect of foreign into non-GAAP measures, certain charges that were previously reported owning our GAAP financial results. We expect this change will increase non-GAAP operating expenses and decrease non-GAAP operating margins and earnings per share.

To help with year-on-year comparison of our non-GAAP measures. You can find a revised workbook in our Investor website, reflecting the updated presentation of our 2020 and 2021 results.

Slide 7 summarizes financial performance in the first quarter of 2022. I'll focus my comments on non-GAAP performance. In Q1, revenue grew 15% excluding COVID -- excluding revenue from COVID-19 antibodies and Alimta, revenue increased 10%, highlighting solid momentum for our core business. Gross margin as a percent of revenue increased 70 basis points to 76.1% in Q1 2022. The increase in gross margin percent was primarily driven by the unfavorable effects of foreign exchange rates on international inventories sold in Q1 2021, partially offset by increased sales of COVID antibodies, which have lower gross margin profile than the rest of our portfolio and to a lesser extent, lower realized prices.

Increase in manufacturing costs and logistics due to inflation had a modest impact on gross margin in Q1. Total operating expenses decreased 6% this quarter, which as a reminder, is now inclusive of acquired IPR&D and development milestone charges. Marketing Selling and Administrative expenses decreased 1% while R&D expenses decreased 4% driven by lower development expenses for COVID-19 antibodies, partially offset by higher development expenses for late-stage assets.

This quarter, we recognized acquired IPR&D and development milestone charges of $166 million or $0.15 of EPS, primarily related to purchase of the Priority Review Voucher. In Q1 2021, acquired IPR&D and development milestone charges were $312 million or $0.27 of EPS. Operating income increased 66% in Q1, driven by higher revenue, primarily due to higher sales of COVID antibodies, lower R&D expenses for COVID antibodies, and to a lesser extent, lower acquired IPR&D and development milestone charges. Operating income as a percent of revenue was 33.4% for the quarter and reflects the benefit from COVID-19 antibodies revenue as well as the negative impact of approximately 210 basis points attributed to acquired IPR&D and development milestone charges.

Other income and expense was income of approximately $38 million this quarter compared with income of $35 million in Q1 2021. Our Q1 effective tax rate was 10.3%, an increase of 140 basis points compared to the same period in 2021. This increase was

driven by a lower net discrete tax benefit this quarter, partially offset by decreased tax expenses related to the implementation of the provision in the 2017 Tax Act required to capitalize research and development expenses.

As the bottom line, we delivered strong earnings per share growth of 63% in Q1, inclusive of approximately 1500 basis points related to lower acquired IPR&D and development milestone charges.

On Slide 8 we quantify the effect of price rate and volume on revenue growth. This quarter, U.S. revenue grew 31% and when excluding revenue from COVID-19 antibodies and Alimta, revenue grew 14% in the U.S. This growth was driven by volume, led by Trulicity, Verzenio, Jardiance, Olumiant, and Taltz. We experienced a net price decline of 1% for the quarter and continue to expect a mid-single-digit price decline in the U.S. for the full year. As a reminder, a single competitor to Alimta launch in the U.S. in February, and we expect broad generic entry in may result in a significant erosion of US Alimta revenue.

Moving to Europe, revenue in Q1 declined 13% in constant currency and when excluding revenue from COVID-19 antibodies and Alimta, revenue grew 14% in constant currency, driven primarily by volume growth for Trulicity, Taltz, Jardiance, Verzenio, and Olumiant. We expect continued growth in Europe, excluding Alimta.

For Japan, Q1 revenue decreased 21% in constant currency as our business there continues to be negatively affected by significant declines in off-patent products primarily Cymbalta and Alimta. Key growth products now represent 65% of total revenue in Japan and we expect to return to growth in Japan beginning in 2023.

In China, revenue grew 10% in constant currency. The NRDL access has driven significant volume growth for newer products like Tyvyt, Trulicity, Verzenio, and Taltz and has been partially offset by related price decreases. We expect this improved access to continue to drive future volume growth, more than offsetting the price decline.

The recent COVID-19 outbreak in China and the subsequent protective measures that are currently being put in place to control the spread of the virus highlight the potential for commercial impact in China in the near term, particularly for infused products, like Tyvyt. Revenue in the rest of the world increased 29% in constant currency this quarter, driven primarily by $95 million in revenue from the sales of rights to Cialis in Taiwan and Saudi Arabia as well as by increased sales of key growth products.

We continue to expect a mid-single-digit net price decline in 2022 for the US, Europe, and Japan, with the worldwide net price decline in the high-single-digit driven by the expanded NRDL access for our products in China.

As shown on Slide 9, our key growth products continue to drive robust worldwide volume growth. These products drove nearly 15 percent points of volume growth this quarter and continue to bolster overall performance and outlook. Slide 10 further highlights the contributions of our key growth products. This quarter, these brands generated $3.9

billion in revenue and made up 61% of our core business revenue, growing 24%. We're pleased with the continued market growth of both the GLP-1 and SGLT2 classes where Trulicity and Jardiance are market leaders, as well as with the strong Taltz prescription growth. We're also encouraged by the significant uptake of Verzenio in Q1, driven by the approval and launch of the adjuvant indication, which has led to an inflection in both new and total prescriptions.

On Slide 11, we provide an update on capital allocation. In Q1 2022, we invested $2.4 billion to drive our future growth through a combination of R&D expenditures, business development outlays, and capital investments. In addition, we returned approximately $900 million to shareholders in dividends and repurchased 1.5 billion in stock. Our capital allocation priorities remain unchanged. As we continue to fund our key market product and expect the new launches, invest in our pipeline, pursue opportunities for external innovation to augment our future growth prospects, and return excess capital to shareholders.

Slide 12 is the updated 2022 financial guidance. As I previously noted, as our (Technical Difficulty) non-GAAP financial measures, we will now include IPR&D and development milestone charges. For guidance, we will include charges that have been incurred or realized as of the date of the earnings release and will not include any impact from potential or pending business development.

We're providing information that should make this change as easy as possible to understand as well as incorporate into modeling. As always, please let us know if there's anything else we can do to be of assistance as you navigate through this transition. I do want to reiterate that margin expansion continues to be priority for our team. Consistent with prior communication, excluding IPR&D development milestone charges, we expect to drive further non-GAAP operating margin expansion over time. Getting into the numbers underline (Technical Difficulty) several items of benefits first quarter results, which are not expected to recur. These include approximately $1.45 billion of COVID antibody sales, U.S. Alimta revenue of approximately $250 million that will be impacted by multi-source generic entrants in Q2 and beyond, a favorable effective tax rate, and a one-time benefit related to the resolution of (Technical Difficulty) patent litigation in Canada.

I would also remind you that as we look ahead to the second quarter, the Q2 2021 revenue benefited from the sale of Cialis rights in China, which will provide roughly 2.5 percentage points of headwind to our topline growth in Q2.

Starting with revenue, we are increasing the guidance range by $1 billion to now be in the range of $28.8 billion to $29.3 billion, reflecting the additional revenue for bebtelovimab sales in Q1. While project an unfavorable impact from foreign exchange rate, we are expecting to offset it with stronger core business performance. We anticipate that any additional revenue from sales of COVID-19 antibodies to be limited begin in Q2 2022, while the U.S. government has an option to purchase additional 500,000 doses of bebtelovimab no later than July 31st of this year, it is uncertain whether this option will be exercised and therefore it is not included in our guidance.

Moving down the income statement, GAAP gross margin percent is now expected to be approximately 76% while non-GAAP margin, gross margin is now expected to be approximately 78%. The majority of this 200 basis point reduction is due to the impact of Q1 bebtelovimab sales which have lower gross margin and to a lesser extent an increase of approximately $100 million in logistics and manufacturing costs due to inflation.

The range for R&D expenses has been increased by $100 million to be $7.1 billion to $7.3 billion driven by investment in our late-stage pipeline, primarily Alzheimer's clinical development, and investment to advance to diagnostics ecosystem. Our guidance includes acquired IPR&D and development milestone charges of approximately $521 million, reflecting Q1 charges of $166 million, with the remainder primarily related to a charge associated with the buyout of future obligations that were contingent upon development, regulatory, and commercial success of our Meudon selective PI3K inhibitor. This guidance does not include any impact from potential or pending business development transaction.

GAAP and non-GAAP operating margin decreased 200 basis points to approximately 28% and 30% respectively, primarily due to the negative impact associated with the acquired IPR&D and development milestone charges to date. Given the accounting change for acquired IPR&D and development milestone charges, in the inherent variability associated with such charges, our non-GAAP operating margin figure will not measure efficiency in the same way it has done historically. However, you contract our operating margin in the way you deem appropriate, knowing that we aim to expand operating margin over time, excluding acquired IPR&D, and develop in milestone charges.

Our Q1 2022 tax rate and EPS include a favorable impact from the provision in the 2017 Tax Act that requires capitalization of research and development expenses for tax purposes. Our financial guidance for the full year is unchanged and assume that this provision will be deferred or repealed over Congress, effective for 2022. If this provision is not deferred or repealed effective this year then we would expect the reported and non-GAAP tax rate to be approximately 10% to 11%. It is notable that while this provision favorably impacts certain tax items, which decreased our effective tax rate, we expect it will increase our 2022 cash payments of income taxes by approximately $1.5 billion.

Based on these changes, we have lowered our reported EPS guidance by $0.70 to now be in the range of $7.3 to $7.45 per share and lower our non-GAAP EPS guidance to be in the range of $8.50 to $8.30. The $0.35 reduction are non-core -- in our non-GAAP EPS range includes the 55% decrease due to the year-to-date acquired IPR&D and development milestone charges, partially offset by improved business performance of $0.20 attributable to the net benefit of Q1 bebtelovimab sales and increased investments in R&D.

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

Daniel M. Skovronsky {BIO 15349505 <GO>}

Thanks, Anat. Let me start with today's exciting announcement. The positive topline results from the tirzepatide SURMOUNT-1 Phase 3 study. Participants without Type 2 diabetes who

have obesity, or overweight with at least one co-morbidity achieved up to 22.5% weight loss at 72 weeks, which translates to a mean weight loss of 52 pounds. Tirzepatide is the first investigational medicines to deliver more than 20% weight loss on average in a Phase 3 study. Indeed most people on 10 or 15 milligrams of tirzepatide in this trial achieved 20% or greater weight loss and up to 63% of patients on 15 milligrams achieved this level of weight reduction.

Obesity is a chronic disease that needs more effective treatment options to patients. We're working hard at Lilly to create new potentially innovative medicines with the aim to modernize how this disease is approached. We hope that there is appetite can be Lilly's first such medicine and the SURMOUNT program has been designed to test just that. I'll cover the SURMOUNT-1 results in more detail, but first let me quickly provide an overview of the SURMOUNT Phase 3 program. The SURMOUNT program has enrolled more than 5,000 people with obesity or overweight across six studies, four of which are global registration studies. On Slide 13, you can see key trial design elements for those four global registration studies. All four studies compared the efficacy and safety of tirzepatide to placebo as an adjunct to a reduced calorie diet and increased physical activity.

SURMOUNT-1 was designed to evaluate treatment with tirzepatide compared to placebo to provide weight reduction and safety data for people without Type 2 diabetes with obesity or overweight with at least one co-morbidity. SURMOUNT-2 will provide weight reduction and safety data for people with obesity or overweight with Type 2 diabetes. SURMOUNT-3 will provide data on maximizing weight loss following an intensive lifestyle program. And SURMOUNT-4 evaluates maintaining weight loss. We expect the remaining three global studies to read out in the middle of 2023.

Note that dose escalation in the SURMOUNT program is consistent with that of the SURPASS program for the treatment of Type 2 diabetes with tirzepatide. Patients start with 2.5 milligrams of tirzepatide and move up every four weeks in 2.5 milligram increments to reach their target dose. In SURMOUNT-3 and 4, study participants who escalate go into the maximum tolerated dose of either 10 milligrams or 15 milligrams, patients escalating the maximum tolerated dose provides opportunity to evaluate the full potential for weight reduction.

Studies vary in duration, from 72 to 82 -- 72 to 88 weeks, and SURMOUNT-1 will continue through 176 weeks to evaluate whether tirzepatide can actually slow the time to onset of Type 2 diabetes in participants who had pre-diabetes at the time of entering the clinical trial. We believe this will be important additional information for patients and physicians. SURMOUNT-1, a large trial which enrolled over 2500 participants met its co-primary study endpoints and also hit on all pre-specified key secondary endpoints.

On Slide 14, you can see the first co-primary endpoint in the SURMOUNT-1 study, where tirzepatide delivered up to 22.5% mean body weight reduction in adults with obesity or overweight. With a mean baseline weight across the study of 231 pounds, this translates into a mean body weight reduction of 52 pounds on the 15 milligram treatment arm of the study.

Along with the impressive results from the 10 milligram dose, which showed 21.4% mean body weight reduction, we were also very pleased to see how well the 5 milligram performed with a 16% mean body weight reduction also at 72 weeks for the efficacy estimate.

Moving to Slide 15. Tirzepatide obviously achieve the second co-primary endpoint of driving at least 5% weight reduction, clearly the vast majority of subjects, including greater than 96% of participants in the 10 and 15 milligram arms achieved this level of weight reduction. We're really excited that a key secondary endpoint is SURMOUNT-1 showed up to 60% of patients achieved at least 20% body weight reduction at 72 weeks, again using the efficacy estimate. This is compared to only 1% for participants who achieved greater than 20% weight loss on placebo as an adjunct to diet and exercise.

Moving to Slide 16. You can see the safety profile from the SURMOUNT-1 study. Tirzepatide was well tolerated in study participants with the overall safety and tolerability profile similar to incretin-based therapies approved for the treatment of obesity. As in the SURPASS program, the most common reported adverse events were GI-related, generally mild to moderate in severity, and usually occurred during dose escalation. Treatment discontinuation rates due to adverse events were between 4.3% and 7.1% for tirzepatide treatment arms compared to 2.6% for placebo.

The overall treatment discontinuation rates range from roughly 14% to 16% in the tirzepatide arms compared to over 26% for placebo. The minimal weight loss seen in the placebo treatment group combined with the observed placebo discontinuation rate of 26% demonstrates the limited efficacy of diet and exercise alone and highlights the significant unmet medical need for people with this disease. We'll continue to evaluate the SURMOUNT-1 study data and are planning to present findings at a medical meeting in the second half of this year. Of course, we plan to submit our manuscript to a top tier peer-reviewed journal.

As Dave mentioned earlier, obesity is a chronic disease impacting over 110 million Americans and there is great need for more effective treatment options. While our current alignment with the FDA is to complete the four SURMOUNT global registrational studies prior to submission, we believe the impressive results from SURMOUNT-1 warrant further discussion. Based on our existing robust dataset, we're looking forward to reviewing the data with the FDA and discussing the potential for an expedited path forward for this indication.

Moving to the rest of the portfolio. Slide 17 shows select pipeline opportunities as of April 27th, and Slide 18 shows potential key events for the year. There have been several other important developments since our last earnings call and I'll cover these by therapeutic area.

In diabetes, along with our partner Boehringer Ingelheim, we're proud of the expanded indication for Jardiance as a treatment for heart failure with preserved ejection fraction, which has been classified as the single largest unmet need in cardiovascular medicine. Jardiance is now the first and only heart failure therapy to demonstrate statistically

significant risk reduction in cardiovascular death or hospitalization for heart failure regardless of ejection fraction.

We also announced (Technical Difficulty) Jardiance for chronic kidney disease will stop early due to clear positive efficacy. The recommendation was made by an independent data monitoring committee and while we've not yet seen results from this interim analysis, we're excited about the potential for this new indication and expect to share detailed results from the upcoming primary analysis at a medical meeting in the second half of this year.

Last month, we began dosing patients in the first of five Phase 3 trials for investigational weekly insulin basal insulin FC or BIF. The trial compares weekly BIF to insulin degludec where patients are currently treated with basal insulin. We intend to start the other 4 Phase 3 trials later this year. You also see we've advanced our long-acting Amylin receptor agonist to Phase 1 development in obesity.

Shifting to immunology. We presented mirikizumab induction data from LUCENT-1 at the Europeans Crohn's and Colitis Virtual Congress, demonstrating superiority over placebo for the primary and all key secondary endpoints. These data show patients with moderately to severely active ulcerative colitis achieved statistically superior rates of clinical remission compared to patients taking placebo, with nearly two-thirds of patients responding to mirikizumab. The results indicated improved symptom relief including decreased bowel urgency and resolution or near resolution of inflammation.

Building upon the positive outcomes from LUCENT-1, we look forward to sharing maintenance data from LUCENT-2 later in Q2. We're also excited to announce that we've submitted to the FDA and expect submissions in Europe and Japan in Q2. Mirikizumab has the potential to be the first in class L-23p19 inhibitor treatment for people with ulcerative colitis.

Last month at the American Academy of Dermatology Annual Meeting, we shared lebrikizumab monotherapy data showing more than 50% of patients with moderate to severe atopic dermatitis experienced at least 75% reduction in disease severity at 16 weeks. Additionally, at the revolutionizing atopic dermatitis conference, we shared data showing 70% of patients receiving lebrikizumab combined with topical corticosteroids achieved at least 75% improvement in overall disease severity. We believe these data could help establish a competitive profile for lebrikizumab and we're looking forward to further data from our maintenance studies in the first half of this year to provide insight into the durability of efficacy. Global submissions are expected by year-end.

Moving to baricitinib. The FDA review for alopecia areata is underway and we're pleased to note that the FDA has granted priority review designation. As expected, we also received a complete response letter from the FDA for baricitinib atopic dermatitis indication as we were not in alignment with the agency on the indicated population.

Finally in immunology, we have discontinued the Phase 2 study for IL-2 in all sort of colitis to do a lack of efficacy based on interim analysis. The safety was consistent with that

observed in previous studies and this decision does not impact the ongoing or planned studies for IL-2 in SLE or atopic dermatitis, as each disease state evaluates a different clinical hypothesis.

Moving on to neuroscience. In the National Coverage Determination issued earlier this month for monoclonal antibodies directed against amyloid, we share the disappointment of patients and their caregivers, with this NCD and we know more generally that the innovation in new medical areas really always starts with data that are less proven and more debated and may proceed initially through regulatory mechanisms such as accelerated approval.

We believe that Medicure's decision to CED in such circumstances is in conflict with FDA's and Congress's intent of expedited regulatory pathways and is likely to have a stifling effect on innovation for new medical areas causing harm to patients that are waiting and in need of new medicines. That said, we're continuing with our rolling submission to the FDA under the accelerated approval pathway. We intend to complete our initial submission yet in Q2, enabling a potential regulatory decision in early 2023.

We believe it would be beneficial for donanemab to obtain accelerated approval proximal to the TRAILBLAZER-ALZ 2 Phase 3 readout in mid 2023, which would enable parallel discussions with CMS regarding outright coverage and expedited review time for full FDA approval. We believe that given the thoughtful and robust design of TRAILBLAZER-ALZ 2 if the study is positive, it should meet the high level of evidence criteria set forth by CMS in the NCD decision. At that time, we will advocate for CMS to reconsider outright coverage of donanemab.

As we've stated previously, it's inconceivable to us that one substantial evidence of clinical benefit has been established for any Alzheimer's medicine, people with the disease won't have access to it. Our view of the mid and long-term opportunity to help patients with donanemab remains unchanged. Shifting now to oncology with pirtobrutinib. We are also working on a rolling submission here under the accelerated approval pathway. In this case for mantle cell lymphoma. Here, we also expect to complete our initial submission in Q2.

We received a complete response letter from the FDA regarding the submission for sintilimab which was in line with our expectation after the oncology -- Oncologic Drugs Advisory Committee meeting earlier this year. Along with Innovent, we're assessing next steps for sintilimab in the U.S. Further in the oncology pipeline, we started two additional Phase 3 studies. The first is an additional study evaluating Verzenio in HR positive HER-2 negative advanced or metastatic breast cancer in combination with fulvestrant following progression on a CDK46 inhibitor and endocrine therapy.

The second is CYCLONE 3, evaluating Verzenio in earlier lines of prostate cancer. We've also advanced our next generation RET inhibitor to Phase 1 development and we've discontinued our Aurora A kinase inhibitor as we did not see sufficient monotherapy activity to warrant further development. Similarly, in our pain therapeutic area, we've decided to discontinue development of EPIREG and TGF Alpha because it did not meet criteria for proceeding.

Finally, as Dave mentioned earlier, the FDA authorized bebtelovimab for emergency use for certain non-hospitalized patients with mild to moderate COVID-19. bebtelovimab neutralizes OMICRON including the BA2 sub limit -- lineage as demonstrated by sudo virus and authentic virus neutralization assays. As you can see, Q1 was another busy but successful quarter for pipeline advancement at Lilly.

Now I'll turn the call back 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 this year. We delivered solid sales growth, driven largely by volume from our key growth products, which represent 61% of our core business. We continue to see opportunity for meaningful operating margin expansion over time, excluding the impact of acquired IPR&D and development milestone charges. We made significant progress developing new medicines with exciting advances, including for Jardiance and HFpEF, the EUA Authorization for bebtelovimab, the submission of mirikizumab, and all sort of colitis as well as positive Phase 3 results for tirzepatide in obesity and Jardiance in chronic kidney disease.

Finally, we returned $2.4 billion to shareholders via the dividend and share repurchase. We are committed to invest for the long term to advance promising R&D opportunities and support launches to bring groundbreaking therapies to patients diagnosed with some of the most challenging diseases facing humankind, like diabetes, obesity, Alzheimer, cancer, and autoimmune disorders. With the progress we've seen to date, we remain extremely confident in our long-term growth prospects.

Now I'll turn the call 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 [ph] 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) And our first question is from the line of Louise Chen. Please go ahead. And she is from Cantor.

Q - Louise Chen {BIO 21301405 <GO>}

Hi, congratulations on the SURMOUNT data and thanks for taking my questions here. So I do want to ask you more in tirzepatide and SURMOUNT. How do you see the market landscape for obesity changing in light of your positive SURMOUNT data today? Is there

an opportunity to file for that indication with the data and what's the larger opportunity for you here? Is it Type 2 diabetes or obesity? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Louise. We'll go to Mike Mason for those.

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

All right. Louise, thanks for the compliment upfront. We appreciate that. I think the market opportunity is -- kind of remains what we thought before. We see it as a sizable opportunity and when we look at the -- just the massive numbers of people who live with obesity, over 100 million people in the U.S., 650 million people globally contributes a burden of over $1 trillion globally. We do think it's a huge opportunity. It should be perceived as a -- and treated as a chronic illness. It not only has health implications, but if you live with obesity, it's a very visible disease, unlike others that really brings with it some unfortunate stigma into society that really hurts individuals both physically and emotionally, and so there is a need to treat this disease. The market is not going to develop overnight. We have to increase awareness that this is a chronic disease that needs to be treated. We do need to establish and grow the access for it.

So we're looking long-term to this. I think it's important for us to be able to build the foundation, build the knowledge that this is a chronic disease, get that appreciated by healthcare professionals and payers, and then grow the market. So we're going to look when investing obviously not only in tirzepatide but early -- many early assets, because we do think this is a need in the marketplace that we need to focus on and obviously, we're quite delighted by SURMOUNT-1, not only the high dose. I mean, obviously, when we saw the 52 pounds of weight loss at the high dose on average, we were wowed by that, but I'm also as excited about the 16% weight loss at the 5 milligram because everyone -- we look at the averages, but there is no averages out there. Every individual is different and we need to have a medication that at different doses offer different weight loss.

And so, I'm very pleased about the dose profile and the weight loss profile across all the doses. As Dan said, we've originally on the -- on your filing question, we have aligned with the FDA on four trials for the SURMOUNT-1, 2, 3, and 4 program. But given the huge market need and given this data, we do think it warrants a discussion with the FDA about whether we can find a path to accelerate it to the marketplace to meet this need. The SURMOUNT-1 data is great. We also have over 4,000 patients in the SURPASS-5 Global Restoration studies that provides a lot of good information on the safety and efficacy of tirzepatide in the diabetes population to go along with SURMOUNT-1.

So we look forward to that conversation. I think when we -- when you look at -- I think your last question was, are we more excited about diabetes and obesity. I think we're equally excited about both of them. Obviously, we will focus our attention on diabetes first, still a huge massive unmet need. We have unfortunately only half of people who live with Type 2 diabetes in good control. So we'll focus on that and then we'll focus long term on obesity as I've said earlier. So thanks for the question. Thanks for the compliments. Appreciate it.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

The next caller is Terence Flynn from Morgan Stanley. Please go ahead.

Q - Terence Flynn {BIO 15030404 <GO>}

Great. Let me offer my congratulations as well on the SURMOUNT-1 data. I have two questions. The first is just based on the timing of the acceptance of the tirzepatide BOA for diabetes, it seems like we're passed the window for the FDA to convene an AdCom panel. So just wondering if you agree, or if the door is still open there and then I was just wondering, probably a question for Mike, if you could share your latest perspective on commercial positioning of tirzepatide. Is this going to be a single brand or two separate brands and then how are you thinking early on just high-level thoughts about pricing here? Is this going to be based on dose level or fixed as is with Trulicity? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Terence. We'll go to Mike for both those questions.

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

Okay. Thanks for the question. I'll answer your second question first on kind of our commercial positioning. Obviously, for competitive reasons, we'll keep that to ourselves at this time, know that we will focus on maximizing the opportunity long term in diabetes and obesity and we'll make the right moves whether that's one or two brands. We'll have dialogs with the FDA on the one versus two brands and it's too early to talk about that at this point.

With regards to the AdCom, we don't anticipate an AdCom for tirzepatide.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

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

Q - Geoff Meacham {BIO 21252662 <GO>}

Hey, guys. Thanks so much for the question. Also want to offer my congrats on the data. Just had a few on the obesity opportunity. Dan, a question for you. The market gating factor still looks to be reimbursement and access, and I think that prevailing wisdom is that an outcome study will be needed. So first, do you agree with that? And second is if you do, how are you guys thinking about the size and scope of obesity outcome study? I wasn't sure if there is a benefit, of a point estimate of a benefit that you think could help drive reimbursement or for example bariatric surgery was a reasonable reference point. Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks. We'll go to Dan and then, Mike, also invite you to weigh in on our MMO study.

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

Yeah, thanks. Of course, we believe, and there is really quite a bit of evidence that weight loss will lead to really strong benefits in outcomes across a variety of diseases. Obviously, cardiovascular disease is near the top of the list, but many others as well. We know a lot from bariatric surgery, which has shown that it can reverse Type 2 diabetes or prevent the onset of diabetes. It can reduce cardiovascular risk. It can decrease even mortality when you get weight loss. That's really in the range of what we saw in this trial.

So we're excited about the potential to change those outcomes. Of course, as you point out, we have to demonstrate that, we will do that over time, but given where we are in our understanding of this disease process and given the depth of unmet medical need in obesity, I don't see that data as a gating factor for user reimbursement of the drug. Maybe Mike can offer more details on that.

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

Yeah, thanks, Dan. Yeah, thanks, and thanks for the compliments on the data. Yeah, the -- I wouldn't look backwardly at the fact that with that obesity agents up to this point really haven't been able to secure good access the weight loss levels that you were seeing 5%, 6%, 7% weight loss. No one was able to produce or no one has produced health outcome benefits at that level of weight loss. So it makes sense for payers not opening access for those probably more cosmetic than true health benefits. But if you're looking at a product like tirzepatide that can deliver up to 22.5% weight loss, we do believe and there's good data out there to suggest that's going to really improve and lead to the good health outcomes. We have to produce that over time and we will do that, but I don't think that will limit us from gaining access in the meantime. I think when you look at novel access we go vis other at 20 million, 25 million people who live with obesity in the U.S. having access. So I think we can continue to build on that. I think there was a real big win for obesity access recently with the Federal Health employees gaining access for obesity agents. So I think that's a important trend.

Also understand that we have -- we're dedicated to produce a series of trials that we hope will demonstrate, and we expect to demonstrate good outcomes with tirzepatide for sleep apnea, HFpEF, as well as our our outcome study that will include cardiovascular. Now, those are indications right now that do have access. So both part you take sleep apnea, for example, that has good coverage in both commercial and part. So we do expect that we show good outcomes there that for those people who have obesity and sleep apnea that we should be able to gain access for it.

So we think we do believe that access will start off and where it is today, and grow it over time, but we are committed long-term to build access and help people who live with obesity for the duration.

Q - Geoff Meacham {BIO 21252662 <GO>}

Great, thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks. Thanks, Mike, and Dan. Thanks, Geoff for your questions. Next caller, please.

Operator

Next caller is Chris Schott from J.P. Morgan. Please go ahead.

Q - Chris Schott {BIO 6299911 <GO>}

Great, thanks. Thanks for the questions and congrats on the data as well. Do you -- I guess a couple of questions on tirzepatide. At first, do you see weight loss plateauing in the study and if so when did it plateau and then do you expect patients will stay on the drug once they've lost weight? I'm trying to sense of just how you're thinking about duration of tirzepatide in obesity. The second question was on an accelerated filing in obesity. Just any clarity of when we could get more details on that? And then finally on the pre-diabetic progression to diabetes endpoint from SURMOUNT-1. I guess could diabetes prevention become a labeled indication or is this just more data that could come on label? Thanks so much.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Chris. We'll go to Mike for all those questions.

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

Okay. I think that may have been more than two, but I'll go through these pretty quickly. So first of all, weight loss plateauing. I think we have to leave some of the data for our medical meetings coming up. So I'll reserve that for that. We do believe that this is a chronic illness that requires a chronic treatment. So we do believe people will need to stay on the drug long term in order to get the benefit. And then pre-diabetes, I look at that as an important population that tirzepatide could provide health outcomes for. So probably more about showing data where our segment could benefit from it versus having a labeled indication for it.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Mike.

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

And then --

A - Kevin Hern {BIO 20557573 <GO>}

Sorry.

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

Go ahead.

A - Kevin Hern {BIO 20557573 <GO>}

Next caller, please.

Operator

Thank you. The next caller is Andrew Baum from Citi. Please go ahead.

Q - Andrew Baum {BIO 1540495 <GO>}

Yeah. Thank you. Couple of questions, please. The long-term commercial potential diabetes, helped by the co-morbidities, I mean, clearly, is there, and I'm sure it will be realized by you and your competitors, could you comment rather on the trajectory near term? You referenced the covered that Novo has attained. But obviously, they had a very expensive bridge program during that period, which makes it difficult to extrapolate what the real reimburse demand is. Separately, we're hearing that PBMs pushing back those patients that converted from the bridge to reimburse. So any comments you have on that will be helpful.

And then second. Would had to (Technical Difficulty) failures with given you have a sense now at the Phase 3 as well as obviously having Verzenio. How are you thinking about how this impacts your development of your SERD program?

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Andrew. We'll go to Mike for the first one on the trajectory in obesity and then Jake for the question around SERD.

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

Yes, as I said earlier, I do think it's going to be one that you're not going to probably spur now the gate on that you'll have a sizable segment, but one that will grow over time. We will provide supportive care bridging programs, as you say at launch to make sure and support people so they can have a good experience and see the benefit to the weight loss. But we do think it's something that this is one that I would look at the obesity market, one that will establish, it'll be decent size, but it will grow for the next decade or two.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Mike. Jake?

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

Yeah, thanks for the question about about about SERDs. Our view of our program in the landscape hasn't really changed all that much in light of the recent announcements. Obviously, as it relates to the two most recent trial readouts, we've yet to see the actual data though at least in one case there were some directional clues given by company management. I think largely speaking we saw those studies as sort of underpowered Phase 2 trials.

And I think in many cases, what we're hearing qualitatively from those companies suggests exactly that. In other words, trends in the right direction but underpowered studies. Our initial second lines randomized trial that we're recruiting right now is a fully powered Phase 3 study. So if anything, we're actually more confident in that study winning than we were previously, but that's not really the -- that may be the first path to market for the agent and impactful for those patients In the late-line setting, but that's not really the ultimate I think most impactful place for the medicine, which is really in the adjuvant setting, and we're working on the trial design there that we'll talk more about later this year.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

Your next caller is Seamus Fernandez from Guggenheim. Please go ahead.

Q - Seamus Fernandez {BIO 7525186 <GO>}

Great, thanks for the questions, and congrats on the data. Just a quick question. Dan, this is a very large Phase 3 program that you're conducting for obesity and more broadly, but the statement that you will be pursuing a potential faster path to market with regulatory authorities on the basis of SURMOUNT-1 data is, it's certainly intriguing. How do you see the likelihood of success and is the real separation there the 20% threshold? Do you really think that's the potential game-changer or is it something else in the data that we have yet to see that you think is unique and compelling?

And then separately, just wanted to follow up on the -- your comments on the Alzheimer's side of things. I think you've said in the past that there are some issues as it relates to how we think about the impact or thoughts around other clinical trials. I'm wondering how you're feeling along those lines and really just wanted to get your general sort of compare and contrast of the Lilly program versus some of those -- some of the other two programs that are coming later this year. Thanks.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Seamus. We'll go to Dan for both of those.

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

Okay. Sure, Seamus. I mean, let me start with tirzepatide and sort of the comments that I made on the regulatory path. The FDA has clear guidance on what's required to get an indication for anti-obesity drug and those guidance documents form the basis of our previous discussions in alignment with the agency. Our BACE case based on those has been and really continues to be the submission will require the full package of Phase 3 data from this trial from this program.

On the other hand, as I said, I think we were impressed and delighted with the data that we got from SURMOUNT-1. It's a very large Phase 3 trial as you pointed out and there are a

number of elements here that encouraged us to open the door for additional discussion with the FDA. You asked what is it specifically. Maybe I'll highlight two or three things. First, the efficacy, as you pointed out, the more than 20% weight loss is really unprecedented level of weight loss in the field. And I think that's exciting for patients and addressing a very significant unmet medical need.

Second is the safety and tolerability data that we got. I think there is a pleasant surprise there if you look at how well tolerated this drug was, how few discontinuations we had. And as I pointed out, more discontinuations for treatment on placebo made more than on the active arms of the drug just indicating that people tolerate this why I want to stay on the drug and appreciate the weight loss benefits they're getting. So the very good safety and tolerability profile that we're seeing, combined with the extraordinary efficacy profile, I think is a major step in that argument.

The last piece of course is that we don't see this data in isolation. This builds on a very significant Type 2 diabetes program, which of course involves many patients with Type 2 diabetes and obesity and demonstrated safety and efficacy in that setting as well. So we'll see how that goes. And I think to circle back to Chris's question, when do we learn more, as we have discussions with regulators. If we learn more, and we see that there is an opportunity for expedited path here, we'll be as forthcoming with investors as possible.

Your second question here was around Alzheimer's and where we're thinking about our profile versus competitors. And when those competitor readouts, what are we going to be looking at. I think we have a number of design elements in TRAILBLAZER-2 that we spoke about previously that we think could be very important, probably starting with our use of biomarkers to select patients not just amyloid positivity but also win doing in on patients with intermediate tau levels.

So these aren't patients who have too much tau in the brain because we think there beyond the point where anti-amyloid drugs will help them nor are they patients with no tau in the brain because we think those patients won't progress even on placebo, and therefore won't get benefit from a drug. So we think selecting those patients will give us the opportunity to see better efficacy in a more homogenous background. Second, we think we have a drug that lowers amyloid faster and to a steeper degree and that should translate to improved benefits. And then third is some of the statistical differences in our analysis plan focusing on a composited measure ADRS, which we're excited about and things should be more highly powered to see a larger effect size.

So all of those things combined lead us to a point where even if competitors trials are negative and I think there's a reasonable chance one or both could be, we won't be discouraged what I expect to see though is when we look at the totality of data from competitor readouts prior to ours, we will see evidence that lowering amyloid in general is having a positive effect on solving cognition and function. Even if some trials on some endpoints at some time points hit or don't hit statistical significance, I think it's that totality data that will encourage us, and then as I said, our trial's designed to hit. So that's what we're hoping for and that's what we expect, middle of next year.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

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

Q - Alice Nettleton

Hi, thank for taking my questions, and congrats on the data. This is Alice Nettleton, on for Tim Anderson. Just on tirzepatide, but based your product and Novo to the go, the weight loss is impressive, but with based products that still about 30% to 40% of patients who placebo who don't achieve at least 5% weight reduction, which is quite a high percentage and it almost seems to suggest a resistance mechanism of some sort to circular. So is there any mechanistic rationale or predictability for those who don't respond? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks. We'll go to Dan for the question.

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

Yeah, thanks for that question. I think you're right, in past studies of different medications for weight loss, there have been a lot of patients who didn't respond. That's not the case with tirzepatide. So we're really delighted that at the 10 milligram and 15 milligram dose, more than 96% of patients had at least 5% weight loss. So this drug is working to some extent in the vast majority of patients in this trial and nearly two-thirds of the patients at the highest dose are getting 20% weight loss, which is really a life-changing level. So I think you're right. Patients are -- have variable degrees of resistance to anti-obesity mechanisms. But I also think that this combination of GIP and GLP that we have in tirzepatide is such a powerful mechanism that it overcomes those resistant patients for the most part. Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

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

Q - Umer Raffat {BIO 16743519 <GO>}

Hi, guys. Thanks for taking my question. And by the way, congrats on the data. It's how I maintain my physique. Well, I'm joking. So donanemab, I have two questions. One, have you been able to finalize the stack line with FDA? And also given your confidence in donanemab, I'm curious why it would not make sense to have a CDR Sum of the Boxes endpoint in there in TRAILBLAZER for the head to head versus.

And then separately, just a quick one, I noticed your slides mentioned the IL-2 conjugate in ulcerative colitis has been removed and I couldn't tell if it's being discontinued in that

because this trial is barely started less than 6 months ago. So just thought I should clarify. Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

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

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

Yeah, sure. So let me start with the Alzheimer's questions. I think we've been public about our stats plan. I think the focus on ADRS is well warranted by all of the data that we've collected by a pretty detailed statistical analysis, many of which have been published on past trials, which just show this is an outcome that performs better from a statistical perspective then things like CDR Sum of Boxes, while still capturing both function and cognition.

So CDR is noisy and also appears unreliable. If you look across sister studies, for example, the two solanezumab studies or the two aducanumab studies, CDR Sum of Boxes can move in opposite directions in different studies whereas ADLs and ADAS-Cog, the two components of ADRS are much more reliable, move together show consistent effects. So that's where we are. I think it's an evolution of endpoints and we'll do our best to justify that with regulators once we have our data.

Why wouldn't we have CDR Sum of Boxes was the second part question. Well, of course, we do. It's -- will be a gated secondary for sure. And I think from our perspective, the worst case scenario is that we're held to achieving ADRS and CDR Sum of Boxes. That's okay. If that happens, I hope and expect that we'll have a good chance to hit CDR Sum of Boxes, but of course, we're going to put what we see is the least noisy, most reliable, most formative endpoint first in our statistical analysis, which is ADRS.

With respect to IL-2, you're right. This was a pretty fast in and out in ulcerative colitis. We were pleased to enroll this Phase 2 study pretty quickly. We triggered interim analysis based on a certain number of patients with a certain amount of follow up and based on that analysis and pre-specified criteria, we do not see enough efficacy to proceed. So it fail that futility analysis. We dropped that indication, wind down that particular study, and all sort of colitis but two other indications persist.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

Next caller is Steve Scala from Cowen. Please go ahead.

Q - Steve Scala {BIO 1505201 <GO>}

Thank you. A couple of questions. The SURMOUNT-1 data was very impressive, but not a huge surprise. It must have been considered as a likely scenario by Lilly, yet Lilly's filing

strategy has shifted. So just to be clear, has FDA or other regulatory body encouraged Lilly to file early based on the SURMOUNT-1 results? So that's the first question.

Second question is, were there any inventory movements or other unusual movements in the quarter? It seems that a number of your key drivers just missed at least our thinking. So I'm wondering if it was inventory movements that accounted for that. Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Steve. We'll go to Dan for the regulatory question, then Anat for the question on inventory.

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

All right. Steve, I think you said, it's not a surprise. I think there are some things here that are quite a bit more positive than maybe most people would have expected. Certainly, the level of efficacy here that was achieved was I think higher than most expectations as well as the tolerability. So the adverse events from nausea, diarrhea, vomiting, lower probably than what most people would have expected treatment discontinuations particularly lower.

So I think on the whole, we have a data package that does exceed expectations. So it's really at the top end of the range of what we thought might be possible for a drug tirzepatide. So we're excited about that. Specifically, you're asking about regulatory interactions. We usually don't want to get into like back and forth on and things like that. But just to be clear, as I said before, our alignment with the FDA was around submitting when the full package is complete, and have not had discussions yet about what other options might exist in light of the state.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dan. Anat?

A - Anat Ashkenazi {BIO 19888043 <GO>}

So for the dynamics in Q1, we typically see dynamic associated with inventory build at the end of each calendar year in December and then following by inventory burn typically in the first quarter of each year. We saw the same dynamic here this year. We saw an impact on Trulicity, and a number of other products, which you may be seeing in as you're looking at the year-on-year comparison.

The other element, if you're looking at Taltz from a year-on-year perspective, we did see in Q1 in comparison to Q1 of 2021 reduction in script size. As you recall, last year we had -- we started our contract with ESI, and the loading dose with associate with multiple devices that each patient started on. So this quarter we're just seeing a reduction associated with that year-on-year comparison.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

The next caller is the Vamil Divan from Mizuho. Please go ahead.

Q - Vamil Divan {BIO 15748296 <GO>}

Great. Thanks so much for taking the questions. Maybe a couple more on the obesity side, if I could. So one, you mentioned the Amylin agonist that you've moved in the Phase 1 here. Can you just maybe talk about that? Is that maybe more of an insurance policy against four competitors you are working on, or do you so expect and when could maybe companies because the mechanisms additional efficacy and that was overseeing now with the blips and lots of issues at the time?

And then second, you talked about this a little bit before around the discontinuation and the duration. So can you just remind us what the current duration or average duration of therapy is with Trulicity, and then maybe if you have any sort of current something that how you want, or when you think patient may eng up staying in a product like yourself? But then, given the -- I think the superior profile, we're seeing for that is diabetes and or will be (inaudible). Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Vamil. We'll go to Dan for the question on kind of early phase obesity and then we'll go to Mike for the question around Trulicity duration and implications in obesity.

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

Yeah. Thanks, Vamil. You're asking about our long-acting Amylin agonist here. We've been interested in biology of other incretins and incretin-like pathways for many years, maybe a decade now or more. Amylin is one of those pathways. We've worked on dual Amylin calcitonin receptor agonist. This is a pure Amylin agonist. We're exploring these and other similar mechanisms as complements likely to tirzepatide. I don't expect any of these packages offer this kind of weight loss, 22.5% weight loss.

But I think it may be for some patients who desire even additional weight loss that you could stack one of these mechanisms on top of tirzepatide. But clearly, we've raised the bar and we'll look through our Phase 1 and Phase 2 portfolio now with even higher criteria for progressing. I think to a new weight loss mechanism now is going to have to be in the very high '20s I think to be an exciting advance beyond tirzepatide, maybe adding something to tirzepatide could accomplish that and offer the majority of patients efficacy similar even better to a bariatric surgery. That's the next frontier.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dan. Mike?

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

Yeah, thanks for the questions. A very good question. We -- when you look at diabetes versus obesity, it's hard to compare I think to suggest that because the nature of the

diseases that you'll have like similar discontinuation rates or our length of therapy, when you look at when someone starts Trulicity in Type 2 diabetes, they only have a fraction of the beta cell health of someone who is normal before the onset and the run-up or pre-diabetes and diabetes has lowered the functioning of the beta cell.

And so what you have in diabetes is that beta cell health continues to decline and then at some point, you may have to go on insulin. We don't believe that it will have that same dynamic and obesity that the effect of weight loss with someone who lives with obesity is not going to have that same effect of kind of wearing off with the beta cell health that you see for Trulicity and our GLPs in diabetes.

So we do believe that the weight loss will be more durable and that patients will be well motivated to stay on therapy. That said, it will be an area of focus for us to make sure that we learn why people stop taking obesity agents and we'll do whatever we can to support patients during the entire length of therapy.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

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

Q - Justin Burns {BIO 16978092 <GO>}

Hi, this is Justin on for Carter. Thanks for taking the questions and congrats on all these exciting updates today. The first one looking at read throughs to heart failure, just wanted to get your thoughts on the implications of this amount data on the ongoing summit study, given the weight loss is a predictor of outcomes there. Does the magnitude of weight loss that today increase your confidence in the outcomes of that study? And then are there any interim analysis, we should be looking for at the summit?

A - Kevin Hern {BIO 20557573 <GO>}

Okay, thank you. We'll go to Mike for those questions on summit.

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

Yeah, I mean, good question. I mean I think the strength of the SURMOUNT-1 data makes us confidence in the entire tirzepatide Phase 3 program for all indications and so obviously our hypothesis, one of the hypothesis was weight loss would help individuals with HFpEF, and obviously SURMOUNT-1 supported that. So we're confident in our HFpEF program for tirzepatide. I don't believe we have, and maybe Dan can lead into that question, off the top of my head, but I do believe we have any interim readouts on our heart failure study.

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

Yeah, Mike. I -- we usually try not to disclose potential interims to preserve the integrity of the study. So sometimes we build those options and sometimes, we're not, but I totally

agree that this weight loss sort of at the high end of expectations as I said earlier, it's just got to increase our confidence in HFpEF and of course, as we dig deeper, we'll look at a number of biomarkers in the study, which could further inform cardiovascular benefits.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dan, and Mike. Justin, thanks for your questions. Next caller, please.

Operator

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

Q - Kerry Holford {BIO 21698599 <GO>}

Oh, hi, thanks for taking questions. Please, another one just tirzepatide first. So is the compelling data today enabled an earlier filing in obesity? Are you also now hoping to secure a quick review? Do you think that that was so you could get that as a supplementary filing or perhaps you would look to use the PLP that you purchased this quarter? And can you also just confirm exact PDUFA date for the diabetes filing?

And then my second question for you, Anat, on IPR&D and guidance. Clearly this cost could evolve yet if you make further acquisitions, collaborations, and so. But can we expect you to provide visibility at the start of each year on what extent, what level of milestones you believe Eli Lilly will make in the year ahead? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Kerry. We'll go to Dan for the questions around regulatory filing around tirzepatide, and then again to Anat on IPR&D and guidance.

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

Yeah, thanks. Thanks, Kerry. just to clarify, we didn't announce plans for an early filing we just said we're moving to the next step and discussing options with regulators. You're right, we do have a PR that we've repurchased. We are excited to have a portfolio with -- rich with opportunities, both new molecular entities as well as the new indications such as the obesity indication. We'll choose based on regulatory path that are available to us and unmet medical needs and competition, of course, what's the best opportunities that factor on.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dan. Anat?

A - Anat Ashkenazi {BIO 19888043 <GO>}

Kerry, so on the IPR&D charges, while we're now building them into our non-GAAP actuals and we'll provide information not just on the quarterly results, but anything, any business development transactions that have been signed between the end of the quarter in our earnings call, but you -- if you look even at our numbers from last year, these numbers are highly variable and highly unpredictable. So you can move from 40 million in one quarter,

400 million in another quarter, or even 0, and when we issue guidance, it is practically impossible for us to provide any detailed view on what those charges will be not knowing what business development transaction we'll be signing.

So what we will do is, as we have those, we'll provide that information to the investment community every quarter, typically if it's associated with the large business development transaction there'll be a press release associated with it within the quarter. So you'll be able to see and track that. But providing it as part of guidance is challenging, practically impossible actually to predict these.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Anat. And Kerry had a question on the Type 2 diabetes PDUFA. We don't give PDUFA dates. We announce it in the quarter when we submitted it, but we -- as we said, we expect that by midyear. Thanks for your questions. Next caller, please.

Operator

The next caller is Evan Seigerman from BMO. Please go ahead.

Q - Evan Seigerman {BIO 18922817 <GO>}

Hi, guys. Thank you so much for taking my questions. I would love to know if you have any additional color to why we saw a higher discontinuation rate in the mid-dose of tirzepatide data. And then more broadly speaking, when you think about in the market between Trulicity and potentially tirzepatide, do you expect to switch patients over? How do you expect it to at the coexist, assuming approval of tirzepatide? Thank you so much.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Evan. We'll go to Dan for the first question around tolerability discontinuations and then Mike, for the second one on Trulicity and tirzepatide.

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

Yeah, thanks. In this study, the tolerability of the 10 milligram and 15 milligram doses were pretty similar. So it's not surprising the treatment discontinuation rates could have been pretty similar. Of course, there is a little bit more efficacy on the 15 milligram dose, which is important driver to stay on therapy. So you probably see the balance of tolerability and efficacy playing out a little bit better, perhaps in the 15, in the 10. But these are all pretty small rates of discontinuation, if you look at sort of mid-single-digit rates of discontinuation for AEs. So that's really great. I think better, better than expected.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Dan. And Mike, on Trulicity and tirzepatide marketing thoughts?

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

Yeah, thanks for the question. Our focus is going to be growing the class as well as growing our share of market in the class. We'll try to maximize the opportunity for our

entire incretin portfolio, I mean what's most important is not necessarily switches for molecules, existing products, but more the new patients that are coming on into the incretin class and winning those new patients and so I think over time, we'll get a mix between new patient starts and switches from other GLPs. But I think primarily, our focus is going to be on really driving tirzepatide wins of new patients coming into the class. And so that will be our approach going forward.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Mike, and Dan. Evan, thanks for your questions. Next caller, please.

Operator

The next caller is Chris Shibutani from Goldman Sachs. Please go ahead.

Q - Chris Shibutani {BIO 3202082 <GO>}

Thank you. Two questions, if I may on tirzepatide and the potential for read across from Nuvo's outcome study that is the next data point I think in terms of thinking about the progress of this ultimate opportunity. Can you frame for us what you think would be your expectations and maybe level set what you think would be a bar there? I know that you mentioned that you don't believe it's necessarily a gating factor. That would be helpful.

Second question on the post-final NCD for donanemab and the language that CMS used. Do you have clarity from perhaps post the final NCD that your current program will adequately address what they believe to be sort of structural requirements for the kinds of studies that need to be conducted in order for CMS to contemplate full reimbursement of Alzheimer's therapy? Thank you.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Chris. We'll go to Mike for just the thoughts on outcome studies in the competitive landscape there in obesity. And then Anne for the question on the NCD in the donanemab.

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

Yeah, good question. We touched on this a little bit early, but I the -- we expect the Step CV study to be successful given the expected weight loss and what he has expressed. We think that will be important to continue to grow the class and for some payers winning access on it. So we hope that the Step program is successful, we expect it will be and obviously, we have a very comprehensive Phase 3 program to demonstrate outcomes for obesity, we also are confident in.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Mike. Anne?

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

Yeah, thanks for the question on donanemab. So as Dan mentioned, our priority will be to advocate for reconsideration with the TB-2 Phase 3 data. So we do remain confident in donanemab and believe that TB-2 and our overall TRAILBLAZER program have extensive data and so as we review the requirements in the NCD, we believe our data should be sufficient to meet the high level of evidence criteria set forth by CMS if TB-2 as positive.

Obviously, we'll need to review this data with CMS and gain their agreement. So we'll do that very quickly. Our intention is as soon as we have that data to request reconsideration for national coverage and we believe that having two positive pivotal trials should meet that high level of evidence. As far as CMS, we've engaged with them throughout the process and so we'll continue to do so moving forward, and there's a number of statements in the NCD that we will see clarity on to gain additional clarity as we move forward. But yes, we do believe that we should meet that high level of evidence, but pending those discussions with CMS.

A - Kevin Hern {BIO 20557573 <GO>}

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

Operator

The next caller is Robyn Karnauskas from Truist Securities. Please go ahead.

Q - Robyn Karnauskas {BIO 15238701 <GO>}

Hi, thanks for taking my question. And I guess I'll keep going on the tirzepatide route. So a lot of you'll have question in the duration of therapy. Have you talked to payers about once you reach a point, where maybe some of your co-morbidities or gone and you're on drug, if they're going to be still reimbursed therapy? And then the second question for you is like when you think about this data now that you have in-house is very robust. What new trials might you think about or new indications whether it be obesity without comorbidities or other indications, might you want to start, now that you sort of have this in-house and it's clear? Thanks.

A - Kevin Hern {BIO 20557573 <GO>}

Thanks, Robyn. We'll go to Mike for both of those questions.

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

Yeah. Good questions. And when we are having discussions with payers, they do -- they are excited about the obesity class, iff we can demonstrate outcomes and if they have a patient who has seen benefits from a anti-obesity medication, they actually want to work with us to make sure that those individual stay on therapy in order to get and maintain the weight loss they've seen.

And so I think there'll be opportunities for us to partner with payers to ensure that we can maintain individuals on chronic medications. I think our expectation is that people do need to stay on tirzepatide long term in order to get the -- and maintain the weight

benefits and we will be working with payers to make sure that we can maintain that weight loss, so people can get the outcomes that they need.

Second question-- remind me, Kevin, what the second question was?

A - Kevin Hern {BIO 20557573 <GO>}

Any new trials or indications as you see this data beyond what we've announced.

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

Yeah, I mean, I think that we're going to talk about and in today's discussion obviously we'll internalize this data. We will -- this is, as we said earlier, this is a important therapeutic area for us, massive unmet needs and one that we are looking to play the long-term game on. So when you put those together, we obviously are, we'll be very thoughtful and aggressive, and if we do feel that there is additional need for trials on tirzepatide that can provide insights to payers and healthcare professionals, we'll do those trials. Thanks for the questions.

A - Kevin Hern {BIO 20557573 <GO>}

Yeah. Thanks, Mike. Thanks, Robyn, for your questions. The queue is exhausted. We'll go to Dave for the close.

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

Okay, great. Well, thanks for joining today's earnings and tirzepatide call, I guess, and your interest, of course, in the Company. It is an exciting moment for all of us. 2022 started in a similar fashion to how we ended 2021 with strong momentum across the business. We remain focused on executing our innovation-based strategy, which of course is to bring new medicines to patients and create value for all our stakeholders.

With strong commercial execution complemented by a pipeline of industry-leading opportunities, we believe Lilly continues to be a compelling investment. So thanks for dialing in today and please follow up with the IR team if you have questions we have not addressed on the call, and have a great day. Thanks.

Operator

Thank you. And ladies and gentlemen, this conference is available for replay beginning after 11 o'clock, at 11.15 Eastern Time today and running through April 28th at midnight. You may access the AT&T replay system at any time by dialing 866-207-1041, and if you're international, 402-970-0847, and entering the access code 472-6957. Again, those numbers are, one, 866-207-1041, and international is 402-970-0847, with the access code 472-6957.

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