Q1 2021 Earnings Call

Company Participants

- Arvind Sood, Vice President of Investor Relations
- David M. Reese, Executive Vice President, Research and Development
- Murdo Gordon, Executive Vice President, Global Commercial Operations
- Peter Griffith, Executive Vice President and Chief Financial Officer
- Robert A. Bradway, Chairman and Chief Executive Officer

Other Participants

- Alethia Young, Analyst
- Carter Gould, Analyst
- Colin Bristow, Analyst
- Cory Kasimov, Analyst
- Dane Leone, Analyst
- Geoff Meacham, Analyst
- Geoffrey Porges, Analyst
- Jay Olson, Analyst
- Kennen MacKay, Analyst
- Matthew Harrison, Analyst
- Michael Yee, Analyst
- Mohit Bansal, Analyst
- Robyn Karnauskas, Analyst
- Ronny Gal, Analyst
- Terence C. Flynn, Analyst
- Umer Raffat, Analyst
- Yaron Werber, Analyst

Presentation

Operator

My name is Erica and I will be your conference facilitator today for Amgen's First Quarter 2021 Financial Results Conference Call. All lines have been placed on mute to prevent any background noise. There will be a question-and-answer session at the conclusion of the last speaker's prepared remarks. In order to ensure that everyone has a chance to participate, we would like to request that you limit yourself to asking one question during the Q&A session. (Operator Instructions)

I would now like to introduce Arvind Sood, Vice President of Investor Relations. Mr. Sood, you may now begin.

Arvind Sood {BIO 4246286 <GO>}

Erica, thank you. Good afternoon, everybody. Welcome to our Q1 call. I think the two key themes for this quarter are continued focus on volume-driven growth and pipeline advancement. Lots to cover, but we'll do our best to stick to an efficient format of limited prepared comments and addressing your one best question.

The slides have been posted. Just a quick reminder that we'll use non-GAAP financial measures in our presentation and some of the statements will be forward-looking statements. Our SEC filings identify factors that could cause our actual results to differ materially.

So with that, I would like to turn the call over to our Chairman and CEO, Bob Bradway. Bob?

Robert A. Bradway {BIO 1850760 <GO>}

Thank you, Arvind. And hello, everyone, and thank you for joining our call. We've had a busy start to 2021 and a first quarter that's something of a mirror image to what we experienced a year ago. Last year, if you recall, we came out of the gate with a very strong January and February and then started to really feel the impact of the pandemic in March. This year, especially in the US, it was almost the reverse. We felt the impact of the pandemic in January and February and we began to see a recovery in March, a trend that seems to be holding in April as well.

Setting aside the pandemic, we executed effectively in the first quarter and this is reflected in the strong competitive performance of our brands globally. Our strong biosimilar showing, the rapid progress of our lead pipeline molecules and the addition of an attractive Phase 3-ready molecule in Oncology.

Altogether, we remain confident in our full-year outlook. We're fortunate to have a diverse portfolio of newer products that continue to show strong volume growth. Repatha, for example, delivered 36% volume growth in the first quarter. It remains the clear leader of the PCSK9 market globally, and will soon reach the milestone of 1 million patients served. We're also the global leader in bone health, with Prolia and EVENITY generating double-digit volume in the quarter. Our industry-leading portfolio of biosimilars is annualizing above the $2 billion mark. And I would remind you that we have three additional biosimilars in Phase 3 development and look forward to a flow of new launch opportunities for these and AMGEVITA over the next few years.

As we've shared with you many times in the past, we're active in business development, looking to complement our internally developed innovation with compelling external opportunities, and our recent acquisition of Five Prime Therapeutics is a good example of that. As you know, one of the molecules we acquired in that deal, Bemarituzumab, was

granted Breakthrough Therapy Designation by the FDA as a first-line therapy for a subset of patients with gastric cancer. More than 1 million new gastric cancer cases are diagnosed annually and the disease is particularly prevalent in the Asia-Pacific region, which we've said previously will account for approximately 25% of our growth over the next decade. Bemarituzumab is now our third late-stage clinical medicine to be granted Breakthrough Therapy status, joining Sotorasib for which the trade name LUMAKRAS has now been provisionally approved for use in the US, and Tezepelumab also has earned that Breakthrough Therapy distinction.

With a strong balance sheet, healthy cash flows and a proven ability to integrate, we'll continue to look for external opportunities that strengthen us in our stated areas of focus.

Before I turn things over to our CFO, Peter Griffith, I want to thank my Amgen colleagues for their continued commitment to serving patients around the world and delivering results for our stakeholders. I look forward to our Q&A session a little later in our call but for now, over to you, Peter.

Peter Griffith {BIO 4299061 <GO>}

Thank you, Bob. I would like to take a few moments to reflect on the strong fundamentals of the business and further, to reaffirm our full-year revenue and non-GAAP EPS guidance. Let me first confirm our predictable consistent capital allocation hierarchy as seen in our Q1 activity. It always begins with investing internal innovation. LUMAKRAS and Tezepelumab, both internally discovered and each granted Breakthrough Therapy Designation are excellent examples of this. We also patiently pursue external business development opportunities that clear our hurdle rate and then are consistent with our areas of therapeutic focus and which we are confident of integrating into Amgen efficiently and effectively on a timely basis.

We allocated $2 billion of our shareholders' capital to the Five Prime acquisition in the second quarter and have committed additional R&D funding to pursue other indications for the lead molecule bema. Our capital expenditures remain a high priority, including investments in our industry-leading protein manufacturing, our ESG initiatives including enabling carbon neutrality by 2027, and digitization imperative.

We continue to return capital to our shareholders. First, we paid dividends of $1.76 per share in the quarter, representing a 10% increase from 2020. This year marks our 11th year of dividends with meaningful increases in each of those years. Second, we repurchased 3.7 million shares in the first quarter at a cost of roughly $865 million. Finally, our capital allocation hierarchy always builds on our efficient capital structure, which results in an optimal weighted average cost of capital.

Now, I will briefly walk through our first quarter financial results. Recall that in 2021, we are now comparing to our recast 2020 results that exclude the impact of fair value adjustments to equity investment that were historically included in non-GAAP OI&E. In Q1, revenues decreased 4%. Historically, first quarter sales have been the lowest quarter as a percentage of the full-year. As we entered 2021, we knew that COVID would likely

introduce some variability. And as the quarter progressed and we saw a continuing cumulative effect of COVID cases on prescribing pattern, we anticipated that Q1 would be more negatively impacted, which led us to disclose in March that it would be moderately below 2020's percentage of the full-year.

First quarter sales benefited from 4% volume growth. Looking back to Q1 2020, we recorded approximately $150 million of favorable changes to estimated sales deductions, creating a negative impact on year-over-year growth comparisons in Q1 2021. As we get underway with the second quarter, we expect there to be some continuing cumulative COVID impact. While we expect to see improvements in the rate of recovery that recovery will be more heavily weighted to the second half of the year.

Total non-GAAP operating expenses for the quarter increased 2% year-over-year. For the full-year, we continue to expect cost of sales as a percent of product sales to be 16% to 17%. Effective Q2 2021, cost of sales will increase as a percent of product sales in connection with our first shipments of antibodies to Lilly. Recall that revenue from shipments of these antibodies will be recorded in other revenue. For the full-year, we expect R&D spend will increase as our innovative pipeline continues to progress, which now includes bema from the Five Prime acquisition as well as the Rodeo acquisition. And for the full-year, we expect SG&A spend to decline. We continue our focus on digitization imperatives.

Non-GAAP OI&E was a net $375 million expense in Q1. This is unfavorable by $79 million on a year-over-year basis due to the recording of our portion of BeiGene's loss this quarter. Recall, the recognition of BeiGene's results did not start until Q2 2020. The effects year-over-year of the adjustments in sales deductions, combined with the recognition of the BeiGene results totaled about $0.29 in decreased EPS on a comparison basis for Q1 '21 and explain a large portion of the 12% decline in EPS year-over-year.

Now, turning to the outlook for the business for 2021. Based on underlying market dynamics and our investment plan, we are reaffirming our 2021 guidance with a revenue range of $25.8 billion to $26.6 billion and a non-GAAP EPS range of $16 to $17. Important additional points to consider as you model the remainder of 2021. We are providing more specific quarter-over-quarter guidance given the unprecedented, continuing, cumulative COVID impact on the operating environment, but we do not expect to provide such guidance on an ongoing basis. We see the recovery from COVID-19 more heavily weighted to the second half of the year. And for the second quarter, we expect total revenues to grow between 7% and 10% sequentially from the first quarter. We continue to expect full-year non-GAAP operating expenses to increase by about 7% over last year.

With an operating margin of roughly 50%, which includes operating expenses for FIve Prime and Rodeo, historically the Q2 quarter-over-quarter operating expense increase is about 10%. But in the second quarter of this year, we expect quarter-over-quarter operating expenses to increase in the mid-teens percentage range, reflecting the impact of our Lilly COVID-19 antibody manufacturing agreement, investments for growth, including the Five Prime acquisition, as well as increasing activity levels including launch preparations.

For the full-year, we continue to anticipate non-GAAP OI&E to be a net expense in the range of $1.3 billion to $1.5 billion. Our capital expenditures guidance remains unchanged at $900 million and based on our confidence in the long-range outlook of the business, we are raising the upper end of our share repurchase range to $5 billion for 2021 versus prior guidance of $4 billion. So our range for share repurchases in 2021 is now $3 billion to $5 billion. Additionally, we are updating our non-GAAP tax rate guidance for 13.5% to 14% versus prior guidance of 13% to 14%. My confidence is strong in the long-term outlook for Amgen, given the strength of the business and the strength of our outstanding and dedicated team of 23,000-plus colleagues that deliver every day to patients and also deliver long-term growth to our shareholders.

This concludes the financial update. I'll turn it over to Murdo. Murdo?

Murdo Gordon {BIO 18450783 <GO>}

Thanks, Peter. First quarter product sales declined 5% year-over-year. Volumes grew 4% driven by double-digit growth for a number of products, including Prolia, Repatha, MVASI, and KANJINTI. Net selling price declined 7% and the year-over-year comparison was negatively affected by 2% due to a benefit in Q1 2020 from approximately $150 million of changes to estimated sales deductions that did not reoccur to the same magnitude in Q1 of 2021.

In the first quarter, the cumulative effect of the COVID pandemic on missed patient visits and diagnoses impacted our business. January and February were clearly affected by post-holiday COVID spikes, and March showed demand improvement across most brands, which has continued into April. Despite the impact of the pandemic, our teams have found solutions to address the continuity of care, stabilizing our continuing patient volume. We also saw improvement in customer-facing execution throughout the quarter across all communication channels, including face-to-face and virtual activities. We expect some COVID-19 related disruptions still in the second quarter with a steady recovery thereafter.

I'll now review some product details beginning with our innovative portfolio. In bone health, Prolia grew 16% year-over-year recording over $500 million of US sales in the US for the first time. As a majority of osteoporosis patients in the US have been vaccinated and diagnoses rates are at approximately 90% to pre-COVID-19 levels, we're confident in Prolia's continued growth in 2021.

EVENITY sales increased 7% year-over-year driven by strong volume growth. Given the severe impact of fractures on the lives of postmenopausal women, EVENITY provides an excellent therapy to build bone first, which should then be followed by treatment with Prolia.

Repatha sales increased 25% year-over-year to a quarterly sales record of $286 million driven by 36% volume growth, and we maintain global leadership in the PCSK9 class. Sales outside the US grew by 40% driven by strong patient demand. In the US, we continue to see strength in new patient starts with new-to-brand prescriptions growing

54% quarter-over-quarter, helped by favorable pharmacy benefit manager formulary changes. US volume growth demonstrates that we've made good progress against our strategy to provide Repatha at an affordable price to patients, particularly those with Medicare Part D coverage. This acceleration in Medicare Part D growth has increased our exposure to the so-called donut hole, which creates some negative impact on overall net price. We remain confident in our ability to grow Repatha globally to address the significant unmet medical need in treating high-risk cardiovascular patients.

Next, to Aimovig, which remains the market leader in the highly competitive CGRP class. Aimovig volumes grew 20% year-over-year in the first quarter, with a 45% average total prescription share and 38% average new-to-brand prescription share. Year-over-year net selling price declined, primarily driven by increased rebates to maintain patient access. Unfortunately, millions of patients suffering from migraine are suboptimally treated with older, less-effective therapies. Given the head-to-head data we've generated showing Aimovig's superiority against topiramate, we are confident we can help many more patients suffering from chronic migraine.

Turning to our Inflammation portfolio, where Otezla has demonstrated a robust safety and efficacy profile with over six years of real-world experience in market with more than 500,000 patients treated globally, and (inaudible) similarly has served millions of patients globally since 1998. Otezla sales were $476 million in the quarter. Volume growth was 9% driven primarily by 11% total prescription growth in the US. Otezla remains the market-leading brand in systemic medication for psoriasis with an approximately 30% share of first-line treatment.

However, new-to-brand prescription volume remained flat as COVID-19 continued to suppress the diagnosis and treatment of psoriasis patients. Year-over-year growth was also negatively impacted given pandemic-related inventory stocking in Q1 of 2020. Otezla has more than 90% commercial payer coverage in the US without requiring a biological step and is an affordable, safe and efficacious option for psoriasis and psoriatic arthritis patients. We see attractive growth opportunities for Otezla as the pandemic recovery progresses. In addition, geographic expansion and the anticipated approval later this year of the mild-to-moderate psoriasis indication will contribute to future Otezla growth.

In 2021, year-over-year comparisons for Enbrel are adversely impacted by $255 million of favorable estimated sales deductions that were recorded in 2020, $115 million of which were in Q1 of 2020. In the quarter, Enbrel sales decreased 20% year-over-year with declines in both unit volume and net selling price. Moving forward, we expect volume and net price trends to continue.

Parsabiv sales decreased 55% year-over-year driven by 60% volume declines. With Parsabiv's inclusion in the end-stage renal disease bundle in the US, we have seen dialysis clinics quickly implement new treatment protocols switching patients from Parsabiv to generic cinacalcet.

Switching to Biosimilars. Q1 sales were $570 million driven by strong volume growth, which was partially offset by declines in net selling price. We continue to hold leading

biosimilar shares in Europe for AMGEVITA, and in the US for MVASI and KANJINTI where we saw average shares of 50% and 43% respectively in Q1. For the remainder of the year, we expect biosimilar volume growth to be offset by declines in net selling price due to increased competition. Longer-term, growth for biosimilars will come from expansion of existing products to new markets and launches of additional biosimilar molecules such as AMGEVITA in the US and biosimilars for Soliris, Stelara, and Eylea.

In Oncology, Neulasta Onpro remains the preferred long-acting GCSF with 54% share of volume in the quarter. In Q1, we surpassed 1 million patients who, with the help of Onpro, were able to receive their GCSF treatment, while reducing the need to return to their doctor's office or other site of care for administration. Consistent with recent trends, Neulasta's US average selling price declined 30% on a year-over-year basis and we expect this trend to continue throughout 2021 driven by intensifying competition.

XGEVA sales decreased 3% year-over-year for the first quarter as volume growth in Asia was offset by lower net selling price in that region. US unit volumes declined year-over-year driven by demand impacts in January and February, with recovery beginning in March and into April.

Kyprolis sales decreased 10% year-over-year for the first quarter as the pandemic has suppressed the number of new patients starting treatment for multiple myeloma. Moving forward, we expect promotion to drive growth in second-line and beyond, as a result of our launch of the combination indication of Kyprolis and Darzalex plus dexamethasone, or DKd. The combination of Kyprolis with Sarclisa and dexamethasone, or IsaKd, was also approved in the quarter.

As Bob mentioned, our team is ready to launch sotorasib, or LUMAKRAS upon approval, and we're excited to establish it as a foundational therapy for patients with advanced lung cancer. We've already launched our Biomarker Assist program, which removes access barriers to testing and helps appropriate patients with out-of-pocket costs. And we're also preparing for the launch of Tezepelumab with our partner, AstraZeneca, and are enthusiastic about the prospect of having a therapy that can help treat the more than 2.5 million people in the world living with severe uncontrolled asthma.

Overall, I'm pleased with our Q1 execution given the pandemic-related disruption of new patient diagnoses and treatment, and we'll continue our focused execution during Q2 and are projecting recovery over the second half of the year. With that, I'll turn it to Dave.

David M. Reese {BIO 19782623 <GO>}

Thanks, Murdo, and good afternoon, everyone. I'll begin with two new programs that are strong strategic fits within our portfolio. First, we are excited to welcome our new colleagues from Five Prime Therapeutics and begin work on bemarituzumab. The integration is going well and we have hit the ground running with Phase 3 planning activities. As Bob mentioned, we received Breakthrough Therapy Designation from FDA and look forward to discussions with regulators on the development program including Phase 3 in the near future. We will also investigate bemarituzumab in other indications

where FGFR2b may play a role, including squamous non-small cell lung cancer, and we'll have more to say on the entire development program as those plans are finalized.

In inflammation, I would like to highlight our acquisition of Rodeo Therapeutics and their 15-prostaglandin dehydrogenase program, which was motivated by compelling preclinical data from Rodeo and valuable insights from deCODE. This is a nice illustration of our use of human genetic data to inform drug discovery and development.

The LUMAKRAS program continues to advance with several regulatory milestones in the first quarter, including global submissions for advanced non-small cell lung cancer and the Priority Review from FDA with a regulatory action date of August 16. We are having productive interactions with the FDA and multiple other regulatory agencies that will include Japan with today's anticipated submission, and we look forward to making LUMAKRAS available to patients as soon as possible.

We are also pleased to receive Temporary Authorization for Use status in France. This designation is to promote fast access to innovative medicines before marketing authorization and conventional access, and we have received a large number of requests.

In the clinical development program, we completed enrollment in the Phase 3 study versus docetaxel in advanced non-small cell lung cancer. Based on the overall efficacy and safety profile of LUMAKRAS and discussions with regulators, we reduced the sample size in this study, while maintaining appropriate statistical power to assess the progression-free survival primary endpoint. The timelines of the study have not changed as the primary endpoint remains event-driven.

While we have demonstrated that the 960-milligram dose is safe and efficacious in advanced non-small cell lung cancer, we continue to explore different doses and regimens as is common in oncology drug development. As part of this effort, we are initiating a new cohort to determine whether a once-daily oral dose of 240 milligrams maintains the safety and efficacy profile of the 960-milligram dose in patients with advanced non-small cell lung cancer. Should a lower dose be as safe and efficacious as 960 milligrams, it may further enhance the patient experience with once-daily LUMAKRAS. We expect the results from this study in late 2022 or early 2023, and do not expect any impact on the timelines of our ongoing Priority Review.

We also continue to make good progress in evaluating combination regimens. Efficacy cohorts are underway for our MEK inhibitor, EGFR antibody and oral EGFR inhibitor combinations, and we expect to present updates on these regimens at medical meetings in the second half of the year. We continue to evaluate doses and regimens to find the optimal options for patients in our other combinations including PD-1 and SHIP2. Finally, we are initiating triplet cohorts in colorectal cancer of LUMAKRAS with standard of care chemotherapy and either an anti-EGFR or anti-VEGF antibody.

In our BiTE programs, we have initiated several new studies, including new indications for AMG 160 targeting PSMA in non-small cell lung cancer; and AMG 757 targeting DLL3, now also being investigated in neuroendocrine prostate cancer. Details on these and

other development programs, including small molecules, can be found in our press release.

Turning to Tezepelumab developed in collaboration with AstraZeneca. The Phase 3 NAVIGATOR data were well-received by clinicians and additional analyses will be presented at the American Thoracic Society meeting in May. We remain on track to submit regulatory filings this quarter and believe the data support Tezepelumab as a first-line biologic therapy for a broad population of patients with severe uncontrolled asthma. We are also investigating other indications with Phase 2 studies in COPD and chronic spontaneous urticaria, and most recently a Phase 3 study for chronic rhinosinusitis with nasal polyps.

Finally on Otezla, we submitted a supplemental New Drug Application to FDA based on the Phase 3 ADVANCE study in mild-to-moderate psoriasis. The positive results from ADVANCE were presented at the American Academy of Dermatology, or AAD, meeting a few days ago.

In closing, I'd like to thank our staff for continuing to deliver for patients. Bob?

Robert A. Bradway {BIO 1850760 <GO>}

Okay. Erica, thank you. Let's turn now to Q&A and perhaps you could remind our callers of the procedure for asking questions. Thanks.

Questions And Answers

Operator

(Operator Instructions)

Your first question is from Geoff Meacham with Bank of America.

Q - Geoff Meacham {BIO 21252662 <GO>}

Hey, guys, thanks for the question. I had a question on Otezla, the head-to-head against deucravacitinib at AAD showed some pretty meaningful differentiation. I just wanted to ask from maybe a commercial perspective, how does that data sit along with the advanced data change your thinking about the positioning of Otezla in the marketplace with respect to psoriasis. Thank you.

A - Robert A. Bradway {BIO 1850760 <GO>}

Murdo?

A - Murdo Gordon {BIO 18450783 <GO>}

Yeah. Thanks, Jeff, for the question. The first thing I would just reiterate is that we anticipated that the Deucra data would indeed show what they did show. And we

assumed that in the model that we put together for the transaction, and we've assumed that for the balance of this year. What I would say is that we continue to believe that Otezla is really ideally positioned in the first-line pre-biologic psoriasis market. As I mentioned in my prepared remarks, we've been on the market for six years now. We have in-market cumulative patient experience with over 500,000 individuals globally. We have excellent commercial and payer coverage at over 90% of covered lives. And we continue to make really good progress, holding a 30% share in the market with really outstanding customer-facing capabilities.

The other thing that we of course look at is positioning in the market and how that holds up against not just Deucra but other competitors. And we think that we really are the first kind of option pre-biologic post-topical. And dermatologists have become very comfortable using Otezla that way. Payer coverage is consistent with that position in the market. And with the mild to -- pending mild-to-moderate indication data which we presented at the same AAD meeting, which was quite compelling, we expect to be able to expand our utilization of Otezla in psoriasis population in the milder patient type.

So overall, we like our position in the market. The way I see it is we still have to see how the full detailed safety data look for the Tyk2 product, given that it is part of the JAK family and it took six years and over 200,000 patients for us to understand the Celgene safety profile. So, I think there is a lot still to be understood here but not necessarily the safety and efficacy of Otezla.

Q - Geoff Meacham {BIO 21252662 <GO>}

Okay, great. Thank you.

Operator

Your next question is from Michael Yee with Jefferies.

Q - Michael Yee {BIO 15077976 <GO>}

I had a question maybe for David. You had a nice update and comments on KRAS. Maybe you could just put some context around the timing of data now for the second half around MEK and maybe talk about what drives the timing of that and disclosure. And then the comment around 240 milligrams versus 960 milligrams, I think there would be different ways to interpret that. Maybe you can make a comment about that because I thought 960 milligrams was pretty well-tolerated and it's got a good profile. So maybe make some comments on that, that would be great. Thanks, David.

A - David M. Reese {BIO 19782623 <GO>}

Yeah. Thanks, Mike. Both great questions. I think our anticipation is that at meetings right after the second -- right into the start of the second half of the year, we'll start to see some of the cohort data that we outlined MEK and then both EGFR antibody and small-molecule inhibitor combinations. And you can probably see those come out sequentially over the second half of the year as we accumulate data. I would say that the combination therapy programs are moving along quite rapidly and as we mentioned, we've opened

some new triplet combinations, so I feel very good about where we are in the status of combination regimens.

In terms of the dose comparison study, we've now got long-term data from both our Phase 1 trial as well as the Phase 2 trial, updated target coverage information, pharmacokinetics, as well as of course efficacy and safety data. And based on modeling, we wondered could we achieve adequate target coverage at 250 milligrams and preserve potentially the same efficacy profile that we've seen at 960 milligrams. And so that's just a question that we're going to ask. It's quite common to continue dose exploration in oncology molecules, and I would view this as a path for the course. We are very pleased with the tolerability profile and as you pointed out at 960 milligrams, we've had an outstanding experience. In fact, this is one of the best-tolerated drugs that I've been involved with in 30 years in oncology drug development. And that's not really what a driver is here, but can we potentially get by with efficacy at a lower 240-milligram dose and enhance the patient experience.

Q - Michael Yee {BIO 15077976 <GO>}

Yeah. Thank you.

Operator

Your next question is from Jay Olson with Oppenheimer.

Q - Jay Olson {BIO 18027199 <GO>}

Hey, thanks for taking the question. I'm curious about the Phase 2 data for Olpasiran that you expect in the first half of next year. Can you just talk about what sort of signals you'll be looking for in that data in terms of your plans to design a Phase 3 study and any potential points of differentiation from (inaudible). Thank you.

A - David M. Reese {BIO 19782623 <GO>}

Yeah. Thanks, Jay. And for those who may not know off the top of their heads what Olpasiran is, this was formerly AMG 890. It's small interfering RNA designed to lower lipoprotein(a) levels in patients with atherosclerotic cardiovascular disease where elevated Lp(a) may be a driver.

As we noted, we completed enrollment in what's a robust Phase 2 trial. That actually completed enrollment ahead of schedule. And what we'll be looking for as we unveil those data, Jay, are, first of all, longer-term follow-up. Meaning, sufficient long-term suppression of Lp(a) levels. Our targets would be in the range of the Phase 1 data that we presented last November at the American Heart Association meeting, and then of course additional safety data. And of course we are exploring different dose levels as is pretty much standard in a program like this, and so this would be in part for dose selection for Phase 3 going forward.

We are very actively engaged already in Phase 3 planning and what the design of that sort of trial may look like. Based on the data that we've seen to date, one of our goals may be

relatively infrequent dosing given the duration of effect that we observed in the Phase 1 trial. And that's one thing that we'll be taking a close look at as well in Phase 2.

Q - Jay Olson {BIO 18027199 <GO>}

Great, thanks.

Operator

Your next question is from Matthew Harrison with Morgan Stanley.

Q - Matthew Harrison {BIO 17603148 <GO>}

Great. Good afternoon. Thanks for taking the question. I was wondering if you could just comment a little more detail on the Repatha trend. It looks like we're really starting to see the product break out a little bit here and not seeing some of those first quarter gross-to-net issues that you've sort of experienced in the past couple of years.

Do you think you're at a point now where you're going to get substantial Part D penetration and also see rest-of-world penetration? Maybe if you could just comment on your outlook there. Thanks.

A - Murdo Gordon {BIO 18450783 <GO>}

Thank you, Matthew. We are pleased obviously with the quarter for Repatha, and it's been a bit of a journey getting here and trying to ensure that patients have affordable access to Repatha, particularly in Medicare Part D, as you point out. I would say that we are anticipating -- with one exception, we are anticipating relatively stable net price for the remainder of the year. And the exception that I'm pointing out is that as we expand our penetration of Medicare Part D, we will have some drag on our net price as a function of patients entering and staying in the donut hole for a period of time. So that's the one downside of helping patients in Medicare Part D. There is still a coverage gap in that benefit and of course given the durability of treatment and the chronic nature of Repatha, they can be in that coverage gap for quite a bit.

So, we do have more exposure to the donut hole over time but as you can tell from the first quarter, we were more than able to offset that small drag on net price. And we anticipate that we'll continue to penetrate that patient population, given the very strong payer coverage we have there with -- between commercial and Medicare, we've got over 80% covered lives for this important product and there are still millions of patients out there who are suboptimally treated for their hyperlipidemia, given that there are at very high risk of cardiovascular events.

And globally, we're seeing some really strong performance in Europe, in the Americas, China is doing quite well despite not having NRDL listing, and we continue to make inroads in Japan where we're the only PCSK9 on the market.

Operator

Your next question is from Yaron Werber with Cowen and Company.

Q - Yaron Werber {BIO 19486720 <GO>}

Great. David, if you don't mind, I just have a follow-up question as well about LUMAKRAS relating to PD-1 combo, specifically. I think you've said in the past that you haven't gotten to the MTD on both drugs as you tested them in combination, and it sounds like you're continuing to explore dose and schedule. You've also recently talked about sequential therapy. So just trying to say, are we actually going to get data in the second half and why are you testing sequential therapy? What are you trying to see? Thank you.

A - David M. Reese {BIO 19782623 <GO>}

Yeah. Thanks, Yaron. We're continuing to look at a variety of approaches in combination with PD-1s, whether that's in combination or sequentially. I think it's fair to say a number of small molecules, EGFR inhibitors, BRAF inhibitors, MEK inhibitors had challenges combining with PD-1s, and I think there is a fair amount of work out here. We are-- we'll provide updates. I don't know if we'll have data that's robust enough to share in the second half of the year. That's possible but I don't want to promise that. But certainly, we'll provide guidance as those different regimens move along and sequential therapy may be actually a preferred approach here.

Operator

Your next question is from Terence Flynn with Goldman Sachs.

Q - Terence C. Flynn {BIO 15030404 <GO>}

Hi, thanks for taking the question. Maybe just one follow-up on that, Dave. I was just wondering does the 940-mg dose exploration have to do with this question on how to best combine KRAS with a PD-1? And then my other question, I just was wondering, Bob or Peter, if you could comment on the tax proposals coming out of DC and any implications for your Puerto Rico -- some of the tax benefits you get out of Puerto Rico on the manufacturing side. Thank you.

A - David M. Reese {BIO 19782623 <GO>}

Yeah. Thanks, Terence. I'll take the first part of that question. Yeah, the 240-milligram dose comparison study doesn't have really anything to do with the combinations dosing. As you're aware, in combination regimens in oncology, one typically explores a range of doses potentially of all of the members of that combination regimen depending on what the backbone may be, but this is really a monotherapy exploration. And again, determine to see whether we can preserve efficacy at a lower dose, at this lower 240-milligram dose.

A - Robert A. Bradway {BIO 1850760 <GO>}

On the tax front, Peter, why don't you share our thoughts?

A - Peter Griffith {BIO 4299061 <GO>}

I would. Terence, very good question there. And look, I think it's premature to speculate on this. We expect the administration's proposal to be subject, I think as everybody does, to significant debate within Congress and other stakeholders. Rest assured, we're active in Washington to ensure that our position (technical difficulty) should continue to be competitive and should continue to really encourage innovation in the United States is well-heard and understood.

And we are very supportive, as you can imagine, of incentives to encourage manufacturing in the United States and the US territory of Puerto Rico. And Terence, I would just let you know that our tax leader, Jackie Crouse, has much expertise in the area of Puerto Rico and not just around tax, but just overall into how the economy down there functions and so forth. She's called upon regularly by the legislature for advice and counsel.

Thanks again for the question.

Operator

Your next question is from Umer Raffat with Evercore ISI.

Q - Umer Raffat {BIO 16743519 <GO>}

Hi, thanks so much for taking my question. David, I have a two-part question on KRAS. First, perhaps if you could just walk us through your thought process on why 240 milligrams in particular. Why not 180 milligrams or 360 milligrams? And I say that in the context of having seen responses as low as 180 milligrams. Perhaps you could even give us a flavor for the PK KRAS [ph] look-like around the 240-milligram doses above and below.

And secondly, I recall back when the Phase 3 was initiated for KRAS, the powering math was really directed at OS not PFS, even though the primary endpoint is PFS. I realize the conversations with FDA have moved towards PFS and it looks like the new powering is more than reasonable for PFS, but I do want to understand the evolution in thought process away from OS and what we can reasonably expect on p-values around OS with data as it emerges. Thank you.

A - David M. Reese {BIO 19782623 <GO>}

Yeah. Thanks, Umer. Good questions. The 240-milligram dose was chosen based on modeling that we've done that really takes account of all of the dose levels, pharmacokinetic data, target coverage data, our accumulated preclinical data regarding efficacy at different target coverage levels. And this was really chosen as a lower bound where we thought we would potentially preserve or could preserve the efficacy that we're seeing at 960 milligrams.

In regards to the Phase 3 trial, as you note, we changed the powering to really have -- we have good power on the progression-free survival endpoint. That was done in concert with regulators. We will be able to take a look at overall survival. The power will be

somewhat reduced in terms of the overall survival endpoint, but I think we'll still have a pretty good sense of what the drug is producing in terms of overall survival. Our part of the thinking here as well is to minimize exposure of patients to the docetaxel control arm.

Q - Umer Raffat {BIO 16743519 <GO>}

Thank you.

Operator

Your next question is from Mohit Bansal with Citi.

Q - Mohit Bansal {BIO 18070890 <GO>}

(technical difficulty) question and maybe one question for Murdo. Onpro has done really well during the pandemic. Could you please remind us how often these contracts are negotiated and should we expect any reversal in Onpro trends, are you seeing anything there as the pandemic subsides? Thank you.

A - Murdo Gordon {BIO 18450783 <GO>}

Thanks, Mohit. The contracts aren't necessarily on a schedule. We have some large networks where we negotiate annually, but we have a lot of smaller, what we call value-based accounts, where we contract on a much more non-calendarized basis. So, they're happening throughout the course of the year.

And is your question, with respect to reversal, are you asking me about price trends, volume trends? Can you clarify that question?

Q - Mohit Bansal {BIO 18070890 <GO>}

I mean the trends -- I mean because there was a trend towards using more Onpro versus the PFS, given it is at-home products. So, do you think there could be some kind of reversal there as the pandemic subsides? Because then, I mean, patients can come in and then get their shots.

A - Murdo Gordon {BIO 18450783 <GO>}

Yeah, thank you for the clarification. Obviously, we're watching that. Clearly, the pandemic was stimulus for many oncologists to think more carefully about the GCSF treatment that they were going to use in order to help minimize the amount of provider interaction that patients would incur. What we have been doing in the meantime, though, is reinforcing that you actually can improve outcomes by using long-acting GCSF and using Onpro in particular. So, we have a promotional effort that I think is helping strengthen the volume demand curve.

The only thing I will continue to point out, though, is with competition come some price erosion. And we have a new competitor entrant in that category in the long-acting GCSF category, so we anticipate more net price evolution -- negative evolution through the remainder of the year.

Q - Mohit Bansal {BIO 18070890 <GO>}

Got it. Thank you very much.

Operator

Your next question is from Geoffrey Porges with SVB Leerink.

Q - Geoffrey Porges {BIO 3112036 <GO>}

Thank you very much for the question. Murdo, could you just discuss the issue of price. Pretty significant negative price effect. First of all, could you tell us whether that's all in the US, or whether it's US and ex-US? And then secondly, since in the US took significant price increases at the end of the year but still have a negative price Q-on-Q, it looks like 8% or 9%, is this going to be a trend that persists throughout the year?

And then, Bob, perhaps you could comment on what we should be modeling in terms of legislative or executive order changes to pricing going forward. You usually have your finger on the pulse in Washington. Thanks.

A - Murdo Gordon {BIO 18450783 <GO>}

Sure. All right, thanks, Geoff. Let me go first on the overall price evolution in the portfolio. We continue to believe that mid-single digit net negative price for the portfolio for the year is the right number and that's what we continue to see. What you know and what we experienced probably more than some of our peer companies in the first quarter, given the nature of our portfolio, is more net negative price evolution because of patients renewing in their benefits and going through benefit re-verification and hitting their kind of out-of-pocket resets. And so our co-pay assistance programs have more drag.

We did activate more payer access at the end of last year into this so we did have on some brands, some increased payer coverage at the cost of some net price negative evolution. But we do anticipate Q1 being the lowest compare, Q2 a little better, and then Q3 and Q4 being better thereafter.

Q - Geoffrey Porges {BIO 3112036 <GO>}

Great, thank you.

A - Robert A. Bradway {BIO 1850760 <GO>}

And Geoff, on Washington, I'm not sure whether executive orders are the concern these days or whether it's something that's attached to reconciliation. If I had to guess, I'd say the greater risk was something being attached to reconciliation. But it's still not very clear how this administration and members of the Democratic Party in general want to try to tackle the question of drug pricing this year. So, we're continuing to stay very involved, as you would expect. And we have the benefit, I think, of being able to demonstrate just how important innovation is with progress you see being made against the pandemic.

And so, we'll continue to stay active and focused on the things that could be done to improve patient access to medicines. And I think the other thing, Geoff, is to continue to shine a light on the role of the middleman and how much of the pharmaceutical dollars now wind up in the hands of the middleman, which I think now across the country is just in excess of 50%. I think it actually is at 51% now. So, we'll continue to draw attention to that as well.

Q - Geoffrey Porges {BIO 3112036 <GO>}

Great, thank you.

Operator

Your next question is from Alethia Young with Cantor Fitzgerald.

Q - Alethia Young {BIO 17451976 <GO>}

Hey, guys. Thanks for taking my question. I just wanted you guys to talk a little bit more about the moderate-to-severe psoriasis market and how you plan on kind of penetrating with the current commercial sales force you have, especially in light of potential competition that may emerge over time with Bristol. And then just also with the SHIP2 program, is that still underway as a combination for you guys? Thanks.

A - Robert A. Bradway {BIO 1850760 <GO>}

Maybe I'll just start very quickly, Alethia. SHIP2, yeah, that's underway and we're continuing to work on that combination. More to come. Murdo?

A - Murdo Gordon {BIO 18450783 <GO>}

Yeah. And Alethia, as I mentioned earlier in response to the question on the Tyk2 data that we recently presented, we -- as I've mentioned in the past, we have begun primary care promotion for Otezla in the currently labeled mild-to-moderate patient population and have seen good response there in terms of uptake with 11% TRx year-on-year performance for the quarter. We're pretty pleased with that evolution.

What we are seeing is a slowdown in the psoriasis patient population, in the newly diagnosed patient population in particular. And we think this is a direct impact of COVID causing patients with psoriasis not to see their dermatologist, starting really at the beginning of the pandemic. But what's happened is the cumulative effect of this is starting now to impact the patients that have passed through some of the topical options. And we depend on bio-naive patients for our growth, so we are definitely pre-biologic option for dermatologists. So, we are watching that closely and we think that that could continue to create some softness in the pre-biologic psoriasis patient market opportunity into Q2 with recovery thereafter because we are seeing much more patient volume in dermatology offices in March and into April. So, we think that things are recovering but it will take a while for that cumulative effect of new patient softness to work its way through the market.

In terms of overall positioning in the market, we continue to think that our safety and efficacy profile is a very attractive option for patients and dermatologists as that first systemic agent pre-biologic. And I think really these days in rheumatology and dermatology, physicians are much more aware of the different categories of options that they have and the different profiles of the different classes of drug. And I think that with recent data in the JAK category, there'll be some speculation and some hesitancy to use a product like the Tyk2 as a first bio-naive option to treat patients.

A - Robert A. Bradway {BIO 1850760 <GO>}

Hey, Erica. Thanks. Let's go to the next question.

Operator

Your next question is from Dane Leone with Raymond James.

Q - Dane Leone {BIO 15203956 <GO>}

Hi, thank you for taking the questions and congrats on the update and the start to the year. So the question for me, which is a follow-up to some of these (inaudible) questions, is really maybe since people have been asking about fairly specific things. I think what everyone is trying to analyze and some of the updates if we're really only getting longer-term follow-up on your pivotal dataset at ASCO, is what the team's view right now of the ability to move sotorasib into the frontline setting in lung. A lot of us had thought that you would need a combination -- successful combination with PD-1 to move into the frontline setting.

Obviously, we haven't seen you guys start a pivotal dataset and you just said might take longer to figure out that algorithm. Alternatively, you go down the SHIP2 pathway. Do you, one, have a timeline for showing us SHIP2 combination data; and two, is there an alternative path for getting sotorasib into the frontline lung setting that we should be thinking about that we might be missing on this call right now? Thank you.

A - David M. Reese {BIO 19782623 <GO>}

Yeah. Thanks, Dane. In terms of potential frontline combinations, I think a number of them that are being examined in the master protocol, if we can enhance efficacy by multiple hits on the pathway could be feasible. For example, the MEK combination, the EGFR inhibitor combinations. And then as well as you mentioned, PD-1. Whether that is in combination or sequentially, for example, to rely on a priming effect is the question that we're trying to answer. SHIP2, I would also consider an additional hit on the pathway and would also fall into that grouping.

So, I think we'll be guided by emerging data, but all of those would be potential avenues into earlier lines of therapy. In addition, also potentially avenues into other indications such as colorectal cancer and some of the other solid tumors where G12C mutations occur.

Operator

Your next question is from Ronny Gal with Bernstein.

Q - Ronny Gal {BIO 15022045 <GO>}

Good afternoon and thank you for fitting me in. Two, if I may. First, just the traditional sotorasib question. I guess we saw some data in (inaudible) about patients having multiple escape [ph] mutations from the first -- when treated with a KRAS G12C inhibitor. And I was wondering, does that concern you that the patient escapes so quickly with multiple mechanism, does that suggest that maybe two agents will not be enough, or is that kind of parth for the course and this is what was expected?

And second, we have seen some of your peers license China developed and tested product to bring to the developed market, especially in oncology. And I was wondering if you consider the strategy, especially as a biosimilar player, as it seems to be a natural complementary strategy? Any (inaudible) come out on that.

A - Robert A. Bradway {BIO 1850760 <GO>}

Maybe I'll start with the first part and then have Murdo address the second part. Yeah, in terms of the mutational patterns that were recently reported, I would say that biologically nothing that we saw surprised us based on everything we've learned about these pathways in the last 30 years to 40 years and the potential mechanisms of resistance. This also points the way, I think, too, to specific combinations that may in fact help to ameliorate those resistance patterns.

I will point out that we will be presenting in short order here also updated comprehensive biomarker data, including mutational data. And I think you'll find that of interest and that is certainly helping to guide our own thinking about the development program as well. And Murdo, you want to take the second half of the question?

A - Murdo Gordon {BIO 18450783 <GO>}

Yes. Ronny, we continue to look globally for product opportunities to license and promote in the world. And I think in oncology in particular, there have been some interesting deals done lately. We obviously have a strong partnership already with a company based in China through BeiGene and we continue to enjoy that partnership in the co-development that we have.

I would also say that given our global footprint, Amgen really is an excellent partner of choice with our global capabilities in oncology and general medicines, so we're open to do business with Chinese companies, Japanese companies, global companies. Absolutely.

A - Robert A. Bradway {BIO 1850760 <GO>}

Okay. Erica, we're pushing up against the top of the hour, so we'll try to get to all of our questions but why don't we bring in the next caller?

Operator

Okay. Our next question is from Carter Gould with Barclays.

Q - Carter Gould {BIO 21330584 <GO>}

Great. Good afternoon and thanks for all the color today. Maybe just switching gears a bit and moving to BCMA, it sounds like you're about to go back into the clinic. Can you maybe just give us some color on sort of the changes to the protocol or dose escalation, any read through to the the broader platform, and just I guess focus more specifically on BCMA with those changes, comment on sort of your competitiveness in a increasingly competitive space? Thank you

A - David M. Reese {BIO 19782623 <GO>}

Yeah, Carter. Thanks for the question. So, we do expect to begin dosing again, hopefully in the next few weeks or so. As you intuited, this would adjust some of the intra-patient dose escalation that is typical with the use of BiTE molecule. And so that -- we'll be pushing pushing that forward. More broadly, obviously we want to be able to deliver a program here that can offer something to patients and physicians that they otherwise might not have, and we'll continually assess the program against that metric.

More broadly, I'm quite pleased with the progress we made on AMG 160 and AMG 757. And as always, would always provide a cautionary note about extrapolating extensively across programs because much of what we witness in the clinic is target dependent. And so all of these programs will have their idiosyncrasies that need to be worked through as part of the development program.

Operator

Your next question is from Colin Bristow with UBS Equities.

Q - Colin Bristow {BIO 17216671 <GO>}

Hi, good evening. Thanks for fitting [ph] me in. Just a quick update from you guys on the business development priorities, what are your current areas of interest, how are you thinking about deal size, and just some overall, I guess, commentary on how you're thinking about valuations in this space. Thanks.

A - Robert A. Bradway {BIO 1850760 <GO>}

Well, Colin, as you know, we've transacted two acquisitions in the first quarter; one at the preclinical stage, one at the Phase 3-ready. And I think that reflects the breadth of interest that we have. We're continuing to look at acquisitions and licensing opportunities in our stated areas of focus. So in particular, immunology, the inflammatory diseases, cardiovascular diseases, cancer are attractive to us. And then we have very strong franchises in a few other therapeutic areas as you know, in migraine, in bone health and nephrology, so we look for commercial opportunities there as well.

Q - Colin Bristow {BIO 17216671 <GO>}

That's helpful. Maybe just one quick question. In terms of protein degradation, obviously you have a platform that's somewhat early. Just any interest in expanding your positioning in that space.

A - Robert A. Bradway {BIO 1850760 <GO>}

Yeah. As we said before, I think going forward we would expect the development of what we call the induced proximity platform to depend both on internal innovation and external partnerships and potentially acquisition. So, we're open to both, we're making a lot of progress there and we'll provide more detail a bit later.

Erica, I gather we have a couple more questions lined up, so we'll take those remaining questions with apologies to the audience. We're going over the allotted hour. Let's get the next question.

Operator

Your next question is from Robyn Karnauskas with Truist.

Q - Robyn Karnauskas {BIO 15238701 <GO>}

Thanks, guys. So, you addressed a little bit of the moderate-to-severe pressure on the competition for Otezla. Could you again address a little bit more now that we have more granular data from (inaudible) and others on the topicals, do you think the topicals being cheaper might push out some of the uptick in the biologics for Otezla?

And then if you want to answer that one. Just throwing out here, you're one of the first to do RTOR application for oncology. With all the FDA controversy at the moment, can you just tell us like how that's going? Is it proceeding as normal? We're all wondering how that application process will go because that could be the faster way to market for a lot of new drugs. Thanks.

A - Robert A. Bradway {BIO 1850760 <GO>}

Try to get them both quickly.

A - Murdo Gordon {BIO 18450783 <GO>}

All right. Robyn, look, we think that there is obviously a role for topicals to play for patients with low body surface area involvement in their disease. But when it starts to become broader surface area or in awkward places on the patient's body, then they're looking for a systemic agent and they're looking for a safe and effective one. And that's really where we think the mild-to-moderate opportunity is for Otezla.

And we're not even considering the millions of patients out there with mild-to-moderate. We're looking at about a 40% to 50% addressable patient population. So, we're giving at least half the market as a topical market, assuming the other half would be addressable with an oral. Dave?

A - David M. Reese {BIO 19782623 <GO>}

Yeah. And in terms of RTOR, or Real-Time Oncology Review, what that does is permit submission of tranches of data as you move through the submission process, as opposed to waiting and submitting either a complete file all at once or very large chunks of a file. We've had very productive interactions with the FDA and in our view, the RTOR process has worked quite nicely here. In the longer term, quite frankly, I think this is the way of the future not only in oncology, but across therapeutic areas for more real-time submission of data probably from the inception of development programs.

A - Arvind Sood {BIO 4246286 <GO>}

Erica, let's take two last questions, please.

Operator

And your next question is from Kennen MacKay with RBC Capital Markets.

Q - Kennen MacKay {BIO 18821382 <GO>}

Hey, thanks for squeezing me in. A question on Tezepelumab. We've recently heard from (inaudible) some thoughts that this actually could be as competitive as some of the other biologics in asthma in the high eosinophil group, not just competitive in the high unmet needs (inaudible) eosinophil market. Just wondering when that data does come out, that full publication does come out, really what we should be looking for in these high eosinophil patients for signs of competitiveness there. Thank you.

A - David M. Reese {BIO 19782623 <GO>}

Yeah. Thanks, Ken. As we've reported, as you saw and will be providing some data updates, additional analyses on the NAVIGATOR Phase 3 trial at the American Thoracic Society meeting in a few weeks now, across the board we saw efficacy that we think is consistent with first-line use. It's important to understand that there are many patients with severe uncontrolled asthma who have disease that is seeking another treatment right now. Meaning, they are not controlled with currently available therapies. And so regardless of the eosinophil count, we think that the clinical profile of this molecule is quite attractive. And my view continues to be that this is just going to be a really important medicine in asthma for patients.

A - Arvind Sood {BIO 4246286 <GO>}

Erica, let's take one last question.

Operator

Your final question comes from Cory Kasimov with JPMorgan.

Q - Cory Kasimov {BIO 3009346 <GO>}

(technical difficulty) updated LUMAKRAS's ability to penetrate the blood-brain barrier, and do you see this as a potential future source of differentiation one way or the other in

the KRAS field? Thank you.

A - David M. Reese {BIO 19782623 <GO>}

Yeah, Cory thanks are quickly. So, we are actually studying specifically LUMAKRAS in patients with brain metastases. I think the clinical data will be definitive here and once we've amassed a large-enough dataset, we'll present that. But it's full-speed ahead, to answer that question.

A - Robert A. Bradway {BIO 1850760 <GO>}

Okay. Well, thank you all for your patience and for dialing into the call today. Remind you as always that Arvind and his team will be around for several hours still if you had other questions that you didn't get answered, but we appreciate your support and look forward to being back with you in July. Thanks.

A - David M. Reese {BIO 19782623 <GO>}

Thank you, everybody.

Operator

This concludes Amgen's First Quarter 2021 Financial Results Conference Call. You may now disconnect.
