Q1 2017 Earnings Call

Company Participants

- Anthony C. Hooper, Executive Vice President, Global Commercial Operations
- Arvind K. Sood, Vice President, Investor Relations
- David W. Meline, Chief Financial Officer & Executive Vice President
- Robert A. Bradway, Chairman & Chief Executive Officer
- Sean E. Harper, Executive Vice President-Research & Development

Other Participants

- Aaron Gal, Analyst
- Alethia Young, Analyst
- Carter Gould, Analyst
- Christopher Raymond, Analyst
- Cory W. Kasimov, Analyst
- Eric Schmidt, Analyst
- Eun K. Yang, Analyst
- Geoffrey C. Porges, Analyst
- Geoffrey Meacham, Analyst
- Joshua E. Schimmer, Analyst
- M. Ian Somaiya, Analyst
- Matthew K. Harrison, Analyst
- Salim Syed, Analyst
- Terence Flynn, Analyst
- Umer Raffat, Analyst
- Ying Huang, Analyst

MANAGEMENT DISCUSSION SECTION

Operator

Good afternoon. My name is Derek, and I will be your conference facilitator today for Amgen's first quarter 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.

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

Arvind K. Sood {BIO 4246286 <GO>}

Thanks, Derek, and good afternoon, everybody. So first of all, thank you for taking the time to participate in our conference call today to review our operating performance for the first quarter of 2017.

Before we begin, I would like to extend a warm welcome to those who are new in their coverage of Amgen, including Umer Raffat of ISI Evercore and Carter Gould of UBS. Each of us very much look forward to working with you.

We made a lot of progress during the quarter both in our commercial execution as well as our R&D efforts, so I'm anxious to get started. I would urge you to listen for specific themes, including volume-driven growth and operational expense management as you hear our senior leaders describe our performance.

Our Chairman and CEO, Bob Bradway, will lead the call today with a brief report on how we are executing against our long-term strategy for growth. Following Bob, our CFO, David Meline, will review our financial results for the first quarter and our outlook for the remainder of 2017. Our head of Global Commercial Operations, Tony Hooper, will then discuss our product performance during the quarter, followed by our head of R&D, Sean Harper, who will provide a pipeline update. And I'll give you a heads-up right now that we have a lot to discuss on our R&D efforts.

As is customary for us, we will use slides for our presentation today, which have been posted on our website, and a link was sent to you separately by e-mail.

We plan on using non-GAAP financial measures in today's presentation to provide information which may be useful in understanding our ongoing business performance. However, these non-GAAP financial measures should be considered together with GAAP results, and reconciliations of these measures are available in the schedules accompanying today's press release on Form 8-K and also on the Investor Relations section of our website.

Just a reminder that some of the statements made during the course of our presentation today are forward-looking statements, and our 2016 10-K and subsequent filings identify factors that could cause our actual results to differ materially.

So with that, I would like to turn the call over to Bob. Bob?

Robert A. Bradway {BIO 1850760 <GO>}

Okay, thank you, Arvind, and thank you all for joining our call.

It's been an active first quarter at Amgen. And before talking about our financial results, I want to put the events of the first 90 days of the year in context because I think they

underscore the reasons why we're confident about achieving our long-term objectives for growth.

As you know, we're focused on six therapeutic categories. And during the quarter, we achieved important milestones in each of them. Core to our strategy is a commitment to differentiated innovation. We aim for products with a big effect size in areas where the unmet need is high. That's what we feel will be required to succeed over the long term in this industry.

In our cardiovascular portfolio, we strongly believe Repatha represents one such product. As all of you know, cardiovascular disease poses by far the biggest health burden on society today. And our outcomes data demonstrated unequivocally that Repatha can play an important role in reducing that burden. And the data also showed to my mind that the rate of cardiovascular events, which approached 10% per year in the optimized statin arm of the trial, is still far too high without Repatha.

Against this backdrop, we expect Repatha to be an important product in the fight against cardiovascular disease and increasingly expect physicians, patients, and other stakeholders to recognize that rejecting an innovative drug for high-risk patients which demonstrated beyond 12 months a 35% reduction in the risk of heart attack, a 24% reduction in the rate of stroke, and a 28% reduction in the rate of revascularizations is simply inappropriate.

The practice of medicine won't change overnight but it won't stall either, not in the face of an innovative new therapy that can prevent hundreds of thousands of otherwise needless and tragic events. In the U.S. alone, cardiovascular disease costs our society in excess of $600 billion a year. And without meaningful innovation like Repatha to change the trajectory of this disease, those costs will exceed $1.2 trillion by 2035.

We believe it's right to embrace innovation not only for patients but also for society. Economic study after study has shown that society benefits financially from adopting therapies like Repatha. Nonetheless, we recognize the access challenges of the day, and that's why we have and will continue to offer innovative value-based contracts to help build a bridge between the medical need and the affordability concerns for patients and payers.

In addition to novel biology, intellectual property is another source of differentiation for our innovation. We were obviously gratified this quarter by the Delaware court's support for our position on Repatha, and we now stand ready for the Appeals Court to hear the case in June.

In oncology, there's no better standard for differentiated innovation than achieving an overall survival advantage for patients. In the first quarter, we achieved that with both KYPROLIS and BLINCYTO. The BLINCYTO results are encouraging for patients with acute lymphoblastic leukemia obviously. But more broadly, they are encouraging as validation for the whole approach of our immuno-oncology BiTE platform. Perhaps because we are the only company with an advanced BiTE platform, this area is not as well understood in

the investment community as other areas of immuno-oncology, but we're excited about the potential of our BiTEs and have several programs moving swiftly in our pipeline. We look forward to sharing data as they become available from these efforts.

The overall survival data for KYPROLIS achieved at an interim analysis in relapsed multiple myeloma patients are also very important and timely. Having established superiority versus Velcade, we expect these data will drive increased share for KYPROLIS, particularly in the second line, and will also be helpful for reimbursement considerations.

Also in multiple myeloma this quarter, we achieved positive results for XGEVA. And subject to regulatory approvals, we look forward to being able to offer this therapy to multiple myeloma patients, many of whom are at risk of skeletal-related events such as those prevented by XGEVA.

Bone health remains an area of high unmet medical need, as still millions of women at high risk for postmenopausal fractures remain untreated. Reflecting on the number of postmenopausal fractures, the World Health Organization called this a global epidemic. Prolia's ongoing significant volume-driven growth, 21% in the quarter, attests to the value of differentiated innovation in this field. Already the leader in bone health, we expect EVENITY will strengthen our hand. And while we await both further clinical data and regulatory reviews, Sean will describe the encouraging results that we received this quarter for the three-year follow-up from the FRAME study.

While discussing our strategy of differentiated innovation, I also want to address our newest therapeutic area, which is of course neuroscience, where we are on the threshold of a novel first-in-class therapy for migraine sufferers. We had the opportunity to present our registration-enabling data at the American Academy of Neurology this week. And not surprisingly, experts in the field were excited about erenumab in an area where there is otherwise precious little to offer those suffering from episodic and chronic migraine.

I've seen some headlines asking whether our expanded collaboration with Novartis signals a waning of our enthusiasm for this opportunity. The answer is absolutely not. We have high hopes for erenumab. And at the same time, we recognize this is a new therapeutic category for us and will likely be a competitive race. So we were very pleased that Novartis, already our collaborator in international markets, shared our enthusiasm for this first-in-class molecule in the U.S. and our determination to resource this product to win. With their decades of experience in neurology and a shared commitment to serve those suffering from migraine, we're excited about our expanded collaboration.

When it comes to strategy, you've also heard us talk about life cycle management, especially for our legacy franchises. The Neulasta Onpro launch is now widely seen as one of the most effective examples of this, with market shares now in excess of 50% in the U.S.

In nephrology, we announced earlier this quarter an extension of our partnership with DaVita for EPOGEN. And of course, we also gained approval for Parsabiv in the U.S. As the established leader in nephrology therapeutics, we continue to look for ways to serve patients with kidney disease and expect this to remain an important franchise for us.

As you know, an element of our strategy includes developing a portfolio of biosimilars, and I'm glad that we made that commitment, as I think there will be a robust market for these products. And while our portfolio of 10 biosimilars is progressing across the board, the highlight for the quarter was in inflammation, where we received EU approval to go along with our U.S. approval of AMGEVITA, our biosimilar to Humira. The first steps in building out this business are to establish biosimilarity and gain registration, and obviously we have done that now for an important molecule in the biggest markets. The next step is to navigate the IP landscape, and the process for that is underway.

Over the past couple of years, we've talked on these calls about our ongoing transformation efforts. We committed to a companywide transformation, real, meaningful change designed to make us more competitive, improve our operating margins, and ensure that we would be in a strong position to return capital to our shareholders during this period of increasing competition for our legacy franchises and while launching nine innovative products, maintaining our investment in innovation, advancing our biosimilars portfolio, and expanding our international presence from 50 to over 100 countries. We have asked a lot of our staff, and they have delivered. In our past results, you've seen our steady progress, and you see it once again this quarter, where our margins have grown and we delivered 9% earnings per share growth.

Looking forward, our orientation is long-term growth with volume-driven products, and we think we can deliver that across our focused therapeutic franchises. But we're also set on managing the business tightly to deliver in the short and medium term too. You should see this in our track record, and that's what you see in this quarter as well.

Our balance sheet and cash flows are strong, and we're looking for investment opportunities, albeit with a determination to add value for our shareholders, not just someone else's. Given valuations across many targets in the sector at the moment, that's challenging, but we'll remain patient and discriminating when it comes to M&A.

We've long advocated the need for corporate tax reform. If innovative U.S. companies are to remain competitive, we need a level tax playing field. We don't have one now, but we're hopeful this administration will deliver that in 2017. Obviously, we think such change would improve our flexibility for capital allocation.

I've taken a bit longer than usual on this call, but with all of the events of the first quarter, I wanted to make sure to reiterate that we're investing in long-term opportunities, managing the business tightly, and are poised to capitalize on investment opportunities which might arise.

With that, let me once again thank our staff for their engagement with our mission, and then turn to David. Thank you.

David W. Meline {BIO 6397419 <GO>}

Okay. Thanks, Bob.

We were pleased with our solid overall results and earnings growth again in the first quarter, as our transformation efforts enabled progress in an environment of strong competition and portfolio transition. We also were encouraged by our 7% volume growth in Europe, reflecting the value of our innovative products in a market where we have experienced similar competition and portfolio transition for a number of years.

Turning to the financial results on page 6 of the slide deck, worldwide revenues at $5.5 billion in the first quarter are flat year over year excluding the impact of foreign exchange and are 1% lower on a reported basis including FX. Worldwide product sales at $5.2 billion in the first quarter are flat year over year excluding the impact of foreign exchange and are 1% lower on a reported basis including FX, as strong unit demand for our newer products was offset by declines in our mature brands. Other revenues at $265 million decreased $23 million versus the first quarter of 2016.

Non-GAAP operating income at $3 billion grew 5% from prior year. Non-GAAP operating margin improved by 3 points to 57.6% for the quarter, reflecting continued favorable expense impacts from our transformation initiatives across all operating expense categories and the expiry of the Enbrel residual royalty payments in Q4 of 2016.

As in prior years, our operating margin is expected to be lower in the remaining quarters of the year, driven by the timing of expenses. On an overall full-year basis, we expect another year of strong operating margins, driven by tight operational expense management. On a non-GAAP basis, cost of sales as a percent of product sales improved by 0.4 points to 13.1%, driven by manufacturing efficiencies, partially offset by product mix.

Research and development expenses at $748 million were down 13% year over year, driven by a first quarter 2016 payment related to a third-party collaboration agreement, lower spending required to support certain later-stage clinical programs, and continued benefits from our transformation initiatives. Research and development as a percent of product sales at 14.4% is lower in Q1, consistent with previous years. Going forward, research and development expense as a percent of product sales is expected to normalize around 2016 levels.

SG&A expenses decreased 6% on a year-over-year basis due to the expiry of the Enbrel residual royalty payments, partially offset by increased investments in new product launches. In aggregate, non-GAAP operating expenses decreased 7% year over year and remain on track to meet or exceed our 2018 commitment of $1.5 billion in transformation savings, while investing to build the business globally, support new product launches, and invest in the long-term pipeline for the business.

Other income and expenses were a net $131 million expense in Q1. This is favorable by $13 million on a year-over-year basis, primarily driven by higher cash balances.

The non-GAAP tax rate was 18.5% for the quarter, a 0.4-point decrease versus the first quarter of 2016. This decrease reflects favorable changes in the geographic mix of earnings, partially offset by a smaller benefit from share-based compensation tax expenses compared to the first quarter of last year. As you may recall, this benefit is a

result of the adoption of Accounting Standard Update 2016-9, requiring these tax impacts to be recognized on the income statement versus the balance sheet. The benefit of this adoption contributed approximately $0.06 to our non-GAAP earnings per share in this quarter compared to $0.09 in the first quarter of 2016.

Non-GAAP net income increased 6%, and non-GAAP earnings per share increased 9% year over year for the first quarter to $3.15 per share.

Turning next to cash flow and the balance sheet on page 7, free cash flow was $2.2 billion for the quarter, an increase of $400 million over last year. This increase was primarily driven by higher profitability as well as timing impacts of income tax payments to the IRS.

We continue to provide significant cash returns to shareholders, consistent with our commitments, as we deployed $0.6 billion to repurchase 3.4 million shares at an average of $163 per share, and are on track to achieve total share repurchase for this year in the range of $2.5 billion to $3.5 billion, as previously communicated. Additionally, our first quarter dividend increased to $1.15 per share, an increase of 15% over last year.

Cash and investments totaled $38.4 billion, an increase of approximately $3.7 billion from the first quarter of last year. This increase reflects continued solid net cash flow generation. Our debt balance stands at $34.1 billion as of March 31, carrying a weighted average interest rate of 3.8% and an average maturity of 12 years.

Turning to the outlook for the business for 2017 on page 8, overall our 2017 revenue guidance remains unchanged at $22.3 billion to $23.1 billion. Our first quarter volume and price performance was in line with our plans, as we experienced a solid contribution from our newer products while managing the impact of competition against the balance of the portfolio. Revenue guidance also reflects the potential impact of the Repatha litigation and improving access for appropriate patients as a result of the positive Repatha cardiovascular outcomes data. Finally, our guidance takes into account potential biosimilar competition against Neulasta commencing as soon as the fourth quarter of this year.

With regard to our non-GAAP earnings per share guidance, we are raising the outlook to $12.00 to $12.60, reflecting our overall solid Q1 performance. In addition, our non-GAAP tax rate guidance remains unchanged at 18.5% to 19.5%, and we expect capital expenditures of approximately $700 million this year.

As previously stated, our 2017 guidance ranges are based on application of existing laws, including the Affordable Care Act and the current U.S. tax code as well as current interpretation of the required notice period prior to commercial marketing of a biosimilar under the BPCIA [Biologics Price Competition and Innovation Act]. We will continue to update guidance going forward for changes in these factors and any other business updates.

Finally, consistent with our 2017 outlook, we remain confident we will meet or exceed the commitments provided for the 2014 to 2018 period, including: double-digit non-GAAP

EPS growth; non-GAAP operating margin improvement from 38% to 52% to 54%; $1.5 billion of transformation savings; and return to shareholders of at least 60% of non-GAAP net income on average during the period.

This concludes the financial update. I now turn the call over to Tony.

Anthony C. Hooper {BIO 6284080 <GO>}

Thanks, David, and good afternoon, everyone. You'll find our product sales starting on slide number 10.

Our business performance is shifting to a more volume-driven growth as we launch innovative products targeting the large patient populations with unmet medical needs. Whilst our focus is on innovation, we have also executed effective life cycle management strategies for some of our legacy brands which are facing potential new competition. Although U.S. revenues declined 1%, our ex-U.S. growth was 3%, excluding the impact of foreign exchange, fueled by a 7% volume growth.

I'll now discuss our specific product performance and will structure my comments by therapeutic area. Let me begin with our bone health franchise.

Prolia is a great example of one of our innovative products that realized robust volume growth during the quarter, with most of its 21% year-over-year sales growth driven by unit volume. Prolia, with a strong value proposition, is uniquely positioned in postmenopausal osteoporosis as the leading branded product on the market. We will continue to invest in Prolia to reach a greater number of patients whilst reinforcing adherence for those already taking Prolia to ensure they continue to realize its benefits. Overall, we expect Prolia will remain a significant growth driver, as the approximately 850,000 U.S. patients on Prolia therapy only represent about 20% of patients presently being treated for postmenopausal osteoporosis.

We also look forward to expanding our bone health franchise with romosozumab, our innovative bone-building molecule for which we now have a trade name, EVENITY. In conjunction with our partners at UCB, we're preparing for a U.S. launch in advance of the July 19 PDUFA date. As Bob pointed out, having the ability to co-position EVENITY and Prolia sequentially will improve our ability to better treat those large patient populations. For thousands of high-risk postmenopausal osteoporosis patients such as those who have fractured, we have a proven therapeutic strategy with EVENITY to first build strong new bone in patients with 12 months of treatment, followed by Prolia for proven continued fracture risk reduction.

Oncology is another area that is benefiting from volume growth with our recently launched products. Let me start with KYPROLIS. KYPROLIS realized 23% year-on-year growth during the quarter. And most of this growth was volume-driven, including our international markets. As you know, KYPROLIS is indicated in the U.S. for second and third-line multiple myeloma. In second-line, triplet regimens are used in approximately

one-third of patients. And despite new entrants, we've been able to achieve about 50% market share for new patient starts in this segment.

The other two-thirds of second-line patients are treated with doublet regimens. And recent data from our ENDEAVOR study had demonstrated that KYPROLIS plus dexamethasone improved overall survival by 21% or nearly 8 months when compared to the Velcade plus dexamethasone.

Improving overall survival is the gold standard measurement when treating cancer. This data clearly establishes KYPROLIS as the proteasome inhibitor of choice and will be a compelling differentiator in our strategy to displace Velcade in this setting. KYPROLIS is well accepted in large academic centers that treat high numbers of multiple myeloma patients. And we are now focusing on extending KYPROLIS's reach into the community oncology practices.

Despite the introduction of new competing products in the U.S., we have also regained share in new third-line patients over the last few quarters. We expect proteasome inhibition to be foundational therapy in multiple myeloma for many years to come and are focused on growing in second and third lines of therapy with plans to expand KYPROLIS's use in newly diagnosed patients. Outside the U.S., we continue to enter into new markets and secure reimbursement with the benefit of the new KYPROLIS overall survival data.

XGEVA grew 6% year over year, mostly due to volume, as we continue to emphasize its clinical benefits. We look forward to having the positive multiple myeloma study data added to our label. This will expand the patient population eligible for XGEVA treatment.

Both Nplate and Vectibix saw another good quarter of volume growth of 9% and 6% respectively.

Neulasta sales increased 2% year over year, as we continue to see a small decline in the use of myelosuppressive chemotherapeutic agents. The first quarter also benefited from accounting estimate changes due to lower Onpro returns, underscoring that Onpro delivery is working better than initially assumed. We continue to drive increasing adoption, and Onpro now represents over 50% share of all Neulasta purchases. This has been a great example of a very successful life cycle management strategy. And as David explained earlier, we expect minimal impact in 2017 from potential long-acting biosimilar competition.

I'd also note that the first quarter historically benefits from heavier purchasing by certain end customers, and we estimate this benefit in quarter one to be about $50 million, which we expect to reverse in quarter two.

For NEUPOGEN, the impact of competition was in line with prior performance. We entered the quarter retaining a 46% share of the short-acting market in the U.S. We expect these competitive dynamics to continue over the course of 2017.

Moving now to Enbrel, I would start by emphasizing that we see no trend break versus 2016. And I will go through Enbrel carefully and in some detail because I don't want you to misinterpret long-term dynamics based on some quarter one peculiarities.

Before getting into quarterly performance, I'd like to highlight that we utilize IMS prescription data to analyze the business. Like many of you, we noticed a slowdown in the first quarter IMS scripts. This has implications for our views on segment demand and end-user inventory levels. We've been in close contact with IMS, and they agree that the first quarter prescription data appears soft in several specialty product categories, including rheumatology and dermatology. As a matter of fact, on a year-over-year basis, unit growth in rheumatology appeared to slow from 9% in the first quarter of 2016 to 2% in this quarter, and from 25% to 9% in the dermatology segment for the same period.

IMS attributes the softness to a combination of several factors, including the number of shipping days in the fourth quarter of 2016 versus the first quarter of 2017, the impact of patient out-of-pocket costs including deductibles, and the Part D donut hole for the start of a new year, as well as the potential increasing use of 90-day prescriptions. This is also consistent with our view of the market.

We noted our expectations that 2016 trends would continue into 2017. On a quarter-over-quarter basis, our share declined 1 percentage point to 32% in rheumatology and declined 2 percentage points in dermatology to 15%, in line with 2016 share trends.

As for the end-user inventory, we previously said that we expected quarter one reductions due to the quarter four 2016 $150 million excess inventory. Based on the IMS data, we calculated an approximate $30 million reduction in inventory levels this quarter. And therefore, we expect the remainder to be used up during the course of the year. Obviously, the accuracy of the IMS data has implications for understanding of both unit demand dynamics and end-user inventory.

Consistent with our previous guidance, net selling price had a minimal impact on year-over-year sales growth during quarter one. On a quarter-on-quarter basis, we are seeing increased commercial patient copay assistance impacting their selling price, which is likely a function of higher patient out-of-pocket costs. This impact typically tapers off over the remainder of the year, and our view on net selling price in 2017 is unchanged.

We are optimistic about a rebound in both Enbrel and Enbrel segment growth in future quarters, as IMS prescription data from the more recent weeks shows improvement versus the beginning of the year in both rheumatology and dermatology.

So in summary, the quarter one results likely reflect a temporary marketplace issue, and we believe the long-term dynamics are intact and in line with our prior expectations. There remain a substantial number of patients for which Enbrel is the best treatment option given its competitive efficacy and long-term safety profile. We will continue to invest in Enbrel to enhance its value it brings to patients and providers. Given its long-term period of patent protection, Enbrel will continue to be a significant cash flow generator for Amgen for many years to come.

Turning now to our nephrology products, beginning with Aranesp, on a worldwide basis, Aranesp declined 4% year over year. In the U.S., it increased by 7%, including the conversion from EPOGEN at numerous independent and midsize dialysis centers. This conversion was substantially completed by quarter three of 2016, with Aranesp now representing over 85% of the ESA usage. Performance outside the U.S. was negatively impacted by foreign exchange as well as the timing of tenders in certain markets.

Now to EPOGEN, as previously disclosed, we recently renegotiated our supply agreement with DaVita. DaVita represents about one-third of the U.S. dialysis market, and they will continue to predominantly purchase EPOGEN through 2022. In exchange for longer supply certainty, we made concessions on net selling prices, which impacted the quarter-on-quarter results. Also, as David mentioned, we do not expect a material impact to our ESA business in 2017 from a short-acting biosimilar competitor.

Sensipar increased 15% year over year, driven by a combination of net selling price and volume growth. Parsabiv, our innovative new cosmetic, delivered intravenously, is now approved in both the U.S. and Europe. And we are working with CMS to secure a reimbursement mechanism in the U.S.

Let me now turn to our cardiovascular franchise and Repatha. Let me first address the quarter-on-quarter growth, which might look a little strange. Quarter four 2016 was slightly inflated due to the booking of a Middle East tender, which was not repeated in quarter one this year. With closer examination of the data, you will see that we recorded positive volume growth in the U.S. of 14% and 28% in Europe. In the U.S., we achieved segment share of 64% in quarter one for new-to-brand patients and briefly touched on 70% as we exited the quarter. In Europe, we exited 2016 with 56% segment share. Our U.S. formulary coverage has greatly improved over last year, especially in Medicare Part D, where we have almost tripled the number of lives covered.

Results of the Repatha cardiovascular outcomes study that were presented at the American College of Cardiology last month are clearly a game-changer for cardiovascular patients, showing significant reductions in MIs and strokes.

We also shared our analysis on the economic value of Repatha at the ACC. This calculation used standard peer-reviewed methodology, using real-world event rates and imputed mortality benefit from the meta-analysis of previous studies, the CTTC relationship, and concluded that prices in the market today are well within the value-based price range. Naturally, this calculation is based on average net selling price and not the list price.

Since the ACC, we've been engaging with payers in the U.S. and across the world on Repatha's clinical data and economic value. We are in active discussions with all of the large U.S. PBMs and payers, and they recognize the importance of Repatha's outcome data to patients.

We are focused on reducing barriers and improving processes to make it easier for a physician to prescribe Repatha and for patients to get access to this important therapy.

We expect payers will start changing utilization management criteria and processes over the coming months.

Several independent groups have studied the access situation and have concluded that current access barriers are inappropriate and potentially harmful to patients. As pointed out in the recent publication by the Partnership for Health Analytic Research, or PHAR, it started with the irresponsible prediction of healthcare costs prior to FDA approval of the PCSK9 inhibitor class. These overestimates resulted in onerous restrictions and lack of patient access from the beginning.

At the ACC last month, two research teams, including one from Duke, presented data showing that patients' clinical characteristics were no different between those denied reimbursement for PCSK9 versus those approved, showing that payer utilization management processes were nothing but an arbitrary barrier to access. And just today, the FH Foundation published a peer-reviewed paper in the journal Circulation showing that 63% of FH patients and 58% of established ASCVD patients had their PCSK9 inhibitor claims rejected despite having suboptimal LDL-C levels and being on moderate or high-intensity statins.

Cardiovascular disease continues to be the number-one cause of death and disability in the world. And in a moment, Sean will remind us of the incredible outcome value that Repatha has demonstrated by its ability to reduce both MI and stroke. This data together with the groundswell of cardiology and patient pressure will result in increasing levels of patient access. Repatha will continue to grow for many years to come, making it one of the largest innovative assets Amgen has brought to market.

Let me conclude by saying a few words about erenumab and our recently announced expanded collaboration with Novartis. We believe that partnering with Novartis, a company that is well-positioned in the neuroscience space, will enable us to maximize the launch of this first-in-class product. We believe that erenumab will offer a strong value proposition to millions of patients suffering from chronic or episodic migraines.

Let me close by thanking all the Amgen staff that worked so hard and tirelessly to get our important products to patients around the world.

Sean?

Sean E. Harper {BIO 16272195 <GO>}

Thanks, Tony, and good afternoon.

I'll begin my comments today with Repatha. As you know, we presented the results of our Repatha cardiovascular outcomes study at the American College of Cardiology meetings in March with simultaneous publication in The New England Journal of Medicine. This represented a major step on the path of getting this therapy to the patients who so desperately need it.

The study had several objectives: first, to validate the PCSK9 mechanism with respect to cardiovascular outcomes; second, to establish the safety of reaching unprecedented low LDL levels, recall that 25% of patients in the Repatha arm had on-treatment LDLs below 19; and third, to understand whether the linear relationship established by statins and ezetimibe between LDL and cardiovascular risk continues down to very low LDL levels, as the human genetics had suggested. This study gave clear positive results on all of these objectives.

The results also validated our dosing approach of maximally inhibiting PCSK9 with Repatha, and that when it comes to LDL, as we began to hear cardiologists coin at the ACC, lowest is best.

Importantly, outcomes data from Pfizer's discontinued PCSK9 program were presented and also published in The New England Journal of Medicine, confirming the efficacy seen in our study and demonstrating that not all PCSK9 antibody therapies are the same with respect to off-target liabilities.

Now there's been a fair amount of speculation in the press and elsewhere about the magnitude of the risk reduction observed in our study, so I'm going to spend a bit of time on the results. We have found that the vast preponderance of experts in this field view this study as highly successful in terms of the observed effect size. Essentially, the results are exactly as what would have been achieved had one been able to reduce LDL to the same degree with additional statin therapy were it possible to do so without unacceptable toxicity.

Specifically, experts understand that the treatment lag that occurs in the first year of therapy, a phenomenon seen in all lipid-lowering trials in this type of population, represented a much larger proportion of the median time on therapy in our study, which was just over two years, versus the average 5.5-year-long statin study. They also understand that adjusting appropriately for duration of therapy, the results line up extremely well with the cholesterol treatment trial as a collaboration or CTTC meta analyses.

When one looks at the pre-specified landmark analyses for this chronic therapy, after the first year when the treatment lag is over and the true chronic value of the therapy can be assessed accurately, the risk reductions in myocardial infarction 35%, stroke 24%, and revascularization 28% are quite impressive, particularly in the setting of such a remarkably clean safety profile. Experts also understand why one should not have anticipated an impact on CV mortality in such a study, and I would refer those who are interested to an excellent editorial on this subject published recently in the Journal of Clinical Lipidology.

And to just remind us of the clinical reality here, many millions of patients like those in our outcome studies have a high annual risk of CV events, despite maximally tolerated statins, and have no other therapeutic alternative to take their LDLs down to levels that significantly protect them from such events. In fact, we were all surprised by the fact that despite optimized therapy with best standard of care, including high-intensity statins, patients in the placebo arm of our CV outcome study had an annual event rate of almost

10%, which clearly demonstrates the unmet need here, as event rates in the real world are significantly higher than those seen in clinical trial settings.

Now one of our highest priorities is to ensure these results are reflected in the Repatha label as soon as possible, and we're targeting regulatory submissions by midyear. I'd also note that the Repatha 420-milligram single-dose delivery option was recently approved in Europe.

Turning to oncology, we completed XGEVA regulatory submissions in the U.S. and Europe for the prevention of skeletal-related events in multiple myeloma patients, providing a potential new treatment option for patients, many of whom are not able to avail themselves of alternative therapies due to renal insufficiency. In multiple myeloma, we received the overall survival data from the ENDEAVOR study in relapsed or refractory patients, which confirm the superiority of KYPROLIS plus dexamethasone over Velcade plus dexamethasone. In fact, ENDEAVOR was the first head-to-head study to demonstrate a survival benefit versus a current standard-of-care regimen in this setting, and we're preparing to submit these results to regulators as well.

We also remain on track to begin enrollment this quarter in our Phase 3 study of KYPROLIS in combination with DARZALEX in relapsed or refractory multiple myeloma, and also recently began enrolling a Phase 1b study of new formulations of oprozomib.

Turning to our immuno-oncology programs, I'll begin with our BiTE platform. We were very pleased that FDA granted BLINCYTO Priority Review for our recent sBLA that includes overall survival data from our Phase 3 study to support conversion from accelerated to full approval. The application also includes new data in Philadelphia chromosome-positive relapsed or refractory acute lymphoblastic leukemia, a small population but an area of significant unmet need. We also continued to roll out our Phase 2/3 BLINCYTO program in diffuse large B-cell lymphoma, the most common form of high-grade non-Hodgkin's lymphoma.

We also had the opportunity in the recent American Association for Cancer Research annual meeting to present preclinical data from some of our new BiTE programs, including half-life extended constructs. We continue to make good progress with the investigation of Enlogic in combination with checkpoint inhibitors, and we'll be presenting the results of our Phase 2 study in combination with Yervoy at ASCO as well as some very interesting human biomarker data at the Congress of the European Association of Dermato Oncology.

Finally, in the early-stage immuno-oncology pipeline, we're making progress on our Advaxis collaboration and have an investigational new drug application in place for a personalized neo-antigen-targeted approach to cancer immunotherapy.

In our bone therapeutic area, our collaboration with UCB on EVENITY continues to advance, and we look forward to our July U.S. PDUFA date for the treatment of osteoporosis in postmenopausal women at increased risk of fracture. Ahead of this, we

expect the primary analysis of our active controlled fracture study, ARCH, in postmenopausal women with osteoporosis in the near future.

I will remind you that the upcoming primary analysis will include the clinical fracture and vertebral fracture primary co-endpoints as well as an interim analysis of the event-driven non-vertebral fracture study secondary endpoint. If statistical significance is not achieved at this interim analysis, the study will continue until the final analysis some months later. We designed ARCH in this manner to ensure adequate powering at the non-vertebral fracture endpoint.

I would also point out that compared to the placebo-controlled FRAME study, the ARCH study compares EVENITY followed by alendronate to antiresorptive therapy with alendronate throughout the study period. These sequences are being assessed in a higher-risk population than our FRAME study, with all subjects in ARCH required to have prevalent fracture. This was possible given the active comparator design, and we were not exposing these higher-risk patients to placebo.

If you recall in the FRAME study, the event rate for non-vertebral fractures was much lower than expected. And at 12 months, the non-vertebral relative risk reduction was 25% in the EVENITY-treated patients but was not significantly significant. In an exploratory analysis reported at ASBMR [American Society for Bone and Mineral Research], the relative risk reduction at two years in FRAME was 25% with a nominal T-value that was less than 0.05. We recently conducted the three-year analysis of this study, which again demonstrated nominal significance for non-vertebral fracture, demonstrating that a year of EVENITY therapy still had high treatment impact through year three, despite the fact that the control group received a very potent antiresorptive agent, Prolia, in years two and three.

Within our neuroscience collaboration with Novartis, we had the opportunity to present the results from our two Phase 3 erenumab studies in episodic migraine at the American Academy of Neurology Annual Meeting yesterday. The data demonstrated the robust and consistent effect of inhibiting the CGRP receptor with erenumab. And feedback from experts at the meeting have been very positive, with many viewing this as a potentially game-changing therapy for a debilitating, highly symptomatic disease. We look forward to making first-in-class regulatory submissions for erenumab that incorporate our episodic and chronic data later this quarter.

AMG 301, our PAC-1 antibody for migraine, also continues to progress. We've seen encouraging pharmacodynamic activity in our Phase 1 study in normal subjects and are currently designing a Phase 2 program in migraineurs, which we expect to begin later this year. Also in the quarter, Phase 3 enrollment in Alzheimer's disease began for the small molecule BACE inhibitor, AMG 520, we are developing with Novartis.

In our inflammation collaboration with AstraZeneca-MedImmune, I am pleased to provide a program update for AMG 157 or tezepelumab, our monoclonal antibody that inhibits thymic

stromal lymphopoietin or TSLP. TSLP is an epithelial-derived cytokine produced in response to pro-inflammatory stimuli that drives inflammatory responses. TSLP expression is increased in the airways of patients with asthma, the magnitude correlating with the severity of disease.

Some of you may recall that our Phase 1b data were quite compelling and were published in The New England Journal of Medicine in 2014. Together with AZ-MedImmune, we've now received the results from a large double-blind Phase 2b study in patients with inadequately controlled severe asthma in which AMG 157 demonstrated a significant reduction in the rate of asthma exacerbations compared to placebo at 52 weeks, successfully meeting the primary endpoint. This is a very encouraging result. And together with AZ-MedImmune, we are currently evaluating the potential for this agent to address a broad population of patients with severe asthma.

Briefly in nephrology, in the first quarter we also received approval for Parsabiv, our innovative IV calcimimetic that is administered thrice weekly at the end of dialysis for the treatment of secondary hyperparathyroidism in patients with chronic kidney disease.

And lastly in biosimilar news from Europe, we received approval for AMGEVITA, our biosimilar Humira, for all available indications and submitted ABP 980, our biosimilar Herceptin, for approval.

In closing, I'd like to acknowledge our staff for advancing these important programs on behalf of patients.

Bob?

Robert A. Bradway {BIO 1850760 <GO>}

Okay, thank you, Sean. I know we've taken more time than usual on our introductory remarks, so let's go straight to questions, Derek, and just please remind our callers of the process for the next step.

Q&A

Operator

And your first question comes from the line of Terence Flynn with Goldman Sachs. Terence, begin your question.

Q - Terence Flynn {BIO 15030404 <GO>}

Hi, thanks for taking the question, maybe just a two-part on Repatha. First, Tony, can you comment if the payers appreciate the details of the four-year data that Sean walked through? And then it looks like net price might have taken a step down in the U.S. in the first quarter. I'm just wondering if you can confirm that and any additional commentary that you can provide. Thank you.

A - Anthony C. Hooper {BIO 6284080 <GO>}

Terence, sure. All our discussions with the payers have been really starting with the discussion on the Repatha outcomes data, and I don't think we've had any pushback at all in terms of people really understanding the robust value. We will continue to work with them. Obviously, each one of them has agreed to go back and relook at the utilization management criteria as we speak.

There does appear to be a slight adjustment in the net price. One was due to a small accounting adjustment. And two, of course, we book our patient copay program to the net price, and the first quarter is normally a lot higher than second, third, or fourth. So we see that normalizing as we go forward.

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

Can we go to the next question?

Operator

And your next question comes from the line of Matthew Harrison with Morgan Stanley. Matthew, you may begin your question.

Q - Matthew K. Harrison {BIO 17603148 <GO>}

Great, thanks for taking the question. Tony, thanks for the detail on Enbrel. I'm sure, as you appreciate, there's a lot of questions that people have on that. If I can just ask two points there, you cited a market slowdown which you think will improve throughout the rest of the year. Could you just talk about your confidence around that? And beyond some of the weekly data points, are there other reasons to believe that broadly the market is not slowing?

And then second, it seems to me that the impact on price in the first quarter is higher than you've seen in quarters past, even when thinking about copay assistance and some of the other factors. Is there anything else going on there, and what's your confidence about price leveling out for the year? Thanks.

A - Anthony C. Hooper {BIO 6284080 <GO>}

Thanks, Matt. So as you know, with Enbrel as a retail product, about 97% of the volume is reported on a script basis, so we can track it quite tightly. For the quarter, it was definitely down, both rheumatology and dermatology. When I look at it sequentially, January, February, March, and then as I see it going into April, each one of those months has shown an incremental growth both in terms of DOT as well as prescriptions and in terms of growth. So January was down a lot. February was better than January. March was better than February, and April is starting to look much better than March as well.

From a net price, we don't see a dramatic change in the net price. Some the new contracts are coming into place, but our outlook on net price for 2017 hasn't changed at all. And when I look at abandonment rates, abandonment rates in the first quarter are

pretty similar for Enbrel to what they were in the fourth quarter or the third quarter last year.

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

And, Matthew, maybe just big picture here, when we look at the flow of patients into the information space, particularly rheumatology and dermatology, we see no reason in the marketplace that the trend of an increasing number of patients into this therapy would have abruptly changed between the fourth and the first quarter. So we think that we'll continue to see growth in the underlying demand for these kind of products.

Operator

And your next question comes from the line of Ying Huang with Bank of America Merrill Lynch. Ying, you may begin your question.

Q - Ying Huang {BIO 16664520 <GO>}

Hey, good afternoon. Thanks for taking my question. I have a question on Repatha. How much have you heard from the physicians in terms of feedback that they have to wait for a treatment guideline change by, let's say, ACC or AHA before they start prescribing more Repatha? And if that's the case, when do you think those professional organizations will change the guideline?

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

I think it's probably a subtle question that you're asking there, Ying, so why don't we just take a moment and really step through it. Tony, why don't you go ahead and take the first go.

A - Anthony C. Hooper {BIO 6284080 <GO>}

So all our discussions with cardiologists have been around their frustration of the administrative burden that has been placed upon them to get a prescription for appropriate patients. A lot of them are having to hire full-time nurses to spend the entire day chasing down required patient data, to chase down interactions between the patient or between the physician and the respective payer or the PBM. The guidelines themselves clearly in everyone's mind would help move the decision-making and the utilization criteria a bit quicker. But our major conversation with physicians is not really around the guidelines; it's more around the inconvenience.

From a guideline perspective, clearly both the AHA and the ACC are busy looking at the outcomes data. They've told us they're busy identifying position papers they wish to put forward. The NLA, the National Lipid Association, was there. The Association of Preventive Cardiology (sic) [American Society of Preventive Cardiology] (54:25), run by Dr. Seth Baum, is in the process of looking at a revised set of guidelines, including a proposed set of utilization management criteria, which they're proposing the PBMs and the payers should be using.

In terms of guidelines themselves, both the AHA and the ACC have said it will take some time before they actually get to a final guideline change.

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

I think the important information here is that the data demonstrated that lower is better, or as Sean said and as we increasingly hear from experts in the field, lowest is best. And I think people recognize that the current guidelines are out of sync with that. So the data make the point clear, and we expect to see white papers and then ultimately changes in the guidelines. But for right now, the data are an important piece of getting people to understand how to manage this disease for patients. Let's go to the next question.

Operator

Your next question comes from the line of Eric Schmidt with Cowen. Eric, you may begin your question.

Q - Eric Schmidt {BIO 1505721 <GO>}

Thanks. Just as a follow-on to Ying's question, it sounds like the major bottleneck is this hassle factor, Tony, that physicians are being put through, and I guess I'm just wondering what kind of leverage Amgen has to reduce that factor. Can't payers just stay entrenched and say our policies are that we'll cover it, but we're going to make you go through X, Y, and Z hoops and maintain the hassle factor and I guess the evidence of better medicine?

A - Anthony C. Hooper {BIO 6284080 <GO>}

So, Eric, I don't think I've spoken to a single cardiologist or general practitioner who hasn't commented on how onerous the process is to gain access to these products.

I think without a doubt, the third-party organizations, the professional organizations such as the ACC, the AHA, as well as patient organizations such as the FH Foundation are the ones who are running the research work at the moment, including Duke, as I said. We actually looked at those patients who received a PCSK9 and those who didn't, and actually show there's no clinical difference in the patients themselves. This type of burden I think is going to start putting the pressure on the payers.

Talking to the payers, they themselves are agreeing with us that the clinical data is important, and they need to expand access to appropriate patients. So we will continue to drive that interaction with them.

Operator

Your next question comes from the line of Cory Kasimov with JPMorgan. Cory, you may begin your question.

Q - Cory W. Kasimov {BIO 3009346 <GO>}

Great, thanks for taking the question. Good afternoon. I have a pretty commercial question on erenumab. I wonder if you can comment on early interactions you're having with payers on that front or maybe just general market research for the product. I guess specifically, I'm wondering how much of an impediment you expect access to be in the early days of that pending launch and how much your research may have factored into the strategic decision to further engage with Novartis.

A - Anthony C. Hooper {BIO 6284080 <GO>}

So let me start, Cory, by just telling you about an interaction I had with my counterpart at Novartis yesterday. He and I have both been in recent contact with neurologists who specialize in treating patients with chronic migraine. And the two of us are quite elated at the level of excitement we're seeing amongst these physicians about having for the first time in decades a treatment opportunity to really help people who have this debilitating disease. It truly is one of those symptomatic diseases where if you've got a migraine, you really know about it, and it impacts how you run your life. Can you run your life or can you be a good caregiver?

We are starting our discussions with the payers right now. We are helping them see the data from a clinical perspective. Obviously, the real negotiation can only start once we have the label, and we look forward to having that in the next couple months or so.

Operator

And your next question comes from the line of Josh Schimmer with Piper Jaffray. Josh, you may begin your question.

Q - Joshua E. Schimmer {BIO 6783077 <GO>}

Thanks for taking the question. If you can, help us understand the market segmentation in asthma, really the issue with AMG 157 again versus some of the other novel biologics targeting the IL4 side pathways (58:46). Thanks.

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

Okay. The question was a little bit hard to hear, Josh, but I think, Sean, why don't you take the first crack at it?

A - Sean E. Harper {BIO 16272195 <GO>}

Yes, what I would say is that it's still early days for a lot of the therapies that are still in development. But as you look across the biologics landscape in asthma, there's a few things that are clear. One is that in aggregate, asthma is an enormous opportunity from the perspective of the unmet need and the number of patients who are, for example, having to take courses of oral corticosteroids throughout the course of the year to manage their disease, which is very problematic for them.

And I think what you're seeing is that many of the mechanisms that are either out there now in biologics or being developed currently are segmented to populations that, for

example, have high eosinophilic counts, atopic phenotype, et cetera. And in the case of TSLP, what we like about TSLP is it is a very upstream kind of a mediator of this inflammation. And our expectation is that we could have a very broad impact on patients with activity across the spectrum of patient phenotypes within the asthma disease spectrum, which would make it a very attractive therapeutic option.

Q - Joshua E. Schimmer {BIO 6783077 <GO>}

Thank you.

Operator

Your next question comes from the line of Ronny Gal with Bernstein. Ronny, you may begin your question.

Q - Aaron Gal {BIO 15022045 <GO>}

Good evening and thank you for taking my question. I guess the Supreme Court have been looking at the biosimilar law today. In the case they side with you and find that shall means will, can you give us a feel for what will happen with the biosimilars that have already launched for Neulasta? Will they have to come back into the full patent dance? Essentially, if you win this case, what does it mean in terms of delay of biosimilar Neulasta approvals or launches?

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

I think there are a couple things in your question there, Ronny. Let me tease apart the two pieces of it. First, as you know, the Supreme Court reviewed this today, and so we'll know within a matter of weeks. Obviously, we think the 180-day needs to be enforced as it was written in the law. But with respect – I think you must have been referring to the short-acting competitors to NEUPOGEN.

Q - Aaron Gal {BIO 15022045 <GO>}

No, I was talking about the patent dance and impact of Neulasta biosimilar launches. Essentially, if you win that, will the biosimilar Neulasta be delayed?

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

I guess I'm not sure what you mean by delayed. I think again, the big picture here, Ronny, is that we've known for some time that we'll face biosimilar competition. We're expecting that that will happen for Neulasta, and we're ready for that. You've seen the actions that we've been taking over the past couple years to be ready for that. And we're ready to embrace the competition, and we've positioned the company from an operating expense standpoint with the knowledge that that competition is coming, and we're launching medicines and entering markets that we think will help us grow beyond that. So the 180-day is obviously post-FDA approval, so we're watching different competitive products make their way through the regulatory pathway.

A - David W. Meline {BIO 6397419 <GO>}

If I could then, in terms of the guidance we've offered, there are none that have been approved yet to compete with Neulasta. There's one that's lined up I think in the third quarter here. So if it were approved and the 180-day stands, then that would imply, as we've indicated, that we could face competition as soon as late this year, and that's how our guidance is built right now.

Q - Aaron Gal {BIO 15022045 <GO>}

Thank you.

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

Yes.

Operator

Your next question comes from the line of Alethia Young with Credit Suisse. Alethia, you may begin your question.

Q - Alethia Young {BIO 17451976 <GO>}

Hey, guys. Thanks for taking my question. Just again on Neulasta, I know Onpro is picking up momentum. But I'm just trying to figure out if you think – how do you think this helps defend you against biosimilar share? Is it as simple as that the market is remodeling itself, and so it delays and prolongs some of the competition that you may see, or is there some other dynamic we should be aware of? Thanks.

A - Anthony C. Hooper {BIO 6284080 <GO>}

Alethia, it's Tony. So let me go back to a comment I made on the last quarter earnings. Let's use MD Anderson as an example of probably one of the premier large oncology teaching centers in the country. It took MD Anderson almost – just over 12 months to go through their P&T committee to get an agreement within the institution to start shifting patients to Onpro. And the rationale was they were really having a good look at the clinical value, the treatment protocols, the discharge protocols, and they finally agreed that this product was certainly worthwhile having.

We spent a number of weeks training their 600 oncology nurses so they were able to really identify the right patient, administer the drug before patients went home, and they have therefore changed the clinical practice. The feedback we get from both the oncology nurses, the oncologists themselves, and patients in fact about the fact they no longer have to come back 24 hours later or a day after their chemotherapy when they're in the middle of chemo-induced nausea and vomiting is a huge advantage and allows them a better quality of life.

So we really believe that the benefit this drug brings is not simply a device. It is really something that allows patients to continue to live their lives whilst being treated for cancer. It also has resulted in changes, definitive changes in discharge protocols, which we think will take some time to be reversed if there's no other alternative.

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

Yes, it's worth keeping in mind the big picture here, Alethia. There's some data in a peer review publication from this week recognizing that there are 100,000 hospitalizations a year in this country from patients who suffer from an infection while undergoing chemotherapy, and of course that's what NEUPOGEN and Neulasta are designed to address. And any product like Onpro that can help prevent some number of those infections is an important product. So there's still an important need in the marketplace. This innovative delivery device enables us to meet a large portion of that need.

A - Arvind K. Sood {BIO 4246286 <GO>}

Derek, let's go with the next question.

Operator

Your next question comes from the line of Geoffrey Porges with Leerink Partners. Geoffrey, you may begin your question.

Q - Geoffrey C. Porges {BIO 3112036 <GO>}

Thanks very much and thanks for taking the question. Just to follow up on the question about erenumab, Bob, could you take us through your thinking about the partnering decision? Because you're in a strong net cash position. You've got robust cash flow. You've got plenty of space in your R&D given the sequential trend, and yet you partner one of your two late-stage products for what certainly looks like it's a fairly specialized prescriber base initially. So could you talk a little bit about that, and then also how you'll be collaborating with Novartis on the launch? Particularly, who will be setting price and how you're thinking about price? Thanks. Sorry for the complicated question.

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

No, that's fine, Geoff. We'll take it in two parts. Why don't I take the first piece? Then we'll have Tony address some of the specifics in your question.

We recognize and we're excited about the opportunity to have a first-in-class and a molecule that we think has a good chance to be best-in-class for a disease where there just aren't good therapies available today, so we're excited about that. But at the same time, Geoff, I think there is a specialty element of this that we don't have experience in. Novartis has been in the neurology neuroscience field for some 60 odd years now, and so they have a real established track record there. And as we interacted with them first with respect to the international markets, I think we came to realize there were opportunities to create a bigger opportunity by combining forces than by going it alone in the international markets.

We've come to know and share and respect each other's capabilities over the time since that agreement went into place. And as we looked at the opportunity in the U.S. and our desire to make sure we resource this to win, including getting off to a strong start with the specialist prescribers, it was our view that our shareholders were going to be better served by our joining up with somebody that had a very established presence in this field.

So that's our view, and I think all of our interactions since then make us feel confident that that was the right decision for the shareholders. But, Tony, why don't you add your thoughts?

A - Anthony C. Hooper {BIO 6284080 <GO>}

Sure, we've been working with Novartis now from a global research perspective and a global marketing perspective for some time. So the teams have gotten to know each other quite well. My counterpart and I have been drawn into these discussions with these experts, as I said, and he and I are becoming even more increasingly excited about the opportunity to deliver a first-in-class product like this to patients in need. He and I both have experience in terms of launching products in the U.S. over the last five years or so, and we understand some of the barriers and some of the challenges. But we also understand the large unmet need over here.

It's clear to us that a strong start in terms of having a clear group of physicians who realize the importance of treating patients properly is going to be important to place pressure on the entire payer system to ensure we can get access. They have a very good presence in the neuroscience market. The feedback we've had from third-party research has shown their team and their medical team are very well regarded, and this strong relationship in our mind will support the ability to launch fast, launch rapidly, and be highly effective in the initial uptake. So they're a good team to be with. We will work closely with them, and I think we can maximize our ability to bring value to patients.

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

And, Geoff, as regard to your questions about operational details, obviously those are topics that we discuss with them in detail before we move forward. And we think between the two of us, we think we've got those details worked out. But again, we're excited to have this partnership in hand and we look forward to getting this molecule approved so we can get out and help patients with it.

Q - Geoffrey C. Porges {BIO 3112036 <GO>}

Great, good luck. Thanks.

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

Thanks.

Operator

Your next question comes from the line of Ian Somaiya with BMO Capital. Ian, you may begin your question.

Q - M. Ian Somaiya

Thank you, just another question on Repatha. You made a comment that payers could potentially make some changes over the coming months. I was just hoping to clarify. Are those changes in prior authorization, or are they just payers being more diligent in

making sure the right patients are getting access to the therapy? And as I think about ACC.8 (1:09:38), the guideline changes in some of the answers you provided, do you need those changes – do you need the new guidelines to state lower LDL goals, or what else, what other type of changes could we see which would benefit the PCSK9 class overall?

A - Anthony C. Hooper {BIO 6284080 <GO>}

So, Ian, it's Tony again. So clearly, everything here is driven from the interpretation and understanding about outcomes data, that fundamentally this product, Repatha, on top of maximally tolerated statins, which is the gold standard to date, is able to drive LDL down further and reduce even more dramatically the risk of heart attack and stroke. So the discussions with the payers are consistently around the utilization management criteria to make sure that the burden is less onerous for physicians, that they and patients are able to get access to products quicker and faster.

White papers or position papers from professional cardiology organizations are really essential to start paving the way to ensure we move towards the guidelines down the road. But they factor, the good clinical data is what's important. Payers have said to us from the beginning that yes, they see the drug lowers LDL, but they need to understand what that means. The outcomes data now shows you what that means, and all our discussions have been, if we are to renegotiate a contract, it is based around the payers' willingness to amend and make more simple the utilization management criteria.

Operator

And your next question comes from the line of Umer Raffat with Evercore ISI. Umer, you may begin your question.

Q - Umer Raffat {BIO 16743519 <GO>}

Hi, thanks so much for taking my questions. I have two pipeline questions, if I may. On romosozumab, the upcoming ARCH trial, what percentage of patients were enrolled in Latin America?

And secondly on CGRP, I noticed you have a TREADMILL CV safety trial that wrapped up earlier in the year. Any update and/or feedback from that, and was that a study that FDA asked you to do? Thank you.

A - Sean E. Harper {BIO 16272195 <GO>}

Okay, so with respect to ARCH, the percentage of patients in Latin America, I don't remember an exact number, but it is substantially less that it was in the FRAME study, but it is still meaningful. So I think it's about 30% roughly, whereas it was higher than that in FRAME.

But I think it's important to recognize that it wasn't the part of the world that the drug was being administered that was the problem. It was the fact that the fracture rates in a placebo-controlled population where physicians were very hesitant to put high-risk

individuals into the trial because of the placebo arm, that the fracture rate was so low that we really didn't have any opportunity to demonstrate a further lowering of the fracture rate. And we don't expect that phenomenon in FRAME because the patients that were enrolled were by definition, by protocol, much higher risk. They had to have had prevalent fracture already. They have had much lower T-scores and so on, because in this case, patients are either getting romosozumab followed by alendronate, or alendronate from the get-go with no placebo control. So I wouldn't focus so much around the question of Latin America, although that was where we saw the problem with the very low event rates.

And then the other piece to keep in mind is that we do have an event-driven analysis for non-vertebral fracture in ARCH which we didn't have in FRAME. And that also, as you know, addresses this event number powering problem that you can run into, which is essentially the wall we hit in FRAME.

With respect to CGRP, I think it's a very good question. One of the things that I learned from talking with people at the meetings in Boston is that the real question in most neurologists' mind right now about the CGRP class remains long-term safety and tolerability. They're very impressed with the efficacy data. They're very impressed with the tolerability and safety that have been observed to date in relatively short exposures in the Phase 2 and Phase 3 study. And so I think there are a number of things that we have been doing specifically as a company, like we have over three years of long-term exposure in open-label extension studies. Other companies, to our knowledge, have not been doing this.

We did the CV TREADMILL study on our own volition because we felt that, again, these were going to be kind of questions that would exist in the marketplace. We have a number of pre-clinical and clinical studies, for example, on the impact on blood pressure and so on that would have been done specifically in anticipation of the kind of questions that prescribers will have around the long-term safety of the product. Many of these data are not broadly appreciated because they haven't come out in peer-reviewed publications and they haven't been necessarily presented in plenary type presentations like the Phase 3 data were. But in aggregate, I think these are going to be important and potentially differentiating data for the product.

Q - Umer Raffat {BIO 16743519 <GO>}

That's very helpful, thank you.

Operator

Your next question comes from the line of Carter Gould with UBS. Carter, you may begin your question.

Q - Carter Gould {BIO 20035589 <GO>}

Good afternoon, guys. Thanks for taking the questions. Sean, I'll stick with the pipeline theme. On the BLINCYTO studies, you referenced the ALL B-cell (1:15:25). When do you

think those data might be presented? Could those be registrational? And on CNP520, is there an interim built into that Alzheimer's study? Thank you.

A - Sean E. Harper {BIO 16272195 <GO>}

Yes, so the BLINCYTO studies are just enrolling now, so it's a little bit hard to project when we would be presenting data from them. That depends, of course, on a number of factors in terms of enrollment rate and when we might hit certain milestones with respect to interim analyses and so on. But the program is progressing on plan, and we're seeing a lot of enthusiasm in the marketplace in the clinical trial investigator space, I should say, for the program.

And then with respect to the CNP520 program, there are some futility analyses built into the Alzheimer's study, which are designed to cut losses if we weren't seeing some kind of an effect. And I believe there may be also an early stopping efficacy interim late in the trial, though. I'd have to go back and look at the protocol to be sure about that.

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

Sean, not everybody might be familiar with CNP520. So you just might remind them (1:16:56)

A - Sean E. Harper {BIO 16272195 <GO>}

Yes, so you might remember that this was highlighted in The Wall Street Journal the other day. Novartis and Amgen I think had come convergently to the opinion that we have extremely high confidence in the target itself, in large part because of the genetic validation work that was done on this target at deCODE. And so the question is really a question of when to intervene. And what we're doing in this study is enriching for a population, who based on their APOE genotype and age are very highly predisposed to converting from a normal cognitive capability to a minimally impaired cognitive capability. So we're going earlier than anyone else has done to date. This actually may be what's required to demonstrate a disease modifying effect.

So the molecule itself is a very high-quality small molecule BACE inhibitor that has been demonstrated to drop A-beta levels dramatically in CSF and all that good stuff. And the main issue strategically is to go in a little bit earlier in this population. And while this is a genetically defined population, about 60% of patients who actually develop Alzheimer's have one of these predisposing alleles. So it's not some tiny little population. It's genetically defined.

Q - Carter Gould {BIO 20035589 <GO>}

Thanks.

Operator

Your next question comes from the line of Geoff Meacham with Barclays. Geoff, you may begin your question.

Q - Geoffrey Meacham {BIO 21252662 <GO>}

Good afternoon, guys, and thanks for taking the question, one for Tony or Sean. So in contrast to Repatha, you haven't had a lot of payer pushback on Prolia. So are there payer or pricing lessons to be learned when you think about the romo [romosozumab] launch in July and its combination with Prolia? Thanks.

A - Anthony C. Hooper {BIO 6284080 <GO>}

Let me take that one, Geoff. The major difference probably between the two is that the majority of Prolia sales are Part B, so it's a buy in bulk model, where Repatha is predominantly a Part D or a retail product we sell.

I think it's all around the value proposition, and we go back again to the day we presented at the ACC just to reconfirm that the present net price of Repatha in the marketplace is well within the range of the value proposition or the value-based pricing in fact for this particular product.

So I think the two things are different. There was a lot of speculation up front about how the PCSK9s could cost the market $150 billion or whatever it was, which resulted in some silly actions, I think, with all due respect. The drugs continue to show real good BAT value. We're happy to stand up and discuss it anywhere. And how the bank (1:19:54) would pay at the moment is how do you change the utilization management criteria, nothing else.

Operator

And your next question comes from the line of Chris Raymond with Raymond James. Chris, you may begin your question.

Q - Christopher Raymond {BIO 4690861 <GO>}

Hey, thanks. So just a broader question on the biologics market structure and maybe as it relates to your biosimilar business. So we were reading a white paper that I think you guys put out recently on the biosimilar market. I think you guys highlight a real problem. Even under a hypothetical scenario, I think your paper talked about how where a biosimilar is priced at, say, a 25% discount to the innovator, you still have a patient copay that's still higher than the innovative drug. I think in your paper it said almost 40% higher under Medicare Part D. So just curious, you guys seem as close as anyone to policy makers and directions to where this may go, and I know you devoted a great deal of time and energy towards your biosimilar business. I assume that there's an expectation here that some of these disincentives will go away. Can you maybe talk in broad terms how you think that might play out?

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

Tony, why don't you go ahead and take that?

A - Anthony C. Hooper {BIO 6284080 <GO>}

Sure. One, I don't remember us putting out a white paper, so I just want to make sure that we're not being given authorship of something we didn't write because I'm unaware of Amgen putting out a white paper. We have said historically in the past that we believe that the biosimilar market will move much like a branded generic market; that the pricing in the beginning will be cautious; that the people who come to market and those who actually use biosimilars will be looking for a combination of quality, continuity of quality, continuity of supply, and the reputations of the organizations coming to market.

We believe that at Amgen we have a lot of good reputation. We have a 38-year history of never shorting a patient, of having quality product consistently on the marketplace. As we've gone through the process of actually developing these biosimilars ourselves, we've realized how tough it is to actually bring these drugs to market or how to develop them. We've spent time with regulators around the world making sure they understand what good looks like, that the rules and regulations are aligned with what we are doing.

There is some debate in the U.S. around linked J-codes between the brand versus the biosimilar. I think those are still being debated at the moment. But until then, it's an unlinked J-code, which means the reimbursement or copays are different. There's a lot happening in the marketplace, and how that could change, I can't speculate now.

A - Arvind K. Sood {BIO 4246286 <GO>}

Derek, as it's going on 6:30 on the East Coast, let's take two last questions.

Operator

Okay, absolutely. And your next question comes from the line of Eun Yang with Jefferies. Eun, you may begin your question.

Q - Eun K. Yang {BIO 4797139 <GO>}

Thanks, a question for Sean. In your collaboration with Arrowhead on RNAi therapies targeting cardiovascular diseases, what's your view on potential safety issues that may be related to RNAi-based therapies? And when do you expect to move into clinic? Thank you.

A - Sean E. Harper {BIO 16272195 <GO>}

Yes, I think that the siRNA technologies right now look good enough that in the case where the only way one can drug a target appears to be siRNA-based inhibition, it's a reasonable thing to pursue. And so that's what we're doing, for example, for LPa where we don't feel there's any other way to drug the target. It's not a derisked platform at this point, and there obviously are concerns. And I think that regulators are going to be very cautious in approving products early on that are based on this kind of novel platform, unless of course it's in a setting where there's very high unmet need and no other kind of options.

So we are exploring siRNA largely in settings in which the drug can't be – the target can't be interdicted in other ways, and also where we feel that the therapy would be unique in

its ability to address that target. So LPa represents an example like that. We have other targets that we feel are potentially that way. And so at this point, we're moving that ahead. The program is really still in a preclinical stage, but it is moving very rapidly. The collaboration has been great. But I can't really give specific timelines of when it would be in the clinic at this point.

A - Arvind K. Sood {BIO 4246286 <GO>}

Let's take one last question, and then Bob will make a few closing comments.

Operator

Your next question comes from the line of Salim Syed. Salim, you may begin your question.

Q - Salim Syed {BIO 16887281 <GO>}

Great. Thanks, guys, for squeezing me in, just a question on romo maybe for Sean or for Tony. The non-vertebral data, guys, how are you thinking about that in terms of uptake? And then also will we be getting that non-vertebral data in the press release, either in a qualitative form or quantitative form, when we get the top line? Thank you.

A - Sean E. Harper {BIO 16272195 <GO>}

Yes. So what I would say is that having evidence of non-vertebral fracture impact is important for cytotherapeutics (1:25:56). Of course, the most important endpoint for physicians, payers, and patients is clinical fracture, which is the symptomatic vertebral fractures which can be very profoundly impactful to patients' quality of life, as well as the long-bone fractures or non-vertebral fractures. And there, we've seen good results, and that's one of the co-primary endpoints for ARCH as well. And I think that it is something that is an important variable. In the end, things like hip fracture are the real dreaded complications of osteoporosis. So having a sense from the aggregate data for a molecule that there can be protection in sites like the hip is important, and that's why we're anticipating ARCH keenly, as it's coming very soon.

I can't comment on what we exactly we'll decide to disclose in a press release. We are always focused on very complex embargo requirements by both the society clinical presentation venues as well as the journals that we're trying to publish in, and this can be quite an elaborate dance to figure out what we can put into our press releases in that setting.

Q - Salim Syed {BIO 16887281 <GO>}

Got it, thanks so much.

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

All right, thank you all for your questions and for your time. We appreciate it. Maybe just a quick couple of quick thoughts from me and then we'll let you back to work. First, as you heard in our discussion, we're pleased with the volume growth, particularly from our

newer products in the quarter. Clearly, there was some noise in the first quarter around Enbrel and the trends. But as you heard us say, we think the long-term trends for Enbrel are on track despite that noise in the marketplace in the first quarter.

And again, lastly, we think we've positioned the company well. And as a group here, we're excited about the future given the long-term growth opportunities that we see for Amgen. So thanks for your interest. We'll look forward to talking to you on the second quarter call.

Operator

This concludes today's conference call. You may now disconnect.
