Q4 2016 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 and Development

Other Participants

- Aaron Gal, Ph.D., Analyst
- Alethia Young, Analyst
- Brian P. Skorney, Analyst
- Cory W. Kasimov, Analyst
- Eric Schmidt, Analyst
- Eun K. Yang, Analyst
- Geoffrey C. Meacham, Analyst
- Geoffrey C. Porges, Analyst
- Jim Birchenough, Analyst
- Joshua E. Schimmer, Analyst
- M. Ian Somaiya, Analyst
- Mark J. Schoenebaum, Senior Managing Director, Head of Healthcare, Biotech & Pharma Analyst
- Matthew K. Harrison, Analyst
- Michael Yee, Analyst
- Robyn Karnauskas, Analyst
- Salim Syed, Analyst
- Terence Flynn, Analyst
- Ying Huang, Analyst

MANAGEMENT DISCUSSION SECTION

Operator

My name is Frederick, and I'll be your conference facilitator today for Amgen's Fourth Quarter 2016 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>}

Thank you, Frederick. Good afternoon everybody. I would like to welcome you to our conference call to review our operating performance for the fourth quarter and full year 2016. So before we start, I would like to welcome back Mark Schoenebaum of ISI Evercore, who has returned from his leave. I would also like to acknowledge those who are relatively new in their coverage of Amgen, including Salim Syed of Mizuho Securities and Leah Cann of Oppenheimer. Welcome. Each of us look forward to working with you. So let's go ahead and get started as we have a lot of ground to cover today.

I'm sure you have seen our press release by now and we are particularly pleased to report that our Repatha four-year outcome study has met its primary composite endpoint and the key secondary composite endpoint with no new safety findings. In order to ensure presentation of this important data at the American College of Cardiology meeting in March, unfortunately we will not be able to provide additional details at this time above and beyond what's in the press release. We will host an investor event on March 17 and look forward to seeing you in Washington, DC.

So leading the call today will be our Chairman and CEO, Bob Bradway, who will provide a strategic report on our performance in 2016 and outlook for 2017. Following Bob, our CFO, David Meline, will review our Q4 and full year results and provide details on assumptions imbedded in our guidance for 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.

As in the past, 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 to 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, our Form 8-K and also on the Investor Relations section of our website.

So just a reminder that some of the statements made during the course of our presentation today are forward-looking statements and our 2015 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.

Robert A. Bradway {BIO 1850760 <GO>}

Okay. Thank you for joining our call. I want to start with the exciting news that we have positive results from our Repatha cardiovascular outcomes trial. In terms of efficacy, the trial met its primary composite and secondary composite endpoints, and importantly in terms of safety, there are were no new findings in the trial. This is obviously an important result for us and for the field as it clearly validates the outcomes benefit of PCSK9 inhibition in cardiovascular disease.

Cardiovascular disease is the most costly disease for society today, and in the absence of new therapies to reduce the risk of cardiovascular events for the millions of patients at high risk in the US and around the world, the burden of this disease is set to rapidly rise. This is why we've been so determined to advance Repatha as an innovative treatment option for those people whose LDL levels and cardiovascular risks aren't well managed by other available therapies.

Today's announcement is the culmination of many years of hard work and investment by Amgen, our scientists and collaborators around the world, and I'd like to thank all of those, including the patients in the trial, for making this possible. We look forward to sharing the data from this rigorous 27,500 patient outcome study at the American College of Cardiology Meeting in mid March and to using the data from our entire comprehensive clinical development program for this molecule to prove the value of this innovative therapy to the health care system.

As our investors know, investment in innovation and a strong conviction to use information available from human genetics to guide that investment are at the core of our strategy. Today's results for Repatha are encouraging on both dimensions of our strategy and also underscore our confidence in our ability to drive our long-term growth.

Now let me turn to update you on the substantial progress we made in our priorities for 2016 with continued solid execution across the business. Our results for the year were strong, with earnings per share growing at twice the rate of revenues as reflected in our 12% growth of EPS on a non-GAAP basis and revenue growth of 6%.

Our commitment to reshape the expense base of the business delivered results once more in 2016, with a decrease in operating expenses on a growing business and a 4% improvement in our operating margin on a non-GAAP basis to 52%.

Through our transformation efforts, we've been able to reshape the business while continuing to invest for long-term growth. International expansion is an important element of our long-term growth plan. Consistent with that aspiration, we continued to roll out our launches of new medicines internationally, with some 94 new product stroke country launches in 2016.

Our pipeline is core to our long-term growth aspiration as well, and here too, we made real progress in 2016 as three new late-stage products rapidly approached the market, including Parsabiv in kidney disease, which is already approved in Europe and we expect soon to be approved in the US; EVENITY, our romosozumab antibody in bone health; and Erenumab, our CGRP antibody for migraine.

We believe our biosimilars portfolio will also be a long-term growth driver, and here too, we continue to invest in our portfolio of molecules and achieved an approval of AMJEVITA, a regulatory filing for our biosimilar to Avastin, and a successful pivotal study for our biosimilar to Herceptin.

We've said for some time that one of the characteristics of our business is its strong cash flows. This year, we generated nearly $10 billion of free cash flow or an 8% cash flow yield. This enables us to return significant capital to our shareholders and to invest externally in innovation, which we did once again this year. Consistent with our confidence in our outlook for long-term growth, we once more raised our dividend, this time by 15%.

As I mentioned before, we are focused on long-term growth. In 2014, we provided five-year financial commitments through 2018. We've just passed the three-year mark, and I'm pleased with our tangible progress against those commitments and we're on-track to meet or exceed them. We will likely face headwinds in 2017 as declines in our mature brands will begin to offset volume growth from our more recently launched products. This is reflected in our 2017 guidance, which David will discuss further.

It's important to note that we began our transformation efforts here several years ago in anticipation of the competitive headwinds we expect to face. Operating leverage from the changes we've made enable us to drive earnings growth in the near term, while our longer-term investments have laid the foundation for growth beyond this period. The elements necessary to drive that long-term growth are clearly coming into focus with our recent launch of six new therapies including Repatha and KYPROLIS and the three we expect to launch in the near feature, as well as the emergence of our biosimilar portfolio.

Shifting focus to Washington, I thought perhaps I should say a few words following our meeting with President Trump and his administration earlier this week. First, I would reiterate my appreciation for the president and his administration's interest in our industry. He was very clear about his desire to promote innovation on behalf of patients, economic growth and job creation.

Second, the president and his team recognized the leading role the United States has played in the field of biotechnology, and we share their desire to strengthen the environment for employees and employers in this sector. Biotech jobs are highly skilled desirable jobs, and there's a global competition for them.

We've long supported corporate tax reform as a way to level the playing field with our ex US competitors, and we look forward to being part of the policy discussions with the new administration around this area as well as regulatory reform, intellectual property protection and trade policy. I think this administration expects to deliver real progress in each of those areas for our industry.

And now on the topic of drug pricing, the President was also clear, as he was throughout his campaign, about the need for us to find ways to bring down the cost of drugs for citizens in the US. We want and expect to work with the President and the administration to be part of the solution in that effort. In participation with the administration and Congress, we will seek to advance changes that enable more Americans to have affordable access to life saving and cost effective medicines.

Now let's turn to David, who will review our financial performance. David?

David W. Meline {BIO 6397419 <GO>}

Okay. Thanks, Bob. Turning to the fourth quarter financial results on page 6 of the slide deck, revenue at $6 billion grew 8% year over year. This quarter, we saw steady product sales performance driven by net selling price and unit demand growth versus last year.

Other revenues at $302 million increased $95 million versus the fourth quarter of 2015. Other revenue benefited primarily from milestone payments, notably a milestone received related to the out-licensing of AMG 139, consistent with our focus on optimizing our portfolio of pipeline assets. Changes in foreign exchange had less than a 1% negative impact to total revenue and product sales in the quarter on a year over year basis.

Non-GAAP operating income at $2.9 billion grew 21% from prior year. Non-GAAP operating margin improved by over 6 points to 50.5% for the quarter, reflecting continued revenue performance, favorable expense impacts from our transformation initiatives across all operating expense categories, and the expiry of the Enbrel residual royalty payment on October 31.

On a non-GAAP basis, cost of sales as a percent of product sales improved by 1 point to 13.3%, driven by manufacturing efficiencies. Research and development expenses at $1.06 billion were flat year over year. SG&A expenses decreased 4% on a year over year basis, primarily due to the expiry of the Enbrel residual royalty payment. In total, non-GAAP operating expenses decreased 2% year over year.

Other income and expenses were a net $202 million expense in Q4. This is unfavorable by $82 million on a year over year basis. This year over year unfavorability was primarily due to higher interest expense due to higher net debt levels, sorry, higher debt levels as well as losses from investment portfolio rebalancing in the fourth quarter of this year.

The non-GAAP tax rate was 18.7% for the quarter, a 7.1 point increase versus Q4 of 2015. This increase reflects unfavorable changes in the geographic mix of earnings this year as well as the realization of the full year benefit of the 2015 federal R&D tax credit in the fourth quarter of 2015. Non-GAAP net income increased 9%, and non-GAAP earnings per share increased 11% year over year for the fourth quarter.

Please find a summary of our 2016 full year results on page 7 of the presentation. Our 2016 full year revenues grew 6% to $23 billion, and non-GAAP earnings per share grew 12% to $11.65 per share. For the full year, non-GAAP operating income at $11.4 billion grew 14% from prior year based on the combination of solid revenue growth and a year over year decline in operating expenses.

Non-GAAP operating margin improved by over 4 points to 52.3% for the year, demonstrating our commitment to improve the profitability of the business as we continue to realize the benefits from our ongoing transformation initiatives. On a non-GAAP basis, cost of sales as a percent of product sales improved by 1.2 points to 13.3%, driven by manufacturing efficiencies. This decrease is a direct result of our continuing

efforts to streamline our manufacturing processes, increase utilization of our factories, and maintain our position as a leader in the field of biologic drug manufacturing.

Research and development decreased 4% as increased new business development activities were more than offset by lower spending required to support certain later stage clinical programs, as well as transformation and process improvement efforts. SG&A expenses were up 5%, primarily due to launch product expense increases, partially offset by the benefits of our transformation efforts as well as the expiration of the Enbrel residual royalty.

In total, non-GAAP operating expenses decreased 1% year over year to $11.5 billion, reflecting continued benefits from our transformation and process improvement efforts. Through 2016, operating expenses have decreased by approximately $200 million versus the 2013 levels, while absorbing significant investments in new product launches, advancing our new biosimilar business and building out our global presence.

We remain on track to our 2018 commitments. To date we have realized approximately $1.2 billion of transformation savings, well on our way to achieving our 2018 commitment of $1.5 billion.

Other income and expenses were unfavorable by $139 million on a year over year basis due to lower investment gains realized in 2016, and higher interest expense due to higher debt balances, offset partially by higher interest income due to higher cash balances. The non-GAAP tax rate was 18.8%, up 2 points versus 2015. The year over year increase was primarily due to unfavorable changes in the geographic mix of earnings, offset partially by the adoption of accounting standards update 2016-09 earlier this year.

Turning next to cash flow and the balance sheet on page 8. For the full year 2016 Amgen continued to demonstrate strong and durable cash flow generation with $9.6 billion in free cash flow versus $9.1 billion last year. This increase was primarily driven by higher profitability. Cash and investments increased to $38.1 billion. This balance included $2 billion in the US and $36.1 billion outside the US. Total debt outstanding increased to $34.6 billion, and carries a weighted average interest rate of 3.8% and an average maturity of 13 years.

In 2016, we deployed $3 billion to repurchase 19.7 million shares at an average of $154 per share. At the end of 2016 we had $4.1 billion remaining on our share repurchase authorization.

Additionally for 2016, we increased our dividend per share by 27% to $1 per quarter with payments totaling $3 billion. Based on our confidence in the future outlook for the enterprise and our continued commitment to our capital allocation strategy, we also announced a 15% increase to the dividend to $1.15 per share in the first quarter of 2017.

Turning to the outlook for the business for 2017 on page 9. 2017 will be an important year for Amgen as we continue to progress towards achievement of our long-term

commitments. We've reshaped the business to deliver top-tier margin performance while continuing to invest for the long-term growth of the business.

As we enter 2017, there are several key assumptions embedded in our outlook that I would like to take a moment to share. First, our revenue guidance range for 2017 includes continued positive momentum from our growth brands and recent product launches. Our guidance also reflects the continued impact of competition against NEUPOGEN and EPOGEN as well as biosimilar competition against Neulasta commencing in the fourth quarter. We also expect competitive dynamics to result in limited net selling price yield through 2017, in particular for Enbrel as well as our contract extension with DaVita related to ESAs as previously disclosed.

Next, we expect an unfavorable impact due to foreign exchange headwinds of approximately 1 percentage point to revenue growth and an approximate $0.20 unfavorable impact to non-GAAP EPS on a year over year basis, assuming current exchange rates prevail through 2017. With respect to other revenue, in 2016 we benefited from rising royalty income as well as several out-licensing transactions, which we do not expect will repeat in 2017. Therefore, we expect 2017 other revenue to be about $200 million less than in 2016.

Finally, today's revenue and non-GAAP EPS guidance ranges are wider than we typically have provided in the past, which is primarily a reflection of the Repatha legal case potential results as well as how quickly payers provide access to appropriate patients as a result of the positive Repatha cardiovascular outcomes data.

With this background, our 2017 revenue guidance is $22.3 billion to $23.1 billion and our non-GAAP earnings per share guidance is $11.80 to $12.60 per share. In addition, our non-GAAP tax rate guidance is 18.5% to 19.5%. We expect capital expenditures to be approximately $700 million this year. As part of our commitment to capital allocation to shareholders, we plan to repurchase shares in a range of $2.5 billion to $3.5 billion in 2017.

As a result of our strong progress through 2016 as well as 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.

Our 2017 guidance ranges are based on application of existing laws, including the Affordable Care Act and the current US tax code as well as current interpretation of the required 180-day notice period prior to commercial marketing of a biosimilar under the BPCIA. If any of these change in ways that are significant to our outlook, we'll provide an updated view on guidance at that time.

In summary, we delivered another year of strong financial results in 2016. And we are increasingly confident in the outlook for Amgen's success in 2017 and beyond. This concludes the financial update. I will now turn the call over to Tony.

Anthony C. Hooper {BIO 6284080 <GO>}

Thank you, David. You'll find a summary of our performance for the fourth quarter on slide number 11. We had a strong finish to 2016, delivering fourth quarter sales growth of 6% year over year. Fiscal year 2016 sales grew by 5% to a total of $21.9 billion. Our team has delivered this growth whilst absorbing significant loss of EPOGEN and NEUPOGEN sales to competition.

Growth in the fourth quarter was principally driven by Enbrel, Prolia, and our newer products, Repatha and KYPROLIS. Growth was also relatively balanced across geographies, with US growth of 7% and international growth of 5% year over year. International growth was 7% excluding the impact of foreign exchange and was fueled by an 11% volume growth.

Our performance in 2016 was successful across several dimensions. We continue to drive strong volume growth of many of our brands, particularly Prolia, XGEVA, Nplate, Vectibix, KYPROLIS and Sensipar. Our international business delivered double digit volume growth. We laid the groundwork for future growth with numerous product launches outside the United States led by Repatha and KYPROLIS, which are off to strong starts in these markets.

Our lifecycle management efforts in the US continue to be effective, evidenced by the uptick of Neulasta Onpro and Aranesp in the dialysis setting. We've also begun our launch preparations for the next wave of product launches, including Parsabiv, EVENITY, and Erenumab.

Let's now turn to our product specific performance beginning with our bone health franchise. Prolia delivered 25% year over year growth for the full year and a 22% year over year growth for the fourth quarter, as we continue to increase share in our core markets. Prolia represents a unique opportunity. It has a strong clinical profile with the proven ability to reduce the risk of fractures, combined with strong long-term safety data. Prolia is the market leader and continues to grow in this significantly unserved disease.

For context, it's estimated that nearly 200 million people worldwide suffer from osteoporosis. In the US, Europe and Japan, less than 50% of these people are diagnosed and only half of those are treated. In addition, between 2000 and 2011, there were 4.9 million hospitalizations from osteoporotic fractures in the US alone. We believe there's an opportunity to improve PMO diagnosis and treatment rates and are focusing efforts in this area. Overall, we expect Prolia to remain a significant growth driver for us into the foreseeable future.

We're also excited about expanding our bone health franchise with EVENITY, our innovative bone building molecule, which is under review at the FDA. We look forward to commercializing EVENITY globally with our partner UCB.

Turning now to ESAs. As we previously announced, we recently renegotiated our ESA supply agreement with DaVita. DaVita represents approximately one third of the US

dialysis market and will continue to predominantly purchase EPOGEN. Our new contract replaces the previous one, extending our relationship to the end of 2022. In order to continue this strong partnership for a longer duration, as well as helping to increase certainty, we made some concessions to net selling price beginning in 2017. I'd point out that we don't expect a biosimilar entrant in the US until late 2017 at the earliest. As David said, this assumes that the current interpretation of the required 180-day notice period prior to commercial marketing of a biosimilar under BPCIA is upheld.

Aranesp grew 5% year over year, primarily from gains in the mid-size and the independent dialysis organizations as they've transitioned from EPOGEN. As we noted in our third quarter call, we believe the majority of this transition is now complete. EPOGEN's rate of decline slowed to 8% year over year in the fourth quarter. Recall that Fresenius' transition to an alternative product began in the fourth quarter of 2015.

Sensipar increased 7% year over year in the fourth quarter due to net selling price and unit growth with underlying TRx growth in the US of over 5% year over year.

We recently launched Parsabiv in a few of the smaller markets in Europe with about 10 more expected by the end of 2017. We look forward to launching in the US following FDA approval. Once approved by the FDA, we'll work with CMS to secure reimbursement, which we expect will take between three to four months after approval.

Moving now to Enbrel, where the market growth continued in the fourth quarter with over 20% year over year growth in value for both the rheumatology and the dermatology segments. Sequentially, market share of Enbrel in both segments remained relatively steady in the quarter. Enbrel fourth quarter sales benefited from an increase in end customer inventory levels. We expect about $150 million of this traversed in the first quarter this year.

As we previously stated, we expect to realize minimal net selling price growth throughout 2017 based on contracts that went into effect on January 1. We also expect volume trends in 2017 to be similar to 2016. We continue to invest strategically in Enbrel including pursuit of new indications and novel delivery systems to enhance the value it brings to patients and providers. Given its long period of patent protection, Enbrel will continue to generate significant cash flows for many years to come.

Let's now turn to our oncology brands, beginning with Neulasta. Neulasta declined 3% year over year due to lower unit volume partially offset by net selling price. Sequential unit volume in the fourth quarter was adversely impacted by heavier purchasing by some customers in the US during the third quarter. Fourth quarter sales of Neulasta also benefited from a single $38 million purchase by the US Biomedical Advanced Research and Development Authority, otherwise known as BARDA.

Based on the best available data, there appears to be a small decline in the use of myelosuppressive chemotherapy regimens. Our Neulasta lifecycle management has helped to compensate for this reduction however. The strategy includes investing in our

DDC campaign focused on raising awareness of febrile neutropenia risk as well as the benefits of Onpro delivery kit.

As expected, we've seen an increase in the average number of Neulasta cycles for patients being treated with the Onpro. Onpro continues to gain traction and exited 2016 with approximately 50% share in the US for all Neulasta sales. We are focused on continued growth given the value Onpro brings to patients and providers and expect Onpro will be a key differentiator for future competition. Finally as David mentioned, we do not expect any long-acting biosimilar competition until fourth quarter 2017, assuming the current interpretation of the 180 days is upheld.

NEUPOGEN exited 2016 holding over 50% of the short-acting market in the US. We expect competitive trends to continue into 2017 from existing and potentially new biosimilar competition. We also now face biosimilar competition in Canada. Overall, we expect the impact from competition in 2017 to be similar in relative magnitude as was in 2016.

XGEVA grew 6% year over year as we continue to emphasize its clinical benefits. We look forward to having the positive multiple myeloma study data added to our label to provide these patients with a new treatment alternative. For Vectibix and Nplate, we see good year on year unit growth.

Moving now to KYPROLIS. Multiple myeloma is a growing but competitive market, given the number of new treatment options. In the fourth quarter, KYPROLIS unit volume grew in both the US and the international markets. We are focused on growing our business in the second-line setting on the compelling ASPIRE and ENDEAVOR data. In the US, the focused messages of our recent campaigns are resonating with oncologists in this crowded and dynamic market. Outside the US, we continue to enter into new markets and secure reimbursement. KYPROLIS has strong uptake internationally in the fourth quarter, with a sequential unit growth of over 10%. In Europe, new patient share exceeded 20% in the second-line setting and exceeded 30% in the third-line setting.

Turning now to our cardiovascular franchise. In two years, we have firmly established ourselves in the cardiovascular space. Our first product, Corlanor, helped us develop relationships and learn the market. Corlanor will continue to play a unique and essential role for certain patients. Nonetheless, we expect Corlanor will remain a niche product with modest sales of under $50 million in 2017 due to its limited label.

Repatha, our second cardiovascular brand, represents one of our largest opportunities. I'm very pleased with the strong competitive execution by our team since launch. We continue to increase our share of new-to-brand prescriptions in the US, and in fact have captured just over 60% to date in January 2017. Our focus here remains on enabling access for appropriate patients. In Europe, we've made very good progress since approval in July 2015. We've now secured reimbursement in 14 markets, with more expected in 2017. We are the market leader in Europe with a 57% market share.

In closing, I'm proud of the team's execution. We delivered results in 2016 in the face of intensifying competition. As we enter 2017, I'm confident that we will continue to increase our level of competitiveness, enabling us to exercise our strategy of delivering innovative therapies to patients suffering from grievous illnesses.

Let me now pass you to Sean.

Sean E. Harper {BIO 16272195 <GO>}

Thanks, Tony. Good afternoon. There's been a lot of progress in R&D since our last call and I'll begin my comments with our cardiovascular therapeutic area. Cardiologists have been looking for many years for an agent that could be used to treat patients already on statins who are nonetheless at high risk for cardiovascular events. At the American Heart Association meetings in November, the cardiology community was excited to see in our intracoronary ultrasound study, GLAGOV. Not only plaque regression when Repatha was added on top of optimized statin therapy in patients with established atherosclerotic heart disease, but also continued plaque reduction down to LDL cholesterol levels in the 20 milligram per deciliter range.

Our hypothesis from inception of the Repatha program has been that one should strive maximally to inhibit PCSK9 and thereby maximally reduce LDL to the greatest benefit in patients at high risk for cardiovascular events, and that it makes no sense to treat to an arbitrary LDL goal in such patients.

Now in our FOURIER outcomes trial, we have met the primary composite endpoint comprised of non-fatal MI, non-fatal stroke, cardiovascular death, coronary revascularization, or hospitalization for unstable angina as well as the key secondary composite endpoint around which the study was statistically powered. This is the more objective MACE or major adverse cardiac event endpoints being non-fatal MI, non-fatal stroke or cardiovascular death. Furthermore, we did not observe any new safety findings in this large placebo controlled study.

We've also seen the results of an approximately 1,900 patient study of patients in FOURIER that evaluated changes in cognitive function over time, which met its primary endpoint of non-inferiority to placebo. From a scientific and medical standpoint, the FOURIER and GLAGOV studies provide a set of landmark results clearly validating the PCSK9 mechanism.

And remember, this is in treatment context of the high hurdle of Repatha being given on top of optimized statin therapy. These are patients with no other meaningful therapeutic options for further LDL lowering. Bear in mind, the population studied in FOURIER has an approximately 50% 10-year residual risk of experiencing a CV event despite optimized statin therapy. And these patients are quite representative of the large number of patients like this out there in day-to-day medical practice. We look forward to presenting the data at the American College of Cardiology Scientific Session in in March.

Since statins were introduced 30 years ago, our industry has been seeking a safe and effective agent to extend beyond the benefits of statin therapy. From the seminal initial association in academia of PCSK9 gene variance in humans to abnormal LDL levels and cardiovascular risk, to Amgen's elucidation of the complex biology involved, and our resulting intellectual property around Repatha, and through our extensive set of clinical trials culminating in GLAGOV and FOURIER, this program's been a remarkable example of the power of human validation of a drug target from the very beginning, based on human genetic insights. I'm proud of the role Amgen has played here and our efforts to drive this paradigm forward in many other programs, with our leading human genetics platform at deCODE and our broad suite of modalities to interdict such targets.

I'm also pleased to report that the Omecamtiv mecarbil program in collaboration with Cytokinetics and Servier is advancing nicely and our 8,000 patient Phase III outcome study in chronic heart failure is now actively enrolling patients. We have also completed enrollment in the Phase II study of chronic heart failure patients in Japan, and expect to see the results later this year. Finally in cardiovascular, we've recently submitted an sBLA for a pediatric indication for Corlanor.

In oncology, we announced a collaboration with Janssen to evaluate the combination of KYPROLIS and DARZALEX, two very powerful agents for the treatment of multiple myeloma. The first study to initiate will be a Phase III registrational study of KYPROLIS plus DARZALEX plus dexamethasone versus KYPROLIS plus dexamethasone in the relapsed setting with enrollment expected to begin in the second quarter of this year.

We also remain committed to the frontline setting, and are in the design phase of the Phase III study of KYPROLIS plus Revlimid and dexamethasone or KRd versus Velcade plus RD in newly diagnosed transplant eligible patients. And we'll provide more details on this study as we finalize our plans.

As is common in drug development, especially in oncology, registration requirements evolve with the science as treatment landscapes change. After initial consultation with regulators, our KYPROLIS weekly administration study, ARROW, had been designed with an overall response rate as the primary endpoint. Based on recent feedback from regulators, response rate is no longer deemed an acceptable endpoint in this clinical context. Therefore, we amended the protocol, making progression-free survival the primary endpoint. As this is an event driven endpoint, we now expect the results from the final analysis in 2019.

We're committed to increasing our footprint in multiple myeloma, and we have several early stage innovative programs ongoing including an MCL-1 inhibitor in Phase I and CD38 and BCMA by specific T cell engaging programs. We also intend to make regulatory submissions this year for XGEVA for the prevention of skeletal-related events in multiple myeloma patients. This remains an important area of unmet need as many of these patients cannot effectively be treated with currently available therapies due to impaired renal function.

In immuno-oncology, our bispecific programs continue to advance. We'll be working with regulators to update the BLINCYTO label with the overall survival data from our confirmatory study in Philadelphia chromosome-negative relapsed refractory ALL. We're also pursuing new indications for BLINCYTO including a submission this year for a small but clinically important population of Philadelphia chromosome-positive relapsed refractory ALL patients.

We're also advancing BLINCYTO into late-stage clinical studies in non-Hodgkin's lymphoma, a much larger indication. While these initial studies will be conducted with our current BLINCYTO construct, we will also be pursuing an extended half-life version in this setting. In fact, we'll be advancing several extended half-life BiTE molecules into the clinic this year directed at various targets.

We're also making good progress with AMG 330, our CD33 BiTE for acute myelogenous leukemia, which is progressing through dose escalation in Phase I. Within our growing multiple myeloma portfolio, we have several immuno-oncology programs we're excited about, including our biospecific CD38 molecule from Xencor and our BCMA BiTE, AMG 420, that's currently in Phase I.

The potency of the BiTE platform also makes target selection critical, and we've developed a world-class proprietary target investigation platform. To augment this platform, earlier this month we announced a research collaboration and exclusive licensing agreement with Immatics, who has a unique target discovery capability in order for us to develop next-generation T cell engaging biospecific immunotherapies.

Switching to bone health, along with our partners at UCB, we continue to make progress with romosozumab, now called EVENITY. We've been having productive interactions with FDA on our BLA filing for the treatment of osteoporosis in post-menopausal women at increased risk of fracture. We're working toward a July 19 PDUFA date. And at this time, it does not appear that we will have an FDA advisory committee meeting for this program.

We also recently submitted an application for marketing approval in Japan for the treatment of osteoporosis for men and women at high risk in fracture. We look forward to the primary analysis of the active controlled fracture study, ARCH, in the second quarter. In this randomized double-blind study, patients receive either alendronate or romosozumab in year one followed by alendronate in year two. The primary endpoints of the study that will be assessed at the primary analysis are the incidence of vertebral fracture at 24 months and the incidence of clinical fractures, which is event-driven.

In addition, at the time of the primary analysis, an interim analysis of the secondary endpoint of non-vertebral fracture will be performed. In order to assure adequate powering in non-vertebral fracture, we will include an event-driven non-vertebral fracture final analysis. If we do not achieve significance at the time of the primary analysis in Q2, we expect the final analysis of non-vertebral fracture some months after the primary analysis.

Turning to our neuroscience collaboration with Novartis, I'll begin with our CGRP receptor antibody for migraine prophylaxis, Erenumab. We have successfully completed our registrational studies and are preparing our global regulatory submissions, which we expect to occur in the second quarter. I'd like to commend our team on their execution of this program, in which we're clearly positioned to be first to market. And we'll be seeking registration in both episodic and chronic migraine.

Migraine is a devastating condition that affects millions of patients, often in their most productive years of life. And we believe that for an otherwise active population, a monthly subcutaneous self-administered presentation with a patient-friendly auto-injector pen would be well received.

In our Alzheimer's program, CNP520, a small-molecule BACE inhibitor, recently received Fast Track designation from the FDA, and patient screening is underway in the Phase III study we and Novartis are conducting in collaboration with the Banner Institute. Recall this study will enroll patients genetically predisposed to Alzheimer's disease who are cognitively normal, an approach that differs from many of the ongoing studies in symptomatic patients.

Quickly on Enbrel, we received an expanded indication in the US, making Enbrel the first and only systemic therapy to treat pediatric patients ages 4 to 17 with chronic moderate to severe plaque psoriasis. This is particularly noteworthy, as safety is always a particular concern when it comes to treating children.

In nephrology we are working toward a February 9 PDUFA action date for Parsabiv for the treatment of secondary hyperparathyroidism in adult patients with chronic kidney disease on dialysis. Parsabiv would be the only calcimimetic agent that can be administered intravenously by a healthcare provider three times a week, coincidence with hemodialysis sessions. And we believe this would allow physicians to have confidence that their patients are receiving the full benefit of the therapy.

We also recently submitted an application to FDA for pediatric indication for our oral calcimimetic, Sensipar.

Finally, our biosimilar programs continue to advance. In Europe we recently received a CHMP positive opinion for ABP 501 our biosimilar Humira. FDA has also accepted our BLA submission for ABP 215, our biosimilar Avastin, with an action date of September of this year.

2016 was a very positive and rewarding year with many significant accomplishments. And I'd like to thank all of our staff for their hard work and commitment to deliver important advances in medicine for the many patients still in need.

2017 is going be another exciting year. And I look forward to seeing many of you at ACC. Bob?

Robert A. Bradway {BIO 1850760 <GO>}

Okay. Thank you, Sean. Let me just quickly wrap up on the year, and then we'll open up for questions. As I hope you can tell from our remarks, we have a clear strategy for long-term growth and we're executing it effectively. That's reflected in our financials with 6% revenue growth, 12% EPS and 4 percentage points of margin improvement. The Repatha outcome study we believe will enable us to show once more how innovation benefits patients and society.

Now the court's recent ruling in our patent litigation is a win for the patent system and patients as it reinforces incentives for the large and risky investments we have to make in innovation to bring forward new medicines to treat serious diseases.

With respect to innovation, we advanced our next set of late-stage innovative pipeline opportunities and our biosimilars program as well. We generated $10 billion of free cash flow as reflected in our free cash flow yield of 8%.

We look forward to working with the administration to advance market-based reforms and solutions that further promote innovation. And as we work to address the headwinds that we've identified for 2017, I'd remind you we've made excellent progress on our long-term commitments for 2018, and we're on track to meet or exceed them.

So with that, Frederick, why don't we open the line for questions, and if you wouldn't mind, let's remind our callers once more what the process is for asking questions of us. Thanks.

Q&A

Operator

Thank you. And our first question comes from the line of Mark Schoenebaum with Evercore ISI.

Q - Mark J. Schoenebaum {BIO 5001077 <GO>}

Geez, Arvind, I need to disappear for three months to get the first question. Thank you so much for your kind words and thanks to your whole team for all the help while I was out. And thanks, Bob, for the nice note while I was gone. And congratulations to Sean on Repatha.

I just had, if I may, I don't know if I'm going get an answer to this, but I thought I might try. Sean, can you give us any information at all around what the predefined non-inferiority margin might have been on the primary endpoint in the neuro cognitive trial? And if you're unwilling to answer that, maybe you can just give me your updated thoughts on the A beta hypothesis in light of the solanezumab failures? Thanks again to everybody.

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

Hey first, Mark, on behalf of the team, great to hear your voice. Welcome back. Sean, go ahead. There's two questions there, why don't you...

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

Yeah.

Q - Mark J. Schoenebaum {BIO 5001077 <GO>}

You only have to answer one.

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

Yeah. The first one I can't answer. The second one I would say that we really don't see any read through on the decision Lilly has made with their antibody to the approach of small molecule BACE inhibition. And I think that I still am a very strong believer in BACE as a drug target and don't believe that really any of the data that's emerging with these antibodies changes the point of view we have on the amyloid hypothesis.

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

Sean, you might also just remind Mark and other listeners that we could also see some setbacks for other small molecule programs directed against BACE before we know that there's only CNP520..

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

Right. Right. We do have the point of view and it's one that exists in the field as a whole, that it may be too late to intervene in patients who have frank Alzheimer's disease already at the time that we begin to administer these products in relatively short-term clinical trials. And this is why we and a few others are focusing on patients who are predisposed to developing cognitive impairment but are cognitively normal when they enter the treatment phase of the trials. And that's the approach we're taking. So I think we could actually see even some failures of BACE inhibitors before we see success of BACE inhibitors and certainly the antibodies are a much tougher proposition in my mind.

Q - Mark J. Schoenebaum {BIO 5001077 <GO>}

Thanks, Sean. Congratulations to you on your trial execution.

Operator

Our next question comes from the line of Eric Schmidt with Cowen & Company.

Q - Eric Schmidt {BIO 1505721 <GO>}

Thanks and my congrats also on the FOURIER data. Sean, I know the press release is silent on the other two secondary endpoints, CV mortality and all cause mortality. Should we take that silence to mean that they were missed or just that there's no ability to give us information on that right now? And when do you think you'll be able to submit the data in sPBA form to an FDA label? Thanks.

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

Yeah, so it's the latter. You should probably not make conclusions (49:53) about the data based on absence of statements in the press release. And we are working. As you might imagine, this is a reasonably high priority for us at the company at the moment, so we have people working right now really hard on putting together a filing. So we'll be doing that as fast as we possibly can.

Operator

Our next question.

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

Yeah, go on.

Operator

Our next question comes from the line of Ying Huang with Bank of America Merrill Lynch.

Q - Ying Huang {BIO 16664520 <GO>}

On the Repatha trial, quick one for Sean. You put on your press release that there's a unequivocally connection between LDL lowering and CV risk reduction. Should we infer that again the data kind of like fits where we saw from the meta-analysis before? And secondly, quick question for Bob. When you met with the President earlier this week, you committed to hiring another 1,500 workers in the States. Can we get some color on that? Is that going be from manufacturing operations or is that going be for promotion of Repatha based on this data? Thank you.

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

Okay. So what I would say about my comment in the press release about the inequivocal is that just if you think about it, we've done this very large trial which is testing the question of whether Repatha versus placebo has an impact on cardiovascular disease and the trial is statistically significant at these key primary and secondary endpoints. So I think just by definition, that is a validation of the connection between the LDL lowering and the cardiovascular and that's all it's meant to provide, not any magnitude of effect kind of a statement.

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

So, Ying, thanks for your question about the job creation. Couple things, first, these were jobs that were expected, contemplated in our plans for 2017. So this is a reflection both of our ongoing confidence and the attractiveness of the environment here in the US, and of the outlook we have for long-term growth. And we were happy to be able to share that publicly because as I said, that reflects what's our current planning assumptions.

So in terms of where the jobs are, really across the business. If you want to look at some specific new areas for us, obviously we look forward to standing up a neurology franchise

with our partners at Novartis and we have exciting incremental opportunity coming in bone health that we expect to be investing in. And we have some staff that we'll be hiring here to support our ongoing international expansion as well.

So as you know, we launched 94 product/country opportunities last year. And so we're continuing to support those with incremental hiring. But generally, in our transformation efforts of the last few years we've been reallocating resources to where we see the most attractive growth opportunities and we'll continue to do that in 2017.

Q - Ying Huang {BIO 16664520 <GO>}

Thank you.

Operator

Our next question comes from the line of Matthew Harrison with Morgan Stanley.

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

Great. Thanks. I'm going to try a Repatha question as well, and if you don't answer that, I have a second one. But you've obviously had a bunch of conversations with payers over the last year and so I know you can't talk about the hazard ratio. But maybe you could just comment if the hazard ratio and the data as a whole gives you a high degree of confidence that you've met the demands of payers with this data set to get broader access.

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

You want to offer your second question now, Matthew, so we have them both?

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

Yeah, sure. Bob, I just wanted to ask you. I mean, you talked about meeting with the President, some of the goals there. I mean, do you have a view on timelines for when we might see some movement around tax reform or some of these other issues?

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

I think the tax reform guidance that's out now in public is probably appropriate. So I don't think tax reform is going to be in the first wave of things to see coming out of the new administration and out of Congress, but I think we will see it this year. And we talked at some length about this, including comprehensive tax reform and repatriation and whether they'll be linked or separate. So we appreciated the administration and the President's updated guidance on that.

But what I'd say, Matthew, is we expect that we'll see it. And generally, I think we're going to find that this is an administration with an action bias and I think they're going to expect to see ideas from us and others in pretty short order here to start addressing some of the concerns that they want to address for the American people. So the good news is we as a company and we as an industry have some ideas and we look forward to being able to sit

down with the administration and Congress and talk about them and see what we can do to work together and make some progress.

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

Thanks.

Operator

Our next question comes from the line of Terence Flynn with Goldman Sachs.

Q - Terence Flynn {BIO 15030404 <GO>}

Thanks for taking the question. Maybe just one on your 2017 guidance. David, I think you mentioned that there was some wider range than is typical and that really reflects two things with respect to Repatha, one is the legal case and then number two is how quickly payers provide access given the data you saw. Can you maybe just give us a little bit more context for both of those? Is the commentary around the quickness of access driven by the data itself or is it driven by having these additional discussions? What's driving that? And maybe just any more detail you could share on both of those. Thank you.

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

Yeah, so what I would say is as it regards to the litigation, obviously there's a range of possible outcomes and positions that we have in the market, so we've tried to capture all of those in the wider range. And in terms of the uptake, what I would say is maybe Tony would like to comment, but we think again there's a range of outcomes that you would see with the uptake in the increased access.

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

Sure. So I mean, our focus remains on helping all payers improve access to Repatha. The utilization management criteria that they have at the moment is beyond the label and we work every day to improve upon that. We look forward to seeing the payer response now that we have the outcomes data. But of course, we won't be able to promote that until it's in the label.

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

Okay, Frederick, let's take the next question, please.

Operator

Our next question comes from the line of Eun Yang with Jefferies.

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

Thank you. So the product that you increased the prices last year, we estimate that on average, increase was about 7.45%. I mean please correct me if I'm wrong. And what was the net realized gain in the price last year?

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

So we haven't provided specific disclosure on that, although if you were to go through each of our quarterly calls, we do provide a summary of list price changes, volume and other factors, right. So I think unless you'd like to comment, Tony.

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

No.

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

I think you can see it's a number obviously less than 7.5%.

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

So, I mean we report every quarter, Eun, the makeup of product changes in terms of units, inventory and of course, at that times net selling price, which is a combination of list price changes and then contractual changes which the impact rebates over time.

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

Thank you.

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

Yeah, maybe just adding to that, Eun, what I think important for us as we look into 2017, as I said in the guidance, we have a limited price uptake net in 2017, which is primarily driven by the fact that as we've said previously, we expect very limited net price on Enbrel, and as Tony mentioned again today, we've given some additional discounts as it relates to EPOGEN with DaVita. So what you can expect is that for Amgen in 2017, you'll see a reduced net price including the US pricing, which will be around inflation specs (58:41).

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

Okay. Let's go to the next question.

Operator

Our next question comes from the line of Robyn Karnauskas with Citigroup.

Q - Robyn Karnauskas {BIO 15238701 <GO>}

Hi, guys. Thank you. So Bob, one last question around the Trump meeting. What can you say that might make us more comfortable that we won't see, because you said he's action-based, or it's an action-based administration, drug pricing pressure ahead of some reform, like more aggressive either tweeting or shaving or something that might be implemented ahead of some sort of reform? Anything that came out of that. And then on the volumes, maybe you could comment a little bit about, is there something nuanced in fourth quarter that makes you feel comfortable that the volumes will not continue to

decline, they'll be less use of these types of drugs over time. What gives you that comfort that you can stabilize that? Thank you.

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

Sorry, Robyn. Just to be clear on the second part, are you talk about a particular product or in general?

Q - Robyn Karnauskas {BIO 15238701 <GO>}

Sorry, I just talking about the Neulasta. You commented that there's less per cycle chemo use of these agents. I was just wondering if you could comment on that. Thanks.

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

Yeah, I mean I appreciate that there's a lot of interest in the discussions we had in Washington, and that's why I wanted to try to address it proactively. Again, genuinely I think that those of us that were there were encouraged by the level of interest that the President has in our businesses and in our industry, I think encouraged by the respect he has for the importance of innovation. He spoke about the need to eradicate disease in his inaugural address, and I think recognizes the power of innovation to do that. So all that, Robyn, gives us great encouragement.

He talked, I think, publicly when we were with him about the need to look at areas of reform, tax reform, regulatory reform, intellectual property protection, trade policy. So all of those, I think, are encouraging for us. He's also been very clear that drug pricing is something that's important to him, and that I'm sure he's going to want to be able to deliver real benefits to the American public on that score. So obviously, I'm not in a position to comment on what he's going say, when.

But I was trying to convey that genuinely we came away pleased that the administration led by the President was interested in engaging with us on the business, and we look forward to working with them and Congress to try to identify things that we all can do differently to help provide access to medicines for the people who need them. So again, I know that there's an interest on the call and by investors to better understand this, but I don't think I could add any other perspective beyond what I've already said Robyn.

And with respect to Neulasta, Tony, maybe you can address her question.

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

Sure. So, Robyn, I mean we always try to be as transparent as possible around the data we see coming and give you guys some heads up as to what we're seeing. The calculation of the number of myelosuppressive regimens in the US, of course, is a complicated process to go through using a number of databases, and then from that we extract from it the number myelosuppressive chemotherapy regimens and then within that, we look at what actually falls within the label of Neulasta itself.

Looking back over the last five, eight years, it continues to fluctuate slightly all the time. And when I talk about a decline, I'm talking about a very low single digit number that I've seen the last quarter. And we're just watching that carefully, but it's been offset by the incremental cycles we're seeing with Onpro as we use Neulasta.

As Bob has said in the past, the number of patients being admitted to hospital with febrile neutropenia continues to increase, and the number of people that die because of that is also on the increase. So the need continues to be there, and we continue to work hard to make sure that physicians and patients are aware of the availability of Neulasta.

Q - Robyn Karnauskas {BIO 15238701 <GO>}

Thank you very much.

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

Thank you. All right. Let's go to the next question.

Operator

Our next question comes from the line of Michael Yee with RBC Capital Markets.

Q - Michael Yee {BIO 15077976 <GO>}

Question, I had a question as it relates to expenses in operating margin. Obviously there's a big benefit windfall from the royalty you won't pay this year. So wanted to understand how much of that do you think could drop to the bottom. And just overall when you think about SG&A and R&D, can you continue to expand operating margins? Because I would think with the CVOT finishing up that there would be some benefit there. So if you look at the two of those, how much operating margin do you have and how much can you drop from the Pfizer benefit? Thank you so much.

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

Sure. So, I would say on the overall operating margin question and then going to the expense. So we finished last year, as we mentioned, at 52%. And what we were able to convey again today is that we expect to meet or exceed all of our commitments and that would include operating at 52% to 54%. So we continue to feel very good about our performance from a margin perspective.

Secondly, if you look at the components of cost, and I think about it in 2017, correct. We have quite a significant improvement in our cost base due to the reduction in the royalty that's effective in 2017 as well as the fact that we'll continue to see additional benefits from transformation initiatives incrementally in 2017 as we continue to march towards the $1.5 billion goal. And partially offsetting that, and Bob touched on it earlier, we do have new expenses that we're building in the business, in particular as we launch more products internationally, that adds cost to the base as well as

standing up a new neuro franchise for the company and expanding on bone, will add some cost.

So I think net-net when you net those out, we'll see most of that reduction of the royalty go to the bottom line but not all this year. But again, we feel very good about the performance of the company in that we're now operating amongst the top tier in terms of not only efficiency and margin, but we're continuing to invest, I think, very appropriately in the long-term future of the business.

Q - Michael Yee {BIO 15077976 <GO>}

Thank you.

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

Yes.

Operator

Our next question comes from the line of Geoff Meacham with Barclays.

Q - Geoffrey C. Meacham {BIO 21252662 <GO>}

Afternoon, guys. Thanks for taking the question, and again, offer my congrats on the outcomes data. So, Tony, trying to determine the commercial path for Repatha with the new data. Are there opportunities to have formulary discussions post ACC or do you think you'll have to wait for the formal PBM negotiation season this fall after legal chips in. (65:25)

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

Geoff, from the revised guidance on section 114 here, we can clearly go out and talk about the top line data and talk conceptually with payers about the value this data brings to them. We can't however, at this particular stage, promote it from a sales perspective because it's not into the label yet, but we can talk to payers, yes.

Q - Geoffrey C. Meacham {BIO 21252662 <GO>}

Got you. Okay. Thanks.

Operator

Our next question comes from the line of Ronny Gal with Bernstein.

Q - Aaron Gal, Ph.D.

Thank you for taking my questions. I'll touch on biosimilars here, a couple of them. With interchangeability guidance, are you guys considering starting any interchangeability trials for your mAb programs? And does that differ between the anti-TNFs and the oncology program?

And then regarding Neulasta, you kind of mentioned the SCOTUS risk for canceling the six months warning. But there's also a chance that they'll reintroduce the patent then. And if they do, does that essentially mean the Neulasta biosimilar will be delayed deep into 2018? Or is that still outstanding?

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

Yeah, I think, Ronny, I'm not sure we want to comment about matters that relate to the ongoing litigation. And with respect to interchangeability, what I would say generally, is that we think that the pathway that looks like going be pursued here in US for

interchangeability is consistent with what we've been advocating for and doesn't represent a change from what we've expected. So I think that's probably, from a competitive standpoint, all I want to say at this point. Again, consistent with what our expectations have been and consistent with what we've been advocating for.

Q - Aaron Gal, Ph.D.

Thanks.

Operator

Our next question comes from the line of Cory Kasimov with JPMorgan.

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

Good afternoon, guys, and thanks for taking my question. So I'm wondering, on the capital allocation front, given that you now have a cash balance of nearly $40 billion to go along with significant ongoing free cash flow generation and potential favorable tax policy from the new administration, does this change the types or the size of organizations that you would potentially being be willing to look at relative to the historic strategy you guys have communicated? Thanks.

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

Maybe David and I can double team this, Cory. Again, we have felt for some time that we have a lot flexibility in our balance sheet to do acquisitions. And I think anything that provides clarity on the tax rate and clarity on the global tax structure would be helpful. It would probably increase our flexibility, but again, I think we have felt for some time that we have considerable flexibility to do transactions. And when we've talked in the past about the kinds of things we're looking at, we've often talked about it in the context of the big plate of things that we have internally that we're working through.

But we feel like we're in a place now where we can look externally for large and small opportunities to help grow the business. So I think the message is, we're confident in the outlook for our company. We're confident in the importance of innovation. And we've got a balance sheet that supports our ability to look at transactions large and small. David, do you want to add anything to that?

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

No, that's right. I mean I would say flexibility. We remain disciplined always in making sure what we're looking at can generate a return for our shareholders, not just the sellers. And I guess from my perspective, I don't really view us even today pre-tax reform as having some arbitrary cap in terms of what we can look at. We think we need to look at all opportunities of all sizes.

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

Okay. Thank you.

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

Yes.

Operator

Our next question comes from the line of Geoffrey Porges with Leerink Partners.

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

Thanks. Congratulations. That's a real milestone. Unfortunately, just a patent-related question. Could you give us a sense of the timing for your expectations for resolution of the PCSK9 litigation? And then related to that, is there any chance of an equivalent patent to the '165 patent in Europe? Do you believe that that might be infringed?

And then lastly, there's some suggestions on Erenumab that some of your competitors have broad IP around the CGRP pathway. Are you confident that you'll be able to launch that product unencumbered and not at risk? Thanks.

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

Okay, Geoff, I think there were three questions there. But with respect to your first question. I think that we expect that the court will rule on the request for a stay of the injunction on or before February 21. With respect to the overall resolution of the case after that, I think it'll probably be something in the four to 10 month timeframe but we'll know more when we've heard from the courts and that will, of course, be public.

And then with respect to your question about the patent outlook in Europe, obviously we don't like to comment about ongoing litigation. So I think I'll hold off on saying anything more than that. And again with respect to Erenumab, we feel confident in both the clinical profile that's emerged for that molecule, as well as our intellectual property portfolio around it.

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

Great. Thanks very much.

Operator

Our next question comes from the line of Salim Syed with Mizuho Securities.

Q - Salim Syed {BIO 16887281 <GO>}

Great. First of all, thanks, Arvind, for the kind comments and congrats to everybody on the FOURIER data. Just two questions. One's a backup because the first one's on Repatha. So, Sean, this is not about the results that you guys now have, but this is more about the design. Can you just remind us what you were assuming in terms of bare minimum benefit in order to hit stats, say, based on how you designed the trial?

And if you can't answer that, my question's around Enbrel 2018 pricing, for Tony. Is the 2017 net pricing, minimal net pricing benefit, is that a 2017 thing? Or should we assume that for 2018 and going forward as well? Thank you.

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

Salim, I think we can answer your first question because that's in public, the answer's public there.

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

Yeah, the design of the trial is published. And I guess what I would say is that, just always remember that the trial was actually designed around this harder MACE endpoint of the cardiovascular death, non-fatal MI and non-fatal stroke. And there we wanted to be able to detect with 90% power a 15% decrease in risk. So that was the design of the study perspective.

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

Okay, let's go to the next question.

Operator

Our next question comes from the line of Joshua Schimmer with Piper Jaffray.

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

The FOURIER results like reshaped the cholesterol management guidelines. How important do you think that is for defining the addressable market and enabling Repatha reimbursement? And then when might those guidelines be revised to reflect the results? Thanks.

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

So maybe I can talk a bit about that. Obviously we look forward to hearing what the ACC and the AHA have to say when they see the full data. Everyone we've talked to has talked about revising the guidelines once they see the outcomes. And I can't give you guidance

on the timing, but obviously if the data is robust enough, we would certainly hope that the guidelines would come forward pretty soon.

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

Thank you.

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

Okay. Thanks, Josh.

Operator

Our next question comes from the line of Ian Somaiya with BMO Capital.

Q - M. Ian Somaiya

Thanks. Just maybe following up on the operating margin question. Tony, can you just give a sense for what the plan is for supporting the drugs that are now or will be facing biosimilar competition? And just your own biosimilar portfolio, how should we think about the impact of the launches of those on gross and operating margins?

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

The plan for supporting existing products base income.

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

Okay.

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

Sorry, we were having a little trouble hearing you, Ian. But I think we got it.

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

So I think your question was what is our plan for supporting existing products that are facing biosimilar competition. Clearly, in places where we believe that the market is evolving to a branded-specific market, we continued to put activity behind the brands. Where they're becoming more commodity like we will reduce activities quite dramatically.

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

And with respect, Tony, do you want to comment with respect to, either the gross or the operating margin context for our own biosimilar portfolio, or leave that for another day?

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

I think we've always believed that our own biosimilar will be in a branded type market in therapeutic areas where we have a strength, and therefore we'll be using existing teams to bring these to the market as effectively as we can.

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

Okay. I think we got a couple more questions queued up. So let's try to get to those, and then Arvind will be here and his team can take any follow-up questions that you all may have. So let's get to our last couple questions here.

Operator

Our next question comes from the line of Alethia Young with Credit Suisse.

Q - Alethia Young {BIO 17451976 <GO>}

Thanks for taking my question, the congrats as well. But on Repatha, maybe you can talk about some of the trends you're seeing with doctors. And are they particularly concerned around the potential for an injunction? I'm just am wondering if you're starting to see people who are Praluent patients move to Repatha. Thanks.

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

Alethia, it's Tony. So let me give you a response. I mean, we don't track anything other than usage by physicians and, yeah, the FDA has approved Repatha for all patients, including those presently taking alirocumab and our expectation is all these patients would in fact become Repatha patients of the future. So we do see, as I said, month to date in January, 60% of new to brand patients are on Repatha. And I'd also add that a vast majority of the physicians that prescribe alirocumab have experience using Repatha, so they know the product and the benefits it provides to their patients

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

Yeah, Frederick, as it's about 15 minutes past the hour, let's take two last questions please.

Operator

Thank you. Our next question comes from the line of Brian Skorney with Robert Baird.

Q - Brian P. Skorney {BIO 15993204 <GO>}

Hey. Good afternoon, guys. Thanks for taking the question. I guess in your comments around the Trump administration meeting, you'd said that you're looking forward to working on market-based reform around drug pricing. I just wonder, in the discussion was the idea of allowing CMS to negotiate directly with manufacturers mentioned at all? Is that something still that might be on the table for the administration? And on the regulatory reform front, he had mentioned that he may be naming a new commissioner of FDA soon. I just wonder if you guys had any insight into how seriously he's taking his Silicon Valley advisors in terms of what seems to be a recommendation for complete reduction of regulatory oversight for new drugs?

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

Brian, I don't think I could comment on that specifically yet. I think you're right that we expect there will be an announcement about an FDA leader here soon. I think this

President takes seriously what he's said about regulatory reform. And I suspect that will be reflected in his choice of a leader for FDA. But again, I think we'll all just have to wait and see. And we didn't talk any specifics about the role of HHS. We talked about the need for all of us to work together to address making medicines affordable and accessible to people who benefit from them, and who need them. But again, it was a constructive discussion, Brian.

Q - Brian P. Skorney {BIO 15993204 <GO>}

Thanks.

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

Okay, Frederick, let's take one last question.

Operator

Our final question comes from the line of Jim Birchenough with Wells Fargo Securities.

Q - Jim Birchenough {BIO 5068439 <GO>}

Hey, guys. Thanks for fitting me in and congrats on the FOURIER data. Just wondering if there's anything to learn from the statin experience when we first saw outcomes benefits there as to whether the key is the data, the data presentation, the publication of the data, or the guideline revision in terms of what really drives the inflection of following these kind of outcomes data. Thanks.

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

Maybe I can respond to that because I'm probably old enough to remember, right. I mean so (78:01) happened in the mid 1990s. The market was dramatically different. It was the first time we'd ever seen real impact of lowering LDL. And clearly, there weren't as many sort of utilization management criteria as exists today. So uptake started quite fast as people saw the value. But it was a brand new concept, so it took a good 10 years to get to the peak of the market.

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

All right. I think at this time, we'll wrap up. As I said earlier, Arvind and his team are around for those of you who have follow-on questions or didn't get a chance to ask your questions in the hour and a bit that we've been together. But let me just again thank you for joining the call and say we're looking forward to the year. We're excited about the outlook for long-term growth and about the progress that we're making towards our 2018 commitments. So with that, we'll look forward to seeing you all at ACC. Thank you.

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

Thanks, everybody.

Operator

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