Q4 2017 Earnings Call

Company Participants

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

Other Participants

- Aaron (Ronny) Gal, Analyst
- Alethia Young, Analyst
- Andrew Peters, Analyst
- Carter Gould, Analyst
- Christopher J. Raymond, Analyst
- Cory W. Kasimov, Analyst
- Eric Schmidt, Analyst
- Geoff Meacham, Analyst
- Geoffrey C. Porges, Analyst
- M. Ian Somaiya, Analyst
- Matthew K. Harrison, Analyst
- Michael J. Yee, Analyst
- Robyn Karnauskas, Analyst
- Salim Syed, Analyst
- Terence Flynn, Analyst
- Umer Raffat, Analyst
- Ying Huang, Analyst

MANAGEMENT DISCUSSION SECTION

Operator

My name is Skinner, and I will be your conference facilitator today for Amgen's Fourth Quarter 2017 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>}

Okay. Thank you, Skinner. Good afternoon, everybody. I'd like to welcome to you our conference call to discuss our business performance for 2017 and our outlook for 2018. Although our results exemplify our focus on volume-driven growth, tax reform has created profound changes and opportunities for our industry and our company. So to begin this dialogue, our Chairman and CEO, Bob Bradway, will provide some perspective, followed by our CFO, David Meline who will review our Q4 and full-year 2017 results, and provide guidance for 2018. Our Head of Global Commercial Operations, Tony Hooper, will review our product and geographic performance in 2017, followed by our Head of R&D, Sean Harper, who will provide a pipeline update.

As in the past, we will use slides corresponding to our presentation today, and a link to these slides was sent earlier. 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 schedule accompanying today's press release, a 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 2017 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. We have more ground than usual to cover with you in our prepared remarks this afternoon. We'll be addressing not only our results for 2017 and our outlook for this year, but also the impact of tax reform, which we see is a very favorable development for our business.

To kick off, I'd offer that with another year of strong performance behind us, we're even more excited about the long-term prospects for our business than we were a year ago. In 2017, we continued to deliver solid operating performance with earnings per share growing 8% and operating margins improving to an industry-leading 53.5%. In capital terms, payout to our shareholders grew by 14%, and we improved our return on capital to 33%. We delivered these results in a period of increased competition for many of our largest products, several of which have lost patent protection, and while continuing to invest heavily in the future of our business. Our steady progress through 2017 places us squarely on track to deliver against the long-term commitments we set several years ago for 2018.

We enter 2018 in a strong position and confident about our long-term outlook. Those franchises which have come off patent in nephrology and oncology have held up well, and we expect them to remain competitive. The brands that we expect to drive our future growth, led, of course, by Repatha, Prolia, and KYPROLIS, with Aimovig and the biosimilars coming close behind, are emerging now, and the strong data we have to support them are encouraging.

And finally, we have stable cash flows and a strong balance sheet, both of which are improved by tax reform. We intend to use our resources to continue to invest in our people and the attractive long-term growth opportunities we see in our history, including M&A where it fits our focus while also returning capital to our shareholders.

To be successful in the long run in our industry, we think it will be essential to have innovative, differentiated medicines that deliver large beneficial effects for patients suffering from serious illness, and to demonstrate that these medicines provide value for all stakeholders in the healthcare system. We have a number of these medicines on the market now and in our pipeline, some of which meet the needs of large patient populations and some of which are for more specialized markets. With pressure on prices globally, we think revenue growth will be more tightly linked to volume growth than was the case historically. In this regard, medicines that serve the needs of large numbers of patients will be particularly attractive growth drivers. Repatha is a clear example of this.

On this call last year, we announced the successful conclusion of the Repatha outcomes trial. Now, following an expedited review by the FDA, we're able to talk to patients, payers, and prescribers about the unique role of Repatha in significantly reducing the risk of heart attack and stroke. Cardiovascular disease is the single greatest problem facing healthcare systems around the world today. And as the population ages globally, this problem will only grow unless we embrace important new innovations.

Repatha is exactly the type of innovation needed today by millions of patients to bring down the risk of cardiovascular disease. Our job now is to see that prescribers, patients, and payers understand this product and recognize the importance of adopting it for high-risk patients. As they do, we expect Repatha to be an important growth driver for us for many years to come. We'll continue to work to ensure that patients gain access to this therapy worldwide, especially those for whom other therapies have not proven effective.

Like Repatha, Prolia represented a paradigm-changing biologic when it was first launched for osteoporosis. Today, it is, of course, the leading osteoporosis therapy. In fact, there are 3.5 million patients worldwide taking Prolia, and the demand for it continues to grow by double-digit percentages. With only 25% of women in the U.S. who might benefit from osteoporosis therapy receiving it, we continue to see significant growth potential for Prolia in osteoporosis.

In our pipeline, I would highlight two products which have similar attractive characteristics but which address more symptomatic diseases. One of these is Aimovig, our first-in-class product to prevent migraine. Current therapies don't work adequately for this debilitating disease, and patients and prescribers are anxious to have a better option. We're hopeful

that Aimovig, which uniquely blocks the CGRP receptor, will be the answer that millions of patients have been waiting for.

The other product I would highlight is tezepelumab, a first-in-class molecule that has shown very encouraging Phase 2 results in treating asthma. There are millions of asthma sufferers worldwide in need of better therapy. We're hopeful that tezepelumab might be just that, and we're actively enrolling a Phase 3 trial to establish the answer. We've enjoyed great success in specialty markets historically and with our innovative medicines, and we expect that to continue. XGEVA represents a good example of this. And with the addition of multiple myeloma to our label, we would expect to see more growth from this product beginning in 2018.

In cancer, more generally, overall survival is the gold standard. We enter 2018 with fresh overall survival data in our labels for KYPROLIS and BLINCYTO. KYPROLIS has established strong share in second and later lines of multiple myeloma therapy, and we expect the addition of overall survival data to strengthen its appeal to physicians, payers, and patients. With overall survival for relapsed/refractory acute lymphoblastic leukemia patients, BLINCYTO is a game-changer in its own right. But importantly, it provides confidence for the long-term outlook for our broader BiTE platform. We have 12 BiTE programs progressing in both liquid and solid tumors, and data over the next two years will inform the future for many of these molecules.

2018 will be another year of new product launches for Amgen. In addition to our launch plans for Aimovig, we are extending our longstanding leadership in nephrology with the launch of Parsabiv, a specialty product for kidney disease, in a number of countries including the U.S.

And finally, I want to highlight that we have clarity now around AMGEVITA, our adalimumab biosimilar, and we look forward to launching that internationally later in the year. This will be first of our biosimilars to launch. We have a strong portfolio coming behind it with one other approval already and several Phase 3 programs awaiting approval and launch. We think these represent compelling growth opportunities for us around the world.

We think tax reform provides a number of important benefits for our company. First, it puts us on a more level playing field strategically with our international competitors, who previously were advantaged by lower rates and global access to their cash. Second, in addition to a more level playing field, tax reform clearly provides incentives for us to invest heavily in innovation and advanced technologies here in the U.S., and that is exactly what we will do.

The timing of tax reform is particularly relevant for us right now as we are on the cusp of deploying our so-called next-generation biomanufacturing technologies, which enable us to make biologics with much improved productivity, a smaller footprint, and much reduced levels of waste and environmental impact. We developed these technologies in the U.S., and thanks to tax reform, we will now build new manufacturing capacity and add highly skilled jobs here in the U.S. to capitalize on them. It's worth noting that with tax

reform, we'll make products in the U.S. and export it to cover 85% of our international sales. With improved clarity on tax reform, we expect to invest on the order of $2.5 billion in capital expenditures in the U.S. over the next five years.

We see tax reform benefiting us in other areas as well. Amgen Ventures, our vehicle for early-stage investing, will also make close to $300 million available for new investments in innovative biotechnology, digital, and healthcare information companies. We'll also grow our already substantial commitment to our communities with plans for the Amgen Foundation's investments in the proven Amgen Scholars and Amgen Biotech Experience programs, which we expect to reach $100 million of commitment within four years. We have engaged some 600,000 high school and college students in person through these programs, consider this our commitment to helping to build a pipeline of talented scientists and biologists in the U.S. and beyond.

Through our foundation's philanthropic giving, we expect to deploy $100 million over the next five years in the communities where we work and live. We've also assessed that tax reform will be generally positive for our staff, especially for our non-executive U.S. staff, who number about 12,000. We estimate that lower personal tax rates, combined with investments we are making in enhancing base wages for these staff, will create literally thousands of dollars of improvement in the average take-home pay for our typical U.S. non-executive staff member. When you pair all this with the fact that some 90% of all Amgen staff members globally have held Amgen stock, you can see that the benefits of tax reform will be quite broad.

Finally, tax reform also provides us with more flexibility for capital deployment. Since 2011, we have invested more than $42 billion in research and development, innovation-based acquisitions, and long-term-oriented capital expenditures. We expect to continue making such long-term investments now while also being able to return excess capital to our shareholders in the form of growing dividends and share buybacks.

Based on our confidence in the long-term outlook for the business, which is enhanced by the benefits of tax reform, we have increased our share repurchase authorization by $10 billion. We expect to retire shares on an accelerated basis this year, as David will describe shortly. As I highlighted for you, the benefits of tax reform for our shareholders do not come at the expense of others but come in addition to the investments that we're making for our staff, the patients we're seeking to serve, and our communities.

So to reiterate, we're operating the business well. You've seen that in our financials and you saw it in our successful response to the extraordinary challenge of Hurricane Maria, too. Our end market products are strong, we have attractive assets advancing in the pipeline, and we have a strong balance sheet. Strategically, we're well-positioned to adapt to the growing pressures in the healthcare environment and to capitalize on consolidation opportunities for our shareholders.

Let me conclude with a word of thanks to our staff around the world for their tireless devotion to our mission. I can assure you they are focused on serving patients and driving growth in 2018 and beyond.

Let's turn to David.

David W. Meline {BIO 6397419 <GO>}

Okay. Thanks, Bob. Before I review our results and guidance, I would hike to take a moment to reflect on our performance over the last several years. As Bob mentioned, we entered 2017 as another year which presented significant challenges related to the transition of our portfolio, as well as the evolving competitive dynamics of the industry as a whole. In the face of these expected and other not so expected challenges including Hurricane Maria, I'm pleased to report that we delivered positive performance again in 2017.

Additionally, with regard to our five-year goals, we have already delivered or have clear line of sight to delivering on the commitments we established in 2014. The first goal was to achieve a substantial improvement in our operating efficiency, agility, and speed, with the resulting outcome of a non-GAAP operating margin between 52% and 54%, representing a 15-point increase at the midpoint. We achieved this objective starting in 2016, two years ahead of our commitment.

Second, in 2017, we delivered the $1.5 billion transformation savings commitment, and we'll exceed that goal in 2018. Third, through our next generation biomanufacturing capability, as well as other efforts to optimize our fixed capital infrastructure, we are on track to meet our 2018 goal of reducing our facility footprint by 23%.

Finally, based on today's 2018 guidance, I'm pleased to confirm our expected delivery on the other key objectives of both double-digit, non-GAAP EPS growth, and providing returns to shareholders of at least 60% of non-GAAP net income on average during the period 2014 to 2018. These commitments are being achieved before benefiting from tax reform, which further enhances Amgen's performance in 2018 and beyond.

Now let's turn to the fourth quarter financial results on page 6 of the slide deck. Revenue at $5.8 billion declined 3% year-over-year. This quarter we saw worldwide product sales at $5.6 billion as unit demand from our growth products largely offset mature product declines. We are particularly encouraged by our 10% year-over-year volume growth in markets outside the U.S., reflecting the value of our innovative products in these international markets, many of which have experienced biosimilar competition and portfolio transition for a number of years. Other revenues at $233 million decreased $69 million year-over-year as a result of the milestone payment received in the fourth quarter of 2016 related to the out-licensing of AMG 139.

Our Q4 non-GAAP operating income at $2.6 billion declined 11% from prior year. Non-GAAP operating margin was 45.9% for the quarter. As previously indicated, our operating expenses reflected the typical underlying fourth quarter pattern. We also experienced a number of additional expenses in the quarter, including $79 million of Hurricane Maria recovery costs, incremental expenses accelerated for tax planning purposes, as well as inventory-related costs.

Finally, we increased our investments in support of volume-driven growth as we expand activities for our products addressing unmet medical needs in large patient populations, including launch preparations in advance of the upcoming Aimovig launch. These increases were partially offset by continued favorable expense impacts from our transformation initiatives across all operating expense categories, and the expiry of the Enbrel residual royalty payment on October 31, 2016.

Other income and expenses were a net $31 million expense in Q4. This is favorable $171 million on a year-over-year basis. This year-over-year favorability was primarily due to higher interest income, gains in our venture portfolio, and gains from investment portfolio rebalancing in the fourth quarter of this year, coupled with favorable compares on both of these items in 2016. A portion of these activities were taken in anticipation of changes in tax and accounting standards effective in 2018.

The non-GAAP tax rate was 16.6% for the quarter, a 2.1-point improvement versus Q4 2016, reflecting favorable changes in the geographic mix of earnings this year. While not impacting our non-GAAP P&L, we incurred a $6.1 billion charge on our fourth quarter GAAP P&L related to U.S. corporate tax reform, including the repatriation tax and revaluation of net deferred tax liabilities. The repatriation tax will be paid to the U.S. government over an eight-year period.

Non-GAAP net income decreased 3% and non-GAAP earnings per share was flat year-over-year for the fourth quarter. Please find a summary of our 2017 full-year results on page 7 of the presentation. Our 2017 full-year revenues declined 1% to $22.85 billion, while our non-GAAP earnings per share grew 8% to $12.58 per share. For the full year, we saw flat worldwide product sales growth at $21.8 billion. Changes in foreign exchange had a 1% negative impact to total revenue and product sales for the full year on a year-over-year basis.

For the full year, non-GAAP operating income at $11.7 billion grew 2% from prior year. Including $146 million of nonrecurring expenses associated with the recovery from Hurricane Maria, our non-GAAP operating margin improved by 1.2 points to 53.5% for the year as we realized the benefits from our ongoing transformation initiatives and the expiry of the Enbrel residual royalty payment.

On a non-GAAP basis, cost of sales as a percent of product sales increased by 0.2 points to 13.5%, driven primarily by expenses related to Hurricane Maria recovery efforts, unfavorable product mix, and other inventory costs, offset partially by lower royalties and manufacturing cost efficiencies.

Research and development decreased 7% year-over-year, driven primarily by lower external business development expenses and lower spending required to support certain later-stage clinical programs. SG&A expenses decreased 2% year-over-year due to the expiration of the Enbrel residual royalty, partially offset by our increasing investments to drive volume growth in our products, which address unmet needs in large patient populations.

In total, non-GAAP operating expenses decreased 3% year-over-year to $11.2 billion. Through the end of 2017, overall operating expenses have decreased by approximately $500 million versus 2013 levels. Included within this total is an incremental annual expense of $1.5 billion required to launch and maintain new products, build out new therapeutic areas, advance our biosimilars business, and increase our global presence.

Other income and expenses were favorable by $255 million on a year-over-year basis due to higher interest income on our higher cash balances, as well as venture portfolio gains and milestones realized across the course of the year. The non-GAAP tax rate was 18% for the full year, down 0.8 points versus 2016. The year-over-year decline was primarily driven by changes in the geographic mix of earnings, offset partially by lower tax benefits from share-based compensation payments.

Turning next to cash flow and the balance sheet on page 8. For the full year 2017, Amgen continued to demonstrate strong and durable cash flow generation with $10.5 billion in free cash flow versus $9.6 billion last year. This increase was primarily driven by higher operating income and favorable changes in working capital. Cash and investments increased to $41.7 billion. This balance included $3.1 billion in the U.S. and $38.6 billion outside the U.S. Total debt outstanding at year-end totaled $35.3 billion and carries a weighted average interest rate of 3.7% and an average maturity of 12 years.

In 2017, we deployed $3.1 billion to repurchase 18.5 million shares at an average of $169 per share. At the end of 2017, we had $4.4 billion remaining on our existing share repurchase authorization. Additionally, for 2017, we increased our dividend per share by 15% to $1.15 per quarter with payments totaling $3.4 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 $1.32 per share for the first quarter of 2018.

Turning to the outlook for the business for 2018 on page 9. 2018 will be another important year for Amgen as we continue investing in the pipeline, building out our global business, and supporting our new product growth. In anticipation of this opportunity, we transformed the business over the past several years to enable us to fully invest from a position of strength. This transformation allows us to deliver industry-leading financial performance while continuing to invest for long-term growth and success.

Our 2018 revenue guidance is $21.8 billion to $22.8 billion, and our non-GAAP earnings per share guidance is $12.60 to $13.70 per share. Our non-GAAP tax rate guidance reflecting the impact of tax reform is 14% to 15%, and we expect capital expenditures of approximately $750 million this year.

There are several key assumptions embedded in our outlook that I would hike to take a moment to share. First, our revenue guidance reflects both continued positive momentum from our newer products, as well as the evolving competitive dynamics related to our legacy products. We have important growth opportunities with the inclusion of outcomes data in Repatha's label, our plan to launch new products including

Aimovig and AMGEVITA, and the added flexibility enabled by tax reform to use our strong cash flow and balance sheet to drive continued growth of the company. We also embrace the potential challenges, including the possible generic competition to Sensipar, continuing competitive dynamics for Enbrel, and expected new competition against Neulasta and Aranesp.

With regard to Sensipar, although the composition of matter patent expires in March, we are involved in litigation over pediatric exclusivity with the FDA, and separately over the formulation patent with potential generic competitors. Although we believe in the strength of our position, uncertainty as to the timing of competition will remain until the outcome of these litigations becomes clear. Also note that historically the first quarter represents the lowest product sales quarter for the year. For 2018, we expect this pattern to continue. Tony will provide further details related to this in his remarks.

With respect to other revenue, for the full year 2018, we expect to see 15% year over year growth. The quarterly run rate will be impacted by an unfavorable true up of a royalty in Q1, offset by incremental milestones in the second half of the year. From an operating margin perspective, since 2016, we have delivered on our commitment of a non-GAAP operating margin between 52% and 54%, and based on today's guidance, we expect to again operate in this range in 2018, as we continue to invest in our products to drive volume growth in large patient populations. Going forward, we will continue to evaluate incremental investments, including acquisitions to drive growth and maximize shareholder value.

The recently passed tax reform legislation provides significant financial flexibility in the form of a globally competitive tax rate and immediate access to the year-end 2017 ex-U.S. cash balance of $39 billion. With regard to 2018 guidance, our non-GAAP tax rate is forecast between 14% and 15%. This incorporates a 21% tax rate on U.S. earnings and a 10.5% tax rate on ex-U.S. earnings.

With regard to capital deployment, our principles over the next several years are as follows: first, we will invest in our business as we continue to expand our pipeline and seek to drive long-term volume growth globally across large patient populations; we will also invest in greater manufacturing capacity to support the volume growth we foresee. For the first time in several decades, tax reform enables us to competitively consider investment in the U.S. As a result, over the next five years, we expect to invest approximately $3.5 billion in capital expenditures. Starting in 2018, approximately 75% of that investment will be in the U.S., up from about 50% in recent years.

As Bob mentioned, a key component of our U.S. capital investment strategy includes a new drug substance manufacturing plant which will be built using our next-generation biomanufacturing capability. We expect to complete this expansion in about half the time of a conventional plant for approximately one-third of the cost. In addition to investing internally, we continued to pursue external opportunities to accelerate the growth of our business in our chosen therapeutic areas, as well as accelerating our global build-out.

Furthermore, we will invest an additional $300 million in our venture fund. Our venture fund is an important tool to ensuring we are appropriately informed, engaged, and invested in cutting edge advances in science, technology, and innovation. Since 2004, we have invested over $0.5 billion in our venture funds. In addition to their scientific importance, these investments have generated returns well above our cost of capital.

Second, we'll remain committed to an optimal capital structure in order to minimize our weighted average cost of capital by deploying any excess accumulated capital and fully deploying cash flows going forward. As a first step to accomplishing this objective, we have received board authorization to purchase up to $10 billion of our common stock. This is in addition to the previously approved share repurchase authorization, which remained at $4.4 billion at the end of 2017.

Given the scale of excess capital we have to deploy, our plan is to proceed with a Dutch auction equity tender offer consistent with the approach we used successfully in 2011. This tender offer would be for up to $10 billion and would commence as early as next week. Further, we may repurchase up to our full authority in the first half of 2018. The optimization of our capital structure will result in higher net interest expense in 2018 and beyond as we will have less interest income due to lower cash balances. For 2018, this results in expected other income and expense of $600 million to $700 million net expense.

As we deploy our excess capital in the most efficient manner over the next several years, we could find that it is prudent to pay some upcoming debt maturities in cash rather than refinancing in the market. This would translate directly into additional financial flexibility and debt capacity that we could choose to redeploy in the future. Third, we will continue to provide meaningful returns to shareholders through both the previously mentioned share repurchases, as well as continued dividend growth.

Finally, today's revenue in non-GAAP EPS guidance ranges are wider than we typically have provided at the start of the year, which is primarily a reflection of a range of Sensipar scenarios in addition to the other ongoing uncertainties outlined earlier. It is important to recognize that our guidance today does not include the impact of potential future M&A activities.

In summary, we delivered another year of strong financial results in 2017, and we remain confident in the outlook for Amgen's success in 2018 and beyond. This concludes the financial update. I'd now turn the call over to Tony.

Anthony C. Hooper {BIO 6284080 <GO>}

Thank you, David. I'd like to begin with a few comments on our overall performance in 2017, followed by a review of our product performance. On a full-year basis, 2017 sales were in-line with 2016's as the growth of our newer products offset the decline in our mature brands. We saw this play out again in quarter four as robust volume growth led by Prolia and our recently launched brands offset volume declines in Enbrel, ESAs, and NEUPOGEN.

Our international performance in quarter four led by Europe, as David said, was strong with 7% growth, excluding the impact of foreign exchange, driven by volume growth of 10%. The European portfolio has already transitioned to a majority of sales from newer brands leading to strong volume growth for the overall portfolio. I'm pleased with our execution in 2017. Our team made excellent progress across a number of strategic fronts in building the foundation for long-term volume-driven growth. We drove volume growth across several important brands led by Prolia. We defended Enbrel and several of our mature brands against increasing competition, and we executed some patient-focused life cycle management strategies.

We continue to advance our recently launched products with impressive new clinical data. The most significant, of course, being the Repatha outcomes data, as well as three new sets of overall survival data, two for KYPROLIS and one for BLINCYTO.

We also began laying the foundation for our next wave of launches as we prepare for Aimovig, our migraine product in the U.S., and AMGEVITA, our Humira biosimilar in Europe, later this year. This will be an exciting milestone as we begin to commercialize our biosimilars in 2018. I am confident that we are well-positioned to capitalize on the opportunities within our portfolio of innovative and differentiated medicines.

Turning now to our product performance. Prolia ended 2017 with another impressive quarter of 24% growth year-over-year. On a full-year basis, Prolia grew 20%, and as Bob said, now at presale with 3.5 million patients globally. In the U.S., we achieved a record number of new patient starts in 2017. After seven years in the market, this growth of new patient initiation underscores the continuing unmet medical need. Once patients are initiated on Prolia, we have a good track record of sustained repeat injections. While this is great progress, there are still 100 million patients worldwide who suffer from osteoporosis. In the U.S., one in every two women above 50 will suffer an osteoporotic fracture. So we continue to work to improve both the diagnosis and the treatment of osteoporosis as we grow Prolia's market share within the market. With its unique profile and through continued and sustained investment, we expect Prolia will remain a very strong growth driver.

Turning now to our oncology brand. KYPROLIS grew 24% year-over-year with strong performance internationally. Uptake in these markets remains robust. Fourth quarter sales in Europe have doubled from the fourth quarter of 2016. In the U.S., KYPROLIS now has two compelling sets of overall survival data in both doublet and triplet regimens that demonstrate a 21% reduction in the risk of death versus standard of care in each setting. The FDA just approved adding the impressive overall survival data from the ENDEAVOR study to the label. KYPROLIS plus dexamethasone is the only preferred doublet regimen in the NCCN guidelines.

We look forward to the equally impressive overall survival data from ASPIRE, being added to our label later this year. These data are without a doubt differentiators and should reset the treatment paradigm as the new standard of care for the relapsed multiple myeloma patients.

Our focus message to physicians is pretty clear. Patients who have relapsed will live longer when treated with regimens that include KYPROLIS, and early indications are showing that this is resonating well as KYPROLIS's share of new relapsed or refractory patients continues to improve.

XGEVA grew 4% year-over-year, driven by a combination of volume growth, changes in inventory, and net selling price. We're pleased to begin the year with the FDA's approval to expand the XGEVA label to include the prevention of skeletal-related events in patients with multiple myeloma. This approval was nearly a month ahead of the PDUFA date, and within five days of approval, the first multiple myeloma patient received an injection of XGEVA.

A large portion of the overall 100,000 multiple myeloma patients in the U.S. are at risk for bone complications. XGEVA can help these patients as many of them cannot effectively be treated with cerebronic acid due to renal insufficiency. CMS has recognized this issue and has designated XGEVA as a novel therapy for these patients. This is another example of our life cycle management strategy and investment in volume-driven growth.

Neulasta sales were flat year-over- year as we continue to see low-single-digit decline in the use of myelosuppressive chemotherapy regimens due to growth in new and less toxic therapies. Onpro continues to gain traction, and we exited 2017 slightly above 60% of U.S. Neulasta units sold. Its compelling value proposition for patients and the healthcare system is clear. It delivers better adherence to therapy, lower rates of febrile neutropenia and hospitalization, and more convenience for patients and oncology practices. Our patent-protected Onpro will be an important point of differentiation in the marketplace against future potential competition.

On the topic of potential new competition to Neulasta in the U.S., we know there continued to be a serious amount of questions about whether the competitors who've been announcing their arrival in the market for some years now will be able to succeed with the regulators and in the courts such that they could finally come to market in the second half of 2018. If they do arrive, we will be ready for them.

With NEUPOGEN, the impact of short-acting biosimilars in the fourth quarter were consistent with prior trends as we exited 2017 with nearly 40% unit share of the short-acting market. We continue to maintain pricing discipline since the entry of competitors.

Now turning to Enbrel, which declined 13% year-over-year. Underlying the volume demand was in-line with prescription trends in the fourth quarter. Segment growth in rheumatology and dermatology, as well as changes in Enbrel's volume share across each segment, were in-line with prior quarters. As I told you last quarter, maintaining Enbrel's strong formulary position and patient access is resulting in a small decline in net selling price. We expect the fourth quarter trends for both unit demand and net selling price to continue into 2018.

You'll also recall that the first quarter last year was the lowest quarter of 2017 as insurance reverifications and patient deductibles reset for the new calendar year. We expect to

experience similar dynamics this year and therefore expect Enbrel's first quarter to be the lowest sales for 2018, representing approximately 20% of full year 2018 sales.

Critical to our strategy with Enbrel is the ongoing pursuit of innovative ways to enhance patient experience and to differentiate our product. The ENBREL Mini with AutoTouch was recently launched along with a new low-pain formulation. This is a multi-use device specifically designed to be used with ease by rheumatoid arthritis patients. Patient feedback has been very positive on these new innovations, and we're also very proud of the positive environmental benefit of this reusable autoinjector.

Switching now to our ESA portfolio. Slide 21 shows the 2017 composition of our ESA business. Aranesp declined by about 7% on a year-over-year basis with lower unit demand, favorable prior-year adjustments, and unfavorable foreign exchange rates.

With EPOGEN, the underlying business remained relatively stable with the primary driver being lower net selling price as a result of our extended Supply Agreement with DaVita until 2022. Over the last couple of years, we have grown our U.S. Aranesp business by converting the medium-sized and independent dialysis centers from EPOGEN to Aranesp. However, we are aware that our long-acting competitor has recently extended their product offering to these dialysis customers. So we expect to lose some of this business as early as this quarter.

We are also preparing to compete with their potential short-acting biosimilar in all customer segments, including hospitals and clinics, if and when such a biosimilar is approved by the FDA. Our long track record of safety, efficacy, and reliable supply is a competitive advantage that Amgen has always had.

Turning now to calcimimetics, beginning with Parsabiv. We continue to launch Parsabiv in new markets throughout the world. This includes launching in the U.S. last month. As the head-to-head clinical data showed, Parsabiv demonstrated a greater level of efficacy when compared to Sensipar. Since the product is administered in the patient's existing IV line during dialysis, it puts control into the hands of the healthcare provider, which could drive an improved level of adherence. Nephrologists continue to be positive and are excited about having the product available. As David mentioned, the 2018 outlook for Sensipar is somewhat uncertain given the ongoing litigations. It is, of course, conceivable that competitors may be able to bring generic products to market at some point in 2018 although we believe we have strong litigation positions.

With Repatha, we continue to execute competitively, maintaining a majority share on a global basis. We were very excited to exit 2017 with the expedited approval by the FDA of the Repatha outcomes data. This is a very important milestone for Repatha and is potential to help cardiovascular patients at high risk for heart attacks and strokes. Our team can now, for the first time, speak directly to the benefits of treating patients with Repatha and its ability to reduce the risk of heart attack by 27% and stroke by 21%, as well as further event reductions after the first year of treatment.

Our sales teams were trained and in the field shortly after the approval and are receiving positive feedback from physicians. It's still early days since the approval, but signs are pointing in the right direction with NBRx gains.

We do, however, expect quarter one sales to be relatively flat sequentially as Repatha faces similar dynamics as Enbrel related to insurance reverification and resetting of patient out-of-pocket costs in the first quarter. We continue to work with payers to improve patient access and are making progress. Our priority remains reaching the large population of high-risk cardiovascular patients. The cost to society of not treating these patients is unacceptable, and we are looking at all options to improve access for appropriate high-risk patients. We also look forward to having the Repatha labels updated for the outcomes data outside the U.S. soon.

So, 2018 will be an important year as we continue our transition of our portfolio and lay the groundwork for sustainable, volume-driven, long-term growth. In closing, I'd like to thank our team for the impressive and competitive execution in 2017. I look forward to facing with them the challenges and more importantly the opportunities in 2018 of bringing our innovative medicines to previously ill patients around the world.

Let me now pass it to Sean. Sean?

Sean E. Harper {BIO 16272195 <GO>}

Thanks, Tony. Good afternoon. I'll begin with cardiovascular. With the recent inclusion of our cardiovascular outcomes data in the U.S. label, Repatha is the first and only PCSK9 inhibitor approved to prevent heart attack, stroke and coronary revascularization in adults with established cardiovascular disease. We now have numerous professional guidelines and treatment pathways along with the FDA, all recognizing the ability of Repatha to reduce life-changing events of stroke and heart attack, and we expect payers to take an increasingly more thoughtful approach to patient access.

In inflammation, we've begun dosing tezepelumab in our 52-week Phase 3 study in over 1,000 patients with severe uncontrolled asthma in our collaboration with AstraZeneca. I would note that the primary endpoint in our Phase 3 program is the same as the one we reported for the Phase 2b study where we demonstrated efficacy across a broad spectrum of patient types. We've also reacquired our IL-15 antagonist antibody, AMG 714, after our Celimmune collaboration generated intriguing Phase 2a data in severe celiac disease. We'll be discussing the data and a potential path forward with regulators as there are not clearly established endpoints for registration in this area.

In neuroscience, we and Novartis are looking forward to the FDA PDUFA date for Aimovig in May. I'm often asked about our approach with the CGR receptor antibody versus the ligand and how it differentiates. We targeted the receptor because we wanted the most potent antibody we could develop to reduce the amount of antibody required for maximal clinical effect, and our expertise in antibody discovery and development allowed us to succeed at this. With Aimovig, we can elicit maximal CGRP inhibition with a relatively low dose. We've submitted 70-milligram and 140-milligram per month to regulators

compared with higher doses for the ligand sequestrants. This translates into monthly subcutaneous self-administration with a pen-type autoinjector that uniquely does not require loading doses, which we believe will be much more attractive to patients and providers.

Also, as we've seen in other diseases, having mechanistic choices is an attractive option for physicians and patients. And Aimovig is the first and only CGRP receptor antibody ever introduced to the clinic. We have also executed a differentiated development program with Aimovig, with a dedicated cardiovascular treadmill study in patients with stable angina, and most recently demonstrated efficacy in a large study of patients with multiple prophylactic treatment failures who are not only considered difficult to treat but also have virtually no other treatment options.

Turning to oncology and KYPROLIS, the U.S. prescribing information was recently updated with the overall survival data from ENDEAVOR, which also received a positive opinion in Europe. The ASPIRE overall survival data have also been submitted in both regions. Having survival data from two studies establishes KYPROLIS as the new standard of care for relapsed multiple myeloma. XGEVA was recently approved for the prevention of skeletal-related events in multiple myeloma for patients in the U.S. As Tony mentioned, this is an important advance as myeloma patients often develop renal insufficiency, which hinders treatment with bisphosphonates, putting them at increased risk for bone complications. XGEVA is not cleared through the kidneys and provides an important new treatment option.

We also received the results of the Phase 3 D-CARE study with XGEVA. D-CARE was initiated in 2010 with the hypothesis that treatment with denosumab could potentially delay cancer recurrence in bone or other tissues in patients with early-stage breast cancer. D-CARE explored an investigational dosing schedule of denosumab as adjuvant treatment for women in high-risk, early breast cancer stages receiving standard of care, neoadjuvant or adjuvant cancer therapy. Unfortunately, the trial was neutral and did not meet its primary endpoint of bone metastasis-free survival. Adverse events observed in patients treated with XGEVA were similar to the known safety profile. Detailed results will be submitted to a future medical conference and/or publication. I'd like to stress this result has no bearing on the approved and well-established indication for the prevention of skeletal-related events in breast cancer patients with bone metastases.

Finally, in other European regulatory news, Nplate received a positive opinion in Europe, recommending approval for the treatment of chronic ITP for patients one year of age or older who are refractory to other treatments. And BLINCYTO received a CHMP positive opinion to include overall survival data from the Phase 3 TOWER trial supporting conversion from conditional to full market authorization in the current indication.

We had the opportunity to provide a detailed update on our oncology franchise and our excitement around our differentiated approach to immuno-oncology at the American Society of Hematology Meeting in December. There we announced that we developed a half-life extended BiTE format and had moved three of these into the clinic with several others in preclinical development. We now have seven BiTE programs in the clinic and expect data generated in the next 18 to 24 months in both hematologic and solid tumors

to provide key insights on the clinical utility of this platform. We're in the unique position to evaluate both BiTE and CAR T programs, in some cases directed against the same antigen, and in fact we have an IND in place for our first CAR T from the Gilead-Kite collaboration. We'll begin dosing patients a bit later this year.

We also highlighted our commitment to multiple myeloma, specifically with our Mcl-1 inhibitor, two BCMA-targeted BiTEs, and a BCMA antibody drug conjugate all moving through Phase 1, and our bispecific T cell engaging antibody directed against CD38 licensed from Xencor, which we'll begin dosing this year as well.

In our bone franchise, UCB recently submitted EVENITY in Europe for the treatment of osteoporosis in postmenopausal women and in men at increased risk of fracture. We continue to systematically reevaluate all registrational clinical trial data to ensure we have the most comprehensive understanding of the cardiovascular safety signal observed in the active-comparator ARCH study, and we will work in close collaboration with the FDA toward our resubmission under the Complete Response Letter timelines in the U.S. later this year.

Lastly, we continue to make good progress on our biosimilars with the European approval of our biosimilar Avastin. We also expect Phase 3 rheumatoid arthritis data from ABP 710, our biosimilar REMICADE, later in the year.

In closing, I'd like to thank all of my colleagues at Amgen for another year of successfully advancing programs for the benefit of patients.

Bob?

Robert A. Bradway {BIO 1850760 <GO>}

Okay. Thanks. Skinner, let's go straight to the questions, and could you please remind our callers of the procedure for asking questions and just give them the heads up that we'll go longer than usual because, as I advertised at the beginning of my remarks, we were going to be a little bit longer in our prepared portion? So we'll stay and take the questions from the analysts, Skinner. Let's jump to it.

Q&A

Operator

Absolutely. And our first question comes from Robyn Karnauskas from Citigroup.

Q - Robyn Karnauskas {BIO 15238701 <GO>}

(54:14) my questions. So can you really be clear about what percentage of your guidance was influenced by biosimilars? What was the real impact? And for Sean, when you think about your pipeline, which is really broad and (54:28) the options that are available. When

you think about the probability adjusted value placed in that pipeline, can you help us understand how to value that pipeline to offset the biosimilar impact? Thanks.

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

Okay, Robyn, we're having a little bit difficulty hearing you, but I think your first question was – it sounded like it was one that we should ask David to address. You were asking how much of the wide range in revenue guidance was attributable to biosimilars. I think David tried to make it clear that a lot of it was related to Sensipar, but go ahead, David, and address this.

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

Yes, right. So, if you look at the guidance that we offered, it's obviously much larger than we would typically have, about double what we would have at the beginning of the year. And certainly a large portion of that is attributable to the uncertainty around the launch, the competitive launches that may occur this year from Sensipar. So that's the primary driver of broader guidance than we typically would offer.

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

And again, Robyn, it wasn't clear what you're trying to get at with your question about the pipeline. But, Sean, go ahead.

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

Yeah. I mean, I think it had to do with the value of the pipeline versus obviously the pressures we're facing on some of our legacy products as they go through the portfolio transition. I would just say that you're right, Robyn, we do have a very broad and deep capability these days. It's best it's ever been at Amgen, in my opinion. And I think that what you can observe is that across the key therapeutic areas that we're focusing in, we have a lot of really exciting opportunities. And I think that we can expect to see the same sort of productivity with respect to advancing the pipeline over the next five years that we've observed over the last five years.

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

Okay, Skinner, let's go to the next question.

Operator

Our next question comes from Chris Raymond from Piper Jaffray.

Q - Christopher J. Raymond {BIO 4690861 <GO>}

Thanks for taking the question. So I have a question that I think is mostly related to Enbrel. There's been some dust kicked up recently with regard to payers and PBMs instituting these so-called copay accumulators, which don't allow copay assistance and other patient assistance to count against deductibles and out-of-pocket maximums. From what I've read, you guys have seemed to have taken a really strong stance against this with some

specific countermeasures, and you're working to ensure that patient support actually benefits the patient. But I'm just hoping if you could maybe put some brackets around the ranges of uptake that this phenomenon could have this year and what other specific countermeasures you could take if your current measures don't work. Thanks.

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

It's Tony. So let me respond to that one. You are correct that Amgen has made it pretty clear that we disagree with the concept of the accumulator, that fundamentally our assistance is there to assist patients who can't afford their copays, that the agreements and contracts we have with these organizations is around making sure patients get access. So we've put that in writing and made it clear to people. As I look at quarter one, I see a minimal impact to our Enbrel business because of these programs.

Operator

And our next question comes from Geoffrey Porges from Leerink Partners.

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

Thank you very much for the question and for all the color in the presentation. Perhaps, David, could you comment a little bit on your balance sheet? You sort of alluded to the fact that there may be some moving parts on your balance sheet and obviously you're bringing a lot of cash back. You're effectively unlevered despite the fact that you have significant debt, given your cash position. As you look at opportunities across the industry, Bob has been sort of quite outspoken about the need for consolidation. I'm just wondering, what kind of leverage would you be comfortable with, given the visibility you have for the future cash flow? Would you be willing to sort of go up on a net basis to several times your EBITDA?

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

Yeah, Geoff. So I guess the way I would think about the balance sheet going forward is I would look at how we've managed the balance sheet over these last several years, and we did that to optimize and get the lowest weighted average cost of , and we did that without consideration of the offshore cash balances. So we set our leverage and it's varied over the last several years at a peak after Onyx, and then it's come down since that time. And I think it would be fair to assume that on a steady-state basis, we would think about those kinds of balance sheet leverage ratios to be similar to what we've had in the past.

Now, what I would say is that in the very near term, given the fact that we have such a large amount of capital that we'll be deploying, it's quite possible, as I mentioned in my comments, that we would pay some debt in the interim, but that wouldn't be mistaken to be where we think the ideal capital structure would be. So I would refer, again without reference to the cash we've been carrying, but just look at our leverage over these last several years, I think it's a good sort of guidepost for how we'll manage the business going forward.

Operator

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

Q - Ying Huang {BIO 16664520 <GO>}

Hi. Thanks for taking my questions. Just a question for David, can you comment whether the guided 14% to 15% tax rate for 2018 is actually also the way we should think about a long-term tax rate? And then in 4Q 2017, your OpEx went a bit higher than usual. Do you expect the margin – the pre-tax operating margin to go back to the level you saw in the first three quarters in 2017 for the 2018 period? Thank you.

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

Sure. Sure. Yeah. So in terms of the tax rate post-2018, what I would say is that if you look at our guide for this year, on a non-GAAP basis at 14% to 15%, our preliminary analysis would suggest to us that that would be a reasonable outlook for the period post-2018. And I use some words, preliminary and that sort of thing, because it's still evolving, but I think as a starting point, I think it's reasonable to think about that as a steady-state-type level of tax rate going forward.

And then in terms of – you're correct, as I tried to articulate. If you look at our operating expense performance in Q4, basically, we typically have, as you know, we typically have – the highest level of expense is in Q4 on annual basis. And to the extent we had expenses beyond that this past year, in Q4 of 2017, those were basically and entirely onetime-type expenses that we wouldn't expect to be recurring, and that was related, as I said, to the hurricane costs, which were extraordinary and onetime, as well as based on the fact that we had last year a 35% tax rate versus taxes this year, 21% in the U.S. We look at choices we might make around the timing of such discretionary expenses and time them into the period where we got a benefit from a tax perspective.

So with all of that, you go to 2018, as I said, our guidance would suggest to you and to us that we expect to operate in the 52% to 54% range again this year, and I think you can expect the quarter-by-quarter patterns of margins and expenses to be quite consistent with what you've seen if you look at an average over the last several years.

Operator

Our next question comes from Matthew Harrison from Morgan Stanley.

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

Great. Thanks for taking the question. David, I was hoping you could just help us break out some items for 2018 guidance, particularly since you've got a couple moving pieces in terms of the bottom line here. If you could help us think about the impact that the tax rate had, the impact of the buyback versus the underlying performance of the business. Thanks.

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

Yeah. So, I guess what I would say is that if you – well, first of all, I think the tax calculation is pretty straightforward in terms of take the 14% to 15% range and apply it to what would be pre-tax profit. I think I gave you a range in terms of both operating margin and what we expect the below the line interest expense and income to be, so I think that hopefully will get you to a pre-tax income that you can apply the tax rate against.

And then in terms of the repurchase activity, we now have authorization in total of a little more than $14 billion for repurchases. And as I said, we could see that deployed as soon as the completion in the first half. Our guidance, of course, takes into consideration that there's some range of timing possibilities that our guidance covers in terms the repurchase effects. So, again, I think you can apply some math to get to the share count and how that would impact our EPS, yeah. Then it's included in the guidance.

Operator

Our next question comes from Terence Flynn from Goldman Sachs.

Q - Terence Flynn {BIO 15030404 <GO>}

Hi. Thanks for taking the question. Maybe just a follow-up to Geoff's earlier question. Bob, during your prepared remarks, you mentioned you're well-positioned to capitalize on consolidation opportunities for your shareholders. Just wondering if you'd consider larger-scale mergers, or is that primarily bolt-on similar to your prior history as Onyx is a recent example. Thanks

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

Well, I said two things, Terence. I said we were well-positioned to address ongoing changes in the healthcare environment and we expect there will continue to be ongoing pressure from the healthcare environment, and that we were also well-positioned to capitalize on consolidation for the benefit of our shareholders. So we've been consistent for some time in saying that we have the financial capacity and we're interested in looking for deals that we think we can add value to in our areas of focus. So we're going to continue to do that.

And as the other question implied, we have felt for some time that there are pockets of excess capacity in the industry, and we'll look to see whether we can help to create some value by being part of the consolidation around those.

Operator

Our next question comes from Michael Yee from Jefferies.

Q - Michael J. Yee {BIO 15077976 <GO>}

Thanks. Good afternoon. Thanks for the question. When I think about your 2018 guidance, I'm sure that people are trying to dig through details of that, but I'm certainly trying to think that there's more uncertainties about beyond 2018. Back in 2014, you gave a long-term strategic outlook and you delivered on that, but I think people are kind of worried

about beyond 2018. What are the factors that you need to get through, Bob or Dave, to think about longer-term guidance? Or maybe there is no need for longer-term guidance. What are you thinking about? Thanks.

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

I think we'll both take a shot at your question, Mike. I think you're right, we felt there was a big disconnect in 2014, and we were confident about the long-term outlook, and we seem to be at a different place from our shareholders. So we found it helpful to try and address that disconnect with longer-term guidance. And we're, as we said – I think each of us said we're confident about the long-term outlook for our business now, and excited about what we see as long-term growth potential of the company, but we continue to talk to our shareholders and take their counsel about the benefit of thinking about the guidance question.

Operator

Our next question comes from Ronny Gal from Bernstein.

Q - Aaron (Ronny) Gal {BIO 15022045 <GO>}

Good evening, and thank you for taking my questions. Just a quick clarification for Tony and then a question for Sean. Tony, you mentioned that you are not seeing impact from the copay accelerator. My understanding was that you do not expect to see one until late in the second quarter when patients begin to hit the maximum out-of-pocket costs. Do I have this wrong or is this something that we should see early in the year?

And then for Sean, on the BCMA program, obviously you guys are putting some resources against it. How good does those bispecifics have to be for you take them forward in comparison to what we are always seeing from the CAR T programs? 50% or 70%? Or maybe just give us the parameters that you're looking for to see if the products are good enough.

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

So, Ronny, to answer your first part of your question – this is Tony – the accumulator programs will, of course, depend on what the individual patient's deductible is. But as I said, we are seeing and projecting minimal impact in first quarter, and by definition, I would therefore see minimal impact in the second as well for Amgen.

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

Yeah. With respect to the BCMA BiTE programs, I think that our view is that it's going to be important for us to be able to demonstrate data, and these comparisons can be very complex. The patient populations and the pretreatment of patients and things of this sort in the CAR T studies is often very different than the calculations that we generate in our data set, so comparisons can be hard. But bottom line is everyone that we talked to in this field believes that if you can take a product like a BiTE off the shelf, administer it, and get a similar degree of efficacy with potentially less of the safety risk and the enormous cost that can be associated with those safety risks in the hospital, that BiTE would be a

preferred modality. As I've said many times, I think there's a role for both of these modalities in the spectrum of care for even an individual patient in an oncology setting.

Operator

And our next question comes from Umer Raffat from Evercore ISI.

Q - Umer Raffat {BIO 16743519 <GO>}

Hi. Thanks so much for taking my questions. I wanted to ask three, if I may. One, on core decisions from PCSK9 antibody patents that we saw last year, do you think they have any read across to the upcoming Enbrel district court litigation?

Second, on Sensipar, and it seems like it's a big swing factor in your 2018 guidance, my question is this, there was an IPR on one of your 2026 patents which was never instituted, so in that context, the question I have how is a generic entry possible, or said another way, are you aware of a non-infringing formulation?

And then finally, just a quick one, how much CGRP in your 2018 guidance? Thank you.

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

I'm sorry, what was the third question? We're trying to track you there.

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

CGRP in the 2018 guidance.

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

How much CGRP in the 2018 guidance.

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

Okay. All right. Okay, Umer, obviously we have ongoing litigation. I don't think it's appropriate to comment on your Sensipar question. And I wouldn't try to read across – I wouldn't try to do the meta-analysis in intellectual property land across the two trials that you referenced. David, do you want to – we're obviously not going to give individual product guidance, Umer, at this point. You know we're excited about the product, we're excited about being first. It's a symptomatic population, and the interest in having a new therapy that makes a big difference is high. But we're not going to give you individual product launch guidance at this point.

Okay, Skinner.

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

Skinner, let's take the next question, and maybe you can just remind our audience to limit themselves to one question since we're running over – way over today.

Operator

Yes. Please limit yourselves to one question, ladies and gentlemen. And our next question does come from Geoffrey Meacham from Barclays.

Q - Geoff Meacham {BIO 21252662 <GO>}

Afternoon, guys. Thanks for the question. Bob, when you think about deals, how much of a priority is a return to top line growth versus just managing cash flow? And then very related, have you guys ever explored a split or some sort of segmentation of the business just to separate the mature franchises from the early cycle products and pipeline? Thanks.

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

Okay, Geoff, our focus when we look at deals is on – we're looking to deploy capital that we think we can earn a return for our shareholders from. So it's very easy to find accretive deals. It's very hard to find deals that are both accretive and add to the long-term return on capital for our shareholders. So we're going to continue to be disciplined. We know the six areas that we're interested in. And with respect to your second question, again, I think you know our track record in this regard. We've been very active and very focused on looking at all ways to create value for our shareholders, and we'll continue to do that.

Operator

And our next question comes from Eric Schmidt from Cowen and Company.

Q - Eric Schmidt {BIO 1505721 <GO>}

Hey, just a question for Tony on Repatha. If I'm doing the math right on slide 23, with the volume and sales gains that you had, it looks like there was a net 15% quarter-on-quarter decline in Repatha's price. Is that true? And maybe you could provide some color what's going on there. Thank you.

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

Eric, I actually couldn't give you the details for that one right now. There was clearly a change in the net price, but I don't think it was that high. We can come back to you guys and give you the details on that, but I don't have them with me.

Operator

Our next question comes from Alethia Young from Credit Suisse.

Q - Alethia Young {BIO 17451976 <GO>}

Great. Thanks for taking my question, one for Sean. What other additional Phase 2 programs would you consider tezepelumab? Maybe anything in allergies or anything like that. Thanks.

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

Yeah. Right now I think the things we're kind of excited about in Phase 2 are AMG 301 in migraine, which is we're in a strong leading position with that mechanism and hope to see that it will be either synergistic with CGRP or address patients that don't respond to CGRP inhibition. And we have also the IL-2 mutein program, AMG 592, I'd highlight, as a program that is moving into multiple Phase 2 autoimmune disorders. And that's a mechanism, as you may know, where we're able to affect the population of Treg cells in a profound way with this engineered form of IL-2.

A number of our BiTE programs are – while they are in Phase 1, the next study for them could, in fact, like it was for BLINCYTO, be registration-enabling. So this Phase 1, 2, 3 line gets pretty blurred in the oncology area particularly. So I consider a lot of the molecules that are in the clinic, including our Mcl-1 inhibitor, to be potentially in a preregistration study as the next study type of status.

Operator

And our next question comes from Cory Kasimov from JPMorgan.

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

Hey. Good afternoon, guys. Thanks for taking the question. Mine's on Repatha, and I recognize it's really recent, but I'm interested in a little more color. On the early feedback you're getting from the field on the drug post the inclusion of CVOT in the label, and really more importantly, how much of a difference would you expect the label to make, given that you guys make it sound like it's still a payer access issue, and payers have been aware of this data for a longer period of time. Thanks.

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

So, Tony here. Let me respond to that one, right. So as I've said a couple of times, since launch we've been able to talk to physicians about the product being able to lower LDL. From a promotional perspective, which is probably 98% of our physicians who don't attend the large congresses, we have not been able to be in a position to talk about the real benefit of Repatha dramatically lowering LDL and thereby reducing the risk of heart attack and stroke.

Just to give you an idea of how fast this has moved, we got the approval on the Friday at about 11:35 AM. By Tuesday we had trained our entire team of managers on actual promotional material. By the Thursday, we trained the entire sales force. By Saturday, we trained 250 cardiologists, speakers, and by the next week, they had completed just over 200 speaker programs with an average of about 15 people attending each speaker program. I've never seen such rapid uptake of a speaker program from an – these are promotional speaker programs, where the cardiologists are talking specifically from the new label.

The feedback from the sales force to-date has been very positive. People are now truly understanding the value of what the drug does. And when I look at the last two weeks'

average NBRxs, they're about 18%, 20% higher than the average of the four weeks for December. So it's tough to read this early on, but we are seeing an uptick in new patients getting through getting approved. When I look at our payer or access environment, I see the commercial plans since January of 2017 have improved by about 8% in terms of the approvals. Our Part D coverage has improved by about 30%.

So we continue to work hard to make sure people understand the value of this drug, and I think more and more cardiologists and physicians are putting forward appropriate patients and fighting for them to get on the drug.

Operator

And our next question comes from Salim Syed from Mizuho Securities.

Q - Salim Syed {BIO 16887281 <GO>}

Yeah. Hi. Thanks, guys, for taking my question. I just had one on Repatha. So, Eugene Braunwald spoke recently at The Medicines Company Investor Day and spoke specifically regarding primary prevention with inclisiran. I was curious what your thoughts were on that and if there's any impact to Repatha as it relates to that. And specifically, also, do you think inclisiran can be inserted between a statin and Repatha? Thank you.

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

Yeah. This is Sean. I'll try to respond. I think obviously the kinds of populations that can be addressed with these agents are identical to the kind of populations that have been treated with statins over the years. We focused on a very high-risk secondary prevention-type population although our label in both the U.S. and Europe is broader than that. And I think that it's perfectly reasonable to study high-risk primary prevention patients. However, when you look at the situation we face right now where it's so difficult to get these drugs to patients who have experienced multiple events and have very high levels of LDL, I'm not sure that's the direction strategically that I would go if I were going to do another outcomes trial, but it's a reasonable thing to do. In terms of sequencing these therapies, that all depends on the effect size that can be achieved, the safety profile of a novel mechanism, a platform technology like siRNA in a very broad population. The bar is extremely high, obviously, from an efficacy safety perspective with Repatha.

Operator

And our next question comes from Ian Somaiya from BMO Capital Markets.

Q - M. Ian Somaiya

Thank you for taking my question. I had another one on Repatha. You'd previously commented on maybe a willingness to speak with the payers or negotiate with payers on rebates and pricing when CVOT was on the label. I guess we've gotten to that point. And then separately, once the guidelines reflected the recommendations, I'm just curious, where are we from a price rebate negotiation standpoint and how much room is there for us to see changes in the sort of the pricing structure of the PCSK9s going forward.

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

So it's Tony. So as we talked last year, we are in constant debate and discussion with payers and providers around the value of this drug, about the value-based pricing we have, and the rebates that have been offered in the marketplace to ensure improved levels of access. So we continue to work with the payers on an ongoing basis to ensure we get a good position on formulary, that we have improved on the utilization management criteria where fundamentally just about every plan has improved on that one quite dramatically. We have worked hard to ensure that we can assist patients where appropriate with copays that they are not able to afford or deductibles they are unable to afford, and I don't think that work's going to stop for a while as we go forward.

Operator

And our next question comes from Andrew Peters from Deutsche Bank Equity Research.

Q - Andrew Peters {BIO 20622504 <GO>}

Hi. Thanks for taking my questions. So I guess maybe to switch gears a bit on a slightly different topic, on the next-gen manufacturing side, just wanted to see how and if this new technology could potentially impact margins. And then more broadly as you talk about kind of the made by Amgen stamp for the biosimilar franchise, as you think about biosimilar production in general, how do you think Amgen is differentiated? And from a margin perspective, as you think about biosimilars, is that something that can fit into your pricing strategy on a competitive basis as well? Thank you.

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

I'll take this in two parts. David and I can respond to your question, Andrew. Yeah, first with respect to next-generation manufacturing, we've been talking about this, as you know, for some time. We're delighted and excited that global regulators have approved our first of these facilities in Singapore. And when we committed to that, first began talking about it some years ago, we were clear that both as a consequence of the lower capital costs and the meaningfully lower operating costs, we would expect over time a benefit to be reflected in our cost of sales line, and that'll happen. And generally, we have said and we still believe that manufacturing is the source of competitive advantage at Amgen. We have a track record of supplying every patient, every time, and we think when it comes in particular to biosimilars, the reliability, the safe supply, and reliable supply of biosimilar medicines from Amgen will be a differentiator.

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

Yeah, I guess I would add, when we set out on the journey to get to our current margin structure, we talked about a number of things that were contributing to us achieving that. And certainly as Bob just talked about the first module of this next-gen manufacturing is now going to be helping us and this next module will continue to enable us to drive our competitiveness. I would caution against thinking that you should think there's a big step-up from where we're operating right now because I think we're operating in a very nice place in terms of our own competitiveness. And so think about driving continued costs down to enable us to then continue and increase our investments in particular in support

of these new products that are going after very large patient population. So we're thinking about continuously driving our cost base to allow us to invest heavily in support of growth for the business.

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

Yeah, Skinner, as it's nearing 6:30 on the East Coast, let's take two more questions, please.

Operator

Absolutely. Our next question comes from Carter Gould from UBS Equities.

Q - Carter Gould {BIO 20035589 <GO>}

Good evening, guys. Thanks for the question and squeezing me in. For Sean, follow-up on the earlier tezepelumab question given all the excitement. Recently we've seen agents' focus on inflammation go relatively broad in terms of indications, yet you're proceeding relatively narrowly despite a central role in inflammation. Is that more because of the rest of your portfolio of assets, risk mitigation approach, or should we expect the list of indications to expand?

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

Yeah, it's a good question. I mean, what I would say is that we believe that there is a particularly profound level of unmet need in asthma. And for a agent, that could be given to sort of all-comers without having to parse patients by fairly complex criteria that are difficult to assess in the average clinician's office. So I personally believe that that is an area of particular opportunity for a biologic therapy like tezepelumab. I think that COPD represents another very substantial opportunity, and because of the nature of this mechanism, one could believe that it might be more likely to have efficacy in a setting like that than some of the other therapies that are directed more at the inflammatory cascades that downstream in asthma.

And there are other disease areas like atopic dermatitis that we continue to explore. And I'm sure as with all of these products in the inflammation space, once a product has a kind of an anchor core profitable indication, virtually every good idea and a variety of not so good ideas get explored by either companies or investigator-sponsored studies trying to find every possible nook and cranny where the product might work.

Operator

And our last question for the call comes from Kennen McKay from RBC Capital Markets.

A - Kennen MacKay {BIO 18821382 <GO>}

Hi. Thanks for taking the question. One for Bob and David here. David, you'd mentioned there was now on the balance sheet strength to really sort of grow the business and really deploy some of that capital. And, Bob, sort of building up what you'd mentioned

surrounding your focus on transformative therapies like Aimovig, like Prolia, like Repatha, I just wanted to get a perspective on what was out there that you really sort of viewed as interesting? We've seen a lot of consolidation in the CAR T space, you have some exposure there, owning a couple of the Kite – now Gilead – programs. Is there anything like in gene therapy or gene editing, or does that really not align with the positioning of sales and volumes converging in the years ahead?

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

Yeah, I guess – this is Meline. And what I would comment on in terms of the opportunities out there, we've been, I think, pretty clear that we're focused, in particular, on the six areas where we've decided to establish a commercial presence, and so we tend to orient ourselves towards those opportunities. And we're quite clear in the market that we want to see everything of any size that might be of interest to us across those areas. In that, Kennen, maybe Sean doesn't want to comment on technologies, but certainly...

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

Yeah, no, I would just – since you mentioned some of these emerging technology platforms like gene editing for therapeutic purposes or gene therapy, that the earlier these kind of things are, the more likely it is that we will look at them even if they aren't in one of these six areas because if we found there's a breakthrough opportunity emerging and we could bring to bear our scientific and manufacturing, commercial capabilities, and so on, we've shown that we'll move on those kind of things.

A - Kennen MacKay {BIO 18821382 <GO>}

Yeah. Okay.

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

All right. Well, I think, Kennen, Sean and David did a good job answering that question. So rather than add to it, let me just again thank you all for your forbearance in a call that went a little longer than usual from us. But just to wrap up, we're heading into 2018. As I think you can tell from our remarks, we're excited. We think we're operating the business well. We have strong products. We have an attractive pipeline that's advancing rapidly, and strategically we think we're well-positioned and focused on delivering growth and value for our shareholders. So we look forward to reconvening with all of you in April and see how we do through the first quarter. Thank you.

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

And I would just like to add my gratitude for your patience. Had a lot of topics to cover today. Of course, between myself and my team, we'll be standing by for several hours, so if you have any other questions, feel free to call us. Thanks again.

Operator

This does conclude today's call. You may now disconnect. Thank you for your participation.