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PFE - Q4 2018 Pfizer Inc Earnings Call

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OVERVIEW:

Co. reported 4Q18 revenues of approx. $14b and reported loss per share of $0.07. Expects 2019 revenues to be $52-54b and diluted EPS to be $2.82-2.92.

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PRESENTATION

Operator

Good day, everyone, and welcome to Pfizer's Fourth Quarter 2018 Earnings Conference Call. Today's call is being recorded.

At this time, I would like to turn the call over to Mr. Chuck Triano, Senior Vice President of Investor Relations. Please go ahead, sir.

Charles E. Triano *- Pfizer Inc. - SVP of IR*

Good morning, and thank you for joining us today to review Pfizer's fourth quarter and full year 2018 performance and 2019 financial guidance and business outlook. I'm joined today by our CEO, Albert Bourla; Frank D'Amelio, our CFO; Mikael Dolsten, President of Worldwide Research and Development; Angela Hwang, Group President, Pfizer Biopharmaceuticals Group; John Young, our Chief Business Officer; and Doug Lankler, General Counsel.

Slides that will be presented on this call can be viewed on our website, pfizer.com/investors. You'll see here that Slide 3 covers our legal disclosures.

Albert and Frank will now make prepared remarks, and then we will move to a question-and-answer session. With that, I'll now turn the call over to Albert Bourla. Albert?

Albert Bourla - *Pfizer Inc. - CEO*

Thank you, Chuck, and good morning, everyone. During my remarks, I will speak about our performance for the year, the continued advancement of our pipeline and the strategy we have put in place to return Pfizer to a period of sustained growth, following the impact of the Lyrica LOE that will negatively impact our growth in both 2019 and 2020. Frank will then provide the details regarding the fourth quarter and our 2019 financial guidance.

Pfizer had another solid year in 2018. Revenues for the year were up 2% operationally. We saw continued growth in several of our biggest-selling medicines and vaccines in emerging markets and in biosimilars. These increases were partially offset by the $1.7 billion in LOE impacts as well as decreases in the Legacy Established Products portfolio in developed markets and in our sterile injectables portfolio, primarily due to continued legacy Hospira product shortages in the U.S.

I will begin with a few words regarding the performance of each of our businesses, starting with Pfizer Innovative Health. This business had another strong year, growing its top line 6% operationally, thanks to the continued strength of several key brands, including Ibrance, Eliquis and Xeljanz globally and Prevenar 13, primarily in emerging markets. I would also remind you that Viagra transferred from PIH to PEH at the beginning of 2018. So if you exclude Viagra from the calculation, the growth would have been 9% operationally. For full year 2018, Ibrance revenues were $4.1 billion, which represented an increase of 32% operationally. While approximately 50% of eligible U.S. patients are getting a CDK inhibitor, in combination with endocrine therapy, many are still receiving endocrine monotherapy or chemotherapy. We continue to educate the oncology community about the benefits of Ibrance therapy. We remain confident in Ibrance leadership in the class based on the strength of our data, significant first-mover advantage, and most importantly, the continued positive patient experience with more than 200,000 patients prescribed the medicine worldwide since its launch. Our current growth driver for Ibrance remains outside of the U.S., particularly in developed Europe and Japan, and we had another quarter of solid growth here. Ibrance has achieved reimbursement in the majority of international developed markets and despite increasing competition has maintained greater than 90% of total CDK class volume in these key markets. For Xtandi, alliance revenues in the U.S. were up 18% for the full year and when combined with our royalty income on ex-U.S. sales totaled nearly $1 billion in 2018. We are continuing to see an increased number of urologists prescribing Xtandi, and our launch of the expanded indication in non-metastatic prostate cancer in the U.S., following the July approval, made the first and only FDA-approved oral medication for both non-metastatic and metastatic castration-resistant prostate cancer. We continued to see growth in Xtandi throughout this year, and we remain focused on demonstrating the value of moving Xtandi into earlier treatment settings. In December, along with our alliance partner, Astellas, we announced that the Phase 3 ARCHES trial evaluating Xtandi plus ADT in men with metastatic hormone-sensitive prostate cancer met its primary endpoint, significantly improving radiographic progression-free survival versus ADT alone. These data further differentiate Xtandi from the competition, both branded and generic. We are engaging global health authorities in discussions regarding the potential of an expanded indication for Xtandi, and we remain confident that Xtandi will be one of the pillars of our Oncology portfolio for years to come. But this year, Xeljanz had a tremendous performance with revenues increasing 33% operationally to $1.8 billion. Our fourth quarter results continued a pattern of extremely strong performance for Xeljanz with scripts up 35% compared with the prior year quarter. This was driven by continued growth in rheumatoid arthritis prescriptions as well as increased contributions from the drug's recent expansion into psoriatic arthritis and ulcerative colitis. We look forward to these new indications becoming even more meaningful contributors in 2019, particularly in ulcerative colitis. Eliquis had another strong year with alliance revenue and direct sales growing 35% operationally to $3.4 billion. Lastly, our Consumer Healthcare business grew 3% operationally for the year with revenues totaling $3.6 billion. In December, we entered into a definitive agreement with GSK, under which we have agreed to create a new Consumer Healthcare joint venture. We expect the transaction to close in the second half of 2019, subject, of course, to customary closing conditions, including GSK shareholder approval and required regulatory approvals.

Turning now to Pfizer Essential Health. While revenues for the year declined, we, once again, saw strong operational growth, both in emerging markets and in our biosimilars portfolio. Emerging markets revenue for the business grew 11% operationally for the year to $7.8 billion. Some of the biggest growth drivers in emerging markets were Lipitor, up 19% operationally; Norvasc, up also 19% operationally; and Sterile Injectables, up 13% operationally. Our biosimilars business grew 41% operationally in 2018 to approximately $769 million.

We received FDA approvals for 2 biosimilars in 2018, and we see the potential for up to 4 additional approvals in 2019.

PEH growth in emerging markets and biosimilars was more than offset by lower revenues for our Legacy Established Products portfolio in developed markets and product supply shortages in the Sterile Injectable business. In the U.S. Sterile Injectable business, manufacturing supply constraints

continued to impact our top line. We expect these issues to be significantly improved by the end of 2019 and continue to expect this business to be a solid growth contributor in the future.

As you are aware, as of the start of our 2019 fiscal year, Pfizer is now organized into 3 businesses: Pfizer Biopharmaceuticals Group, a science-based innovative medicines business led by Angela Hwang; Upjohn, an off-patent branded and generic medicines business headquartered in China and led by Michael Goettler that is bringing 20 of our most iconic brands to more than 100 markets around the world; and our Consumer Health Care business led by Chris Slager, which is preparing to become part of a joint venture I mentioned earlier.

Now let me turn my attention to our R&D pipeline. This year, we saw a wave of new approvals from our pipeline, including 4 targeted cancer agents over the last 4 months of 2018. In total, we received 7 key approvals in 2018, spanning both new molecular entities and line extensions which will allow us to serve a broader patient population.

In terms of the recent news, let me touch on some of the key milestones we have achieved since our third quarter call. In rare disease, FDA accepted our NDA filing for tafamidis for the treatment of ATTR cardiomyopathy with a PDUFA date in July. As a reminder, we estimate less than 1% of ATTR cardiomyopathy patients have been diagnosed. And currently, there are no approved treatments for this disease, making it an incredibly underserved market. In Oncology, we have several promising developments. We received FDA approvals for LORBRENA, a third-generation ALK inhibitor for lung cancer; and for DAURISMO for acute myeloid leukemia. In the oncology biosimilar space, we received a positive CHMP opinion for ZIRABEV, a potential biosimilar to Avastin. We have initiated clinical studies for a second cancer vaccine applicable in major solid tumor types, and we advanced a second CDK inhibitor for Ibrance-resistant cancer into clinical studies. In Vaccines, we've started a Phase 3 trial for our next-generation 20-valent pneumococcal conjugate vaccine for adults 18 and older. In Inflammation & Immunology, our JAK3 inhibitor for moderate to severe alopecia areata started a pivotal Phase 2b/3 trial. In Internal Medicine, Pfizer and our partner, Eli Lilly, announced this morning positive top line results from a Phase 3 study evaluating tanezumab 2.5 milligram or 5 milligram in patients with moderate to severe osteoarthritis pain.

Looking ahead, we see the potential in 2019 for several inflection points that will further advance our pipeline. These include potential U.S. approvals for the combination of BAVENCIO and Inlyta for first-line renal cell carcinoma as well as for up to 4 biosimilars: trastuzumab, bevacizumab, rituximab and adalimumab, which, when taken together, represent a potential blockbuster opportunity for Pfizer.

We also expect Phase 3 readouts for rivipansel in sickle cell disease and for our JAK1 in atopic dermatitis as well as further Phase 3 data readouts for tanezumab, which has the potential to address the serious unmet needs of the more than 27 million Americans living with osteoarthritis and the more than 33 million suffering chronic low back pain. Thanks to these achievements and expected milestones, we believe we are extremely well positioned for what we expect to become an era of sustained top line growth with leverage to the bottom line growth rate, following the impact of the Lyrica LOE. We view this as a significant opportunity because 3 very positive trends are intersecting at the same time: first, macro trends such as an aging population and a rising middle class in emerging markets increasing the number of people seeking access to both innovative and established medicines; second, the continued advancement of what we believe is the best pipeline in our history with good breadth and strong innovation. And finally, after Lyrica, we expect to enjoy the benefits of a dramatic abatement in LOEs until the second half of the next decade.

Our job now is to stay the course, take the steps necessary to pivot to growth. Our strategy for doing so can be summed up in 3 words: innovating for growth. This means we must advance both scientific innovation that significantly improves current standards of care and commercial innovation that addresses patient access and affordability issues. To deliver these innovations, we have taken steps to ensure we have the right organizational structure in place and that our resources are focused in the right areas. To improve operational effectiveness and create capacity for value-creating work, we have reorganized our operations to simplify them. We are initiating an enterprise-wide digital effort to speed up drug development, enhance patient and physician experiences and access and leverage technology and robotics to simplify and automate our processes. And we are significantly reallocating capital across the enterprise by investing more aggressively in profitable growth drivers and reducing resources in areas of lower strategic importance. This includes significant planned reductions in indirect SI&A spending, much of which will be reallocated to R&D. And within R&D, the entire increase in spending will be project related with overhead costs actually anticipated to come down. In addition, of course, to all of this, we have the financial flexibility to continue to undertake additional shareholder-friendly capital allocation initiatives. We see a growing dividend as an important part of our investment thesis. We also have the ability to deploy capital, as appropriate, in other areas, whether that be share repurchases or business development initiatives. Where at the current time, we are focused on smaller tuck-in type acquisitions and licensing opportunities for mid-stage compounds.

Of course, our business isn't without its challenges. Most significantly, we need to ensure that our innovation and risk-taking is rewarded in the marketplace while doing all we can to ensure affordable access for patients.

To this end, we continue to work with governments, policymakers, payers and other players in the healthcare ecosystem to advocate for pro-innovation policies that benefit patients, our company and our industry as a whole. All the steps we are taking are designed to enable us to achieve our purpose of delivering breakthroughs that change patients' lives.

In summary, we see our improved growth profile coming more clearly into focus, and we believe we remain well positioned to deliver new medicines for patients, prepare the company for accelerated growth in the future and create enhanced shareholder value.

I will now turn it over to Frank to provide details on the quarter and our outlook for 2019. Frank?

Frank A. D'Amelio - *Pfizer Inc. - CFO & EVP, Global Supply & Business Operations*

Thanks, Albert. Good day, everyone. As always, the charts I'm reviewing today are included in our webcast.

Now moving on to the financials. Fourth quarter 2018 revenues were approximately $14 billion, which reflects operational growth of $657 million or 5% and the unfavorable impact of foreign exchange, $383 million or 3%.

Our Innovative Health business recorded 10% operational revenue growth in fourth quarter 2018 driven primarily by Ibrance in international markets, Eliquis and Xeljanz globally and Prevenar 13 in the emerging markets, all of which were partially offset by the loss of exclusivity of Viagra in the U.S. in December of 2017 and the resulting shift in reporting of Viagra revenues in the U.S. and Canada to the Essential Health business at the beginning of 2018 and decreased revenues for Enbrel in most developed Europe markets, mainly due to continued biosimilar competition.

Revenues for our Essential Health business in the fourth quarter decreased 3% operationally, primarily due to a 13% operational decline in the Legacy Established Products portfolio in developed markets, driven mainly by industry-wide pricing challenges in the U.S. and generic competition; a 14% operational decline in the Sterile Injectables portfolio in developed markets, primarily due to increased competition across the portfolio and continued legacy Hospira product shortages in the U.S.; and a 10% operational decline in the Peri-LOE Products portfolio in developed markets, mainly as a result of expected declines in Lyrica in developed Europe and Pristiq, all of which were partially offset by the addition of Viagra revenues from the U.S. and Canada that were previously recorded in the IH business; a 10% operational growth in emerging markets, primarily reflecting growth across the LEP and SIP portfolios in China; and operational growth of 31% from biosimilars in developed markets, primarily from Inflectra in certain channels in the U.S.

In the fourth quarter, we recorded a $0.07 loss per share compared with earnings per share of $2.02 in the year ago quarter, which was primarily due to the unfavorable impact of the non-recurrence of a $10.7 billion benefit recorded in fourth quarter 2017 to reflect the December 2017 enactment of the Tax Cut and Jobs Act; higher asset impairment charges, primarily associated with generic sterile injectable products acquired in connection with Pfizer's 2015 acquisition of Hospira and higher restructuring/implementation costs, partially offset by the non-recurrence of net losses on the early retirement of debt recorded in the fourth quarter of 2017 as well as higher revenues in fourth quarter of '18 compared to last year.

Adjusted diluted EPS for the fourth quarter was $0.64 versus $0.62 in the year ago quarter. The increase was primarily due to higher revenues and lower SI&A expenses. I want to point out that diluted weighted average shares outstanding declined by 152 million shares versus the year ago quarter due primarily to our ongoing share repurchase program, reflecting the impact of shares repurchased during 2018, partially offset by dilution related to share-based employee compensation programs.

As I previously mentioned, foreign exchange negatively impacted fourth quarter 2018 revenues by approximately $383 million and positively impacted adjusted cost of sales, adjusted SI&A expenses and adjusted R&D expenses in the aggregate by $408 million. As a result, foreign exchange had a negligible impact on adjusted diluted EPS compared to the year ago quarter. As you can see on this chart, we've met or exceeded all components of our 2018 financial guidance.

Turning now to our 2019 guidance. I'd first like to note that our guidance reflects a full year contribution of revenue and expenses from Consumer Healthcare. Our revenue guidance of $52 billion to $54 billion reflects an anticipated $2.6 billion headwind from products that have recently lost or are expected to lose marketing exclusivity shortly, including the LOE for Lyrica in the U.S. in June 2019 as well as an anticipated $900 million negative impact from unfavorable changes in foreign exchange rates relative to the U.S. dollar compared to actual FX rates from 2018, partially offset by continued strong growth expected from key product franchises, including Ibrance, Eliquis, Xeljanz and Xtandi as well as contributions from newly launched products and indications.

Moving on to other elements of our 2019 financial guidance. Compared with 2018 actual results, the midpoints of these ranges imply higher adjusted cost of sales as a percentage of revenues, resulting primarily from the anticipated LOE of Lyrica in the U.S.; lower adjusted SI&A expenses, reflecting a 3% to 4% increase indirect spend for product marketing promotion being offset by a reduction in indirect spend; and higher adjusted R&D expenses to support our late-stage and emerging early-stage pipelines. In addition, we anticipate significantly lower adjusted other income this year compared to 2018.

As I highlighted on our third quarter earnings call, we expected the core components of other income, net interest income and expense, income from royalties and the ViiV joint venture as well as our pension credit to net to approximately flat or 0. We have since refined our forecast and are now estimating approximately $100 million of income for 2019. This is approximately $1.2 billion less in 2018 adjusted other income, which included $586 million of net gains on equity investments as well as $464 million of income from collaborations, out-licensing arrangements and the sale of compound rights. In 2019 and forward, we will exclude gains or losses on equity investments from adjusted results because of their inherent volatility and because we do not believe they reflect the results of our core business. As we report our quarterly results in 2019, the 2018 adjusted results will be presented, excluding these gains, while income from collaborations, out-licensing arrangements and the sale of compound rights will remain in adjusted results. Our guidance does not assume any potential future milestone income until it is actually recorded.

We expect our effective tax rate on adjusted income to be approximately 16%, which we believe is sustainable for the foreseeable future. We expect 2019 adjusted diluted EPS to be in the range of $2.82 to $2.92. As I just mentioned, this range now excludes gains and losses on equity investments, which favorably impacted 2018 adjusted diluted EPS by $0.08. This range also reflects an anticipated $0.06 negative impact from changes in foreign exchange rates and expected share repurchases of approximately $9 billion in 2019.

Now I want to highlight how our 2019 guidance compares to 2018 revenue and adjusted diluted EPS. The midpoint of our 2019 revenue guidance, excluding the anticipated $900 million negative impact from foreign exchange, implies flat to slightly improved operational performance compared to 2018 despite facing an anticipated $2.6 billion of LOE headwinds this year, which is $900 million more than 2018. On adjusted diluted EPS, the midpoint of our 2019 guidance, excluding the anticipated $0.06 negative impact from foreign exchange, also implies comparable operational performance compared to 2018 after removing the $0.08 gain on equity investments. I want to highlight that despite the significant challenges of the Lyrica LOE this year, we expect our 2019 operational performance for revenues and adjusted diluted EPS, excluding foreign exchange, to be comparable with 2018.

Moving on to key takeaways. We delivered strong Q4 2018 financial results with 5% operational revenue growth and 3% adjusted diluted EPS growth compared with the year ago quarter. Our 2019 financial guidance ranges imply comparable operational performance for revenues and adjusted diluted EPS when excluding the impact of foreign exchange in 2018 net gains on equity investments despite the anticipated loss of market exclusivity in the U.S. for Lyrica on June 30, 2019. We accomplished multiple product and pipeline milestones since our previous quarterly update, and we returned $20.2 billion to shareholders in 2018 through a combination of dividends and share repurchases. Finally, we remain committed to delivering attractive shareholder returns in 2019 and beyond.

Now I'll turn it back to Chuck.

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Thank you, Frank, and thank you, everybody. Operator, can we please poll for questions now?

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Your first question comes from Steve Scala from Cowen.

Stephen Michael Scala - *Cowen and Company, LLC, Research Division - MD and Senior Research Analyst*

Congratulations on a strong 2018 and a solid 2019 outlook. A couple of questions. First, to clarify, has BAVENCIO plus Inlyta been filed in first-line renal cell? And if yes, was this based on the PFS data or was OS met since ESMO? And if only PFS, then how will the regulators view this given that KEYTRUDA plus Inlyta achieved both PFS and OS? So that's the first question. Second question is can you craft an expectation for us for the tafamidis rollout? Will this be more like a traditional cardiovascular rollout which can be sluggish or more like a novel orphan drug filling an unmet need which can be much more rapid?

Albert Bourla - *Pfizer Inc. - CEO*

Thank you, Steve. I think maybe John can answer the BAVENCIO-Inlyta question?

John D. Young - *Pfizer Inc. - Chief Business Officer*

Yes. Thanks for the question, Steve. So we obviously would confirm filing when it's formally -- a filing has formally been received by the FDA. So what I can at this point in time is that we're in the filing phase for that study and that indication.

Albert Bourla - *Pfizer Inc. - CEO*

Yes. Thank you, John. And Angela, maybe you can speak a little bit about the tafamidis rollout plans.

Angela Hwang - *Pfizer Inc. - Group President, Pfizer Biopharmaceuticals Group*

Sure. So we're really excited about the potential launch of tafamidis for ATTR cardiomyopathy. We do see this as a rare disease, but it is a severely underdiagnosed rare disease, particularly because there is no treatment today and diagnosis involves the use of invasive heart biopsies. We know that from autopsy data that there are about probably 100,000 potential patients in the U.S, the prevalence of this disease, but we also know that only about 1% of these patients are diagnosed today in the U.S. So really, from a launch perspective, diagnosis is going to be a key focus of our launch plans. And in this regard, diagnosis and market development is a key area for Pfizer. It's a key area of expertise for Pfizer. Let's just take example the diagnosis of the ALK mutation for Xalkori in non-small cell lung cancer. At the launch of Xalkori, the diagnosis rate here was about 1%, but we know that today, it has reached diagnosis rates of 80% to 90%. So we have a strong record of success in developing new markets across not just the ALK example but many therapeutic areas, but the one thing we've also learned from this is that it does take time. So our launch is going to be focused on a number of factors: first, in creating suspicion for this disease by both cardiologists as well as patients through education around the symptoms of cardiomyopathy. In parallel, we also want to increase the utilization of noninvasive scintigraphy versus heart biopsy as a means of diagnosis. We know that there are about 15,000 scintigraphy machines in the U.S. today, and these machines are already being used routinely to diagnose other cardiac diseases. So we know that this is a routine procedure, and it is already reimbursed. So when we look in totality, what we see for tafamidis is the following: we have excellent data. We have compelling patient benefits. We have deep expertise and commercial footprint in cardiology. We also have a track record of success in creating new markets, and we plan to bring all of this to bear in diagnosing and treating the cardiomyopathy patient.

Albert Bourla - *Pfizer Inc. - CEO*

Thank you, Angela. And needless to say that for both BAVENCIO and Inlyta and tafamidis, we are really very excited about the future based on the strength of the data of both studies.

Operator

Your next question comes from Umer Raffat from Evercore.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

First, just wanted to -- since this has been such a topical thing, your commentary on large M&A, maybe for the broader audience, can you reiterate your thoughts? Would be very curious what your preference are in large versus mid and how you define smaller acquisitions in terms of dollars. Second, just quickly on R&D. On tafamidis, my question, I guess, is there wasn't a free acid -- couldn't you have developed a free acid form for 20 milligram also? And I ask because presumably that could have helped with the European pricing structures given your existing 20-milligram approval there. And finally, Frank, just your thoughts on absolute SG&A and R&D dollar changes in the next 5-year time frame, just mostly trying to understand your thought process on operating margin evolution plus therapy.

Albert Bourla - *Pfizer Inc. - CEO*

Thank you very much, Umer. I will recap my thoughts on M&A, and then Mikael can deal with the R&D question about tafamidis. Look, as we have said consistently and we started saying that from the second quarter last year and the third quarter last year and now we are repeating in the fourth quarter earnings call, business development is not a strategy. It is a way to execute your strategy, and our strategy has been very clear. Our strategy is top line growth through the introduction of breakthrough medicines. And we sounded, as I said in my comments, into innovating for growth. And we believe that right now, we are very well positioned to have seen this strategy because of the combination of one virtual LOE-free period after the Lyrica LOE until '25, the mid of the decade; and also the introduction of a great pipeline, what we think is the greatest pipeline ever. So with that in mind, when we have that hand to play, what we need to do is to make sure that we maximize the chances of achieving the potential that those new launches are expecting to bring. And this means that execution is extremely important. Right now, execution can make the difference. And the large M&A, it's not that we'll not have right now, matching our growth profile, but it could take -- derail us from execution because a large M&A requires thousands of people to work together thus to integrate the 2 companies. That being said, first of all, we never say never, so we are examining all opportunities. And also, we do plan to deploy capital to enhance our growth profile. It's just that this time, the capital that we plan to deploy has a very different -- slightly different direction and focus than before. Before, we were trying to do revenues now or soon. This was, more or less, the focus of our M&A dogma and is exactly what we needed at the time. We were dealing with lack of revenue growth, and we needed to bring either thesis that could enhance the strategy to break the company at the time or it could bring revenue streams that will enhance the growth profile that was actually very bad at the time. Right now, the dogma is changing, and it is how can we bring assets to enhance even further a pipeline to make our growth sustained. And because we have a very strong R&D machine that right now I fully trust their ability to choose assets and also develop them. This is why our strategy is to deploy capital towards this direction. As I said, though, we never say never. And of course, we will never lose our flexibility to deploy capital if we see the opportunities in the best way to achieve our premise. And with that, I will ask Mikael to comment.

Mikael Dolsten - *Pfizer Inc. - Global President, Worldwide Research & Development and Medical*

So thank you for the question. We have under breakthrough designation moved tafamidis registration and the 20-milligram formulation for once-a-day administration was to unused in clinical studies, and it has priority review. And Albert pointed out potential FDA action date in July. We have also filed a 61-milligram formulation that we think is a very convenient alternative that is under standard review as expected and would potentially be approved in the fall. This would offer patients the very best choices for a therapy that has this really strong data set and a consistency in cardiomyopathy.

Albert Bourla - *Pfizer Inc. - CEO*

And also, I would ask Frank to comment on the question about SI&A and R&D expenses.

Frank A. D'Amelio - *Pfizer Inc. - CFO & EVP, Global Supply & Business Operations*

Yes. So if you think about SI&A, just -- we've printed, what, $14.2 billion in 2018. We guided to $13.5 billion to $14.5 billion, so the midpoint is $14 billion, a couple hundred million lower than what we showed in 2018 on actuals. And we actually swung a few hundred million from indirect SI&A to direct SI&A. So in SI&A is we're working our way through the Lyrica patent cliff, so think about that will take place in 2019, 2020. We'll remain tough on SI&A. On R&D, as you look at R&D, we guided $7.8 billion to $8.3 billion. We spent about $8 billion last year. We'll watch the R&D number. But given how our late-stage pipeline we expect to grow, we think R&D will continue to grow. Once we get past the Lyrica LOE, beginning 2021 with 2020 as a base, we expect that top line to grow in the mid-single digits, and we will make sure we leverage that relative to the bottom line, get operating leverage, margin expansion so that the revenues are growing at a rate that's more than what the expenses are.

Albert Bourla - *Pfizer Inc. - CEO*

Thank you very much. And I see, Mikael, do you want to make a comment?

Mikael Dolsten - *Pfizer Inc. - Global President, Worldwide Research & Development and Medical*

I just wanted to make sure since you had this keen culmination interest rumor that the 61-milligram free asset formulation is equivalent to the 80-milligram top dose that we used in the clinical trial. So that would be a single tablet as an alternative and potential available latest for pending review.

Albert Bourla - *Pfizer Inc. - CEO*

So there is no difference in dose. It is just the dosage form.

Mikael Dolsten - *Pfizer Inc. - Global President, Worldwide Research & Development and Medical*

Perfect.

Operator

Your next question comes from Chris Schott from JPMorgan.

Christopher Thomas Schott - *JP Morgan Chase & Co, Research Division - Senior Analyst*

So just 2 here. The first was on tanezumab. Can you just talk about the profile that you see emerging from these first 2 studies, I guess, specifically on RPOA type 2 and this case of osteonecrosis. I just want to understand, you've had some dialogue as you're starting the studies on acceptable levels of these signals, can you just confirm that what you're seeing so far is below what you think's an acceptable threshold in terms of safety? And then my second question was about Xtandi and key drivers going forward. And here, I guess, do you see the traction you'd hope to see with the label expansion and do you expect any impact as we think about generic ZYTIGA, Eliquis on 2019?

Albert Bourla - *Pfizer Inc. - CEO*

Thank you, Chris. Let's have John start the tanezumab -- answer the tanezumab question and then maybe Mikael can jump in. And then Angela, can you please take the Xtandi question?

John D. Young - *Pfizer Inc. - Chief Business Officer*

Okay. Thanks for the question, Chris. So let me just sort of context it just by saying from our review of the 2 studies that have read out today, we continue to believe that tanezumab has the potential to offer a new nanoguide treatment for sustained efficacy for moderate to severe OA, osteoarthritis, and chronic lower back pain patients who are not receiving adequate relief or can tolerate other analgesics and also for cancer pain patients, and those are the patient populations in our pivotal studies. We also see that tanezumab has the potential to address serious high unmet need for those patients. We estimate that there are around 27 million Americans living with osteoarthritis, 33 million patients living with chronic lower back pain. And many of those patients failed to achieve adequate pain relief despite treatment with various types of pain medications. Additionally, we also know that the misuse of an addiction to opioids leads to more than 115 deaths everyday in the United States. And so it's estimated that 21% to 19% of patients prescribed with opioids for chronic pain misuse them and 8% to 12% development an opioid use disorder. So we remain encouraged by the emerging clinical profile for tanezumab although we recognize that many questions still need to be answered. Last year, we saw data from 1 Phase 3 OA study, which was study 1056. That population represented about 10% of the total number of patients in our Phase 3 program, which overall includes 6 Phase 3 studies and around 7,000 patients in osteoarthritis, chronic lower back pain and cancer pain. So today's study, we announced earlier on today, we shared top line results from our second Phase 3 OA study, which is 1057. And that population represents another 12% of the total number of patients in our Phase 3 program. So in summary, I would say we continue to see data sets read out. We have more than 3/4 of the total number of patients in our Phase 3 program still to read out although the profile is still emerging, and that's to say there are many questions that we still need to answer about the profile of the product. But overall, we remain very positive. Mikael, maybe you can add specific answer to Chris' question.

Mikael Dolsten - *Pfizer Inc. - Global President, Worldwide Research & Development and Medical*

Thank you, John. That was a terrific overview of why we are excited about this new emerging potential pain drug class for patient in great need for new opportunities to treat difficult disease. With the 1057 study, it was -- as we have projected and believe to expect RPOA in low single-digit percent. In 1057, it was just above 2%, versus 1056, above 1%. This is the range that we have assumed will come out in these trials. And across now 1,000 patients, we have RPOA at 1.7%. Within the RPOA, I just wanted to punctuate that the majority of them are of Type 1, the milder case, with only joint narrowing -- joint space narrowing and infrequent symptomatology, and only 1/3 of them about -- are tied with more significant radiological changes. Finally, we had one case of osteonecrosis, which is in line with our expectations that it's going to be a rare event. We have now more than 1,000 patients in osteoarthritis treated with tanezumab, which gives us quite good opportunity to see an emerging drug profile with robust efficacy and as expected, adverse event profile, that for these patient type seems to me provide really favorable benefit risk, given the alternative treatments are few and would offer a way for us to treat difficult pain, avoiding abuse dependencies such as with opioid. And let me just conclude and say please remember that the type of patients in 1057 and 56 have been through at least 3 different classes of analgesics and on average, had OA for more than 6 years and have reported OA with significant impact on their ability to function in everyday life. So for them, it certainly is an important opportunity to treat their disease. And let me conclude with reminding you that total joint replacement was similar across placebo and tanezumab treated, again, an important finding for us.

Albert Bourla - *Pfizer Inc. - CEO*

Thank you very much, Mikael. And Angela, key drivers of growth for Xtandi, please?

Angela Hwang - *Pfizer Inc. - Group President, Pfizer Biopharmaceuticals Group*

Sure. So let me begin by talking a little bit about how well Xtandi did in 2018 and how pleased we are with its performance but also very optimistic about its future. As you heard Albert say, it is -- Xtandi is one of the pillars of our Oncology business. So full year 2018, we grew 18%. Q4 versus Q4

'17, we grew 12%. And then if you include royalty revenues, Xtandi actually achieved over $1 billion in 2018. But when we step back and take a look at its growth strategy, I would describe it as follows:

First, it's our base business in metastatic castrate-resistant prostate cancer. This was our first indication, and our growth strategy here has been focused on driving uptake around urologists, and we're really pleased with the progress that we've seen here. Today, more than 30% of our new scripts are written by urologists, and we're continuing to see market share growth in this segment. The second segment and growth segment is the non-metastatic castrate-resistant prostate cancer segment, and this is the PROSPER data. And we've seen very positive trends here as well since the launch of PROSPER in July of 2018. Just in 6 months, our market share is quadruple that of ERLEADA or if you look at it a different way, it's equivalent to the combination of chemo use and ERLEADA combined. You may not see it in total sales yet, but that's because the new patients are coming into therapy, new patients are coming every day. So you may not see the full impact of this pool of patients, which is still accumulating, so it will take time to realize. Finally and our last opportunity and the one that we're really excited about is in the hormone-sensitive prostate cancer patient population because this is where the duration of therapy would be the longest. And here, there are 2 patient segments. The first is based off of our ARCHES data, is the metastatic hormone-sensitive patient and there are about 38,000 new patients coming in a year. As you know, the results of ARCHES was announced in December and it will be presented at ASCO in February. We look forward to our discussions with the FDA to potentially support an expanded indication for Xtandi here. The second segment of growth is going to be in the non-metastatic hormone-sensitive patients. And here, there are about 30,000 new patients a year. This is being studied in the EMBARK trial, which will read out next year. So in totality, we believe that we have excellent data, and we also have the potential for new indications, and this will enable Pfizer to make significant impact on patients' lives but importantly, to change the standard of care for prostate cancer. You also asked a question on the impact of generic ZYTIGA. And here, we expect the ZYTIGA generics to have a minimal impact on our business. Typically, generic impact is greatest with the originator brand. In this instance, Xtandi also has indications that are different from ZYTIGA. And in addition to that, our dosing frequency is different. We also are -- we also don't have the requirement for steroid co-administration, and we also have differences in our monitoring requirements. So I think that all of these will stand well in terms of making switching less likely and for the impact on Xtandi to be minimal as we expect.

Albert Bourla - *Pfizer Inc. - CEO*

Thank you, Angela. And as I said before, for the BAVENCIO-Inlyta and tafamidis products equally excited about tanezumab and the Xtandi, particularly with the new indications that are coming.

Operator

Your next question comes from Alex Arfaei from BMO Capital Markets.

Alex Arfaei - *BMO Capital Markets Equity Research - Pharmaceuticals Analyst*

Great. First on Xeljanz, you obviously have strong momentum there. You have a formidable competitor coming expected this year. They have a lot of rebates leverage. You have more JAKs coming, TNF biosimilars, TYK2, obviously a lot of activity in this market so I'm just wondering how you're thinking about the commercial dynamics in major immunology markets. And then a follow-up in emerging markets. Obviously, very strong performance for your legacy products like in cardiovascular disease, Lipitor and so on. Just wondering how sustainable is that in your view.

Albert Bourla - *Pfizer Inc. - CEO*

Yes. On Xeljanz, I will ask Angela to comment, but just to make an initial comment about -- Xeljanz already has, this year, has $1.8 billion. So Xeljanz already have crossed the threshold, but it is quite important to be able to be stopped by exclusionary practices that maybe leaders can have in contracting. But I will ask Angela to comment on the growth prospects of Xeljanz in '19 and beyond.

Angela Hwang - *Pfizer Inc. - Group President, Pfizer Biopharmaceuticals Group*

Sure. So first of all, just beginning with '18, as Albert said, I mean, tremendous growth that we've seen in Xeljanz. 37% growth Q4, over last year Q4 and particularly in the U.S., really strong double-digit growth, about 26%. What we're seeing here in Xeljanz, and I'll start with the U.S., is really the mobilization of all of the indications for Xeljanz. We see strong uptake for Xeljanz in rheumatoid arthritis and really great experience, and I think in comfort by rheumatologist in prescribing Xeljanz. So just as an example, about 53% of U.S. patients now are using Xeljanz without methotrexate, so as monotherapy, which is just great progress in terms of, I think, demonstrating the confidence that rheumatologists have with Xeljanz. But what we also saw towards the end of last year was the launches of PsA and UC and another example here of the growth that we've experienced in terms of the Q4 volume growth, 1/3 of that volume growth came from these 2 new indications. And just as another example of why we're excited about these new indications, in UC, specifically, our early data shows that we've also recently surpassed SIMPONI in terms of new patient market share. So I think in the U.S., we continue to see our tremendous growth possible across all of these indications. And as you know, we have other indications that are part of our life cycle management that we will be continuing to work on. Globally, we have launched RA, UC as well as PsA, but what we are in the middle of is gaining reimbursement for these new indications. We're encouraged by recent signs from payers of their acceptance of Xeljanz in these new indications such as the NICE approval that we've got in 2018 for both UC and the PsA indications. But net-net, when we sort of bring together all of these indications, RA, which is our base business, but now tagging on UC and PsA, we see between both of these 2 new indications a market that's approximately $10 billion large. And I think, over time, with reimbursement, but also the increased comfort level and experience that rheumatologists, gastroenterologists will have with prescribing Xeljanz, we expect to see continued and strong growth from this franchise. I think you also questioned about competitors as well, and certainly, this is a class that is hugely competitive. But I think that Pfizer's long experience, and I think our track record of success in JAK science as well as our deeply entrenched in commercial footprint in rheumatology and now in gastroenterology will stand as well as we deal with this increased competition.

Albert Bourla - *Pfizer Inc. - CEO*

Thank you, Angela. And I will ask Frank to give us some numbers and comment on Emerging Markets. Just an initial comment from my side, but the Emerging Markets is and will continue to be a key strength for us and a key pillar of growth and particularly, in the context of the new organization. Let's not forget that a very big part of the Emerging Markets business has become part of the Upjohn Group. And this is -- and this was exactly engineered so that we will be able to maximize the growth, and particularly in areas like Asia and particularly China where they have the biggest potential. But Frank, why don't you give us some numbers to color the picture?

Frank A. D'Amelio - *Pfizer Inc. - CFO & EVP, Global Supply & Business Operations*

Sure. So Alex, Emerging Markets for the quarter, $3.3 billion in sales for the year, $12.65 billion in sales, each up 13% on an operational basis, strong performance. China, for the quarter and the year, more than 20% growth. So you asked what to expect going forward? We believe we can continue to grow Emerging Markets in the low double digits on going forward basis.

Operator

Your next question comes from Vamil Divan from Crédit Suisse.

Vamil Kishore Divan - *Crédit Suisse AG, Research Division - Senior Analyst*

So a couple if I could. So one, just around 2019 guidance, can you just elaborate a little bit more what you're assuming in terms of net price increases in the U.S. into that guidance and maybe just with all the discussions on a DC, what -- are there any significant changes that you're assuming may take place in the 2019 time frame? And then just the second one is more on the oncology side, any update around when we might see some of the adjuvant breast cancer data from Ibrance? I know that's a key part of the next sort of part of the growth story for that franchise. So maybe you can share anything there. And then similarly with BAVENCIO, which is more around the immuno-oncology adjuvant opportunity, it doesn't look like there's a lot of work being done with BAVENCIO there. Maybe you can just comment on any adjuvant opportunity for that product.

Albert Bourla - *Pfizer Inc. - CEO*

Right. On 2019 guidance and the pricing, I will ask again, Frank, to run some of the numbers.

Frank A. D'Amelio - *Pfizer Inc. - CFO & EVP, Global Supply & Business Operations*

Sure. So Vamil, in terms of price in the U.S. for 2019, we assume that price will be flat. And worldwide, we're assuming price that's in the negative low single digits. So minus low single digits and U.S, flat.

Albert Bourla - *Pfizer Inc. - CEO*

And I just want to make a comment here about it's very clear that pricing is not going to be a growth driver for us now and, I think, in the future. It's very clear. So this is all included in our guidance and is also included in our projections for mid-single-digit growth post Lyrica LOE for the 5 years. And that will come from breakthrough medicines and based on volume rather than in price increases. And with that, the oncology question about Ibrance, let me pass it to Angela, please.

Angela Hwang - *Pfizer Inc. - Group President, Pfizer Biopharmaceuticals Group*

Sure. So we're really excited about the adjuvant opportunity. And as you said, it is the third part of our growth strategy, so a very important part of our growth story for Ibrance but also for oncology, in general. The 2 studies, PENELOPE and PALLAS, are the studies that we are looking forward to. Both of them are going well and have recruited faster than expected. And these studies are important because they give us the potential to double the number of patients that are eligible for Ibrance. But we have to remember that these studies are event-driven and based on our projections, should read out some time next year. So I think more to come on that as we progress through the clinical trials. And then I think you had a second question on...

Albert Bourla - *Pfizer Inc. - CEO*

BAVENCIO. I think John maybe can take it, and then you can add, Angela.

John D. Young - *Pfizer Inc. - Chief Business Officer*

Yes. Thanks for the question, Vamil. So we are obviously continuing our effort with the execution of the avelumab development program. It includes 30 ongoing studies, 7 of which are potentially registration enabling, involving more than 9,000 patients across 15 tumor types. I think it's always important when we talk about IO to say that we have always recognized, believe that the real value of IO is expected to be in effective combinations. And we believe that solid pre-clinical science, where we're in a good position to be competitive in a number of tumor types, it really underpins our development strategy. One example of that, I think Albert's already commented on is the JAVELIN Renal 101 trial combined, BAVENCIO with Inlyta in previously untreated advanced renal cell carcinoma patients and the combination provide a superior progression-free survival compared to SUTENT. There are 2 additional immunotherapy Phase 3 studies ongoing, including axitinib with pembrolizumab in first line renal cell carcinoma, which is a study sponsored by MSD and, also enzalutamide and atezolizumab and CRPC, which is sponsored by Genentech and Roche. But I think in terms of the wider development program, which is kind of where you're driving, we're currently testing up to 10 Pfizer combinations with checkpoint inhibitors, including 5 targeted Pfizer therapies. We also have a number of studies combining avelumab and talazoparib across a range of indications. So that really speaks to just the way that we see BAVENCIO as being potentially valuable therapy in some important areas of high unmet need for patients where we believe combinations could really advance standard of care.

Operator

Your next question comes from Tim Anderson from Wolfe Research.

Timothy Minton Anderson - *Wolfe Research, LLC - MD of Equity Research*

I have a few questions. I don't want to put your cart before the horse on this but 2020 consensus has earnings growth being nearly flat. There are a variety of pushes and pulls. You're launching new products. You have some strong growing in-line brands, but you still have Lyrica, LOE spilling over into 2020. I'm wondering if you can comment on how you kind of view where consensus sits on the earnings line. Is 2020 likely to be a flattish year as well? Second question is on this other income deductions line. Just wondering why the change in heart in how you account for the impact of unrealized and realized gains and losses, why different in 2019 versus 2018? Was that at the advice of your accountants or the IRS or someone else? And then last question, on the JAK1 inhibitor for atopic derm, you have a Phase 3 reading out 2019. Can we assume you'll need 2 Phase 3s for approval in that indication, and when will the second one read out if it does require 2?

Albert Bourla - *Pfizer Inc. - CEO*

Thank you. Frank, why don't you deal with the question about the consensus and the OID, and then Mikael can discuss the JAK1 Phase 3 study.

Frank A. D'Amelio - *Pfizer Inc. - CFO & EVP, Global Supply & Business Operations*

Sure. So first, Tim, on the OID question, now that was my decision in terms of taking the gain or loss on equity securities, equity investments out of adjusted income. New accounting was put in place on this on the beginning of 2018 in terms of realizing or booking gains and unrealized gains into results. The amount of -- the size of the gains in 2018 surprised us quite frankly, introduced a lot of volatility into our numbers. So I decided at the beginning of 1/1/19, we'll take that out. And by the way, please note, I actually think that if we left it in, that the probability of that being a good guy is much higher than if it were a bad guy to our 2019 results, but I thought the best thing to do was just take it out because it was introducing a level of volatility that isn't part of our core business. So we removed it for that reason. But we tried to show that on the guidance figures that we've provided to you all in our release at the bottom of Page #2. Then in terms of the 2020 numbers, and I won't comment on consensus, obviously, but in terms of our rhythm of the numbers. For job one is we got to deliver on what we've just said for 2019. 2020, we will still have the challenge of Lyrica LOE. We get the full year effect of that in 2000 -- in 2020, so we'll have to work our way through that relative to the business, and obviously, we do everything we can to work our way through that relative to earnings.

Albert Bourla - *Pfizer Inc. - CEO*

Thank you, Frank. Mikael, what about the JAK1, how many Phase 3 studies do we need?

Mikael Dolsten - *Pfizer Inc. - Global President, Worldwide Research & Development and Medical*

So I would say it like this. We think it's very large opportunity for the JAK1 in atopic dermatitis, and we're very excited about the profile as you remember from our Phase 2 studies that this drug class seems to have real rapid activity, both in clearing skin eczema and in pruritus itching. We have actually 2 trials reading out in 2019, one in May and one in September range, give or take, with some time as these trials conclude. And we actually have a significant program here to potentially establish these as a very significant product with also trials reading out in 2020, including a comparator trial to the [peak's end] and I think particular there is to look at the rapid onset of JAK versus biologicals. There is a mechanism of action started to provide additional insight and also a 52 weeks longer-term studies. So it's a very comprehensive data package. But please look out for our 2019 data readout that would tell us the initial outcome of this exciting new drug class.

Albert Bourla - *Pfizer Inc. - CEO*

The strength of the profile as it will emerge.

Operator

Your next question comes from Louise Chen from Cantor Fitzgerald.

Louise Alesandra Chen - *Cantor Fitzgerald & Co., Research Division - Senior Research Analyst & MD*

So first question I had was on tanezumab. Do you think the RPOA and the other safety imbalances are result of the drug or the patient population? And then second question I had was if you could provide any sort of efficacy data with respect to the 2 arms? Or if you can't, how does it compare to what we saw on 16-week data? And then last question I had was just on your leverage as you move past these LOEs, what kind of leverage can we assume to the bottom line? And how much better will it be than what we see now?

Albert Bourla - *Pfizer Inc. - CEO*

Mikael, can you please deal with the tanezumab question, please?

Mikael Dolsten - *Pfizer Inc. - Global President, Worldwide Research & Development and Medical*

Yes. I mean, certainly, we known from historical trials that patients with advanced OA are more likely to develop RPOA than patients with chronic lower back pain that, in general, have healthier joints. That's #1. #2, about tanezumab relationship to this, I think we will get a better understanding as we see this year the comparator trial with NSAIDs for OA and with opioids in chronic lower back pain. That will allow us to understand the incidence of RPOA on different treatment, but please let me just underline each drug class has its profile. And of course, opioid, as you know, which is the major comparator for us in chronic lower back pain are associated with a range of very difficult side effects, including fatal outcome for tens of thousands Americans every year, very different from low single-digit orthopedic injury that we have discussed. And let me even remind you that NSAIDs which, in general, has been not very effective on advanced OA are, of course, associated with gastrointestinal risks of bleeding and also been associated with cardiovascular risk. So overall, we think that tanezumab represent a new emerging drug class with a very interesting efficacy, and we'll learn more about the exact tolerability safety profile later this year, but we remain very positive about this offering for patient pending of course finalization of studies and potential regulatory process.

Albert Bourla - *Pfizer Inc. - CEO*

Thank you, Mikael. And as regards to the levers of the bottom line, let me ask the master of levers, Frank D'Amelio, to comment.

Frank A. D'Amelio - *Pfizer Inc. - CFO & EVP, Global Supply & Business Operations*

So Louise, here's how I think about this and to kind of connect back to Tim's question, we need to work our way through 2019. We need to work our way through 2020, work our way through the Lyrica LOE and the major impact of the Lyrica LOE in those 2 periods. We get to 2021, LOEs decline materially. Our pipelines kicking in, our in-line products are kicking in, our emerging markets are continuing to grow, that's where we see this inflection point in terms of the rhythm of the business, the rhythm of the numbers. We think we can grow that top line mid-single digits. So approximately 5%. We think, clearly, we can grow the top line when we grow the top line mid-single digits. We can clearly grow the bottom line more than mid-single digits. And hopefully, our actions over the years have demonstrated our ability to do that. So that's how I think about this in terms of rhythm of the business.

Albert Bourla - *Pfizer Inc. - CEO*

Well said, Frank.

Operator

Your next question comes from David Risinger from Morgan Stanley.

David Reed Risinger - *Morgan Stanley, Research Division - MD in Equity Research and United States Pharmaceuticals Analyst*

Just a follow-up on 2020. So obviously, the patent expiration of Lyrica annualizes in June of 2020, so do you think that Pfizer can return to revenue growth in the second half of 2020 after that annualizes, Frank? Or are there other factors that could preclude or return to growth in that second half period? And then with respect to Ibrance, I was just hoping for some perspective on what we should expect for U.S. sales in 2019 relative to 2018. Obviously, sales have been flattening out according to the IMS data. But should we be expecting U.S. sales to be flat in '19 versus '18? Or could they be down slightly due to competition gaining share? Any color would be helpful.

Albert Bourla - *Pfizer Inc. - CEO*

Thank you. And obviously, we do not provide guidance for the year after. And also, we do not comment, provide guidance on individual products, particularly on individual reason of an individual product. But I'll ask Frank to give some color on the 2020 and what happens after the second quarter, and then, of course, Angela, to give at least the dynamics of the market.

Frank A. D'Amelio - *Pfizer Inc. - CFO & EVP, Global Supply & Business Operations*

So Dave, I'll do my best to try to answer this, but to Albert's point, trying to provide 2020 guidance and breaking it down into quarters and halves is extremely difficult. What I would say is this, there will still be material LOE impacts from Lyrica in 2020. And so we still view 2020 as a challenging year. I think the real pivot point, the real inflection point becomes 2021 using 2020 as the base year. And that's where I think we can really show some major-league progress on the top line and then dropping that to the bottom.

Albert Bourla - *Pfizer Inc. - CEO*

I'm going into quarter-after-quarter, of course. It's just something that we don't want to speculate on. And Angela?

Angela Hwang - *Pfizer Inc. - Group President, Pfizer Biopharmaceuticals Group*

So I think as we think about Ibrance in the U.S. certainly, we have been very pleased with the performance of Ibrance to date. I mean, just really strong growth quarter-over-quarter or even full year over full year, but the way we look at it, in the 3 phases of growth is how we think about its growth prospects. So Phase 1 is this U.S. launch in metastatic breast cancer, which includes our growth of the CDK class as well as our own leadership of that class. And in this regard, being that we had such rapid uptake initially, we have now reached a 50% class share, which we're very pleased with though we know that this is the point that we will need to continue to expand on in order to generate the growth. But certainly, the fact that we've been able to treat 95,000 patients in the U.S. with metastatic breast cancer is very positive for us. And then in the other phase of our growth is our international launches, which really began in 2018. And here, we've exceeded our expectations as well. We have treated more than 85,000 patients ex U.S. through the launches in Japan, in the EU, in China and Brazil towards the end of last year. So I think in 2019, that's going to be another focus area of growth for us. And then Phase 3, we talked about already a little bit earlier, which is our adjuvant population, which is coming up. But maybe sort of coming back to the U.S. and specifically where the growth is coming from, we do see the class growth at 50% as one that -- as one where additional opportunities can be found. And I think that what we are now focused on is breaking the entrenchment with the single agent endocrine therapy, which will then allow us to grow the CDK class. But we're also clear about what it is that we need to do here. So just as

an example, we know that 25% of our key accounts have more than 40% share in the single-agent endocrine therapy. So we're really focused on targeting our HCP education very carefully in this area. We also know that educating a newly diagnosed HR+/ HER2- patients about the significant clinical benefits of adding Ibrance to -- in first line therapy is an important aspect of our work. And here, we know that the data show that in the first line setting, when you add Ibrance to endocrine therapy, you achieve a longer progression-free survival of about 12 months. So we think that this is really important information for patients to have. So when you look at the totality of our data, our access, our strong leadership position, but also the strategy that we have, we believe that we can really make a difference from a patient impact perspective, and we see great potential for growth for Ibrance.

Operator

Your next question comes from Jason Gerberry from Bank of America.

Jason Matthew Gerberry - *BofA Merrill Lynch, Research Division - MD in US Equity Research*

I guess, just -- I'm not sure that you'll be able to answer this, but just on tanezumab. Was there any sort of dose response with respect to the RPOA rate? I believe in the prior study at ACR, there was a bit of a dose-related response. So I was just curious to what extent you can comment on that. And then also just with the RPOA, did -- I know there's an additional dose that was provided in this trial versus prior trials, so just sort of curious if the inclusion of an additional dose if events were skewed early or late in the treatment period. And then one housecleaning item. Do you expect to be in the market for Rituxan at time of market formation, which is, I think, the Street's thinking around mid to second half of 2019?

Albert Bourla - *Pfizer Inc. - CEO*

Mikael, do you want to take the tanezumab question?

Mikael Dolsten - *Pfizer Inc. - Global President, Worldwide Research & Development and Medical*

Thank you for the interest in the product. And as we have said previously, we were very pleased with the readout of 1057 and 1056. More than 1,000 patients with robust efficacy we reported on the 5-milligram plus across 3 primary endpoint and on 2 of them on 2.5-milligram. We have not seen on these 2 doses any difference in the tolerability or safety profile and feel that we understand the profile very well. And we're also pleased to report that total joint replacement was similar versus placebo. So I think that speaks to the strength of the data set we have. And we look forward to share data in more details at upcoming conference and report out additional studies this year.

Albert Bourla - *Pfizer Inc. - CEO*

Yes, very nice interest on tanezumab over here. Angela, about the biosimilar, Rituxan?

Angela Hwang - *Pfizer Inc. - Group President, Pfizer Biopharmaceuticals Group*

So our plans are on track, and we are planning to launch Rituxan in 2019, and we look forward to receiving the approvals and then planning for our launch.

Operator

Your next question comes from Geoff Meacham from Barclays.

Geoffrey Christopher Meacham - *Barclays Bank PLC, Research Division - MD & Senior Research Analyst*

Sorry to ask another one on the 2019, 2020 growth profile. But Albert, is there a willingness to be more active on commercial stage M&A just to change the growth profile until 2021 or even divesting lower growth franchises? I'm just trying to see how proactive Pfizer will be versus just waiting until after the Lyrica LOE. And then another one on biosimilars, there's obviously lots of launches coming up, including Rituxan. How will the strategy evolve from a pricing and access perspective and what are the main lessons you guys have learned so far from Inflectra just of late that could help accelerate the launches?

Albert Bourla - *Pfizer Inc. - CEO*

Angela will answer in a moment with biosimilars question about our -- that you asked, pricing and what is our strategy there. But look, on '19 and '20, as I said, we will be proactive, but proactive doesn't mean that our focus it is how to change the profile of '19. Proactive means how we're going to enhance the growth profile of Pfizer in the pivotal moment that is happening after the June-July of 2020, or in '21, we will see this a full year. So in the commercial space, again, we are looking for opportunities with our -- to deploy capital that will help, but the direction right now, it is to enhance our growth profile and not to dilute it. And the direction right now, it is not to disturb operationally the business in this very critical phase that we are trying to get the pipeline through the finish line, prepare the markets commercially and then launch the products. And this is the focus, really. Angela, what about biosimilars?

Angela Hwang - *Pfizer Inc. - Group President, Pfizer Biopharmaceuticals Group*

So we are looking forward to the launch of 3 additional oncology biosimilars in our portfolio in 2019. And I think that what we've learned about the biosimilar market is that there, it is a -- we believe in it and -- from a potential perspective and from a growth perspective. What we're also seeing are differences in the EU and in the U.S. So in the EU, we see a very rapid uptake and actually great acceptance of biosimilars. And if I just use infliximab molecule as an example, the infliximab biosimilars are about 65% of the total molecule. And we've seen rapid uptake and great acceptance by customers, by payers. We see a market that, I think, is evolving and developing in the U.S. and I think that our experience with infliximab in the U.S. really is not a great analogy for what might be to come with our new oncology biosimilars. Just because they're very different dynamics in the I&I space compared to the oncology space. The big difference in the I&I space in the U.S. is the exclusionary contracting from J&J, which has really prevented and been a great impediment to our ability to grow the I&I biosimilar. Rebates, rather than net price has really driven, I think, formulary access, and that has been a great barrier to our ability to grow. However, we see different dynamics in the oncology space, and that is because oncology drugs are shorter in duration of therapy. So that allows new patients to turn over faster. And it will make it easier for the physicians to initiate new patients on oncology biosimilars. And we believe that this will enable customers to benefit from the cost savings that they can derive from biosimilars much more quickly than what you might see in the I&I space where the duration of therapy is very long. It's a long chronic disease. So we are excited about the upcoming launches of our oncology biosimilars, and we expect our entire biosimilar portfolio to be a strong contributor to growth to Pfizer in 2019.

Albert Bourla - *Pfizer Inc. - CEO*

Thank you, Angela.

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Thanks for the insights. And we'll take your last question please, operator.

Operator

Your final question comes from Seamus Fernandez from Guggenheim.

Seamus Christopher Fernandez - *Guggenheim Securities LLC, Research Division - Former MD, Major Pharmaceuticals and Biotechnology*

So my question really was on tanezumab. I know there's been a lot of questions around the safety side, but the low dose didn't separate from placebo on one of the co-primary endpoints. And just wanted to understand a little bit better how you guys are feeling about the differences in this particular patient population to really give you strong convictions that the assumed benefit of efficacy of this novel mechanism are going to be sustained.

Albert Bourla - *Pfizer Inc. - CEO*

Mikael?

Mikael Dolsten - *Pfizer Inc. - Global President, Worldwide Research & Development and Medical*

Thank you. First, let me point out that the 5-milligram dose in 1056 and 1057 performed very well, consistent, robust on all 3 primary endpoints in both the studies. The 2.5-milligram performed with statistical significance in 1056 on all 3 primary endpoint. And on the 2 most important, it was positive, pain and physical function. It was positive on overall assessment of OA at several time points, but narrowly missed at the 24 week. Often what happens in this type of trials in pain is that you may have variability in placebo response at various time points that is likely to influence. But please note that numerically, we are still pleased with the response to 2.5 milligram at all time points. And we think we have 2 doses that offer, so far, robust consistent efficacy and very advanced patient populations. And we feel that we consistently have reported the tolerability and safety profile. So we look forward to conclude the trials with another osteoarthritis later this spring and a chronic lower back pain and so far, we are very pleased with tanezumab.

Albert Bourla - *Pfizer Inc. - CEO*

Thank you, Mikael, and just thank you, everyone, for your great questions. I was very pleased to see that the majority of the focus right now is on our pipeline. And I think you're right. This is where it should be. And we are looking forward for equally great '19 as we had in 2018. Chuck?

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Great. Thank you, everybody, for your attention this morning. This will end the call.

Operator

Ladies and gentlemen, this does conclude Pfizer's fourth quarter 2018 earnings conference call. Thank you for your participation. You may now disconnect.