Q4 2018 Earnings Call

Company Participants

- Albert Bourla, Chief Executive Officer & Director
- Angela Hwang, Group President-Pfizer Biopharmaceuticals Group
- Charles E. Triano, Senior Vice President, Investor Relations
- Frank A. D'Amelio, Chief Financial Officer & Executive Vice President, Global Supply & Business Operations
- John D. Young, Group President, Chief Business Officer
- Mikael Dolsten, Global President, Worldwide Research and Development & Medical

Other Participants

- Alex Arfaei, Analyst
- Christopher Schott, Analyst
- David R. Risinger, Analyst
- Geoffrey Meacham, Analyst
- Jason M. Gerberry, Analyst
- Louise Chen, Analyst
- Seamus Fernandez, Analyst
- Steve Scala, Analyst
- Tim Anderson, Analyst
- Umer Raffat, Analyst
- Vamil K. Divan, Analyst

MANAGEMENT DISCUSSION SECTION

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 {BIO 3844941 <GO>}

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, our General Counsel.

The slides that will be presented on this call can be viewed on our website, pfizer.com/investors. You'll see here that slide three 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 {BIO 18495385 <GO>}

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 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 of 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 [PIH]. 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 Prevnar 14 primarily in emerging markets. I would also remind you that Viagra transferred from PIH to PEH [Pfizer Essential Health] 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, our 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 it 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 [Androgen Deprivation Therapy] in men with metastatic hormone-sensitive prostate cancer, met its primary endpoint, basically 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.

For this year, Xeljanz had 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 two biosimilars in 2018, and we see the potential for up to four 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 three 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 Healthcare business, led by Chris Slager, which is preparing to become part of the 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 four targeted cancer agents, over the last four months of 2018. In total, we received seven key approvals in 2018, earning 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 a 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 started a Phase 3 trial for our next-generation 20-valent pneumococcal conjugate vaccine for adults 18 and older.

In Inflammation and 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 a combination of Bavencio and Inlyta for first-line renal cell carcinoma, as well as for up to four biosimilars, trastuzumab, bococizumab, 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 a serious unmet need for 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 three very positive trends are intersecting at the same time: first, macro trends, such as an aging population and the 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 three 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 of 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, policy makers, 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

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 of $383 million or 3%.

Our Innovative Health business recorded 10% operational revenue growth in the fourth quarter 2018, driven primarily by: Ibrance, international markets; Eliquis and Xeljanz globally; and Prevnar 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: 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; to 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 and 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 2018 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 in direct 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 expect that 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 zero. We have since refined our forecast and are now estimating approximately $100 million of income for 2019. This is approximately $1.2 billion less than 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 to 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 to 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 and 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 {BIO 3844941 <GO>}

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

Q&A

Operator

Your first question comes from Steve Scala from Cowen.

Q - Steve Scala {BIO 1505201 <GO>}

Thank you very much and congratulations on a strong 2018 and a solid 2019 outlook, a couple 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.

The 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? Thank you very much.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you, Steve. I think maybe John can answer the Bavencio/Inlyta question.

A - John D. Young {BIO 17639257 <GO>}

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

A - Albert Bourla {BIO 18495385 <GO>}

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

A - Angela Hwang {BIO 20415694 <GO>}

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's 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. with 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 end market development is a key area for Pfizer, is 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 benefit. 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.

A - Albert Bourla {BIO 18495385 <GO>}

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.

A - Charles E. Triano {BIO 3844941 <GO>}

All right, thank you. Next question, please, operator.

Operator

Your next question comes from Umer Raffat from Evercore.

Q - Umer Raffat {BIO 16743519 <GO>}

Hi, thanks so much for taking my questions. First, I 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? I would be very curious what your preferences are on large versus mid and how do 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 five-year timeframe. I'm just mostly trying to understand your thought process on operating margin evolution post-Lyrica.

A - Albert Bourla {BIO 18495385 <GO>}

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 it 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 summed it, as I said in my comments, into innovating for growth. And we believe that right now we are very well positioned to achieve this strategy because of the combination of, one, virtually LOE-free period after the Lyrica LOE until 2025, the mid of the decade, and also the introduction of a great pipeline that we think is the greatest pipeline ever.

So with that in mind, when we said 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 expected to bring, and this means that execution is extremely important. Right now, execution can make the difference. And large M&A, it's not that we'll not add right now marginal growth profile, but it could take – derail us from execution because a large M&A requires thousands of people to work together just to integrate the two 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 on our M&A dogma, and this is exactly what we needed at the time. We were dealing with luck for revenue growth, and we needed to bring either pieces that could enhance the strategy to break the company at the time or we 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 with this, how can we bring assets to enhancing further our 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 plans.

And with that, I will ask Mikael to comment.

A - Mikael Dolsten {BIO 16368411 <GO>}

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 the one used in the 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 consistency in cardiomyopathy.

A - Albert Bourla {BIO 18495385 <GO>}

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

A - Frank A. D'Amelio

If you think about SI&A, we've printed $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, as 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 that R&D will continue to grow. Once we get past the Lyrica LOE, we get into 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 and margin expansion so that the revenues are growing at a rate that's more than what the expenses are going to be.

A - Albert Bourla {BIO 18495385 <GO>}

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

A - Mikael Dolsten {BIO 16368411 <GO>}

I just wanted to make sure since you had this key formulation interest, Umer, 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. But there is no difference in dose, it is just the dosage form.

A - Albert Bourla {BIO 18495385 <GO>}

Perfect, thank you.

A - Charles E. Triano {BIO 3844941 <GO>}

Thank you. Next question, please, operator.

Operator

Your next question comes from Chris Schott from JPMorgan.

Q - Christopher Schott {BIO 6299911 <GO>}

Great, thanks very much for the questions, just two here. The first was on tanezumab. Can you just talk about the profile that you see emerging from these first two studies, I guess specifically on RPOA Type 2 and this case of osteonecrosis? I guess my understanding that you've have some dialogue as you're starting new studies on acceptable levels of these signals. Can you just confirm that what you're seeing so far is at least below what you think is an acceptable threshold in terms of safety?

And then my second question was about Xtandi and key drivers going forward. And here, I guess are you seeing the traction you had hoped to see on the label expansion, and do you expect any impact as we think about generic ZYTIGA looking out into 2019? Thank you.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you, Chris. Let's have John start with tanezumab, answering the tanezumab question, and then maybe Mikael can add something. And then, Angela, can you please take the Xtandi question?

A - John D. Young {BIO 17639257 <GO>}

Okay, thanks for the question, Chris. So let me just context-set just by saying from our review of the two studies that read out to date, we continue to believe that tanezumab has the potential to offer a new non-opioid treatment with sustained efficacy for moderate to severe OA, osteoarthritis, and chronic lower back pain patients who are not receiving adequate relief or can't 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 needs 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 medicine.

Additionally, we also know that the misuse of an addiction to opioids leads to more than 115 deaths every day in the United States, and it's estimated 21% to 29% of patients prescribed opioids for chronic pain misuse them and 8% to 12% develop an opioid use disorder. So we remain encouraged by the American clinical profile for tanezumab, although we recognize that many questions still need to be answered.

Last year we saw data from one 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 six 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 three-quarters of the total number of patients in our Phase 3 program still to read out, although the profile is emerging. And as I said, there are many questions that we still need to answer about the profile of the product, but overall we remain very positive. But, Mikael, maybe you can add a specific answer to Chris's question.

A - Mikael Dolsten {BIO 16368411 <GO>}

Thank you, John. That was a terrific overview of why we are excited about this new emerging potential pain drug class for patients in great need for new opportunities to treat difficult disease. You know, with the 1057 study, it was, as we have projected and believed, 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 of course, now in 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 space narrowing and infrequent symptomatology. And only one-third of them about are of a type with more significant radiological changes.

Finally, we had one case of osteonecrosis, which is in line with our expectation 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 a quite good opportunity to see an emerging drug profile with robust efficacy and, as expected, a adverse event profile that, for these patient types, 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 opioids.

And let me just conclude and say, please remember that the type of patients in 1057 and 1056 have been through at least three different classes of analgesics, and on average had OA for more than six years, and they reported OA with significant impact on their ability to function in everyday life. So for them, this 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.

A - Albert Bourla {BIO 18495385 <GO>}

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

A - Angela Hwang {BIO 20415694 <GO>}

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, Xtandi is one of the pillars of our oncology business. So full-year 2018, we grew 18%. Q4 versus Q4 2017, we grew 12%. And 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 among 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 six months, our market share is quadruple that of ERLEADA. Or if you look at 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 the 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 will be the longest. And here there are two patient segments. The first is based off of our ARCHES data. It's 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 patient, 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're we expect the ZYTIGA generics to have a minimal impact on our business. Typically, generic impact is greatest with the originator brand. And in this instance, Xtandi also has indications that are different from ZYTIGA. And in addition to that, our dosing frequency is different. 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.

A - Albert Bourla {BIO 18495385 <GO>}

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

A - Charles E. Triano {BIO 3844941 <GO>}

Thank you, Albert. Next question, please, operator.

Operator

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

Q - Alex Arfaei {BIO 15433937 <GO>}

Great. Thank you very much. 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 by your legacy products like in cardiovascular disease, Lipitor and so on. I'm just wondering how sustainable is that in your view? Thank you very much.

A - Albert Bourla {BIO 18495385 <GO>}

Yes. On Xeljanz, I will ask Angela to comment. But just to make an initial comment that Xeljanz already has this year $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 2019 and beyond.

A - Angela Hwang {BIO 20415694 <GO>}

Sure. So, first of all, just beginning with 2018, 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 I think and comfort by rheumatologists in prescribing Xeljanz.

So just as an example, about 53% of U.S. patients now are using Xeljanz without methotrexate 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; a third of that volume growth came from these two 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 tremendous growth possible across all of these indications. And as you know, we have other indications that are part of our lifecycle 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 got in 2018 for both the 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 two new indications a market that is 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 asked a question 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 commercial footprint in rheumatology and now in gastroenterology will stand us well as we deal with this increased competition.

A - Albert Bourla {BIO 18495385 <GO>}

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 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 was exactly engineered so that we would be able to maximize the growth, and particularly in areas like Asia and particularly with China, where they have the biggest potential. But, Frank, why don't you give us some numbers to color out the picture?

A - Frank A. D'Amelio

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 do we expect going forward. We believe we can continue to grow emerging markets in the low double digits on a going-forward basis.

A - Charles E. Triano {BIO 3844941 <GO>}

Thank you. Next question, please, operator.

Operator

Your next question comes from Vamil Divan from Credit Suisse.

Q - Vamil K. Divan {BIO 15748296 <GO>}

Great, thanks so much for taking my questions, 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 of the discussions out of D.C., are there any significant changes that you're assuming may take place in the 2019 timeframe?

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 part of the growth driver of that franchise, so maybe you can share anything there. And then similarly with Bavencio, we did some work around immuno-oncology as an opportunity, and 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. Thanks.

A - Albert Bourla {BIO 18495385 <GO>}

Right, on 2019 guidance and for the present, I'll ask again Frank to run some of the numbers.

A - Frank A. D'Amelio

Sure. So, Vamil, in terms of price in the U.S., for 2019 we assume net 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.

A - Albert Bourla {BIO 18495385 <GO>}

And I just want to make a comment here, Vamil. 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 the Lyrica LOE for the five 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.

A - Angela Hwang {BIO 20415694 <GO>}

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 two 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 sometime 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...

A - Albert Bourla {BIO 18495385 <GO>}

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

A - Angela Hwang {BIO 20415694 <GO>}

Okay.

A - John D. Young {BIO 17639257 <GO>}

Thanks for the question, Vamil. So we're obviously continuing our effort with the execution of the avelumab development program. It includes 30 ongoing studies, seven 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 I-O to say that we have always recognized and believe that the real value of I-O is expected to be in effective combinations, and we believe that solid preclinical science where we're in a good position to be competitive in a number of tumor types really underpins our development strategy.

One example of that that I think Albert has already commented on is the JAVELIN Renal 101 trial that combined Bavencio with Inlyta in previously untreated advanced renal cell carcinoma patients. And the combination provided superior progression-free survival compared to Sutent. There are two 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 in CRPC, which is sponsored by Genentech and Roche.

But I think in terms of the wider development program, which is where you're driving, we're currently testing up to 10 Pfizer combinations with checkpoint inhibitors, including five 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 a potentially valuable therapy in some important areas of high unmet need for patients where we believe combinations could really advance standard of care.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you.

A - Charles E. Triano {BIO 3844941 <GO>}

All right, thank you. Next question, please, operator.

Operator

Your next question comes from Tim Anderson from Wolfe Research.

Q - Tim Anderson {BIO 3271630 <GO>}

Thank you. I have a few questions. I don't want to put the 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 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. I'm just wondering why the change in heart on 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 the last question on the JAK1 inhibitor for atopic derm, you have a Phase 3 reading out in 2019. Can we assume you'll need two Phase 3s for approval in that indication? And when would the second one read out, if it does require two?

A - Albert Bourla {BIO 18495385 <GO>}

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.

A - Frank A. D'Amelio

So first, Tim, on the OID question, 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 in 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. It introduced a lot of volatility into our numbers. So I decided that at the beginning of 1/1/2019, we would take that out. 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. And we tried to show that on the guidance page that we provided to you all in our release at the bottom of page number 2.

Then in terms of the 2020 numbers, I won't comment on consensus obviously. But in terms of our rhythm of the numbers, so our job one is we've got to deliver on what we just said for 2019. 2020, we will still have the challenge of the Lyrica LOE. We'll get the full-year effect of that in 2020. So we'll have to work our way through that relative to the business. And, obviously, we'll do everything we can to work our way through that relative to earnings.

A - Albert Bourla {BIO 18495385 <GO>}

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

A - Mikael Dolsten {BIO 16368411 <GO>}

So I would say like this, we think it's a 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 two trials reading out in 2019, one in May and one in the September range, give or take some time as these trials conclude.

And we actually have a significant program here to potentially establish this as a very significant product, but also trials reading out in 2020, including a comparator trial to DUPIXENT. And I think in particular there is to look at the rapid-onset of JAK versus biologicals. There is a mechanism-of-action study to provide additional insight and also a 52-week longer-term study. So it's a very comprehensive data package. But please look out for our 2019 data readout that will tell us the initial outcome of this exciting new drug class.

A - Albert Bourla {BIO 18495385 <GO>}

The strength of the profile as it will emerge. Thank you, Mikael.

A - Charles E. Triano {BIO 3844941 <GO>}

Next question, please, operator.

Operator

Your next question comes from Louise Chen from Cantor Fitzgerald.

Q - Louise Chen {BIO 6990156 <GO>}

Hi, thanks for taking my question. So first question I had was on tanezumab. Do you think the RPOA and the other safety imbalances are a 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 two arms. Or if you can't, how does it compare to what we saw in the 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? Thank you.

A - Albert Bourla {BIO 18495385 <GO>}

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

A - Mikael Dolsten {BIO 16368411 <GO>}

Yes. I mean, certainly we know 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 number one. Number two, 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 of Americans every year; very different from a 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 being associated with cardiovascular risk.

So, overall, we think that tanezumab represents a new emerging drug class with a very interesting efficacy, and we learn more about the exact tolerability/safety profile later this year. But we remain very positive about this offering for patients, pending, of course, finalization of studies and potential regulatory process.

A - Albert Bourla {BIO 18495385 <GO>}

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

A - Frank A. D'Amelio

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 two periods. We get to 2021, LOEs decline materially. Our pipeline is 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 to rhythm of the numbers. We think we can grow that top line mid-single digits. So approximately 5%.

We think, clearly, if 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 the rhythm of the business.

A - Albert Bourla {BIO 18495385 <GO>}

Well said, Frank.

A - Charles E. Triano {BIO 3844941 <GO>}

Thanks, everybody. Next question, please.

Operator

Your next question comes from David Risinger from Morgan Stanley.

Q - David R. Risinger {BIO 1504228 <GO>}

Yes, thanks very much. Just to 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 would preclude a 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 2019 versus 2018, or could they be down slightly due to competition gaining share? Any color would be helpful. Thank you.

A - Albert Bourla {BIO 18495385 <GO>}

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

A - Frank A. D'Amelio

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, 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 line.

A - Albert Bourla {BIO 18495385 <GO>}

Going into quarter-after-quarter of course is something that we don't want to speculate on. And, Angela?

A - Angela Hwang {BIO 20415694 <GO>}

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 three 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 have such rapid uptake initially, we have now reached a 50% class share, which we are very pleased with, though we know that this is the point that we will need to continue to expand on in order to generate further 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, 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 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-positive HER2-negative patient about the significant clinical benefits of adding Ibrance 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.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you.

A - Charles E. Triano {BIO 3844941 <GO>}

Next question, please, operator.

Operator

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

Q - Jason M. Gerberry {BIO 17237298 <GO>}

Good morning and thanks for taking my questions. I guess just – I'm not sure if you'll be able to answer this. But just on tanezumab, was there any sort of dose response with respect to the RPOA rates? I believe in the prior study at ACR, there was a bit of a dose-related response. So I was curious as to what extent you can comment on that.

And then also just with the RPOA, there was an additional dose that was provided in this trial versus prior trials, I was just 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? Thanks.

A - Albert Bourla {BIO 18495385 <GO>}

Mikael, do you want to take the tanezumab question?

A - Mikael Dolsten {BIO 16368411 <GO>}

Yes, 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 across all three primary endpoints, and on two of them on 2.5-milligram. We have not seen on these two 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 strengths 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.

A - Albert Bourla {BIO 18495385 <GO>}

Yes, very nice interesting tanezumab overview. Angela, about the biosimilar on Rituxan.

A - Angela Hwang {BIO 20415694 <GO>}

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

A - Charles E. Triano {BIO 3844941 <GO>}

Great, thank you, Angela. Next question, please, operator.

Operator

Your next question comes from Geoff Meacham from Barclays.

Q - Geoffrey Meacham {BIO 21252662 <GO>}

Hey, guys. Thanks for the question. 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, 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 are 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 can help accelerate the launches? Thank you.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you. Angela will answer in a moment the biosimilars question about that you asked pricing and what is our strategy there. But look, on 2019 and 2020, as I said, we will be proactive, but proactive doesn't mean that our focus is how to change the profile of 2019. Proactive means how we're going to enhance the growth profile of Pfizer in the pivotal moment that is happening after June-July of 2020, or in 2021 we will see it a full year.

So in the commercial space, again, we are looking for opportunities 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?

A - Angela Hwang {BIO 20415694 <GO>}

So we are looking forward to the launch of our three additional oncology biosimilars in our portfolio in 2019. And I think what we've learned about the biosimilar market is that we believe in it 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 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 of biosimilars, just because there are just 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.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you, Angela.

A - Charles E. Triano {BIO 3844941 <GO>}

Great, thanks for the insights, and we'll take our last question, please, operator.

Operator

Your final question comes from Seamus Fernandez from Guggenheim.

Q - Seamus Fernandez {BIO 7525186 <GO>}

Thanks very much for the question. 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 I 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 conviction that the assumed benefits of efficacy of this novel mechanism are going to be sustained.

A - Albert Bourla {BIO 18495385 <GO>}

Mikael?

A - Mikael Dolsten {BIO 16368411 <GO>}

Thank you. For us, let me point out that the 5-milligram dose in 1056 and 1057 performed very well, consistent, robust on all three primary endpoints in both of the studies. The 2.5-milligram performed with statistical significance in 1056 on all three primary endpoints, and on the two 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 24 weeks.

Often, what happens in these types 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 two doses that offer, so far, robust consistent efficacy in a very advanced patient population, and we feel that we consistently have reported the tolerability and safety profile. So we look forward to conclude the trials in either osteoarthritis later this spring and chronic lower back pain. And so far, we're very pleased with tanezumab.

A - Albert Bourla {BIO 18495385 <GO>}

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 are right. This is where it should be. And we are looking forward for an equally great 2019 as we had in 2018. Chuck?

A - Charles E. Triano {BIO 3844941 <GO>}

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 all. Thank you for your participation. You may now disconnect.