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Day Call

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PRESENTATION

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Thank you, everyone, for coming this afternoon. We are very proud on behalf of all my Pfizer colleagues to have you here today. As you can imagine, a lot of work from -- a lot of people has gone into today. So we're putting this all together for you. So we hope you enjoy it. We hope you find it very valuable.

Before we get started, I know people have been asking about WiFi connectivity. So I'm just going to read the network name to you. It's called Investor Day Guest, 3 separate words. You'll find that if you look for the WiFi network and the password is 12, 1-2; December, D-E-C 2-0-2-2. So 12DEC2022. So today's date in other words, hopefully, that's simple.

All right. So thank you all for coming. I need to make my favorite part of the day, the forward-looking statements. So today, we are going to make some forward-looking statements. These statements are valid only as of today, and we undertake no obligation to update them in the future. And if you have questions about our forward-looking statements, you can see our SEC Forms 10-Q and 10-K, the latest ones for more information, specifically under the section entitled Risk Factors and information about forward-looking statements.

All right. All the material for today -- well, most of the material for today is posted already on the IR section of our website under Events and Presentations. And at the end of the day, we will post updated materials, which include an appendix and other material right at the end. And in addition, there will be some posters and other things that you can access on that portion of our website as well under the event.

Okay. The focus of the day is going to be what we've been talking about very recently, these 19 high-impact launches in the near term. So we ask you to focus on the launches and the next wave of pipeline behind them. So any questions not on that, we're happy to handle that offline with the IR team or in another setting, but we want to keep the questions as much as possible, tightly focused on the agenda for today.

In terms of logistics, there are going to be 2 main sessions, 1 session now, and then we're going to have a brief break, and then there's going to be a second session, which is going to be followed by a Q&A, and then we'll come back for closing remarks and then a reception.

And just to remind you, when it's about time for the Q&A section to start, only then do we ask that you queue up on these 2 mics that are here on line, 1 on the right of the stage, 1 on the left of the stage. In addition, for those of you who are viewing us online, thank you for viewing us remotely, and there's a section towards the bottom of your screen where you'll be able to ask questions that we'll be able to respond to.

And again, if there's any questions any of you have that we're not able to answer today, we can take them offline and answer them later. Okay. So I guess that is it. Now we have our first session, which is going to be hosted by my colleague, Angela Hwang. And then our second session will be hosted by Andy Schmeltz, my other colleague from c\Commercial Strategy and Innovation. And then we will have a closing from Dave Denton, and then we will have a reception after that, as I said, on site here.

And now I would like to invite my colleague, Angela Hwang to come up to the stage. Angela, as you know, is our Chief Commercial Officer and our President of Pfizer's Biopharmaceutical Business. Angela? Please.

Angela Hwang - Pfizer Inc. - Chief Commercial Officer & President of Global Biopharmaceuticals Business

Thank you, Chris, and hi, everyone. It is great to be here. I am super proud to be in front of all of you and to help set the stage for our first in-person Investor Day since before the pandemic. So you can imagine how excited we are to be here.

There's great energy in the room. I'm hoping you guys will ask all the questions that you have on your mind because we plan to be here today to show how confident we are in our pipeline, in our business and particularly the launches that are coming up.

As Chris mentioned, our goal is for all of you to walk away with strong confidence in Pfizer's growth story and specifically to understand our near-term launches and select pipeline products. But before handing it over to our leaders, and you're going to hear from all of our business leaders today, what I wanted to do was to share some perspectives around why we believe we are truly in the most unique and exciting time in Pfizer's history.

Simply, we're just not the same company we were a few short years ago. We went from delivering \$40-plus billion in revenue to one that is expected to reach between \$99 billion to \$102 billion. Those are the figures that we've given you at Q3 earnings. So that's kind of more than doubling our revenue in 2 short years.

Of course, this is a direct result of the remarkable innovations in our COVID franchise, but this level of revenue growth is unprecedented and would be absolutely a first in the pharmaceutical industry. Applying the lessons that we have learned from both COMIRNATY and PAXLOVID, we are now pushing ourselves to reimagine our traditional ways of working so that we can move at maximum speed but also efficiency across our entire portfolio. We want to bring these breakthroughs. This is what we call our Lightspeed behaviors.

And we do this, of course, while still operating under the highest integrity and the highest scientific standards. Reputationally, we're seeing tremendous gains. As you all know, Pfizer has become a household name. The powerful brand equity that we have built over the last 170 years has now been further enhanced over the past 2 years.

And according to a recent survey, our brand awareness now stands at an impressive 82% and the latest round of reputation polling shows that 61% of the general population views Pfizer favorably, and that is compared to 42% for the industry as a whole. And this represents a significant 3-point increase since June.

Following the industry-wide declines and the economic pessimism that we saw this year related to factors such as the conflict in Ukraine, high energy costs, lessened consumer confidence across all sectors of industries.

Now if you go back to January 2020, only 28% of the general population viewed Pfizer favorably then. So of course, we're so encouraged that we've been able to sustain our reputation gains. We are also steeped in our customer transformation through the evolution of our go-to-market model.

And this is important because the speed of change is so high, and you see it everywhere with our governments, with our competitors, with our customers and we, in turn, are responding with agility, creativity and impact. In our company and in our industry, it's all about, what's next? The next breakthrough medicine or vaccine, the next game-changing technology that make solution to an unmet patient need. And this continued pursuit of what's next is embedded in our DNA. And it's a foundational driver of our purpose, which you all know is breakthroughs that change patients' lives. And it's also why we have confidence that our story is one of growth.

We have a growth plan from now to 2030. In the 2020 to the '25 period, we believe that we are on track to achieve a 6% revenue CAGR in our current in-line business. So this would mean that we exclude foreign exchange, COVID-19 revenues, future business development.

Additionally, even with the anticipated flattening out of our COVID franchise after the decline from its peak in 2022 sales we believe that this franchise will remain a multibillion-dollar revenue generator for the foreseeable future. So that's why it is important to see COVID as a growth -- as a contributor in our portfolio and part of our growth story.

As we previously said, we expect a negative impact of approximately \$17 billion through LOEs in the '25 to 2030 time frame. However, we believe that we have the substrate to not only mitigate that loss but to grow beyond it. So let's take a look at each one of those expected growth contributors. Our strong capital position has given us the ability to pursue business development opportunities with the potential to add at least \$25 billion of risk-adjusted revenues to our 2030 top line.

When we review sell-side models, the market estimates that we're approximately 1/3 of the way to delivering this \$25 billion -- and this would come from the recent BD deals that we did in Arena, Biohaven and Global Blood Therapeutics.

Next, we have an exciting wave of expected launches from our own R&D pipeline in the next 18 months. And we believe that these have the potential to generate \$20 billion in revenue. And then beyond the next 18 months, we have the potential for launches beyond that throughout the back half of the decade. And that would include interferon beta, GLP-1, inclacumab, GBT 601, our mRNA vaccines that include flu, zoster as well as a flu-COVID combo.

We believe that all of these have the potential to bring more growth towards 2030.

So these are the building blocks to our growth plan. And because we're already executing against this plan, we have the confidence that we can achieve our 2030 growth goals. So let's look more closely at the expected launches in the next 18 months. We expect to have up to 19 new products

or indications in the market, including 5, Ngenla, the COVID vaccine variant; Cibinqo, Nurtec, Oxbryta, that have already begun commercializing this year. These 19 launches, of which we believe that more than 2/3 of them have the potential to be blockbusters would be the most ever in Pfizer's history in such a short period of time.

The 15 internally developed projects alone could potentially represent \$20 billion in 2030 sales, which would more than offset the expected LOE impact. And many of these programs are already largely derisked from a clinical perspective.

Now beyond that, we know that we have to deliver and execute these launches successfully. So we need to look at our launch planning and execution, and we need to redefine what it means to be best-in-class at bringing products to market at speed and at scale.

We believe that we have to establish a standard of excellence that will enable us to outperform our internal expectations, external expectations and formidable competition. So we've approached this in 2 ways. First, we're evolving our go-to-market model to create a more relevant and impactful engagement with physicians and patients.

Second, we've reorganized our biopharma business to help us simplify decision-making, resource prioritization and execution, as well as fortifying our industry-leading capabilities in marketing, medical and access, all of this to support our new go-to-market model.

So let's talk more about this model. We began this evolution in 2019, but the pandemic has really served as an accelerant of this because during this time, many of our health care professional partners and patients required greater flexibility in their interactions with us.

And we all relied on digital tools and technology to meet their health care needs. This new model is focused on delivering a superior customer experience via an omnichannel approach that is centered around the established and strong in-person relationships that our representatives already have with customers.

Specifically, what we want to do is to give our customers a more personalized experience that is customized to their needs. For some, that could be a high-touch in-person interaction, right, much like what you know today, while others may want more of a hybrid engagement. Equally important is access to medical experts on demand who can answer specific questions when and where our physicians need it in order to help them treat their patients.

Our omnichannel offerings are underpinned by data and predictive analytics. So this is what enables us to better customize our engagement with our customers to meet their needs and their questions. And in doing so, what we will do is to create more memorable and more impactful customer and patient experiences.

So we first launched this new approach in the U.K. in late 2021. And this was followed by the U.S. in April of 2022. And then ensuing from there with 68 markets that are now leveraging this new approach. So that's not where it ends. This is planned to grow to 78 countries by the end of this year. And our final 2 major markets, which are Japan and China, will progress in 2023.

We have also enhanced our customer-facing capabilities by including a wider range of roles that serve our customers. So for example, we have more medical roles, more access roles, more virtual reps all of this beyond the traditional in-person sales rep that we all know and love.

And the thousands of customer-facing colleagues we have globally are now better equipped with hybrid engagement tools to support the customers when and how they want. And recent customer feedback tells us that we're on track, we're on the mark, and Pfizer remains a leader in customer experience.

Once fully scaled, we believe that this will be a truly differentiating capability and we are very excited to continue to advance this go-to-market model.

Now let me talk more about how we reorganized our biopharma business. Biopharma has been constantly evolving since we launched the BU or the business unit construct in 2016. After spinning off Upjohn, we were able to pivot to a pure innovative pharma company, and it was this focus that enabled us to create COMIRNATY and PAXLOVID in record time as well as deliver on the pipeline that you're hearing about today.

We reorganized our commercial operations into 3 global customer-focused units. So that would be Primary Care, Specialty Care and Oncology as well as 3 geographies, the U.S., international developed markets and the emerging markets. In addition, we have streamlined our in-country structure and decision-making processes. We've created a much greater connectivity between the development of global strategy and local execution. And we've enhanced our marketing, medical and access capabilities globally.

And we believe that our new organizational construct, coupled with this new go-to-market model will amplify our patient impact, help us to focus on the most important priorities and in that way, deliver on these world-class execution launches. Overall, our confidence to execute this plan stems from our leadership track record. And let me just give you a few examples of what we're particularly proud of.

Pfizer's U.S. field force continues to rank #1 in the industry and now for the fourth year in a row in the 2022 Sales Force IQVIA rankings. The Pfizer field team has also moved to #1 position with several key customer segments, including cardiology, nurse practitioners, OB/GYNs and urologists.

We were also recognized as one of the world's most ethical companies by Ethisphere. And finally, Pfizer ranked #4 on Fortune's annual Most Admired Companies list, the highest ranking that we've ever received. So hopefully, with all of this, I've been able to convey to you why we have such great confidence in our growth plan and how well Pfizer is positioned for both near-term as well as long-term sustainable growth.

So now let's turn to the next segment of our program, which is a review of some of our expected key launches in 2023. And for the next section, you'll be hearing directly from our senior leaders of each of these therapeutic areas. All of the presentations that you're seeing today, including the details on certain other expected key launches can be found on our website.

And so now it is my pleasure to turn it over to Rodrigo Puga, Pfizer's U.S. Commercial and Global Business Lead for Internal Medicine, who's going to kick off our first session for us. So thank you, and welcome, Rodrigo.

Rodrigo Puga - Pfizer Inc. - U.S. Commercial & Global Business Lead for Internal Medicine

Thank you very much, Angela. It is a real pleasure for me to be with all of you today to talk about our recently acquired migraine portfolio. I am Rodrigo Puga and I lead the Internal Medicine business, the U.S. commercial and the business globally. And I am here to talk about migraine. I have 2 main goals for the next 10 minutes or so. The first one is I want to demonstrate why NURTEC ODT is truly a breakthrough medication. And the second 1 is to share why we believe our potential CGRP portfolio has the potential to reach \$6 billion of revenues at peak.

And since the brand launch in early 2020, we have received countless of messages from patients expressing their gratitude. It has been incredible to witness the impact that this medication is having on patients and on the treatment paradigm and even more so to imagine the growth that this could generate in the near future.

Migraine is a huge market. And migraine is not just a headache. Migraine is a life-disrupting disease affecting more than 1 billion people worldwide. In the U.S. alone, we have 40 million people living with migraine. 1 in 5 women need to fight with this disabling disease.

And it's not only about the burden on patients and their families. It's also about the significant impact that this disease is having on the global economy, accounting for around 5.6% of the global disease burden. Migraine alone, it's more than all the other neurological diseases combined.

And at the same time, unfortunately, 30% to 40% of the patients cannot find or have not found the right solution for their migraine yet. Let's talk about the disease and the treatment approaches. Migraine, again, is a debilitating neurological disease and it can be categorized in episodic if you have 14 or less headache days per month or chronic, if you have 15 or more.

Important for you to understand is that 94% of the patients are in the episodic stage of the disease and only 6% are chronic migraine patients. In terms of treatment approaches, you can treat migraine acutely or preventively. And it's also important to understand that all patients, even if they are taking a preventive treatment, will need at some point some acute treatment when they experience a breakthrough migraine.

And all this is important because later on, I will talk and explain how our potential CGRP portfolio has the potential or the possibility to cover the full migraine spectrum. Unfortunately, when we talk about the current standard of care, there are many limitations. If we talk about acute treatment where treatments are the standard of care. They face tolerability issues, cardiovascular contraindication, the need for repeat dosing, the risk of developing medication overuse headache which actually exacerbates the frequency and the severity of the migraine, which is exactly the opposite of what you're trying to obtain with the migraine treatment.

If we talk about preventive treatment, again, patients face tolerability issues, suboptimal discontinuation rate. The long duration of time required to obtain efficacy and many of the available treatments are injectable treatments that, as you can imagine, is not the most preferred route of administration for patients.

And this is why we believe that Nurtec or Vydura, which is the brand approved in the European Union can help address the needs of many, many patients. On the acute setting, it has demonstrated strong efficacy with 86% of the patients not needing a rescue medication. It has not been associated with the risk of medication overuse headache. It does not have cardiovascular contraindications. And if we talk about the safety and tolerability profile, the most common adverse event is nausea at 2% versus placebo, 0.4% giving this new medication a very good safety and tolerability profile.

Talking about the preventive indication. Again, strong efficacy. This drug has demonstrated to reduce 30% the number of migraine days at week 1. It's an oral treatment, and it's preferred in most cases, over injectable and very well tolerated. Adverse events, the most common adverse events are again nausea at 2.7%, abdominal pain and dyspepsia are 2.4% versus 0.8% of placebo in both cases.

And something that I want to highlight is, if you remember, if you see the rates in the acute setting and the preventive setting, they are very similar. And for the preventive indication, you are taking this medication every other day. So a very good safety and tolerability profile.

Before NURTEC ODT, there was a in the migraine treatment paradigm because you either had options to only treat acute or only treat prevention. And NURTEC bridges that gap being the first and only approved for both acute and prevention, providing flexibility to physicians and patients in managing both with only 1 pill.

And this is why we believe this new drug is changing the treatment paradigm. And we believe that this is a unique characteristic that will only continue to differentiate the brand over time. On top of that, NURTEC ODT is the only CGRP that comes in an oral disintegrated tablet, which is very convenient for patients because they don't require water for the intake.

Talking about the clinical profile of this new medication. On the acute setting, it has demonstrated freedom of pain and the most bothersome symptoms at 2 hours. In a secondary endpoint in the pivotal clinical trial also demonstrated pain relief and return to normal function in as little as 60 minutes. And for the 4 endpoints that I've just mentioned, the effect was sustained during 48 hours, again, with only 1 dose.

If we talk about the prevention indication, it reduces the monthly migraine days, more than 50% in half of the patients at month 3, and it has a strong safety and tolerability profile.

But let's talk now and let's see how this clinical profile is being translated into market results. And the first thing that you can see on the slide is that NURTEC ODT is already the market leader. It's the most prescribed oral CGRP, and it has more than 50% of the market with 50 -- more than 50% of the TRx share.

And something that I would like to highlight is that since we announced the acquisition in May this year, we see -- we saw no disruption. On the contrary, we keep separating from the competitors, and we gained 6.4% in TRx share. In the U.S. alone, NURTEC ODT was already used by more than 600,000 unique patients and also by more than 90,000 unique prescribers.

If we talk about the most important leading indicator, new-to-brand prescriptions, we are also leading there with 51.6% of share. So this is why we only expect even stronger growth in the coming months and year for this brand. And if we review the migraine market dynamics, what we can see is a high-growth brand in a high-growth market.

We believe this market could grow in the next 5 years to 40 million prescriptions. And despite being new, the oral CGRPs are disrupting the broader U.S. market. Biohaven mentioned many times that it was a matter of time for our CGRPs to overtake the injectable CGRP monoclonal antibodies.

And this is exactly what happened during this summer, as you can see on the screen. But also, they are disrupting the standard of care in general. If we talk about acute where triptans are the standard of care. You can see on the chart how triptans are declining. If we talk about preventive, you can see how topiramate, which is the standard of care is also declining. Still, if you see the right-hand side of the slide, oral CGRPs only represent 16% of the TRx share and 23% of the NBRx which tells about the significant growth opportunity ahead. And again, in this new market, NURTEC is the market leader.

And this is why we believe oral CGRPs can be the first line of therapy and can reach around 40% of the overall migraine market. One additional data point that I want to leave with you is, today, only 22% of NURTEC ODT scripts are coming from primary care physician, a space where Pfizer really excels and where we are planning to leverage all our capabilities.

This slide shows you how we are building a franchise in the CGRP and in the migraine space to meet the needs of the patients. I mentioned that you can treat migraine acutely or preventively. And the prescription will depend on the number of headache days per month and the severity of those.

NURTEC ODT can cover all the blue space that you can see there. The full acute range for both episodic and chronic migraine and also it's indicated for episodic prevention, where you can find the majority of the patients, actually 94% of the patients and is already the market leader.

But on top of that, if approved by the FDA, we are planning to launch zavegepant who has the potential to be the first CGRP in an intranasal formulation for the acute treatment of migraine. This new drug has demonstrated pain relief in as little as 15 minutes, and we believe it could be suitable for patients where speed of onset is paramount.

And also, it could be very suitable for patients who experience nausea and vomiting who would, of course, preclude them of taking an oral medication. And we are developing these NURTEC and zavegepant together, we think, are complementary. And as you can see, the only missing space is the chronic prevention. We are not participating in that space. And this is why we are developing a Phase III clinical trial as an oral formulation for zavegepant for the prevention of chronic migraine. And if successful, and the takeaway here is that we are working to build a franchise that can help the full migraine spectrum.

Now I want to share with you our key revenue assumptions and why we believe this could be a \$6 billion franchise. The data that you can see on the screen is the data that we are using for our forecast and that you can use for modeling purposes. We think that if you run the numbers, you will be able to get -- you have here rimegepant, which is NURTEC or Vydura, and you have zavegepant, both in the intranasal and in the oral formulation.

And if you run those numbers, you will be able to get to our assumption, which is that this portfolio could reach \$6 billion at peak. I would like now to highlight some of the key commercial strategies that we are putting together to amplify this portfolio.

So starting from the very successful foundation that Biohaven built, we are adding more to that equation. We are leveraging the Pfizer scale, deploying our best-in-class key account management organization to the 250 leading health care system in the United States and that -- those systems cover 75% of all the patient care and 88% of all the health care practitioners.

We have already doubled the number of sales reps covering an additional number of 72,000 HCPs. We have multiplied 8x the number of medical field support for this brand. And again, these are some of the things that we are doing by leveraging the Pfizer scale to take the migraine portfolio to the next level.

And I think that you all know that we do have the global scale to launch this asset that today is only in the U.S. to launch it globally. And we are working, as Angela mentioned, at Lightspeed to launch NURTEC or Vydura around the world. This medication is already approved in the European Union, the U.K. and some parts of the Middle East, and we are expecting regulatory approvals from around the world in the coming months and years.

We have also submitted for the acute indication in China and if successful, we will be able to help the 130 million people living with migraine in that country. And on top of that, as I mentioned, we are expecting the approval of zavegepant intranasal as the potential first-in-class intranasal formulation and working with a Phase III clinical trial with zavegepant oral.

And this is why we believe that Pfizer is well positioned to be a leader in migraine. We have potentially a best-in-class portfolio for migraine. We have the history of building blockbusters. Our sites are set high for this recently acquired asset, and we are aiming to help the 1 billion migraine sufferers around the world with a high unmet need.

So I hope that by now, I was able to achieve my 2 goals, which is to demonstrate why NURTEC ODT is truly a breakthrough medication and that our potential CGRP portfolio has the potential to reach \$6 billion of revenues at peak.

Thank you very much. And I would like now to hand it over to Sinan Atlig. Thank you again.

Sinan Atlig - Pfizer Inc. - U.S. Commercial & Global Business Lead for Vaccines

Good afternoon, everyone. My name is Sinan Atlig and I am the U.S. Commercial and Global Business Lead for Vaccines. It is my 22nd year now at Pfizer, and I have worked across a variety of geographies and brands.

In my previous role, I was leading Pfizer Vaccines in international developed markets and have been the face of Pfizer to the European Commission and to different governments around the world during the launch of our COVID-19 vaccine together with our partner, BioNTech.

But today, I won't be talking about COVID-19 but another contagious virus that can cause serious -- potentially serious respiratory illness, which is RSV, Respiratory Syncytial Virus. I feel very proud to be talking about RSV vaccine candidates because of the unmet need that we see across the globe.

There is not a day that goes by in which we don't see a news clip or an article about RSV epidemic in the U.S. and across the world. In the U.S., ICU beds have been overflowing and there are recent calls to declare public health care emergency.

As you see on the first point in the slide for the maternal, the unmet medical need for babies is clear and well characterized. But there is also a significant burden for older adults, which is similar to influenza. As there are currently no vaccine or specific treatment options available, RSV is causing a significant burden on the health care system, on the economic system and on the individual level, whether we talk about older adults, babies, caregivers or parents.

That is why I am so proud to present our unique approach to RSV. Our vaccine candidate is a bivalent protein-based vaccine, helping protect against both RSV A and RSV B strains. Because of this, our vaccine candidate does not rely on cross protection. Another very important aspect of our vaccine is that it does not include any adjuvant or viral vector components. We have 1 single vaccine candidate, the same formulation that we are filing regulatory applications for 2 distinct indications based on the compelling data in these 2 separate populations.

Our vaccine candidate is the only late-stage asset with potential indications in both older adults and maternal immunization. As you may have heard, last week, we have announced the BLA acceptance and the priority review for our older adult indication by the FDA with a PDUFA date in May of 2023.

And as we have announced earlier in the year in our older adult Phase 3 study, our vaccine candidate showed strong efficacy and more importantly, higher efficacy in more severe symptomatic cases. In addition, we have seen consistent efficacy different -- across different patient subgroups.

The DMC noted that the vaccine was well tolerated with no safety concerns for vaccinated individuals. And again, I want to emphasize that our investigational vaccine does not have any adjuvant or viral vector component. Before going over the Phase III interim study results on maternal indication, I would like to underline Pfizer's pioneering approach in RSV prevention, immunizing women during pregnancy to help provide protection for their babies immediately at birth and continuing up to 6 months, which is the -- which is the period with the highest vulnerability for the infants.

Seeing this innovative approach producing these results makes me again feel very proud. As we shared earlier in the year, at the recommendation of the independent data monitoring committee and in consultation with the FDA, we have stopped enrollment in our trial and plan to submit our BLA to the FDA by the end of the year.

The Phase 3 data results demonstrate our vaccine candidate has a high level of efficacy, and the DMC indicated it was well tolerated with no safety concerns for either the vaccinated mothers or their infants. If approved, this will be the first investigational vaccine to help prevent RSV immediately at birth or better set from the first breath.

At Pfizer, we are uniquely positioned to commercialize our vaccine candidate in both indications. We rely on our best-in-class commercial capabilities and decades of launch excellence that we have recently proven with our COVID-19 vaccine rollout and our Prevnar 20 adult launch in this indication. We have robust and differentiated contract model -- contracting models, both with IDNs, the integrated delivery networks and with retailers.

We also have proven reliable manufacturing supply and distribution capabilities and expertise in educating customers across various channels. As we look towards the commercial opportunity and the significant unmet need, we believe we have the potential to make a public health impact.

Based on our Phase 3 interim analysis results in both potential indications, coupled with the unmet need, we project potential blockbuster revenues for our vaccine candidates. First, there are 2 distinct and big population groups that can benefit from this protection. Although the pregnant women population is relatively smaller, the burden of RSV is much better characterized with a clear need.

Hence, we believe we can potentially reach a high uptake rate between 60% to 70%. As there are no other maternal immunization candidates in late-stage development, we anticipate 100% market share. If approved, we anticipate our data to support a favorable and year-round recommendation by ACIP.

Monoclonal antibodies can be important complementary options, especially for babies who may need additional protection if they are approved. Let's move to the older adult side. For older adults, the burden of the disease is less well known and often mistaken with flu and other causes of respiratory diseases. Despite this, we believe our vaccine can reach peak uptake rates of 50% to 60%.

In this indication, we will have competition. But based on our vaccines clinical profile, our commercial capabilities and our anticipated launch timing, we believe we can potentially reach and sustain a market share between 45% to 60%. If approved, we anticipate our data to support a routine and age-based recommendation by ACIP.

The key to success will be education. Educating everyone on the burden of the disease and on the favorable profile of our vaccine candidate, whether they are HCPs, providers, retailers, expecting mothers, older adults or caregivers. That will be the key to launch our investigational vaccine to address the significant unmet need and to reach our vaccine candidate's potential which rolls up to be a potential multibillion dollar opportunity, again, if approved and recommended.

Finally, our RSV vaccine candidate has the potential to strengthen our ever-growing respiratory portfolio of Prevnar franchise and COVID-19 franchise. Like with COVID-19, Pfizer's commitment does not stop at the vaccine candidate, complementing our efforts to advance our RSV vaccine candidate, we also have Sisunatovir, an investigational therapeutic with the potential to help treat RSV-related illness. That is why we believe Pfizer is uniquely positioned to deliver successful launches and build upon our legacy as a leader in helping prevent and treat respiratory diseases.

Thank you all for your attention. I would now like to hand it over to Kevin Sullivan, who leads our Specialty Care business globally, and who will provide details on Etrasimod and Ritlecitinib.

Kevin Sullivan - Pfizer Inc. - Global Specialty Care & U.S. President

Good afternoon, everyone. It's great to be here with you today. My name is Kevin Sullivan, and I lead Specialty Care globally. The Specialty Care business plays a critical role as we work to address patient needs in the hospital inflammation, immunology and rare disease areas.

But today, I'm pleased to speak with you about 2 near-term potential breakthroughs in inflammation and immunology. And I'd like to start with ulcerative colitis. The best way to frame all ulcerative colitis, the disease overview is to see ulcerative colitis through the eyes of a patient. "UC diagnosis is a life sentence that have it on the body it turns any day to chaos in an instant."

That quote really sparks something we need to keep in mind as we dive in. Ulcerative colitis is a chronic and often debilitating inflammatory bowel disease. We hear all the time about the impact that this disease has on patients' lives. Many are dealing with severe symptoms, such as chronic diarrhea with blood, pain and weight loss.

And even with all the treatments available today, up to 30% of UC patients still progress to surgery, where all or part of their colon is removed, which has a significant impact on the quality of life. UC an estimated 1 million people in the U.S. alone. And this is a disease that impacts younger people, half are diagnosed with UC by the age of 35. So they're dealing with all of this disruption and pain during very active years of their lives when they're attempting to advance their careers or raise their family. And while those statistics I share speak largely to hardships of UC patient experience, that's really just the beginning. We must also empathize with the deep emotional turmoil that many are forced to live with.

Young often healthy people get thrown into a life of perpetual uncertainty and a sheer loss of basic control. Another quote, "You don't know when it's going to strike, and I mean that sincerely." Some can't even think about going anywhere if they're not 30 seconds away from a bathroom.

And what's more is the quote continues to say, "It's not only the physical feeling but it's the mental and emotional aspects as well." Frankly, they're robbed of their dignity. And at the core, they're looking for stability and relief.

So now let's take a look at the current UC treatment landscape. The majority of diagnosed patients are earlier in their disease, often with mild to moderate UC and are being treated with conventional therapies and/or steroids. That's the area in blue that makes up 64% of the treated patients on this slide.

However, when -- upon failure of conventional therapies, UC patients progress to advanced therapies such as biologics and JAK inhibitors, that's the area in right in green. These advanced patients are most often further progressed and are diagnosed with moderate to severe UC.

But what we also know, however, is that a large portion of patients on conventional therapies are either suboptimally maintained or have failed, but are hesitant to progress to advanced therapies. And the top reasons ACP cite for this hesitancy are patients are either concerned about the safety or side effect profile of current advanced treatments and patients are concerned about switching from an oral conventional therapy to an IV or subcutaneous injection advanced therapy.

And these are real concerns that keep patients on conventional therapies for too long, hindering their opportunity to reach remission. And for patients that do convert to advanced therapy, 52% still are not retaining long-term remission today. So let's apply a treatment lens to the patient journey, hopefully, paint a clear picture of what we see as a significant unmet need in this area.

On the left, you have what we call conventional therapy. These are 4 milder disease inclusive of corticosteroids, which is still used sparingly to gain quick controls of a flare. And on the right are the more advanced treatments prior to the entrance of S1Ps. This is comprised of largely biologics and JAKs. We'll talk more about S1Ps on a later slide.

But if I could bring your attention to now the green shaded area in the middle. When patients require a step-up from conventional to advanced therapy, most often, this moves the patient away from oral treatments, even though 89% of advanced naive patients prefer an oral treatment.

Instead, patients are often moved to biologic therapies that either require an IV or a subcu injection. Because of limited oral options in the first-line advanced setting, doctors are regularly having to put patients on therapies with more challenging routes of administration.

The only oral option on the advanced side was JAKs, but remember, they're most often prescribed after first-line failure for their label. So let's take a closer look at etrasimod. Etrasimod is a small molecule S1P receptor modulator that selectively activates S1P receptors 1, 4 and 5. By partially and reversibly reducing the number of lymphocytes in peripheral blood, etrasimod reduces the number of activated lymphocytes in gut tissue, which is believed to be how it exerts therapeutic effects in UC.

And more specifically, this what has us believing that has the potential to become not only just the next S1P to come to market, but the S1P to carry with it the clinical profile that you guys are looking for and make it potentially best-in-class.

Let's start with what's on the left side of the slide. And while all this is subject to regulatory approval and labeling, some of the key potential differentiators are, the safety profile of etrasimod supports the potential for a no-box morning. It's a once-a-day oral, tablet is about the size of a baby aspirin and the data supports initiation without the need for titration, so it's simple.

Very importantly, the efficacy profile is generally on par with what physicians are looking for with the most prescribed biologics in first line, but etrasimod is not a biologic. Notably, we saw strong clinical efficacy in the bio naive patient population. So to be clear, this is the segment of patients taking their first advanced therapy after failing conventional, so simulating the first line advanced position.

And the long-term remission after 1 year is 100% steroid-free remission, which is so important for patients. Now if we look to the right side of the slide, this takes a closer look at the data emerging from our clinical trials. The ELEVATE program was a huge success in demonstrating a strong efficacy profile.

ELEVATE was comprised of 2 independent Phase 3 trials. ELEVATE UC 12, which was a 12-week induction study only and ELEVATE UC 52 was a separate trial composed of a 12-week induction followed by a 40-week maintenance period through -- in a treat-through trial design.

And this is noteworthy because it's a little different than some of the more recent Phase 3 trials in UC. A benefit of this design is it provides a sense what the clinician and patients can expect after a full year of treatment because all patients randomized on day 1 are included in the efficacy calculation at week 52, both the induction responders and the nonresponders.

In contrast, when you rerandomize a trial design and evaluate efficacy at 52 weeks, but only among a subset of patients that achieve response, and then you exclude the ones that did not achieve clinical response after induction. We didn't do that. We did a pull-through trial design. So for etrasimod across both induction endpoints, 1 in 4 patients were in clinical remission after 12 weeks of treatment and that further increased at week 52, that proportion. 1 in every 3 patients enrolled in week 0 were in remission at week 52. And to reiterate, that's across everyone enrolled, not just the responders after the induction.

When we turn to safety, we're very pleased with the overall risk benefit profile as well. Treatment-emergent adverse events, including serious AEs were similar between treatment groups in both trials, and you can see them listed here on the slide. Let's now take a look at the UC competitive set. When you look at the growth of this category and all the new options that have arrived in the last 5 to 10 years, before the arrival of S1Ps, a couple of points are clear.

Number one, the UC patient is better off today than they were a decade ago. However, having said that, there's still an opportunity -- it's still open in this growing disease to bring a treatment profile that could be highly attractive for advanced naive UC patients. Then in mid-2021, there was the arrival of the first S1P into the UC treatment landscape. That's the column furthest to the left.

And with that was the possibility with this new MOA that we were another step closer to delivering on the desired profile of a first-line advanced treatment, helping to address the remaining unmet needs for advanced naive patients. Remember the stat I mentioned earlier, 89% of advanced-naive patients prefer an oral therapy. And yet today, less than 3% of patients receive an oral as their first-line advanced treatment in the U.S.

So if I could just recap for a minute, let's think back to the patient we showed earlier and the hardship and the loss of the most basic and normal human freedoms. And now let's think of the GI doctor, the one meeting to make an important first-line advanced treatment decision. The GI, of course, would want what's best for the patient clinically but also wants a treatment that could meet the patient's preference for an oral therapy.

In our U.S. patient ATU survey, when you see patients were shown etrasimod's blinded target product profile, 74% responded that they were very likely to ask their HCP about etrasimod. And you can see from the checkmarks on this page, etrasimod may be the kind of treatment option to meet the needs of both patients and physicians.

And therefore, if approved, we aim for etrasimod to be considered a go-to first-line oral treatment for patients that fail conventional therapy. A focus area for Pfizer I&I is addressing the unmet need in gastroenterology. And here, I'd just like to take a minute and demonstrate how we're committed to fulfilling that purpose. First, with the potential approval of etrasimod, Pfizer could become the only company to offer a UC therapeutic portfolio that addresses the need for additional oral options in the first line with etrasimod, include biosimilars for the well-known TNF therapies with Inflectra and Abrilada and includes the first oral JAK inhibitor approved in UC.

Investing in a robust portfolio of UC treatments is just one way we're demonstrating our commitment. Secondly, since we acquired Arena Pharmaceuticals earlier this year, we have doubled down in assessing every way we could potentially accelerate commercialization of etrasimod. And I'm thrilled to highlight that we've been able to accelerate regulatory submissions in over 50% of priority markets by investing in the strength, scale and expertise of Pfizer's global regulatory team.

And finally, we know that patients are at the center of Pfizer's purpose, breakthrough that change patients' lives. So it's our ambition to raise the standard of caring for all IBD patients. We have the insights, we have the scale and we have the drive to become the preferred partner dedicated to patient engagement and advocacy providing holistic support for IBD patients.

So if I could, I'd like to close with a few key figures on the market potential for etrasimod in UC. To start, there are more than 1.7 million patients in the top 5 developed markets alone were diagnosed with UC. Across global markets, we also see for etrasimod in 80% Rx treatment rate, up to about 35% of patients treated with advanced therapies and a 50% market growth expected over the next 5 years all leading to \$1 billion to \$2 billion blockbuster revenue potential for etrasimod.

But just as important, of course, it also makes us extremely excited about the opportunity etrasimod has, if approved, to ignite a paradigm shift for UC patients and providers around the world. Now if we could, I'd like to now turn my attention to medical dermatology and alopecia areata. Excuse me for one second. Before diving in, like we did before, I think it's important to take a minute to talk a little bit about what alopecia areata is and who it impacts. Alopecia areata or AA is often shocked up as being mostly cosmetic, but it is, in fact, an autoimmune disease that impacts up to 2% of the global population.

The hallmark feature is partial or complete hair loss that can occur on the scalp, face or body and as you've seen here, the degree of hair loss can range from patchy to total loss. Contrary to what most people think, AA, can affect any age, gender, race, ethnicity does not discriminate. And in addition to the physical effects and the burden of hair loss like losing, say, the protective effect of eyebrows or eyelashes on the face, there are deep psychosocial impacts that can significantly affect someone's daily life.

The reflection in the mirror is constantly changing and morphing into something else. And often patients tell us they no longer feel like they recognize the person that they were before. In fact, studies of patients with AA have shown that a majority, 85% report that coping with AA is a daily challenge. And more than 60% stated that they have withdrawn from social activities due to their AA. This disease typically happens before the age of 40. So there are a lot of young people impacted at a time in their lives when they're looking to lead active lives. But instead, they often withdraw and feel isolated and alone.

45% of patients report that they missed work or even left their job. And with more than half acknowledging that they feel insecure, inadequate, self-conscious, one thing is definitely clear this is a disease with impact that goes well beyond hair loss. The quotes on this slide are from an FDA patient panel that took place a few years ago and may reflect with both we and dermatologists here regularly, that AA can make patients feel, "Damaged or abnormal," battering their self-esteem because AA has changed their life.

These are all very powerful words, and it's clear that these patients continue to suffer and they deserve better. So when we look at the current treatment paradigm, we need to acknowledge that until June of this year, there weren't any approved treatment options for AA in the U.S. or Europe. This let patients and physicians treating with off-label therapies like steroids that are commonly administered topically or via intralesional injection into the hair follicle, which could be, of course, very painful.

This also had a high level of dissatisfaction with these treatments because of limited efficacy plus the burden on patients is significant, including the need for painful injections every few months. And for patients a more extensive disease, local and injectable steroids may not even be effective or appropriate.

And oral steroids are not appropriate for long-term use. So with no approved treatment options for adolescents and only 1 other treatment approved for adults with severe AA, these patients and their physicians need more options. And if approved, ritlecitinib has the potential to become a first-line oral treatment that potentially delivers hair regrowth that can be maintained over time with continued use.

And as the first in a new investigational class of oral kinase inhibitors, ritlecitinib is a dual tech JAK3 inhibitor with a selectivity profile distinct from other approved JAK inhibitors. The clinical results from our registrational study, ALLEGRO-2b/3, support the breakthrough potential of ritlecitinib if approved. Let's look at the top side of this graph.

You can see the primary U.S. endpoint of SALT being less than or equal to 20, just for context, that measure corresponds to patients achieving 80% or more scalp hair coverage. It's also important to note that the patients in ALLEGRO-2b/3 at their baseline had at least 50% or more scalp hair loss. And you can see in blue that nearly 1 in 4 patients achieved 80% or more scalp hair coverage at 6 months on the 50-milligram dose. This is compared to only 1.5% in on the placebo arm.

Moving now to the bottom, the line graph on the bottom. If we continue treatment with ritlecitinib out to 48 weeks, you can see that even more patients can achieve 80% or more scalp hair coverage with 43.2% of patients in the 50-milligram arm.

Not all patients achieved these results, but it gives you an appreciation of the impact that this could have on the life of a patient with AA. The pictures on the right side of the slide illustrate what that potential effect for patients might be. These pictures were taken from our clinical program and show 2 different patients at baseline at week 24, which was the primary endpoint, and then at week 48, and the results are quite significant.

If you look at the week 24 photos, this is what 80% or more scalp hair coverage looks like. And again, not all patients taking riles achieve these results, as I just mentioned, but the pictures on the potential response are compelling. With regard to safety, ritlecitinib's profile in ALLEGRO-2b/3 and was consistent with previous studies.

Overall, the percentage of patients with AEs, serious AEs or discontinuing due to AEs were similar across all patient groups. And you can see the most common AEs listed on the bottom right of this slide. Also, our Phase 3 long-term study continues to investigate the safety and efficacy of ritlecitinib beyond 48 weeks up to 3 years for adults and adolescents.

Interim results from Allegro LT are consistent with the primary Phase IIb/III study, ritlecitinib was generally well tolerated with sustained clinical and patient reported efficacy up to month 24 in patients aged 12 years and up with AA. So in summary, the Phase 3 data results demonstrated robust efficacy, delivering sustained, complete or near complete scalp payer regrowth. And that's why we're confident with that ritlecitinib, if approved, has the potential to redefine the standard of care as a potential treatment option for AA that's well differentiated from current treatments.

So if I could summarize our view of the potential commercial opportunity on ritlecitinib, subject to regulatory approval. As a first in a new investigational class of oral kinase inhibitors, ritlecitinib has the unique selectivity profile in AA distinct from currently approved JAK inhibitors, including the one currently approved for AA.

Ritlecitinib reduces AA inflammation in 2 ways by targeting 2 different types of kinases, TEK family and JAK3, while remaining devoid of JAK1, JAK2 and TYK2 inhibition. Our studies included patients down to age 12, and if approved, ritlecitinib would be the only approved treatment option for adolescent patients aged 12 to 17 years old.

The Phase III data results demonstrated robust efficacy delivering sustained complete or near complete scalp regrowth. And while there are no head-to-head trials with other therapies, we believe that if approved, ritlecitinib has the potential to become a significant advance compared to the traditional treatment approaches for this disease, which are not appropriate for long-term use and present limited efficacy.

And that's why we're so excited about ritlecitinib. We can now pivot to how we're laser focused in delivering a best-in-class launch for ritlecitinib. Our approach is anchored on 3 core areas. First, we continue to develop the AA market, which we're already doing via omnichannel approaches, to educate stakeholders about AA and its associated burden.

This includes payers, dermatologists and consumers as well as through close partnership with patient advocacy groups like the National Alopecia Areata Foundation in the U.S. and others in other key markets.

Second, we plan to unlock access by advocating for adequate coverage and reimbursement by articulating the unmet need and impact of AA to payers and through Pfizer's dermatology patient access platform. And third, if approved, we'll strive to drive adoption through industry-leading patient activation initiatives, leveraging our dermatology field for us and Pfizer's scientific leadership in I&I and executing with excellence on all of this will help position ritlecitinib as the treatment of choice for systemic appropriate patients.

And I'd like to close again with a few figures on the market potential. As we stated, AA is an area of significant unmet need and with very limited treatment options. So in assessing addressable market potential, even when using conservative estimates to assess eligible patients, ritlecitinib has the potential to reach revenues of \$1 billion globally at peak, breaking it down and taking the G7 countries alone, about 6.4 million adults live with alopecia areata, of which 43% have the 50% or more scalp hair loss. This is aligned with the inclusion criteria that I mentioned in our clinical trial.

Of those, we estimate about 28% to 49% regularly see their dermatologists. And of those, we estimate up to 46% would be candidates for advanced treatment. Therefore, we're confident that if approved, ritlecitinib has the potential to transform the AA treatment paradigm, address the unmet patient need, deliver substantial value to Pfizer and redefine the standard of care in how patients manage their AA.

And going beyond AA, we're also excited about the next potential opportunity for ritlecitinib with vitiligo. So in closing, hopefully, you can see that we're extremely excited about both ritlecitinib and etrasimod and their potential to change patients' lives. And thank you so much for your time and attention.

I'd like to now turn it over to Suneet Varma who leads the Oncology business globally. Thank you.

Suneet Varma - Pfizer Inc. - Global Oncology & U.S. President

Good afternoon. I can take a breath now. We've had a number of presentations. I know it's a lot of material, I'll be the last presenter of the day presenting 2 different opportunities, and then we'll have time for Q&A.

My name is Suneet Varma, I'm the Global Oncology and U.S. President for Pfizer. As you may know, I came into this role from Rare Disease in September. And I now oversee our growing oncology portfolio of 24 different medicines that treat 30 types of cancer and we had more than \$12 billion in revenue last year.

We continue -- we expect Oncology to continue to be an important business for Pfizer. And not just now and not just for the next few years, but frankly, for the rest of the decade. Today, I'm going to highlight 2 exciting potential launches from our oncology portfolio that are expected in 2023. I'll start with elranatamab, our BCMA bispecific in multiple myeloma. Now I may sometimes refer to elranatamab as elra for short. Hematologic malignancies are cancers that affect the blood, bone marrow and lymph nodes.

While the prevalence for these cancers is relatively small there are significant unmet needs. And this can be very deadly depending upon the specific type of blood cancer. The 3 main types of blood cancer are leukemia, lymphoma and myeloma.

Multiple myeloma is a blood cancer that affects plasma cells made in the bone marrow, causing them to grow and divide. Multiple myeloma is the second most common blood cancer worldwide and is associated with a poor overall prognosis. There are several multiple myeloma drugs on the market, but none are curative. This leaves a significant unmet need with only half of the patients surviving 5 years or more.

Second and later relapses are unfortunately all too common in multiple myeloma and they can be devastating to patients because after each relapse, patients see a higher risk of treatment resistance, shorter remissions and shorter response durations. This amplifies the effect of the disease and the need for new treatment options.

A global prospective study found that the medium duration of response for later line treatments are triple-class exposed is only around 7 months. 7 months, that's it. Therefore, new treatments with novel mechanisms of actions or MOAs that counter mechanisms leading to resistance, including immune evasion are essential to improve outcomes for these patients.

Multiple myeloma, as we all know, has been a mix of older and recent more new drugs. BCMA is an antigen highly expressed in multiple myeloma cells and is emerging as a very promising new immunotherapeutic target with the potential to transform treatment in this space.

Three types of BCMA therapies are currently being developed, including CAR-T and ADC and the newest modality bispecific antibodies. As you know, CAR-T cell therapy is a type of treatment in which patients' T cells are changed in the laboratory, so they will attack the cancer cells. Despite high efficacy, CAR-T is complex, personalized and is a process that limits the utilization to qualifying academic centers.

ADCs, on the other hand, are targeted therapies that are purposely designed to deliver cytotoxins to cancer cells. They've been shown they've shown a lot of promise in both solid tumors and hematologic cancers. However, there is mixed enthusiasm amongst HCPs for ADCs in multiple myeloma due to moderate efficacy. And lastly, we have BCMA-targeted bispecific antibodies.

By now, most of you are familiar with bispecifics and the MOA. Among the BCMA targeted therapies, we believe bispecifics have the potential to become the next standard of care specifically across the full treatment paradigm, and I'll show that later, because their promising efficacy, safety profile and combination and convenience opportunities are many. In particular, BCMA bispecifics have the potential to put transformative efficacy in reach of a broad range of patients. What we are hearing from HCPs or health care professionals supports this vision.

Given the factors that I discussed previously that are currently limiting the availability of some of these novel therapies, elranatamab has the potential to reach an even greater number of patients as an off-the-shelf option. And based on the emerging efficacy and safety profile, combined with the ease of administration, we believe we have a winner with elranatamab. It is potentially the BCMA-targeted agent of choice subject to regulatory approval.

As I highlighted previously, there are high rates of relapse with multiple myeloma with outcomes declining significantly after relapse. This area -- the area -- sorry, with the highest unmet need is the late-line setting where there are the fewest treatment options. Pfizer set out to attack this problem by studying elranatamab in this severe patient population.

But before we dive into the emerging efficacy data, let me share with you more detail about the patient population we are looking at in the first pivotal trial for elranatamab MagnetisMM-3. MagnetisMM-3 is a Phase 2 study evaluating the safety and efficacy of elranatamab as monotherapy in patients whose disease has relapsed or is refractory to 3 primary classes of existing treatments. This is a broad, heavily pretreated population. This comes to life when you compare some of the characteristics from MagnetisMM-3, sometimes I'll refer to it as MM3 to real-world triple class-exposed patients shown on this slide.

In particular, I want to call your attention to the high percentage of patients enrolled in MM3 who were considered penta-drug refractory at approximately 1 in 2 compared to only 1 in 6 in the real-world setting. In addition, MM3 included a significantly high number of patients who were previously exposed to extramedullary disease or EMD, which is also associated with poor outcomes. Nearly 3x more in our MM3 population than the real-world setting.

All of this highlights a very severe advanced patient populations with characteristics associated with poor outcomes representing an area with, therefore, the highest unmet need. Conducting this trial in this difficult-to-treat patient population also set a significant high bar for efficacy and also safety measures for MM3.

Remembering that high bar that I noted on the last slide, the MM3 results to date highlight the potential for LRA to be a leader in the bispecific class. It makes us bullish about the opportunity, frankly, when moving into earlier lines of therapy 2. 2 days ago at ASH, and I was at ASH just got back yesterday, we presented an updated longer follow-up update on elranatamab from Cohort A of MagnetisMM-3 in patients who are BCMA naive. And look -- we looked at this in 3 separate areas that frankly got us pretty jazzed, early and deep response, manageable safety profile and also the dosing convenience.

In the primary cohort, which was not BCMA exposed, data showed early and deep response after 10.4 months of follow-up, a high objective response rate of 61% with 84% probability of maintaining response at 9 months. So real durability on top of that response.

The data also suggests a manageable safety profile as it relates to cytokine release syndrome or CRS. We believe these AEs may be mitigated by the step-up dosing. These results are really compelling in a heavily pretreated patient population, and I heard it in the room when I was in the symposium as well.

And when we think about factors that influence HCP preference and choice, elranatamab has the potential to have a preferred combination of efficacy, of safety, and also the accessibility with its dosing convenience, including off-the-shelf, subcu dosing, the potential for every other week dosing and less frequent dosing for responding patients. This makes it a good option in academic institutions, of course, but also community settings.

In fact, nearly 70% of our surveyed HCPs are highly impressed with the overall elranatamab portfolio. And by the way, that's a top 2 box, not on a 5-point scale, but on a 7-point scale. This underscores our belief that elra has the potential to be the leading bispecific. And in turn, the leading BCMA agent across all stages of multiple myeloma.

In summary, we, I, all excited by the potential for elra to reach a rapidly expanding number of patients globally across the treatment paradigm. Of course, this is subject to approvals and positive readouts in ongoing studies, and there are many. We expect bispecifics to play a major role in the treatment paradigm for multiple myeloma, and we believe elra has a right to win in the bispecific space because of the data that I just highlighted.

We see this momentum as the start of something great. We're studying elra across many different patient populations. Starting with triple class refractory, we expect to move to double class exposed and then ultimately moved to the newly diagnosed setting. As I mentioned, we start here and given the profile, we move to earlier lines of use.

As you see on this slide, we start with about 15,000 triple class-exposed patients. And then we build over time. We move upwards to approximately 90,000 possible patients treated across all lines of therapy. As the populations are added, we expect the duration of therapy to be longer as well. Across the treatment paradigm, we anticipate a possibility of over \$4 billion in potential peak revenue for elranatamab.

I'm going to do what Kevin did before I move to the next one. The only difference is I didn't come with an open bottle. So just give me a moment. Sorry, that's Angela's seat for the Q&A, and just dropped a little bit of water.

Now I'll shift to another exciting launch. The second one that I mentioned I talk about in the oncology portfolio, Talzenna, and prostate cancer. Great progress has been made in prostate cancer in the last decade. Prognosis is far more hopeful today than it was 10 years ago. But our work is far from finished.

Because despite great advancements in treatment, it is still the fifth most common cause of cancer death among men globally with a relative 5-year survival rate of only 31% and when metastatic, so 1 and 3. And within 5 to 7 years of diagnosis, approximately 10% to 20% of prostate cancer patients develop metastatic castration-resistant prostate cancer, and I'll refer to that as mCRPC. This is where the cancer has spread beyond the prostate gland and has progressed despite medical or surgical gold treatment, which is attempted to lower testosterone.

Lastly, this is a disease associated with aging. There's a higher incidence in men over the age of 65. And in particular, in the U.S., most of those patients, about 70% are covered by Medicare. Prostate cancer, as I mentioned, is a progressive disease, characterized by multiple stages where patients progress from castration-sensitive to castration resistant. The journey though, is different for each patient.

Most patients start in the upper left -- upper level of this graphic in either the purple or the blue boxes. The cancer is either localized or metastatic, but it is castrate sensitive where the disease responds to hormone therapy or surgical treatment to lower testosterone in turn slowing the growth of the cancer. After initial treatment, though, patients move to the bottom boxes.

Disease progresses to castration-resistant when hormonal therapy to lower testosterone levels is no longer effective. Ultimately, if a patient lives with the disease long enough they will end up in the lower red box mCRPC. Patients with mCRPC experience poor outcomes, shorter duration responses and high rates of morbidity. So you're getting a theme here, not different than what we just talked about in the last as things progress to a point, then you end up with these challenging situations clinically.

So new strategies are needed to address resistance and prolong survival in mCRPC. That's where you're going to get the maximum utility from these kinds of products because you've already exhausted your other treatment options, including hormone therapy and chemotherapy.

The first line mCRPC setting accounts for 50% of all treatment-eligible mCRPC patients, and that is where we explore the novel combination of Talzenna and XTANDI in our Phase 3 TALAPRO-2 study. Back in October, we announced by press release positive top line results from our TALAPRO-2 trial.

We are very pleased with the strong findings, a statistically significant and clinically meaningful improvement in radiographic progression-free survival. I may refer to that as rPFS or PFS. A significant benefit in patients with or without homologous combination repair or the HRR gene mutation. That makes Talzenna the first PARP inhibitor combined with XTANDI to demonstrate clinical benefit in this patient population. And most interesting, although no definitive conclusions can be made across trials, especially when they're not head-to-head, the rPFS appears to be the longest observed in a randomized clinical trial in this setting.

These data highlight the potential for Talzenna in combination with XTANDI, if approved to become a new standard of care for mCRPC irrespective of HRR gene mutation status. We are currently under embargo, but you will see more details from TALAPRO-2 at an upcoming scientific meeting in early 2023.

Given the challenges with the resistance we've discussed, I believe and we believe the future of advanced prostate cancer is, in fact, in these rational combinations. And the results of TALAPRO-2 provide a compelling reason to believe in this particular combination, Talzenna plus XTANDI for first-line mCRPC, all-comers patients. And as a novel hormonal therapy XTANDI has a distinct mechanism of action as it directly inhibits the androgen receptor.

The positive results from TALAPRO-2 align with our preclinical and clinical data that supports the rationale for combining PARP inhibitors and androgen receptor inhibitors. This suggests a potential synergistic impact of the combined mechanisms of action in mCRPC. And synergy is something that really caught my attention when I saw this and I was talking to my partner in R&D, this is not a case of 1 plus 1 equals 2. This is a case of 1 plus 1 equals 3.

And this also makes this the first combination with XTANDI as an ARI backbone, and we already know that XTANDI is the global standard of care and the leading branded novel hormonal therapy with overall survival demonstrated in 3 types of advanced prostate cancer already. The strong efficacy results from TALAPRO-2 were in an all-comer patient population with the potential to demonstrate consistent effects across clinically relevant subpopulations. And we believe these factors position the TALZENNA-XTANDI combination to be competitive in this space and differentiated from other combinations.

In first-line mCRPC, 2 competitor PARP inhibitors plus NHT combinations, which are known under the PROPEL study heading and the magnitude study heading have different study designs and therefore, as you would expect, demonstrated different results. We believe TALZENNA plus XTANDI will compete directly with LYNPARZA plus abiraterone that's PROPEL in the all-comers first-line mCRPC space.

Our Phase 3 design is differentiated also by key stratification factors and prior treatment eligibility criteria. Randomization of patients in TALAPRO-2 was stratified by DDR mutational status and prior treatment with hormonal therapy like AbbVie or abiraterone or taxane-based chemotherapy docetaxel and mCSPC. This is very much like what we expect to see in a real-world setting.

And so our clinical trial really mirrors that. TALAPRO-2, we're pleased to say, showed robust, highly consistent efficacy in all comers, mCRPC in patients both with or without HRR gene mutations and therefore, has the potential to demonstrate consistent effect in patients previously treated with AbbVie or docetaxel.

Over the next 12 months, we expect all of these novel combinations to launch. However, if approved, we believe the profile emerging from the TALAPRO-2 data positions TALZENNA plus XTANDI to be the leading standard of care in this space. The PARP inhibitors plus and HT combos are expected to drive significant growth within the global prostate cancer therapeutics market, a market that is overall expected to nearly double, potentially reaching beyond \$30 billion by 2028.

In first-line mCRPC, there are 110,000 to 120,000 treatment-eligible patients in the G7 markets. In the all-comers population, we believe that about 1/4 to 1/3 will get a PARP inhibitor plus NHT combination. And based on the data, we believe that TALZENNA plus XTANDI has the potential to garner 40%, 60% of the class share depending upon the geography. And this translates to over \$1 billion in peak revenue potential.

Based on the compelling TALAPRO data -- TALAPRO 2 data, sorry, we believe TALZENNA in prostate cancer has the potential to be our next blockbuster in the Pfizer Oncology portfolio.

We have built extensive prostate cancer knowledge and expertise through our in-line portfolio already. We're in the market with XTANDI. We also are in the market with Orgovics. So that allows us basically to position ourselves to continue to investigate Talzenna plus XTANDI in earlier segments of prostate cancer and know that we're going to be able to pull it through and execute in the market. But we're doing additional work, nonetheless.

And I'd like to just mention our Phase 3 TALAPRO-2 study. So not TALAPRO-2 but TALAPRO-3. And this is being done in men with HRR deficient metastatic castration-sensitive prostate cancer or MCS PC. And that's something that's going to come after this beyond 2023. So we're lining ourselves up again for more impact over time.

All this to say, these results underscore our long-standing commitment to men living with prostate cancer and our pursuit of scientific breakthroughs that define new standards of care across the treatment continuum. Everybody with me? Thank you so much for your time.

I'll now turn it over back to Chris, who can begin the Q&A. Thank you very much.

QUESTIONS AND ANSWERS

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

All right. I'd like to invite my other colleagues up from the first section. While I just go through the rules for the Q&A session again with you. So again, there will be microphones here. To the left of the stage to the right of the stage, you're welcome to start lining up right now.

And also, we have about 30 minutes to take your questions. We'll answer as many as we can as time allows. We ask you to please ask 1 question per person, and then get back in the queue if you have additional questions. We also ask that you state your name and firm affiliation for the microphone, please. And finally, we'll take questions from online as well. So with that, why don't we begin? Our first question from the left.

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

Louise Chen from Cantor. I wanted to ask, you talked about business development being a big your new revenues going forward. I'm curious how you think about the impact of the Inflation Reduction Act and the types of acquisitions that you'll make.

Angela Hwang - Pfizer Inc. - Chief Commercial Officer & President of Global Biopharmaceuticals Business

I mean maybe I can begin, but I can also just ask any of my colleagues who are actively looking at deals right now to chime in. So I think, first of all, -- we know that they are -- the IRA is hugely complex, right? There are multiple dimensions. There's a lot of different facets to the IRA that we're still continuing to understand and to analyze and to develop the assumptions from. So generally, I think whatever we say now, I'm sure we'll continue to evolve and to change and as our knowledge becomes deeper. But suffice to say that we are embedding what we know about the IRA into all the models that we're running as we look at our business development deals.

And so if you factor in small molecule, biologics, the timing of the price changes, that's one aspect. I think that is maybe on more on the negative side. However, on the positive side, let's not forget that the IRA also gives us tremendous access to Medicare patients, right, with the threshold of \$2,000 out of pocket and the ability for a patient to now access a tremendous amount of medication that they previously were not able to.

I think those are sort of like 2 assumptions. To give you an example of how like we need to really look at it layer by layer and factor every single one of these in. So I think with everything, there's going to be some puts and some takes. But in general, I mean, just rest assured that we're obviously cognizant of these changes, and we are already baking them in. I know there's -- I mean, there are examples that any of you want to tee up put this to paint a more -- a big picture of what this looks like. I welcome.

Suneet Varma - Pfizer Inc. - Global Oncology & U.S. President

Yes, absolutely. And just from a BD point of view, I just want to highlight, again, BD is not a strategy unto itself. It's a way that we can advance our current strategies, for example, and we look at our patient impact first then we look at strategic fit, what are the capabilities, especially in oncology with our tumor types, and we look at the financial case, of course, including especially where Pfizer can add value and also what would be the IRA impacts.

And you're right, it will be different on dose versus biologics. Although generally speaking, when we consider patient impact and strategic fit, we're agnostic to modality, agnostic to size as well. And in oncology, which, as you may know, has 24 products I mentioned in my talk right now, 1/3 of them are developed in-house, about -- Ibrance is an example of that. 1/3 of them are through M&A, Talzenna, which I just talked about is an acquired asset and some of them are partnered as well, and XTANDI, which I also mentioned, is also a partnered asset.

So our cases for our launches, let me just say, don't change. And in BD, to Angela's point, we factor that in. with what we know, short-term boost on utilization for Medicare out-of-pocket capping and smoothing. And then really, I think what I've observed is the effects of IRA that we're still analyzing it as enterprise are really a post 2030 impacting factor, but we're factoring in a less.

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Next question from the right, please.

Trung Huynh - Credit Suisse Securities - Security Analyst

Trung Huynh from Credit Suisse. Just one on RSV and a clarification if I can. You highlighted some high rates of uptake there, but you also highlighted that you're building a de novo market. So you're going to get some help from J&J and GSK.

But the disease in itself is still relatively well unknown outside of specialist physicians, physicians or people who have been hospitalized by the disease. So I guess my question is, how do you think about building that awareness? And how do you come to the conclusion of that -- those uptakes which you gave us? And then just on the clarification, you noted over \$2 billion opportunity. Is that simply for both? Or is that for 1 each?

Angela Hwang - Pfizer Inc. - Chief Commercial Officer & President of Global Biopharmaceuticals Business

Sinan, this one is definitely over to you.

Sinan Atlig - Pfizer Inc. - U.S. Commercial & Global Business Lead for Vaccines

Yes, definitely. So just for clarification, when we say over \$2 billion is for both in total. And coming back to your question on the uptake rates. Yes. So when we compare RSV it is definitely underreported and underdiagnosed, but the burden is there.

So the number that I have shown in the slide, which was 177,000 cases in the U.S. It is there out there. And this year, CDC also said the case numbers have been almost 10x versus pre-COVID. So on one side, the burden is there. On the other side, unfortunately, but this year has been a very significant RSV epidemic.

It's very unfortunate from a patient point of view, but it was all over the news and hit out increased the awareness. So when we look at how this disease progresses and the epidemiology of it. This year was a year in which RSV came to the forefront.

On the other side, as Pfizer vaccines, we have launched multiple products in respiratory space. And we really know how to work and educate different sets of customers, whether they are HCPs, patients. So we are hopeful that, as you said, the awareness is low, but that's our job as Pfizer, and we have proven in the past that we do that really well. And we hope to approach near flu right like uptake rates.

So flu uptake rate is around 75%. And our projections show between 50% to 60% uptake rates. So given the burden and the need and our own capabilities as Pfizer, we believe we can reach these uptake rates for the peak year, not, of course, specifically in the first year. But when we move to the peak year, we believe we can reach that.

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Next question from the left, please.

Christopher Thomas Schott - JPMorgan Chase & Co, Research Division - Senior Analyst

Chris Schott at JPMorgan. I just had maybe 2 questions. Maybe just a quick follow-up on RSV. Can you just talk about kind of pricing analogs to think about here. And I guess, specifically, when we think about either coming already commercial pricing or high dose flu, are those reasonable comps to think about as you think -- I don't know if you can say on pricing, but as we think about trying to model that piece of it.

And then my second question was just for Angela. Just kind of bigger picture. You're launching a lot of products here. Help me a little bit about how much of this infrastructure you already have in place and how much we need to think about Pfizer building out?

And I know your OpEx base has stepped up, but a portion of that has been COVID kind of franchise related. So help us a bit of just -- is there a lot of spend we should think associated with these new product introductions.

Sinan Atlig - Pfizer Inc. - U.S. Commercial & Global Business Lead for Vaccines

Yes. So from a pricing point of view, as you said, we cannot give you a precise pricing point. All we can say is we are going to -- we are planning to target a price point that help support a broad recommendation by ACIP. And when I say broad, I mean year-round recommendation for pregnant women, a routine year-round recommendation for pregnant women and also a routine age-based recommendation for the older adults.

So that's the price point that we are targeting.

Angela Hwang - Pfizer Inc. - Chief Commercial Officer & President of Global Biopharmaceuticals Business

I mean I can add to that. As you know, when it comes to vaccines, the way they're priced is through their cost effectiveness, right? And the burden of every disease is very different, COVID to pneumococcal to flu, to RSV. So that pricing will ultimately be determined by the cost effectiveness of what this medication -- what this therapy is able to bring to the community.

And so this that sort of the band of pricing that we have to consider is going to factor all of that in. So I don't think you can look at it like if flu is this and if COVID is that then therefore RSV is that. You have to look at the disease of RSV, the population that's impacting the cost of hospitalization zone. And so all of that needs to be factored in to ultimately help us understand what is then the price of RSV. And for us, we'll have to think about across 2 populations, right, adults as well as maternal. And then on the second. So yes, -- we -- I mean, one of the beautiful things about what we have in our portfolio and even all the products that you've seen today, they build off of infrastructure that we already have, right?

They build off of expertise. I wouldn't say just the actual infrastructure, but its skills and expertise and tremendous amount of partnerships and relationships that we have in the marketplace. And so I think the synergies there, we believe, will help us to get into market faster and be able to do a really great job.

However, as you know, in as much as there are many places where we can share resources, right? So if you have a primary care rep field force. The primary care rep will be able to carry additional products in their portfolio of products. But there's a limit to that, too, right? Because only so much they can do beyond which they are not effective, which means it can't just be a single field force for all of these primary care products that you've seen.

We have to have multiple field forces. But of course, we'll be able to do it much more efficiently because we can plan the deployment across a large portfolio of primary care products. However, as you all know, that -- but that's not the only cost, right? We are also promoting to very specific audiences to very specific prescribers, there are -- every interaction with the physician is a cost unto itself. So depending on also how many people you're trying to reach, whether that's through medical education, whether that's through search, whether that's through the multitudes of marketing tactics that we have, there is also a per reach cost that you have to consider.

And so I would say that the expectation is that there is a large step-up in our investments and in our expenses next year for 2 reasons. One is to invest in the products that are launching in 2023, but also fast behind us are another set of products in '24 and '25.

So that OpEx that you're seeing in our P&L covers the market development for the other 2 years as well. But the expectation is that those costs are going to be high because we just think impacts a little bit alone. There's billions of people that we're trying to reach, right?

And every outreach has a cost associated with it even if you have a contained infrastructure. So I think that's the way you should think about it. We're going to build off of what we have, achieve as high an efficiency and synergy as possible. But beyond that, you have to -- we have to reach everybody that we intend to and our customer base. And that will be incremental.

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Thank you, Chris. Next question on the right, please.

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

Steve Scala from Cowen. Great presentation so far. So you've given lots of very helpful data points on pools of revenue, but it's still a challenge to kind of pull it all together given the COVID declines, which are inevitable over time.

So I'm just curious, do your internal models show biopharma growth in each year of your 6%-plus revenue guidance duration? And if each year, is that because biopharm is so strong or COVID remains durable. And if it's not each year, then how should we think about the cadence?

I know you don't want to be pinned down, but I think it's very important to investors to anticipate or know whether we're headed for some down years or whether it's all up from.

Angela Hwang - Pfizer Inc. - Chief Commercial Officer & President of Global Biopharmaceuticals Business

So I'd be happy to answer that. I think from the outset, we've always spoken about our 6% as a compounded annual growth rate over 5 years from 2020 to '25. So that means that over the 5 years, the compounded -- it's compounded for the 5 years, it will be 6%. So that does mean that every year may not be identical, right?

And we saw that this year. You've seen already over the last 3 quarters that 2022 is not a 6% year, it's less than that. However, over the 5 years, we believe that it will contribute towards a 6% CAGR. And from that perspective, we continue to be confident that, that's what you should be able to see over the 5-year mark. So it's not identical every year.

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

Right. I know it's not identical, but are we anticipating down years? Or do you think you'll deliver growth each of those 6 years?

Angela Hwang - Pfizer Inc. - Chief Commercial Officer & President of Global Biopharmaceuticals Business

We will deliver -- well, this year, we grew 3%, which -- so it's a growth, but it grew less than 2021. So each year will be growth. It will be a matter of how much growth. But yes, it's growth every single year.

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Yes. And just to clarify that, as you know, Steve, that 2025 ambition excludes COVID, and that's on a constant currency basis. So I hope that helps. Next question from the left, please.

Robyn Kay Shelton Karnauskas - Truist Securities, Inc., Research Division - Research Analyst

Sure. Robyn Karnauskas from Truist and I realized we had similar questions. So we thought we'd just grouped them together. Evan Seigerman from BMO. So there was a lot of talk about the bispecifics at BCMA at ASH and in particular, the high infection rates, you guys are way in the lead.

But can you talk a little bit about how you see the space evolving how you're mitigating these infection rates. I don't know if you have a theory if it's because BCMA is more on B cells. And then I wanted to touch on the new targets, the GPRC5D and FcRH5 targets that were highly talked about at the meeting. Yes. That's the same thing afterwards.

Suneet Varma - Pfizer Inc. - Global Oncology & U.S. President

And Chris Boshoff, I'm going to ask you to take the infections point, if you wouldn't mind stepping up to the mic and Chris is our Chief Development Officer of Pfizer Oncology.

But if I could, I'll just answer your other question first, which is essentially yes, we're aware of the non-BCMA. And you said all the letters, I just say non-BCMA bispecific, -- and I think that -- and that was announced at ASH. So for us, I mean, our first reaction just as human beings was this is a great because in terms of options for patients, they need more treatment options, the severity of the disease, the incidence of the disease and multiple myeloma, having more treatment options is better.

It also further supports, let's say, the proposition that we believe bispecifics are the modality of the future that are ultimately kept broader and earlier use overall as more bispecifics coming to the market. However, we believe that when you look within bispecifics as a class, that the BC BCMA bispecifics are going to be used before the non- bispecifics.

And so we believe that those will come in and be used after the bispecifics that we were talking about today. So that's kind of our view of how the marketplace is going to develop over time. In terms of the infection rate, I can just say, obviously, patients of safety is super important. We're actively monitoring and managing it. And of course, we're looking at the risk benefit, of course, in the multiple myeloma space of all these factors. We did hear chatter about infections at ASH as well, and I'll ask Chris to comment on that.

Chris Boshoff - Pfizer Inc. - Senior VP, Chief Development Officer, Oncology & Rare Disease

That's a very good question. As you know, the disease, especially penta-refractory multiple myeloma patients are already very prone to infections because they are already severely immunosuppress from previous fourth, fifth, sixth lines of therapy. With BCMA, bispecifics as can be expected, we are ameliorating plasma cells. .

So immunoglobulin transfusions have been very proactive to educate physicians for the use of immunoglobulin transfusions as well as prophylactic antibiotic regimens. So educating patients but also physicians of how to deal with this. One of the other issues to just point out is that a lot of infections were in our program specific regional associated with COVID, including we had some COVID deaths in our program. And that coincided with almost an epicenter of cover cases that occurred in Central Europe. But we are mitigating what we can and is an important issue to proactively address for us in the whole program.

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Sorry, Evan, did you have another part with that? Or was that good?

Evan David Seigerman - BMO Capital Markets Equity Research - MD & Senior BioPharma Research Analyst

(inaudible)

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Okay. Great. So then let's take a question from the right, please.

Chris Shibutani - Goldman Sachs Group, Inc., Research Division - Research Analyst

Chris Shibutani from Goldman Sachs. If I can ask a question about etrasimod largely highlighting the opportunity here in ulcerative colitis. And as we think about 1 of the fundamental opportunities in premise of many of these compounds in INI is that there's this essence of there being kind of a gift that keeps on giving with additional indications.

And historically, for etrasimod, some of the indications that had been in mid-stage clinical trials included for Crohn's disease as well as atopic dermatitis and discussion by the company prior to Arena being acquired some other more than perhaps boutique or maybe not a sizable indications such esophagitis, alopecia areata, et cetera.

So can you update us on the status of where you are in terms of thinking about potential further development and commercial opportunity for etrasimod across some of these other indications, obviously being very directly related to the IVD opportunity.

Kevin Sullivan - Pfizer Inc. - Global Specialty Care & U.S. President

Sure, I'd be happy to. And I'd also maybe ask Mike Corbo to who heads development for I&I to maybe pitch in. But I'd start with, we are very excited about the possibility of additional indications for etrasimod. You heard me mention Vitiligo. Vitiligo has 3 million patients in the U.S. alone and about 1 million of them have disease where it's in a large area of their body where a systemic treatment may be appropriate for them.

Across all other indications, we also remain very excited. But as we do with all of our medicines, we look to file the science, and we look forward to exploring where etrasimod may be more appropriate for additional indications for I&I patients on some of those other indications you mentioned. And maybe, Mike, if I could ask you to step in.

Michael Corbo - Pfizer Inc. - Senior VP, Chief Development Officer, Inflammation & Immunology

Sure. Yes. Thanks, Chris. I think from the GI perspective, not only are we looking at the moderate to severe population, but also we do have Gladiator running, which is more moderate population. We do think that's a really important population that is not well treated. Disease is still on track. We expect to make a decision of a dose in 2023, and that is a seamless adaptive trial. So that is really pivotal phase right now.

We do have Phase 2 data coming in on EoE in the next couple of months as well as alopecia areata we'll make data-driven decisions as to does this fit a good population is their medical need. And also in AB, we do have a Phase 2 or, let's call it, a 2-part portion of the AD program, and we hope to get some data out of that towards the end of next year. So still active in derm, still active in GI, still looking to expand and continue to look for life cycle development from there.

We will probably be staying away from neuro just because we feel that's a very well -- really well met need in the. So what we will be branching out beyond that.

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

And one small correction. Vitiligo is obviously for rituximab. Okay. Then Evan, on the left.

Evan David Seigerman - BMO Capital Markets Equity Research - MD & Senior BioPharma Research Analyst

Evan Seigerman from BMO. So I do have a follow-up on BCMA then 1 on NURTEC. So we are giving some position feedback that they would not use a bispecific ahead of CAR-T therapy. And with this in mind, I guess, how would you position for patients? And then on NURTEC, what are you doing differently than what Biohaven did to help accelerate the sales growth trajectory?

Angela Hwang - Pfizer Inc. - Chief Commercial Officer & President of Global Biopharmaceuticals Business

Suneet, do you want to grab that first and then word read.

Suneet Varma - Pfizer Inc. - Global Oncology & U.S. President

Yes, absolutely. No, no worries. It's pretty exciting stuff. We believe ultimately that BCMA bispecifics and bispecifics in general, are going to gain broader and earlier use over time.

Unfortunately, CAR-T, while enjoying high efficacy, has many other availability issues in terms of where it can be administered, the personalization, the customization, et cetera. So I think that it will be obviously a physician decision, the different patient journeys, but ultimately, I think that breadth or that broadness of use really will come from the bispecifics.

And I think if you look at the convenience factors, which is where you go with the patient part of that question, which is off-the-shelf, flat dosing, subcutaneous every other week dosing over time, I think that's very appealing to a patient who, especially, let's say, a choice in one of those limited academic centers.

But once you get out to the community, a quite an appealing option for patients as well.

Rodrigo Puga - Pfizer Inc. - U.S. Commercial & Global Business Lead for Internal Medicine

So thank you for the question. I think it's a very good question because we are starting off from a great foundation from Biohaven. And we are adding a lot to that equation. On top of the already implemented fill force that Biohaven had that we are keeping we are doubling the sale force in the U.S., covering 72,000 additional HCPs.

We are deploying all our key account management team, reaching 250 health care systems in the U.S., helping them to identify migraine and how to better treat patients we are putting 8x more medical field support. And on top of that, we are reviewing every lever of the marketing plan, including the gross to net. We believe that the way that Biohaven did it, it's the right one, which is to create a lot of trial, and this brand has 95% commercial access, and we want to keep that.

But of course, now this is part of Pfizer, and we believe that we have a different leverage in our ability to review gross to net. And so in general, we are deploying all our commercial footprint in the U.S. And then what else are we doing? We are launching this globally, which is something that Biohaven was not -- didn't have the infrastructure to do that.

So we are deploying all our infrastructure capability to launch this incredible assets across the globe and it's already approved in the European Union. So we are hoping to launch it very soon. And we are expecting regulatory approvals across the globe in many, many different regions. And also, we already submitted an acute indication in China this year, the second half of this year. So we are expecting to have an acute launch, hopefully, in the coming future.

So we are adding all our infrastructure to make this an even more successful launch in the rest of the world and to accelerate what is happening in the U.S. And just an additional data point, we didn't wait until the acquisition. We actually signed SLA with Biohaven and we deploy some of the things that I mentioned, doubling the file force and some additional things prior to the acquisition.

And we are starting to see that the market leadership is increasing, and this is something that I mentioned in the recent months, we saw that 2 curves compare NURTEC and the competitors are actually separating, and we have gained 6 points of market shares in the recent months.

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Thank you for the question. I have questions for the right, please.

David Reed Risinger - SVB Securities LLC, Research Division - Senior MD

Dave Risinger from SVB Securities. I have 2 questions. First, with respect to NURTEC, could you comment on the rough breakdown. So the greater than \$6 billion, how much of that is in the U.S. versus ex U.S.?

And then with respect to RSV, obviously, what's going to matter is the answer on the durability of protection in terms of the pricing. So could you comment on when you expect to have that clarity on durability protection and how that's going to inform your launch pricing next year?

Angela Hwang - Pfizer Inc. - Chief Commercial Officer & President of Global Biopharmaceuticals Business

Do you want to go first?

Rodrigo Puga - Pfizer Inc. - U.S. Commercial & Global Business Lead for Internal Medicine

Yes, sure. So the first thing that I would like to mention is the \$6 billion at peak is included in the whole portfolio. which is NURTEC or Vydura in the EU and zavegepant in the intranasal formulation plus zavegepant in the potential oral formulation for chronic migraine.

And then in terms of how the sales are going to be divided, we expect more sales to come from the U.S., but we still expect that what we call developed market is going to be a significant add to that. And we are planning to launch this brand in at least 70 markets. So it's more going to come from the U.S., but the rest of the world is still going to be very important.

Sinan Atlig - Pfizer Inc. - U.S. Commercial & Global Business Lead for Vaccines

On the duration of protection question, yes, of course, that will be one of the inputs that is going to help us determine the price. And as Angela has said, we have 2 indications, maternal and older adults. And -- we are still awaiting the results of the duration of protection of more than 1 year because as of the interim study analysis results are only based on 1 year duration of protection.

So as soon as we are going to have this data, that will be an input to our decision on how to price our product.

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

And we've previously talked before about having those ahead of an ASI recommendation and making a pricing decision. So next year. Next question from the left, please.

Mohit Bansal - Wells Fargo Securities, LLC, Research Division - Senior Equity Analyst

Mohit Bansal from Wells Fargo. So I have a question regarding etrasimod. So there's no doubt that the profile of the product does allow for first-line issues because of the safety and efficacy of the product.

But historically, in I&I space, it has been challenging for these products to be used ahead of an anti-TNF. You are launching in an environment where anti-TNF are going generic, especially Humira has been biosimilar. So what is the go-to strategy to make sure that the payers step through this product and then go to anti-TNF. Is it pricing? How would you position this part of product?

And #2, in second line, do you foresee any use as induction maintenance where you use a JAK inhibitor first and then use an S&P as a maintenance.

Kevin Sullivan - Pfizer Inc. - Global Specialty Care & U.S. President

So thanks for the question. I would say, to answer the second question first. We're looking at a position as first line. You saw the statistics I mentioned about the amount of patients that are coming off of conventional looking for an advanced therapy but having those reservations about going to an injectable.

This is a busy market, as you mentioned. This is a crowded market, but it's a market that we know very well. There was another data point that I didn't speak to in my session. It was around symptom relief within the ELEVATE study. And it was also quite good -- the more patients on it taking etrasimod through the trial versus those taking placebo reported symptomatic remission as early as 14 days.

And you add that on top of 1 in every 3 out of 52 weeks, achieving remission and that remission being steroid-free 100% of the time and all the other concerns are that people have about moving to biologics. I think that we stack up very favorably based on that profile to compete in a first-line setting.

What we need to do, though, is just educate stakeholders, HCP's, physician, patients about this option. And we believe that the risk-benefit profile for so shapes very well against the current competitive set.

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Thank you, Mohit. Question then from the right and then a flip question from the left before we end the session.

Joe Thomas - BofA Securities, Research Division - Research Analyst

I'm Joe Thomas from Bank of America here for Geoff Meacham. I have 2 unrelated questions, if I may. First 1 is on etrasimod. Since you already have Xeljanz in UC, are you expecting any cannibalization there as that rollout occurs? And then my second question is in RSV in adults.

Since you're on a similar time-line with GSK regarding approval and ASIP. How are you thinking about differentiating during the RSV season next year in order to capture that dominant market share that you described?

Kevin Sullivan - Pfizer Inc. - Global Specialty Care & U.S. President

I'll start with etrasimod, and thanks for the question. I think what we have to remember is that this is a very large space, okay? And there are a lot of options out there. There are options for biologics that are options for JAKs. And what we're looking to do step in front of that with an oral first line. There is not a -- let's say, I think space in the JAK space in UC will continue to exist.

Where we're looking to go is to bring more -- let's say, more opportunity to etrasimod as a first-line oral away from injectables taking into account the patient's preferences on many of those patients, say, 2/3 of them that are on conventional therapies that are looking or need to move over to advanced therapies. So coming to your question on the RSV older adult space. So we rely on our first our vaccine candidates clinical profile and also on our commercial capabilities as Pfizer.

So when I look at our vaccines clinical profile. So first, it's a bivalent vaccine that won't rely on cross protection. Second, as I have mentioned, it doesn't have any adjuvant or viral vector component and these components have been associated with higher reactogenicity. And when we look at the clinical results, the results were very strong with higher efficacy in more severe and symptomatic cases.

and with a favorable safety profile. So from our vaccine candidate profile, we believe in our vaccines profile. -- but also even more importantly, as Pfizer, we have proven in the last decade to have very successful launches and also in competitive spaces. So our last 2 launches have been the COVID-19 rollout and also the Premna20 launch in the adult space.

And in both spaces, we have launched in a competitive area, but we also have leading market shares in both areas because we believe that we have the, as I have mentioned, the right contracting models with both integrated delivery networks with retailers. We have an industry-leading field force, and we know how to educate consumers across various channels. So when I combine all of that, I feel really confident that we can have a leading market share going into this season.

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Thank you for the question, Joe. And then last question to the left.

Andrew Simon Baum - Citigroup Inc., Research Division - Global Head of Healthcare Research and MD

Andrew Baum, Citi. A couple of questions. Firstly, for Chris, on your bispecific elranatimab, could you -- 1 thing that struck me is the peripheral neuropathy which does not seem to be certainly related to the number of lines of prior therapy. It seems to be something unique about the molecule.

While this is not an alien phenomenon with other bispecifics, it does seem quite different from the other BCMAbs, so I'm curious how we should think about this and whether it could be a competitive disadvantage in what is a crowded field.

And then second, on the oncology side, could you talk to the likely label as it compares to AstraZeneca for talazoparib in prostate cancer. I was trying to pass it out by the inclusion criteria. But I think Astra is anticipating a label only for patients who are naive to androgen blockade, I'm just trying to work out whether that's the same or different, assuming that talazoparib gets approved for prostate cancer and to what extent that could provide a commercial advantage.

Angela Hwang - Pfizer Inc. - Chief Commercial Officer & President of Global Biopharmaceuticals Business

Chris, do you want to do BCMA first. And then Suneet, do you want to take the label?

Chris Boshoff - Pfizer Inc. - Senior VP, Chief Development Officer, Oncology & Rare Disease

So BCMA in general, is expressed at very low levels on some neuronal cells. So if there is any gripeuropathy, it likely will be a class effect. Regarding in the Phase I study, we did experience peripheral neuropathy that was of concern, and it turned out here there were 2 patients that were treated also with pomalidomide, which can also cause peripheral neuropathy.

In the registration study you've seen or the registration 10 study mechanism 3 today you've seen almost all the patients with proven neuropathy had preexisting neuropathy due to lenalidomide or pomalidomide. And most patients, as you know, have to see both of those. So we do not think it's any different from any of the other BCMA bispecifics or BCMA-targeted therapies.

And it's also encouraging now in the earlier lines we'll be testing. As you know, we've got an ongoing Phase 3

trial and double-class exposed in the study that have started mechanism in the post-setting early lines and that it's encouraging that we haven't seen anything that's a signal of concern to us. Good question. Thank you.

Suneet Varma - Pfizer Inc. - Global Oncology & U.S. President

Yes. And I'll do this 1 quickly, although Andrew, what I would say is that when we go to the reception later, we can spend a little more time on Tala label. But I think right now, I can't comment on where the competitors labels may end up. But what I can say is that we're obviously going for the XTANDI as a standard of care backbone. We're going for the, let's call it, robust and long progression-free survival amongst the longest that we have.

And we're going to really highlight the highly consistent results of the mutated and nonmutated population. So that's what we expect our label. I think 1 of the things about the stratification factors that's very important to us. is that prior treatment with docetaxel or AbbVie essentially put us in, we think, the most realistic application that we see in real-world setting and practice. And so that's the approach that we're going for with our product. But we can talk about it more in the session.

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Great. Well, thank you for your questions in this session. Okay. We're going to have an approximately 30-minute break by my clock, that puts us at approximately 3:38 and there'll be refreshments outside, as Suneet said, and he's buying. So thanks very much.

Angela Hwang - Pfizer Inc. - Chief Commercial Officer & President of Global Biopharmaceuticals Business

Thank you.

(Break)

PRESENTATION

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

All right. Thank you for all coming back. Hopefully, you enjoyed the first module of the afternoon. And in a few minutes, we have our second module, which will be hosted by my colleague, Andy Schmeltz. But before Andy begins, I just want to repeat the forward-looking statements we made earlier.

Again, we'll be making forward-looking statements in the course of this afternoon. Any statements we make are applicable only as of today, and we undertake no obligation to update those statements in the future. If you have more questions on our forward-looking statements, you can see our SEC filings under Forms 10-K and 10-Q under the sections entitled Risk Factors and forward-looking statements.

And with that -- Okay, that's strange. It doesn't seem to be working, but -- there we go. Okay. And now I'd like to invite my colleague, Andy Schmeltz, to this podium.

Andy Schmeltz - Pfizer Inc. - Senior VP, Commercial Strategy & Innovation

There you go. Good afternoon. It's great to be here today with everyone. My name is Andy Schmeltz, and I oversee Commercial Strategy and Innovation here at Pfizer. While our focus so far today has been on our exciting near-term launches, we now turn to Pfizer's high-value pipeline, which we're very enthusiastic about.

Earlier, Angela showed this slide and outlined how we plan to grow from 2025 to 2030, not only mitigating the gap from our LOEs, but setting course for continued growth. Through ongoing purposeful business development activity, akin to our 4 acquisitions over the past 12 months, which have put us more than 1/3 of the way to our stated goal of \$25 billion in incremental revenue by 2030.

And as Angela and our leaders just covered with our exciting wave of 19-year term launches, we're poised to deliver \$20 billion in revenue by 2030. Now we'll focus on our pipeline contribution to this growth ambition, which we believe offers significant value and opportunity.

As you see, Pfizer has a very robust pipeline across all 6 therapeutic areas of focus: inflammation and immunology, internal medicine, oncology, rare disease, vaccines and anti-infectives. And while Pfizer's customer and country facing commercial and medical organization under Angela, our biopharma division, is now structured as Primary Care, Specialty Care, and Oncology, it's important to highlight that Pfizer's category-based model, enabling therapeutic area-specific Chief Scientific Officers, Chief Development Officers and commercial leaders to partner closely to champion mid- to long-term strategies, investments and capital deployment, not only remains intact, but in fact, is strengthened in our new model.

While we're very excited about our overall pipeline and many of the programs you see here, today, we're going to double-click on a subset of these that benefit from a deeper dive, and we look forward to future opportunities to showcase many more of our pipeline programs in the future. But for today, these programs include anti-interferon beta, a potential breakthrough in dermatomyositis and polymyositis, danuglipron and PF15322-1532

potentially best-in-class oral GLP-1 receptor agonist; TTI-622, a potential backbone combination agent for hematologic malignancies and inclacumab and GBT 601 from our Global Blood Therapeutics acquisition, potential transformative therapies for sickle cell disease and our mRNA pipeline vaccine programs for flu, shingles and a flu COVID combo.

So let's start with anti-interferon beta, and I'll turn it over to our inflammation immunology Chief Development Officer, Mike Corbo to get things started. Mike?

Michael Corbo - Pfizer Inc. - Senior VP, Chief Development Officer, Inflammation & Immunology

Well, thanks, Andy, and good afternoon. You'll notice a word on the slide here that we've actually used quite a bit, and that's the word breakthrough. It's not one that we take very lightly. And when we think about a disease like dermatomyositis, we're thinking about a disease that has significant unmet need, high morbidity and mortality. And right now, it's treated with modalities that basically originated in the 1950s.

That's in need of a breakthrough if we've ever seen one. So Dermatomyositis is characterized by really significant issues from an autoimmune perspective in the skin and in the muscle. It is a very debilitating disease. Patients cannot typically function in normal daily life. Symptomatically, the skin is very characteristics, a variety of rashes that are very much the hallmark of the disease. These are bothersome, disfiguring and really impacts patients' lives. But most significant is the effect on muscle. It's not just being weak, muscles are damaged.

Diatrophy. I'll remind you that your heart and lungs are muscles. If you talk to a rheumatologist, typically, rheumatologists don't lose a lot of patients. They do, but not a lot. You'll often find that on that list of patients they lost is a patient with DM. It is a very significant disease of morbidity and mortality. It's a rather rare disease, 40,000, 60,000 patients and again, decreased life expectancy.

The other part of this is, since it's a rare disease, it's not totally well known and patients tend to wander in their diagnosis journey, some up to 5 years. So really, this is a disease that has a huge unmet need is looking for new targeted therapies and potentially this can really change patients' lives. So a little bit about DM. Now let's start talking about interferons.

So interferons, for those who are not totally familiar are key communicators within the immune system is actually 3 families of them, type 1, type 2, type 3, that's the simplest part of immunology. Once you get into the CDs, we just kind of lose track of all the numbers. But when we think about type 1 interferons, they are the key family of interferons that interact with our immune system in autoimmunity. So a lot of the inflammation, a lot of the destruction that you see are driven by this family of type 1 interferons.

Now growing up, I guess, for a few decades now. In immunology, we've always kind of thought of this as a broad brush. That whole family is bad. You should trim the whole forest and you should be able to affect the disease. And that is true, and there are great drugs that are able to do that. It's a little novel to think about just going into the (inaudible) and picking 1 tree out of the 17 to say this is really going to affect disease.

But that was the approach that we were taking when we came to this. And this originated with some good basic research from folks at Brigham & Women's Hospital in Harvard with understanding that there was a signature for interferon beta in dermatomyositis. Now this is novel. This is a little different than the way we normally think.

So they brought this to Pfizer and through our organization of the centers for therapeutic innovation started partnering with the researcher. And actually, we designed a molecule, monoclonal antibody specific to inhibit interferon beta. That's all it does. It doesn't do anything else. It only inhibits interferon beta. So -- and thinking about this, we had to kind of come up with how do we test this? How do we look at this from an experimental perspective?

So as I mentioned, DM has both a skin and a muscle component. It's easier and faster to understand what happened to the skin. There's good established measures. So the first Phase 2 study that we actually designed together with Mike Vincent and WRDM at Pfizer was to look at the effect of this molecule on skin. So inhibition of interferon beta in DM, do you see anything that actually happens by really inhibiting 1 of these 17 type 1 interferons.

So -- what we did find in the skin portion of the study was if you look on the left-hand panel, this is the overall SODAS D score, which is a continuous measure of disease activity in the skin. This is a very substantial, low is good mind you, okay? And this is a very substantial reduction. This was really a small study. We got this going. I remember the night Mike Vincent called me when he saw the data for the first time.

And the first thing we said is this is phenomenal, what are we going to do? Because this is too important to just tinker around with. So we looked at the data, we looked at it from a responder perspective, which is on the right-hand panel, also incredibly impressive. But what we needed to do is say, well, look, we can stop here if we wanted to and do a Phase II design, talk to the FDA, think about what doses we want and plot along in our normal way.

But going back to what Angela said in the very beginning, that's not how we're doing our job anymore. And also, these patients are waiting. There's no reason to do our job that way anymore. So instead of just stopping and designing a new Phase II, all we did was start to add cohorts to the existing study. The first was for dose. So we needed some dose information.

It's hard to go to an end of Phase 2 without some dose information. And then importantly, we really needed to understand what was going on with the muscle. So in that part of the study on the next slide, we looked at patients that had primarily muscle involvement in their disease. And we took a number of different measures, there's many ways to look at muscle improvement and involvement.

On the left panel is the patient response. Patients know what's going on. Okay, sometimes better than physicians, no events to physicians. They know that they're weak. They know if they can't raise their hand. There's a very clear response from the patient perspective. Another way to look at this is actually from a really objective perspective and looking at CK. CK is a byproduct of muscle degradation. We use it in a lot of different diseases, you use this in muscular dystrophy, in fact. But again, we see an objective and a subjective very clear signal.

So if you look at this orthogonally, it works on the skin, it works on the muscle in multiple different directions. This is something of significance. So this was all well and good. We said, "Great. Where do we go from here? Well, we could have again just said, let's go right into a Phase 3 program, which, by the way, we were designing and planning and working on our end points. But at the same time, we said, well, is there more that we can do.

This is kind of novel that we found an interferon beta signal in a disease. Are there other ones out there that we may be able to be considering in parallel? And talking to key opinion leaders, working with a company in Israel called Cyto Reason, which is an IA-based company, using some of our own data and outside data and doing some of our own research, we did find that there's another disease, polymyositis that has a very similar signature to dermatomyositis. So it is a different disease.

Andy will tell you a little bit about that. But in a gene expression profile that you see here, we see very similar patterns of genes being turned on in interferon. So again, we said, well, look, that's great. We could do 2 programs. That's not really the right way to do things. Again, if we go back to Angela.

So now what we're doing is actually building a program that looks at multiple indications in a single Phase 3 study. So basically a basket approach, things that we've learned from our friends in oncology like Chris. But again, it's pretty novel for rheumatology. So if we think about this story and how it's kind of come together, I think it kind of summarizes where Angela was going about working differently and thinking differently.

So an early sign of efficacy didn't stop. All we did was adapt, adapt, adapt, get the information and the data that we needed. From there, what else can we do? And in doing so, we now are going to be designing or actually have designed a Phase III program that has dermatomyositis, polymyositis and juvenile dermatomyositis, slightly different disease than DM and is a population that we can't simply ignore.

So we've already had discussions with regulators, and this is a little bit novel. Oncologists get this. The vision get this from oncology, the response has been very favorable. They like the concept of a basket approach. So Again, we've decided to look at this very differently, accelerating the Phase II, making the Phase III to look at 3 indications at once.

So that's really the approach we're trying to take. And that's just this initial part of the development for interferon beta -- anti-interferon beta, sorry, Andy. I always forget, you shorten everything. So that's where we are today. What Andy is going to come back and tell you is a little bit more about polymyositis, how all this comes together and how doing really good for these patients potentially can do really good for Pfizer. So Andy?

Andy Schmeltz - Pfizer Inc. - Senior VP, Commercial Strategy & Innovation

Thanks, Mike. Mike described dermatomyositis in pretty good detail. So let me take a moment to characterize the unmet need specifically in polymyositis. Polymyositis, or PM, is another disease in the idiopathic inflammatory myopathy subtype, sharing clinical characteristics with dermatomyositis, or DM. PM involves similar debilitating life-threatening muscle and extramuscular manifestations as DM, but without skin involvement.

Today, PM is both harder to diagnose and treat than DM. And the number of U.S. cases is estimated to be in the range of 40,000 to 60,000, so pretty comparable to dermatomyositis. It's important to note there are no targeted therapies approved to treat polymyositis. Steroids and off-label immunosuppression medicines are used with limited efficacy and with safety considerations.

Turning to the market opportunity. We believe the combined DM and PM total addressable market could grow to \$3 billion to \$6 billion in the U.S. and up to \$12 billion globally by 2030, the appropriate market development efforts and the introduction of multiple novel breakthrough therapies, including interferon beta. Let me break it down.

Based on claims data, we estimate there are about 100,000 U.S. diagnosed patients today across dermatomyositis and polymyositis and that's anticipated to grow by about 50% and to 150,000 patients by 2030. Hence, the range we're showing here, 120,000 to 180,000. Now why this growth? It's driven by the approval of novel medicines over the coming years and the education of physicians, which should help faster diagnosis.

Now we've seen this before in nascent autoimmune diseases, where the approval of innovative medicines with breakthrough profiles have triggered patient diagnosis and market growth. Think hidradenitis operotiva and ankylosing spondylitis over the past 10 years where the approval of innovative medicines significantly increased diagnosis and treatment rates.

Now let me comment on the use of advanced therapies. Currently, 20% to 30% of treated patients are prescribed advanced therapies, and we expect that to grow to about 40% of with novel medicines, including anti-interferon beta with a differentiated benefit risk profile. And touching on pricing. DM and PM are rare diseases where IVIGs are considered the gold standard for steroid refractory and intolerant patients.

Today, the net prices are about \$150,000 a patient a year in the U.S. So following the math outlined here, we envision a \$3 billion to \$6 billion U.S. opportunity in 2030, which doubles at the global level. And this international multiplier is informed by market research in key countries and triangulation with Pfizer benchmarks, hence, the global opportunity of \$6 billion to \$12 billion. So in terms of any interferon beta market or commercial potential now.

Within this \$6 billion to \$12 billion total addressable market for advanced DM and PM therapies, interferon beta could achieve a significant share given the attractive competitive landscape and the potential to be a first -- the first approved targeted therapy in polymyositis.

With once monthly 60-minute infusions and potentially compelling efficacy and safety, anti-interferon beta could represent a much needed breakthrough for these patients. We believe interferon beta has the potential to generate \$1 billion to \$3 billion peak revenue globally. And this exciting program is not currently included in any analyst models to the best of our knowledge.

So to sum up, anti-interferon beta has breakthrough potential for 3 reasons: one, in targeting a single pathway to achieve potentially superior efficacy while avoiding pan interferon safety signals; two, with a strong mechanistic fit and compelling Phase II data in dermatomyositis, as Mike described; and three, with a clear scientific rationale for registrational enabling basket study across dermatomyositis and polymyositis.

Ani-interferon beta could potentially translate into a differentiated medicine with a much needed benefit risk profile for DM and PM sufferers and deliver up to \$3 billion in peak revenue. Needless to say, we're excited with what we have in our hands with anti-interferon beta, and we really look

forward to initiating the pivotal program. Thank you. Let me now turn things over to Jim Rusnak, our Chief Development Officer for Internal Medicine, to speak to our GLP-1 portfolio. Jim?

Jim Rusnak - Pfizer Inc. - Senior VP, Chief Development Officer, Internal Medicine & Hospital

Well, thank you very much, Andy. So it's really a pleasure to be here. I just want to have the opportunity to be able to share a little bit about the great opportunity we have for Pfizer in both type 2 diabetes and in obesity. And as you know, these are very large patient populations with a tremendous amount of unmet medical need. And for obesity in particular, we view this as a serious medical condition, not merely a lifestyle choice. And this condition is going to affect more than 1 billion people globally by 2030.

Obesity confers a comorbidity risk in over 200 medical conditions, but yet there is a very low treatment rate less than 5%. Similarly, type 2 diabetes affects about 0.5 billion people with a growth trajectory similar to that of obesity. And despite there being multiple classes of agents available, only about half of the patients in the U.S. with type 2 diabetes achieve their A1C targets.

So for both conditions, a convenient, highly effective, once-daily oral treatment could be really transformational. GLP-1 mediates key drivers for both obesity as well as type 2 diabetes. The GLP-1 receptor agonists have shown to decrease appetite, delayed gastric emptying increased insulin secretion. This translates into weight loss, glycemic control as well as lower cardiovascular risk.

And this class over the years has really been demonstrated with continuous innovation. Subcutaneous BID injections were replaced with once daily injections were replaced with once weekly injections. And despite all of the tremendous amount of efficacy in terms of the A1c that they can deliver, the weight loss as well as the cardiovascular outcome.

This class of medicine remains heavily underutilized. We believe that further innovation in oral GLP-1s will keep fueling the growth opportunity as well as address this underutilization. The GLP-1 receptor is really a challenging drug target with failed efforts in the small molecule approaches. Our 2 candidates show our tremendous science as well as our resilience in this capacity.

Both danuglipron and 1532 are potential best-in-class chemical profiles and the exhibit full agonism of the GLP-1 receptor has good oral bioavailability and has very wide therapeutic indices. Overall, there were 3 key developments that led to danuglipron in 1532. Initial screening efforts were very difficult for obtaining lead compounds. Until an allosteric modulator was added, which represented a conformational change in the GLP-1 receptor, which then allowed us to develop novel screening activities for lead candidates.

We screen 2.8 million lead molecules for potential candidates. And then we took those leads, and we further optimize them through tremendous amounts of medicinal chemistry efforts increasing the potency over 50,000 fold. Generally, we increased the potency by about 100 to 1,000-fold during this process. These efforts resulted in 2 clinical candidates, danuglipron, which is a 4 to 6 life of BID medication, but with the potential for once daily with a modified release formulation and life cycle management as well as PF1532, which is a true once-daily profile with an 18 to 21 hour half-life.

Both of these molecules are true full agonists of the receptor and have no fasting requirements. Importantly, we believe the full agonism may be required to achieve the same level of response as an injectable GLP-1. So here, I'd just like to remind you a little bit about our clinical data. Overall, we did observe robust dose-dependent decreases in A1c and body weight. And here, we see danuglipron that results from our Phase IIa study at a 12-week dosing.

And on the left-hand side, we see the decrease in A1c at our top dose, which was 200 milligrams BID, nearly a 1.6% reduction in the hemoglobin A1c at that 12-week time point. and a corresponding 5.4 kilogram weight loss amongst these patients. We have some earlier data that it's also been shared with our 1532 compound. This has also resulted in dose-dependent reductions for baseline hemoglobin A1c, mean daily glucose, fasting plasma glucose as well as body weight.

On the left, there is a consistent dose-dependent reduction of mean daily glucose. And this is actually a very good measure in short-term trials with type 2 diabetes. And based upon these 4 to 6 weeks results for main daily glucose, we would anticipate that 1532 would have a very robust A1c lowering with longer treatment durations.

On the right, body weight reduction, again, about 5.1 kilograms and about half the time at 6 weeks. And this is tested at 180 milligrams over that time period in type 2 diabetic patients. So I'd just like to make the point that early weight loss can actually help increase the compliance with this category of medicine. I think everyone knows that there are some GI toleration issues, the patients need to push through in order to get to a place where they can tolerate the medicine over a longer period of time.

And these substantial weight loss at the early point can really help with that. And while we expect the glucose to plateau, we do expect that the weight effects will continue to increase over time and with higher doses. With respect to the clinical development program, we've actually already begun to enroll our Phase 2b study for 1532.

We have 2 different strata, One is a type 2 diabetic strata in which we'll compare 1532 both placebo as well as oral semaglutide in our non-type 2 diabetic obesity strata will compare 1532 to placebo. Of note, we will be testing higher doses up to 260 milligrams rather than stopping at 180 milligrams as we did in Phase 1b. We had our first subject first dose in November of this year. And so far, we've had good patient experiences.

We believe that using oral sema as a comparator in this type 2 diabetic arm should help us actually see early signs of differentiation of efficacy, tolerability and safety. And this, we anticipate to read out in the first quarter of 2024. Our danuglipron program, we've added an additional cohort of 200-milligram on a monthly titration schedule to really help understand the minimization of GI side effects as we put in slower titration regimens for danuglipron. And assuming clinical success, data from these studies will allow us to pick one of these molecules based upon the efficacy, tolerability and dosing to advance the Phase 3 in both type 2 diabetes and obesity. And now I'll turn it over to Andy to discuss the market opportunity we have in this space.

Andy Schmeltz - Pfizer Inc. - Senior VP, Commercial Strategy & Innovation

Thanks, Jim. We see the potential for GLP-1s to become a \$90 billion market by 2030 across type 2 diabetes and obesity, a view that is increasingly shared by many of you in the analyst community. Now the primary focus here is the U.S. market, which today, due to pricing considerations, accounts for 90% of GLP-1 sales, a ratio we do not see changing materially in the future.

Let me walk you through this calculation. More and more U.S. patients will seek treatment as type 2 diabetes and obesity become more and more prevalent. And while the type 2 diabetes therapeutics category is well established with strong reimbursement, we also see an anticipate reimbursement for obesity increasing to 50% overall and with 80% coverage for commercial insurance. The recognition of obesity is a serious health condition with significant consequences is playing out real time as we see reimbursement rates improving for REGOVI.

In terms of adherence and pricing, they're in line -- our assumptions are in line with current GLP-1s. And I want to note that the higher projected pricing for obesity is due to the anticipated higher dosing for patients here than with type 2 diabetes. So let me double-click a little bit on GLP-1 class share. Globally, the GLP-1 class is growing at a 30% rate. Yet GLP-1s are only representing 17% of type 2 diabetes total prescription volume and 14% for the obesity category.

For type 2 diabetes, we expect GLP-1s to capture 25% to 30% of the market by 2030 and due to an increased recognition of the class as a leading mechanism for HbA1c control and weight loss as well as with type 2 diabetes guidelines, changing and moving GLP-1s closer to first-line treatment for many patients. In obesity, we believe the step change in weight loss efficacy and the dramatic increase in reimbursement will create a large obesity market for GLP-1s with a 50% to 60% share. So within this \$90 billion GLP-1 market opportunity in 2030, let's now talk about the blockbuster potential for a Pfizer oral GLP-1. We expect oral GLP-1s to capture a significant 30% share due to a strong patient preference for orals over injectables, which per market research is attributed to both the convenience of orals, and patients' resistance to injections.

And within that potential \$27 billion oral GLP opportunity, we believe a Pfizer oral GLP-1 -- if successful in clinical trials and approved would be in a prime position to differentiate based on efficacy, tolerability, no food restrictions and a simple dosing regimen, potentially contributing more than \$10 billion in peak year sales globally.

Put simply, we expect oral GLPs to capture about 1/3 of the overall GLP-1 opportunity and Pfizer's GLP-1, either danuglipron or PF1532 to secure about 1/3 of overall oral GLP-1 share. Clearly, a lot to play out via the forward development program, but that's the math for this potential \$10 billion-plus revenue opportunity. And I want to note this is significantly different than current analyst consensus in the range of \$2.5 billion peak sales.

All of this leads us to a compelling value proposition in the setting of a rapidly expanding GLP-1 class and easy-to-take oral GLP-1 with simple dosing is poised for category leadership. Both danuglipron and PF1532 are well positioned due to differentiators shown here, and we eagerly await the results of the ongoing Phase 2 programs to trigger Phase 3.

We believe Pfizer's deep experience and expertise in drug development and commercialization put us in a prime position to deliver a potentially best-in-class therapy to meet the needs of these patients. And we believe that our #1 rated primary care field force enables a potential shift in prescribing from specialists today to primary care physicians, which could improve accessibility for patients and the ability to treat type 2 diabetes and obesity.

I hope you now see and share our enthusiasm for this potential best-in-class oral treatment option, either danuglipron or PF1532a poised to make a meaningful difference for diabetic and obese patients and for Pfizer shareholders. Thank you.

Now I'd like to shift gears and turn things over to Chris Boshoff to speak about TTI-622 and the opportunity in hematologic malignancies. Chris?

Chris Boshoff - Pfizer Inc. - Senior VP, Chief Development Officer, Oncology & Rare Disease

Thank you very much. It's really a pleasure to be here to share with you some of our development programs, which have not really discussed much. You've heard earlier about elranatamb. So we're going to start with one of our malignant hematology programs, which is TTI-622. And then we'll also discuss in benign hematology, our sickle cell disease portfolio. Malignant hematology, as Suneet mentioned earlier, you all know these are tumors are blab born marrow lymph nodes, including the leukemia, lymphoma, myeloproliferative disorders and multiple myeloma.

Approximately 10% of all malignancies will be a hematologic malignancy. More importantly, in the U.S., every 3 minutes, 1 person will be diagnosed with the hematologic malignancy. And this still a significant unmet need with many patients not surviving 5 years. But as you all know as well, this is the area in biomedicine where there's been some of the most incredible innovation over the last decade with some of the most innovative therapies that's being developed with still a significant space to improve duration of treatment, especially with a safe, well-tolerated backbone and also potentially to lead to cure for some of these patients.

TTI-622, SERP alpha, CD47 access, as you know, is emerging as an important immune checkpoint specifically on hem malignancies or hematological cancer cells. Perhaps think of it as PD-1, PD-L1 on solid tumors. We know specifically in hematologic malignancies over expression of CD47 is associated with a poor outcome, puraprognosis, often more aggressive disease and often resistance to current therapies.

SIP Alpha is a receptor that inhibits is a receptor on myeloid cells that inhibits immune attack of cancer cells where CD47 will be expressed on. TTI-622 targets, the SIRP-alpha CD47 access. TTI-622 is differentiated from some of the other CD47 agents being developed. It maintains an active Fc region. It can, therefore, have an effector function, which means that potentially, there's a rational combination to also combine with other antibodies with effective function.

TTI-622 is also differentiated in other dimensions when it was developed and selected at Trillium. It was specifically selected because it binds less to rate blood cells, and this could have significant advantages. In the first instance, we know that anemia and hemolysis has been a challenge or vulnerability for some of the other CD47 targets being developed.

We also know that it prevents the big red blood cell sync. So the rate blood cells sync, if the antibodies bind to red blood cells have already scooped up go to red blood cells, and there'll be less antibody to bind to the tumor cell. So all in all, it means you can get a broader therapeutic index and potentially more effective therapy or antibody to this interaction between cancer cells and immune cell.

And then what I'll also show and share with you is that so far, TTI-622 is the only CD47 targeted medicine that has shown single agent activity, including complete remissions across a range of lymphoid malignancies. If we look at the waterfall plot from early data from our Phase I data, just a reminder, these are single-agent data just with TTI-622 non in combination across a dose range across various lymphoid malignancies.

We see responses, some of them very durable. This includes 2 complete remissions, one ongoing for more than 125 days, one patient was in remission and could go on to it and stem cell transplant curative intense stem cell transplant. And -- but overall, more importantly, it's very well tolerated, as you can see on the right. In fact, only one case so far of Grade 3 or 4 anemia, inferring that the preclinical data of less binding to red blood cells that does appears to be translated into the clinic with less vulnerability for anemia.

Because of the preclinical data that's been generated in combinations with various targeted therapies, small molecules, antibodies bispecifics for potential rational combinations, we started a broad development program. We're focusing specifically on multiple myeloma, acute myeloid leukemia and diffuse large B-cell lymphoma. In multiple myeloma, we've got an ongoing study with izatizumab, cafetuzumab and Kyprolis and dexamethasone and this study should read out in 2023.

We also will start in the beginning of '23 a study in combination with elranatamb, our CD3 BCMA bispecific. And this should be the first combination of the CD47 targeted agent with the BCMA bispecific. In AML, we've got an ongoing study with azacitidine. For those AML tumors harboring a P53 mutation, we also have an ongoing study in combination with venetoclax plus azacitidine. I'm pleased to say that the last study has now recruited over 40 patients.

Most patients deep duration of responses, deep responses, long duration of responses and we're looking forward to present those data at a conference in 2023. And then diffuse large B-cell lymphoma, we have an ongoing study with rituximab because of the infective function, rational combination and which should also present those data in 2023.

We are starting a combination with tafasitamab plus lenalidomide. In that instance, we will enable both antibody-directed cellular cytotoxicity and antibody-directed seller phagocytosis and a combination that's supported by preclinical data and then also starting a study with our colleagues and partners at Roche for Glofitamab the CD20, CD3 that they also presented this weekend at ASH.

So overall, a substantial body of data will be generated and that will start now is already being generated, and we're looking forward to update you in 2023 on the progress of this program.

Andy Schmeltz - Pfizer Inc. - Senior VP, Commercial Strategy & Innovation

Thanks, Chris. So we see significant market opportunity across hematologic malignancies, particularly for these 3 indications. The total addressable market for these cancers is sizable and growing, reaching 46 billion worldwide by 2030. Multiple myeloma, of course, is considered an incurable disease with inevitable relapse. And the multiple myeloma market is expected to increase by more than \$10 billion and grow beyond \$30 billion by 2030 driven by continued emerging novel modalities with the potential for improved treatment options, replacing or combining with traditional agents across lines of therapy.

For diffuse large B-cell lymphoma and acute myeloid leukemia, both are areas of expected double-digit market growth given the significant unmet need today with shorter duration of treatment and limited options. There's an opportunity for more efficacious and tolerable therapies and novel combinations to improve and extend treatment, particularly in transplant ineligible and second-line diffuse large B-cell lymphoma and in unfit acute myeloid leukemia.

Moving to commercial potential. We're really encouraged by the promising emerging profile of TTI-622 with early signs of efficacy, differentiated tolerability and potential as a combination agent of choice. Combinations of TTI-622 with novel agents are expected to be either first to market or in the first wave in their respective areas.

In multiple myeloma, we see a major opportunity for TTI-622 as a potential combination with future standards of care, CD38s and novel therapies, including BCMA. We're excited for the combination with our own BCMA bispecific elranatamab. TTI-622 plus elranatamab would be the first CD47-plus-BcMA bispecific combination to market.

In diffuse large B-cell lymphoma, we're -- we see the opportunity for TTI-622 to be the combination partner of choice in the high-risk setting to produce durable response in patients with relapsed or refractory DLBCL. And through our collaboration with MorphoSys and Incyte, we have the opportunity to have a first-to-market combination with Monjuvi and lenalidomide.

In acute myeloid leukemia, there's a potential to be in the first wave of CD47s, where this mechanism has already demonstrated efficacy. Here, TTI-622 may offer compelling tolerability and combinability with standard of care agents, such as azacitidine. Given the potential for TTI-622 to differentiate on efficacy, including duration of response, safety and combinability, we see this as a \$3 billion-plus worldwide peak year sales opportunity across these hematologic malignancies. And I want to note this is materially different than current consensus forecast that are in the range of \$200 million peak revenue.

So in summary, TTI-622 is a potential game changer for patients with hematologic malignancies with a strong value proposition. The early efficacy and differentiated safety profile position TTI-622 as a best-in-class CD47 agent and a combination partner of choice. The strong monotherapy results in minimal red blood cell binding offer a major opportunity to combine with novel agents with the goal of extending duration of therapy and remission across hematologic malignancies. And we're advancing, as Chris showed an extensive clinical development program with unique combinations to enter multiple lines of therapy across these malignancies. And building on our strong track record of leadership in oncology, we believe elranatamab and TTI-622 provide a compelling core to win in this space.

We're bullish on the opportunity for TTI-622 to become the backbone combination partner of choice across hematologic indications. Thank you. Now we're going to go back to Chris to speak to our sickle cell disease portfolio.

Chris Boshoff - Pfizer Inc. - Senior VP, Chief Development Officer, Oncology & Rare Disease

Thank you very much. It's now really a pleasure for me to update you on 2 of our programs, inclacumab and GBT 601. As you all know, sickle cell disease, a monogenic lifelong devastating disease, affecting quality of life, significant morbidity, but also affecting lifespan. And in fact, in Sub-Saharan Africa, 90% of children born with sickle cell disease will not survive until they're 5 years old.

In the West, the lifespan is approximately curtailed by 25 to 30 years. In the U.S., currently, 100,000 people live with sickle cell disease. In Europe, 50,000 in Saudi Arabia 75,000, Brazil, 100,000 and many hundred thousands more in sub-Saharan Africa, significant unmet need. In the U.S., less than 50% of current patients with -- people living with sickle cell disease actually get adequate therapy partly because of access, access to care, access to therapy, but also the limitations of current therapies, side effects, adverse events from current therapies and compliance and adherence to therapy.

This is a disease of hemoglobin polymerization. So hemoglobin A, which is the majority and adult healthy adult hemoglobin, hemoglobin A consists of 2 alpha globin sub units and 2 beta globin sub units. When this is a single nucleotide substitution in the gene encoding for beta globin, that results in sickle hemoglobin or hemoglobin S.

Sickle hemoglobin when -- if it's not bound to oxygen or in low oxygen conditions in Epoxy or when its deoxygenated will undergo polymerization and hemoglobin S polymerization lead to these crescent or sickle cells or crescent or sickled erythrocytes, red blood cells. These red blood cells are very unstable resulting in hemolysis, resulting in anemia resulting in chronic fatigue and all the other sequela of chronic anemia. Sickled red blood cells or sickled erythrocytes, also clump together with platelets and with leukocytes to obstruct small blood vessels, leading to so-called vaso-occlusive crisis.

The pathognomonic feature of this disease, VOCs, vaso-occlusive crises, vaso-occlusive crises in the long term, lead to end organ damage, including brain ischemia resulting in neurocognitive defects, renal failure, acute chest syndrome, pulmonary hypertension and many other sequela with significant consequences for morbidity but also affecting life span.

Oxbryta was the first approved medicine tackling the root cause of sickle cell disease, hemoglobin polymerization GBT-601 is being developed to be a next-generation best-in-class, potentially best-in-class inhibitor of polymerization. Crizanlizumab was the first P-selectin inhibitor that was shown to reduce VOCs. Inclacumab is now being developed as a potentially best-in-class and differentiated molecule that will be administered once quarterly or once every 3 months.

Bone marrow stem cell transplants or stem cell transplants are really reserved for those with an HLA much sipping for those with severe sickle cell disease, but most importantly, for those with access to a tertiary center because of the significant acute and long-term CQA of bone marrow transplantation. On the other end of the spectrum is the future, 2030, 2035 and beyond, ex vivo but eventually in vivo gene editing or base editing, which could result in a clear for this disease.

And this is an area which you all know that Pfizer is also significant -- where we have a significant interest and where we are building capability. VOCs, as mentioned, a significant impact on quality of life. Inclacumab is a fully human IgG4 monoclonal antibody against P-selectin. It's got a unique binding to P-selectin and the binding site overlaps completely with the natural ligand with the potential for optimal blocking of ligand and receptor interaction.

It is only -- is also the only piece selection being developed, which could be quarterly administered every 3 months intravenously. Also to mention that over 700 patients so far have been treated for nonsickle cell disease for cardiovascular disorders, and that is where we saw the tolerability and the safety of inclacumab. What is shown on the graph is platelet leukocyte aggregation with peers in preclinical models from blood from patients with sickle cell disease that inclacumab is more effective than crizanlizumab to block aggregation, which is, of course, the root cause of VOCs.

GBT-601, as mentioned, is being developed a potentially best-in-class molecule based on the mechanism of action of Oxbryta. Preclinical data illustrate or show that we get higher hemoglobin occupation with 601, which results in increases in hemoglobin, decrease spleen size in animals and also decreased hemolysis. 601 was also selected because of the differentiated pharmacokinetic profile, longer half-life and a better ratio between red blood cells and plasma, better demarcation, which means most of the drug is concentrated within red blood cells, improved PK.

Also to mention that early clinical data from the first 6 patients treated with GBT-601 in an ongoing multiple-ascending dose escalation study showed that what was seen in hemoglobin increase, it was higher than previously reported with Oxbryta. With Oxbryta in a Phase 2 study, the median increase was 1.1 gram per deciliter. And we can see here the majority of patients are over -- or 4 of 6 patients over 2.5 grams of deciliter. Importantly to point out, this is part of a MAD study, of the multiple ascending dose escalation study, and this was with 100 milligrams per day maintenance. We've since moved to 150 milligrams per day maintenance.

Also important to just show here is hemoglobin occupancy. With GBT-601, 4 out of 6 patients -- or 2 out of 6 patients achieved occupancy over 40% and 5 out of 6 patients hemoglobin occupancy more than 20%. And that compares very favorably, which was seen previously with Oxbryta which was where 50% of patients achieved hemoglobin occupancy more than 20%. And then on the right, we can see significant reduction in biomarkers for hemolysis with GBT-601, again compared to Oxbryta. This is LDH data, but a similar data obtained for other biomarkers of hemolysis like indirect bilirubin or reticulocyte count.

If we look at the updated data, and these data presented over the weekend at ASH on the first 4 patients now treated at a higher maintenance dose of 150 milligrams a day. What we can see a further increase in hemoglobin levels and in particular, there's 2 patients where hemoglobin levels are starting to be normal between 12 and 14 grams per deciliter.

There's one patient, patient #3, where the levels are declined. This patient was not adherent to the regimen of 150 milligrams per day outside of the clinic, and that's why the levels are declining. I'm happy to say now that we've since we've now treated 12 patients at 150 milligrams per day. These patients will be followed up for 6 weeks, and then we intend to go on to 200 milligrams per day. We hope early next year to make a decision between 150-milligram maintenance or 200 milligrams maintenance and then to initiate the Phase III trial towards the end of next year.

The clinical development program for inclacumab and GBT-601. Inclacumab, there's 2 studies, ongoing Phase 3 studies. The first study is specifically looking at reduction of VOCs. So these are patients 12 years and older that have 2 to 10 VOCs per year that in coming to the study and followed for 48 weeks to look at the reduction of VOCs and inclacumab once every 3 months injection.

The second study is a very unique study and probably the first such study, important study for patients with sickle cell disease. These are patients presenting or being hospitalized with the VOC. They become an index case -- this is an index case of VOC, provided with 1 dose of inclacumab and then followed for 90 days. We know in the real world that 50% of patients will be readmitted within 90 days after an episode of VOC. So it's a reduction of rehospitalization, which is an important endpoint for this population. And as mentioned, GBT-601, we hope to start the Phase III randomized trial towards the end of next year. It will be GBT-601 versus placebo with a co-primary endpoint of hemoglobin increase and reduction of VOCs.

Thank you very much.

Andy Schmeltz - Pfizer Inc. - Senior VP, Commercial Strategy & Innovation

Thanks, Chris. Let me touch on the market opportunity or total addressable market for sickle cell disease prophylaxis, which has been growing with 45% of sufferers treated today, up from about 1/3 in 2015. And we expect to see continued expansion to 2/3 or more of all people with sickle cell disease over the coming 10 years. So 50% growth from today.

Here's the rationale. For years, the only available prophylaxis treatment for sickle cell disease was hydroxyurea with limit uptake due to modest benefit risk, and hence, only 1/3 of patients treated. Recently though, with the approvals of several medicines, including Oxbryta, there's been an uplift in the prophylaxis treatment rate now at 45%, as I mentioned. And in the future, with the availability of newer therapeutics like inclacumab and game changers like GBT-601 and our E-selectin program, the prophylaxis treatment rate could reach 2/3 of patients or more.

We're especially excited about the potential of inclacumab and GBT-601. Inclacumab offering substantial VOC reduction with quarterly dosing and could reduce hospital readmissions following a VOC and GBT-601 could offer a more profound benefit to people with sickle cell disease than Oxbryta, including significant VOC reduction, while also offering once daily oral dosing and a favorable benefit risk profile.

So how does this translate into commercial potential? We expect the future prevalence of sickle cell disease to reach about 120,000 people in 10 years with prophylaxis treatment rates growing to about 2/3 of all patients as outlined. We expect inclacumab to be using about 15% of prophylaxis patients, predominantly those already on oral therapy, but struggling to control VOCs. And we believe GBT-601 could be a foundational therapy for sickle cell disease, reaching approximately 60% of prophylaxis patients.

GBT-601 has the potential to deliver meaningful clinical benefits in combination with a favorable benefit risk profile and simple one pill, oral once-daily dosing, the ideal potential therapeutic for all people with sickle cell disease. In the future, we hope patients will start treatment with GBT-601 as the backbone in lieu of hydroxyurea and then add on current or future potential options to optimize their outcomes. We see the combined revenue opportunity across the board here in the range of more than \$3 billion peak year sales.

So the bottom line is we're really excited about making an impact in sickle cell disease. GBT-601 has the potential to reduce red blood cell sickling and homologous, meaningfully reduce vaso-occlusive crises and offer convenient single pill, once-daily oral dosing. We envision GBT-601 as a strong foundational therapy for people with sickle cell disease. And inclacumab has the potential to offer once every 12-week infusions and reduce VOCs at rates similar to or better than current agents, making an important therapy for people struggling to control their VOCs.

Finally, we believe our sickle cell disease drug development expertise in our existing commercial footprint in rare hematology position us well to meet the global needs of people with sickle cell disease.

Thank you. Now let me introduce Liesa Anderson, who will take you through our exciting mRNA pipeline portfolio. Liesa?

Annaliesa Anderson - Pfizer Inc. - Senior VP and Chief Scientific Officer, Vaccine Research & Development

Thank you, Andy. I'm delighted today to have the opportunity to share how at Pfizer we're broadening the use of our mRNA platform for vaccine development. So we're really building upon the success of both our infrastructure as well as our talent in how we bring new vaccines to market after delivering a successful portfolio that includes Prevnar 13, Prevnar 20 and community, we're also looking to build upon our RNA platform for RNA development.

With RNA development and the work that we have done with BionTech on community, it really puts us in a strong position to look and see how we can continue with mRNA technology to really disrupt how we develop vaccines at Pfizer. And today, I'm going to focus on the vaccines that are listed in the box, which are our next-generation RNA vaccines.

So let me first start with influenza or flu. And so there are licensed vaccines for flu. However, despite that, we still see between 3 million and 5 million cases of severe flu globally every year. And we think that we can do better when it comes to mRNA, and we can think that we can disrupt this picture in 3 different ways. First of all, the mechanism of action.

So mRNA vaccines, we know from our experience with community induce both neutralizing antibodies but also T cells, and we think T cells are very important for vaccine effectiveness. The next piece, the second piece, is the fact that mRNA vaccines don't take as long to produce. And with the current flu paradigm, currently, the flu strains for the flu year has elected 6 months in advance to meet those manufacturing time lines. And as we all know, a lot can change in 6 months. And so by having a technology that you can move manufacturing forward could help have more efficacious vaccines.

And then finally, going back to the manufacturing for the third point, is, again, the time, the flexibility. If new strains come along, mid-season or if we see pandemic flu variants arise, we have the flexibility with the mRNA platform to address that.

Here, I'm showing you some data that's taken over many years, and it really highlights the ineffectiveness of current flu vaccines, where we see variable efficacy year-by-year. This efficacy is driven by 2 main things, which are colored in the graph. In the dark blue, we see low effectiveness because of antigenic drift. And then in the light blue, we see low effectiveness due to egg adaptations that happen whilst the flu vaccines that are made in eggs are being produced, causing mismatches when the vaccine is then administered to the population. In some years, you see that you actually get both things happening.

So again, for an mRNA-based approach, we think that we can solve a lot of these problems. We have a 3-pronged approach for how we're looking to solve this. And these are pictured in the boxes in the slide. The first, building upon the proof of concept that we have had with the mod technology, we have a mod flu vaccine, that's in Phase 3 and is expecting to readout later next year. We're also looking at combination vaccines, starting with respiratory combo of flu and COVID using the COVID vaccine that we partnered with BioNTech and our investigational flu vaccine. And we believe that by combining them, it offers 2 justifications. The first is that currently, COVID isn't a seasonal disease, but we think that over time, it will become seasonal and by then, therefore, putting the COVID vaccine with the flu vaccine, it provides an opportunity for both simplification and increased vaccine compliance.

And then the third approach that we're taking to address flu vaccines is by increasing antigens. So current vaccines are really driven by raising antibodies to hemagglutinins. And there are 4 different hemagglutinins that are included in each vaccine represented by 4 different strains. Neuraminidases are also associated with protection and flu. However, the way these are included in the inactivated vaccines is very inconsistent. And in the protein-based vaccines, it's not included at all.

And so by finding ways to improve the technology that we have so that we can increase the number of antigens that go into that vaccine. We also think that, that is going to be a way to help improve the flu paradigm. And we're looking at increasing antigens by changing some of the technologies we use, and I'll go into that in a little bit more detail later.

So here's just some preclinical data that we're showing for the first time. And this is our data with our investigational mod flu vaccine, put in combination with our COVID bivalent vaccine. And on the left of the slide, you can see data for our COVID vaccine. And so what we did is we vaccinated mice with either the COVID vaccine alone, the investigational flu vaccine alone or both of them together. The left shows neutralization

data for the COVID component of the vaccine, both the vaccine alone, the COVID vaccine alone in blue -- and gray actually. And then against the Wuhan strain, and the 4, 5 variants. And you can see there's really very similar levels of neutralization when you have the vaccine as monovalent vaccines with just the COVID or when combined.

And then on the right of the slide, you can see very similar data for the flu components where you have the flu vaccine alone and then the flu vaccine with the COVID tested against the 4 different hemagglutinin antigens, and we see little or no interference when we combine those vaccines. So we're currently in Phase I with this study, and we're looking forward to having a readout early next year to then move that program forward.

So the next piece of the strategy, I mentioned, was potentially adding more antigens. And this provides the advantage of being able to dose spare. As we've seen with RNA vaccines with the mod platform, as you add more antigens and go higher in dose, you see reduced tolerability. And so as we want to put more antigens in these vaccines, we're looking at ways of how can we be dose sparing and put less antigen in there so that then we can put more antigens in there. And here's just a cartoon that compares the 2 different technologies that we're working with. So the upper one is the mod technology which is how we make the COVID vaccine. And you can see on the top that essentially once the vaccine enters the cell, the RNA portion replicates to make the antigen.

And on the bottom of the figure is the saRNA or the self-amplifying RNA. And this differs in the fact that once that RNA enters the cell, it amplifies as the name says, and it has more copies of RNA. And those additional copies of RNA are then translated into antigens. And so by that way, you can put less RNA in the vaccine because you're going to make more once it's been administered.

So again, some preclinical data. This is data that we've not shown before. And it's really looking at what happens if you make an sRNA construct that contains both the hemagglutinin and the neuraminidase that I mentioned, and you compare it against a licensed flu vaccine. And on the left of the slide, you see the hemagglutinin assay data with the -- and then on the left -- sorry, get my left, right wrong -- on the left, we get the neuraminidase data as well. And we're really seeing really good strong responses in preclinical models that are comparable or better to what we see in compared to the control.

So we have an exploratory study ongoing, where we're looking at different combinations and constructs of saRNA to understand what will give us the most potent tolerable results, and then we're expecting those results to read out next year as well at which time we will share them.

I'd now like to switch gear to Varicella Zoster Virus or VZV, as we call it. And there are effective VZV vaccines that are associated with preventing shingles. And in the U.S., there's a shingle vaccine that's used. Despite being effective, they contain an adjuvant, which is associated with a high rate of adverse reactions and low tolerability. And we think that with RNA vaccine, we can do better and help to drive uptake of this important vaccine by making it less reactogenic.

Why do we think this? We haven't put our vaccine into the clinic yet. But what we do know from both our COVID vaccine and the investigational mod flu vaccine is that they have very similar reactogenicity profiles. And this is shown on the left of the slide. And essentially, we are expecting to see something similar for our VZV vaccine. And what I'm showing you here is considerably lower to what has been reported to the current licensed shingles vaccine. So we're very confident that by inducing both antibodies and a reduced tolerability profile, we'll be in a good position to be very competitive in the market. But we do have some data, again, it's preclinical and showing this again for the first time.

So on the left of the slide, I'm showing the antibody responses when you vaccinate animals with our mod RNA vaccine compared to the current U.S. standard of care. And you see very similar levels of antibodies, so that's good. And then on the right of the slide, I'm showing you our T cell responses. T cells again are very important in efficacy and memory. And on the one side, there's a CD4 responses and then the other, there is CD8 responses. And what we see from a T cell perspective is either a trend for higher or significantly higher responses. And so we're really excited about our VZV vaccine and the prospect of moving this vaccine into the clinic early next year.

So I'd like to finish with that and just say that we have high confidence that our mRNA vaccine platform can deliver both the effectiveness and the safety tolerability profile that's required and therefore, result in better uptake of the vaccines that we currently see today.

So with that, I'd like to hand over to Navin Katyal.

Navin Katyal - Pfizer Inc. - U.S. Commercial & Global Business Lead for mRNA Portfolio

Okay. Thank you, Annaliesa. All right. I know that it's me, a short Q&A and closing remarks between me and the cocktails. So thank you for hanging in there. Again, it's a pleasure to be here with all of you today, and we're really looking forward to this last discussion.

I want to start just by underscoring our belief that at Pfizer, we are uniquely positioned, and we are very well positioned to deliver on the future of our mRNA-based vaccines portfolio. And I think the conviction that we have here, the confidence that we have here is really fourfold. First, because of the proven global leadership that we've seen to date with our commercialization of community. The role that community has played in the pandemic, I think, is incredibly obvious. But we are very, very proud of that, the role that it's played.

And if you just take a step back and look at that impact, we've seen that we've delivered over 4 billion doses to over 180 countries and territories across the world date. And if you also take a step back and look at sort of the administrations of the vaccines, we see that almost 2 out of every 3 COVID-19 vaccinations to date across the world have been with community. So it's just remarkable, remarkable tailwinds, I would say, as we move forward.

Our second source of conviction is the power of our broad and growing portfolio of vaccines. So as we move forward into the commercial markets and as we move forward commercializing our growing mRNA portfolio, we intend to continue to leverage the decades of experience that we have in commercializing vaccines but also couple that with this growing portfolio. And as we move forward in terms of contracting and creating agreements with customers, I think we have an enormous opportunity to really construct differentiated agreements that will really advantage and position our mRNA portfolio in a very, very positive way.

Our third source of conviction here is our industry-leading development, regulatory and manufacturing capabilities once again recently demonstrated by the agility of our bivalent booster delivery this past year around the world. In the U.S. alone, we delivered over 30 million bivalent doses just to the U.S. after authorization. And when you take a step back and just look at the 30 days after we got that authorization, that first authorization in the U.S., we were responsible for over 70% of the supply in the U.S. alone. And I think what that highlights is not only the sort of agility and the power of mRNA technology, but I think even more importantly and more interestingly, the power of that technology in the hands of Pfizer.

So I think our fourth source of conviction here as we move forward with our mRNA portfolio in the vaccine space is our deep conviction and our confidence in our global commercial operations. I think it's no surprise to anyone that the relationships that we have with our customers all over the world, they're long-standing, they're deep and they're incredibly trusted. And our infrastructure to educate, to reach, to engage both consumers, patients, vaccinators all across the world is simply unmatched. And we've seen that time and time again.

So I think all told, we are, again, very, very confident that we're very well positioned to lead in mRNA and including in some of the competitive vaccine markets that we're going to be entering into moving forward. So I think as a result, we do see a very large and very durable, sustainable portfolio, particularly as we transition out of the pandemic. So let's take a quick look.

So in influenza, as Annaliesa said earlier, we anticipate that we will see a broad immune response with our vaccine candidate. And we couple that with the speed and with the agility, again, that we've seen with mRNA, particularly in Pfizer's hands, I think we do have a real exciting opportunity to really address the volatility and effectiveness that we've seen year-over-year, either due to strain mismatch, strain drift, et cetera, that sort of phenomenon that Liesa was talking about earlier.

And then in terms of supply, like I just said, right, the sort of global scale and the reliability that we were able to sort of demonstrate in the COVID-19 experience, I think we bring to bear again in the influenza space to bring reliability to the influenza space, which has been a challenge in certain years and I think is an incredibly important part of customer decision-making as they think about who they want to partner with. So I think that is another tailwind that we expect to capitalize on.

With the COVID and Influenza combo space, as Annaliesa said, we are aspiring and really targeting a strong clinical profile. We also think this offers another opportunity to continue to drive compliance, to continue to drive uptake given the convenience both to vaccinators and to consumers alike. And we've seen in all the research that we've done, that there's very strong desire to see a combo product launch in the market.

And then again, just given the strong preference that we've seen for Comirnaty amongst both vaccinators as well as consumers, and it's very, very strong. So when you look at the sort of preference time and time again, we see that we enjoy with Comirnaty a very substantial margin of preference among vaccinators and consumers. And when we take that tailwind and we apply it to our combo, I think we're very confident that we're going to have an opportunity to lead in this space as well.

And then finally, for shingles. As Annaliesa said earlier, we aim and we're optimistic for a strong clinical profile with high efficacy and opportunity to improve upon tolerability, which we know is important. And then finally, once again, leverage the scalability and the power of the global manufacturing network in another space that has seen some supply disruption and frankly, some shortages across the globe. So have an opportunity to really make a mark in this space as well.

And when we take all of this into account, and we couple this with our leadership capabilities, all those capabilities that we just talked about, again, we see a very large, durable business for these mRNA vaccines going forward and we estimate a potential annual portfolio revenues between \$10 billion to \$15 billion by 2030.

So in closing, we have tremendous confidence in our mRNA vaccines portfolio, especially given the very strong compelling value proposition we see against each of the vaccine candidates in these programs. And I think we believe that we have an unparalleled opportunity to develop and to commercialize our pipeline. And again, we expect this to translate into a very meaningful and durable business and value into 2030 and beyond. So I want to thank you all for your time and attention today. I'm going to invite the rest of my colleagues up for Q&A. Thank you.

QUESTIONS AND ANSWERS

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Okay. Great. So the logistics of this Q&A session are going to be very similar to the last time. We're going to alternate between left and right. If we have questions from the Internet, we'll try to take them as well. And Ama Amoah is also going to assist us with any questions from the Internet if they come in. And then after the 30 minutes, we will have a brief closing statement by Dave. Dave Denton, our CFO, excuse me. So with that, why don't we take the first question from the left, please.

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

Louise Chen from Cantor. I wanted to ask you about your oral GLP-1 franchise. So I wanted to ask you, do you think you'll be able to move fast enough to be competitive with the injectables that are already on the market or coming to market? And what do you think payers need to see to give broad coverage for obesity drugs?

Andy Schmeltz - Pfizer Inc. - Senior VP, Commercial Strategy & Innovation

I'll take that. We're very excited, as I tried to articulate about what we have in our hands with our oral GLP-1 portfolio. It's a huge market opportunity, the unmet need here. I think in obesity, it's like over 650 million patients, they anticipated to grow to over 1 billion and over 0.5 billion diabetics. And GLPs are increasingly becoming important. All the market research we have is that people prefer an oral option to being to injections, whether it's a weekly injection, a monthly injection or a quarterly injection. And specifically with an oral option, something that's once a day or twice a day, but it's convenient, most importantly, you don't have a food restriction is really, really important. And because the space is so large, obviously, we expect and aspire for a compelling profile, but we believe there's a real opportunity in the space for oral GLP-1.

And in terms of reimbursement, I think we're going to be able to see a lot play out over the near term. But everything we see right now is that obesity, as I mentioned, is becoming recognized as a serious medical condition with downstream consequences, reimbursements going up, we're seeing it with today. And look, if anything changes, we'll have plenty of time to make sure we're generating the evidence for that are needed for payers to enable reimbursement. So we're setting the stage. I don't know, Jim, if there's anything you want to add from a technical standpoint.

Jim Rusnak - Pfizer Inc. - Senior VP, Chief Development Officer, Internal Medicine & Hospital

Yes. I mean I think that's very well said. With respect to some of the programs that are of the highest importance. So this is one that's been given what we call designation. And we've sort of developed some of those programs, the COVID vaccine is one of them. I was responsible for Paxlovid. And there is a true enterprise-wide backing for programs that have the Lightspeed designation like GLP-1, and I'm confident that we'll be able to deliver this in a timely fashion.

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

I'm Steve Scala from Cowen Company. I guess maybe they don't qualify as near-term launches or high-value pipeline agents, but there were 4 things that didn't get mentioned today that I'm kind of surprised it. One, and I apologize if I missed it, -- but gene therapy for hemophilia despite the fact that we're getting data next year and the year after.

Two, Prevnar got passing mention but you have competitors pursuing more balance, GSK and Sanofi, and you have a follow-on, presumably with. Maybe you could tell us how many?

Third, Eliquis follow-on, Albert said on the second quarter call, you were looking. Are you still looking? And how confident are you you'll have an answer by May of 2028?

And then lastly, Alzheimer's, despite the fact that -- with was the pioneer, is your lack of activity in Alzheimer's, the fact that you haven't found anything interesting yet? Or you think current therapies have no value?

Chris Boshoff - Pfizer Inc. - Senior VP, Chief Development Officer, Oncology & Rare Disease

Maybe I can address the gene therapy issue. Liesa, I don't know if you want to talk about Prevnar and then for Eliquis follow-ons, maybe Jim can address that. And then Andy, do you want to talk about Alzheimer's disease.

Okay. So in terms of gene therapy, Steve, what I would say is, we focused on the biggest opportunities today. So we still remain very excited about our gene therapy programs, but we just have so many good things going on that we couldn't talk about everything today. So we're happy to talk about those and other venues in the future, and our enthusiasm is unchanged.

Annaliesa Anderson - Pfizer Inc. - Senior VP and Chief Scientific Officer, Vaccine Research & Development

Yes. And so for Prevnar, again, our focus today was on mRNA vaccines. We're very confident with our position with the pneumococcal vaccine space. We've submitted the licensure our 20-valent pediatric vaccine, which provide the broadest coverage for any pneumococcal vaccine, and we currently have adult 20-valent vaccine as well.

Looking to the future, we still remain confident that we're going to maintain our leadership position. As you pointed out, we do have something in early clinical studies. It's not something that we're ready to talk about yet, but we certainly will share it when -- as we get data and as we move forward.

Jim Rusnak - Pfizer Inc. - Senior VP, Chief Development Officer, Internal Medicine & Hospital

With respect to Eliquis, I think that we're very careful in monitoring this space. For a follow-on to Eliquis, Eliquis has had a fairly high bar. So we're very cautious to the opportunities in the space. But should one come along that we're interested in, we'll provide updates in due course.

Andy Schmeltz - Pfizer Inc. - Senior VP, Commercial Strategy & Innovation

And just briefly on Alzheimer's disease, I actually worked on that program, bapineuzumab back in the day with Wyeth at the time of the Pfizer acquisition. And I think it's just an indicator that this space, although the unmet need is so significant is challenging and will take a long time to play out. And while in the therapeutic areas that I mentioned, neuroscience is not one of the areas of focus for Pfizer today. If the science is compelling and something looks exciting, of course, we're going to take a look at it from an opportunistic standpoint.

And maybe just one overarching comment. There was a lot in the portfolio that we could have talked about today. We tried to focus on the areas where we thought there was an underappreciation in the investment community of what we believe the prospects we have in our hands versus what's the current perception, but there's a lot more areas beyond those that you just asked about that we'd love to talk about.

Andrew Simon Baum - Citigroup Inc., Research Division - Global Head of Healthcare Research and MD

Yes, Andrew Baum, Citi. Just on the GLP-1. Lilly will have data from their Phase 2 internally about now. I'm sure they'll start the Phase 3 next year. Obviously, you haven't seen the data, neither of you. But given the lead time that they have and given the enormous leverage they have as a function of their franchise in diabetes and obesity, it seems that a very high mountain to climb even if you do deliver a drug because they will have a once day, no food interaction, 1 year plus lead time and probably the world's largest drug potentially to leverage off. So how do you think about entering that franchise against those competitive forces?

And then following on from that, Pfizer is one of the few companies with a large primary care presence. Many have disbanded that. To what extent do you think there's any issues with Pfizer potentially licensing an IV? We obviously saw the Amgen [data] recently. Is that a conflict of interest? Do you think a sponsor may think that as a conflict of interest given that you have your established drug well, I don't expect you to comment on Amgen specifically, but just in general, whether you think 1 precludes the other for whatever reason?

Andy Schmeltz - Pfizer Inc. - Senior VP, Commercial Strategy & Innovation

So I can speak to the kind of commercial business considerations. I don't know, Jim, if you want to comment anything on the profile that we have on our hands.

Jim Rusnak - Pfizer Inc. - Senior VP, Chief Development Officer, Internal Medicine & Hospital

Yes. So I think that we're actually very fortunate that we have not 1 but 2 molecules to choose from that were developed in-house firstly. And I think that the key characteristics that we look at as a potential very important differentiator is us being a full agonist of the receptor. And we do believe that, that full agonism may be required to really replicate what can be seen with peptides administered subcutaneously. So we will, again, go very quickly in development, and we have a high degree of commitment for these drug assets.

Andy Schmeltz - Pfizer Inc. - Senior VP, Commercial Strategy & Innovation

And maybe just to add, I think we think we have in our hands a best-in-class opportunity. And we're going to have the -- we'll obviously monitor the competitive environment, see the profiles of what are out there and we will design our pivotal programs to exploit areas of potential differentiation with our substrate relative to the competition. And we are undeterred by the reality of competing versus other major biopharma players. If you go back over the years, we do it in almost every one of our major categories, and we have the infrastructure, the capabilities to it successfully. So that's not -- we're not intimidated there. And the opportunity here is significant and the space is large.

In terms of building upon a portfolio in type 2 diabetes and obesity, we have internal programs that we're working on, and we're always looking to complement our internal substrate with bringing things from the outside. And I think you make a fair point, injectables are going to have an important role just as orals. We'll have an important role in the spaces. So that would be on the table.

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Sorry, Andy, maybe I can ask you a question. What is our market research thought is about consumer preferences with regards to once daily oral versus other?

Andy Schmeltz - Pfizer Inc. - Senior VP, Commercial Strategy & Innovation

Yes. I spoke in kind of alluded to market research that we have. But all the data that we see is that patients prefer orals over injectables and in particular, a convenient, whether once or twice a day and something without a food effect is going to be appreciated. That's why in the assumptions I shared while a lot of the GLP space is going to be injectable, we think that orals will take about 1/3 of it.

Chris Shibutani - Goldman Sachs Group, Inc., Research Division - Research Analyst

Yes. Chris Shibutani from Goldman Sachs. A question about the mRNA-based flu vaccine opportunity. On Slide 126, you identified a potential \$10 billion market opportunity there. Several components go into this. You were very clear about some of the potential advantages, which seem clear. Agility, it seems to be a particularly appropriate word in that regard. What is your confidence that you're going to be able to demonstrate superiority as opposed to just non-inferiority?

And to get to that \$10 billion number, can you perhaps weigh in on the extent to which you think increased uptake is a factor versus potentially premium pricing? And I'd like to also just see potentially a response that David may be able to provide in his closing commentary. You've made some decisions overall about the structure of how you're making R&D investments.

And some of that, in particular, was highlighted by a decision recently to out-license or to structure TL1A investment, which was in late Phase II clinical development using a partnership there. Perhaps we can understand how you're thinking about triaging this. I know that the level of R&D investment has been increasing, but we'd love to -- perhaps it would be helpful to get some further insight into how you're thinking about adding that as part of the strategy.

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Navin and Liesa on the mRNA question. Don't take the superiority one or...

Annaliesa Anderson - Pfizer Inc. - Senior VP and Chief Scientific Officer, Vaccine Research & Development

So I can start, and then I'll hand over to Navin. So the question was what's our confidence for superiority. So a couple of things. First of all, as I showed -- as I discussed, we have the T cell responses, which Mikael Dolsten showed, I think, in second quarter earnings. And we think that the T cells really will help drive the effectiveness of the vaccine, and we're conducting the study, so we will see. So that's the first thing.

The second piece is that we're developing this vaccine from 18-year-olds and above. And so one step is noninferiority, which is fine, obviously, for the younger guys. But as people get older, you need to be able to show that you're better than the current standard vaccines. And so that's, again, where we'll see where the T cells plays out. And then the other thing that I didn't mention is so traditionally, when flu vaccines are licensed, they're licensed using noninferiority immunity. And then after that, it's an accelerated approval and they then go ahead and do post-marketing efficacy studies to show that it's actually efficacious.

We're not doing it that way, again, because we're looking at a different mechanism of action. We're looking for the contribution for the T cells as well as the antibodies, which is why we've gone straight ahead to do the efficacy study and not do the immune noninferiority.

Navin Katyal - Pfizer Inc. - U.S. Commercial & Global Business Lead for mRNA Portfolio

Yes. And then I would just say in terms of the commercial potential and the opportunity. I think the reason why we're bullish is sort of multifactorial. I think first, you hit on it, which is the fact that the technology will allow us to be more agile, right? So if we can get away from being 6, 7 months out from when the season starts and actually start to find a new regulatory framework, which we expect we will have to allow us to match later in the season, then I think you have sort of a very disruptive sort of environment than what's sort of the environment has been for decades. I think that's sort of number one to sort of underpinning the mRNA technology first and foremost.

And then I think secondly, then we have the sort of Pfizer commercial machine sort of underpinning our ability to sort of take that and really amplify the awareness that we now have an opportunity to really do something as a step change in terms of driving better efficacy as a result of just having better strain match because what you see historically is a lot of people just don't bother. And the reason they don't bother us because they've seen some that say that historically, the efficacy hasn't been very high.

So I think that's where, just like we've done with really leverage our field force, our customer-facing colleagues, our consumer engagement and all of the other things that we can bring to bear to make sure that we can drive sort of that step change in awareness that we have something new that can offer something different on top of, I would say, the contracting prowess that we continue to deliver on with all of our vaccines. And now that we'll have this sort of broader portfolio, I think we'll be well positioned to really make a mark and succeed in the flu space.

Andy Schmeltz - Pfizer Inc. - Senior VP, Commercial Strategy & Innovation

And to your question on TL1A, and I'll let Dave speak more perhaps in the closing. But the formation of a new company with Roivant, I think was very purposeful. As I showed the slide with all our clinical substrate at the beginning, we have a lot on our hands. And while we have significant capital in R&D resource. At the end of the day, it is limited, and we're trying to find creative ways to make as much impact as possible. And forming this new code, we have a 25% equity stake and we have commercialization rights in some territories going forward is one example of that ability to be able to advance more with finite resources.

Christopher Thomas Schott - JPMorgan Chase & Co, Research Division - Senior Analyst

Chris Schott at JPMorgan. I just want to come back to the roughly 1/3 market assumption for the oral GLP-1s in that broader market. And I guess kind of a twofold question. Is that a similar view in both diabetes as well as obesity? And I guess, the core of the question is, I know Rybelsus isn't a perfect drug, but does have single-digit market share. And we're seeing injectables not just targeting GLP-1, but cutting adding other kind of mechanisms on top of that, and that hurdle keeps going higher and higher. So can you just come back to -- as we're thinking about this market in '27, '28 with products beyond potentially in the market. How are we getting 1/3 of the patients starting on an oral when that oral may not have the same efficacy that you can get with injectables?

Andy Schmeltz - Pfizer Inc. - Senior VP, Commercial Strategy & Innovation

Yes. Very good question. I do think that it's going to be different in diabetes and obesity. Diabetes is, I mean, a more mature established marketplace. And so that's the paradigm that oral GLPs are operating into. And obesity is more nascent. It's emerging now and things are going to evolve. And I think there's an opportunity for orals to come on -- oral GLPs to come on earlier in obesity as the market is being shaped and growing and particularly for prospective obese patients to say, you don't have to contemplate an injection, which is kind of one of the things that we know that that's a deterrent to an oral is going to be an exciting opportunity, which is why when we think about the share, we said oral 50% to 60% in obesity versus 25% to 30%.

Could we have the exact numbers wrong in terms of the GLP penetration for diabetes and obesity and then the share of orals for diabetes and obesity? We're projecting out into the future. So we're trying to give broad strokes with margins of air. But we'll have to see how it plays out. And that's, I think, one of the -- from where we are today, we have enough lead time to monitor how the market is evolving and to optimize our approach and calibrate it based on how the market paradigm is crystallizing. So that's what we're looking forward to.

Trung Huynh - *Credit Suisse Securities - Security Analyst*

Trung Huynh from Credit Suisse. One on interferon and another one on GLP-1. So just on interferon, thanks for pointing out, none of us have got it in our models. Just wondering could you just tell us about the catalysts we should expect for that one going forward? When is the Phase 3 start? When should we get the Phase 3 data? When do you expect launch?

And then just on GLP-1, again, sorry, another one on perhaps pricing pressure of the class. You noted 17% TRx in diabetes, 14% TRx in obesity is going to be a \$90 billion market, it's going to be one of the biggest classes in the world, if not the biggest class in the world. So how are you thinking about how PBM is going to react to that going forward, especially as we get more and more GLP-1s entering the market?

And then specifically on your potential oral, whatever one that's going to be, how do you disassociate that from oral pricing, which is a significant step down from GLP-1 pricing?

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

Mike, the interferon?

Michael Corbo - *Pfizer Inc. - Senior VP, Chief Development Officer, Inflammation & Immunology*

I can start with interferon beta. So from a Phase 3 or a pivotal program perspective, we are working already with regulators. So those end-of-Phase II discussions are actually imminent. Our intent is to start that basket Phase 3 program in 2023 as quickly as we can. Again, it depends on the feedback that we get. And then from a -- really from a recruitment perspective, recruit that as quickly as possible. I can't tell you today because we're not recruiting today, but our intent is to be able to contribute to the overall bottom line in that '26 to '30 time frame and be able to contribute those numbers that Andy was showing you.

Andy Schmeltz - *Pfizer Inc. - Senior VP, Commercial Strategy & Innovation*

And in terms of the future pricing paradigm in the diabetes and obesity marketplace, 2 things. One, we aspire to have a clearly differentiated profile with the Pfizer oral GLP-1, whether danuglipron or PF-1532. But let's assume for a second that these offerings are more similar than different. Then I think that it's going to be much more of an access -- pricing and access strategy and how you place, what your strategies in terms of getting access and coverage. And so it's a little bit the gross pricing to a net pricing contracting paradigm.

And again, here, the beauty is we don't have to make those decisions right now. We're going to be able to see how everything evolves and be very purposeful once we have the profile clear, that we will make sure we're generating the data to support access and the value proposition, and then we'll make the pricing assumptions. But we're pretty confident that kind of the general range that we're believing from a net standpoint is viable in the future.

Evan David Seigerman - *BMO Capital Markets Equity Research - MD & Senior BioPharma Research Analyst*

Evan Seigerman from BMO. So you had a lot of information about various peak commercial potentials across assets, but I noticed there wasn't any about the go forward for your COVID-19 program. So maybe without providing guidance, provide us some broad strokes about how you're thinking about the go-forward commercial opportunity for either boosters or boosters plus influenza?

Navin Katyal - Pfizer Inc. - U.S. Commercial & Global Business Lead for mRNA Portfolio

Sure. I can take that. So I think -- yes, so as Andy highlighted earlier, our intent was to really focus on the launches moving forward. But just in terms of COVID-19, I think we know, first and foremost, COVID is here to stay unfortunately. So we do expect that there will be moving forward a sort of a durable business around stand-alone community as well as the combo with influenza moving forward. I think many countries around the world have already started to signal that they will move towards an annual recommendation for most of the population or large parts of the population.

And then for some, potentially those at high risk or maybe immunocompromised, maybe something somewhat more frequent. But that is the basis for our strong view that this will be a durable annual business that looks like flu. I think as we think about the, we also think about the influenza sort of paradigm given all the reasons I just talked about, I do think that the adult market will quickly emulate the flu in terms of uptake. And I think the pediatric space is given what we've seen in terms of uptake to date will take a little bit longer to mature. But over time, I think we do see that, that will start to converge.

And then I think to your point on combination, we're very bullish on combination because we know that the adult vaccination market is getting a bit more crowded and there is a lot of interest particularly amongst the healthcare system, but also amongst consumers for something that's more convenient. And I think that will have a synergistic effect in terms of driving uptake, both for flu as well as for COVID moving forward. So we're -- I think we're very confident, and we definitely are continuing to invest given the large and durable business that we see moving forward.

Carter Lewis Gould - Barclays Bank PLC, Research Division - Senior Analyst

Carter Gould, Barclays. Maybe I think I asked you to ask this at EADV, but I'll ask it again. Just in terms of the decision-making process between 1532 and danuglipron, a, will that Phase 2 data provide enough information to make a decision? And should we still be thinking about it as an either/or are there scenarios in which you split indications or do something creative on that front?

And then maybe just, Andy, at the risk of hearing you say you'll make a decision down the road when you have more data. I guess just when we think about -- it seems like it's been discussed much more of like a zero-sum game here, but we think about potentially integrating with the injectables, maybe leading off with injectable and then transitioning to an oral is maintenance. Can you talk about how -- if you have market research supporting that or internal thoughts on that potential paradigm going forward and how you might be able to shape that?

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Jim, do you want to?

Jim Rusnak - Pfizer Inc. - Senior VP, Chief Development Officer, Internal Medicine & Hospital

Yes. So we'll be having the data readout for the, that add-on cohort to our existing Phase IIb study reading out in the second half of next year. And then we anticipate the 1532 data, both the obesity cohort as well as the type 2 diabetic cohort reading out in that first quarter. So we will have data essentially contemporaneous with one another. We have started the Phase IIb study for 1532. It's actually recruiting fairly robustly. So we're optimistic that we'll be able to meet those time lines. And we're going to look at the totality of the data, the overall reduction of A1c, the tolerability.

We have 13 different dose regimens within the type 2 diabetic cohort and the obesity cohort. There are some similarities between them. There are some differences between them so that we can actually explore differences in titration and the toleration within the study itself and make this comparison within danuglipron but it would be to make that decision in the first quarter, it would be to select the winner, if you will, out of those 2 rather than to parse out individual indications.

Andy Schmeltz - Pfizer Inc. - Senior VP, Commercial Strategy & Innovation

And in terms of your second question of course, we're going to see the Phase 2 data and what we have in our hands, glad to know you've been listening. But I think what we're going to do is then set course to generate data that maximizes the opportunity in the utility for patients. And I think it's fair that both diabetes and obesity, you're not generally treated with one medicine, you're treated with a combination of medicines and then different medicines over time. And so how can we build upon what we have in our hands with our oral GLP-1 and then add on to the data. So there will be a subset of patients that are out there that already have used injections. And they're not -- it's not de novo to avoid moving to an injection.

Do we have data that can make compelling to initiate use with our oral GLP-1s after they've already experienced an injection? So I guess what we've been speaking to is kind of in a perfect world, kind of what the vision is. But of course, when it gets real and we were ready to trigger the generation of that pivotal data, we will wrap around it to make sure we're maximizing the opportunity across the populations who could benefit from our oral GLP-1.

Robyn Kay Shelton Karnauskas - Truist Securities, Inc., Research Division - Research Analyst

Robyn Karnauskas, Truist. Two quick ones. On CD47 or 622, you focus on lymphoma, leukemia, but other companies are looking at combinations and breast with ADCs, you don't have an ADC program that could open up value to that program I want to get your thoughts on value outside of blood cancer?

And then again, another question on the oral GLP. With prior care doctors, are you focusing just on primary care? Do you think that will be your strategy with the \$15 to \$20 price point? Because you're right, they don't really use it. And if you're going to do it, how do you really get them comfortable with maintaining patients' compliance and keeping sure that they are titrated the right way because we've heard some very interesting ways that specialists are titrating Ozempic to make people get through that rough patch?

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Chris, do you want to take the TTI?

Chris Boshoff - Pfizer Inc. - Senior VP, Chief Development Officer, Oncology & Rare Disease

So for TTI-622, we are focusing on hematological malignancies. There's another molecule in the portfolio, TTI-621, which is IgG1 base with increase even in a higher FC activity -- effective function, and that molecule is being currently sold tumors. But TTI suited to focusing on hematologic.

Andy Schmeltz - Pfizer Inc. - Senior VP, Commercial Strategy & Innovation

And regarding our oral GLP portfolio, the intent was that it's both and both specialists and primary care physicians, leveraging the Pfizer infrastructure to really bring this exciting mechanism into primary care physicians' offices because of the expected prevalence of type 2 diabetes and obesity, there are not enough endocrinologists out there to appropriately treat this disease. And of course, assuming we're going to move down that path, we will put in place all the right market development, education opportunities. We'll benefit from actually the experiences going on today with some of the competitors kind of experimenting in primary care, so that we make sure that we overcome any hurdles or challenges.

Robyn Kay Shelton Karnauskas - Truist Securities, Inc., Research Division - Research Analyst

With the \$90 billion, I think, number you have on the class, are you assuming that all the class is pricing compression because there'll be more competitors out there? Or are you assuming that the orals are going to be separate priced like Andrew asked earlier than the injectables.

Andy Schmeltz - Pfizer Inc. - Senior VP, Commercial Strategy & Innovation

I think we're going to have to see how it plays out. We're going to make sure that we price competitively, given the circumstances at the time to enable access and patients to benefit.

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Joe, you get the last question.

Joe Thomas - BofA Securities, Research Division - Research Analyst

Joe from Bank of America on for Geoff Meacham. I have 2 just relating to the vaccines. Regarding the \$10 billion to \$15 billion portfolio potential you gave for the mRNA vaccines, I was wondering if you could break down what the mix looks like for that. Like is COMIRNATY going to still have a large share of that? Are you thinking that maybe it's going to be a little more split between the products?

And then my second question is for the combo vaccines, we have had a bit of conversation about kind of shortening the formulation time for the flu vaccines and how important that is. And I'm just wondering what considerations need to come for the combo vaccines because now you have to consider matching strains for 2 different viruses, essentially, if you're thinking seasonally. And so I was wondering what strategies you might have to address that during the development?

Navin Katyal - Pfizer Inc. - U.S. Commercial & Global Business Lead for mRNA Portfolio

Great. Thanks for the question. So in terms of the COMIRNATY portion of combos and sort of moving forward, I think obviously, time is going to tell as the sort of the virus continues to evolve. But what we do know is COVID is year-round right now, right? It certainly has peaks and troughs and it starts to peak, we see, during the winter months, but we also see that it continues to be with us year-round. And so what we expect is that there will continue to be vaccinations that happen year-round. So we do think that COMIRNATY as a stand-alone product will have meaningful sort of contribution to the overall sort of high, if you will.

But we also know that based on all the research that has rolled in thus far, what we see routinely, right, is that there's a preference to have combinations for obvious reasons, right, for the convenience. And so as we move to the fall season when we expect the bolus, right, of the population to be getting a vaccine, we expect that at that point, we'll see sort of the meaningful contribution from the combo. So between the fact that we have year-round COVID, between the fact that we might see some populations having to do perhaps an additional boost, we do see a meaningful sort of contribution from the stand-alone. And then sorry, can you repeat the second part of your question?

I think strain selection. Strain selection, yes. So yes, something that we're spending a ton of time on because we think there's an opportunity both for COMIRNATY and for COVID rather, but also for flu to do have better strain match. And so what we are going to be doing and we're already doing is actively having discussions with regulators around the world, institutions like the CDC, WHO to make sure that we have a fit-for-purpose strain selection that allows us to get closer.

And then as you highlighted, it's going to be complex because you are going to have potentially shifting strains both for flu and for COVID. But I think as we've spent a lot of time meditating on this, I think we at Pfizer, we're going to be uniquely and, I think, really well positioned for sort of working through all those different sort of moving parts. I mean, we just did that this past year, right? When you think about, we didn't know if it was going to be BA.1, if it was going to be BA.2, if it was going to be a BA.4-5, if it was going to be a monovalent or a bivalent.

And we ended up, right, figuring those things out, like 2, 2.5 months before we had to launch all across the world. And what we saw was in the U.S., as I said earlier, we were able to more than supply, right, the entire population. We were 70% of the market shares in the first 30 days in the

U.S. alone. And the vast majority of the BA.4-5 bivalent in developed markets as well. So I think we've seen, right, that we have, given our scope, our scale and our expertise in sort of being agile with supply that I think we're very confident that we can deal with the complexity of a combo.

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Thank you for your time. Now the rest of us are going to head off the stage, and I'd like to invite our Chief Financial Officer, Dave Denton, to come and make some closing remarks.

David M. Denton - Pfizer Inc. - CFO & Executive VP

Thank you, Chris, and thank you, team. It's my pleasure just to spend a few minutes this afternoon to just really wrap up the program. First, just what an exciting day. I just want to thank all the presenters. And I want to thank you specifically for spending some time with us to learn just a little bit more about Pfizer. And clearly, as you can see, it's just an exciting time at Pfizer as we continue to invest for future growth.

As Angela shared with you earlier this morning or this afternoon, this slide represents our long-term growth plan. Hopefully, today, we've set the stage for why we believe Pfizer has the right products, the right team and the culture to fulfill our goal of creating \$20 billion of in-house developed product revenues by 2030. Additionally, we are well on track of achieving our target of \$25 billion of risk-adjusted sales by 2030 generated through business development.

And finally, we also gave you just a glimpse of what we believe will fill the last key drivers box on the right side of this chart with exciting products like our GLP-1 agonist and new vaccines generated by our mRNA platforms, just to name a couple. And all of that obviously is subject to clinical and regulatory approval. We plan to update you regularly on the execution of our commercial and development plans.

And I know you've heard a lot today. So as a reminder, these are the upcoming potential launches and products to just get us there. An unprecedented number of potential launches over the next 18 months. If successful, these launches, of which we believe more than 2/3 will have the potential to be blockbusters, would be the most ever in Pfizer's history in such a short period of time.

In summary, based on what we've discussed this afternoon, we've laid the foundation for you that Pfizer has a very bright future. The unprecedented number of potential launches are critical for our long-term growth. So specifically, let me switch gears and think about next year. And specifically regarding 2023, we are confident that we have a clear line of sight to deliver a year-over-year revenue growth in the range of 7% to 9%. That's excluding COVID-19 products and excluding the impact of FX.

Furthermore, to help ensure that we can successfully execute against our plan in such a short period of time, you should expect to see us continue to make important investments to Pfizer. Our 2023 plan contemplates increased investments of both resources and fundings in both our R&D operations as well as our commercial organizations.

And maybe to address the point that was raised during the Q&A, we will invest in R&D but we're going to invest creatively such that we can bring innovation to market more rapidly and create more medicines more quickly, at the same time, do it in a way that maximizes economic value and long-term profits and return on invested capital for Pfizer.

We believe these investments are important and critical long-term growth for Pfizer, particularly in the 2025 to 2030 time frame. We look forward to sharing more of these details of our plan during our Q4 2022 earnings call in late January. Again, thank you for attending our session today, either virtually or here with us in New York City. In the upcoming days, you'll receive a short survey asking for your feedback on the time that you spent with us today. We want to make sure that your feedback is incorporated such that we can help make this time even better fit your needs in the future.

And as always, the slides that you have seen today are already available on our website to help you with your models. And in the upcoming days, we will upload the transcript of this event as well. And for those of you that are here in person, I wish you safe travels home. But before you leave, I invite you to join us for a short reception that you can intermingle and talk with the speakers as well as some of our Pfizer leaders.

And for the entire -- from the entire Pfizer family, I would love to wish you and your family a really happy holiday and a happy and healthy new year. So with that and for those of you online, I appreciate you joining us today. You can sign off. But before we close, I'd ask Chris to come back and make a couple of just logistic comments.

Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

I think you actually handled it pretty well. So the reception is going to be downstairs as we had lunch earlier today and the brief break. As Dave said, updated materials, including this last closing segment, will be posted on the website immediately after this call, and then the transcript will be coming in a day or 2.

And again, if there's any follow-up questions, including any questions which are online and we weren't able to address here, we'll be happy to address those offline with Investor Relations later. So thank you once again, and we appreciate your coming. Be well.

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