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PRESENTATION

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

Welcome, everyone, and thanks for joining us virtually for our first of 2 sessions, where we will share some exciting updates from Pfizer's portfolio and R&D pipeline. Today's program will be a combination of prerecorded prepared remarks and then, of course, live audience Q&A sections. Today, we'll hear from members of our executive leadership team as well as leaders of our Internal Medicine and Vaccines teams, the 2 therapeutic areas in focus for today's session. We will have a Q&A session following each of the therapeutic area presentations.

The presentation at today's Investor Day include forward-looking statements about, among other things, our anticipated future operating and financial performance, business plans and prospects and expectations for our product pipeline our in-line products and product candidates. By their nature, all these statements about future events and expectations for our pipeline products are forward-looking. Each forward-looking statement contained in these presentations is subject to risks and uncertainties that could cause actual results to differ materially from those projected in such statements. Additional information regarding these factors are included in the slide entitled Forward-looking Statements and Other Notices and under Risk Factors in our 10-K and 10-Qs. The forward-looking statements in these presentations speak only as of the original date of the presentation, and we undertake no obligation to update or revise any of the statements.

The slides that will be presented during this session will be posted on Pfizer.com/investors after each session. You can also find speaker bios and today's agenda on a separate tab at www.pfizerinvestorday.virtualeventsite.com. Again, there will be time for a Q&A via the operator following each business unit's presentation.

Now we're going to play a video that articulates our commitment to science.

(presentation)

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

Now I'll be handing it over to our executive leadership team. Today, we'll hear from Albert Bourla, our Chairman and CEO, who will speak to the broad transformation that has been in place at Pfizer and how it will make a difference; Mikael Dolsten, our Chief Scientific Officer and President, Worldwide Research, Development and Medical, who will speak to how our R&D organization has evolved to become a highly focused and agile leader in science and identify for us some of the exciting breakthroughs that may be available for patients; Rod MacKenzie, our Chief Development Officer, who will speak to some very important metrics regarding our R&D productivity; and Angela Hwang, Group President, Biopharmaceuticals Group, who will speak about our commercial organization and provide detail as to the drivers of our projected 6%-plus revenue CAGR from the time of the close of the Upjohn-Mylan transaction through the end of 2025 and, importantly, quantify our current view as to peak sales potential for selected pipeline assets that could drive growth well beyond 2025.

I'll now turn it over to Albert Bourla.

Albert Bourla - *Pfizer Inc. - Chairman of the Board & CEO*

Welcome, and thank you for joining us today. We are thrilled to introduce you to the new Pfizer by doing a deep dive into the scientific engine and culture of innovation that we expect to drive our growth for the next decade and beyond.

Over the next 2 days, we will share our excitement about our pipeline, including some of the projects about which we are very excited, but with which you might not be as familiar. It is this pipeline that makes us confident that following the completion of the pending Upjohn-Mylan transaction, we can drive at least 6% revenue CAGR over the next 5 years and continue to deliver longer-term top line growth beyond that period.

With the separation of Consumer Health last year and the expected separation of Upjohn later this year, we are significantly transforming our company. We are evolving from a diversified enterprise to a more focused and innovative biopharma company, from a scientific fast follower to a first-in-class scientific powerhouse and from growing EPS through large-scale M&A and share repurchases to accompany with organic growth at our core, supplemented by bolt-on acquisitions where and when they make sense. We believe this structure not only makes Pfizer more relevant to patients, but we'll also earn a higher PE multiple. The transformation of this magnitude could not happen within 1 or 2 years. It started in 2010 when my predecessor, Ian Read, recognizing that our historic R&D productivity lagged the industry, set a priority to strengthen our scientific engine. This 10-year journey resulted in a dramatic turnaround of our R&D organization. The increased R&D productivity, as well as the depth and breadth of our pipeline, gave us the confidence to move so quickly over the past year to transform into the new Pfizer. The new Pfizer will be very different. It will combine the agility and innovative spirit of a biotech with the scale of a big pharma.

To be successful, a company like this needs to have a purpose that inspires all its employees, a small set of clear strategic priorities and a culture that allows innovation to flourish. Last year, we launched what we call our Purpose Blueprint, the road map that will guide our company for the foreseeable future. It includes, on one page, all the why, what and how of Pfizer. Our Purpose, which is breakthroughs that change patients' lives, represent the why we exist and do everything we do. Our Bold Moves represent the what do we need to do to be successful, unleash the power of our people, deliver first-in-class science, transform our go-to-market model, win the digital race in pharma and lead the conversation on science and reputation. Every plan we develop, every action we take and every dollar we spend is aligned with these 5 bold moves. Finally, our Values represent the how we do things. Our new Pfizer's culture will be characterized by courage, because breakthroughs favor the bold; by excellence,

because we can only change patients' lives when we perform at our best; by equity, because every person deserves to be seen, heard and cared for; and by joy, because we take our jobs seriously, not ourselves.

In order to prevent our scale from becoming an impediment innovation, we organized Pfizer into 6 vertical integrated business units. Each of these units possesses deep scientific, commercial and patient experience expertise that make them uniquely effective to address the distinct needs of the patients and physicians they serve. We see these 6 business units as 6 individual biotechs within Pfizer. Each of them is led by a triad, consisting of a Chief Scientific Officer, a Chief Development Officer and a Global Commercial President. They manage their units independently within the boundaries of their assigned strategic priorities and budgets. All the operational decisions of each business unit, regardless of whether they are scientific or commercial, are made within the unit. This allows for greater agility, speed and executional excellence. It is this operating model that allowed our Vaccines business unit, for example, to move so fast with the development of their COVID-19 vaccine candidate, and our Hospital unit with the development of their antiviral protease inhibitor candidate. These biotechs compete with each other for capital and resources for the internal and external projects. These resources are allocated by a committee of 5 executive leadership team members, which applies the same criteria to both internal and external programs. We have removed all previous incentives that were favoring internally versus externally sourced science.

This operating model was implemented in 2016 and has resulted in better decision-making regarding which projects we pursue and which we deprioritize. To realize our full potential as a more focused and innovative biopharma company, we must also radically simplify the ways in which we work and the interactions between our business units and corporate functions. Bureaucracy and innovation are like oil and water. They don't mix well together. Over the past several months, we have worked to reimagine the way we work and begun to redesign major corporate processes with an objective to radically simplify. Going forward, we will also reduce the number of interfaces we have between our core and enabling functions from 15 to 5, and we'll consolidate our search services centers from 20 to 6 These changes will create a more nimble and efficient company, improve our ability to get things done and rightsize our corporate expenses to have smaller revenues base to ensure our culture of innovation continues to flourish. It also is essential that our incentives align with the focus on science and our pipeline. That's why we have made an important change to our short-term incentive plan for all colleagues who are bonus-eligible. Going forward, the funding of the variable compensation, which is approved each year by the compensation committee of the Board, will be based on both our financial performance and the success of our pipeline.

Previously, only our R&D colleagues compensation was impacted by our pipeline performance. This sends a clear message to our entire organization about how important the success of our pipeline is. As a purpose-driven, science-based biopharma company, and in line with our values, we are committed not only to delivering strong financial results but also to ensuring that environmental, social and governance principles are hardwired into our DNA. We recognize the adverse impact climate has on health and are proud to have achieved a 23% reduction in greenhouse gas emissions from 2012 to 2019. That's ahead of our science-based goal to achieve a 20% reduction by 2020 and build on the progress we have made to reduce emissions by approximately 55% since 2000.

In 2019, we conducted also our first global pay equity study. The study confirmed that Pfizer has equitable pay practices between women and men globally as well as between minority and nonminority colleagues in the United States. And our annually elected Board of Directors is comprised entirely of independent directors, other than me, with more than half of them being from diverse background based on gender or ethnicity. To signify our commitment to ESG, we recently renamed the Board's Corporate Governance Committee to become the Governance and Sustainability Committee, which speaks volumes about our Board-level interest and involvement to sustainability.

As we evolve into a world-class science-based biopharma, we also have strengthened our Board of Directors by infusing more global business leadership and scientific expertise. Since 2019, we have added to our Board 4 highly accomplished directors: Dr. Scott Gottlieb, special partner of the New Enterprise Associates, resident fellow of the American Enterprise Institute and the 23rd Commissioner of the FDA; Mr. James Quincey, Chairman and Chief Executive Officer of the Coca-Cola Company, the world's largest nonalcoholic beverages enterprise; Dr. Susan Hockfield, Professor of Neuroscience and President Emerita at MIT. Susan was the first woman and the first life scientist to lead MIT as its 16th President; and Dr. Sue Desmond-Hellmann, Board member of the Bill & Melinda Gates Medical Research Institute, a former CEO of the Bill & Melinda Gates Foundation and the first female chancellor of the University of California San Francisco. With these additions, we clearly strengthened the scientific depth of our Board, while maintaining a balance of strong financial, business and scientific expertise.

Together with our longer-serving board members, Professor Helen Hobbs from the University of Texas Southwestern and Professor Dan Littman from NYU, our Board now includes 5 highly accomplished scientists that form one of the best science and technology board committees in our industry. Each not only have spent their career focusing on a different therapeutic area, including metabolic diseases, immunology, cancer, neuroscience and clinical medicine, but they also greatly complement one another in terms of early science, clinical development and regulatory expertise. Each of these actions have been essential to our transformation, and we think that now is the exact right time for the genesis of the new Pfizer for many reasons. First, our existing portfolio of innovative medicines and vaccines continued its strong growth. Last year, it generated 8% operational revenue growth. And for the first 6 months of the year, it generated 9% operational growth. We have a long runway of high-performing, patent-protected brands with no significant LOEs anticipated until 2026. We expect a 5-year revenue CAGR of at least 6% on a risk-adjusted basis following the completion of the Upjohn separation and continued growth beyond that from the next wave of our patent-protected portfolio. Should we be successful with our COVID-19 vaccine and antiviral programs, we will obviously update this projection. Our adjusted EPS during that same 5-year period is expected to grow in the double digits.

Investment in Pfizer shares today provides healthy dividend income that we expect will continue to increase. Our pipeline is as strong as it's ever been with 89 projects spread across 6 targeted therapeutic areas with 4 programs in registration and 23 in Phase 3. Last, but not least, we have the financial strength to supplement our internal pipeline where appropriate with external business development. As we have already said, we are biased towards Phase 2 and Phase 3-ready assets.

And now let me offer a few points regarding our longer-term revenue growth view. The sell-side community expects $18 billion to $20 billion in lost revenue during our LOE period, which is expected to begin in 2026, 6 years from now. We have a similar expectation in our longer-term forecasting. On a risk-adjusted basis, we see our current pipeline excluding any revenue from a COVID vaccine or treatment and excluding any future business development revenue as serving to at least replace the LOE revenues at risk. We are eager to show you why we think this is the case over the next 2 days.

In closing, we believe we have taken the steps to create the focus and culture needed to drive our success as a science-driven company. What you will see over the next 2 days is the Pfizer of the next decade. I believe you will walk away with the new appreciation of the value our science can deliver to patients, to society and to our shareholders. We look forward to showcasing our people, our culture and our science. And with that, let me turn it over to Pfizer's Chief Scientific Officer, Mikael Dolsten. Mikael?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical*

Thank you very much, Albert, and welcome, everyone. In this next session, I would like to share with you Pfizer's R&D turnaround over the past decade or so and our journey to get here. I will also review our robust and innovative pipeline with an emphasis on what we see as promising but underappreciated assets.

Along with most of our peers in the early 2000, Pfizer found itself following a volume-oriented R&D strategy that sought to get as many shots on goals as possible. During the period leading up to 2010, our R&D efforts were thinly spread across 10 key therapeutic areas, seeking to advance as many programs into the clinic as possible. By 2010 year-end, we had 104 NMEs in the clinic, predominantly small molecules. Our major R&D sites were located outside of major scientific hubs, isolating our R&D colleagues, and our decision-making was often siloed. But in 2011, we embarked on a significant R&D turnaround effort, focused on reinvigorating our innovative core.

As part of the turnaround, we made a conscious decision to focus our resources on 5 key therapeutic areas, where we felt we could make the greatest impact. In addition, we shifted away from a volume-based development strategy to one in which we focused on high-quality NMEs. We recorded 54 NMEs in second quarter 2020 and broadened our modality base beyond small molecules. During this time, we also co-located our R&D sites in scientific hubs, which enable us to better attract scientific talent in our core therapeutic areas.

The impact of our turnaround was profound. Our decision-making became more integrated with enhanced objectivity and a high bar for success. And Pfizer began racking up successes that included first-in-class blockbuster therapies developed internally at Pfizer, such as Xeljanz, Prevnar, IBRANCE, and complemented by partnership or acquisitions of molecule from external sources, including Eliquis with BMS, XTANDI from Medivation,

which has significantly benefited millions of patients around the world. Over the next few minutes, I would like to take a deep dive into each of these elements, describe the impact they have had on our success and how they put us in an outstanding position for success well into the future.

The success of this strategy is reflected in the substantial improvement that we have seen in Phase 2 trials. In the 3 years leading up to 2017, Pfizer's Phase 2 success rate, which is defined by successful transition into Phase 3 was 17%, which was well below the industry median and put us in the bottom quartile. I'm proud to say that, today, we have tripled our Phase 2 success rates on a 3-year rolling average, going from 17% in 2017, to 47% in 2019, to currently 53% in 2020 year-to-date, and we're now among industry leaders in this metric.

Between 2015 and 2017, for every successful Phase 2 to Phase 3 transition, Pfizer needed 6 to 7 readouts. By 2019, Pfizer was achieving 1 successful transition into Phase 3 from every 2 Phase 2 readouts.

Another measure of success is survival rate from first-in-human to approval. These 2 have significantly improved with 76% relative increase since 2015 and has surpassed the industry peer group. 2015, Pfizer had 5% end-to-end success rate versus industry at 10.6%. 2019, Pfizer is at 8.8% versus industry at 8.3%.

Another factor in our success was the decision to concentrate on 5 therapeutic areas, where there's great unmet need and a strong biological foundation and where our expertise and capabilities can be leveraged to improve the likelihood of success. Our 5 core therapeutic areas include: oncology, with a focus on targeting cancer vulnerabilities and drug resistance; inflammation and immunology, leveraging our world-leading experience in cytokine biology; vaccines, where we can leverage our industry-leading experience to develop high-impact bacterial and viral vaccines; rare disease, with a key focus on the molecular pathology of genetic diseases; and internal medicine, where we now focus on metabolic dysfunction and cardiovascular risk.

Along with our sharpened focus in 5 key therapeutic areas, Pfizer has broadened its scientific and clinical toolbox to tackle diverse disease pathophysiology. We expanded our core technology platforms beyond small molecules and monoclonal antibodies to include conjugate and engineered vaccines and AAV gene therapies. But we have gone beyond that and have been focusing on building novel emerging platforms, which includes protein degraders, expanding our small molecule expertise; multi-specific biologics like bi and trispecifics; RNA vaccines like our potential COVID-19 vaccine in partnership with BioNTech; gene expression modulators, which includes zinc fingers in ALS; translation and splicing acting drugs in cancer, such as PRMT5 or EIF4E; artificial intelligence, multi-omics and epidemiology, which utilizes big data, real-world evidence, genomic profiling and enhanced epidemiology information to guide early decisions.

To place Pfizer's R&D at the forefront of the evolution in biopharmaceutical space, we have co-located our key R&D facilities in globally recognized scientific hubs. Together with our focus on science, locating to these hubs has enabled Pfizer to attract top scientific talent and effectively leverage the collaborative environment such locations naturally offer. Our therapeutic area hubs are distributed in scientific centers of excellence, including for oncology, La Jolla, California and Boulder, Colorado; Inflammation & Immunology, Rare Disease and Internal Medicine, Cambridge, Massachusetts; and Vaccines in Pearl River, New York.

Our science and technology centers include small molecule centers at Groton, Connecticut and Sandwich, U.K.; large molecule centers at St. Louis, Missouri and Hanover, Massachusetts; a new modality in therapy sites at Kit Creek and Sanford, North Carolina. These efforts have yielded an innovative pipeline that has positioned Pfizer to be a leader in the next wave of therapeutic breakthroughs. We are confident that we're on the right road and have set an ambitious goal to put up to 25 breakthroughs in the hands of patients by 2025. In short, up to 25 by '25. 2026 to 2028 opportunities include a significant number of potential breakthrough medicines across our therapeutic areas, and we're exploring potential acceleration paths to enable earlier approvals of these medicines.

There are a total of 62 key programs shown on the slide, which included 38 key assets that could potentially contribute to up to 25 by '25, and 24 key assets shown in the 2026 to 2028 time frame. More than 70% are beyond Phase 1 and more than 35% are in Phase 3 registration all recently approved. There is strong contribution from all TAs, with oncology being the main contributor, 29%; followed by immunology and inflammation, 20%. Our Internal Medicine portfolio sees its initial potential launches in the second half of this decade and includes multibillion potential blockbuster opportunities in the period 2026 space.

If we look at up to 25 by '25 cohort in terms of non-risk-adjusted peak sales potential, we see approximately $35 billion to $40 billion in revenue. This includes PCV20 revenues and, as you know, is a potential replacement for Prevnar 13. We recognize these will not all achieve peak sales in the same year and are subject to attrition. But this should give confidence in the overall size of the opportunities we see. Of the $35 billion to $40 billion, major contributions are coming from Vaccine, Rare Disease, followed by Immunology & Inflammation. Achieving up to 25 by '25 will require a combination of developed Pfizer-generated molecules and external partnership BD deals. Of the 62 programs shown here, close to 1/3 of part of business development and bolt-on M&A, we will continue to look for breakthrough bolt-on assets and deals, which will further bolster our pipeline.

In the next 2 days, our scientific leaders will present therapeutic area deep dives, covering nearly half of these assets. These programs were predominantly chosen based on expected launch by 2025, clinical data we're excited to share, assets we believe are underappreciated assets by the analyst community.

Finally, I want to highlight our near-term catalyst among the programs you see on the potential slide. They include up to 10 potential approval, 10 anticipated pivotal study readouts and 10 anticipated early-stage clinical readout by 2021. Up to 10 potential approvals include key programs like a COVID-19 vaccine, abrocitinib in atopic dermatitis and PCV20 valent adult vaccine. Up to 10 potential pivotal readouts includes key programs, like ritlecitinib in alopecia, XTANDI and TALZENNA combination in TALAPRO-2 study in prostate cancer, and IBRANCE-PATINA study in double positive hormone receptor and HER2-positive advanced breast cancer. Up to 10 potential early-stage clinical readouts include key programs like BCMA IO therapy in multiple myeloma, Lyme disease vaccine and topical brepocitinib in atopic dermatitis.

Finally, I would like to introduce our highly accomplished scientific leadership team, Jeff, Nick, Mike, Kathrin, Seung and Morris, who have a strong record of drug-hunting abilities and proven history of translating pipelines into products that can help millions of patients. Across these therapeutic areas' CSOs, we have more than 1,000 scientific publications and more than 50 years of Pfizer work experience.

Thank you very much for your attention. Now I will hand over to Rod.

Alexander Rod MacKenzie - *Pfizer Inc. - Chief Development Officer & Executive VP, Global Product Development*

Thank you, Mikael, and thank you to everyone for joining us today. It's my pleasure to take you through some of the very impactful ways we've been revving up our clinical development engine in recent years and how we're continuing to reduce our cycle times across development.

To get us started, let's go back to 2015. Quite frankly, we were in a poor spot in terms of our operational performance metrics and nowhere close to where we knew we should be based on our talent and experience. You can see some examples here. We were bottom quartile with double-digit rankings. Needless to say, that's not where we expect to be.

Well, if we fast forward from 2015 to 2019, I'm pleased to say that we've moved to the top quartile. More important, though, than the ranking is what that ranking reflects. And as you can see, we've achieved very significant reductions in cycle times across the board, ranging from 18% to more than 50% in some cases. So we're in a much better place today, and I'm pleased to report that we expect that trend to continue through 2021 and beyond. Here, you can see that we expect to further reduce these key cycle times by up to another 60% by the end of next year.

So how did we get here? We focused on 3 key dimensions of performance. The first was the most important. It was to build an integrated patient-centric development organization with a deeply embedded culture of performance, quality and continuous improvement. The second dimension was to put all of our colleagues to work on all of our processes, systems and tools with a strong focus on internal and external innovation. It really was optimization on steroids. And then with the first 2 foundational elements in place, the third dimension was, and it still is, reinventing the way we operate with a laser focus on quality and cycle time reductions.

To give you a sense of the ambition we have, we're in the process of taking out a further 2.5 years from our average times for end-to-end clinical development. So let me spend a few minutes on each of these 3 dimensions. And let's start with organization culture and our people. Our first action was to consolidate all of our clinical operations. Back in 2015, these were somewhat fragmented and sitting in different parts of Pfizer. All in all, we took 4 different organizations and brought them together under one leader. And from the outset, global product development has been

an organization which is obsessed with patient centricity, quality, speed, cost and simplicity, in other words, all the elements of operational excellence.

So what does it mean to be patient-centric? Remember that every participant in the clinical trial is a volunteer. All of them are pioneers in science and medicine. So patient centricity is primarily about building trust in the communities that we work with. Recently, you may have seen that we've made a public commitment to enrolling clinical trial participants who reflect the racial and ethnic diversity of the countries where we operate and better represent the epidemiology of the diseases we're addressing. More specifically, we are keenly aware that we must build trust in the communities that continue to suffer from racial injustice and socioeconomic disadvantage, and they have good reasons to mistrust the health care system. This won't happen overnight, but these are important principles that we're holding ourselves accountable to.

We're also working to build awareness. Today, far too few people know what clinical trials are available to them. We need to make it much easier for them to find information and to make that first connection with clinical trial sites. And finally, when someone participates in a clinical trial, it needs to be less burdensome. For example, fewer visits to sites means less need to take time off work, and fewer invasive procedures means just a better experience for everyone. This is what it means to be patient-centric. It's really about doing the right things, which is at the heart of why we're doing all of these things. And by doing the right things, we will also enhance the quality of our clinical data sets because they will better reflect the real population and clinical practice.

Any organization is only as good as its people. And I'm pleased to say that we have one of the most experienced and talented groups of clinical development leaders in the industry. Between them, Jim, Bill, Mike, Brenda and Chris have played key leadership roles in bringing more than 30 medicines and vaccines to patients with cumulative lifetime revenues in the region of $150 billion. So these are leaders who have done it before, and they have a state-of-the-art clinical engine now to work with. So I know that we can trust them to deliver the pipeline that you will hear about throughout this meeting. But the good news is that you don't have to take my word for it because you will hear from each of these leaders during the meeting.

Let's now look at the second dimension of performance, and that's operational excellence. When we created our organization, we spent a full year examining every aspect of our clinical development operations and optimizing them. The work was entirely done by volunteers across the organization, more than 700 of them in 44 work streams. And the result was very significant improvements in operational performance. For example, we saw reductions in cycle times, in some cases, up to 30%.

In addition, we created cost efficiencies that allowed us to reinvest approximately $750 million back into the portfolio. But in addition to optimization of our processes, we recognize that we can't change the practice of clinical trials without the type of experimentation that leads to innovation, and we're beginning to see the fruits of that now. We're conducting, for example, a decentralized trial, where we're bringing the entire study to patients. They can participate in the trial without ever leaving their home. We believe this is the first regulatory grade study, which is completely remote in that way. We hope to see a significant increase in retention of participants in the study. And if we do, we'll scale that approach up in other studies.

Another example is automated clinical documentation, which will reduce the time it takes for authors to review documents, allowing colleagues to focus on higher-value work. And finally, in this dimension of operational excellence, we placed a premium on being externally focused. Collaborations with other innovative companies are really important to us. For example, we're working with TrialSpark, a young, energetic company based in New York City, who provide infrastructure to doctors and clinics who have not traditionally conducted clinical trials, and we gain access to patients we couldn't otherwise reach.

With Oceanor Healthcare, we have access to our first rate, extensive and growing network of hospitals that use electronic health records, enabling the seamless transfer of anonymized data into Pfizer databases. And as a founding member of TransCelerate, we're helping harmonize industry practices, thereby facilitating patient centricity by providing them with our clinical trial partners a similar experience, no matter which sponsors they're working with.

Let's move now to the third dimension of our transformation, which is laser-focused on reducing cycle times. As you know, in the world of patented medicines and vaccines, the faster we bring our breakthrough products to patients, the better we fulfill our purpose and the better we meet the goals of our investors. There's a perfect alignment between these 2 things. When we began our work, on average, from a first-in-human study start

to an approval took us about 9.5 years. That's too long for everyone. So we look very carefully at every moment of that timeline. We took apart every transaction, every technology, every process, every human-to-human interaction and every tool. We look minute to minute to understand in great depth how our time was being spent.

In the end, we decided to split those 9.5 years into 2 buckets. The first bucket was what we felt was operationally addressable. For example, white space, where really nothing is happening, decision-making time and the time to recruit our clinical studies. All of that is addressable. We have control. The second bucket is what we felt was operationally fixed, where we have less control. For example, regulatory review periods or the study period of a trial. If we're studying a medicine for a year in a trial, no matter how quickly we recruit in that study, it cannot take less than a year. In other words, the 2 buckets were based on what we have strong control over and that which we have little control over, at least in the short term. When we added it all up, the addressable time turned out to be 5.2 years, and so we set ourselves a breakthrough goal to reduce that by a full 2.5 years by the end of 2021. And I'm pleased to say we are making great progress. Here, you can see the cadence of the actual and anticipated reductions in average cycle times. Up to and including 2019 are actuals, and 2020 and 2021 are projections, but I'm very confident we'll continue to do well.

So how are we doing it? We're working in 5 areas, and you can see the relative contributions here. The first is in changing the investment profile of our programs. As Mikael described to you, with our Phase 2 success rates going up, our confidence in making earlier investments in programs is getting higher. That, in turn, reduces white space while we wait for clinical trial supplies for pivotal studies, on the average, we think by about 8 months. We've also speeded up our study starts, which accounts for a couple of months. Now the clinical trial recruitment phase is the single longest cycle time we have when you look across the entire continuum. By moving faster in recruitment, we expect to gain up to an average of 5.5 months. Then on the back end of studies, we're moving much faster from the last patient in the study to the database release. We expect that to contribute an average saving time of 3 months.

However, the biggest impact is in the automation of processes. Right now, every aspect of clinical trials is very human-intensive and requires many, many manual processes and transfers of data and other information. Through automation, we're creating an environment where data can flow directly from a patient into an electronic database and on into Pfizer systems after anonymization and to populate clinical trial submission documents without them being touched by human hands. And because automation can positively impact every aspect of end-to-end clinical development, we anticipate that the overall automation of processes will contribute nearly 1 year to our cycle time reductions.

Let me finish by showing you how we are putting all of this to work. I thought you might like to see how this new clinical development engine and our culture of operational excellence at Pfizer has come together in our COVID-19 vaccine work. Tomorrow, you'll hear in some detail a full description of Pfizer's overall COVID-19 response. But just to give you a little bit of a preview, you'll see here that from the time we had the first approved protocol for our potential COVID-19 vaccine to the first subject first visit was only 12 days. Then when we received regulatory approval to start our Phase 2/3 study, we had our first subject first visit 2 hours later. We had 6,000 people dosed in the study in just 18 days and more than 20,000 in just 35 days from the start of the study. I think you'll agree that these are extraordinary timelines, and these timelines would not have been possible without the culture of operational excellence that we've been building.

Let me finish with LORBRENA. This is an important medicine for non-small cell lung cancer that took less than 5 years in clinical development, under half of our previous median and significantly shorter than the industry median of the day. LORBRENA is a lifesaver and is a life prolonger. It was discovered by our own scientists using state-of-the-art medicine design, developed with patient centricity and quality and speed and with love and respect for the patients that we serve.

Well, that was a whistle stop tour of our transformation journey in clinical development. We expect to continue to get better, but there's no question in my mind that we now have a clinical engine that will deliver the portfolio that you will hear about in this meeting and to deliver it with quality and speed.

Thank you for your attention. And now it's my pleasure to turn it over to my colleague, Angela Hwang, Group President for Pfizer's Biopharmaceuticals Group.

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

Thank you, Rod, and hello, everyone. I am pleased to be here today to review the Biopharma portfolio with you. As you saw in Mikael's and Rod's presentations, our pipeline is robust and has great prospects from an unmet need and a market perspective. What you heard from Mikael was a broad review of our pipeline until 2028. But during this presentation, I'm going to focus on 2020 to 2025.

What I see is a business that has the potential to deliver 6% CAGR or more in the next 5 years. And this is a function of 3 things. First, a strong in-line portfolio that's already delivering strong growth today and will continue to grow. Despite the impact of the pandemic, which drove a downside of $250 million, Biopharma in-line brands grew 9% in the first half of 2020. The momentum in our current portfolio is strong. And the 7 in-line products, namely, IBRANCE, XTANDI, Oncology Biosimilars, Braftovi/Mektovi, VYNDAQEL, Eliquis and Xeljanz are expected to drive 50% of the revenue growth over the next 5 years.

Second, the potential of 25 launches by 2025, including 9 potential blockbusters that have a total of $15 billion in non-risk-adjusted revenue in 2025. Third, no significant LOEs anticipated until 2026. We have a unique portfolio of medicines and vaccines housed in 7 business units, each with commercial capabilities and resources that are focused specifically on their therapeutic areas and customer needs.

Having all of the business units within one biopharma group also gives us unparalleled scale and capital allocation abilities. This combination allows us to achieve both focus and leverage across the BUs and is what makes our commercial model unique and competitive. Our commercial engine and our capabilities give us great confidence to deliver best-in-class launches for every pipeline product to come.

So let's introduce the business units. The 7 units are led by my outstanding leadership team, our global presidents. Together, they comprise $41.6 billion of revenue in 2020, this being the midpoint of our 2020 guidance. Each of these leaders have deep expertise within Pfizer. They bring unique experiences and capabilities to biopharma. They work side-by-side with the Chief Scientific Officers and Chief Development Officers that Mikael and Rod already introduced to you, and they shape and advance the pipeline in addition to their commercial responsibilities. We call this group of 3, the triad. And together, they create and execute on their respective parts of the end-to-end strategy for each business unit. This is also the group who will be discussing the pipeline with you later this afternoon. Each of these business units is a leader in the market segment they operate in today, and all of them have deep pipeline potential.

Let's start with Internal Medicine. Today, it is a business unit that is $9 billion in revenue. And in the pipeline are 6 potential first-in-class medicines. We have deep expertise in cardiology and primary care, and those capabilities will be leveraged for our pipeline assets in hypertriglyceridemia and obesity. Vaccines has the potential to become a top 2 player in the next few years especially if the COVID vaccine is successful. You will hear more about the potential of our COVID vaccine tomorrow. Currently, this vaccine is not reflected in the $6 billion of vaccine pipeline potential that we believe we have.

I&I has a leading medicine in Xeljanz. And we are one of the largest targeted JAK portfolios across the industry with 12 potential NMEs across 24 indications. We feel we are well positioned to maintain leadership in I&I.

And the Rare Disease BU will be the only company with 3 Phase 3 gene therapy programs, building on the momentum of exceptional launches like the one that we've seen with VYNDAQEL. Our oncology BU has been a strong growth driver in recent years and will continue to contribute to biopharma's growth with up to 14 approvals of NMEs and indications by 2025.

The hospital BU is a leader in sterile injectables and anti-infectives and is focused on building out its pipeline with innovative molecules and platform technologies. This includes 3 NMEs, namely the ATM-AVI asset and both the IV and oral protease inhibitor.

Our emerging markets BU encompasses all the products from the 6 business units and commercializes those products in over 100 countries. Our emerging markets footprint is one of the largest in the industry with significant scale. In 2020 alone, over 140 product launches are expected. This is the road map of how we plan to achieve our 6% revenue CAGR from 2020 to 2025. 50% of the revenue is expected to come from the 7 in-line brands. And together, these 7 brands have the potential to contribute $8 billion of incremental revenue by 2025.

The other part of our growth will be led by our pipeline. Nonrisk-adjusted, the revenue potential for this in 2025 is about $15 billion. The assets we're showing here are either in Phase 3 or will be by the end of this year. Risk adjustment gives the pipeline about $8 billion, making up the other 50% of our revenue growth. We have 3 mega blockbusters in abrocitinib, DMD gene therapy and Vupanorsen. Abro and Vupa have more than $3 billion in peak revenue and DMD gene therapy more than $2 billion in peak revenue. We also expect PCV20 to be a mega blockbuster, but we are not factoring this into our incremental revenue growth because we see this replacing PCV13. And these expected launches are not only a contributor to revenue growth in 2025. They also help Biopharma to fuel the growth through the LOE period that begins in 2026. This is truly an exciting portfolio and one that is meaningful for every single BU. Never in the 23 years that I have been here have I seen as exciting a launch and growth story as the one that we have today. And when you consider that this growth is off a $41-plus billion base in 2020, it's all the more significant, but it doesn't stop here. We continue to pursue business development, which will drive incremental revenue growth to what we are discussing here today.

Over the next 5 years, this is the cadence of launches that you can expect. As you can see, each business unit has a role in contributing to Pfizer's growth. I won't go through and name each of these now. But as you can see, they are the following themes here. We have a strong Vaccines portfolio that includes the potential of a COVID vaccine later this year. The investments we have made behind our Rare Disease portfolio and gene therapy gives us a consistent series of launches until 2025. And the depth of our JAK portfolio, which builds off the strong foundation on Xeljanz, expands into new disease areas like dermatology.

So let's get into some specific details around a few of our growth brands to help show how we see their future growth potential. VYNDAQEL has seen exceptional performance in ATTR-CM and should be close to $1 billion global brand by the end of 2020. We're seeing strong launches across the world. Today, just in the U.S. alone, we have diagnosed approximately 15% of all ATTR-CM patients. This is remarkable given the short period of time since the product has been on the market and the challenges that we've seen from the pandemic. We previously talked about peak diagnosis rates for rare diseases being in the range of 30% to 50%. With the momentum we have, we would expect to drive a higher-than-average diagnosis rate for a rare disease. We also expect peak diagnosis rates to occur earlier than we originally thought if we follow the shape of the curve.

Xeljanz. We believe in the growth potential Xeljanz has. In a heavily rebated class like this one, we have to contract. These contracts we executed over the last 18 months helped us to gain access to an incremental 64 million lives. But with any contract, there is a lower net price. This has had a negative double-digit pricing impact over the last several quarters. But this gained access is a major driver of Xeljanz' excellent volume growth. We expect in 2021 and beyond for the volume impact to significantly outpace any pricing impact. Since launch, we have consistently grown volume over 30% a year, excluding the impact of COVID recently.

As for the JAK class, we see the entrance of competitor JAK as being a positive. In the U.S., 32% of all new-to-brand advanced therapy scripts are now from JAKs. Given the high unmet need in rheumatology and UC, the attractiveness of an oral therapy and a significant biologics market that can still be penetrated, this gives us great growth potential in the JAK class. We look forward to launching ankylosing spondylitis to further strengthen our leadership in rheumatology. AS continues to have a significant unmet need for the 1.7 million adult patients in the U.S. and the EU. We have a strong field force footprint and deep customer relationships, giving us a competitive advantage in rheumatology. In the Phase 3 trials, Xeljanz was found to be an efficacious and safe oral option for those who had an inadequate response to NSAIDs, meeting both the primary and the secondary endpoints at 16 weeks. And data was submitted as an sNDA to the FDA, and we expect our PDUFA to be the second quarter of 2021.

Our Oncology Biosimilars portfolio is an exciting one and is now the largest in the industry with 6 biosimilars approved, including MABs as well as supportive care products. Over the next several years, we expect the growth of our Oncology Biosimilars to be driven by global launches and increasing utilization, especially here in the U.S.

IBRANCE is the leading CDK4/6 inhibitor in metastatic breast cancer. In the U.S., IBRANCE holds an 87% share in first-line CDK use, and we expect to defend our market-leading position. Oncologists view IBRANCE'S profile favorably with over 5 years of patient and physician experience. And real-world data recently showed a statistically significant benefit of 42% in overall survival.

We conducted research with KOLs and oncologists as recently as July and August, and consistently, prescribers reiterated their positive view of IBRANCE as the leader in metastatic breast cancer now and in the future. Since the category is large, growth will naturally moderate as it's difficult to maintain the same growth on such a large and growing base. Despite the monarchE results, we do not anticipate an impact on IBRANCE

prescribing in metastatic breast cancer. We expect patients treated with a CDK in early breast cancer to be retreated with a different CDK if they progress to metastatic. And currently, Pfizer is aware of at least 5 studies evaluating CDK off the CDK usage, with results anticipated in the late 2022, early 2023 time frame. So we remain confident in IBRANCE'S leadership as the preferred CDK in metastatic breast cancer.

We believe we have a best-in-class commercial organization in Pfizer biopharma. We have breadth and depth of therapeutic areas with a proven track record of capital allocation that drives growth. Our strengths are founded in our disease knowledge, legacy of customer relationships and execution excellence. Everything that we're doing today is directly applicable to launching our pipeline. We've also demonstrated that we can set new standards for launch with industry-leading capabilities. This is evident in our recent launches such as VYNDAQEL and our Oncology Biosimilars, and we will do this again if we're successful with our COVID vaccine. The triad structure integrates our commercial, clinical development and research organizations, allowing us to introduce commercial insights early in the development process. And our end-to-end capabilities also help us to be a partner of choice in business development. And we've seen this play out successfully as in recent examples like Array and BioNTech.

Strong fundamentals position biopharma for continued growth. We have 7 key in-line drivers. We have limited LOEs. We have a commercial engine that delivers customer focus and global scale with capabilities that are directly applicable to our pipeline, and we have a prolific and exciting pipeline that is truly focused on breakthroughs. These are the reasons why we are confident we can deliver 6% or more revenue CAGR from now till 2025.

I know you will enjoy hearing from our triad teams about the strength of our pipeline and how we will fuel the next stage of growth in biopharma. And now, Chuck, back over to you.

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

Thanks, Angela. So now we're going to take a break. So please stand by and we'll resume in 10 minutes with the presentation from our Internal Medicine leadership team.

(Break)

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

Welcome back. Now we're going to move into our Internal Medicine program. To kick it off, we'd first like to share a video, featuring Roger Ortega, a NASH patient.

(presentation)

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

Now I'd like to turn it over to the Internal Medicine triad.

Michael Gladstone - *Pfizer Inc. - Global President, Internal Medicine*

Hello, and welcome. Internal medicine is a legacy of discovering, developing and commercializing best-in-class therapies, and many of these are not only household names, but they've been the backbone of Pfizer's long-standing success. Through our focus on cardio-metabolism, Internal Medicine is well positioned to continue to address diseases that impact patients on a massive scale. We're pleased to discuss our R&D strategy with you today, and we're excited to share data on several development programs that we believe have either first-in-class or best-in-class potential.

So here's the team presenting today, and between the 3 of us, we have over 75 years of internal medicine experience. My name is Mike Gladstone. I'm the Global President of Internal Medicine, and Jim Rusnak is our Chief Development Officer. He leads both the Internal Medicine and the Hospital categories. Morrie Birnbaum is our Chief Scientific Officer and Internal Medicine.

So let's take a closer look at our expertise and our reach. Internal medicine drives innovation that diagnoses, treats and prevents the most prevalent health care challenges facing our societies. And in 2019 alone, we reached approximately 59 million patients. First, we have an aging population with chronic metabolic conditions that are at an epidemic level. Second, the diseases we focus on, such as obesity, cardiovascular disease and type 2 diabetes, these are some of the largest cost drivers in our health care systems. And we've got an unmatched track record in developing and commercializing massive primary care medicines like Zoloft, LYRICA, LIPITOR, Norvasc and Eliquis. And while some companies have backed away from CV med, Pfizer continues to invest here because we recognize the tremendous unmet patient need that still exists. We've got an industry-leading footprint in cardiology and primary care. That means we know the health care providers. We know the patients, and we know how to get medicine into the hands of patients that need them. Our experience and reach make us a compelling partner. We strategically engage with other industry members in order to complement our already strong portfolio.

Our footprint with PCPs will also be an advantage when we launch tanezumab, and we're excited about tanezumab as a potential first-in-class non-opioid treatment for patients with chronic pain due to moderate to severe osteoarthritis who've experienced inadequate pain relief from other analgesics. Our regulatory applications for tanezumab are under review by FDA, EMA and Japan's PMDA. And we're looking forward to FDA's decision in December later this year.

Now I'll turn it over to Morrie to introduce the internal medicine R&D strategy. Morrie?

Morris J. Birnbaum - *Pfizer Inc. - Chief Scientific Officer of Internal Medicine*

Thanks, Mike. Our Internal Medicine pipeline strategy addresses the increasing global burden of metabolic disease. Because of the incredible advances in the treatment of life-threatening diseases, people are living longer. And this, coupled with increased food intake and sedentary behavior, has led to a worldwide epidemic of obesity and with it, what we at Pfizer call the dysmetabolic state. Now this dysmetabolic state, the hallmark of which is insulin resistance, puts people at risk for diabetes, nonalcoholic fatty liver disease and cardiovascular disease. With our expertise in cardiometabolic conditions and our deep commitment to use this knowledge in the development of novel therapies, Internal Medicine is well positioned to make significant contributions to the fight against these global epidemics.

To address the needs of so many people with cardiometabolic diseases, Internal Medicine has assembled novel, science-driven and balanced early and mid-stage pipeline that spans multiple diseases and indications. We currently have 9 medicines in active clinical studies and more following in the preclinical pipeline made up of potential medicines discovered and developed in-house. Today, we would like to share exciting data and development plans for several investigational therapies. We'll focus on our combination of ACC and DGAT2 inhibitors for NASH, 2 drugs that were recently given INN of clesacostat and ervogastat. We'll also talk about danuglipron, the INN for our small molecule oral GLP-1 receptor agonist for diabetes and obesity.

But first, we'd like to bring you an update on Vupanorsen, a promising potential treatment for cardiovascular disease that we acquired through an in-licensing agreement with Akcea and Ionis.

Michael Gladstone - *Pfizer Inc. - Global President, Internal Medicine*

Thanks, Morrie. Vupanorsen is a great example of our strategy to identify external opportunities to further strengthen our internal portfolio. Vupanorsen has shown promise in early studies of reducing atherogenic lipoproteins that could help reduce residual CV risk. Cardiovascular disease continues to be the leading cause of death and disability worldwide. Elevated levels of LDL-cholesterol are an established risk factor for coronary heart disease. However, substantial CV risk remains even after levels of LDL-C have been lowered by statins and PCSK9 inhibitors. You'll see that here in the 4-year study with PCSK9 inhibitor, evolocumab. The residual risk here shows that we need to address other risk factors beyond LDL-C, such as non HDL-C and triglyceride-rich lipoproteins.

We estimate that over 6 million U.S. patients are of a high-risk of a major CV event, despite already being treated with statins. Jim's going to talk more about the role of Vupanorsen and how it can play a role in addressing this residual risk. Jim?

James Rusnak - *Pfizer Inc. - Chief Development Officer, Internal Medicine*

Angiopoietin-like 3, or ANGPTL3, is a protein produced and secreted by the liver that is a key regulator of lipid and cholesterol metabolism. Individuals with a genetic loss of function mutation in ANGPTL3 have lower lipid levels and a reduced risk of coronary artery disease by approximately 35% to 40%. Amongst dysfunctions, ANGPTL3 regulates lipoprotein lipase, or LPL; and endothelial lipase, or EL, controlling the conversion of VLDL to VLDL remnants. VLDL remnants are thought to be highly atherogenic, pro-inflammatory and can be directly inserted into the arterial wall without modification. It has been proposed that on statin CV risk is strongly associated with these VLDL remnants. We believe Vupanorsen, an investigational antisense oligonucleotide, which leads to enhanced clearance of VLDL remnants, will result in reduced cardiovascular risk as the reduction of ANGPTL3 causes increased production and clearance of these VLDL remnants as well as reductions in triglycerides, LDL, non-HDL and other lipids.

A large meta regression analysis that includes 49 trials with 375,000 patients showed that a reduction of non-HDL, in addition to triglycerides, is strongly associated with a lower risk of major cardiovascular events, as demonstrated on the chart on the left. The charts on the right are from Akcea and Ionis' Phase 1b study in healthy volunteers with elevated triglycerides. Once-weekly doses of Vupanorsen led to dose-dependent reduction in non-HDL cholesterol and triglycerides. At the recent ESC Congress, Akcea presented results from a 2a study of Vupanorsen in patients with nonalcoholic fatty liver disease, type 2 diabetes and hypertriglyceridemia. The Phase 2a study evaluated a lower dose range than the earlier Phase 1b study. It met its primary endpoint of triglyceride reduction and several secondary lipid parameters.

While the overall Phase 2a result met the primary endpoint, the maximal effects on some lipid parameters, particularly non-HDLC, were not as robust as originally observed at the higher doses of the Phase 1 study. Pfizer is leading the development of Vupanorsen moving forward, with a focus on cardiovascular risk reduction. We are initiating a Phase 2b study to complete additional dose-ranging in patients representative of our planned Phase 3 population. The Phase 2b study will be initiated later this month and is a placebo-controlled trial in 260 patients with elevated non-HDL cholesterol and high triglyceride levels who are on stable statin therapy, plus or minus ezetimibe. We are collaborating on this study with the TIMI Group. It will assess the safety and efficacy of different doses of Vupanorsen, along with assessing the safety and efficacy of the same monthly dose of Vupanorsen given at different dosing intervals. Our Phase 3 program will include a large-scale cardiovascular outcome study, which will enroll patients with elevated non-HDL cholesterol who are at increased risk of cardiovascular events.

Two additional Phase 3 studies will support a severe hypertriglyceridemia indication and will seek to demonstrate superiority of Vupanorsen to placebo and to Vascepa in reducing triglycerides, LDL cholesterol, non-HDL cholesterol and ApoB.

In closing, we're very encouraged by the human genetic data that demonstrates lots of function variants of ANGPTL3, having a reduced incidence of coronary artery disease and the early data that we've seen with Vupanorsen. We see great potential for Vupanorsen as a new approach for patients who need additional treatment to lower their on statin residual life-threatening cardiovascular risk. Now I'll turn it back to Mike to introduce our NASH program.

Michael Gladstone - *Pfizer Inc. - Global President, Internal Medicine*

Thanks, Jim. Before we move on to NASH, I want to take a minute to highlight the potential opportunity with Vupanorsen. Subject to approval, we'll launch in 2025. The indication will be severe hypertriglyceridemia. This is for triglyceride levels above 500 milligrams per deciliter. Over 2 million patients fall into this category. The larger unmet need and also the larger opportunity for Vupanorsen are in cardiovascular risk reduction. We'll launch that indication in 2028. We estimate that there'll be over 6 million statin-treated patients with significant residual risk by 2028. This means triglyceride levels above 200 milligrams per deciliter or other risk factors, including elevated non-HDLC. Vupanorsen will be an add-on therapy to statins plus other lipid-lowering agents. Now the goal here is to further reduce residual CV risk, and we're really excited about its potential.

Now let's take a look at NASH. NASH is a serious and growing condition for which there are currently no FDA- or EMA-approved treatments. Our expertise in metabolic disorders, coupled with our differentiated approach in NASH, will enable us to develop breakthrough medicines for patients.

While a lack of treatment and a validated noninvasive diagnostic leaves some question about the prevalence of NASH, I want to be clear: this disease has significant consequences, and it carries a growing burden for patients and health care systems. NASH significantly increases morbidity, and it's one of the leading causes of liver transplants in the U.S.

Now by the way, the severity of hepatic fibrosis is defined in stages. And they range from F0 or no fibrosis to F4, which is cirrhosis. Evidence suggests that significant to advanced fibrosis, that's Stages F2 and F3, are associated with both liver-related and all-cause mortality.

Now I'll turn it over to Morrie who'll tell us more about our NASH strategy and our pipeline.

Morris J. Birnbaum - *Pfizer Inc. - Chief Scientific Officer of Internal Medicine*

NASH pathogenesis is complex and multifactorial, involving fat accumulation, inflammation, liver scarring and, if left untreated, progression to life-threatening liver failure or cancer. At Pfizer, we view NASH as fundamentally a metabolic disease. We believe that by targeting core metabolic pathways, we can drive the fat out of the liver and, by doing so, not only prevent NASH in susceptible individuals but actually reverse the inflammation and fibrosis in patients who already have the disease, ultimately preventing the life-threatening downstream consequences of NASH.

Let's take a closer look at the key biochemical pathways we are targeting with our potential first-in-class therapeutics. Acetyl-CoA carboxylase or ACC catalyzes the first step in the synthesis of new fat and is a key regulator of fat oxidation, making it an attractive therapeutic target for hepatic fat reduction. Additionally, emerging preclinical and clinical evidence suggests that ACC in addition may have direct effects on reducing inflammation and fibrosis.

At the other end of the pathway, Diacylglycerol 2 or DGAT2 is the enzyme that catalyzes the terminal step of lipid synthesis, the production of triglycerides, which is the form of fat that accumulates in the livers of NASH patients. Interestingly, inhibition of DGAT2 has an indirect effect to shut down those genes that encode the enzymes of fat synthesis. Though we don't understand how this happens, it is important to the rationale for combining the DGAT2 and ACC inhibitors.

But first, let's take a look at the early clinical profiles of each of these inhibitors when used as monotherapy. Here are the results from a Phase 1 study of our potential first-in-class DGAT inhibitor, ervogastat, in subjects with NAFLD, that is individuals with excess fat in the liver but no signs of NASH. As you can see in the bar graph, treatment led to dose-dependent decrease in liver fat, with a higher dose achieving a 40% reduction in fat in just 2 weeks compared to a 10% decrease in response to placebo. In addition, ervogastat reduced circulating triglycerides, an important risk factor for cardiovascular disease and pancreatitis.

Now let's take a look at what happens when ACC activity is inhibited. Like DGAT2, inhibition of ACC also reduces liver fat. In a 16-week study in patients with NAFLD or presumed NASH, ACC inhibition with clesacostat reduced liver fat by more than 60% at the highest dose tested, again, with placebo-dependent decrease of less than 10%. Clesacostat also caused 40% in ALT, a circulating marker of liver injury. However, as shown in the panel to the right, the marked decreases in liver fat were accompanied by a significant increase in serum triglyceride, a recognized consequence of ACC inhibition. Since ACC had such a profound effect on steatosis, it has the potential to directly reduce inflammation and fibrosis. We saw the way of mitigating the increases in serum triglycerides while maintaining or even enhancing the positive effects of ACC inhibition.

As I described earlier, because of the indirect effects of DGAT2 inhibitor to reduce the levels of enzymes essential to fat synthesis, we reasoned that by adding it to the ACC inhibitor, we might suppress the increase in circulating triglycerides. We're pleased to share with you today the results of a Phase 2 trial evaluating the combination of our ACC and DGAT2 inhibitors. These exciting data were recently presented at the International Liver Congress.

As shown in the panel on the far left, after 6 weeks' treatment, both DGAT2 and ACC inhibitor monotherapy reduced hepatic fat in subjects with NAFLD, with the combination offering efficacy comparable to ACC alone. As shown in the second panel, a larger proportion of subjects achieved a greater than 50% liver fat reduction on the combination relative to DGAT inhibitor on its own.

Now let's take a look at what happened to serum triglycerides. As shown in the far right panel, as expected, the ACC inhibitor increased circulating triglycerides while the DGAT2 inhibitor offered a slight reduction. Importantly, the combination of the 2 agents yielded a fasting triglyceride profile indistinguishable from placebo, completely correcting the adverse effects of ACC inhibitor monotherapy.

Further, as shown in the table at the bottom of the slide, the ACC-DGAT2 inhibitor combination significantly reduced the number of times fasting triglycerides rose above the threshold levels of 400, 600 or 800 milligrams per deciliter, again producing a profile comparable to placebo. These are very exciting data as they reveal a potential way to realize the efficacy of ACC inhibition and still maintain a favorable safety profile.

While the early ACC and DGAT2 inhibitor data are highly encouraging, currently, the only definitive way to evaluate NASH efficacy is by assessing histological changes in the biopsy study. Hence, we have progressed both the DGAT2 inhibitor monotherapy as well as the ACC-DGAT2 inhibitor combination in a Phase 2b liver biopsy study, which began enrolling this past June. The outcome of this study will guide which candidate or combination we progress to Phase 3.

Unfortunately, there isn't enough time today to discuss the emerging data for our KHK inhibitor or other early innovative approaches. Nonetheless, I hope you got a sense of our commitment to NASH, our excitement about our novel metabolic approach and the many different ways we are attacking the problem. We are rapidly progressing a robust pipeline of first-in-class agents designed and developed within our own laboratories. We believe that the strong scientific rationale for these mechanisms will increase the likelihood of their success as NASH therapies.

Now Mike and Jim will talk about another area of significant patient need, type 2 diabetes and obesity, and discuss our small molecule oral GLP-1 program.

Michael Gladstone - *Pfizer Inc. - Global President, Internal Medicine*

Thanks, Morrie. The obesity and type 2 diabetes epidemics represent the largest medical challenges confronting the world today. We believe there's a significant opportunity to reach many more patients with our potential first-in-class small molecule oral GLP-1RA danuglipron. The numbers here are astounding: 650 million of these patients today, and less than 5% of them have been treated with medicines. The cost of managing the 200-plus comorbidities associated with obesity is significant. We know for most patients that diet and exercise simply are just not enough to make a meaningful difference. When you look at type 2 diabetes, about half of the patients remain undiagnosed. About half of those that have been diagnosed still are not at their Hba1c treatment goals. The end result here drives significant cost to the health care systems.

Now the GLP-1 class has a proven mechanism of action that offers compelling diabetes and weight loss efficacy with cardiovascular benefits. However, the current injectable GLP-1s are underutilized for type 2 diabetes. That's why our scientists set their sights on identifying a breakthrough approach to managing these conditions with a small molecule oral GLP-1RA. The compelling Phase 1 data we shared with you in June leads us to believe that we have a potential breakthrough treatment on our hands for both obesity and type 2 diabetes.

Now I'll turn it over to Jim to share more about this exciting program. Jim?

James Rusnak - *Pfizer Inc. - Chief Development Officer, Internal Medicine*

The discovery of non-peptide small molecule GLP-1 receptor agonist has been a significant challenge. Pfizer Internal Medicine has remained committed to this pursuit, however, due to the large patient need and the promise that a true small molecule agonist holds.

Our Phase 1 data suggest that danuglipron will yield a differentiated profile that is expected to deliver potent benefits on blood sugar and weight loss, safety and tolerability comparable to the peptide GLP-1 class, good oral bioavailability with no food or dose restrictions. And unlike the peptide-based oral GLP-1, danuglipron may be suitable for both monotherapy and combination therapies.

Let's have a look at the data. This is very exciting Phase 1 data, and it was shared in an analyst briefing in June of this year. This is an inpatient study conducted in subjects with type 2 diabetes on stable metformin background. For the higher doses, subjects were titrated for the first 2 weeks and

then stabilized at the target dose for the second 2 weeks. We observed robust reductions in fasting plasma glucose and hemoglobin A1c at all doses. This study was only 4 weeks in duration, so the changes in hemoglobin A1c likely have not reached maximum effects. Study subjects experienced robust reductions in body weight at higher doses. Danuglipron was well tolerated in the study with an adverse event profile that was consistent with the GLP-1 class.

I would also like to proactively address the questions we've heard on GI tolerability. As expected, we did observe dose-dependent increases in GI-related adverse events, including nausea, diarrhea and vomiting. When looking at GI tolerability in this study, it is important to keep in mind that this was a short 4-week Phase 1 study where we utilized an aggressive dose titration scheme to reach the higher doses.

On average, uptitrations occurred every 2 to 3 days. This aggressive titration was required because we sought to evaluate doses for at least 2 weeks at steady state. As a result, the tolerability data from this study is not comparable to more typical Phase 2 and Phase 3 data reported with other agents where longer and slower titration schemes were used. In fact, our upcoming Phase 2 studies, dose titration will occur at weekly or biweekly interims. Since these studies will titrate more slowly and are of a longer duration, they will provide a more representative picture of the tolerability profile of danuglipron.

Based on the Phase 1 results, we are poised to continue to progress our oral small molecule for both type 2 diabetes and obesity and have an ambitious program in place. Our aspiration is to develop the most efficacious oral therapy for type 2 diabetes and develop the first small molecule oral GLP-1 receptor agonist for treating both obesity and type 2 diabetes. We are also exploring this asset in NASH, and we believe danuglipron may ultimately be best utilized in combinations with one of our other NASH assets.

I'll now turn it back to Morrie to help close us out.

Morris J. Birnbaum - *Pfizer Inc. - Chief Scientific Officer of Internal Medicine*

We began today's discussion by describing how the modern lifestyle has led to an epidemic of diseases that share as their basis the dysmetabolic state. We also shared with you how Pfizer Internal Medicine is building on the newest science to develop an innovative pipeline to treat some of the most prevalent health challenges facing society today and over the next decade. While many other companies are exiting the cardiometabolic area, we chose to redouble our commitment, recognizing the tremendous impact of these conditions on human health and the economy and understanding the responsibility of Pfizer to make a real difference in such a challenging but important area of health care.

With Pfizer's deep knowledge of the basic biology of human metabolism, our years of experience in the discovery, development and bringing to patient of therapies for cardiometabolic disease and our passion for turning that knowledge into first-in-class or best-in-class medicines, we are confident in our ability to address multiple diseases stemming from the dysmetabolic state. In doing so, we have the potential to improve the lives of millions of patients and make a significant positive impact on society.

On behalf of Jim, Mike and the more than 7,000 internal medicine colleagues working every day to advance breakthroughs that change patients' lives, we thank you for your time and attention and look forward to answering your questions.

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

Great. Thanks. So now we've got Jim, Morrie and Mike available here, ready to answer your questions about the portfolio and the pipeline. So operator, at this point, can we please now poll for questions for the Internal Medicine triad? Thanks.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Your first question is from the line of David Risinger with Morgan Stanley.

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

Thank you, Chuck and team, for hosting the sessions. We really appreciate it. So Chuck, I don't know if it's appropriate or not, but I wanted to ask about the higher-level pipeline projections. So just to confirm, the $35 billion to $40 billion pipeline peak, is that in 2030? And the 50% risk adjustment, is that the average risk adjustment for that pipeline that you're assuming?

And then with respect to the team that just presented, I just wanted to better understand a little bit your philosophy with respect to developing assets considering the competitive landscape. So for example, as you think about NASH, could you talk about that competitive landscape and Pfizer's positioning and time to market relative to other companies?

And in addition, with respect to the oral GLP-1 if you could speak to that as well, how you assess the competitive landscape and how you make decisions on the appropriate level of investment spending in light of those considerations?

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

Yes, Dave, Chuck here. So your first question, before I turn it over to the IM team, that -- the $35 billion to $40 billion represents potential peak sales. Now remember, not every potential compound has peak sales in the same year. So if we normalize and said at peak for each compound, that's where you get that number as opposed to a single estimate for a given year, so that if you said all of them achieved peak sales in the respective years where they would be hitting peak sales, that's where we see the potential. But again, we're not pinpointing that to a specific year. That's in a sense totality and really on a continuum basis.

And then regarding risk adjustment, yes, as we look at each compound, we assign each compound a different risk adjustment based on what we've seen in terms of the data so far. But our view is the reality, as we all know, is you either have a compound or a compound fails. So it's either a 0 or you have a successful compound. So that's how we're looking at this rather than to say somewhere in the middle, some will win, some will lose. So that's what the risk adjustment does, but that's when we take this as a totality of the pipeline just to give you all the sense of what we see in this situation where they were all successful and hit peak sales. And then from that point, we would take a general risk adjustment.

So on that sense, let me leave it there, and then I'll turn it over to Mike to kind of moderate with his group here on your specific internal medicine questions. Thanks, Dave.

Michael Gladstone - *Pfizer Inc. - Global President, Internal Medicine*

Thanks, Chuck. I think we'll start off with the competitive set situation, and I'll ask Morrie to start there, and then I'll follow with GLP-1 and commercial considerations. So Morrie?

Morris J. Birnbaum - *Pfizer Inc. - Chief Scientific Officer of Internal Medicine*

Thanks, and thanks for the question. You're absolutely right. We're not in the first wave of potential NASH therapies. But we do have the advantage of seeing what's happened before us, and I think the message is very clear, and you know the results of the study so far. They've been largely disappointing. And we interpret that as validation of our underlying philosophy, which is the only way to effectively treat NASH is by going at those core metabolic pathways. And quite honestly, the late-stage clinical trials that have failed have not addressed that strategy. They've largely been repurposed drugs, drugs that were initially developed for other diseases and were now switched over to a NASH therapy.

So yes, we're not first, but we're still pretty confident based on the results of other studies and also, I should say, based on the human genetic results that have come out over the last couple of years, again, validating the metabolic basis of the disease and really providing reinforcement that our metabolic strategy ultimately will have the most efficacious outcome.

Michael Gladstone - *Pfizer Inc. - Global President, Internal Medicine*

Thanks, Morrie. And the big challenge remains here with screening diagnosis and monitoring of NASH. And this is still a very, very big opportunity. It's been estimated that there are 18 million NASH patients in the U.S., and roughly about 30% of these patients have fibrosis Stage F2 and 3, which is what we're targeting. And there's a wide range of opinions as to what the external community thinks will be the diagnosis and treatment rate. And the range is somewhere between 20% and 75% expected diagnosis rate for F2 and F3. We believe that our assumptions are on the more conservative end of that. At the end of the day, this is a pretty large opportunity for us. And as this landscape evolves, so will we in terms of our assumptions. But we think we're well prepared to bring a competitive product to the marketplace here.

Now I'll shift over to GLP-1. And I think the important thing to keep in mind here is that if you look at type 2 diabetics treatments, the GLP-1s have about 44% share of the non-insulin diabetes dollar sales in the U.S. But they only had about 9.6% share of the total prescriptions. And we think the treatment gap here is due in part to the limitations available at the -- with the current GLP-1. It's in their route of administration. They're either injectables or they're very difficult to take with significant food restrictions. And we believe that the opportunity here with danuglipron is significant if we achieve our target profile, and we have an oral product that delivers total reduction of A1c and body weight without food restrictions, and it can be combined with other compounds. If it hits its target profile and it's approved, we believe it will be competitive, as competitive as the best first-in-class agents that we have, best-in-class agents in the GLP-1 class.

So with that, Jim, do you have anything else to add on GLP-1?

James Rusnak - *Pfizer Inc. - Chief Development Officer, Internal Medicine*

Yes, Mike. So thank you very much. I think the GLP-1 opportunity is very exciting. Again, what we're striving for here is to be the most efficacious oral treatment for diabetes and a treatment for obesity.

I think what's exciting about the data that we've seen to date, what was in short duration, at steady state after 2 weeks, we have a hemoglobin A1c reduction that is comparable to what is seen with marketed agents at 3 or 6 months. And we know that it takes quite a while to stabilize hemoglobin A1c over that time period. So we do anticipate that we will get additional efficacy data over that intervening time period in Phase 2 and Phase 3 studies.

I think that this will allow us to demonstrate superiority in the oral agent class. It's also exciting because we can use danuglipron in combination with other agents, not only for diabetes but also potentially for NASH, and really close that treatment gap that you spoke about earlier, Mike.

Michael Gladstone - *Pfizer Inc. - Global President, Internal Medicine*

Thanks, Jim.

Operator

Your next question is from the line of Umer Raffat with Evercore. Okay, your next question is from the line of Louise Chen with Cantor.

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

I've got a few. First question is, how much upside to that 6% CAGR do you think we could see if your COVID-19 vaccine is successful and revenues turn out to be recurring? Secondly, on NASH, how long do you think your studies have to be to show a reversal of fibrosis? And do you think a combo therapy will be more effective than monotherapy here? Any thoughts? And then last one, just on this oral GLP-1. How do you think about oral versus injectable and how that debate will play out?

Michael Gladstone - *Pfizer Inc. - Global President, Internal Medicine*

Okay. So I'll turn the CAGR question over to Chuck, and then we'll go to NASH with Morrie on the length of the study in combinations. So Chuck, I don't know if you want to comment on that first question.

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

Yes. Sure, Louise. So we said -- we have said that if we're successful with the COVID vaccine, that is something we would then make any appropriate updates to the 6%-plus CAGR. So we aren't making that update today. But certainly, if the time comes, we will let you all know how that changes our thinking. Thanks, Louise.

Michael Gladstone - *Pfizer Inc. - Global President, Internal Medicine*

Then Morrie, perhaps we can go to you and just talk about the length of the studies needed for reversal and/or combination -- pipeline combination.

Morris J. Birnbaum - *Pfizer Inc. - Chief Scientific Officer of Internal Medicine*

Thanks, Mike. Let me start with combinations. There's been a lot of enthusiasm in the NASH field for combinations, and it's rational in the sense that most metabolic diseases end up with combination therapy. They're complicated multifactorial diseases, and NASH falls within that class.

So we are going to be testing combinations for a number of the agents, some you've heard about today, going forward. But ultimately, whether we end up with a combination or we can get enough efficacy with monotherapy will be determined by our Phase 2 biopsy studies, and we'll make a decision off of that. But we're certainly open to combinations and agree that it might be necessary, but the data will ultimately tell us.

I'll turn it over to Jim to talk about the clinical plans for NASH.

James Rusnak - *Pfizer Inc. - Chief Development Officer, Internal Medicine*

Thanks, Morrie. Yes. So currently, we have the DGAT and DGAT-ACC combination in a Phase 2b study. The primary end point of that study is a biopsy timed at 48 weeks. We believe that a 52-week, a 72-week biopsy for Phase 3 will be appropriate and will be guided by our Phase 2 data as well as other data as it emerges in the field.

Michael Gladstone - *Pfizer Inc. - Global President, Internal Medicine*

Great. Now as we turn to look at -- to move over to oral GLP-1, how will the oral versus the injectable game play out? I'll probably have a few words, and I'll kick it over to Jim to see if you have anything to add.

As I stated earlier, I think one of the big challenges here with -- is the utilization with the GLP-1 since their administration, it's injectable. And the only oral out there has significant food interactions. And we think the advantage here will be that we can deliver our target profile. We can have a

full product that doesn't have the food restrictions that are currently available or the inconvenience of an injectable. And this product can be combined with other compounds.

Jim, is there anything to -- else to add there?

James Rusnak - *Pfizer Inc. - Chief Development Officer, Internal Medicine*

Yes, Mike. I think that while speculative, there is some real promise for an oral agent. And that's because an oral agent that actually is a true small molecule gets absorbed in the intestines where GLP-1 is endogenously produced and GLP-1 receptors reside. Subcutaneous injection, while it certainly can reach those areas, wouldn't necessarily reach to the same extent. And of course, the other oral agent, which is available, gets absorbed through the gastric wall. So that may be a potential theoretical benefit for this oral agent.

Morrie, anything else?

Morris J. Birnbaum - *Pfizer Inc. - Chief Scientific Officer of Internal Medicine*

No, I think you covered it well, Jim. Just to reiterate, it's a controversial field. There's no doubt that there are receptors outside the brain, and those receptors are in the portal complex as well as the wall of the intestines, in the plexus. So -- and it's also pretty clear that these get activated with an oral -- with oral -- when you take food because GLP-1 is secreted from the intestines. So there is some reason to believe and some data to support the idea that a gastrointestinal absorption of the -- of an activator will lead to a differentiated response. If anything, it's been associated with the satiety response after a meal.

So we'll see. We have to do the experiments, but at least there's a basis to be optimistic about getting a different profile with an oral drug than an injectable.

Michael Gladstone - *Pfizer Inc. - Global President, Internal Medicine*

Thanks to both. And I think I'll probably just end off and say the weight loss efficacy of the currently approved therapies for type 2 diabetes is limited with single-digit reductions in body weight. And we need to do better than that. Obesity also needs to be understood as a metabolic disease instead of a lifestyle issue. And this is going to require some market development. Pfizer has got the history of understanding what it takes to bring medicines like this to market, and we're working with that in mind to bring this to the hands of millions of patients. Thank you for your question.

Operator

Your next question is from the line of Chris Schott with JPMorgan.

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

My first was on vupanorsen. Can you just help us put the efficacy here into context relative to other products in the market? And I guess specifically, are you expecting the benefit driven from this drug to be largely triglyceride lowering in terms of the driver? Or do you think there's other elements of the profile that will also drive the CV outcomes benefit for this product?

And then my second question was just on tanezumab, just as we're approaching the approval of that drug. Just the latest update about how you're thinking about the commercial opportunity here, I guess, given the need in the market balanced against some of the safety profiles that we've seen emerge with that one.

Michael Gladstone - *Pfizer Inc. - Global President, Internal Medicine*

Great. I think I'll -- perhaps, Jim, if you can start off with vupa, then I'll follow back with the tanezumab question.

James Rusnak - *Pfizer Inc. - Chief Development Officer, Internal Medicine*

So we see the opportunity of vupanorsen to be addressing lipoprotein and residual cardiovascular risk in sort of a broad perspective. We do believe that there's a substantial opportunity beyond just triglyceride lowering. Vupanorsen reduces non-HDL cholesterol in a dose-dependent fashion. And Akcea in their 2a study studied a lower end of the range, which was initially studied in the Phase 1 program.

What we intend to do in our Phase 2b study is actually expand that dose range beyond what was studied in the Phase 2a trial to really understand the efficacy that we can derive on non-HDL. Non-HDL is tightly linked to cardiovascular risk reduction, and we'd be seeking to take that data and design a cardiovascular outcome trial to show the inpatients that are already receiving very efficacious lipid-lowering therapy so that we can reduce their cardiovascular risk largely through non-HDL reduction with vupanorsen.

Morrie, anything else to add on that?

Morris J. Birnbaum - *Pfizer Inc. - Chief Scientific Officer of Internal Medicine*

Yes. Thanks, Jim. Increasingly, we're basing our prediction on how these drugs are going to work on human genetics. And we do have a lot of information on the phenotype of individuals who are deficient for angiopoietin-like 3 protein. And yes, there is a market decrease in triglyceride, but equally important, there's a decrease in not only non-HDL cholesterol, as Jim said, but there's also a decrease in LDL cholesterol. And importantly, the decrease in non-LDL cholesterol was by an LDL receptor independent mechanism, which gives knocking down angiopoietin-like 3 the potential of lowering LDL cholesterol further even when maximally treated with one of the drugs on the market, which -- both of which work through the LDL receptor.

So there's a lot of reasons to believe that angiopoietin-like 3 is going to reduce cardiovascular risk by multiple mechanisms.

Michael Gladstone - *Pfizer Inc. - Global President, Internal Medicine*

Great. Thank you for the question. I'll answer the question about the tanezumab opportunity. I guess when you think about tanezumab opportunity, first, we need to think about the unmet need. There's a large unmet need in osteoarthritis. And I think -- we think tanezumab can play an important role. When you think about in the U.S., we've got 27 million people who have osteoarthritis, 11 million of those have moderate to severe osteoarthritis. Couple that with the fact that 80% of these patients have tried and failed 3 or more analgesics. There haven't been any new classes of medicines in this category for over a decade. You put those factors together, there's a lot to be excited about tanezumab, and we're looking forward to hear from the FDA about our BLA in December of this year. So thanks for the question.

Operator

Your next question is from the line of Geoff Meacham with Bank of America.

Geoffrey Christopher Meacham - *BofA Merrill Lynch, Research Division - Research Analyst*

Just had one on -- one question on R&D strategy and one on NASH. For Albert or Michael, on the strategy, I know you guys have raised the pipeline success rate. What would you say mostly drove that? Was it broader deployment of biomarkers? Was it a more dynamic clinical trial design? And is there an opportunity to further increase your Phase 2 and ultimately Phase 3 success rate?

And then on NASH, I know the long-term approach, as mentioned before, is likely combo therapy with 2 or 3 mechanisms. Is there one that you view as foundational? And how would you characterize the FDA environment for NASH just with respect to shortening the studies and maybe more rapidly derisking in the clinic?

Michael Gladstone - *Pfizer Inc. - Global President, Internal Medicine*

Thanks for the question, and this will be our last question. So with that, I'll turn it over to Morrie to talk about NASH and combinations, and then I'll ask Chuck to see if he has any comments on the first.

Morris J. Birnbaum - *Pfizer Inc. - Chief Scientific Officer of Internal Medicine*

Right. Thanks, Mike. Yes, I think at this point, it's too early to commit to one therapy as -- that we're particularly optimistic about. Obviously, you heard about the excitement of being able to inhibit ACC1 and -- to a fairly large degree and not be concerned about the increase in triglyceride. So we're very excited about that.

But as always, we're going to have to see -- we'd have to see what the biopsy studies show. And as we mentioned earlier, we've got a number of different mechanisms -- independent mechanisms coming through the pipeline. So we will find out which works the best. But right now, we're very excited about our lead studies, which are the ACC-DGAT combo and the DGAT2 inhibitor alone.

Jim, do you have anything to add on the clinical side?

James Rusnak - *Pfizer Inc. - Chief Development Officer, Internal Medicine*

I think that the question regarding the acceleration and FDA, I think that FDA has been very responsive to all of our interactions. And this is an emerging field. This is a field that we're looking for that initial standard of care to be developed. And I think that right now, the field is still open.

Michael Gladstone - *Pfizer Inc. - Global President, Internal Medicine*

Great. Thank you. Chuck, any comments on the first question? That was a little bit broader than internal medicine.

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

Yes. Sure, Mike. So yes, Geoff, of course, we're always trying to have continuous improvement here. So I think it's a combination of those factors that you referenced. We took -- as Rod pointed out in the presentation, we took a hard look at some of the areas where we were below average, identified those issues and took very specific steps to improve them. So I think it's a combination. And yes, we're always going to continue to see ourselves improve. But a lot of progress made there. And so it really, as I think Rod and Michael pointed out, a very different scientific organization here driven by a whole different set of parameters and really a different way to assess our success and a lot more accountability here certainly.

So thanks for the question, Geoff. And thanks for your questions. Now we're now going to move into our Vaccines program, and we'll transition there. And before we do that, we'd first like to share a video featuring Emma Harris, who's a former RSV patient.

(presentation)

PRESENTATION

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

Now I'd like to turn it over to the Vaccines team.

Nanette Cocero - *Pfizer Inc. - Global President, Vaccines*

I am Nanette Cocero, President of Pfizer Vaccines. And I am thrilled to be joining you this afternoon to share some of the exciting work our team has underway. There is certainly no more relevant time to be discussing the profound importance of vaccines to society as the world has been turned upside down by what we are very familiar with now, the COVID-19 pandemic. Yet we're also driven every day by the personal stories and the experiences of families like the one you just watched in the video.

It is personal for all of us. And for me, it is especially because like baby Emma, my son Javier contracted RSV when he was only 2 months old. Thankfully, he made a full recovery and today is a thriving 24-year-old, but it was a scary and difficult time for our family. And the potential to bring forward a vaccine that can help other families is what drives me and inspires me every day.

I'm also inspired by our Vaccine team, which includes experts and leaders in vaccine research and development, infectious disease epidemiology, medical affairs and vaccines commercialization.

You are all familiar with our flagship product, Prevnar. And several of the leaders with you today were instrumental in bringing this vaccine to millions of people around the world. I am joined for today's presentation by Kathrin Jansen, our Head of Vaccines Research and Development. And later for the Q&A, you will meet Luis Jodar and Bill Gruber, who round out our vaccine leadership team. We and the thousands of vaccines-focused colleagues working besides us every day have a true passion for helping to protect lives and meaningfully impact public health through the power of our vaccines.

Since the acquisition of Wyeth just over a decade ago, Pfizer has worked with focus and rigor to build the capabilities that have allowed us to quadruple the number of vaccine programs we have in the clinic and most recently to move quickly and effectively to take on COVID-19 virus. Our efforts over the last 10 years have transformed Pfizer's presence in the vaccine space from the Prevnar company to an end-to-end global vaccine leader anchored in 3 key strengths: innovation, portfolio breadth and depth and scale. We have invested significantly in our vaccine infrastructure. And today, we operate one of the most sophisticated and reliable supply chains in the industry, enabling us to deliver more than 1 billion vaccine doses since 2010 and without stock-outs.

We also continue to fuel our research and development engine. Currently, we have 9 programs in active clinical development. Dating back to Prevnar 13, we have received 10 Fast Track Designations and 3 Breakthrough Therapy Designations, underscoring the innovation they represent and the unmet medical need that they address. Best of all, with our robust pipeline, we are now aiming with regulatory approval to deliver 6 innovative breakthrough vaccines by 2025.

Another way to look at this is that with regulatory approval, we expect to be able to launch more than one innovative vaccine every year for the next 5 years on average. These 6 vaccines by 2025 include the 4 Phase 3 assets you see outlined here in red. These are the candidates we will focus our discussion on today: our next-generation pneumococcal conjugated vaccine candidate, PCV20, in development for adults and pediatric populations; and our potential first-in-class C. difficile, pentavalent meningococcal and RSV maternal vaccine candidates. Also included in the 6 by 2025 are our Lyme vaccine candidates in collaboration with Valneva and our COVID-19 vaccine candidate in collaboration with BioNTech. These programs will not be discussed in detail today, but we're looking forward to sharing more on our COVID-19 vaccine tomorrow and online in the near future.

Before moving on, I do also want to underscore how much progress there has been with our pipeline in the last 6 months alone. This slide you see today looks quite different from the version you would have seen had we held this meeting back in March. Since that time, we have initiated 5 new Phase 3 trials and added the Phase 2 Lyme program to our pipeline.

We are incredibly proud of the momentum we are building even in the face of a uniquely challenging year. With this strong pipeline, in addition to our current portfolio, we are working towards protecting more than 0.75 billion additional lives by 2028. We expect to deliver sustained growth year-over-year and to be a strong contributor to the long-term growth goals of the overall company while making a profound impact on global public health. This represents an acceleration of our growth profile compared to our recent past driven by the 6 anticipated vaccine launches between now and 2025.

Bottom line, we have the infrastructure, we have the expertise, and we have a passionate and committed team to successfully deliver against this growth goal. And what drives us the most are those 0.75 billion lives across the globe that are depending on us to make it a reality.

And with that, I'd like to turn it over to Kathrin Jansen.

Kathrin U. Jansen - *Pfizer Inc. - SVP & Head of Vaccine Research & Development*

Thank you, Nanette. My name is Kathrin Jansen. I'm Senior Vice President and Head of Vaccine Research and Development at Pfizer. I'm passionate about vaccine R&D and have focused my scientific career on improving public health through the development of high-impact vaccines, such Gardasil while at Merck and Prevnar 13 and TRUMENBA at Pfizer.

As noted by Nanette, today I will review our 5 late-stage programs, starting with our third-generation pneumococcal conjugate vaccine, PCV20, which aims to address the unmet pneumococcal disease burden in adult and pediatric populations. We established our leadership in the area of pneumococcal conjugate vaccines, first, with the introduction of PCV7 in the year 2000, followed by PCV13 in the 2009, 2010 time frame. PCV7 and PCV13 had a tremendous impact on public health, reducing the global pneumococcal disease burden, but we knew that we could do more.

Streptococcus pneumoniae remains a significant cause of disease and deaths globally for adults, infants and children, as you can see here, with an estimated 500,000 deaths a year in adults and 320,000 deaths annually in children. To help further address this considerable burden, we now are advancing a 20-valent pneumococcal conjugate vaccine in adult and pediatric populations. Based on our estimates shown here, we believe that PCV20, once approved, could provide the most comprehensive coverage against pneumococcal disease in both adults and pediatric populations compared to the standard of care and compared to other pneumococcal conjugate vaccines in late-stage clinical development, of course, also with advantages of a PCV that induces immune memory, lasting protection and particularly in older adults, proven efficacy against non-bacterimic pneumonia. If Phase 3 is successful and receives regulatory approval, PCV20 adult will provide 33% more IPD coverage, and PCV20 pediatric will provide 42% more invasive pneumococcal disease coverage than any other pneumococcal conjugate vaccine in late-stage clinical development.

I'm thrilled to present for the first time today, the clinical data from our PCV20 pediatric Phase 2 study based on which the FDA granted breakthrough therapy designation on August 17. Licensure of PCV20 pneumococcal conjugate vaccine requires demonstration of comparable serotype-specific immune responses to PCV13 for the serotypes in common.

As you can see here for our pediatric 4-dose regimen, immune responses across serotypes are indeed comparable. We also see substantial immune responses for the additional 7 serotypes not in PCV13 that mirror those seen in PCV13 and for which efficacy was demonstrated previously. These data will be presented at IDWeek next month. Registration for PCV20 pediatric is targeted for late 2022, and potential approval is targeted for mid-2023. These milestones are tracked closely to assess any potential COVID-19 timeline impact.

Now to turn to our PCV20 adult vaccine. I'm very excited to share that we are close to the finish line. The PCV20 adult submission is on target for early October with a potential approval expected mid-2021. Our team is looking forward to sharing the Phase 3 results from our PCV20 adult vaccine next month as a virtual presentation at IDWeek.

Next, I'd like to update you on our Phase 3 C. difficile vaccine program. C. difficile is a potentially life-threatening disease that has been recognized by the CDC as an urgent public health threat and is classified by WHO as a priority pathogen. C. difficile infections cause symptoms ranging from diarrhea to life-threatening inflammation of the colon and affect mostly older adults. This is the disease that can truly be everywhere. It is highly contagious given that it is transmitted through heat-resistant spores.

In the past, it was thought that the disease is mainly hospital-acquired. That is no longer the case. We now know that community-associated infections are on the rise and represent about half of all C. difficile infections. Compared to shingles, which can be prevented by a 2-dose vaccine that is recommended in the United States for adults 50 and older, C. difficile causes a higher number of annual deaths in the United States and has a higher cost to the health care system, as shown here. Our vaccine candidate is composed of 2 inactivated toxins, Toxin A and B, that have been inactivated through genetic and chemical detoxification procedures. Shown here are our Phase 2 proof-of-concept data that give us high confidence in our ongoing Phase 3 program. Our bivalent vaccine induces high-toxin neutralizing antibody responses after 3 doses, as shown here, for Toxin B. You can see that the responses plateau and then persist at substantially elevated levels above baseline. Similar response is observed also for Toxin A.

So what is the relevance of these Phase 2 data? The majority of vaccinated subjects had antibody titers that exceeded the serum levels of a monoclonal antibody license to protect against recurrence of C. difficile disease. Our Phase 3 CLOVER study is an end point-driven study that is fully enrolled. As publicly reported, end points are accruing slower than originally anticipated. Given our confidence in the vaccine and in consultation with the FDA, we have added additional interim analysis to our study, and we expect to have the first interim analysis occurring at the end of this year.

The next program I would like to share with you is our pentavalent meningococcal vaccine, or in short penta, a vaccine designed for the broadest meningococcal disease coverage. It is heart-breaking when we hear stories of how parents watch their child suffer from the serious consequences of meningococcal disease. There are currently separate vaccines for meningitis, ACWY and meningitis B with separate recommendations, which is very confusing to health care providers and parents. This is unfortunate because only 17% of U.S. adolescents receive at least 1 dose of a MeningB vaccine and far fewer receive the full schedule of meningococcal vaccines needed for protection. But we think we can do something about this confusion and help simplify the schedule to protect more adolescents and young adults.

Through our acquisition of the effective meningococcal ACWY vaccine, Nimenrix, we had an excellent opportunity to combine it with our own meningococcal B vaccine, Trumenba, aiming to provide one pentavalent vaccine to help address meningococcal disease caused by serogroups A/BCWY in adolescents and young adults. Assuming clinical success and FDA approval, we envision a future schedule with our penta vaccine that would only require 3 doses, shown here in light blue, compared to the 4 doses in current schedules.

If we are successful, this simplification should avoid confusion and help ensure comprehensive protection from this potentially deadly disease in larger numbers of adolescents and young adults. In addition, Pfizer could potentially be the leader in the meningococcal U.S. market.

To show that we are on track to potentially achieve this goal, I'd like to share new clinical data from our penta Phase 2 proof-of-concept study. Shown here are the immune responses of penta in dark blue bars compared to Trumenba in light blue and MenACWY in gray. Similar to pneumococcal conjugate vaccines, meningococcal vaccine licensure requires demonstration that penta, again in the dark blue bars, has comparable immunogenicity to MenB and ACWY vaccines. We are pleased to show you here that penta, indeed, in almost all cases, induces comparable, if not better, immune responses than the comparators. Given these data, we believe that if reproduced in Phase 3, such data will help support licensure and put us in a good position to offer a more comprehensive pentavalent meningococcal coverage to help prevent this devastating disease. Additional results from this study will be presented at IDWeek next month. Our Phase 3 study start occurred on June 17, 2020. As you can see on this timeline, we believe that if Phase 3 indeed is successful, a BLA filing of a penta vaccine could potentially occur in early 2023.

I'd now like to switch to RSV, a vaccine candidate that we believe can revolutionize how we think about protection of newborns from infectious diseases through maternal immunization, a new frontier for vaccines. For too many newborns, respiratory syncytial virus, or RSV, can cause severe respiratory disease causing families to experience fear, anxiety and despair as they see their newborn baby struggling to breathe, as you saw in the video played earlier in our session. RSV disease is particularly devastating in newborns, causing approximately 1.4 million hospitalizations in those less than 6 months of age and unfortunately, deaths in many newborns across the globe. There is currently no cure or vaccine, and the standard of care treatments that exist today simply are not enough for this vulnerable population.

Scientists and researchers have worked on the development of an RSV vaccine without success for over half a century, including Pfizer. Based on the discovery by Jason McLellan and his team in 2013, we now know that while we all have the right vaccine target, we all had the wrong structure. The left-hand side panel shows the vaccine target antigen that was the root cause of all prior failures.

This structure or the postfusion structure of F is not the predominant form that exists on the virus and not the structure that antibodies must bind to, to neutralize the virus. Instead, note the structure on the right, the prefusion F form, which is the right form and is the target of most naturally produced virus-neutralizing antibodies. The reason the pre-F structure was so elusive for so long is that pre-F is extremely unstable like a spring-loaded device that flips into the wrong form after the slightest trigger. Using our protein engineering expertise at Pfizer, we used our numerous inventive protein design and engineering capabilities to optimize the stability of the pre-F form and lock it down.

Based on our clinical Phase 2 data in healthy women and men, we believe that we have the most stable and immunogenic vaccine candidate for maternal vaccine. Compared to prior attempts with our pre-F vaccine candidate, we see never-before observed fold rises of RSV-neutralizing antibodies, over 15-fold for RSV A and 18-fold for RSV B in women of child-bearing age compared to the mere 2 to 3-fold rises seen prior with postfusion F or insufficiently stabilized forms of F. Having these high fold rises to both subtypes is critical as RSV A and B circulate almost at equal rates in any given RSV season.

What do these this data mean, though? We modeled efficacy data from an RSV monoclonal antibody to estimate the fold rises likely needed for a substantial protection, while rises from prior vaccines were not sufficient to achieve meaningful protection, and our model actually predicted this.

We believe that our vaccine fold rises suggest a high probability to demonstrate substantial efficacy in newborn babies. These data provide us with confidence that our vaccine candidate, if proven successful in Phase 3, could be the very first maternal vaccine licensed and most importantly, would offer protection for the most vulnerable population from RSV in the first days, weeks and months of life.

Our Phase 3 RSV study began on June 18, 2020, with pregnant women receiving a single vaccine dose between 24 and 36 weeks of gestation. This study is on a Pfizer accelerated pathway to bring faster forward promising vaccine candidates. Due to COVID, we are tracking the RSV disease epidemiology very closely to understand any potential impacts on our timeline. We do have an interim analysis built into the program at 50% of cases. If efficacy was met at the interim analysis, the submission could occur as early as mid-2023 based on our current timeline projections.

To summarize our late-stage vaccine portfolio, we have built a robust and exciting vaccines pipeline with the potential to launch 6 innovative vaccines by 2025, the 5 you see here on the slide, plus our COVID-19 vaccine candidate, which I look forward to discuss with you in detail tomorrow.

With that, I would like to hand it back over to Nanette. Thank you.

Nanette Cocero - *Pfizer Inc. - Global President, Vaccines*

Thank you, Kathrin. As I talked about earlier, our work in the pneumococcal space is well-known. Today, in addition to hearing about our next-generation Prevnar vaccine, PCV20, you have also heard about Phase 3 assets such as C. difficile, RSV maternal and meningococcal pentavalent vaccine candidates. And you have gotten a closer look at these disease areas, the compelling data we have generated to date and an overview of clinical timeline. Additionally, I wanted to share some information on how we are thinking about the commercial opportunity of these 3 assets.

For C. difficile, the prevalent population ranges from 90 million to 130 million people depending on the ACIP recommendation that we receive. We anticipate vaccinating up to 5% of the target population each year in the United States, ultimately reaching nearly half of those 90 million to 130 million people on a cumulative basis. We also expect 100% market share for the first 4 to 5 years before competition potentially enters the market.

For RSV maternal, we anticipate a strong market uptake among our population, which is the number of pregnant mothers based on the annual birth cohort. We also expect to maintain a 60% to 70% of the RSV maternal vaccine market given our lead over the competition and our projection that there will be complementary usage of maternal immunization and monoclonal antibody.

And finally, within the total meningococcal market, we expect to push current penetration rates even higher to what you see here with the potential introduction of our pentavalent meningococcal vaccine. We anticipate our share of the pentavalent market to range between 40% to 55%, yielding peak sales in 2029.

By now, I'm sure you all can see why we're so excited about our portfolio. We're entering a new era for Pfizer vaccines that will be driven by these 6 breakthrough vaccines. 2020 is a pivotal moment in our journey, not only because of COVID-19 but because of how we have accelerated and expanded our pipeline overall. We are incredibly proud of how far we have come in the last 10 years and yet even more important and exciting, where we're heading in the next 10 years because the best is yet to come.

Thank you all for your time and attention. And now I'll turn it back to Chuck to get us started with the Q&A session.

QUESTIONS AND ANSWERS

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

Great. Thanks, Nanette. Certainly a lot going on in the vaccines area. So we're going to get ready to move to the Q&A session for the vaccines team. And just a reminder, we're going to have a separate COVID section tomorrow with Michael, Angela and Kathrin presenting on COVID, and then Albert will join for the Q&A session as well for that tomorrow. So if you can hold your COVID questions until tomorrow. This way, the vaccines team can talk about all the other vaccines that they've just gone through.

So with that, operator, now please poll for questions for the vaccines team.

Operator

(Operator Instructions) Your first question is from the line of Vamil Divan with Mizuho Securities.

Vamil Kishore Divan - *Mizuho Securities USA LLC, Research Division - MD*

I do have some COVID questions. I guess I'll save those for tomorrow. So one on your pneumococcal franchise and one on the meningitis side. So just in terms of the pneumococcal franchise, I guess, I'm curious on how you think about the sort of near to mid-term commercial outlook for your franchise because Merck does seem to be a little bit ahead of you with their vaccine, the 15-valent. I can see why yours is maybe a better vaccine and maybe the leader over time. But maybe if you can talk about how you see the next sort of 1 to 3 years playing out if Merck -- if they're able to get to the market ahead of you, especially in the pediatric setting.

And then on the meningitis side, I guess, we've been surprised, I guess, by the relatively limited uptake for your current vaccine. You did seem to give pretty bullish sort of projection in terms of market share and penetration. And I guess, I just -- maybe if you can dive a little deeper into that. I know there's a 3-shot series instead of a 4-shot series. But what, I guess, maybe drives your confidence there in terms of -- is that the main driver in terms of why the uptake would be a lot more? Or I guess, I'm just trying to understand that one a little bit more to see why this one might turn out to be a bigger opportunity than what we've seen so far.

Nanette Cocero - *Pfizer Inc. - Global President, Vaccines*

Okay. Well, thank you for your question, and I'll begin with the question on pneumo. And we are confident that we will be maintaining our leadership position given our strong history of safety and efficacy and expect to be 12 months behind our competition for the pediatric space. And for the adult space, we are going to be coming to market by mid next year, which is right head-to-head with competition.

While current pipelines indicate a potential 12 months in the pediatric space, we are leveraging our clinical expertise to explore closing this gap, just as we did with the adult vaccine. PCV13 efficacy and even more important, the safety are well-established and recognized among physicians and patients. And this is why we expect physicians to be very comfortable continuing prescribing PCV13 in the period before PCV20 is potentially launched. And as you mentioned, both PCV13 -- I mean, PCV20 adult and pediatric do add additional coverage, 42% additional coverage in the

pediatric space and 33% more coverage in the adult space. So for all these reasons, we are confident that we will maintain our leadership in the pneumococcal space short term and L-O-N-G term.

Now to your question on mening. We are also confident and very excited about the opportunity to address the current patchwork, like Kathrin mentioned, which is complicated and inconsistent recommendation in order to simplify the vaccination schedule, allowing more adolescents to be fully protected. We -- with the 5 additional serotypes, this will give us A/BCWY, which covers the majority of the meningococcal devastating disease. Our timing -- because of our timing that puts us ahead of our competition as first to potentially launch, and based on strong Phase 2 data that Kathrin mentioned, we do see a high probability for a Phase 3 success and licensure. And by entering the market in the U.S. first, we do anticipate maintaining a strong share of the market, resulting in a blockbuster commercial opportunity.

And to the third question on the 3-shot series, I will pass on that question to my colleague, Luis Jodar. Luis, please?

Luis Jodar - *Pfizer Inc. - Chief Medical & Scientific Affairs Officer, Vaccines*

Yes, Nanette. Thank you very much. So I think as Kathrin and Nanette said, there is now a patchwork of recommendation. So just to remind everybody, at 11 years of age, there is a dose of the tetravalent vaccine and a booster dose at 16 years of each, and those have routine recommendations. Those are the former ACIP category A, and the uptake is very high.

I think you've mentioned why you were thinking that the 2 doses for MeningB at 16 years of age the uptake is a little bit lower. And that's for a number of reasons, but presumably because it's a category B or shared clinical decision-making. So what we are expecting when a pentavalent is introduced, it is to reduce the 4 current shots into 3 shots and going to the universal or routine immunization both at 11 years of age as the tetravalent containing vaccine, and then 2 doses to replace the 3 doses in the 16 years of age. For that reason, we are very, very confident that the uptake is likely to be very high and even higher than the current tetravalent uptake right now. Thank you. Back to you, Nanette.

Nanette Cocero - *Pfizer Inc. - Global President, Vaccines*

Thank you, Luis.

Operator

Your next question is from the line of Geoffrey Porges with SVB Leerink.

Geoffrey Craig Porges - *SVB Leerink LLC, Research Division - Director of Therapeutics Research & Diversified Biopharma and Senior Research Analyst*

A couple for Luis. I just want to follow up on the question about pneumo conjugator. And how do you expect the ACIP to handle a time difference between the availability of the package for your data and then your competitor's data? So is there a threshold where the ACIP will lump them together and just take a vote and then issue a recommendation? Is that 6 months, 3 months, 1 month? Just trying to figure out whether there'll be a switch in the recommendation to your competitor's product and then theoretically, a switch back to yours assuming the pivotal trials are correct.

And then a question for you, Kathrin. It's something that I'm sure is near and dear to your heart, but do you need a proprietary adjuvant system? We've been surprised with the performance of all the proprietary derived adjuvant, and I know you're headed towards MRNA. But do you think that that's something you would like to have in your portfolio and toolkit given all the opportunities you're looking at?

Nanette Cocero - *Pfizer Inc. - Global President, Vaccines*

Excellent. Well, thank you for your questions. You did my job. So Luis will do -- will take the first question, and Kathrin will take the second question. Luis, please?

Luis Jodar - *Pfizer Inc. - Chief Medical & Scientific Affairs Officer, Vaccines*

Sure, absolutely. About the timing of ACIP, well, first of all, of course, I cannot speculate around what the ACIP is going to do, but that's an interesting question. And I think I would answer it in 2 ways. First, for adults. And I think as you've heard Kathrin, we are filing in October the PCV20. So again, we'll see how it goes. But in principle, we expect that licensure is going to be in mid-2021.

Now we do not know whether Merck is going to be up there or not. But the idea would be that both vaccines would be either looked into the grade and recommendations for June 2021 or in October 2021. So that, I think, it's pretty clear that both vaccines in adults are going to be sort of recommended at the same time.

As for the pediatrics, well, right now, there is -- we are a year behind. But I think, as Kathrin mentioned, we are trying to do our best to shorten that gap as much as possible. And if we shorten that gap to less than 1 year, it might be prudent to have sort of a holistic review of the recommendations of pediatrics just together. But really, that would depend on the gap between the 2 vaccines. And of course, I cannot give you whether it's 3 months or 6 months, but it would be 1 or 2 ACIP meetings, I would say. That's the difference. And then I'll pass it to Kathrin.

Kathrin U. Jansen - *Pfizer Inc. - SVP & Head of Vaccine Research & Development*

Thank you, Luis, and thank you, Geoffrey, for your question about the adjuvants. We actually have been working for a long time on the evaluation of different adjuvants. Our strategy has been to invest in a focused manner in new technologies such as adjuvants when we believe that the current approaches may not be sufficient to develop a successful vaccine. And actually, case in point is our collaboration with BioNTech on a seasonal flu vaccine. We believe that BioNTech's RNA platform may address the current shortcomings of seasonal influenza vaccines and provides a platform that we believe could be -- provide better protection each year. Back to you, Nanette.

Nanette Cocero - *Pfizer Inc. - Global President, Vaccines*

Well, thank you very much. Yes. Thank you, Kathrin.

Operator

Your next question is from the line of Terence Flynn with Goldman Sachs.

Terence C. Flynn - *Goldman Sachs Group, Inc., Research Division - MD*

First, it's kind of a follow-up to a prior one with respect to the 20-valent market opportunity. Do you guys see that as more of a straight conversion opportunity? Or is there actually a chance you could expand usage and grow your revenues over time in that segment above and beyond Prevnar 13?

And then one on the messenger RNA platform. How are you guys thinking about that more broadly? Is that something that, again, as you think about your partnership there, you do see a broader range of opportunities? And maybe you could talk to us about that.

And then the third question is just on the C. diff vaccine. Any way to lower the number of injections there needed from 3 to less than 3?

Nanette Cocero - *Pfizer Inc. - Global President, Vaccines*

Okay. So I'm going to start with the C. diff question and then -- and pass it on to Kathrin, please, and then I'll take the PCV20 question. And actually, I'm so sorry, but I do not get the second question. Can you repeat it?

Operator

His line is closed.

Nanette Cocero - *Pfizer Inc. - Global President, Vaccines*

Okay. All right. So let's go then to Kathrin. Can you please then address the C. diff question on the number of doses, and then I'll address the PCV20 question?

Kathrin U. Jansen - *Pfizer Inc. - SVP & Head of Vaccine Research & Development*

Yes. Thank you very much, Nanette, and thank you for the question. As you know, of course, we are very excited about our collaboration with BionTech and the RNA platform, and you will hear much more about this in our session tomorrow. So given the exciting data that we are seeing out of this technology, you are absolutely correct. We are thinking about widening our -- the platform to encompass additional disease targets. So that is a -- in addition to the influenza vaccine. So this is something that we are working on, but we haven't decided yet on the details of those additional programs.

We are also working in the context of the seasonal influenza on an RNA platform that is called self-amplifying RNA that we believe has the best chance of success to develop a more potent seasonal influenza vaccine. This self-amplifying RNA could potentially be very potent, and we believe that there may be an opportunity to make this a 1-dose vaccine.

Nanette Cocero - *Pfizer Inc. - Global President, Vaccines*

Thank you. Thank you, Kathrin. Now to the PCV20 question, we are confident in the potential of PCV20, of course, given that went to coverage that we have mentioned. Yet we also do recognize that there will be a period where we will have both PCV20 and PCV13. While our strategy is to transfer all of our PCV13 business to PCV20, there will be a period where we'll have both because the registration timeline is not the same on every country, especially for the emerging markets countries. So there will be a period of time where we will have PCV20 in the U.S. and in Europe and we might still have PCV -- well, we will have PCV13 in emerging markets. So thank you for your question.

Luis Jodar - *Pfizer Inc. - Chief Medical & Scientific Affairs Officer, Vaccines*

So Nanette, perhaps you can pan to Bill. Bill, I think there was a question about the 3 doses versus 2 doses of the C. difficile clinical program. Perhaps you want to elaborate that.

William Gruber - *Pfizer Inc. - Senior Vice President, Vaccine Clinical Research & Development*

Yes. So maybe I can just speak to that briefly. So obviously, if the C. difficile efficacy trial, the CLOVER trial, demonstrates efficacy with a 3-dose regimen, there is the potential by showing that an immune response with a 2-dose regimen spread 6 months apart, if that shows a comparable immune response, there's the potential for a 2-dose regimen to be part of an indication. And so it's a good question, and it's something that we're interested in.

Nanette Cocero - *Pfizer Inc. - Global President, Vaccines*

Okay. Thank you. Thank you, Bill and Luis.

Operator

Your next question is from the line of Seamus Fernandez with Guggenheim.

Seamus Christopher Fernandez - *Guggenheim Securities, LLC, Research Division - Senior Analyst of Global Pharmaceuticals*

Great. So just a couple. First on the pneumococcal conjugate, just wanted to get a better understanding of the threshold, particularly in the pediatric patient population, that's been demonstrated with your 20-valent. Historically, I think the threshold that had been established by regulators was the 0.3 or 0.35 microgram per ml target for the antibody threshold. So I'm just wondering if that threshold has been achieved with all of the 20 serotypes.

And then as a separate question to that, if it hasn't been achieved but non-inferiority has been clearly established to Prevnar 13, is it possible that the agency's bar has shifted to some degree given the efficacy with Prevnar 13?

And then second question I have is actually on -- around the RSV program. Can you help us understand 2 questions: number one, is passive vaccination with an antibody like nirsevimab, which we saw recently published in The New England Journal versus maternal vaccination, can you help us understand the advantages of maternal vaccination over potential passive vaccination?

And then separately, just in terms of the percentage uptake that we typically see with maternal vaccination. What would be the estimated acceptance because it would seem like that might be more challenging versus a passive vaccination approach?

Nanette Cocero - *Pfizer Inc. - Global President, Vaccines*

Thanks, Seamus. Thank you very much for your questions. The first 2 questions on the threshold, I think that Kathrin, you can take those and Luis could probably then also after that. And I will take the RSV question. Thank you, Kathrin.

Kathrin U. Jansen - *Pfizer Inc. - SVP & Head of Vaccine Research & Development*

Yes, thank you. So just as I described earlier, the polysaccharide conjugates vaccines will be licensed against existing pneumococcal conjugate vaccine. So PCV20 will be licensed by demonstration of noninferiority to PCV13 for the serotypes in common and then also using the 0.35 threshold for the 7 additional serotypes. So what we have demonstrated so far, what you have seen here, are data from our Phase 2 study. That study was not powered to actually demonstrate noninferiority. When we go to the adult program, that study was our Phase 3 data, and that study was powered to demonstrate noninferiority. So what regulators do and what we have done in the past with PCV13, because of the large number of statistical noninferiority comparison that we have to do, and for PCV20, that will be 20, we have established precedents that in -- if by chance one or more of the serotypes would miss the noninferiority margin, that regulators will look at additional data and take the totality of the data into consideration.

And that is actually a very wise decision, if you want, because we have seen exactly the same for PCV13 when we compared it to the original Prevnar 7. We found that 2 of the serotypes did indeed miss the noninferiority margin, but then other data such as fold rises, the reverse cumulative distribution and how the extent to the miss of the noninferiority margin were all taken into consideration as well as functional antibody, which led to the licensure approval of PCV13. And what turned out then in real life after the vaccine PCV13, as it was rolled out, that the serotypes that actually did miss noninferiority were very effective and continue to be effective in -- after the use of the PCV13 vaccine.

And we expect, should we see something like this in the Phase 3 program -- in our pediatric Phase 3 program, that we would expect and believe that the same approach would be used to license PCV20 for the pediatric population. Thank you.

Nanette Cocero - *Pfizer Inc. - Global President, Vaccines*

Okay. And then Luis for the antibody question for RSV.

Kathrin U. Jansen - *Pfizer Inc. - SVP & Head of Vaccine Research & Development*

RSV.

Luis Jodar - *Pfizer Inc. - Chief Medical & Scientific Affairs Officer, Vaccines*

For the...

Kathrin U. Jansen - *Pfizer Inc. - SVP & Head of Vaccine Research & Development*

Yes. Maybe I'll start, Nanette, and just discuss some of the advantages, and then Luis can put into context how a monoclonal in the vaccine assuming both are successfully approved could coexist.

So from our perspective is it is our intent to -- and we have designed the RSV maternal program to really address the global unmet medical need of RSV in newborns up to 6 months of age, where we really do see the highest unmet medical need. So one of the advantage of a vaccine is that the protection of the newborn starts at birth because it's actually provided by the mom.

The second advantage of a vaccine approach is that you do induce a, what we call, polyclonal RSV-neutralizing antibody response, and that is in contrast to a monoclonal that only targets a single epitope on the virus. And when you think about this, the RNA viruses, even though they are more stable than flu, nevertheless, they do mutate, and we have already seen a number of mutations that are circulating. So there's not just one strain. And there is a high liability with the monoclonal to actually lose effectiveness should the epitope that is recognized by that monoclonal change over time.

And so, Luis, if you would like to discuss, though, how a monoclonal can be used in the context of a successful maternal vaccine, please?

Luis Jodar - *Pfizer Inc. - Chief Medical & Scientific Affairs Officer, Vaccines*

Sure. Thank you, Kathrin. And Seamus, I think your question was about, okay, suppose that you have the monoclonal and the vaccine, similar characteristics, how do they coexist together based on ACIP recommendations. And again, we're very confident about our approach. And I think Kathrin has summarized it well, our approach with our RSV vaccine for the ACIP. Again, I cannot expect without the ACIP and the CDC is going to decide to make these recommendations. But the way that we are seeing it is that it seems to us that a structural recommendation makes more sense than just having 2 recommendations with 2 different providers, 2 intervention tools, 2 target populations, pregnant women or kids, and then 2 time points as well. So at the end of the day, what we believe is that if safety and efficacy is demonstrated, then there's going to be a universal recommendation for pregnant women. And then the monoclonal, with the complementary intervention, either for high-risk groups or either for unvaccinated or for older age populations, that's how we see this play now. So thanks very much. Back to you, Nanette.

Nanette Cocero - *Pfizer Inc. - Global President, Vaccines*

Thank you, Luis. And yes, just to address the last piece of the question, which is regarding the uptake of RSV in the maternal space. We are very confident that our penetration estimates, given the strength of the data that we have today, we do believe that we can reach the 60% to 70% market share, especially because RSV is the #1 cause of hospitalization in infants younger than 6 months old, and the treatment is really limited to only fluids and oxygen. So we do believe that with appropriate education and awareness as well as continued strong clinical results, all stakeholders, including pregnant mothers, will see the value that the RSV vaccine is bringing.

So thank you so very much for your questions. We have run out of time. So thank you to the panel for answering all the questions. And again, thank you for the audience for all your great questions, and now I pass it on back to Chuck.

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

Great. Thanks, Nanette, and thanks, everyone, for your engagement today.

A couple of things. We certainly look forward to reviewing our other therapeutic areas within the organization tomorrow. As a reminder, that will be inflammation and immunology, rare disease, oncology and then the COVID section. And as a reminder, tomorrow's session is going to begin at 10:00 a.m. New York time.

And then if you refresh your screen, you'll see at the top a survey. So if you could take a moment to fill out the feedback survey, we'd certainly appreciate that. And we look forward to reconnecting with you all tomorrow, and this will end today's session. Thank you.

Project Matrix
Post-EGM Legends

Forward-Looking Statements

This communication contains "forward-looking statements". Such forward-looking statements may include, without limitation, statements about the proposed combination of Upjohn Inc. ("Newco") and Mylan, which will immediately follow the proposed separation of the Upjohn business (the "Upjohn Business") from Pfizer Inc. ("Pfizer") (the "proposed transaction"), the expected timetable for completing the proposed transaction, the benefits and synergies of the proposed transaction, future opportunities for the combined company and products and any other statements regarding Pfizer's, Mylan's, the Upjohn Business's or the combined company's future operations, financial or operating results, capital allocation, dividend policy, debt ratio, anticipated business levels, future earnings, planned activities, anticipated growth, market opportunities, strategies, competitions, and other expectations and targets for future periods. Forward looking statements may often be identified by the use of words such as "will", "may", "could", "should", "would", "project", "believe", "anticipate", "expect", "plan", "estimate", "forecast", "potential", "pipeline", "intend", "continue", "target", "seek" and variations of these words or comparable words. Because forward-looking statements inherently involve risks and uncertainties, actual future results may differ materially from those expressed or implied by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to: ongoing challenges and uncertainties posed by the COVID-19 pandemic for businesses and governments around the world; the parties' ability to meet expectations regarding the timing, completion and accounting and tax treatments of the proposed transaction; changes in relevant tax and other laws; the parties' ability to consummate the proposed transaction; the conditions to the completion of the proposed transaction not being satisfied or waived on the anticipated timeframe or at all; the regulatory approvals required for the proposed transaction not being obtained on the terms expected or on the anticipated schedule or at all; inherent uncertainties involved in the estimates and judgments used in the preparation of financial statements and the providing of estimates of financial measures, in accordance with U.S. GAAP and related standards or on an adjusted basis; the integration of Mylan and the Upjohn Business being more difficult, time consuming or costly than expected; Mylan's, the Upjohn Business's and the combined company's failure to achieve expected or targeted future financial and operating performance and results; the possibility that the combined company may be unable to achieve expected benefits, synergies and operating efficiencies in connection with the proposed transaction within the expected time frames or at all or to successfully integrate Mylan and the Upjohn Business; customer loss and business disruption being greater than expected following the proposed transaction; the retention of key employees being more difficult following the proposed transaction; Mylan's, the Upjohn Business's or the combined company's liquidity, capital resources and ability to obtain financing; any regulatory, legal or other impediments to Mylan's, the Upjohn Business's or the combined company's ability to bring new products to market, including but not limited to where Mylan, the Upjohn Business or the combined company uses its business judgment and decides to

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