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EDITED TRANSCRIPT

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CONFERENCE CALL PARTICIPANTS

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

PRESENTATION

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

Okay. I think we've begun here. So thanks for joining us. I'm Tim Anderson. I'm the large-cap pharma and biotech analyst at Wolfe Research.

Today is the first day of our 2 day healthcare conference, where we'll be interviewing different companies in a fireside chat format.

We've got Pfizer with us for this next session. 3 members of the R&D team, Mikael Dolsten, President, Worldwide R&D, Chief Medical Officer. He came to Pfizer through the Wyeth acquisition in 2009. We have Annaliesa Anderson, who is SVP and Chief Scientific Officer in Bacterial Vaccines and Hospitals. She's been with the organization since 2007. We have Charlotte Allerton, SVP and Head of Medicine Design with the company since 1993. And we have Chris Stevo from Investor Relations. And Chris, I think you want to make some opening remarks here.

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

Yes, I'm not a scientist, so all I'm good for is reading forward-looking statements. So I just want to note that we are going to be making forward-looking statements in our conversation today, and they're only current as of today, and we undertake no obligation to update them in the future. And if you have any questions on our forward-looking statements, you can see the disclosures in our Form 10-K and 10-Q. Thank you.

QUESTIONS AND ANSWERS

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

Great. Okay. So yes, with that, we'll go ahead and begin. So exciting times for the company. You really deserve lots of credit. You're helping lead the world out of COVID. So it really is a remarkable achievement, and congratulations to all of you. We have an R&D Day coming up in December. You guys have an R&D Day coming up in December. Any details you want to share programs you'll highlight the most, what the nature of the discussion will be?

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

Well, thank you, Tim. We have such a broad pipeline with really great momentum. So I don't think we'll reveal the agenda right now. We want to have everyone come in with curiosity and excitement. And the general message is that in this COVID era, we were able to contribute with what seems to be the premier vaccine and probably the most promising oral protease inhibitor, oral antiviral basically 2 of the most powerful tools to manage the pandemic.

And as we can talk more about, I think, actually, they are synergistic, both at the individual level and at the population level. So what we really want to do at the R&D Day is to show that this just didn't happen in isolation. We have built biomedical understanding a technology platform, human and AI learning, how to design medicines and vaccines. We have built through decision-making and other processes, a leading success rate in the industry for R&D.

And during COVID, we particularly also managed to with the support of our CEO, Albert Bourla established the Lightspeed platform of how you move things swiftly and how you invest boldly when you see certain signals. So we'll take that lens and share more broader in the pipeline promise of the future.

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

You have the longest running tenure as Head of R&D, I think, of any of the multinationals. Can you trace -- I'm giving you a chance to brag about your accomplishment. Can you trace some of these improved R&D metrics that you've talked about in Q3, referencing the pharmaceutical benchmarking for data to continuity within the organization? Or what have been some of the bigger drivers of that? It seems that things like major mergers often disrupt R&D. Pfizer has been through its fair share of those. You've lived through one of those at the company. But what is helping Pfizer to kind of outperform its peers along various things like phase success rates?

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

No, happy to say a few words about kind of a decade plus journey. I did actually hear from one of the consultant teams, I think it was actually BCG that leaders that are longer in their service for a high-tech company like a pharma are able with the colleagues together to assemble more of deeper insights and more of continuity of change and less of disruptiveness as may happen in an early phase of a turnaround, so you become more of an engine with a real rhythm in pulling off innovations. So I would attribute what actually, I and my colleagues that all have been working here and these are 2 of my key colleagues had done over a decade is to build that culture that strong talent pool, the commitment to science that can deliver breakthroughs, and we have been able to work with many outstanding business leaders.

Of course, the last few years with Albert, I think, has been the peak and more to come, the peak of this decade, particularly with him and the company as a whole, feeling that we have built such a strong R&D engine. And when you're prone to invest, you have to have the metrics on success rate and cycle time, if you invest as a pioneer, not just incrementally too, where you follow others.

If you have high success rates and right now in the KMR benchmark, we are about 20% from Phase 1 to approval, which has been unprecedented. I think Tim for you and me over a decade to note, it used to be high single digits.

And actually, our competitors are around 10% to 11%. We were now actually going about 20%. When you have that success rate, it's possible when you start to see exciting science coming through Phase I with an initial human signal to rely on that and say, "We Pfizer can invest at risk to accelerate the programs with manufacturing, in pharmaceutical sciences, hundreds of millions, maybe 1 billion because we know that disproportionately we'll succeed more than others."

So having built that capacity allows you in a way to go to the Premier League, where it's difficult for others to follow because if you have just after success rate, you will burn a lot of cash rather than disproportionally use the cash well. So that was one part of our journey to build that translation, whether on the molecules or on the biomedicine to get that high success rate.

And the number two where I think Albert inspired us a lot is, once you go into that race, others may follow you, and they may learn from you. So it's very important that you have that extra gear to rev up the engine and we came out during COVID with this new way of working that we call Lightspeed.

I think you have probably never written an analyst report about anyone that have concluded from the lab to an EUA approval in less than 10 months a complex vaccine for new disease. Well, if you thought that was maybe a one-off, you've probably never written about a team that have designed

a small molecule against the protease. That is one of the more difficult and sematic targets and actually had to do hundreds of different compounds. It was not just having a starting point with all great attributes and then to get it through highly positive Phase 3 and announced filing in 20 months. So these are some examples why I think we feel much more confident that it's not about a single project. It's about a systematic approach to R&D that involves close partnership with colleagues.

When COVID started, I and many of the colleagues here, Lisa was part of many task force with an age on small molecules and consulting with Charlotte, I was part on the acting leadership team. I think a lot of companies were willing to contribute, but very few are investing heavily. And I think they may have underestimated how much pandemic will take a toll on unmet medical need and society as a whole. And I think, many thought that this would be just an effort that wouldn't pay off and would disappear as society went into lockdowns and the pandemic disappeared.

So I think us working with a broader team in Pfizer, CDC, FDA really lit the light in the front of our eyes. Now it's the time to rise as a company for this tremendous pandemic, and there are ways to make this successful for patients, for many countries and for shareholders at the very same time. And that's when the ecosystem works at, its best. It reinvents itself and incentivize for future innovation.

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

The company has major cash windfall from both vaccine and oral treatment. And that segues into the question about business development. So from a Head of R&D perspective, how are you looking at this? I mean I think and I think others are thinking this too. We almost have to see a flood of additional deals by a company that otherwise wouldn't have happened that you're allowed to do now with all this excess cash that could really help address, what is sometimes cited bear case of lots of patent expiries when you get to the later 2020s. So the business development outlook from here, would you agree that it has probably changed from what you would have thought it was 1.5 years ago?

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

Yes. I'll say a few words, and then I'll ask Charlotte and Lisa also to comment an example of areas by medical areas, technology areas that are high on our radar that can disrupt the future or supplement what we have.

Clearly, the opportunity of COVID was to deal with the pandemic. And I think we have learned that it's going to transit into a mix of pandemic in some regions of the world staying for quite some time and then an endemic situation with ability to manage disease through very active use of medicines and vaccines to manage the viral load in the globe. And we feel that the 2 can be very synergistic.

So that, of course, suggest to us that this is a very durable business and that we're also fortunate to have a very durable vaccine and therapeutic defense to manage the threats to people and to business or society maintaining its open structure.

We have seen that the vaccine when deployed effectively can really immediately take off the fear in society, but it's not a one and done. We see with surveillance that the infection can rise again vaccination needs to be combined with boost and a proper surveillance system. We know that in parts of the world, there are either resistance to vaccinate or it's just not possible to have the logistics to do repeat vaccination sufficiently consistent.

So a therapeutic, I think, will be as sizable in its impact as a vaccine over time, and there were some really intriguing studies from Fred Hutch Center in U.S. -- in Seattle showing that they made a mathematical modeling, how much would an oral pill that can be convenient to use of the type of efficacy that we have, not just moderate efficacy but very high. How could it combine with various extent of vaccination and all of their scenarios showed that the pill would augment the impact of the vaccine in a synergistic manner for the individuals that get infections to spare them from long-term sequelae for their neighborhoods and for the overall transmission rates.

So I think what -- you talk about the windfall, it's not just 1, 2 years. I think we have created a very unique leading medical business for many years to come, and we see ample opportunity to accelerate our internal engines with the product acquisitions, technology that drives the whole portfolio

coming from that technology, early-stage product that can benefit by our success rate and cycle times to have more competitive edge, and late-stage product that can fit our existing portfolio.

So we will be very active and the type of acquisition of companies like Trillium we announced, the deal was closing today. We announced a more product-specific deal with Arvinas. We acquired earlier Array in Boulder as an example of a deal with both capability products and royalties.

So you will see all of that come into play. I'll ask Charlotte and then Liesa, just to give example of areas externally that may represent one of the many opportunities for how business development can supplement us and where we may be a preferred player because many biotechs today are not just looking for cash. They're looking for someone that can accelerate our success like we did with BioNTech from a small regional biotech to one of the household names in the partnership with us. So Charlotte, what's your view on BD for small molecules of the future?

Charlotte Allerton - *Pfizer Inc. - Senior VP & Head of Medicine Design*

So Mikael was asked earlier, what's one of the transformations we've made under his leadership? And I think grounding ourselves in a deep understanding of what brings about transformational medicines and important pathways to modulate has been a key part of that and then expanding our modality base to make sure that we're well placed to bring forward therapeutics against those targets that are truly transformational to the disease. So leading with the biology and then making sure we put the right toolbox in place. And so in our small molecule therapeutic area, one of the places that we've been focusing is protein degraders, as an example of where we can do that well.

We have our collaboration with Arvinas, and also enhancing our efficiency and our speed with which we can bring forward therapeutics and that's leading to a lot of investments in AI and machine learning. We obviously have the advantage of having been working in small molecule drug design for a long time, having big databases of data, which we can really leverage to our advantage. So those are two areas that I would select.

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

Do you have any quick comment, Lisa?

Annaliesa Anderson - *Pfizer Inc. - Senior VP & Chief Scientific Officer, Bacterial Vaccines & Hospital*

I do. Thank you, Mikael. And I think going back to how under your leadership, we've really focused the research and the development organization. So we've gone from 13 areas to 6 highly targeted therapeutic areas. And so it makes it much easier to be able to identify within those areas where do we have gaps, where can we maybe bring things in to support the late-stage programs. And specifically, in the anti-infective space, this year, we bought in Amplyx, which then gave us a broad spectrum antifungal that we could move into late-stage development.

From a vaccines perspective, Mikael mentioned that we partnered with BioNTech. We also have a similar partnership with Valneva, a company that's based in France and Austria to bring forward the Lyme vaccine. So we do have very strong capability internally. And so we're really looking to see how we can supplement that to really broaden what we can do within our focused target areas.

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

Great. Okay. So let's shift the discussion to talk about first Paxlovid which is your oral antiviral. So the first readouts from Pfizer and Merck were both in high-risk unvaccinated patients. What it means to be unvaccinated, that's clear. But my question is, how is high-risk defined? Could that just merely have been that they weren't vaccinated? Or did they have to have other medical conditions? And really, what was the baseline characteristics of these patients? How many medical conditions did they have that made them high-risk? Because I think the inclusion criteria was something like one or more to say. So I'm just trying to understand that baseline demographics of that first readout.

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

Lisa, do you want to start?

Annaliesa Anderson - *Pfizer Inc. - Senior VP & Chief Scientific Officer, Bacterial Vaccines & Hospital*

Certainly, yes. So at the beginning of the pandemic, as Mikael mentioned, we worked with urgency to bring a vaccine forward that could help to stem the path of the pandemic. And then in parallel, we were working on the antiviral compound in designing the initial clinical study, we looked at where the most medical need was, and there were clearly evidence that people with different comorbidities, such as obesity, old age, hypertension and other things were at greater risk of more severe outcomes of COVID-19 disease.

And so for this first study, the EPIC-HR or high-risk study, this was a population that was selected. So patients had to have one or more of standard comorbidities that had been defined by the CDC and other groups to be enrolled in that study. We didn't include people who had been vaccinated because at the time that we were developing the study, we didn't consider that the high-risk vaccinated population was going to be a high-risk of more severe disease. We are since seeing now as immunity wanes in some populations so we are seeing some people who are having severe outcomes who have been vaccinated. But then we have our second study, which is the EPIC-SR or standard-risk study. And in that study, we have included both patients who have and who haven't been vaccinated, the patients included who have been vaccinated are all what are considered high risk. So they all have the similar comorbidities that I mentioned for the high-risk study.

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

I just wanted to add one clarification. This was a terrific description by Lisa. That the definition of patients are based on that they have mild-to-moderate symptoms and are at high-risk for hospitalization. We measure hospitalization death, and we had a stunning result of about 90% reduction in hospitalization, 100% in death, really unprecedented. So it doesn't really say whether you are vaccinated or unvaccinated in the overall description of which patients can benefit. We have left that open. We enrolled mainly unvaccinated because of getting a high hospitalization rate. But it certainly is up to regulatory agency if they would just call it high-risk patients.

And just to give an example why it's likely that you would respond if you are a high-risk patient, immunocompromised, which is a large segment, because the study contained about half that were -- had previously been exposed to COVID. So they were naturally vaccinated and they did equally well, Tim, on our Paxlovid as the vaccinated -- as the unvaccinated. So natural vaccinations through infection did equally well as unvaccinated. So I -- we have left it open to the agency to consider a broad label that could allow anyone defined as a high-risk patient to be eligible for the treatment pending approval.

And we are pleased to see that efficacy was consistent, safety, tolerability across the study. So that's why we filed with urgency. And fingers crossed, hope to see this opportunity to deliver this oral treatment very broadly. And we invested $1 billion or more in preparing for a launch, which could come very soon, pending review.

And of course, next year, we have had a goal of 50 million treatment courses. Now like we did with a vaccine, we anticipate to substantially exceed that with a vaccine we said 1 billion doses when we made 3. So I think you will see the same that, pending approval, we'll be able to provide much more than originally stated. But for now, we have said 50 million treatment courses and a substantial amount in first part of '22.

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

Another question, Merck with molnupiravir they -- that product will be put up for an FDA advisory panel in late November. What should we expect on Paxlovid, you guys likely to be put up before a panel?

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

Charlotte, do you want to comment on the molecule and the type of profile we've seen and where do you think it's necessary need to be an advisory committee?

Charlotte Allerton - *Pfizer Inc. - Senior VP & Head of Medicine Design*

So we're very confident in the profile of small molecule. I think everybody has seen the clinical data that we shared in the high-risk population showing that the patients who are treated within 5 days of symptom onset, it saved 9 out of 10 hospitalizations, and we saw 0 deaths on placebo.

We're also very encouraged by our safety profile. We saw less serious adverse events and discontinuations on study drug than we did on placebo in line with the great efficacy that we saw. And it's also underpinned by a robust preclinical safety package, including a clean genetic toxicology package. So we are excited to have submitted for Emergency Use Authorization, and we look forward to hearing back from the agency regarding whether they see us as needing an advisory committee or not.

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

Yes. And just to add to that, we know the agency already started to review our file. Certainly, from our point, we are prepared for an advisory committee, but it seems like our safety, tolerability profile is more similar, not identical, but more similar to the antibodies that did not need a safety review with the advisory committee while polymerase inhibitor as a drug class are often more scrutinized given that enzyme is more similar to the enzymes that are involved in controlling the human genome and to make sure you don't get any risk from mutagenicity. In contrast, the viral protease, the 3CL protease is uniquely as a viral existing enzyme, we know close to homologous so that's why we don't think that there is at all the same type of risk for these drugs. And as anticipated, the tolerability profile was very good.

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

Yes. Okay. So a big question here, and you've touched on this partly as how these drugs will work in vaccinated patients. We talked about showing efficacy if I just heard you right, in patients that had disease induced immunity, albeit they were high-risk, but they still showed sounds like an equal benefit rephrasing what you said. So with the next trial coming up, being the EPIC-SR or standard-risk trial, that will have both vaccinated and unvaccinated patients. Are you guessing that the magnitude of the benefit in EPIC-SR is going to be really compelling and maybe just as high as the EPIC-HR, it seems like it would almost have to be lower.

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

Lisa, you want to start?

Annaliesa Anderson - *Pfizer Inc. - Senior VP & Chief Scientific Officer, Bacterial Vaccines & Hospital*

Yes, certainly, I can make a start. So the study where we saw the efficacy that read out 2 weeks ago, the high-risk patient population study. This one, the endpoints were hospitalization and death. And the patients who enrolled in this study were at high-risk of reaching those endpoints. With the SR study or the standard-risk study, the patients there are not at such high risk of hospitalization and death. And so we actually have different endpoints. We're looking to see how the disease progresses, the patients are recording information as to how their disease progresses. So I don't think one can compare between the 2 and say, "Will we be as successful or not" because the endpoints are different.

What we do know is from our reactogenicity profile or the adverse events that we monitor during the study that we saw most events in the patients on the placebo group for a high-risk study, which was indicative of them having more severe symptoms of disease. And so there's a good chance

that this may also pass through to our standard-risk study, and we should have a good sign of efficacy. As far as the study's progression is going, we're hoping to be able to read out in the near future. And so we'll be able to answer the question with some real data.

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

That's terrific. And we have recorded a very potent effect on viral load, very high, even the effect is like a logarithmic reduction if you have high virus load. But of course, many standard-risk patients may have lower viral load as they don't have the comorbidities. So a reduction that's prominent in those patients, Tim, will likely, if intervened early, have a very beneficial effect on them. So at least I believe the effect -- it's a different endpoint, as Lisa spoke to. But personally I have no doubt that it's reasonable to assume that the product will show a really compelling profile in that study too.

As always, we need to let the study readout, but also take note we're the only company running a study for that at the moment. So it's really important for public health for those that are at standard-risk that want to have a treatment, this would end in any only near-term opportunity for them, antibodies are not there and antibody not probably here, polymerase drug is not running there either.

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

And then the vaccinated population that you enrolled, it was a little unique because these were patients that had medical conditions who were vaccinated. And so when you add those together, you guys seem to have standard-risk. Are you guys likely to run any other trials in completely normal health patients that have been vaccinated? Or will you get enough of your answers out of the like SR such that it won't be necessary?

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

We always try to make sure we provide a science-driven product profile. So right now, I think we have the largest antiviral program with high-risk, standard-risk and prophylaxis. We will continue as we conclude that program to make sure we provide good guidelines for any patients that may benefit from the drug. So by no means, this means that we shouldn't generate more data. I think the label that could come out basically doesn't need to have any restriction, Tim.

If you show dramatic effect on viral load, tolerability and safety across many populations, it certainly is up to regulators to project that in a much broader population. As always, we may do specialized studies in patients that have severe kidney or liver impairment, where special dose advice may be possible. There may be certain patient groups that are highly susceptible, newly transplantation, et cetera, that we may want to supplement. But right now, I think the study program covers, we said potential more than 150 million people that could be a target for using a product of this profile, assuming we continue to extend the very promising high-risk data into the other populations.

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

Okay. Just a couple of final questions on this, and then we should shift to different areas. Any utility of this drug in non-COVID settings and other viral diseases?

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

Charlotte on the profile across coronaviruses, what would you say? And could you see additional opportunities for having this drug available?

Charlotte Allerton - *Pfizer Inc. - Senior VP & Head of Medicine Design*

So one of the pieces, actually, Mikael already mentioned that we really liked about the main protease target is the ability to get specificity for that target over human proteases, which leads into the safety profile. But the active sites in the main protease, the sites could be 2 main protease is actually quite well conserved in other coronaviruses. So we do know that our molecule has antiviral activity in vitro for MERS and for SARS which gives us reason to believe that we hope that it could have potential as a broad coronavirus therapeutic, and we're doing additional follow-up work on that.

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

The other -- that was terrific. The other area is, as I spoke to this as a supplement to the vaccine, right now, COMIRNATY does really well across all viral SARS-CoV-2 mutants. And of course, we continue to monitor the convergence in mutations that may indicate immune evasion versus increased transmission.

And some days, likely there are going to be a mutant virus that will not be as efficiently controlled by the current vaccines. The 2 mRNA players, we and the Moderna have, of course, an opportunity to act very fast, but it's still maybe 100 days to change the production and then come out to 1 billion of doses.

So during such a period, you may see many more breakthrough infections. And you may see unvaccinated again hit by new strain. That could, of course, be an opportunity for use of stockpiling and be able to immediately clamp down on new mutations or new coronaviruses in the population.

So that's an opportunity where I think we are able to profoundly improve pre-pandemic preparedness among coronaviruses, including SARS-CoV-2 variants of the future before sufficient vaccine is available.

And we are pleased to see that so far, it looks like this is a drug that could have a very long shelf life, and we'll continue to expand stability tests that could allow pending guidelines to have this drug, whether in a personal medicine cabinet, if you're a person at risk or in pharmacies, et cetera. So beyond the 150 million patient pool we target annually, this could be another very sizable opportunity for many countries.

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

Last question on this topic. And it's really -- it's a commercial question, but I'm sure you've thought about it. What does this mean to vaccination rates? So as a seller of the vaccine and as a seller of oral antiviral, do you think the availability of this is going to actually cut down on vaccination rates, when I told someone who was not in health care field about this oral product and the very first thing on their mouth was, "Okay, now I don't need to go get a vaccine." So what's going to happen to vaccination?

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

Tim, as I mentioned, the mathematical modeling of having a potent pill and a potent vaccine, both well tolerated shows that in synergy complementary. I think we have seen now that those that are eager to vaccinate or are welcoming as a general approach prophylaxis, they will continue to vaccinate likely on an annual basis. Some groups are more vulnerable, and it will be hard to know exactly when they should vaccinate. Is it 6, is it 12 months, should they stay with the general guidelines? Those patients will, of course, have a tremendous medical tool if they get an infection to have Paxlovid. There are families or work environment or schools to use a potential Paxlovid pending our study for prophylaxis could immediately clamp down on an outbreak.

And of course, we have then to vaccinate the refusing population. That for them, this would be a life-saving tool. So I don't really see it as impacting vaccination. If we are to manage an endemic decade or decades of this virus, we need to use both, and we will continue to say vaccination is critical, but the therapeutic can be complementary or even synergistic.

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

Okay. Great. I want to shift to mRNA vaccines and really kind of broader question with mRNA, not on the COVID vaccine. But really looking at mRNA, flu vaccine is the next opportunity for this technology. And you guys are already pursuing this in partnership with BioNTech. And Moderna is raising to come up with mRNA flu as well. So I'd like to kind of probe on this.

So the first question is, the time line for seeing data from you guys on mRNA flu, you have a quadrivalent candidate I think, already in the clinic. And then the second question is what's required for registration? I know commercially, ultimately, you need to show vaccine efficacy, but can you file just on titers? And is that something that could actually occur in 2022?

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

Well, we are eager to expand mRNA platform, the one we have with the BioNTech partnership broadly into a variety of different viral diseases, and we will reveal more about the many opportunities we see there. Flu is just one among many and several others, whether alternative vaccine or no vaccines will become part of our future pipeline.

I think the main advantage with mRNA in flu is the ability to have a consistent conformity between new vaccine and the circulating strain. As you know, current flu vaccines are anywhere between 20% to 60% in efficacy, in average 40% because the strains may shift during the season or drift maybe rather.

So certainly, we are going all-in, in this flu vaccine studies and hope to have data early next year on the modRNA platform. We actually also have interest in the self-amplified mRNA platform and have made considerable progress on that platform, which we believe can be utilizing much lower amount of mRNA and may be ideal over time when you want to construct a [pan airway] vaccine, airway virus vaccine or vaccination that embrace many different mRNAs targeting adult or pediatric needs. So that's also a platform that we expect early next year to be generating clinical data.

So keep your eyes open, and I think it will be very, very exciting 2022, not just with our mRNA and flu and self-amplified many other areas, including I think Liesa mentioned Lyme vaccine, we will have data. Of course, the pediatric vaccine will come next year. C. difficile will come.

So it's a whole flurry of vaccines using a variety of different technologies. What's unique with Pfizer is that we can choose between conjugate vaccines, where we are, I would say, the most experience in the world. We do very sophisticated protein engineered C. difficile is an amazing story there.

And we do protein in certain confirmations to be naive when it comes to the virus prefusion stage such as RSV, and then, of course, mRNA, and we have also tested adenovirus that we think are more fit for cancer vaccines. So you will hear a lot, including flu.

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

And I just bring you back to the question of what's required to file for mRNA flu? Is it just titers?

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

Oh, that question, well, it's really up to regulatory authorities to look at your data. I think you could certainly technically file for that you have some advantage in your immune surrogate endpoints versus standard of care, assuming you have tolerability and safety that's comparable. I think ACIP and CDC probably will be much more compelled once you have that plus efficacy data. I think the uptake will be much more significant. So while it's a possibility that we never exclude, I think the most powerful approach like we have done in COVID here for many different age groups even to come with immune endpoint and vaccine efficacy.

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

And then the timeline could that actually -- in an absolute best-case scenario could that be fileable in 2022? It seems like that's probably a stretch in our assessment is probably more like 2023.

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

'22 will be a very busy year. With Lightspeed, I have learned working now with Albert and Liesa and Charlotte, nothing is impossible in the hands of Pfizer. So that could be magnified in '22, not just a flu that you asked about. I won't promise a flu filing since it's a relatively early project, but we always make the unimaginable become imaginable. We are, of course, on track for filing potential peds PCV20. I think we'll file for RSV, and we'll see what happens with flu.

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

And then last mRNA flu question. Reactogenicity of an mRNA flu, do you think it would be acceptable enough in a flu setting, such that it's not a commercial impediment?

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

When we chose the dose of COMIRNATY, we did based on decades of experience of based on our coworkers Kathrin Jansen and others, Bill Gruber, very thorough work in the balancing between local reactogenicity in the arm, and a systemic reactogenicity fever, headache, chills, and risk for any long-term safety issues imbalance with the efficacy.

And I would say we were very pleased with the 30-microgram dose that we have selected. And we think that tolerability profile is compatible with any existing marketed vaccine, including flu. And you have seen worldwide that including publication in JAMA that show that this is the best tolerated mRNA vaccine.

And worldwide, you have seen that I think our thorough work on tolerability also translates into higher safety. I was just catching up last week when I was in Europe, Sweden, there are a number of countries that report preference or only use of COMIRNATY, whether below 30 or below 40. Denmark, Sweden, Finland, Norway, France, Germany, U.K., Japan. So I think that's based on the profile of selecting a dose that is very compatible. So I think us or any other flu maker that using mRNA will need to stay with that type of tolerability profile. When you go above that, I think you are not competitive beyond maybe first period of a pandemic.

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

Last question because we're out of time here. It's on the JAK space. And is there a decision to essentially divest your TYK2 inhibitor and your JAK TYK combo? So Pfizer has talked about having a broad JAK portfolio, that kind of came as a surprise decision, how do I interpret that? Do I interpret that, that Pfizer thinks that a TYK2 is just another JAK?

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

I would say we should interpret this, I spoke about our success rates being twice the industry. And our Phase 2 success rates are also twice the industry. So the great job that Charlotte, Liesa and our colleagues do is generating so many exciting proof of concepts. And even with an R&D budget that's projecting in the range of $10.5 billion, you have to make your strategic choices on what you want to develop.

And we actually have benefited a lot from also having partnerships. So right now, in the JAK space, we have gotten approval now of abrocitinib in atopic dermatitis, as you know, in Europe, Japan, positive opinion -- sorry, in U.K., Japan, positive opinion in Europe. Regulatory discussions ongoing now in U.S.

Ritlecitinib, we are planning to file in alopecia. And I'll ask later Charlotte just to say a few words. I think it's a really unique molecule. We want to invest in more indication behind this. Brepocitinib that we co-creating a new company with another investor group that we will share the name of a very experienced group that we have worked with before. We retain certain commercialization rights. We see it just an opportunity to partner. It's a great drug. It's the only TYK2/JAK1. It has very strong data in rheumatology and great data in topical atopic dermatitis treatment.

It's just we have to make choices how to use our efforts most wisely and welcome others to co-invest. It's been successful before. We've spun out Cerevel neuroscience company with a good valuation. We are a significant owner of that. We did the same with Allogene et cetera. So Tim, it's just a strategy to be able to have participation in more things, whether we partner with someone else's drugs or sometimes lets others be part of our drug. Charlotte, could you just conclude a bit around why we're doubling down on ritlecitinib?

Charlotte Allerton - *Pfizer Inc. - Senior VP & Head of Medicine Design*

We see ritlecitinib as a very different profile to others in JAK class. It's got a different pharmacology and selectivity profile. It's got good potency against JAK3 in the TYK family and a different selectivity profile that we expect to turn into a differentiated efficacy and safety.

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

Great. Okay. I'm going to wrap the call up. I want to thank Mikael, Annaliesa and Charlotte, and congrats again for all the work you guys have been doing in COVID. Thank you for the discussion today. It's been very helpful. And we look forward to kind of watching all the future developments as we move into 2022. So thank you, and have a nice day.

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

Thank you.
