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EDITED TRANSCRIPT

PFE.N - Pfizer Pflash: A Spotlight On Clostridioides difficile (C. diff) Vaccine Development

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OVERVIEW:

Company Summary

REFINITIV

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PRESENTATION

Operator

Good day, everyone, and welcome to Pfizer Pflash: A Spotlight on Clostridioides difficile Vaccine Development. Today's call is being recorded.

At this time, I would like to turn the call over to Francesca DeMartino, Chief Investment Relations Officer and Senior Vice President. Please go ahead, ma'am.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Thank you, and good morning, everyone. I'm Francesca DeMartino, Chief Investor Relations Officer. On behalf of the Pfizer team, thank you for joining us for our second Pfizer Pflash webcast. Today's call will be recorded and will be available for replay on our IR website at pfizer.com.

As a reminder, our Pfizer Pflash series is intended to serve as an educational deep dive into our pipeline, products, and leadership. Each call will spotlight a specific product, therapeutic area, or growth initiative and give you an opportunity to hear from and interact with our business leaders.

Today's session will begin with a short conversation followed by a live Q&A. As a reminder, this call is intended only for the investment community, including our sell-side analysts and institutional investors. If you are unable to join the entirety of the event, you can find the replay available on our IR website.

I want to note that on today's call, we will be making forward-looking statements. I encourage you to view slide 2 in our presentation and the disclosures in our SEC filings, which are all available on our IR website at pfizer.com.

Forward-looking statements on the call are subject to substantial risks and uncertainties, speak only as of the call's original date. And we undertake no obligation to update or revise any of the statements. With that, let's get started.

As you know, vaccines are a key area of focus for Pfizer, with a portfolio that seeks to address both viral and bacterial pathogens. Today, we will provide insight into a program that we believe has the potential to be a key driver of growth for our bacterial vaccine franchise.

It is a privilege to have you all with us as we delve into C. diff. Before we move to the main discussion, let me take a moment to introduce our speakers: Annaliesa Anderson, Senior Vice President and Head of Vaccine Research and Development; Alejandra Gurtman, Senior Vice President and Head of Vaccine Clinical Research and Development; and Julie Skinner, Vice President, Bacterial Vaccines and Technology.

Annaliesa, Alejandra, and Julie are central to our innovative work focusing on vaccines from early discovery through licensure. Annaliesa, Alejandra, and Julie, welcome and thank you so much for joining today. Can you please start by introducing yourself and giving a brief overview of your current role and experience?

Annaliesa Anderson - *Pfizer Inc - SVP, Head, Vaccine Research & Development*

Thank you, Francesca. I'm thrilled to be here today with my colleagues, Alejandra and Julie, to talk about the impact of C. difficile infections and our progress in developing a potential vaccine.

In my role as Pfizer's Senior Vice President and Head of Vaccines Research and Development, I'm responsible for leading the end-to-end research and development for all infectious disease vaccine programs in Pfizer's portfolio.

During my time at Pfizer, I've helped to lead the strategy and execution of multiple programs leading to the licensure of numerous vaccines and therapeutics, including the 13-valent pneumococcal conjugate vaccine, PREVNAR 13; the first-ever US licensed vaccine against invasive meningococcal disease caused by serogroup B, TRUMENBA; strain change and next-generation research and development for the first-ever licensed mRNA-based vaccine, COMIRNATY; the first-in-class antiviral, PAXLOVID; and the most complex vaccine ever marketed for both adults and pediatrics, PREVNAR 20; and the first-ever bivalent pre-fusion F RSV vaccine, ABRYSVO, for use in both older adults and pregnant people for the protection of newborns against RSV disease.

And with that, I'll turn it over to Alejandra.

Alejandra Gurtman - *Pfizer Inc - SVP, Head, Vaccine Clinical Research and Development*

Thank you, Lisa. I'm Alejandra Gurtman, Senior Vice President of Pfizer, Vaccine Clinical Research and Development. I am responsible for early- and late-stage clinical development of Pfizer's vaccines pipelines.

I had to lead the RSV vaccine program, resulting in approvals for adult and maternal indications in the US and Europe; and Pfizer's COVID-19 vaccine program supporting development and strategy and advancing the adolescent and pediatric programs for emergency use authorization. Before this role, I was the global clinical lead for the Staphylococcus aureus vaccine and also led the PREVNAR 13 pediatric program.

I supported the PREVNAR 13 program and studies in high-risk, immunocompromised populations. I am trained in medicine at the University of Buenos Aires and completed my post-doctoral training at Mount Sinai School of Medicine in New York City, where I also served as an Associate Professor and the Founder of the travel medicine program before coming to Pfizer nearly 20 years ago.

And next, we will hear from Julie.

Julie Skinner - *Pfizer Inc - VP, Bacterial Vaccines & Technology*

Thank you, Alejandra. In my role as Pfizer's Vice President of Bacterial Vaccines and Technology, I am responsible for leading Pfizer's portfolio of bacterial vaccines and early discovery through development. This includes leadership and oversight of our C. difficile vaccine program.

Prior to joining Pfizer, I completed post-doctoral training at the CDC before moving to vaccine development with roles at the biotechnology company Intercell followed by 15 years at Merck leading their bacterial vaccine programs, including work leading to the approvals of the pneumococcal vaccines, VAXNEUVANCE and CAPVAXIVE. I am thrilled to have joined Pfizer and have the opportunity to lead our bacterial vaccine programs.

With that. I will bring it back to Francesca.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Thank you all for your introductions. Liesa, can you briefly speak to Pfizer's overall strategy in developing bacterial vaccines?

Annaliesa Anderson - *Pfizer Inc - SVP, Head, Vaccine Research & Development*

Yes, of course. As we all know, vaccines are one of the greatest public health advancements of all time, resulting in the control, elimination, or near elimination of numerous infectious diseases that were once pervasive and often fatal.

Today, more people are benefiting from safe and efficacious vaccines to help prevent infectious diseases than ever before. And vaccines provide an essential health benefit at all ages, from maternal and infant populations to seniors. However, our work is not done given the many infectious diseases remaining with high unmet medical need that cause a significant burden to society.

At Pfizer, we're focused on three pillars to target emerging health threats and drive potential for long term growth. Speaking to only our bacterial programs, we are enhancing our core pneumococcal franchise. Our fourth-generation pneumococcal conjugate vaccine or PCV candidate is in Phase 2 for adults and pediatrics after demonstrating encouraging immunogenicity and an acceptable safety and tolerability profile in first in-human Phase 1 study.

As a reminder, our fourth-generation PCV candidate covers 25 serotypes, including potentially improved immunogenicity for serotype three, which is one of the largest remaining contributors of disease. Our second pillar is focused on executing on our mid- to late-stage pipeline portfolio. Today, we will spotlight C. difficile.

Lastly, we're focused on growing our pipeline. We have some very exciting preclinical programs targeting both bacterial and viral pathogens, and I look forward to providing an update on these in the future.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Great. Thank you. So diving in, could you please give us a little background on C. diff and why it would be so important to have a vaccine against this disease?

Annaliesa Anderson - *Pfizer Inc - SVP, Head, Vaccine Research & Development*

Of course. Clostridioides difficile is a gram-positive, aerobic, spore-forming bacillus. We also call it C. diff, and it causes -- it produces two virulent toxins that are responsible for the illness known as Clostridioides difficile infection or C. difficile.

Lastly, we're focused on growing our pipeline. We have some very exciting pre-clinical programs targeting both bacterial and viral pathogens, and I look forward to providing an update on these in the future.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Great. Thank you. So diving in, could you please give us a little background on C. diff and why it would be so important to have a vaccine against this disease?

Annaliesa Anderson - *Pfizer Inc - SVP, Head, Vaccine Research & Development*

Of course. Clostridioides difficile is a gram-positive, aerobic, spore-forming bacillus. We also call it C. diff, and it causes -- it produces two virulent toxins that are responsible for the illness known as Clostridioides difficile infection, or CDI for short. These toxins are called toxin A and toxin B.

C. diff colonization is often enabled by disruption in the normal gut flora due to factors such as antibiotic use, age, and recent hospital stays being additional common risk factors for the disease. We have a slide here that provides a visual of how CDI happens.

If C. diff colonizes the gut and releases its toxins, they can cause severe damage. CDI causes inflammation in the bowel, and manifestations range from asymptomatic or mild to more serious complications, such as severe diarrhea, toxic mega colon, intestinal perforation, and other life-threatening complications.

Unfortunately, individuals contracting an initial case of C. difficile are frequently susceptible to recurrent infection, with the CDC estimating that approximately one in six will be recurrent in the subsequent two to eight weeks.

In recent years, C. diff has emerged as a major cause of infectious diarrhea. In fact, it is estimated that there are nearly 500,000 infections a year in the US.

1 in 11 people over the age of 65 is diagnosed with healthcare-associated CD will die within one month. In 2019, C. difficile was categorized by the US Centers for Disease Control and Prevention as an urgent public health threat, its highest infectious disease threat designation.

Patients with C. diff requiring medical intervention are typically treated with antibiotics such as vancomycin, fidaxomicin. Though, in some instances, surgical or fecal microbiota transplantation techniques may be employed.

In addition, orally or rectally administered fecal microbiota products are approved to prevent recurrence of CDI, though not for protecting against a first infection. Treating and managing patients with CDI places a substantial burden on the healthcare system, with prior peer-reviewed publications estimating the annual US healthcare cost at approximately $5 billion to $6 billion.

Given the current landscape, there is a pressing unmet medical need for a vaccine that can prevent primary or recurrent CDI to reduce C. diff-associated healthcare burden. With our development program, we aim to address this need and deliver the first such vaccine to providers and patients.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Alejandra, a question for you. Who would be the target population for a C. diff vaccine?

Alejandra Gurtman - *Pfizer Inc - SVP, Head, Vaccine Clinical Research and Development*

Well, CDI incidence increases dramatically after the age of 50. And a significant proportion of the burden of disease is in individuals aged 65 and older.

Moreover, prolonged exposure to healthcare settings can increase the risk of CDI, and individuals are 7 to 10 times more likely to get CDI while they are on antibiotics and during the months following. Our C. diff vaccine candidate trials have focused on adults that are 50 years of age or older.

While we cannot speculate on decisions of regulatory agencies or recommending bodies, potential populations could include those who are 50 years of age or older. As we get older, our risk factors increase. And so it could potentially be a good strategy to be vaccinated before the risk period starts when it may be too late to get a vaccine.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Pfizer had a first-generation C. diff vaccine candidate that advanced through Phase 3 testing. Alejandra, can you give us a little background on that?

Alejandra Gurtman - *Pfizer Inc - SVP, Head, Vaccine Clinical Research and Development*

Oh, happy to. Our first-generation candidate is a genetically and chemically detoxified investigational vaccine formulated with modified C. diff toxin A and B antigens. It received FDA fast track designation in 2014. Phase 1 and 2 data indicated that three doses of this vaccine candidate were well tolerated and elicited robust, neutralizing antibody activity against toxins A and B for up to four years in adults aged 50 to 85.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Thank you. And can you tell us about the Phase 3 trial?

Alejandra Gurtman - *Pfizer Inc - SVP, Head, Vaccine Clinical Research and Development*

Of course. Based on the Phase 1 and 2 data I just mentioned, we then evaluated the safety and efficacy of our first-generation C. diff vaccine candidate in the Phase 3 CLOVER trial, an overview of which you can see on the slide.

CLOVER was an important innovative study. The trial began in 2017 and spanned the height of the COVID-19 pandemic, with top-line data being announced in the first quarter of 2022. I have a schematic here that summarizes the trial.

We'll randomize more than 17,000 adults aged 50 older who are at increased risk of C. diff infection. Participants received three doses of investigational vaccine or placebo over a six-month period.

The first and second primary endpoint of the trial track the first C. diff infection episode that took place 14 days or more days after the participant had taken the third dose or the second dose of the vaccine, respectively. Given the innovative nature of the global study, we work with regulators such as the FDA and the EMA as well as key infectious diseases experts to align on a clear definition of the primary C. diff case.

In the middle of the slide, I am showing you the trial uses a single rigid criteria that demanded specific clinical symptoms and left confirmation that the participant was positive for C. diff toxin. Notably, this definition did not distinguish between mild, self-limiting cases and more severe cases that require medical attention.

Data from the trial showed that the primary endpoint was not met as the lower bound of the vaccine efficacy, 96.4 confidence interval, fell below the pre-specified cut of 20%. However, when looking at secondary endpoints and additional analysis, we saw encouraging signals of efficacy that highlighted our candidate's potential to lower C. diff-associated healthcare burden.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Can you tell us more about the secondary and additional analysis and how they give you confidence in the CD program going forward?

Alejandra Gurtman - *Pfizer Inc - SVP, Head, Vaccine Clinical Research and Development*

Sure. These analyses showed the vaccination with our first-generation candidate led to reductions in medically attended CDI and the duration of infection. Starting with the table on the left, the first row shows data on the primary end point, which I just mentioned was not met.

However, looking at the second and third rows, you will notice that none of the C. diff infections reported in vaccinated participants in the relevant per-protocol population require medical attention or antibiotic intervention. This is indicative of 100% vaccine efficacy for these posthoc end points.

And looking on the right, you can see that the median C. diff infection duration dropped from four days with the placebo to only one day with vaccination. Taken together, these results suggests our first-generation vaccine candidate may have alleviated CDI severity from moderate to severe cases to mild self-limiting disease.

Furthermore, by showing 100% efficacy against medically attended CDI, they suggest that a vaccine, including our toxin A and toxin B antigens, may have the potential to play an important role in protecting at risk patients and reducing the healthcare burden of this potentially fatal disease.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Thank you, Alejandra. Julie, following the CLOVER results, what were the next steps for the program? And what is its current status?

Julie Skinner - *Pfizer Inc - VP, Bacterial Vaccines & Technology*

Looking at the totality of CLOVER data, we came away from the trial encouraged. Though we were, of course, disappointed to miss the primary endpoint, we saw a clear signal suggesting our vaccine candidate may protect against medically attended and more severe forms of infection, which is a critical piece for reducing disease burden.

And as the CLOVER study was ongoing, we had actually already began working on an updated C. diff vaccine formulation that could simplify the dosing schedule. Specifically, we wanted to develop a formulation that would induce a robust and durable immune response with a two-dose regimen. Compared to the three-dose regimen evaluated in CLOVER, we believe a two-dose vaccine could improve completion of the dosing series and enable us to help protect more patients.

So following the CLOVER readout, we continue to focus on developing this updated formulation and designing a clinical program to demonstrate our candidate's ability to meaningfully reduce C. diff disease burden. A key early step in this process was assessing the potential of our updated formulation to induce immune responses against toxin A and toxin B similar to or better than that displayed by our first-generation candidates, but faster and with less doses.

This would provide an early indication of the new formulation's potential to protect against medically attended and/or severe C. diff infection. To pursue our objectives, we advanced three updated formulations of our vaccine candidate into Phase -- into a Phase 1/2 trial in the first half of 2023.

Based on safety and immunogenicity data from the Phase 1 portion of the study, we selected our preferred formulation to bring into Phase 2. The Phase 2 portion of the study remains ongoing and is exploring multiple dosing schedules. We expect data from the trial in 2025. And pending positive results and alignment on a regulatory path of agencies, we would aim to potentially start a Phase 3 trial in late 2025.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Thanks, Julie. Alejandra, one final question for you. If we get the results we're hoping for in a Phase 2, what would be -- what would the planned Phase 3 trial look like?

Alejandra Gurtman - *Pfizer Inc - SVP, Head, Vaccine Clinical Research and Development*

It's too early to speak to the specifics of a potential Phase 3 trial design, but this would be informed by both the Phase 2 findings as well as regulatory interactions.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Okay, thank you. And thank you all for a great discussion. So in summary, our C. diff program targets an urgent and serious public health threat with no vaccines approved to protect against C. diff infection. This highlights a pressing unmet need, with 1 in 11 people over the age of 65 diagnosed with healthcare-associated CDI passing away within one month.

With our first-generation vaccine candidate, we saw reductions in disease duration and medically attended cases in Phase 3 demonstrating its potential to reduce C. diff-associated healthcare burden. We are now building on these prior results by advancing an updated formulation of our investigational vaccine that has the potential to be administered as a two-dose regimen.

This updated formulation displayed encouraging safety and immunogenicity in Phase 1 and is now advancing through Phase -- through a Phase 2 proof-of-concept trial. Pending positive Phase 2 data and alignment on a regulatory path forward with agencies, we would aim to potentially start a Phase 3 trial in late 2025.

QUESTIONS AND ANSWERS

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

We'll now begin the Q&A session with Liesa, Alejandra, and Julie. As a reminder, our Pfizer Pflash series is designed as an educational deep dive into our pipeline programs. I'll therefore kindly ask participants to keep questions focused on the C. diff vaccine development program discussed today and to avoid those that would require us to provide forward-looking financial projections.

While we're happy to clarify any information shared during the presentation, we will not be offering estimates beyond what has already been communicated. We will do our best to provide as much clarity as possible within these guidelines. And thank you for your understanding.

With that, we're ready to take the first question. Operator, if you could please assemble the queue.

Operator

(Operator Instructions) Evan Seigerman, BMO Capital Markets.

Evan Seigerman - *BMO Capital Markets - Analyst*

Okay. Thank you so much for taking my question. Thanks for this presentation. So as you think about the unmet need in C. diff, I know there's clearly -- it's clearly a big issue for seniors. I guess, how do you envision this product actually -- how do you say this? How do you envision this product being used in the real world?

Is it for a specific type of at-risk senior? Is it for a broad population? And secondarily to that, what would the potential uptake curve look like, knowing that -- assuming that the Phase 3 trial for this is successful? Thank you, guys.

Alejandra Gurtman - *Pfizer Inc - SVP, Head, Vaccine Clinical Research and Development*

This is Alejandra Gurtman. Thank you for the question. We obviously need to do the Phase 3 trial and expect that the vaccine will show efficacy and then be approved. And part of your question is related to how the vaccine will be recommended.

And as you know, that will be part of, in the United States, ACIP recommendations. As I mentioned before, as you get older -- as we all get older, the risk for disease increases. And especially as we go in and out of medical care and you may be exposed to antibiotics, the risk is even higher.

So ideally -- again, this would be an ACIP recommendation, a vaccine that is age based where you can get it, for example, at age 50 will hopefully be protective of those events that you may have before you are exposed to that medical care I mentioned. Did I answer your question?

Evan Seigerman - *BMO Capital Markets - Analyst*

Yeah. I guess the follow-up is -- the second part is, who would be the best candidate for this vaccine, assuming the data is successful? Is it a wide variety of patients or is it going to be more focused at those who would be higher risk? And how would that be defined?

Alejandra Gurtman - *Pfizer Inc - SVP, Head, Vaccine Clinical Research and Development*

Yeah. I would just say that commenting on recommendations is something that we, at this point, are not able to do. Obviously, this is an unmet medical need. But I will also ask Lisa if she wants to add to what I just said.

Annaliesa Anderson - *Pfizer Inc - SVP, Head, Vaccine Research & Development*

Thank you, Alejandra. So as we get older, one can't always predict when you're going to get -- be at risk of C. difficile disease. When you look at the population who gets disease, it's people who are older. It's people who have frequent contact with healthcare facilities. And it's people who have to take certain antibiotics for a period of time.

And so really, when one looks at an age-based recommendation, it means that you can vaccinate before you reach those periods of risk. And again, we don't always know when we're going to fall into those periods of risk.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Great, thanks. Thanks, Evan. Operator, we will take the next question, please.

Operator

Trung Nguyen, UBS.

Trung Nguyen - *UBS - Analyst*

Hi, guys. Thanks for the presentation. Just two from me, please. So in the intro, you noted C. diff is caused by toxin A and toxin B, which is what you're targeting with your vaccine. There's actually some strains that produce a third toxin, binary toxin, which is associated with more severe infections.

So does your vaccine generate any immunity to that? And if not, I'm wondering how common the third toxin is in some C. diff strains.

And then secondly, you noted C. diff is common in elderly patients. I'm curious, in the data that you've seen, if you're seeing any waning of efficacy as you get older. Older people may not be able to mount as much of a strong immune response to vaccines, so anything that would be helpful. Thank you.

Julie Skinner - *Pfizer Inc - VP, Bacterial Vaccines & Technology*

Sure. Thank you for the question. So as Alejandra noted, our C. diff vaccine is a toxoid-based vaccine, and it's derived from native toxins which have been modified and then activated to maintain immunogenicity. Our vaccine contains toxoid A and toxoid B. It does not contain binary toxin.

Annaliesa Anderson - *Pfizer Inc - SVP, Head, Vaccine Research & Development*

And if I can add to that, it's Annaliesa here. And so, yes, we acknowledge that binary toxin does cause some disease. But even in studies that have been done preclinically, vaccines that contain both the toxin A and the toxin B are effective at protecting against disease even in the presence of binary toxin.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Okay. Thanks, Trung. Operator, we will take the next one.

Operator

Chris Schott, JPMorgan.

Ethan Brown - *JPMorgan Chase & Co - Analyst*

Hi, this is Ethan on for Chris. Thanks for taking my questions. Just two for me. The first is, how do you think about the timeline of the potential Phase 3 trial this time around, given the CLOVER trial took around five years to be announced but was affected by COVID?

And then on the duration of the C. diff vaccine, any information you have here? It seems like this is a regimen that patients will only need to take once. Is that fair to say? Thank you.

Alejandra Gurtman - *Pfizer Inc - SVP, Head, Vaccine Clinical Research and Development*

Yeah. So it's Alejandra here again. Thank you for the question. So the timing of the study, as it was alluded, we're hoping to start the study in 2025.

When you refer to CLOVER, most of the CLOVER, as I mentioned, study was implemented and executed during the pandemic. And as you might remember, during the pandemic, medical care really changed, right? So surgeries were -- elective surgeries were canceled. Many procedures and, actually, medical visits were postponed and were done through telehealth.

And therefore, the incidence of disease probably went down based on the fact that patients didn't have the exposure that you will need of what we're expecting to have during the study. So by the time that we conduct the next Phase 3 study, hopefully, we will not be in a pandemic.

And this will be, again, a case accrual design, which means that you need to accumulate sufficient cases to be able to then declare efficacy. We will execute the study, and we will select the right institutions and networks to be able to do the study.

And I cannot tell you the timing, but we want to have this vaccine as early as possible. So we will be very diligent on how we design and who we bring into that.

In terms of duration of protection, which I think was your second question, for the -- one of the good things about the CLOVER study, among many of them, is that we were clearly able to show that the vaccine protects during at least four years, right? So we expect that the new vaccine will be -- will have a duration of protection as such.

And even when you design a Phase 3 and you declare your efficacy, we will potentially be able to follow, patients for longer to assess the duration. In the current Phase 1 and 2 studies, actually, we have duration of immune response for many years to start -- to see again. Hopefully, the vaccine actually induces antibodies that stay there for some time to be able to protect. So if I answer your question -- yes?

Annaliesa Anderson - *Pfizer Inc - SVP, Head, Vaccine Research & Development*

So if I could just interrupt -- sorry. So just to clarify, with the current Phase 1/2 studies, we will have the data by the time of the potential license. So we don't have the data yet. Thank you.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Okay. Thanks, Ethan. Operator, we'll take the next one.

Operator

Vamil Divan, Guggenheim Securities.

Vamil Divan - *Guggenheim Securities LLC - Analyst*

Great. Thanks for hosting us, for taking questions. So couple of questions, if I could. So one, you shared your Phase 2 data over the prior vaccine Phase 3 data. And now, you're mentioning you might be able to go to a two-dose regimen. Can you just share a little bit more on what you've seen in terms of immunogenicity data that gives you comfort that this could be potentially a two-dose regimen?

And then my other question is maybe a broader question. This may not be fully accurate, but I feel like there's been a number of other companies that have also worked on C. diff vaccines previously that have not been successful. So appreciate reviewing what Pfizer has done, but maybe you can just provide some broader perspective on the broader attempts that have been made here and what have been some of the challenges and why things might turn out differently this time?

Julie Skinner - *Pfizer Inc - VP, Bacterial Vaccines & Technology*

Sure. Thank you for your question. So regarding the two-dose regimen that we're looking at, we do have an ongoing Phase 2 trial looking at dosing. And as part of the formulation of our next-generation vaccine candidate, we have evaluated adjuvants.

And we do believe that adjuvants can increase the strength or magnitude of the immune response to the vaccine. As such, if the immune response is stronger, the number of vaccinations may be able to be reduced.

So if the adjuvant selected for use with our next-generation C. diff vaccine formulation proves to induce higher antibody responses to our vaccine antigens, there may be potential to reduce the number of vaccinations while still achieving optimal and impactful immune responses. And for the second part of your question, I'm going to turn to Annaliesa Anderson.

Annaliesa Anderson - *Pfizer Inc - SVP, Head, Vaccine Research & Development*

Thank you, Julie. So you appreciate we can't really comment on other people's studies and other people's programs. What we can say is in the Phase 3 study that we conducted, as Alejandra explained, in those key secondary and investigational analysis, we were able to see very high efficacy, especially against the medically attended disease that clearly show this vaccine can have a strong clinical benefit.

And we're really excited to be able to move forward with this vaccine with the new formulation to not only, yes, repeat that efficacy, but also to have a more optimized dosing schedule.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Thanks, Vamil. Operator, we'll take the next question.

Operator

Geoff Meacham, Citibank.

Geoff Meacham - *Citi - Analyst*

Hey, guys. Thanks for hosting this. I really appreciate it. Just have a couple of quick ones.

The first one -- I know it's hard to assess, but just given what could be newer regulatory attitudes towards vaccines and development, what's your guys' view of whether you'll need a bigger safety database or, for example, longer follow up versus what you normally would design, thinking just of the Phase 3 trial?

And then on C. diff, I think when you look historically, you see outbreaks and at risk populations like the elderly that really drive the infection rates. Yeah. How does Pfizer maybe raise the bar for awareness to justify this being part of a broader vaccine regimen? Thank you very much.

Alejandra Gurtman - *Pfizer Inc - SVP, Head, Vaccine Clinical Research and Development*

Well, thank you for your question. It's S Alejandra here. I may start and then ask my colleagues to add more. So I think that your first question was about regulatory attitude.

We are engaging with regulatory authorities in the same way that we have done before. We expect that the required safety database that you ask would be similar to what we have done before. For many vaccines, the required database is about 3,000 exposed participants. The study will be larger than that, so we will be able to really have a database that will support that the vaccine is safe and well tolerated.

I think that your second part, your second question, was about a longer follow up. And as I alluded, this will be a case accrual study design. And as I mentioned as well, the study design, as I also share, is a little bit too early to share at this point.

But we will -- we are aware of the of the need for this vaccine to have a longer follow up. And so we will -- we potentially will introduce that as well to follow patients for longer periods of time. You mentioned outbreaks, I think, and I was wondering if you were referring to -- maybe you can clarify if the outbreaks that you're talking about, the ones that you may see in hospitals or nursing homes.

Geoff Meacham - *Citi - Analyst*

Yeah, I think that's the right -- when you follow the epidemiology, that is concentrated in those settings.

Alejandra Gurtman - *Pfizer Inc - SVP, Head, Vaccine Clinical Research and Development*

Yeah. So as you know, unfortunately, at the current time, there is not really any vaccine or any of it -- any other, sorry, available therapies for primary recurrence in CDI. So those outbreaks are usually controlled with basic hand washing with soap and water and proper cleaning and disinfection.

As you're probably aware, there is infection control practices with isolation to ensure that you can control the outbreak. We -- that would be something that will come eventually that we will be able to evaluate after the vaccine is approved. But the study design will not incorporate to look into outbreaks at this time.

But maybe I will just ask my colleagues here if they have additional points that they want to call.

Annaliesa Anderson - *Pfizer Inc - SVP, Head, Vaccine Research & Development*

I think one of the questions, Geoff, if I got it correctly, was how can we increase awareness of this disease, particularly in the context of more vaccines that are available for older adults. So older adults obviously, are much more vulnerable population. And vaccines are one of the most cost-effective tools that we have for preventing and mitigating serious infections.

As we mentioned earlier in this call, the Centers for Disease Control and Prevention already, yes, highlight the importance of C. difficile on society, targeting it as the highest hazard from an infectious disease perspective. And so I think there's already acute awareness of the importance of preventing C. difficile and the potential benefit that the vaccine could have.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Thanks, Jeff. Operator, we'll take the -- thanks, Jeff. Operator, we'll take the next one.

Operator

Steve Scala, TD Cowen.

Steve Scala - *TD Cowen - Analyst*

Well, thank you so much. I have a couple of follow-ups and then a question. So first, relative to uptake, how might uptake of C. difficile vaccine compare to that of a pneumococcal vaccine among older people? So would you expect it to be more robust than a pneumococcal vaccine, less robust, or would it be similar?

Second, did you approach regulators with the first-generation data? Pfizer thought it was provocative. But if you did approach regulators, should we assume that they didn't agree?

And then lastly, my question, if C. diff is such a significant problem, then to what do you attribute the modest success of the therapeutic DIFICID? Thank you.

Annaliesa Anderson - *Pfizer Inc - SVP, Head, Vaccine Research & Development*

Okay, I can start with this and hand over. Regarding the last question for the antibiotic with trade name, I think, fidaxomicin, we can't comment on that. We're focusing on vaccine development.

Regarding uptake and how we see a comparison of uptake of different vaccines, once we demonstrate that the vaccine is efficacious and the FDA approves it for licensure, that will then be reviewed by the ACIP. And they will look at what they call their grading process, and they will assess the population who should be taking this vaccine.

And so I don't think we can comment on a comparison of uptake of vaccines because there's still some more work to be done there. And then your middle question was around discussions that we have had with regulators.

We conducted a Phase 3 study which we call CLOVER, and we did not meet the primary endpoint. And it's important from a vaccine licensor perspective to be able to meet primary end points. So I think that's all we can say then.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Thanks, Steve. Operator. We'll take our final question, please.

Operator

Kripa Devarakonda, Truist Securities.

Nicole Germino - *Truist Securities, Inc. - Analyst*

Hi, good morning. Thanks for taking our question. This is Nicole on for Kripa. On the Phase 2 for the next gen vaccine, can you just remind us what the endpoints are and what the bar for success is for the Phase 2 dose that you would potentially use for the Phase 3?

Alejandra Gurtman - *Pfizer Inc - SVP, Head, Vaccine Clinical Research and Development*

Yeah .Can I ask you to repeat the question? Your volume wasn't good for me, so -- thank you so much.

Nicole Germino - *Truist Securities, Inc. - Analyst*

Sure. Sorry about that. So for the Phase 2, can you remind us what the endpoints are and what the bar is for success for the Phase 2 dose that you would use for the Phase 3 trial?

Alejandra Gurtman - *Pfizer Inc - SVP, Head, Vaccine Clinical Research and Development*

So I will start by saying the Phase 2 is evaluation immunogenicity and safety of the vaccine. As Julie mentioned, we had three candidates, and we moved one to Phase 2.

So we are testing different doses and different regimens. And we want to ensure that the vaccine is safe, well tolerated, and generates immune responses that we will then -- when we have confidence and we see the results, that's when we start the Phase 3. Did that answer your question?

Annaliesa Anderson - *Pfizer Inc - SVP, Head, Vaccine Research & Development*

I think I can add to that a little bit, if you want. So essentially, we reviewed with you the data that we got from CLOVER. And what we saw from that study with a three-dose vaccine was something that can provide significant medical benefit in preventing severe C. difficile disease.

And so with our second-generation program, first thing is that we want to see something that is safe and well tolerated. And secondly, we need to see immune responses with the two-dose schedule that are going to be at least the same as what we saw in that initial case study that we did.

Nicole Germino - *Truist Securities, Inc. - Analyst*

Will you also be having the first episode of CDI also as one of the endpoints that you would be looking at, too?

Annaliesa Anderson - *Pfizer Inc - SVP, Head, Vaccine Research & Development*

Not in the Phase 2 study. That will be something we'll assess in Phase 3.

Nicole Germino - *Truist Securities, Inc. - Analyst*

Thank you.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Thanks, Nicole. Operator, are there any more questions?

Operator

I'm showing no additional questions at this time.

Francesca DeMartino - *Pfizer Inc - SVP, Chief IR Officer*

Okay. Thank you again to everyone who took the time to join our call today. I would also like to offer a very special thanks to Liesa, Alejandra, and Julie for sharing their insights and expertise.

Our vaccines unit is an important piece of our R&D engine, and we remain committed to delivering innovative solutions to protect against harmful pathogens. We appreciate your engagement today and look forward to continuing our Pfizer Pflash series in 2025, which will resume after our Q4 call early next year.

And thank you, everyone. I would like to wish everyone a happy holiday season, and we'll see you in the new year.

Operator

This does conclude today's program. Thank you for your participation. You may disconnect at any time.