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EDITED TRANSCRIPT

PFIZER INC SPOTLIGHT ON CANCER CACHEXIA AND PONSEGROMAB

EVENT DATE/TIME: November 01, 2024 / 2:00PM UTC

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PRESENTATION

Operator

Good day, everyone and welcome to Pfizer Flash, a Spotlight on Cancer Cachexia and Ponsegromab. Today's call is being recorded. At this time, I would like to turn the call over to Francesca DeMartino, Chief Investor Relations Officer and Senior Vice President. Please go ahead, ma'am.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

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

We're very excited to kick off these calls which will serve as educational deep dives into our pipeline and products. 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.

Each of these educational sessions will begin with a short conversation followed by a live Q&A. As a reminder, this call is intended for the investment community, including our sell side analysts and institutional investors. We intend to host one to two episodes per quarter.

I want to note that on today's call we will be making forward-looking statements. I encourage you to view the slide 4 in our presentation and the disclosures in our SEC filings which are all available on our 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.

It is a privilege to have you all with us as we delve into one of our most innovative programs and share some of the latest advancements Pfizer is making. This first episode will focus on cancer cachexia and our internally discovered and developed investigational drug, ponsegromab.

As you know, Pfizer has been dedicated to developing innovative therapies that improve patient outcomes with cancer and cardiometabolic disorders being two key areas of focus. Today, we will provide insight into our ongoing work at the intersection of these two areas and discuss our clinical trial program in cancer cachexia and how we are developing a potential treatment that we believe could make a significant difference in the lives of patients.

We hope today's discussion will help you understand the importance of continued research and progress in this area and also how it fits into our broader oncology and cardiometabolic pipeline.

We -- before we move to the main discussion, let me take a moment to introduce our speakers: Charlotte Allerton, Head of Discovery and Early Development; and Bill Sessa, Chief Scientific Officer of Internal Medicine. In addition, Aditi Saxena, Vice President and Clinical Research Head, Internal Medicine, will participate in the Q&A.

Charlotte, Bill and Aditi are central to our innovative work in cancer cachexia and today, they will guide us through an overview of the condition and exciting Phase 2 study results with ponsegromab that we presented earlier this year at ESMO and published in the New England Journal of Medicine.

Charlotte, Bill and Aditi, welcome and thank you so much for joining us on this inaugural Pfizer Flash call. Can you start by introducing yourself and giving us a brief overview of your current role in Pfizer and your previous experience.

Charlotte Allerton *Pfizer Inc - Head, Discovery & Early Development*

Thank you, Francesca. In my role as Pfizer's Head of Discovery and Early Development, I oversee R&D efforts from discovery through clinical proof of concept for our anti-infectives, inflammation and immunology and internal medicine research units. In addition, I lead our enterprise wide small and large molecule design teams as well as additional scientific and clinical lines.

And with that, I will hand over to Bill.

Bill Sessa *Pfizer Inc - Chief Scientific Officer, Internal Medicine*

Thanks, Charlotte. As for my team's role, we sit within Charlotte's Discovery and Early Development organization and are focused on delivering molecules from discovery through clinical proof of concept in areas such as cardiovascular disease, renal disease and metabolic diseases.

I am also the Alfred Gilman Emeritus Professor of Pharmacology and Medicine at Yale University School of Medicine. I led a research and discovery group in cardiovascular disease for 30 years prior to joining Pfizer. Over to you, Aditi.

Aditi Saxena *Pfizer Inc - VP, Clinical Research Head, Internal Medicine*

Thanks, Bill. For those on the call, I'm the Clinical Research Head in Bill's Group and Senior Author of the Ponsegromab New England Journal of Medicine paper. I'm an endocrinologist and completed my training and served on faculty at Brigham and Women's Hospital and Harvard Medical School. Pleased to be here with you today.

QUESTIONS AND ANSWERS

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Okay, great. Charlotte, let me start with you. Talk to me about cachexia, what is it and how it is -- how is it diagnosed?

Charlotte Allerton *Pfizer Inc - Head, Discovery & Early Development*

Thanks, Francesca. Cachexia is a complex disabling and life-threatening metabolic condition that affects about 9 million people worldwide. It's often an unrecognized consequence of many chronic illnesses, including cancer and heart failure. Cachexia leads to a significant loss of skeletal muscle and body fat, typically resulting in more than 5% loss of total body weight over a period of six months.

Cachexia is particularly prevalent among cancer patients affecting about 50% of them at some point in their cancer journey and being implicated in up to 30% of cancer related deaths. In addition to the weight loss, symptoms of cachexia include decreased appetite, reduced muscle strength and function and fatigue, and these symptoms can severely impact quality of life and the ability of patients to tolerate their cancer treatments.

Cancer cachexia is not fully understood but believed to be driven by several factors with cytokines being a main contributor. In this condition, cytokines are released that cause inflammation and accelerate fat and muscle loss. Additionally, cancer symptoms and side effects such as pain, nausea, vomiting and depression can lead to reduced appetite and food intake while also impacting swallowing and the body's ability to absorb nutrients.

Diagnosing cachexia is based on international consensus criteria. These criteria define this syndrome as weight loss of more than 5% during a six-month period or weight loss of more than 2% in patients with a BMI of less than 20 or sarcopenia, with sarcopenia defined as loss of skeletal muscle.

The workup for cachexia patients may involve a physician conducting a physical examination, evaluating eating habits, performing tests to understand overall fitness and muscle strength, imaging techniques like CT scans and Dexa scans may be used to measure the amount of lean tissue in the arms and legs to estimate muscle mass.

These tests help to establish the stage of cachexia. These stages include cachexia , which I just defined, as well as pre and refractory cachexia. With pre cachexia, there is unintentional weight loss that amounts to 5% or less of overall weight over six months, often accompanied by appetite loss.

Tests can show metabolic changes indicating that the patients are losing both muscle and fat. And then there is refractory cachexia which is associated with metabolic factors that can render strategies to manage weight loss unsuccessful. Patients with refractory cachexia may not be strong enough to tolerate cancer treatment and their cancer may be unresponsive to therapy. Sadly, patients with refractory cachexia may have a life expectancy of less than three months.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

So let's continue with the unmet medical need in cachexia and who does it impact.

Charlotte Allerton *Pfizer Inc - Head, Discovery & Early Development*

There is a critical unmet need as cancer cachexia is implicated, as I said before, in up to 30% of cancer related deaths with no treatments approved by the FDA for the condition. Current treatment options are therefore very limited and mainly focused on easing symptoms, improving nutrition and using nutritional supplements.

Recently, a guideline has supported the use of low dose Olanzapine to improve appetite and weight in patients with advanced cancer; however, this recommendation is largely based on a single center study.

Other options include short term use of progesterone analog or glucocorticoids that offer limited benefits that come with the risk of unfavorable side effects such as thromboembolic events with the use of progestins.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Can you share why it's been so difficult historically to develop treatments for this disorder?

Charlotte Allerton *Pfizer Inc - Head, Discovery & Early Development*

Cachexia is a complex condition that often goes underdiagnosed and undertreated. Anamorelin, a ghrelin receptor agonist is approved in Japan for the treatment of cancer cachexia; however, it has not received approval from the EMA or the US FDA.

In the past research on cachexia treatment faced challenges because it often focused solely on therapies to reverse muscle wasting, which is only one aspect of the disease. In contrast to prior attempts at drug development in this indication, our efforts with ponsegromab aim to improve multiple components of cachexia all at once by targeting the cytokine GDF-15. These improve -- these components include addressing the weight loss but also measures of patient quality of life such as symptoms and functional limitations that can be very debilitating to cancer cachexia patients.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Okay. Thank you, Charlotte. Bill, a question for you. Charlotte just mentioned GDF-15, can you explain what exactly that is?

Bill Sessa *Pfizer Inc - Chief Scientific Officer, Internal Medicine*

Sure. Thanks, Francesca. GDF-15 stands for growth/differentiation factor 15, which is a cytokine that significantly increases in response to pathological stresses, associative inflammation or tissue injury.

Normally, GDF-15 expression is low in most tissues, but it's highly expressed in some patients with cancer. Though the full host of consequences of elevated GDF-15 is still being understood, the cytokine has been established as a cancer biomarker that is associated with cachexia and poor survival.

The effects of GDF-15 are believed to be the result of its interaction with its receptor, which is called the glial cell derived neurotrophic factor family receptor alpha, also known as GFRA, which is localized in the brain. This interaction is thought to be a key modulator pathway, affecting appetite control and body weight regulation.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

So staying with you, can you explain how ponsegromab works?

Bill Sessa *Pfizer Inc - Chief Scientific Officer, Internal Medicine*

Sure. As you can see here, ponsegromab is an investigational monoclonal antibody designed in our own labs at Pfizer to target GDF -15. This antibody binds the GDF-15 in the blood, thereby preventing it from acting in the brain where it may drive the onset and progression of cachexia. Ponsegromab is administered subcutaneously and was dosed every four weeks in our recent Phase 2 trial. It has the potential to be the first FDA approved treatment for cancer cachexia, subject to validation in a registrational clinical trial with regulatory approval.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Okay. Let's dive into the Phase 2 trial. Can you tell us about the study design?

Bill Sessa *Pfizer Inc - Chief Scientific Officer, Internal Medicine*

Absolutely. The design of the trial is shown on the slide here. As you can see, the trial randomized 187 patients with either non-small cell lung cancer, pancreatic cancer, or colorectal cancer, who also had cachexia and elevated levels of GDF-15.

These patients received three subcutaneous injections of ponsegromab at doses of either 100, 200 or 400 milligram or a placebo, and these injections occurred once every four weeks. Primary goal of the Phase 2 study was to assess the effect of ponsegromab on body weight and participants at week 12.

Additionally, the study included secondary and exploratory objectives, including changes from baseline in appetite and cachexia symptoms, digital measures of physical activity and the lumbar skeletal muscle index.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

And can you tell us about the data that Pfizer presented at ESMO and is now published in the New England Journal of Medicine? What did we see in that study?

Bill Sessa *Pfizer Inc - Chief Scientific Officer, Internal Medicine*

In the Phase 2 study, it met its primary endpoint demonstrating significant and robust increases in body weight with ponsegromab compared to placebo after 12 weeks across all doses evaluated. Ponsegromab was generally considered safe and well tolerated in this study. Specifically, we observed placebo adjusted increases in body weight of about 2% in the 100 milligram group, about 3.5% in the 200 milligram group and about 5.6% in the 400 milligram group after 12 weeks.

Achieving a placebo adjusted weight gain greater than 5% at the top dose within 12 weeks was notable as a cancer cachexia endpoints working group has suggested that a 5% weight gain is indeed clinically meaningful to the patient.

In addition to the weight gain, benefits were seen with the top dose of ponsegromab, including, compared to placebo, adjustments across multiple secondary and exploratory endpoints. These included those assessing patient reported outcomes, overall physical activity and muscle mass.

Looking at patient reported measures adjusted for placebo, we saw posttreatment increases on the FAACT anorexia/cachexia subscale which consists of 12 questions.

Additionally, we saw a placebo adjusted increase when focusing on the five questions within the FAACT anorexia/cachexia subscale that make up the five item anorexia symptom score. Taken together, these results point to a moderate improvement from baseline compared to placebo on appetite in cachexia symptoms after only 12 weeks.

In addition to patient reported measures, we also tracked physical activity during the treatment period. The results of our analysis showed, on average, clinical trial participants spent an additional hour and 10 minutes plus per day being physically active on the 400 milligram ponsegromab dose compared to their baseline after adjusting for placebo. These data are encouraging as they highlight ponsegromab's potential to improve physical activity and function.

Lastly, CT imaging analysis showed an increase in lumbar skeletal muscle mass at 12 weeks with the top ponsegromab dose compared to placebo indicating that the overall weight gain observed was driven in part by muscular gains.

The results therefore suggest that ponsegromab has the potential to deliver meaningful weight gain, which is consistent with the improvements in symptoms and physical activity observed alongside these data. Collectively, we believe these Phase 2 results signal a potential breakthrough in cancer cachexia.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Thank you, Bill. Charlotte, I want to come back to you and ask what's the next step in ponsegromab's development program for cancer cachexia?

Charlotte Allerton *Pfizer Inc - Head, Discovery & Early Development*

Well, based on these positive results, we plan to start a registration enabling study in 2025. We're currently discussing the design of that study internally and with regulators and we look forward to updating more.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Okay, great. What about the competitive landscape? What other treatments are in development for cancer cachexia?

Charlotte Allerton *Pfizer Inc - Head, Discovery & Early Development*

As mentioned earlier, there currently are no FDA approved treatments that address the underlying causes of cachexia. With ponsegromab, our goal is to obviously change this and deliver a first-in-class therapy.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

And what about other diseases? Are you investigating ponsegromab in any other areas?

Bill Sessa *Pfizer Inc - Chief Scientific Officer, Internal Medicine*

Yeah. We believe ponsegromab has potential across a broad range of diseases beyond cancer cachexia and are currently exploring its use in heart failure. The Phase 2 study of ponsegromab in people with heart failure is ongoing, which builds on data from our prior external studies showing an association between GDF-15 levels and the symptom burden hospitalization rate and death in patients with heart failure.

We look forward to providing updates on this trial when they are available. And while the current focus is on cancer and heart failure, we plan to continue to explore other areas where ponsegromab may hold potential for other indications.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Okay. So let's say, I'm an oncologist, what final message would you want me to walk away with when I'm thinking about the potential for this molecule and what it could mean for patients? Charlotte, you want to take that?

Charlotte Allerton *Pfizer Inc - Head, Discovery & Early Development*

At this stage where we have encouraging Phase 2 data that we hope to validate in a registrational study, I would highlight two key takeaways for oncologists. First and foremost, ponsegromab has demonstrated promising Phase 2 results and the potential to improve patient quality of life. This is supported by data across multiple endpoints that highlight how ponsegromab has the potential to partially reverse cachexia effects and drive improvements in not only weight but also symptoms, muscle mass and physical activity.

Secondly, by increasing weight, muscle mass and other factors, ponsegromab could potentially put patients in a position where they can better tolerate anticancer therapy, though this would need to be determined in future trials.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Okay. Bill, Charlotte, thank you for the great discussion. So if I were to summarize our conversation, I would say that in sort of three points: one, ponsegromab has the potential to treat multiple facets of cachexia; in a Phase 2 trial, ponsegromab demonstrated the potential to increase weight and improve quality of life as assessed by multiple measures and participants with cancer cachexia; this confirmed the role of GDF-15 as a driver of a novel target for cachexia, highlighting ponsegromab's potential to be a breakthrough

therapy for patients.

Secondly, ponsegromab may have a role in enhancing treatment tolerance by increasing weight, muscle mass and other factors. Ponsegromab could potentially put patients in a position where they can better tolerate therapy. This could potentially lead to better overall treatment outcomes, though this would need to be determined in future trials.

And then lastly, ponsegromab's future development and broader potential. Based on the positive results from the Phase 2 study, we expect to advance to a registration enabling study for ponsegromab next year. While the current focus remains on cancer and heart failure, we plan to continue to explore if ponsegromab may hold potential in other indications.

So now I'd like to open the floor for a Q&A session with Charlotte, Bill, and as I mentioned, Aditi will join that session. Before we begin, I would like to remind everyone that this is an educational deep dive into our pipeline. Therefore, I kindly ask that you avoid questions that would require us to provide forward-looking financial projections which we cannot do today.

While we're happy to clarify any information shared during the presentation, we will not be offering estimates beyond what has already been communicated. Additionally, we ask you to keep your questions focused on topics specifically discussed today. We'll do our best to provide as much clarity as possible within these guidelines and I appreciate your understanding. And as always, the IR team is available for follow up after the call is over.

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

Operator

(Operator Instructions) Evan Seigerman, BMO Capital Markets.

Conor MacKay *BMO Capital Markets - Analyst*

Hi there. This is Conor MacKay on for Evan. Thanks for taking our question. With these really impressive data in hand, can you maybe walk us through how you're thinking about designing a potential Phase 3 program? Understanding that you might not be able to do a basket study in all tumor types, are there any indications that you would think about going after first?

And then, I guess, on top of that as well, you mentioned that with ponsegromab, patients might be able to tolerate additional treatment or sort of give physicians greater treatment flexibility, would you consider maybe evaluating overall survival in Phase 3 study as well?

Charlotte Allerton *Pfizer Inc - Head, Discovery & Early Development*

Thank you very much for the question. So we're pleased with the data from our Phase 2 study, which shows the gain in the body weight and the improvement in functional endpoints as a measure of patient quality of life, which is particularly important.

And as I said, we're currently discussing this data internally and with regulators and we're using it to guide our registration study design. The Phase 2 study was not powered to show a survival endpoint, but we know that cachexia is associated with up to 30% cancer related deaths and patients with cachexia have a poor prognosis. So these considerations are being discussed as part of our Phase 3 planning.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Okay, great. Thank you. Operator, let's take the next question, please.

Operator

Vamil Divan, Guggenheim Securities.

Edouard Mullarky *Guggenheim Securities - Analyst*

Hey, good morning. This is Edouard on for Vamil. I guess I'm still -- I guess this -- I think this will be clear up a little bit when we see more of the trial and how the data pan out. But I guess one thing I'm trying to think of is this more going to be sort of a supportive care therapy or do you think it would actually be really a -- kind of a therapeutic and sort of the implications on pricing there?

And then in the conservative case, it does end up being more of a supportive care therapy, can you help us think about pricing and supportive care? Are there sort of any good analogs that we should think about in supportive care therapies and sort of what sort of pricing point do those agents get? Thank you.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Aditi, can I turn that one over to you, please?

Aditi Saxena *Pfizer Inc - VP, Clinical Research Head, Internal Medicine*

Sure. So I don't think I could comment on implications related to pricing, but we do believe that, as we've discussed, cancer cachexia is a very serious condition. And so exactly how this will be used with respect to patients' care therapies still is subject to the registrational trials that are coming. And so we look forward to providing updates at that time.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Okay, thanks. Operator, we'll take the next question.

Operator

Louise Chen, Cantor.

Louise Chen *Cantor Fitzgerald & Co. Inc. - Analyst*

Hi, thanks for taking my question here. I was wondering if you're going to have any data or studies to show how ponsegromab can prevent cancer deaths or help patients better tolerate their treatments. Anything objective? Thank you.

Charlotte Allerton *Pfizer Inc - Head, Discovery & Early Development*

Thank you for the question. I think as you know, we mentioned earlier, we feel encouraged by the Phase 2 data. And one of the queries we have regarding the impact of quality of life is whether it will enable patients to tolerate more of their treatment. Of course, there's also the question of, if you treated earlier in disease, would that enable an impact on overall survival and greater toleration of treatment?

So those are all discussions that we're having currently as part of our Phase 3 planning. We do believe the data that we have in hand from our Phase 2 study which was focused on the gain in body weight and the impact of quality of life is also very impactful for patients. And we will be using that data to design the Phase 3 studies and we look forward to updating you on that.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Great. Thanks, Charlotte. Operator, we'll take the next one, please.

Operator

Chris Shot, JP Morgan.

Ethan Brown *JPMorgan Chase & Co. Inc. - Analyst*

Hi, this is Ethan on for Chris. Thanks for taking our question. Just in general, how heterogeneous do you view this condition? And are you seeing similar responses across most patients or are there any notable patient profiles that could suggest a higher or lower likelihood of responding to the drug? Thank you.

Bill Sessa *Pfizer Inc - Chief Scientific Officer, Internal Medicine*

Yeah. Well, thank you for the question. As you know, from Phase 2 study, there was sort of a cutoff that we used for -- criteria for entering into the trial of GDF-15 levels. And ironically, when you look at the data, about 97%, 98% of the participants actually achieved those levels.

So we think that the GDF cutoff -- it really hasn't been established yet, but we believe that high levels of GDF-15 will be really important for entering into these trials. And it seems like it works across a range of GDF-15 levels above what was considered a normal level.

Charlotte Allerton *Pfizer Inc - Head, Discovery & Early Development*

Thank you, Bill. And I think in the Phase 2 study, we had three cancer types, we had the non-small cell lung cancer, the colorectal cancer patients and the pancreatic cancer patients. We do know that GDF-15 is upregulated in other cancer types and that's something we're exploring.

And we also know that GDF-15 is up regulated in other chronic conditions and we have a study running in heart failure and we're looking forward to seeing that data and sharing it with the community and also exploring other indications and chronic illnesses in which GDF-15 levels are elevated and seeing if ponsegromab could have a therapeutic impact there.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Great. Thank you. Operator, we'll take the next question, please.

Operator

Kripa Devarakonda, Truist Securities.

Billal Jahangiri *Truist Securities, Inc. - Analyst*

Hi, good morning. This is Billal on for Kripa. Sorry if I missed this. Can you remind us what sort of impact it has on muscle given -- cachexia affect muscle significantly. Like, what's the mix of healthy weight gain between fat and lean muscle?

Charlotte Allerton *Pfizer Inc - Head, Discovery & Early Development*

If I could just clarify the question, the question was asking about the weight gain and the balance between fat and lean muscle?

Billal Jahangiri *Truist Securities, Inc. - Analyst*

Yeah.

Charlotte Allerton *Pfizer Inc - Head, Discovery & Early Development*

Correct. So what we saw in our Phase 2 study was actually we did measure the lean and the fat gain as part of it and we were very encouraged to see a healthy balance in there. And it looks like around a 5% gain in the lean muscle mass, which we consider to be significant.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Operator, we'll take the next one.

Operator

Trung Huynh, UBS.

Trung Huynh *UBS - Analyst*

Hi, guys. Thanks for taking my question. Trung from UBS. Thanks for hosting this event. I have a couple here. Just one on the enrollment of patients for the Phase 3 cachexia trial. So you noted that there's people across various parts of their cancer journey. There's some patients that are at different stages. There's people who are on different treatments. Just thinking about how you're thinking about some of these issues in getting that homogeneous patient population so you don't have any baseline population distortions there.

And then you touched on your Phase 2 in heart failure, there's certainly other diseases out there like HIV, kidney disease that are associated with cachexia. You noted that you're looking at this. Can I clarify that GDF-15 is also the issue with cachexia in these diseases? And is there a way the FDA could oversee a broader cachexia approval or do you have to specifically conduct these studies in these diseases? Thank you.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Aditi, can we ask you to start with the first part of the question, please?

Aditi Saxena *Pfizer Inc - VP, Clinical Research Head, Internal Medicine*

Sure. So I think the first part of the question was looking at patient populations in future trials. I think we've mentioned that there -- this is -- we are actively working on these efforts and look forward to sharing details with you in the future. But maybe to comment on the study design for the Phase 2 trial and what was informing us of that

So we saw consistent responses across the three different cancer subtypes that were studied in that trial, which is very encouraging. Bill spoke to the GDF-15 minimal threshold, which was chosen to, not in any way, overlap with a healthy population and really the vast majority of our screened participants met that GDF-15 threshold. And we believe this to be the case across other cancer cachexia populations as well.

The second piece about other indications for an elevated GDF-15 cachexia population. So as you mentioned, there are implications to other cachexia populations. We do believe the pathophysiology could be very, very relevant. But ultimately, we are testing it separately in heart failure that will provide us some really key information in testing this hypothesis outside of a cancer cachexia population and certainly, will be helping us to consider other indications as well.

Welcome, Bill and Charlotte, additional input as appropriate.

Bill Sessa *Pfizer Inc - Chief Scientific Officer, Internal Medicine*

Yeah, I think this is a really great question in terms of other indications. And I think within the group, we have this belief and feeling that there is a GDF-15 syndrome associated with a variety of diseases. And we know that this is not just a bystander, it's actually a driver of a lot of the cachectic symptoms. So we're very much interested in looking at these opportunities.

Charlotte Allerton *Pfizer Inc - Head, Discovery & Early Development*

I think there was an additional part of the question asking about whether there could be a broader label obtained ultimately, based on the access of the GDF treating or lowering the GDF-15 across a broad range of diseases? I think that's an interesting suggestion. It's certainly one we're discussing, but that will be something that we need to discuss with regulators as more data emerges.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Okay, great. Operator, we'll take the next question.

Operator

Dave Risinger, Leerink Partners.

Dave Risinger *Leerink Partners LLC - Analyst*

Yeah, thanks very much and thanks for hosting this call. So I have a couple questions. First, with respect to GDF-15, could you just provide more color on the mix of patients and how you're thinking about this biomarker in terms of what percentage of patients would fall into different categories of elevation and thus what percentage of patients would benefit significantly versus modestly? And then second, could you just speak to the administration of the drug and whether you're working on a more convenient administration? Thank you.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Aditi, we'll start with you, please.

Aditi Saxena *Pfizer Inc - VP, Clinical Research Head, Internal Medicine*

Sure. So in our Phase 2 trial in cancer cachexia, as mentioned, we -- the vast majority of participants really met the elevated GDF-15 criteria that we had set for the trial. So we don't expect that. Once people have actually demonstrated the clinical signs and symptoms of cachexia, we actually believe that we're already selecting for an elevated GDF-15 population.

So what we also saw is that looking at gradations of GDF 15 baseline levels within the trial didn't significantly impact their response, we actually saw really consistent responses regardless if they were in the sort of lower end of GDF-15 relative to the trial population versus higher end.

So we actually believe that the clinical signs and manifestations of cachexia really speak to the underlying pathophysiology, which we believe is GDF-15 driven. But thank you for the question regarding the drug products. So we are looking to make that very patient friendly for upcoming trials and also for ultimate administration in the clinic.

Dave Risinger *Leerink Partners LLC - Analyst*

Thanks so much. So can I just ask a few more then? So you're not planning on this being a biomarker selected drug in terms of patient selection, correct? And then could you just explain what the administration of the drug is today and what could be improved?

Aditi Saxena *Pfizer Inc - VP, Clinical Research Head, Internal Medicine*

So in terms of the use of the biomarker for ultimate clinical use is still something that is a developing strategy. So -- and in terms of the drug product in the -- for the current clinical trials, it is administered via syringe and as a subcutaneous injection. Ultimately, we will be looking for methods that are more amenable to dosing by patients in the home setting.

Dave Risinger *Leerink Partners LLC - Analyst*

(multiple speakers) And what's the frequency of administration? And what are you -- I'm sorry, I was just looking for a little more color. What is the frequency of administration and when would you work on a less frequent solution for patients?

Aditi Saxena *Pfizer Inc - VP, Clinical Research Head, Internal Medicine*

The frequency of administration in the Phase 2 trial was every four weeks. And so we believe that that frequency of administration will be carried on through the next trials, but we'll provide updates as appropriate.

Dave Risinger *Leerink Partners LLC - Analyst*

Sorry. If I could --?

Bill Sessa *Pfizer Inc - Chief Scientific Officer, Internal Medicine*

Sorry. Also, just to follow up on the Phase 2 trial, four weeks after the last top dose, about 97% of the GDF-15 was tied up with the antibody with only 3% or less remaining. So we know that the drug is onboard, is tying up GDF-15 even at time points beyond the last dose.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Okay. Operator, we'll take the next question please.

Operator

Xiaobin Xu, Bernstein.

Xiaobin Xu *Bernstein - Analyst*

Hi, this is Xiaobin Xu from Bernstein. Thank you for your question. Could you provide more detail on why Pfizer's considerations on the Phase 3 cachexia endpoint design and what anticipate the timeline for bettering this endpoint results. And given the importance of the outcome data for the pricing, will there be a focus on demonstrating long term benefits beyond the weight gain such as extended survival or improved of patient quality of life? Thank you.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

I think it was on the Phase 3 end point or --

Charlotte Allerton *Pfizer Inc - Head, Discovery & Early Development*

Thank you for the question. I think what we shared today or gone into more details on is our Phase 2 results. As Bill spoke through, that was based on weight gain and then showing improvements in quality of life and to show that data is underpinning our discussions on Phase 3 trial design and discussions with regulators.

As we discussed earlier, cancer cachexia is associated with up to 30% cancer-related deaths and patients with cachexia do have poor prognosis. So we are discussing that data as part of the design of our registration studies as well. Ultimately, the label for ponsegromab will be dependent on data from registration studies and discussions with the regulators.

And while 12 weeks was the time of our primary analysis in the Phase 2 trial, we also have an open label extension study running and the details of our Phase 3 study and the length of it, what we're currently discussing. But ultimately, the goal would be to provide a treatment option to cancer cachexia patients for as long as they need it.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Thank you, Charlotte. Okay. Operator, next question, please.

Operator

Steve Scala, TD Cowen.

Steve Scala *TD Cowen - Analyst*

Thank you so much. I have two questions. First, what commercially successful cancer supportive agents should we look at as analogs for the launch ramp and peak usage of ponsegromab?

And secondly, it looks like the product was in Phase 1 in January of 2020 and maybe well before that, so it took four and a half years to get to this point. Why did it take so long?

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Do you want to start the first part? The supportive agent.

Charlotte Allerton *Pfizer Inc - Head, Discovery & Early Development*

So I think regarding that, I don't want to comment on other people's products or [previous] care. What I would say that I think we speak about ponsegromab is it's getting to the mechanistic basis of treating cachexia and therefore, is impacting not only the weight gain but also aspects of the quality of life. And we look forward to seeing the additional benefits of that in future studies.

And in terms of the timing of the study, I think initially we did undertake a Phase 1b study in patients and that study took a little bit longer. We worked closely with patient advocacy groups and actually our Phase 2 study in cancer cachexia recruited ahead of schedule and ran ahead of schedule. So we continue to look at optimizing the timing for our trials.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Thank you, Charlotte. Okay. Operator?

Operator

I'm showing no further questions at this time.

Francesca DeMartino *Pfizer Inc - Chief Investor Relations Officer and Senior Vice President*

Okay. Thank you once again to everyone for joining us today and a special thank you to Charlotte, Bill and Aditi for sharing more details on the incredible work that is being done every day.

Pfizer remains deeply committed to innovation in cancer and cardiometabolic treatments and we're excited about the progress being made in potentially addressing cancer cachexia. We really appreciate your time today. We look forward to continuing these conversations in future sessions. The IR team is always open to hearing what's on your mind, what we could add to future sessions. And thank you and have a great weekend.

Operator

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

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