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PFE - Pfizer Inc Analyst and Investor Call to Review Tafamidis Data Presentation at ESC Congress 2018

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OVERVIEW:

PFE discussed about data from ATTR-ACT study presented at ESC Congress 2018.

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PRESENTATION

Operator

Good day, everyone, and welcome to Pfizer's Analyst and Investor Call to review tafamidis data presentation at European Society of Cardiology Congress 2018. Today's call is being recorded. At this time, I would like to turn the call over to Mr. Chuck Triano, Senior Vice President of Investor Relations. Please go ahead, sir.

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

Thank you, Sylvia, and good morning, everyone, and thanks for joining us today to discuss the Phase 3 tafamidis data that were presented here at the European Society of Cardiology Congress, and also published today in the New England Journal of Medicine. Before we start, I want to remind everybody that we will be making forward-looking statements on today's call and actual results may differ from those statements. The forward-looking statements speak only as of the original date of this presentation, and we undertake no obligation to update or revise any of these statements. With that, I will turn the call over to John Young, Group President of Pfizer Innovative Health. John?

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Thank you, Chuck, and good morning, everyone. Today, we are speaking to you from the European Society of Cardiology Congress in Munich, Germany, where we were proud this morning to share for the first time the primary results from the tafamidis Phase 3 transthyretin cardiomyopathy ATTR-ACT study, the only Phase 3 study to date specifically in transthyretin amyloid cardiomyopathy or ATTR-CM. These late-breaking data were presented in a hotline session here at ESC and simultaneously published online in New England Journal of Medicine, and we look forward to discussing them further with you all this morning. I'll start by providing a brief overview of the increasingly promising clinical potential of our broad,

Rare Disease portfolio. I'll then turn it over to Dr. Brenda Cooperstone, our Chief Development Officer for Pfizer Rare Disease, to discuss these results in more detail. We also have here with us today our Global President for Pfizer Rare Disease, Paul Lévesque, who will join us for the Q&A segment of the call.

Pfizer has long been a significant player in the Rare Disease arena. With a growing pipeline of therapies to address a variety of rare diseases, we continue to leverage our knowledge and expertise, built over nearly 3 decades of experience across a wide spectrum of disease areas, with the goal of helping these patients with unmet medical needs. Our work spans a number of disease areas of focus, including hematology, neurology, pulmonology, endocrine and inborn errors of metabolism and nephrology. Importantly, we are also building on our rich heritage in cardiology to explore areas such as ATTR-CM. Pfizer has 7 approved rare disease medicines, providing much needed treatment options for approximately 76,000 patients in more than 100 countries worldwide.

Currently, we have multiple compounds in preclinical and clinical development across a broad range of disease areas, with 4 new clinical entities in pivotal trials. And importantly, we have dedicated Rare Disease colleagues around the globe supporting this important work on behalf of patients each and every day. But today, we are here to discuss ATTR-CM, a rare, progressive and universally fatal disease associated with progressive heart failure, and for which there are no approved pharmacologic treatments. Adding to the challenge is the fact that diagnosis rates for this disease are extremely low. Patients with ATTR-CM face an incredibly long and arduous disease journey, as they cycle through misdiagnoses. The disease is often initially misidentified as more common types of heart failure but the symptoms persist and patients may consult with several cardiologists over time. If ATTR-CM is ultimately suspected, they are referred to a center of excellence where the disease can be confirmed through diagnostic measures such as cardiac biopsy or scintigraphy. Unfortunately, once patients receive the accurate diagnosis of ATTR-CM, the median life expectancy in untreated patients is reported to be only 2.5 years in those with the hereditary form and 3.6 years for those with the wild-type form. We have a large task in front of us to first and foremost help cardiologists to better understand this disease and drive patients to centers of excellence. As such, it's imperative that we truly put patients first to collectively work to improve the time to diagnosis to help these people earlier in their disease. We look forward to leveraging our deep experience with cardiologists and our heritage in this space to help these patients.

At this time, the precise prevalence of ATTR-CM is unknown. But it's believed that less than 1% of patients with the disease are currently diagnosed. Current estimates suggests there are approximately 400,000 to 500,000 patients living with this disease in developed markets and approximately 15% to 25% of those patients are in the U.S. It's important to note that there are 2 distinct types of this disease: those with the variant or hereditary form, which is caused by a mutation in the transthyretin gene; and those with the wild-type form, which is not hereditary and may occur as people age. We believe there are approximately 10,000 to 15,000 patients at this time with hereditary ATTR-CM, and potentially 390,000 to 490,000 patients living with the wild-type form. These figures represent an incredible opportunity to help patients with either manifestation of the disease. If tafamidis is ultimately approved for an indication in ATTR-CM, we have the potential to provide an oral treatment option for patients, where no pharmacological therapy currently exists. At this time, ATTR-CM represents a significant burden on the healthcare system, associated with both high mortality rates as well as rates of cardiovascular-related hospitalization. Moreover, because widespread awareness of this disease is low among physicians, including the cardiologists to whom the symptomatic patients often present, those living with ATTR-CM, either with hereditary or wild-type, are often stuck in a seemingly never-ending cycle of treatments that do not address their actual disease. Even in the rare instances when these patients are accurately diagnosed, the only treatment a physician can potentially offer is liver or heart transplantation, which is often unfeasible or unavailable. And today, there is no approved medicine to help them. However, as you'll hear from Brenda, today we have shared the results observed in the Phase 3 ATTR-ACT trial, which evaluated tafamidis and patients with ATTR-CM. And these results suggest that tafamidis, if approved, can potentially offer an oral treatment option to help address the significant unmet need of these patients. So let me now turn it over to Brenda who will talk about the data in more detail.

Brenda Cooperstone - *Pfizer Inc. - SVP, Chief Development Officer, Pfizer Rare Disease*

Thank you, John. Good morning, everyone. Today, I'm thrilled to be able to discuss the primary results for our Phase 3 ATTR-ACT trial, which evaluated tafamidis versus placebo for the treatment of patients with ATTR-CM. But first, I'd like to provide some background on why the data from this trial are so significant for this patient population.

Transthyretin, a protein that naturally circulates in the blood, is inherently unstable. Both mutation of the TTR gene or age can affect its structure, potentially resulting in protein breakdown and amyloid deposits. ATTR-CM is a form of transthyretin amyloidosis, a rare progressive disease

characterized by the buildup of abnormal deposits of amyloid in the heart, resulting in restrictive cardiomyopathy and progressive heart failure. Specifically, ATTR-CM is caused when transthyretin becomes unstable and misfold. This misfold of protein can build up in the heart as amyloid fibrils, which causes the heart muscle to become stiff, resulting in heart failure. Signs of ATTR-CM typically manifest around 60 years of age and patients often present with symptoms similar to more common types of heart failure, such as dyspnea on exertion, fatigue, effort intolerance, orthostatic hypotension, syncope and conduction abnormalities. Tafamidis, designed as an oral capsule, is a small molecule that selectively binds at specific sites on the transthyretin tetramer to prevent destabilization of the transthyretin transport protein, the first step of the cascade leading to the formation of amyloid. The Phase 3 ATTR-ACT study is an international multicenter double-blind placebo-controlled randomized 3-arm clinical trial in 441 patients with ATTR-CM that investigated the efficacy, safety and tolerability of an oral dose of either 20 or 80 milligrams of tafamidis meglumine capsules compared to placebo. The study included both patients with the hereditary and wild-type form of the disease. The primary endpoint of the study, which compared tafamidis to placebo with the hierarchical combination of all-cause mortality and frequency of cardiovascular-related hospitalizations over a 30-month period. The results presented by Professor Rapezzi this morning and published online in the New England Journal of Medicine shows that tafamidis was associated with a statistically significant reduction in the hierarchical combination of all-cause mortality and frequency of cardiovascular-related hospitalizations compared to placebo, with a P-value of 0.0006. Digging at this deeper into one of the components of the primary endpoints, the data showed tafamidis was associated with a 30% reduction in the risk of all-cause mortality compared with placebo over a 30-month treatment period, with a hazard ratio of 0.7 and a P-value of 0.0259. For the purpose of this analysis and in the Cox Proportional Hazard Model on this slide, heart transplant and implantation of a cardiac mechanical assist device were treated as death. Removing transplant and mechanical assist patients increased the reduction in all-cause mortality to 33%, with a P-value of 0.018. Additionally, looking at the other component of the primary endpoints, tafamidis was associated with a 32% reduction in the rate of cardiovascular-related hospitalizations compared with placebo over the same timeframe, the relative risk of 0.68 and a P-value of less than 0.0001. As Professor Rapezzi shared this morning, it is important to note that tafamidis demonstrated a consistent directional mortality benefit and reduction in frequency of hospitalizations in the tafamidis treated arms across subgroups -- all subgroups, including hereditary and wild-type. The only exception to this was in the frequency of hospitalizations in the NYHA Class 3 subgroups, where we do not see a reduction versus placebo. The higher hospitalization rate observed in this group may be attributable to longer survival during a more severe period of disease. Furthermore, when looking at key secondary endpoints, a significant improvement in functional capacity and quality of life measures were observed in those treated with tafamidis versus placebo. Specifically, tafamidis reduced the decline of the 6-minute walk test distance, a measure of functional capacity and reduced the decline in quality of life, as measured by the Kansas City Cardiomyopathy Questionnaire Overall Score compared with placebo at month 30. The safety data shows that tafamidis was well tolerated in this population at both oral doses of 20 and 80 milligrams, with an observed safety profile comparable to placebo. Additionally, discontinuation of study drug due to treatment emergent adverse events occurred at a lower rate with tafamidis than placebo. And now, I will turn this back to John to close.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Thank you, Brenda. And I hope you all share in our enthusiasm after hearing more about these important findings from the ATTR-ACT trial.

In summary, ATTR-CM is a challenging and underdiagnosed disease and will require significant market development. We're committed to doing everything we can to help to educate and raise awareness for this rare disease and ultimately help patients in need of treatment. Whilst accelerating time to diagnosis of these patients require significant work, we believe we can uniquely leverage our heritage and capabilities with cardiologists, including our Eliquis field force to raise awareness of this disease and drive diagnosis. Tafamidis, our investigational oral therapy for this condition, remains the only potential treatment that has been evaluated in a Phase 3 trial designed to assess the safety and efficacy, specifically in patients with ATTR-CM. Tafamidis demonstrates there is statistically significant benefit in the reduction of both all-cause mortality and cardiovascular-related hospitalizations in patients with this disease at rates of 30% and 32%, respectively. This benefit was shown across all prespecified subgroups with the exception of cardiovascular-related hospitalizations for patients classified as NYHA Class 3 at baseline and was well tolerated at both oral 20-milligram and 80-milligram dose groups. And we are delighted to share these results today. Given the data demonstrated across endpoints in the ATTR-ACT trial, the safety profile in this study and from years of experience in the polyneuropathy indication outside of the U.S. as well as oral dosing, we are excited about the opportunity tafamidis represents for patients as a potential treatment option in ATTR-CM. Now, we look forward to answering your questions, and I'll turn it back to Chuck to start the Q&A session.

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

Thank you, John and Brenda, for the comments. Sylvia, can we please poll for questions.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Your first question comes from Geoff Meacham from Barclays.

Jason Eron Zemansky - *Barclays Bank PLC, Research Division - Research Analyst*

This is Jason on for Geoff. Real quickly, can you give us a sense of where the 20-milligram dose is priced in the EU, and then how are you thinking about pricing on both doses moving forward? And then, I have a quick follow-up.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Okay. Thanks for the question, Jason. So I'll ask Paul Lévesque just to comment on where we stand in regard to EU pricing.

Paul Lévesque - *Pfizer Inc. - Global President, Pfizer Rare Disease*

So, Jason, thank you for the question. The EU pricing has been, as you can understand, it's been priced on the 20 milligrams based on the value of the data that was presented back then for polyneuropathy. So the average price per year per patient in EU and Japan is probably 75,000. We are certainly not in a position today to give you more information about the pricing associated to cardiomyopathy -- ATTR cardiomyopathy simply because we certainly need to have an approval, a label and a final value proposition.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Thank you, Paul, and thanks, Jason, for the question.

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

Next question please, operator.

Operator

Your next question comes from Chris Schott from JP Morgan.

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

Just two questions for me. First, I think you touched on this during the call, but can you elaborate on how you go about building this market and increasing the number of diagnosed patients? I guess, realistically, where do you see diagnosis rates and treatment rates going over time? So any color on that would be appreciated. The second question was just when we think about the benefit we saw with the data today, were the death and hospitalization rates seen with the placebo group in line with your expectations and trial designs? Just trying to get a sense of how that baseline performed versus expectations.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Great. Thanks for the question, Chris, I'll ask Paul to talk about the -- how we see the work that we need to do to build and progress diagnosis rates. I'll ask Brenda to talk about how we see the deaths in the placebo group. So, Paul?

Paul Lévesque - *Pfizer Inc. - Global President, Pfizer Rare Disease*

So of -- for sure increasing diagnosis is a key success factor so thank you for the question. Improving diagnosis rates will rely on several factors, including expanding the number of centers of excellence and driving patients in those centers, use of scintigraphy, we saw that on a previous slide, development of diagnosis checklist, we are going to try to make it easy on doctor and the availability of an approved therapy, which we don't have today, which is the reason why the diagnosis rate is so low. Pfizer will continue to remain active in educating cardiologists and collaborate with key stakeholders in organizations to support awareness, training, tools to accelerate and expand diagnosis ahead of the potential launch of tafamidis. When it comes down to how it's going to ramp up over time, it's, obviously, linked to our capacity to execute and it'd be premature, at this time, to release a number.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Thanks, Paul. Brenda, would you like to answer the question about how we see the death rates in the placebo group?

Brenda Cooperstone - *Pfizer Inc. - SVP, Chief Development Officer, Pfizer Rare Disease*

Yes, thanks for this question. So when this trial was originally designed back in 2011 or so, there was very little epidemiology available to understand exactly what the mortality rate would be, and we took a conservative approach. However, the mortality rate that was seen in the placebo arm in this trial with further information available is perfectly in line with expectations for this uniformly stable disease.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Great. Thank you, Brenda.

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

Next question, please, operator.

Operator

Your next question comes from Jami Rubin from Goldman Sachs.

Jamilu E. Rubin - *Goldman Sachs Group Inc., Research Division - Equity Analyst*

I was just wondering if you think there was any indication that tafamidis was less effective in the mutant population. We did see in the data that, that population did not hit statistical significance, although there were many fewer African-Americans enrolled in that population and they tend to be patients with the mutant type of the disease. So if you would talk about that. And also, just was curious if you knew how -- if you see how physicians are going to choose between tafamidis and patisiran in the U.S.? And also how you see that playing out in Europe?

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Okay. Thanks for the question, Jami. So I'll ask Brenda to talk about how we saw tafamidis efficacy in the mutant population, and Brenda and Paul probably can both comment about how we actually see this playing out in the marketplace given that we anticipate a likely conclusion here will be that -- it will be the only approved treatment for this patient population. But, Brenda?

Brenda Cooperstone - *Pfizer Inc. - SVP, Chief Development Officer, Pfizer Rare Disease*

So thank you for your question. So we did see, across all subgroups, that there were -- was directional benefit, both for survival and with respect to cardiovascular hospitalization and this was also true within the various populations for ATTR-CM. This was especially true for the mortality analysis and with respect to cardiovascular hospitalizations, you should understand that the variant populations tends to present at a more severe point within their disease, so there is overlap with the Class III patients, which is why you'd see a pull with respect to that cardiovascular hospitalization.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Thank you. So I think the second question was competitors and how we see this playing out. Jami, I think, it's -- as we said, I think, the -- given our competitors haven't studied this in a -- their products in a wild-type population, they've only studied for polyneuropathy, I think the likely conclusion is that we'll certainly be the first and only product approved for the patient population that we've studied here. So I certainly don't want to speak for competitors and their data, but I think the likelihood is that this will set -- our data set will set a very high bar for others to be able to demonstrate their effectiveness in this patient population. Thank you for the question.

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

Next question please, operator.

Operator

Your next question comes from Vamil Divan from Crédit Suisse.

Vamil Kishore Divan - *Crédit Suisse AG, Research Division - Senior Analyst*

So just maybe following up on the subgroup question. Also, I know you touched on this a little bit, but the performance of the drug is maybe better in the less-advanced patients. So just maybe if you can comment on that in terms of, is that consistent with what you're expecting? Is it different than what you are expecting? And also, as you think about the commercialization efforts, how does that, sort of, impact your thinking in terms of trying to get the patients much earlier in the disease?

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Okay. Thanks for the question, Vamil. So I'll ask Brenda to talk about the data and the subgroups and how we see performance in the less-advanced patient population.

Brenda Cooperstone - *Pfizer Inc. - SVP, Chief Development Officer, Pfizer Rare Disease*

So with respect to the more-advanced patient population or Class III, as for all patients with congestive heart failure, earlier treatment is better. I think that is uniformly understood. Even within the Class III, mortality was directionally correct, and we've already discussed with respect to CV hospitalizations that living longer with more severe disease could be reflected within the data. The trial itself was not designed to look for statistical

significance within each individual subgroup. We really just looked for directionality in order to support the overall conclusions. And furthermore, there will be further analysis within the secondary endpoints, biomarkers and exploratory endpoints that will support benefit at all stages of disease.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

So thanks. So maybe just I'll ask Paul to comment in just a minute about our commercialization efforts, Vamil. But just to say, I think the work to and the urgency to diagnose patients is very clear. I think the data certainly has supported as Brenda has just said most definitely a benefit of early diagnosis and treatment, which is not surprising for many forms of chronic disease, and that's what we see here. And so, I think, the efforts, frankly, that we'll put into place in order to make sure that we work with cardiologists and other healthcare professionals to identify and differentially diagnose these patients will capture in early patients as well as patients suffering from more severe forms of disease. Paul, would you like to add anything?

Paul Lévesque - *Pfizer Inc. - Global President, Pfizer Rare Disease*

Yes, while it's just a bit of what we covered earlier, but, obviously, we need the medicines to be approved, finalize our labeling, finalize the value proposition. Once that is done, I think that the awareness is going to be increasing and we're certainly permitted to remaining extremely active in educating the cardiologists, making sure that the ecosystem is optimal so that the patients can be referred to the centers of excellence so we have a plan. Our tradition in the cardiovascular medicines, cardiovascular field that we have with the Norvasc, the Lipitor, the Eliquis of the world makes us certainly in a good position to accelerate that development.

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

All right, thank you. Next question please, operator.

Operator

Your next question comes from Louise Chen from Cantor.

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

(inaudible) hereditary, and do you think the diagnosis of ATTR-CM will increase and why or why not, and why has diagnosis historically been so low? And then, the last question I had here is what percent of your practice is hereditary versus nonhereditary, and how do you expect this to change over time?

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Okay. I don't think we, sort of, caught the first question, but I think I heard one thing around how you see the -- how we see the diagnosis of ATTR cardiomyopathy increasing over time. And the second question was really around, I think, the mix of patients in clinical practice. I think that's what we picked up here. So, Brenda, maybe you could just like to touch on those questions, around the mix of patients, what do we see?

Brenda Cooperstone - *Pfizer Inc. - SVP, Chief Development Officer, Pfizer Rare Disease*

So the mix of patients in clinical practice, the epidemiology estimates that it's approximately 10% of ATTR cardiomyopathy would be secondary to the genetic variance and approximately 90% would be secondary to wild-type.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Okay. So, I think, in terms of how we see that developing. Obviously, our ability to find patients, we can only find the patients to the extent that the other numbers that Brenda just quoted proves to be accurate. Those are the patients that, obviously, we will then help physicians to discover. And I think, that really is the fundamental here that we are working with the best epidemiology that's available. But I think to your point about how we see the market developing, I think, undoubtedly, from everything we've heard here at the ESC today, the availability of a medicine that actually has data as compelling as we believe we have here, certainly is one of the factors that's very likely to motivate physicians to be able to diagnose and then ultimately offer treatment options for these patients. So thank you for the question.

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

Can we move to the next question please, operator?

Operator

Your next question comes from John Boris from SunTrust.

John Thomas Boris - *SunTrust Robinson Humphrey, Inc., Research Division - MD*

The first one just has to do with the value proposition and the 20-milligram dose priced at an annual basis of 75k. Since this is a new or different indication, can you just walk us through what percent of patients were treated with 20 versus 80? And does that imply that on a 20-milligram per unit basis an 80-milligram could potentially secure price in around 300k on an annualized basis? Second, how many centers are there in the United States that actually use the current diagnostic tool? If you could just quantify the number of treatment centers that actually have it? I would assume it's very, very low based on the number of patients that actually get diagnosed, and what do you have to do to be able to expand that going forward?

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Okay. Thanks for the question, John. So I'll ask Paul to talk about the work that we have been doing to identify diagnostic centers in the U.S. and also to make comments on pricing. And, I think, your second question was about the proportion of patients in the trial that were on 20 versus 80 milligram. Paul, first off?

Paul Lévesque - *Pfizer Inc. - Global President, Pfizer Rare Disease*

So the -- we -- our understanding today is there are just about 50 centers of excellence in the U.S. We suppose that this number is going to increase significantly with the enthusiasm related to the publication of this trial today. But also with the approval that will be coming early next year. So that's certainly something that is important. We have also found evidence that scintigraphy was more available in the different hospitals than we first anticipated. So all this to say that I believe that the diagnosis rate is going to improve over the years, and we will be committing to, obviously, carrying education programs that will make sure that these patients are identified and funneled through the centers of excellence. When it comes down to pricing, you have to understand that the 20 milligram is available related to polyneuropathy in many countries except the U.S., UK, Canada and Korea. So over there, that was linked to a value proposition that was made then with the data set that was presented. With the data set associated to ATTR-CM, we believe that the value propositions will be different, the targeted population will be different, and therefore, we are going to need to sit down with the health technology assessment bodies of the world, and, obviously, find a way for finding quick access for the patients. But we are committed to making sure that we come with creative solutions so that patients can have access to this medicine as fast as possible after approval.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

And, Brenda, question about the mix of patients on 20 versus 80 milligrams study?

Brenda Cooperstone - *Pfizer Inc. - SVP, Chief Development Officer, Pfizer Rare Disease*

Right. So within this trial, which enrolled 441 patients, randomization was 2:1:2 and that was twice as many patients on 80 milligrams as on 20. And then as many patients on placebo as were on 80 milligrams.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Thanks, Brenda. So maybe just one other comment just to, sort of, build what Paul mentioned about pricing and just to, sort of, emphasize. Obviously, we are in the very early days of really evaluating the value proposition for tafamidis in this indication. But the one thing that we do know is that given the median age in our study was 75, we expect approximately 75% of the targeted population fall under Medicare for reimbursement. And we intend to approach CMS with a creative value proposition to ensure that most patients with cardiomyopathy -- ATTR cardiomyopathy can have access to tafamidis as soon as possible after the introduction of this medicine. So that's something that's just very much fore -- at the forefront of our minds and we are going to be actively working on that as we engage with regulators in parallel with those payer discussions.

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

Great. Thank you for those responses. Next question please, operator.

Operator

Your next question comes from David Risinger from Morgan Stanley.

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

So I just wanted to go back to the high-level topic of developing the market. Could you just discuss the cost of scintigraphy so we can understand that a little bit better? And then the availability of it to cardiologists.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Thanks, David. So maybe I'll ask, Paul, again, just to talk about what we know of the development of the market and the cost of scintigraphy as a diagnostic test.

Paul Lévesque - *Pfizer Inc. - Global President, Pfizer Rare Disease*

So I don't have the exact cost of diagnosis, but this is one of the least expensive of the nuclear imaging tests that can be run. And the wide distribution of scintigraphy equipment across the U.S. leads us to believe that providing that we have an approved medicines with a clean label, we could actually have fast enthusiasm for diagnosis patient.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Okay, Thank you, Paul.

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

Next question please, operator.

Operator

Your next question is from Umer Raffat from Evercore ISI.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

First, do you think the 30-month trial duration underestimated the true mortality benefit with this drug? I'd be very curious about what you think of that. And then secondly, I was surprised to see the 400,000 to 500,000 patient estimate on your slide for the TTR cardiomyopathy. So I was curious first what's the source for that? I'd love to be able to read whatever paper that is. And then also, I noticed the footnote on that slide, which says 400,000-plus prevalence and it's for NYHA class II to IV whereas this trial was Class I to III. So I just wanted to get a better sense for what you think the true target population is.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Okay, so thanks for the questions, Umer. So I'll ask Brenda to talk about the 30-month duration and our views on that, we obviously don't want to speculate. And then I'll ask Brenda and Paul to comment on your second question as well. So thank you.

Brenda Cooperstone - *Pfizer Inc. - SVP, Chief Development Officer, Pfizer Rare Disease*

So with regard to the 30-month duration. Yes, it is certainly possible that with further follow-up, we will see further separation in terms of the mortality and therefore an increasing survival benefit, and we do have an ongoing open-label extension, which will give us further information with regard to the mortality in the longer term. Beyond that though, I can't really -- I don't have any further information.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Brenda, do you want to comment on the prevalence data? So with the -- you talked about an estimated prevalence that has reasonable content (inaudible) that you want to make any comments about the prevalence data that we have available?

Brenda Cooperstone - *Pfizer Inc. - SVP, Chief Development Officer, Pfizer Rare Disease*

No, just that the prevalence data that we have available to us is really based on multiple sources, where individual centers or regions have looked at the amount of patients who would test positive for amyloid for other when they have -- they come in for other diagnoses such as aortic stenosis or other types of congestive heart failure or pathology. And combining that with what we know from experts within the field then we put together our best estimate on an epidemiological model, but these numbers will certainly be refined over time as people become more knowledgeable about the disease and pursue better avenues for diagnosis.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Great. Thank you, Brenda.

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

Next question please, operator.

Operator

Your next question is from Jason Gerberry from Bank of America.

Jason Matthew Gerberry - *BofA Merrill Lynch, Research Division - MD in US Equity Research*

First question. Just your strategy for studying tafamidis or your thoughts on studying tafamidis in combination with some of the TTR knockdown agents given the relatively benign safety profile of tafamidis. It would seem like that's a possibility and one school of thought might be that the reduced benefit in Class III might be that these patients have already built up amyloid deposits and may be harder to show benefit with tafamidis but perhaps in combination with the TTR knockdown agent, perhaps, that makes sense. So in terms of, sort of, shoring up your longer-term positioning in the market, just kind of curious on your thoughts there. And secondly, will you include polyneuropathy in the -- is that included in the updated U.S. filing? Those are my two questions.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Great, thanks for the questions, Jason. So I'll ask Brenda to talk about the possibility of combination with other agents and how we see that.

Brenda Cooperstone - *Pfizer Inc. - SVP, Chief Development Officer, Pfizer Rare Disease*

So as of today, we are the only medicine that has been tested specifically in patients with cardiomyopathy. So it's difficult to comment on any of our competitors. I will say that the combination is certainly a possibility, but beyond that, there's really no information to inform further how practice may change in terms of the treatment for these patients.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Thanks, and in relation to your question, Jason, about possible polyneuropathy indication in the U.S. Obviously, given the excitement that we have about these, the first priority is to make sure that we can quickly file, and we hope gain approval for TTR cardiomyopathy in the United States. We are in active dialogue with the FDA in regard to that, and we are very excited about, hopefully, being able to bring tafamidis to that patient population as quickly as possible. In terms of a potential polyneuropathy indication, which as Paul mentioned in his response to an earlier question, we have a number of -- approval for a number of -- in a number of markets outside of the U.S. We certainly will look at opportunities to continue the dialogue with the FDA on the potential path forward for tafamidis in that indication and we'll engage the neurology division on the data from ATTR-ACT as well. And so there is a different division -- review division of the FDA than for the cardiomyopathy indication. So that's certainly something that we have every intention of doing. But our first priority is to make sure that we can, as swiftly as possible, bring tafamidis to the ATTR cardiomyopathy patient population just given the power of this data and the unmet need that exists in the marketplace. So thanks for the question, Jason.

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

Thanks, John. Next question please, operator.

Operator

Your next question comes from Steve Scala from Cowen.

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

I have a few questions. First, can you speak to formulation? We understand the soft gel is not ideal and if reformulation were required, how would this impact the timelines? Secondly, is Pfizer confident that one trial is sufficient for approval? And then thirdly, is there anything else in the pipeline from the FoldRx acquisition that investors have been overlooking?

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Okay. Thanks for the questions, Steve. So one question about formulation, one question about whether one trial is sufficient for approval and then another question about FoldRx. So I'll ask Brenda to talk about the view that have around the strength of these data and how we view the likelihood of approval. And I'll ask Paul to talk about the reformulation question.

Brenda Cooperstone - *Pfizer Inc. - SVP, Chief Development Officer, Pfizer Rare Disease*

So this particular protocol was done under special protocol assessment with the agency. So discussion about what was necessary for approval was actually had prior to conduct of the trial. So we are confident that we will be able to work with the agency to bring this medicine quickly to patients.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Great, thanks, Brenda. Paul, do you want to ask about the -- answer the question about formulation and any impact on the timeline?

Paul Lévesque - *Pfizer Inc. - Global President, Pfizer Rare Disease*

The 20-milligram capsule is already in the market in many places associated with the -- to polyneuropathy. This, to my knowledge, doesn't actually link to any -- is linked to any issue, and we are pursuing a 61 milligram that actually delivers 80 milligram as a supplement that will actually be filed with the agency as well, which is going to facilitate the use of the 80 milligram should that be the starting dose.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Last question was about FoldRx. Just to say plainly the -- by an order of magnitude, the most exciting asset that came out of that -- this acquisition was tafamidis. So thank you, Steve.

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

And, operator, can we take our last question, please.

Operator

Your final question comes from Greg Fraser from Deutsche Bank.

Gregory Daniel Fraser - *Deutsche Bank AG, Research Division - Research Analyst*

It's Greg Fraser on for Gregg Gilbert. I would like you to comment on whether the time to separation of the mortality curves differ between the wild-type and the hereditary patients? And then can you also comment on the regulatory strategy for the cardiomyopathy indication in Europe?

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Okay. Thanks for the questions, Greg. So I'll ask Brenda to comment about the time to separation on the mortality curves.

Brenda Cooperstone - *Pfizer Inc. - SVP, Chief Development Officer, Pfizer Rare Disease*

So thus far we really looked at the pool analysis across all subgroups. I can tell you that it looks consistent across all subgroups with respect to the time for separation.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

And in relation to regulatory timelines, we, obviously, don't disclose dates. We will inform our shareholders and the analyst community when we file. We have commented already about the engagement that we have had with the FDA and our expectations there. In the EU, I think, we just shared the same sense of urgency, and we are looking to file in the European Union at the earliest possible opportunity.

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

Great, thank you. And thanks to everybody for joining us today on the call today. Thanks to John, Paul, and Brenda on the Pfizer side.

John D. Young - *Pfizer Inc. - Group President of Pfizer Innovative Health*

Thanks, everyone.

Operator

Ladies and gentlemen, this does conclude today's conference. Thank you for your participation. You may now disconnect.