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PFE.N - Pfizer Inc to Review Oral GLP-1 Data Call

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PRESENTATION

Operator

Good day, everyone, and welcome to Pfizer's Analyst and Investor Call to review oral GLP-1 data presented at the European Association for the Study of Diabetes 2022. Today's call is being recorded.

At this time, I would like to turn the call over to Mr. Ronen Tamir, Vice President, Investor Relations. Please go ahead, sir.

Ronen Tamir - Pfizer Inc. - VP of IR

Thank you very much, and thank you all for joining us today. We're very happy to be presenting some exciting GLP-1 clinical data to you all.

Today, we will be making forward-looking statements that are subject to substantial risks and uncertainties. And I'd just like to remind you that these forward-looking statements speak only as of the webcast's original date, and we undertake no obligation to update or revise them in the future. You can find additional information on forward-looking statements in our SEC filing, including Forms 10-Q and 10-K, under the section labeled Risk Factors and Forward-looking Information and factors that may affect future results.

Now allow me to introduce you to your speakers. We have Aditi Saxena, Vice President and Clinical Research Head of Internal Medicine; Bill Sessa, the Chief Scientific Officer of our Internal Medicine Research unit; and Andy Schmeltz, Senior Vice President of Commercial Strategy and Innovation. And for our Q&A session, Aditi, Bill and Andy will also be joined by Jim Rusnak, Pfizer's Chief Development Officer for Internal Medicine and Hospital.

So with that, let me turn it over to Bill Sessa to begin.

William C. Sessa - Pfizer Inc. - SVP, Chief Scientific Officer, Internal Medicine

Thank you, Ronen, and thank you all for joining us today to discuss a truly exciting area of clinical development for Pfizer.

First, I wanted to remind you of the massive unmet need and market opportunity in type 2 diabetes and obesity, conditions that impact hundreds of millions of people worldwide that's continuing to grow over the next decade. There are also significant gaps in the current treatment paradigms. For example, less than 5% of patient's obesity receive medical treatment. And only about 50% of U.S. patients with type 2 diabetes are able to get their HbA1c below treatment goals.

Obesity, in particular, is a driver of comorbidities, including type 2 diabetes, and over 200 health-related complications that impact every organ system in the body. The most well characterized in obviously for obesity is cardiovascular disease, which impacts cardiovascular outcomes, the #1 cause of death worldwide.

We believe the GLP receptor, and GLP meaning glucagon-like peptide receptor, is a very promising target in obesity and type 2 diabetes, one that we think has untapped potential. We know that GLP, if the ligand for GLP receptor mediates insulin signaling and satiety in response to food intake, these are key drivers of both obesity and type 2 diabetes.

GLP receptor agonist to take by GLP RAs are a class of medicines that target the GLP receptor, have been shown to provide clinical benefits such as decreasing appetite, delaying gastric emptying and increasing insulin secretion, resulting in weight loss, glycemic control and reducing cardiovascular risk.

I'd like you to take you through the discovery story behind Pfizer's promising GLP receptor agonist candidates. They represent a tremendous achievement on behalf of our scientists at Pfizer. The GLP receptor was a challenging target in the drug industry plagued by failures to develop small molecule agonists. Pfizer's in-house expertise in small molecule design and medicinal chemistry enable the discovery of a potential best-in-class oral GLP agonist, danuglipron and PF-0781532 or for conventional purposes, 1532 for today's call. To overcome the challenges associated with the discovery of GLP receptor agonists, we developed a sensitized screening assay that lowered the activation energy barrier for GLP-1 receptor, increasing assay sensitivity and facilitating detection of agonists. Using this high -- nontraditional high-throughput screen being screen close to 3 million compounds, followed by careful medchem structure activity relationship optimization ultimately increasing potency over about 6 logs.

Additional optimization for pharmacologic potency, safety and other attributes led to our 2 oral GLP agonist candidates, which are full agonist at the GLP receptor similar to injectable peptides, but of course, with the convenience of oral administration.

As you can see on the right side, data from Phase 1 single ascending dosing studies in healthy volunteers support a twice-daily dosing for danuglipron of a half-life between 4.3 to 5.7 hours, further optimization of drug attributes yielded 1532 with a longer half-life of 18 to 21 hours, which supports once-daily dosing may provide benefits, including improved compliance that may lead to better health outcomes.

Now with this background, I'd like to turn it over to Aditi Saxena, who will walk us through some of the exciting clinical data recently presented at EASD. Aditi?

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

Thank you, Bill. Today, I'll be providing an overview of the clinical data from studies of our oral -- Pfizer oral small molecule GLP-1 receptor agonist, which were presented at the EASD 2022 sessions. We had 3 presentations at EASD, 2 of which covered 2 separate Phase 2 studies with danuglipron and one covering the Phase 1b study with our once-daily oral GLP-1 receptor agonist PF-07081532, which will be referred to as 1532.

First data we'll review is from the 16-week Phase 2b dose-ranging study of danuglipron in participants with type 2 diabetes. This Phase 2b study was a randomized placebo-controlled parallel group dose-ranging study to examine the effect of danuglipron over 16 weeks on the efficacy, safety, tolerability and pharmacokinetics in adults with type 2 diabetes. The primary efficacy endpoint was changed from baseline in HbA1c at week 16, and key secondary endpoints were changes from baseline and fasting plasma glucose, body weight -- and body weight at week 16.

This was an outpatient study conducted globally during the earlier stages of the pandemic from July 2020 to July 2021. 411 participants were randomized and dosed, of whom 77% or 316 participants completed the double-blind treatment phase.

The study design scheme are presented here. After the screening and placebo run-in periods, participants were randomized to placebo or 1 of 5 doses of danuglipron. For participants randomized to danuglipron doses of 40 milligrams BID and above, a prespecified dose escalation scheme was incorporated, and weekly dose escalation steps to reach the -- and have weekly dose escalation steps to reach the randomized target dose. For participants randomized to higher target doses of danuglipron, the target was reached later relative to lower doses. After dosing was completed, participants progressed to the follow-up period, which lasted approximately 1 month.

In this study, over 16 weeks, there were dose responsive declines in HbA1c across all of the danuglipron arms compared with placebo, with declines up to almost 1.2% at the highest dose of danuglipron. The right panel shows the time course of the changes from baseline in HbA1c over the dosing duration. Declines in the danuglipron arm separated from the placebo arm as early as week 2 of the study and continue to increase in magnitude in a dose-dependent manner over the duration of the study.

Significant reductions were also observed in fasting plasma glucose, with reductions up to approximately 32 milligrams per deciliter over 16 weeks. Similar to the pattern with HbA1c, significant reductions in fasting plasma glucose with the danuglipron arms were observed within 2 weeks of dosing.

Significant declines in body weight were also observed over 16 weeks at the 2 higher doses of danuglipron compared with placebo. Declines in body weight were observed throughout the dosing period and had not yet reached a plateau at the highest dose of danuglipron by week 16. The key takeaway here is that study participants saw weight loss benefit even within the first few weeks, the experience of which can often help with compliance in the face of initial mild GI side effects.

Now I'd like to touch very briefly on the data from our 12-week Phase 2 study of danuglipron. Data from this Phase 2 study were previously reported, and the full 12-week data will be available after the call, and the slides posted to our website. But I do want to take a moment to highlight the HbA1c and body weight reduction seen after 12 weeks of treatment with danuglipron in the study, which were significant compared to placebo.

We conducted the study to refine our understanding of the top doses used in the 16-week study, and we believe that these data provide a better picture of danuglipron's potential efficacy at the higher dose levels. We see reductions here of up to 1.5% -- 1.57% in hemoglobin A1c and 5.4 kgs or 5.7% change for baseline in body weight.

Now I'll provide an overview of the Phase 1b study data with our once-daily GLP-1 receptor agonist 1532. This Phase 1b study was conducted as an inpatient study at 2 clinical research unit sites in the United States. This randomized double-blind placebo-controlled study was the first time that multiple doses of 1532 were administered with the objectives to assess safety, tolerability, pharmacokinetics and pharmacodynamics of escalating multiple oral doses of 1532 in type 2 diabetes and obesity. Six cohorts were enrolled, of which 5 cohorts were participants with type 2 diabetes, and one cohort was nondiabetic participants with obesity. 1532 or placebo were administered once daily with breakfast. Dose titration was used to achieve higher doses of 1532. Dosing took place during the early stages of the COVID-19 pandemic from mid-2020 to mid-2021, and the study design is provided here. Across cohorts 1 through 4, participants with type 2 diabetes were randomized to target doses ranging from 10 milligrams up to 120 milligrams or matching placebo with a dosing duration of 28 days. In cohort 5, type 2 diabetes participants were randomized to 180 milligrams or matching placebo with a dosing duration of 42 days, and a single cohort of obesity participants were randomized to either 180 milligrams or placebo over 42 days.

Here, we see the pharmacokinetic profile for 1532, which is predictable and linear with proportional increases in Cmax and AUC across the dosing range administered with a consistent half-life across the doses administered suitable for once-daily dosing.

Here, we see robust declines in mean daily glucose with 1532 across the dose range with dose-dependent reductions in mean daily glucose. Mean daily glucose was utilized as a comprehensive assessment of glycemic control in the study. Plasma glucose was assessed over a 24-hour period, both at baseline prior to dosing and at the end of the 4- to 6-week dosing period as a pharmacodynamic biomarker for this study. These robust

dose-dependent declines were observed at all doses of 1532 over the 4- to 6-week dosing period in patients with type 2 diabetes, and all of the dose levels were statistically significant relative to placebo. Declines up to 99 milligrams per deciliter were observed.

Based on these results from mean daily glucose, we anticipate that 1532 could have very robust Hba1c lowering over a longer dosing duration.

Robust declines in fasting plasma glucose were also observed with 1532 over 4 to 6 weeks, with model declines up to 86 milligrams per deciliter over the dosing duration. This was equivalent to observed average reductions from baseline up to 79 milligrams per deciliter over 28 days and up to 102 milligrams per deciliter over 42 days. By day 28, all of the 1532 treatment groups above 10 milligrams had an observed average fasting plasma glucose of less than or equal to 126 milligrams per deciliter approaching nondiabetic thresholds.

We also saw dose-responsive declines in body weight with 1532 over the same dosing duration relative to placebo, with higher doses of 1532 declines in body weight up to 5.1 kilograms were demonstrated in participants with type 2 diabetes and up to approximately 5 kilograms in nondiabetic participants with obesity over 6 weeks. These declines were equivalent to approximately 5.5% decline in body weight in the type 2 diabetes population and a 5.2% reduction in the obesity population.

Similar to danuglipron, the key takeaway here is that study participants saw weight loss benefit even within the first few weeks, the experience of which can help with compliance when experiencing mild GI side effects.

So in summary, administration of both danuglipron and 1532 in clinical studies led to dose-dependent reductions in HbA1c glucose and body weight. Both investigational drugs demonstrated a safety and tolerability profile consistent with the GLP-1 mechanism of action, with the most common adverse events being mild in intensity and gastrointestinal in nature. And critically, unlike currently available oral treatments, study participants were not required to fast while taking danuglipron or 1532.

As we've discussed today, we've seen exciting data in the recently completed studies of both danuglipron and 1532. We believe both candidates are promising novel oral small molecule GLP-1 receptor agonist. We want to ensure we possess robust data to inform the candidate, doses and profile that advances to Phase 3.

To do this, we expect to initiate a Phase 2 program with 1532 in the fourth quarter of 2022 and to expand our Phase 2 study of danuglipron in nondiabetic patients with obesity to include a monthly titration cohort expected to complete in the second half of 2023. Our Phase 2 programs will evaluate both assets in type 2 diabetes with obesity, and we plan to advance the optimal candidate based on efficacy, tolerability and dosing to Phase III studies and the indications of type 2 diabetes and obesity expected to begin in 2024.

Now I'll turn it over to Andy Schmeltz.

Andy Schmeltz - Pfizer Inc. - SVP, Commercial Strategy & Innovation

Thank you, Aditi. I'd like to conclude our speaking program by sharing how we believe a small molecule oral GLP-1 could be a breakthrough medicine for patients.

There has been significant innovation in the type 2 diabetes and obesity treatment spaces with the development of the GLP-1s, which, as we've seen, offer substantial A1c lowering in weight loss. And the GLP market is growing rapidly, now at \$25 billion globally with 30% growth versus last year. This class growth is fueled by demonstrated cardiovascular outcomes in type 2 diabetes and treating guideline updates that have moved GLP-1s earlier in the treatment paradigm.

And while historically, there have been reimbursement challenges for obesity medications, we've been monitoring the payer environment. Our market research with payers indicates that there is significant increase in U.S. commercial payer coverage over the past year, which we believe is here to stay.

We are seeing strong growth in the GLP-1 market and a clear patient preference for oral dosing that may lead to a significant share capture for oral GLP-1s. The data shown here come from market research with approximately 300 patients living with type 2 diabetes on the left, obesity shown on the right, or both conditions shown in the middle. About 1/4 of respondents for the first 2 groups, patients with type 2 diabetes or both type 2 diabetes and obesity indicated that they are currently taking an injectable GLP-1 medicine. Patients were asked about their preference for 3 forms of GLP-1 medication, a twice-daily oral without fasting shown in dark blue, a once-daily oral with fasting in light blue and a once-weekly injectable shown in teal.

As shown in dark blue, across all patient types, the clear preference is for a simple oral GLP-1 dosing without fasting restrictions. Now note that a once-daily oral without fasting wasn't provided as an option in this market research. However, that appears to be the emerging profile of PF-1532.

In summary, we're excited by danuglipron and PF-1532, 2 candidates in Phase 2 with the potential to offer a uniquely differentiated profile and secure a significant share of the oral GLP-1 market.

The reasons to believe here are very clear. Number one, GLP-1s are rapidly emerging as an increasingly compelling option for the treatment of type 2 diabetes and weight loss. Number two, we believe an oral GLP-1 without fasting restrictions would be in a prime position poised for class leadership. And number three, we're particularly enthusiastic about the promise of Pfizer's 2 shots on goal to deliver a potential breakthrough medicine for these patients.

That concludes today's prepared remarks. So let me turn it back to Ronen for the Q&A.

Ronen Tamir - Pfizer Inc. - VP of IR

Thank you, Andy. Operator, we can start the Q&A.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) And our first question will come from Umer Raffat with Evercore ISI.

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

I have 3 quick ones today, if I may. Perhaps, first, could you lay out for us why the Phase 2b has less than 4-kilogram weight loss at week 12, but the Phase 2a has 5.4 kilograms? Maybe there's something on baseline, if you could expand on that, number one.

Number two, could you also get into the tolerability profile more particularly? And I ask that because when we last saw the big data updates you guys showed, there was up to 12 beats of heart rate increases. There was a real GI tolerability issue, up to 80% vomiting, 44% diarrhea. And it looked like doses above 50 milligrams BID in danuglipron were going to be very hard. But I noticed you guys are persisting with those doses right now, not only in the trials showed today, but also in the upcoming obesity study where you're actually dialing it up to all the way up to 200 milligrams BID. So I'm just trying to understand how you're threading the needle on tolerability.

And finally, if you could expand on any changes in titration and whether they're actually helping so far or not.

Ronen Tamir - Pfizer Inc. - VP of IR

Thank you, Umer. Aditi, why don't you start?

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

Yes, I can take those. So thanks for the great questions. So in terms of the weight loss differences between the Phase 2b and the Phase 2a study. So I think I mentioned that the Phase 2b study really began at the earliest stages of the pandemic. We do believe that people's background behavioral patterns were slightly different at that time relative to -- when our Phase 2a study began, which was about 6 months later. They ran in parallel to each other, but they were slightly staggered. And so we do believe that our Phase 2a study may have represented people starting to return to their normal behavior patterns.

We also explored multiple dosing titration schemes with those highest doses. So it just -- it offered more opportunity to understand what those doses could do in a relatively short period of time.

Also, the Phase 2b was conducted globally, so across multiple regions, whereas the Phase 2a was conducted in the U.S. So it does speak to sort of some differences in the study population. Do believe that the Phase 2a presents some very compelling data regarding the weight loss potential of the compound at the highest doses and a short duration of time. So we do believe we've seen across multiple doses in that study. So we do believe that, that is representative of the effects of dani with those doses.

Coming to the tolerability profile. So you remember our Phase 1b data really well. That was similar to the Phase 1b that we presented for 1532. It was the first time that multiple doses were administered in an inpatient setting. We were pushing the dose in that Phase 1b, and we had rapid titration -- more rapid than what we took into our outpatient studies where doses were being increased in our inpatient setting every 2 to 4 days. And in that setting, we did see that with increased doses, there were increased incidents of GI adverse events. That was not unexpected, honestly, with this mechanism. And so we did believe that slowing down the titration would improve the tolerability profile, which it did in an outpatient setting. We do believe that additional improvements will be possible with slower titration. That has been shown across the GLP-1 class. We do believe that our agents will have a similar profile with slower titration.

And then I believe the last question was how we would be changing the titration -- is that -- if I'm remembering correctly. And so I think I spoke to it, which is we are expecting to take in slower titration schemes to our longer duration studies.

Operator

Our next question will come from Chris Shibutani with Goldman Sachs.

Chris Shibutani - Goldman Sachs Group, Inc., Research Division - Research Analyst

(inaudible) the future and the (inaudible) opportunity on this (inaudible). Any recommendation how you would position these products? What do you think (inaudible) or are you talking about (inaudible) injectables to realizing that still (inaudible) clinical data, how you see the position (inaudible)

Ronen Tamir - Pfizer Inc. - VP of IR

Chris, I'm sorry, I'm having a really hard time hearing you. I think that your question was about the commercial opportunity and how are we going to position our GLP-1, and I'm going to hand it over to Andy. But operator, if you can get a clearer line. So Chris may repeat his question, I would appreciate that.

Chris Shibutani - Goldman Sachs Group, Inc., Research Division - Research Analyst

Yes. No, I think you got the tone. Apologies I'm at the airport. Yes, looking for your perspective on the positioning and what the commercial opportunity could look like given that the landscape will have different offerings, including presentations oral subcu, ID, et cetera.

Ronen Tamir - Pfizer Inc. - VP of IR

Andy?

Andy Schmeltz - Pfizer Inc. - SVP, Commercial Strategy & Innovation

Sure. Thanks for the question, Chris. So let me try to frame it out. As I mentioned, the global GLP-1 class is already sizable at about \$25 billion, and it's growing at a 30% rate. Yet, GLP-1 only represents about 17% and 14% of type 2 diabetes and obesity categories, respectively, in the U.S. So with continued adoption and expansion in these areas as well as just the growing prevalence of these diseases, we could envision the GLP-1 class to be a \$90 billion opportunity perhaps over the next 10 years. And with the breakthrough potential of an oral option, such as danuglipron or PF-1532, with compelling benefit risk, vis-a-vis the alternatives and without a food effect, it's not that hard to imagine oral GLP-1s, and in particular, a potential Pfizer medicine supported by our industry-leading sales, marketing, medical, account management access teams capturing a sizable share of appropriate patients across type 2 diabetes and obesity. So that's kind of our current vision of how the category will evolve. The role of orals, we think, is quite compelling with the right profile. And needless to say, we're very excited about the potential here that we're working on. Thanks for the question.

Operator

Our next question comes from Louise Chen with Cantor.

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

Congrats on the data. So could you provide more color on what gives you confidence that payers will cover obesity as an indication given how chronic it is for a lot of people?

And then secondly, would you consider advancing one of your candidates for type 2 diabetes and one for obesity? Or is it either or when you move forward with these 2 different molecules?

And then last question is, what do you think is a competitive profile for HbA1c lowering and weight loss? Or what would your ID like to see to be competitive in the market?

Ronen Tamir - Pfizer Inc. - VP of IR

Thanks, Louise. So Andy, why don't you take the payer question, and Aditi, you can take the -- which product we're going to advance forward and if we're going to have one for different indication. And Bill, why don't you take the last one about that profile?

Andy Schmeltz - Pfizer Inc. - SVP, Commercial Strategy & Innovation

Sure. So let me start with your question regarding the payer environment. We have been engaging with payers on a regular basis, conducting market research, getting their feedback in terms of reimbursement. And in our most recent primary market research, the feedback was that particularly in the obesity market, given the step change in efficacy that's been demonstrated now, not a 5% weight loss, but a 15% weight loss as well as the promise of potentially cardiovascular outcomes in this trial on the -- in this category in obesity on the horizon with the trial reading out, that, that really changes the paradigm and that commercial plan coverage will change significantly. So that's our perspective now. And of course, as things play out, we'll continue to monitor to affirm that, that's an appropriate assumption. Aditi?

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

Thanks, Andy. So the overall plan is really to advance an agent for both type 2 diabetes and obesity. So I think that, that was speaking to the second question and not necessarily to dissociate the 2 development paths by compound. So the intent is really to take forward the optimal agent dosing scheme for the 2 indications.

And in terms of the competitive profile, I mean, we're really seeing that the oral -- an oral small molecule GLP-1 receptor agonist with all the benefits of the mechanism would really make a big difference in the care of patients with type 2 diabetes and obesity, represents ideally a very easy-to-take medicine that could offer multiple benefits from glycemic control to weight loss.

And I'll see if Bill or Jim maybe wanted to offer any additional comments.

William C. Sessa - Pfizer Inc. - SVP, Chief Scientific Officer, Internal Medicine

Yes, I could chime in here. I think one of the clinical profile of noninferiority to injectables on A1c as well as weight is the beneficial profile. And we think we can be potentially best-in-class for orals for type 2 diabetes. So that's one of the aspirational goals.

Operator

Our next question will come from Mohit Bansal with Wells Fargo.

Mohit Bansal - Wells Fargo Securities, LLC, Research Division - Senior Equity Analyst

Two, if I may, one is -- one may be related to the safety of the once-daily oral. So from the presentation, we saw that at higher doses, they were higher -- there was higher nausea, vomiting, all those GI side effects. And there was a little bit of -- the trial was -- the dose escalation was a little bit rapid. So could you talk -- speak a little bit about that? And how do you think it could pan out with a more slow dose titration?

The other question, I just wanted to probe a little bit more on the comment you just made, noninferior data versus injectable GLP-1. Do you think you really need that given it is -- it may be an oral? Do you think a little bit -- inferior data would be sufficient for an oral to become the first-line treatment ahead of injectables here?

Ronen Tamir - Pfizer Inc. - VP of IR

Aditi, why don't you start?

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

Sure. Thanks. So I'll speak to the safety and tolerability profile of 1532. So with this mechanism, it's typically expected to see dose-dependent increases in GI tolerability. That's not a surprise with the mechanism of action. And so we did expect that higher doses would have a higher incidence of GI side effects relative to lower doses. We do believe that with slower titration in an outpatient setting, we'll be able to optimize the tolerability of the higher doses of 1532. And our lower doses actually was well tolerated.

Our lowest dose had absolutely no nausea, no vomiting. Several lower doses had no vomiting at all. So I think that we really see that this profile is attractive, and that with slower titration and outpatient dosing, we'll see a tolerability profile that will be very much satisfactory. Thank you.

I think there was a second question, too, about noninferiority. I don't know, Bill, you wanted -- Bill or Jim wanted to take that one.

Jim Rusnak - Pfizer Inc. - SVP, Chief Development Officer, Internal Medicine & Hospital

Yes, I could take that one, Aditi. Thanks. So I think that we're very excited about the profile of these molecules. And clearly, the data that Aditi shared around 1532 with the changes and the reductions of mean daily glucose and fasting plasma glucose is -- once those are extrapolated out and measured with A1c over longer course trials, I think that we're going to actually have a very substantial reduction in hemoglobin A1c, and that will provide a very beneficial profile. In addition, we will couple that with a more protracted dose escalation strategy to really optimize the benefit risk.

Operator

Our next question will come from Evan Seigerman with BMO Capital Markets.

Conor MacKay - BMO Capital Markets, Research Division - Research Analyst

This is Conor MacKay on for Evan. Congrats on the data. I have a couple of questions. First, would you be able to comment a bit more on how you're thinking about the Phase 2 trial design for 1532? And then also, would you consider pursuing any other indications outside of diabetes and obesity for these molecules?

Ronen Tamir - Pfizer Inc. - VP of IR

Thank you. Bill, why don't you take this question?

William C. Sessa - Pfizer Inc. - SVP, Chief Scientific Officer, Internal Medicine

Aditi might be better. Aditi, can you take this question?

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

Sure. So we are anticipating bringing in slower titration schemes to support 1532's Phase 2 study in type 2 diabetes and obesity. So we'll have a longer duration of dosing, but we are anticipating getting started later this year and hoping to have data to support Phase 3 start in 2024. So I think some of the details of the study will be forthcoming. But I think in high level, you'll see longer dosing durations exported with danuglipron really to explore those slower titration schemes and get up to higher doses.

Jim, did you have any additional comments?

Jim Rusnak - Pfizer Inc. - SVP, Chief Development Officer, Internal Medicine & Hospital

Just we will be starting this in the fourth quarter. It will be a single trial, and we'll be looking at both diabetes as well as nondiabetic obese patients.

Operator

Our next question will come from David Risinger with SVB Securities.

David Reed Risinger - SVB Securities LLC, Research Division - Senior MD

Can you hear me?

Ronen Tamir - Pfizer Inc. - VP of IR

Yes.

David Reed Risinger - SVB Securities LLC, Research Division - Senior MD

This is very helpful. I have a few questions, please. First, with respect to the next-gen 1532 candidate's profile, clearly, the differentiation is once-daily dosing versus twice daily. But could you expand on any other differentiating features?

And then with respect to thinking about that once-daily potential, is that only with 1532?

And then finally, the slide indicates that you're planning a Phase 2b study in diabetes and obesity to initiate in the fourth quarter of '22. Should we expect top line results from that about 2 years later? Or would you envision a different timeline to obtain top line results?

Ronen Tamir - Pfizer Inc. - VP of IR

Thanks, David. Aditi, why don't you start? And...

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

So in terms of the profile of 1532 relative to danu, so it is -- as you saw with the pharmacokinetic profile, it is suitable for once-daily dosing that at this stage appears to be the primary differentiating factor. We do have a goal for bringing forward a single asset with once-daily dosing. And so it's important to note actually that we have tested other formulations of danuglipron that did support once-daily dosing as well. Those were tested in our Phase 1b study. So those remain an option for the danuglipron asset as well.

But we do believe that 1532 certainly has a PK profile at its outset that is suitable for once-daily dosing, and that was what we've taken into the clinical studies, and we'll be exploring in the upcoming Phase 2.

Perhaps I'll let Jim answer the plans for the Phase 2 study.

Jim Rusnak - Pfizer Inc. - SVP, Chief Development Officer, Internal Medicine & Hospital

Thanks, Aditi. Yes. With respect to our Phase 2b study, as I mentioned, it will be in both type 2 diabetics as well as obese nondiabetic patients. It will be initiated in the fourth quarter of this year, and we plan to have the top line report out for that in the first quarter of '24.

Operator

Our next question will come from Carter Gould with Barclays.

Carter Lewis Gould - Barclays Bank PLC, Research Division - Senior Analyst

This has been very helpful. I want to ask kind of 2 bigger picture questions. Just given sort of the sort of arms right across diabetes and obesity, just from a franchise approach, do you think longer term, having just sort of GLP-1, albeit oral will be enough here? Or I guess against a world where there's increasing duel in tri-agonist, are you going to have to have your hand, I guess, in multiple pots there? And if there are any internal efforts at Pfizer on those fronts, could you highlight those?

And then you highlighted on the slides from an interest in fixed dose combinations. As you think of then about potentially rolling those out, is that something you think you be able to do in Phase 2? Just thinking about the appropriate timing for those efforts.

Ronen Tamir - Pfizer Inc. - VP of IR

Thanks, Carter. Andy, why don't you take the first question? And Jim, you can take the second one.

Andy Schmeltz - Pfizer Inc. - SVP, Commercial Strategy & Innovation

Sure. So Obviously, these patients are taking multiple medicines, and there is a possibility for fixed dose combinations, co-formulations and the optimal regimen choice, that's definitely right up our alley. And I'll let maybe Jim comment more there.

But to your -- I think the core of your question, which is this is a pretty competitive environment. You referred to it as an arms race. I mean I would just say that we're undeterred by the competition, and we really look forward to engaging in the best interest of patients to commercialize a potentially breakthrough medicine for type 2 diabetes and weight loss. And we have a proven track record competing successfully in the competitive cardio metabolic environment over the last 25 years. And we've done a pretty good job of bridging initially specialist-driven therapies into a primary care setting.

Our track record with Norvasc and Lipitor many years ago, and more recently, with Eliquis and VYNDALIQ in addition to proven success in many competitive situations across all our major therapeutic areas. So we're excited to have the opportunity to engage and to demonstrate leadership in this space.

Jim, do you want to add on to the question on combinations?

Jim Rusnak - Pfizer Inc. - SVP, Chief Development Officer, Internal Medicine & Hospital

Yes. Thanks, Andy. I mean for -- we are from a development perspective, it's a little bit early for us to speculate on the complete development program for GLP-1s as well as fixed dose combinations that may have very important implications into life cycle management. But obviously, the opportunity to combine these oral agents with other very prominent mechanisms in this space would be highly advantageous. And I think that we can provide those updates in due course.

Operator

Our next question will come from Geoff Meacham with Bank of America.

Joseph Thomas - BofA Securities, Research Division - Research Analyst

This is Joe Thomas on for Geoff Meacham. I just have 2 related questions. I was wondering if you can provide some more clarity on the titration dosing scheme at dose levels that you might move forward into the Phase 3. And then related to that, are you expecting to see greater magnitude of HbA1c and weight loss in trial to go beyond 16 weeks?

Ronen Tamir - Pfizer Inc. - VP of IR

Thanks, Joe. Aditi, why don't you take that?

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

Sure. So I did present sort of the target doses that have been tested in Phase 1b, and most of our titration schemes really began in that Phase 1b study at 10 milligrams. We are using those clinical data to develop the titration schemes for the Phase 2 study. So it's very much informed by that. But there are additional steps, et cetera, that will be tested there that will really allow us to pick the optimal paradigm to take into Phase 3. And so those will be available once we have started the study.

I think that in terms of greater HbA1c and body weight loss, we know with this mechanism that you do need longer durations to see the full effects on HbA1c and body weight typically sort of moving out to sort of more of the 6- to 9-month time frame. So our longer-duration studies will be able to really show us what the compound can do in Phase 2.

I don't know, Jim, if you have any additional comments on that.

Jim Rusnak - Pfizer Inc. - SVP, Chief Development Officer, Internal Medicine & Hospital

Actually, I think that you've covered that well, Aditi. Thank you.

Operator

(Operator Instructions) And our next question will come from Robyn Karnauskas with Truist Securities.

Nishant Shailesh Gandhi - Truist Securities, Inc., Research Division - Research Analyst

This is Nishant on for Robyn. We have a couple of questions. So number one is considering 1532 once daily, which would have better compliance, would you consider advancing that versus danuglipron in Phase 3 even if the data is, let's say, not superior to danuglipron?

And second one is we are in the price reform act era, which is being effective in 2026. So how do you take that into consideration to develop an oral in this environment?

Ronen Tamir - Pfizer Inc. - VP of IR

I'm sorry, I cannot understand the second question. Can you repeat that?

Nishant Shailesh Gandhi - Truist Securities, Inc., Research Division - Research Analyst

Yes. With price reform act, the bill passed and it's going to be effective in 2026, so how do you take that into consideration to develop oral medication in this environment?

Ronen Tamir - Pfizer Inc. - VP of IR

Thank you. Aditi, why don't you take the first question?

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

Sure. So we did talk about 1532's pharmacokinetic profile relative to danu, and it is suitable, and it's standard formulation for once-daily dosing. We do a once-daily formulation for danuglipron that's been tested in our Phase 1b study. So we do have an opportunity to develop that potentially if that were the compound to go forward. So we don't believe that we -- necessarily that the decision would be made only on -- whether or not the

compound itself is once daily, we would be able to be -- we would be hoping to bring forward a once-daily profile for either one. So that's the answer. I think -- I don't know, Ronen, if you had for the second question, who would field that one.

Ronen Tamir - Pfizer Inc. - VP of IR

Andy, would you take the second question?

Andy Schmeltz - Pfizer Inc. - SVP, Commercial Strategy & Innovation

Sure. I think you're referring to the pricing and reimbursement environment in the U.S. post implementation of the Inflation Reduction Act. And certainly, our eyes are wide open to the implications of that legislation going into effect. And we're modeling in our forecast and expectations the forward environment for pricing and certainly expect there to possibly be some downward pressure on pricing in the future, but we're taking that into account in our modeling.

I think there's also the recognition with capping out-of-pocket costs for patients, particularly Medicare, that, that also has a little bit of a balancing effect as well. So that's our current perspective. And of course, we'll continue -- the most important thing is the profile of the medicine playing out as we continue along the development path. Thank you.

Operator

Thank you. At this time, there are no further questions. So I would like to turn it back to our speakers for any additional or closing remarks.

Ronen Tamir - Pfizer Inc. - VP of IR

Thank you, everybody, for joining us today. And as a reminder, you can find the scientific slides represented in the conference on our website in the IR section.

And with that, I would like to wish everybody good afternoon, good night, and have a great day.

Operator

Thank you, ladies and gentlemen. This does conclude today's teleconference and webcast. We appreciate your participation, and you may disconnect at any time.

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