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EDITED TRANSCRIPT

MRK.N - Merck & Co Inc at AHA Investor Event

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OVERVIEW:

Company Summary

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PRESENTATION

Operator

Welcome to the Merck & Co., Inc., Rahway, New Jersey, USA AHA Investor Event. (Operator Instructions) This call is being recorded.

If you have any objections, you may disconnect at this time. I would now like to turn the call over to Mr. Peter Dannenbaum from Senior Vice President, Investor Relations. Sir, you may begin.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Thank you, Ivy. Good evening, and welcome to Merck's investor event coinciding with the American Heart Association Scientific Sessions 2025. Thank you to those of us here in New Orleans and also to those participating via the webcast. We appreciate your interest in Merck.

Before we get started, I'd like to remind you that some of the statements that we make today may be considered forward-looking statements within the meaning of the safe harbor provision of the US Private Securities Litigation Reform Act of 1995. Such statements are made based on the current beliefs of our company's management and are subject to significant risks and uncertainties. If our underlying assumptions prove inaccurate or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Our SEC filings, including Item 1A in the 2024 10-K, identify certain risk factors and cautionary statements that could cause the company's actual results to differ materially from those projected in any of our forward-looking statements made today. The Merck & Co., Inc., Rahway, New Jersey, USA undertakes no obligation to publicly update any forward-looking statements.

During today's call, a slide presentation will accompany our speakers' prepared remarks. These slides and our SEC filings are all posted to the Investor Relations section of our company's website.

Now moving to the agenda. Speaking on today's call will be Dr. Dean Li, President, Merck Research Laboratories; Dr. Joerg Koglin, Senior Vice President, Head of General and Specialty Medicine Global Clinical Development; and Jannie Oosthuizen, President, US Human Health.

The full biographies of the speakers can be found in the appendix of the slide presentation.

Dean will start our prepared remarks with an overview of our cardiometabolic and respiratory portfolio. Joerg will then highlight the enlicitide data presented at AHA and our development strategy. And Jannie will conclude by discussing how enlicitide fits into Merck's effort to address the silent CV epidemic.

Our upfront remarks will take about 30 minutes, after which we will turn to Q&A. Kshama Roberts, Senior Vice President, Global Pharmaceuticals, is also here to assist in responding to potential questions.

With that, I'll turn the stage over to Dean.

Dean Li - *Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories*

Thank you, Peter. Thank you very much, and thank you for joining us in the room and online. Welcome to our investor event in conjunction with the American Heart Association Congress in New Orleans. I am privileged to share the stage with my colleagues across both our research and commercial organizations. And I'm very much looking forward to provide an overview in sharing my enthusiasm for Merck's cardiometabolic and respiratory portfolio.

We have built a broad cardiometabolic and respite to our portfolio that can redefine how these diseases are treated. Starting left to right, for WINREVAIR, we are very pleased with the impact WINREVAIR is having in the real world with positive results from both ZENITH and HYPERION, WINREVAIR continues to generate a wall of data. We look forward to additional opportunities, including showing results of the Phase 2 CADENCE study and providing updates on the development of the auto-injector.

Next, to Ohtuvayre, it is the first novel mechanism for inhaled maintenance treatment of COPD in more than two decades. As a dual inhibitor PDE3 and 4, Ohtuvayre has both bronchodilatory and nonsteroidal anti-inflammatory properties. The strong Phase 3 data culminated in FDA approval in June 2024. There is an ongoing Phase 2 trial in non-cystic fibrosis bronchiectasis, which has a primary completion date of September 2026.

And then for enlicitide, we were pleased to share compelling data this weekend for enlicitide, our oral PCSK9 inhibitor. We now have three positive pivotal trials from the CORALreef program. This weekend, we presented data from the CORALreef Lipids study as well as a CORALreef study focused on familial heterozygous hypercholesterolemia. This has the potential to be the first choice, add-on lipid-lowering therapy with monoclonal antibody-like efficacy. We expect filings to begin in early 2026, and longer term, enlicitide has the potential to be an anchor for combination therapy.

The focal point of this event and the data at AHA is WINREVAIR and enlicitide. Evidence continues to accumulate for WINREVAIR's strong clinical benefit across a broad spectrum of patients with pulmonary arterial hypertension. WINREVAIR has generated positive clinical data demonstrated by the sequential studies published in the New England Journal of Medicine. WINREVAIR is having a real impact on patients and has the potential to transform the treatment of PAH.

I'm pleased with the data shared for WINREVAIR this weekend presented by Vallerie McLaughlin from the University of Michigan. In these data, there was a pooled post-hoc analysis from all three studies that show the effect of WINREVAIR on major morbidity and mortality outcomes in a broad range of the population. There was a 75% reduction in the risk of composite morbidity and mortality endpoint. There was a 56% reduction and risk of lung transplantation or death and a 51% reduction in the risk of death.

On the right is a ZENITH label update for the expanded indication. WINREVAIR is now the first PAH therapy with an indication that includes components of the clinical worsening events hospitalization for PAH, lung transplantation and death.

Ohtuvayre is the first novel mechanism for inhaled maintenance treatment of COPD in more than 20 years in an area with significant unmet need. It is the only product to combine bronchodilatory and nonsteroidal anti-inflammatory properties in a single molecule. With Ohtuvayre as a broad label and favorable benefit risk profile, it has the potential to redefine the maintenance treatment paradigm. Ohtuvayre improved symptoms of COPD, enabling better breathing where patients start to feel good. We continue to build on the positive real-world experience, and we have additional opportunities and follow-on indications.

Now to the main event. Enlicitide was designed to target PCSK9 in the same way as the antibodies and deliver antibody-like efficacy. It has shown profound reduction in LDL cholesterol. The CORALreef Lipids study demonstrated a reduction of 55.8% in primary analysis and 59.7% in the post hoc reanalysis. In the CORALreef study focused on familial heterozygous hypercholesterolemia demonstrated a reduction of 59.4%.

We are pleased with the degree of lipid lowering for the secondary endpoint in ApoB with a 50% reduction, non-HDL cholesterol with a 53% reduction and Lp(a) with a 28% reduction. These percentages for ApoB and non-HDL cholesterol are aligned with what has been reported for anti-PCSK9 monoclonal antibodies.

The main takeaways before handing it to Joerg, enlicitide achieved LDL-cholesterol reduction surpassing other oral lipid-lowering therapies used as an add-on to statins. Over two-thirds of patients received or achieved rigorous prespecified LDL-cholesterol reduction goals and the ease of use, including an oral formulation with no adverse drug-drug interactions, and more than 97% compliance and strong safety and tolerability.

In closing, with efficacy similar to the monoclonal antibodies, enlicitide is a simple, easy-to-use pill that can help address the ongoing cardiovascular disease epidemic with the potential to significantly impact cardiometabolic health globally.

And with that, I will now turn the stage over to Joerg.

Joerg Koglin - *Merck & Co Inc - Senior Vice President, Head - General & Specialty Medicine, Global Clinical Development*

Thank you, Dean. Good evening, and hello, everyone. I'm Joerg Koglin, and I lead clinical development for general and specialty medicine at Merck. It's my pleasure to be here today and to provide an overview of the results from our Phase 3 CORALreef Lipids and CORALreef heterozygous HeFH studies evaluating the safety and efficacy of our oral PCSK9 inhibitor enlicitide. These studies were presented yesterday and earlier today in late-breaking science sessions at the conference here in New Orleans. The heterozygous HeFH study also has been published by now in JAMA. The lipid study has been accepted by the New England Journal of Medicine and will be published at a later date.

When I went through my own training as an internist in cardiologist obviously, many years ago, Merck's legacy cardiovascular diseases in general and in atherosclerosis in specific was very obvious. Merck led the way in developing therapies that changed cardiovascular medicine.

In atherosclerosis, the approval of lovastatin as the first statin in the late '80s, followed by statin as a better second-generation, as well as the development of ezetimibe as a preferred statin add-on spearheaded a new wave of products focused on lowering LDL cholesterol levels and reducing strokes and myocardial infections. Merck scientists played a foundational role in establishing the current standard of care in lowering in lipid-lowering therapies.

Later this upcoming week, actually, the role of the Merck Research Laboratories will be acknowledged by the American Chemistry Society with the designation of the Rahway and West Point sites as ACS National Historic Landmarks for the pioneering work that led to the discovery and development of the first statin.

Yet, despite all that progress in developing increasingly potent lipid-lowering medicines, we remain in the middle of a cardiovascular disease epidemic. Cardiovascular disease remains the leading cause of death in adults worldwide claiming roughly 19 million lives every year. 85% of those deaths are attributed to atherosclerotic cardiovascular disease, or ASCVD.

For over a century, cholesterol has been recognized as a major driver of ASCVD, and yet, it is estimated that half of the US general population has elevated blood lipid levels. Even with major advances in lipid-lowering therapies, residual cardiovascular risk remains high. Less than 30% of all patients actually treated for ASCVD achieved their guideline-recommended LDL goals, reinforcing the need for additional and more effective interventions. So programs that culminated in the discovery and development of enlicitide started with the bold goal to deliver the most effective LDL lowering pit and to make it accessible to a broad range of patients worldwide.

Injectable PCSK9 monoclonal antibodies have set a high bar in clinical studies, achieving LDL lowering by 50% to 60% with significant reductions in major adverse cardiovascular events and a favorable safety profile. However, their use has been limited by the need for injections and by remaining

access barriers. Developing an orally bioavailable PCSK9 inhibitor with antibody-like properties, represented a significant medicinal chemistry challenge.

Enlicitide is a novel macrocyclic peptide that has been shown to disrupt the binding of PCSK9 to the LDL receptor in a manner similar to that of approved monoclonal antibodies, but is administered only once a day. Similar to antibodies, it absorbs its action at a cell surface without really getting into the cell. And this comes with the expectation to avoid any major safety signals or adverse drug-drug interactions. However, unlike monoclonal antibodies, it can be stored at room temperature, circumvents the need for cold chain transportation, and it can be manufactured and distributed at scale, offering the potential for broad global access.

The Phase 3 enlicitide development program spans across a broad range of patients with ASCVD. The development program includes the CORALreef Lipids, heterozygous HeFH, and AddOn studies, all focused on changes in LDL cholesterol as a basis for an initial filing. In parallel, we have now fully enrolled the CORALreef Outcomes study designed to show that enlicitide can safely and effectively lower the risk of major adverse cardiovascular events. Today, we'll talk about CORALreef Lipids and heterozygous FH and will present the results of the add-on study at a later point of time.

Let me start with CORALreef Lipids, our broad hypercholesterolemia study. The study randomized 2,912 participants, 2:1 to enlicitide or placebo. So study focused on patients in need of primary prevention with an LDL of at least 70, or patients following a prior ASCVD event requiring secondary prevention with an LDL higher than 55. All participants had to be on optimized and stable lipid-lowering therapies. The primary endpoint was the placebo-corrected mean percent change in LDL at week 24, with secondary endpoints, including LDL changes at week 52- and 24-week changes for non-HDL-C, ApoB, Lp(a), and goal attainment rates.

The study population was balanced enrolling a broad and very diverse primary and secondary prevention population. The mean age was 63, 40% were female, almost half of the patients had type 2 diabetes, 60% already had a first event. Most patients were already receiving statin therapy with a mix of moderate and high-intensity regimen. The baseline of the LDL cholesterol averaged 96-milligram per deciliter.

Enlicitide in this study was very well tolerated with a safety profile similar to placebo. The rates of adverse events, serious adverse events, or discontinuation due to adverse events were comparable between those groups deaths were rare and were also completely balanced. Adherence rates for study drug intervention and for fasting instructions, where with 97% or higher, exceptionally high, documenting the ease of use for this medication in our study population.

There were no apparent differences in the proportion of participants with adverse events across any of the major system organ classes between enlicitide and placebo. Please note the absence of any difference in gastrointestinal AEs or musculoskeletal AEs. So in these almost 3,000 patients followed for over a year, the enlicitide safety profile was remarkably similar to placebo.

Now with regard to efficacy. Enlicitide demonstrated robust, statistically significant, clinically profound and durable reductions in LDL-C. When using the data handling rules as specified in the statistical analysis plan which resulted in biologically impossible baseline values in 5 out of the 2,909 patients, the calculated LDL reduction at week 24 was 55.8%. And correcting for these biologically impossible values to obtain the most accurate estimate of the true effect size, the placebo-corrected LDL reduction was 59.7%.

The LDL reduction was seen early, was durable over the entire duration of the 52-week study. These levels of LDL reduction delivered on the promise of enlicitide as an oral PCSK9 inhibitor designed to have antibody-like efficacy while surpassing reductions seen with all other oral lipid-lowering therapies, approved or currently known to be in development and used on top or instead of statins.

Designed as the most potent oral lipid lowering solution, we used an exceptionally rigorous definition for goal attainment. Aligned with both the European treatment guidelines and the 2022 ACC/AHA consensus statement, we define goal attainment as an LDL reduction by at least 50% and an absolute LDL attainment of lower than 70- or 55-milligram per deciliter.

Even with these ambitious definitions, close to 70% or two-thirds of participants receiving enlicitide achieved these goals regardless of their intensity of background therapy, and this compares to only 1.5% and 1.2% in the placebo group. And using more liberal definitions, such as those used for other compounds approved or in development, goal attainment reached or exceeded 80% as should be expected for best-in-class LDL reductions.

Prespecified secondary endpoints. We also looked at other atherogenic lipoprotein biomarkers. ApoB as a marker of the number of atherogenic particles is recognized as an even stronger predictor of ASCVD risk than LDL-C and is expected to replace LDL-C in treatment guidelines at some point in time. Non-HDL, quantifies the total amount of atherogenic cholesterol including, but not limited to, LDL. As such, it also has been shown to be a better predictor of heart disease than LDL-C alone. Lp(a) is an independent genetic risk factor for ASCVD, and in the past has not been addressed by statins or other widely used lipid-lowering therapies in contrast that slightly increase Lp(a).

Looking at these parameters, enlicitide, again, produced reductions in each of these endpoints with an effect size aligned with the original goal to have antibody-like efficacy. These biomarker findings provide further support for the promise of enlicitide to have a profound impact on outcomes for patients at risk of ASCVD.

Let's quickly look at the CORALreef heterozygous HeFH study, our second pivotal lipid study focusing on patients with heterozygous familial hypercholesterolemia. The study enrolled 303 adults with heterozygous FH, randomized 2 to 1 to either enlicitide or placebo on top of statin therapy. The primary endpoint again was LDL-C change at week 24 with similar secondary endpoints as the CORALreef Lipids study.

Again, enlicitide achieved placebo-controlled of 59.4% mean reduction in LDL-C from baseline at week 22 -- week 24 in the heterozygous FH population with evidence of efficacy seen early and being durable over the full duration of the study. Comparable to our findings in the main lipid study, these results reinforce the agent's potential in these high-risk genetic populations.

In summary, across the full development program, enlicitide showed consistently robust LDL-C lowering in the range of 57% to almost 60%. These values are consistent with placebo-corrected reductions of approximately 60%. Again, these levels of LDL-C reduction across all studies delivered on the promise of trying to come up with a PCSK9 inhibitor that could be antibody-like in its efficacy. So consistency in the effect size was also observed for changes in ApoB, non-HDL, Lp(a) as atherogenic predictors of cardiovascular risk with reductions of minus 50%, 53% and then 28%, respectively, across all studies.

These results support our original ambition to bring the best oral lipid-lowering agent with antibody-like efficacy to a broad population globally. Enlicitide offers profound LDL reduction translating into a robust LDL-C goal attainment with broad reductions in atherogenic particles. It was easy to use and came up with placebo-like safety profile.

Together with recent outcome results presented here at AHA, yesterday's data make us very excited for the future readout of our CV outcome study to confirm enlicitide's role in reducing the risk for stroke, MI, and cardiovascular death.

The presentations here at AHA this weekend are just the start. Data from the CORALreef Lipids and studies will support regulatory filings in early 2026. We've already announced the successful readout of the -- study and are planning to present detailed results in early 2026, too. As a reminder, this study will compare enlicitide to other mechanisms used as add-on to statin therapy.

Beyond that, we've now fully enrolled the CORALreef Outcomes study, a study that includes both primary and secondary prevention patients with a primary completion date projected in late 2029. We also initiated a pediatric heterozygous HeFH study and have announced the upcoming start of a co-administration study with rosuvastatin.

In conclusion, enlicitide is designed to address the global cardiovascular epidemic. The studies presented here at AHA established the foundation for an initial filing early in 2026. Together with the AddOn study, we strongly believe that these data will position enlicitide as the first choice oral add on lipid-lowering therapy.

The CORALreef outcome study is designed to provide a definitive measure of the potential of enlicitide-reduced stroke, MI, and CV death in both high-risk primary and secondary prevention patients. The development of a statin fixed-dose combination would allow to further simplify and optimize management of LDL-C in most patients, a potent oral medication with the potential for further -- for appropriately managing LDL-C with a vast majority of patients with further transformed treatment and expand the field into other orthogonal mechanisms that have been shown or hypothesized to drive the prevention of ASCVD beyond LDL-C lowering. We believe that enlicitide is uniquely positioned as a cornerstone of future combination therapies, and that, our pipeline offers multiple different options to try to solve the CV epidemic.

And with that, I'll hand it over to Jannie.

Jannie Oosthuizen - *Merck & Co Inc - President - Human Health U.S.*

Thank you, Joerg, and good evening, everybody. There's an urgent need for additional new treatment options to address the global cardiovascular disease epidemic. Cardiovascular disease is the number one cause of mortality worldwide. And each year, about 85% of CV disease related deaths are due to atherosclerotic cardiovascular disease. Despite the widespread availability of statins, LDL cholesterol control is still falling short in routine practice.

In the United States, nearly 70% of patients on lipid-lowering therapy are not at their LDL-C goal. The result is substantial economic cost to health care systems as well as to society. Globally, the vast majority of treated patients are on statin monotherapy, which speaks to the significant opportunity that remains for add-on therapies to improve outcomes for patients. We are very excited about the potential to bring enlicitide to patients given the substantial impact it can have in addressing the silent CV epidemic.

As we plan to bring enlicitide to market, there are some current market dynamics to highlight. There is a lack of patient awareness as CV disease typically progresses over time and leads to serious complications without noticeable symptoms. Many individuals may not be aware of their risk factors, which may put them at increased risk for serious disease. For those who are treated are not at goal, there is an opportunity for patient awareness and activation given the silent nature of the disease.

Additionally, there are varying LDL-C targets and performance metrics across geographies. Even where clear targets exist, they're not always consistently applied in practice. This is leading to suboptimal outcomes for patients. And in terms of current state, there has been limited use of PCSK9 therapies to date.

Across the US, Europe, and Japan, more than 80 million treated patients have LDL-C levels that are above guideline recommended goals. Our early launch focus will be on treated patients who are not at goal and need additional LDL-C lowering. This includes secondary prevention patients with ASCVD and high-risk primary prevention patients whose LDL-cholesterol remains above target on statins, including those with familial hypercholesterolemia, as well as individuals who cannot tolerate higher intensity statins.

We anticipate that initial prescribing will be more weighted towards patients with established ASCVD with the opportunity in those patients who are at risk of ASCVD contributing to additional growth beyond the early launch years.

Over the long term, there are significant opportunities to shift toward earlier routine combination therapy through future fixed-dose combinations. Additionally, there's a large eligible cohort of people who are not receiving any lipid-lowering therapy today. As Dean and Joerg said, enlicitide is designed to deliver antibody-like LDL-cholesterol lowering with the simplicity of a daily pill. We believe it has the potential to be -- to be a very significant contributor in helping address the silent CV epidemic.

In the Phase 3 study, enlicitide achieved 59.7% LDL-C reduction. We believe this sets a new high bar for oral add-on lipid-lowering therapies. Importantly, a substantial majority of patients made rigorous LDL-C targets, including both absolute goals and percentage reductions from baseline. This level of goal attainment could become even more important should more rigorous guideline targets be established in the future. As a daily oral pill enlicitide offers ease of use with safety comparable to placebo and no adverse drug interactions. These features make it simple for patients to use and support broad real-world uptake.

As we have previously communicated, our intent is to enable broad access for enlicitide. We are committed to working with payers to reduce barriers and to support patients that need additional therapy beyond statins. And oral formulation also opens up enlicitide to a much broader target prescriber base than traditional specialists such as cardiologists to also include primary care professionals. This combination of efficacy, safety and ease of use as well as broad access and a wider prescriber base position enlicitide to be a very important treatment option and to help address the CV epidemic.

Earlier this year, we communicated the components of our expansive late-stage pipeline that comprise a potential non-risk-adjusted revenue opportunity of over $50 billion by the mid-2030s. This included approximately $50 billion from our cardiometabolic and respiratory portfolio.

Our confidence in the cardiometabolic and respiratory opportunity is largely underpinned by enlicitide and WINREVAIR, each of which, we believe, have multibillion dollar commercial potential. Additionally, we have recently added an important new growth driver in Ohtuvayre, which we also believe is a multibillion-dollar revenue opportunity. We, furthermore, have many promising early phase programs, which represent incremental commercial opportunities.

Overall, we are confident in our ability to leverage our commercial engine and global footprint to advance our cardiometabolic and respiratory portfolio to positively impact patients around the globe.

With that, I turn it over to Peter.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Okay. Ivy, we're now ready for questions. If you could please repeat the instructions to those on the line.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Chris Schott, JPMorgan.

Unidentified Participant

Hi. This is Taylor on for Chris. Thanks so much for taking our question. I was just wondering if you could provide a little more color about how your thinking about enlicitide food effect? And how this would be reflected on the product label? And then what's the latest on how you're thinking about potential fasting requirements from this type? Thank you.

Dean Li - *Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories*

So why don't I ask you to do a little bit of response to that. And then Jannie can speak about some of the other, more commercial implications. And then I'll maybe make a comment or two.

Joerg Koglin - *Merck & Co Inc - Senior Vice President, Head - General & Specialty Medicine, Global Clinical Development*

Good. Yes, I can get started. So enlicitide is recommended to be taken first thing in the morning, and then to wait for 30 minutes before taking food. After that, in our study, an exceptionally high adherence rate to these recommendations with a compliance of over 97% suggests that participants really had no problems with this approach and supports the ease of use for enlicitide.

And as a physician, I think this is not surprising given that commonly used medicines are taken first thing in the morning, and the practice actually for many patients is to take some medicines, brush their teeth, get ready for their day and then go on with their lives. And enlicitide would fit very well in that routine. At the end of the day, I think for patients, it's most important in how effective a treatment will be and if it is able to get them to their treatment goals.

Jannie Oosthuizen - *Merck & Co Inc - President - Human Health U.S.*

Yes. Thank you, Joerg. I fully agree. I think from our perspective, we strongly believe that this will not be a barrier to use. And in fact, it could be a positive.

If you think about a patient establishing a very simple routine of taking enlicitide first thing in the morning when you wake up, and before you know it 30 minutes have passed, and you get on with your day, with the most potent lipid-lowering oral agent that is available. So we really think this could actually be a very positive aspect in terms of driving compliance. And that's what we saw in the trial. We saw a 97% compliance rate. So I think that's a great confirmation this truly is not a barrier for us.

Dean Li - *Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories*

I don't have much more to say, except that's how I take my medicine.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

So Ivy, we'll take a few here in the room.

Daina? And if you could please state your name and firm, that would be really helpful.

Daina Graybosch - *Leerink Partners LLC - Analyst*

Daina Graybosch from Leerink Partners. Congrats on the data. I'm actually going to ask a different one but also on adherence. And that is you did have 3% that were adherent. Did you see -- is that enough to see whether that actually had a negative impact on the outcome, just in case patients aren't as adherent in the real world? Is that a risk or not?

Dean Li - *Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories*

Joerg, did you want to take that in terms of the clinical trial?

Joerg Koglin - *Merck & Co Inc - Senior Vice President, Head - General & Specialty Medicine, Global Clinical Development*

I think so. The clinical trial adherence that we observed is exceptional, even when you compare that to drugs that are not given with specific fasting instructions. Of course, the regulatory filing will be supported by much more detail pharmacokinetic fasting studies. And at the end of the day, this is something that was easy to take for patients.

They didn't struggle with it. They stayed on drug. You see that the patient -- and the durability of effect over time, I think, supports that.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Great. Next question. Nick?

Unidentified Participant

Nick Jennings for Goldman Sachs. So the 52-week LDL-C lowering seemed a little bit lower than the 24-week period. What do you think is driving that difference? And we did not see that in the AGF -- HeFH study, I believe, so difference between those two studies?

Joerg Koglin - *Merck & Co Inc - Senior Vice President, Head - General & Specialty Medicine, Global Clinical Development*

So we start just with the observation. There was a profound treatment effect see it early, it is durable over time. I think a small diminution of treatment effect is something that actually consistently observed in almost every lipid-lowering study. It's actually something that you can see when you look at the product circular for some of the injectables. And it's something that you see in the Phase 2 and Phase 3 results, essentially for everything that is in development or has been recently published.

And then you're right, sometimes it doesn't happen in our heterozygous HeFH study. As you point out, 24-week LDL reduction of 59.4% compared to 61.5% at week 52. So in easier case, I think in the end, what we take from this results to durability of the LDL effect over time.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Great. Any others in the room? Malcolm?

Malcolm Hoffman - *Bank of Montreal - Equity Analyst*

Hey. Malcolm Hoffman here for BMO. Looks like we may get Phase 2 data for MK-7262 potentially any day now. Thinking about that trial and what we have seen with enlicitide so far, how do you think about these two agents and their potential to be combined further? What more may you need to see to pursue this in a clinical trial? And are there any specific considerations that you would need to think about in such a combo given the food effect we already discussed.

Dean Li - *Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories*

So I'll just answer it more broadly. We think these results with enlicitide and also other data that was presented about how important being monoclonal antibody like because there was data about monoclonal antibodies really suggest a tipping point of being able to address LDL. And I think that's a profound impact for the field. And I think the field felt that this weekend. I also think that's going to be a tipping point because it's going to allow people to begin to ask themselves what other risk factors could be important.

And I'm not going to go through what precisely every combination. But the three buckets after LDL that you might consider is, clearly, inflammation has to be looked at as something that could be important in terms of cardiovascular epidemic and rigs.

Clearly, LP(a) will be important in relationship to that. In fact, those patients who have high LP(a), really, the number one thing you have to do with the cardiologist is you need to drop their LDL cholesterol as close to 0 as possible. And I think the last one is, clearly, there is important for cardiovascular outcomes is to understand what's the relationship of obesity in relationship to that.

So we look at as LDL, inflammation, LP(a), and obesity. And we have agents in all four categories. And as with those advance, we will make decisions as to when to advance them, how to advance them and whether they should be advanced in monotherapy or in fixed-dose combinations.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

(Event Instructions) Ivy, if we could take a few more from the phone line, that would be great.

Operator

(Operator Instructions) Vamil Divan, Guggenheim.

Vamil Divan - *Guggenheim Securities LLC - Equity Analyst*

Great. Thanks for taking my question. I just had a question, you touched on this in the prepared remarks about the primary prevention data we saw from Amgen at the conference. So I'm just curious your thoughts on what we saw there in terms of the impact, the path ahead and how does that impact your views on what -- and we show your control and also just overall the market potential now if you -- has it gone up or change in any way based on what we're seeing in the outcome?

Dean Li - *Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories*

So I'll turn it over to Joerg. But I do think the data presented, as you discussed, emphasizes how important PCSK9 as a pathway and how important the specific mechanism by which the antibodies work, which is to interrupt PCSK9 and LDL receptor interactions can really have a profound impact.

And with that, I'll turn it to Joerg.

Joerg Koglin - *Merck & Co Inc - Senior Vice President, Head - General & Specialty Medicine, Global Clinical Development*

Yeah. So VESALIUS is a great study. It provided a 25% reduction in MACE. And I think it's fair to believe that the results will reset the urgency in the field to initiate LDL therapy perhaps a little bit earlier in patients and to think about more ambitious LDL goals. The results get us more excited -- even more excited about the future readout of our CORALreef study, based on a we have established that we have LDL lowering effects that would predict an outcome in the same range.

And we also, of course, acknowledge that certain design features in the VESALIUS study and in the CORALreef outcome study are pretty similar that makes us pretty excited about these results.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Great. Next question, please, Ivy.

Operator

Courtney Breen, Bernstein.

Courtney Breen - *Sanford C Bernstein & Co LLC - Equity Analyst*

Hey, everyone. Thanks for taking my question. Good evening. I wanted to just asked a little bit about the dimensions that you're considering when it comes to commercialization of the product. I think there's been a few questions on adherence so far. But I also wanted to ask in the context of kind of some of the pricing conversations and your language previously around democratizing access to these products.

We now have Amgen offering Repatha at $239 in the patient channel. We've now also kind of just had a big GLP-1 deal land in the US with the Trump administration. And so can you talk a little bit about the positioning of this product in the context of others that might be launching such as the oral GLP-1 that would be considered for many of the same patients around the same time.

Dean Li - *Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories*

That's a great question, and I'll hand it to Jannie to take a stab at that.

Jannie Oosthuizen - *Merck & Co Inc - President - Human Health U.S.*

Yeah. Thank you for the question, Courtney. First of all, from a pricing perspective, we will price to get broad access in the United. States and in terms of democratizing treatment, this really is a global cardiovascular epidemic. And I think we have a unique opportunity to impact this disease on a global basis with a small molecule that, as Joerg said, it's easy to ship, and we can hopefully get the price points also in ex US markets where we can open up access. So that's part of the democratization.

But certainly, in the United States, we have an objective to make sure that we remove barriers as much as we can in order for patients with a need for further intensification and on to statin to have access to enlicitide. That really is the objective.

In terms of using technology, whether it's digital means to continue to remind patients for compliance, those are all great tools that we can increasingly deploy from a tactical perspective and make sure that patients get the full advantage and benefit of this great potent lipid-lowering treatment.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Great. Next question, please, Ivy.

Operator

Steve Scala, TD Cowen.

Steve Scala - *Cowen and Company LLC - Analyst*

Thank you so much. I'm curious, how did Merck define adherence or compliance in the enlicitide trials? And is that a standard validated definition used in similar trials.

And I don't know if we're limited to one question, but if we aren't limited, then I would like to ask, are there interim looks at efficacy in the outcomes trial? And could you speak to the split between primary and secondary patients?

Dean Li - *Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories*

Steve, I'll give you the expert, Joerg Koglin, to go through the details of the clinical plans.

Joerg Koglin - *Merck & Co Inc - Senior Vice President, Head - General & Specialty Medicine, Global Clinical Development*

So the assessment of adherence in our clinical study was based on patient questionnaires. Patients were asked two different questions, were asked a question where you're able to take the drug reliably. And they were asked to, were you're able to adhere? And then there were prespecified criteria that were laid out in the protocol.

We'll publish, of course, the results in the protocol that will be in the New England Journal that will detail that further. Is that a standardized approach? No, this was a more rigorous approach to really address the question, are patients able to use this drug easily, and then we are really pleased with the outcomes and the high adherence rate. We wanted to understand how easy is it to use.

With respect to the outcome study, yes, the protocol prespecifies an interim analysis after three-quarters of the events are collected. The study is now fully enrolled. We designed to study in a way that it includes both primary and secondary prevention patients, three-quarters of the patients

in the study, the study has 14,707 patients enrolled. I think that's a number. Three-quarters of those patients are primary prevention patients, one-quarter are secondary prevention -- sorry, other way around. Three-quarters are secondary prevention patients and 1/4 are high-risk primary prevention patients.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Great. Thank you, Steve. And to be clear, multiple questions are permitted today because we have plenty of time. Next question, please.

Operator

(Operator Instructions) Geoff Meacham, Citi.

Unidentified Participant

This is Mary Kay on for Geoff. I would like to ask a quick one on WINREVAIR here. How might this new data further strengthen your confidence in the clinical profile and potentially impact is used in clinical practice beyond what we're seeing now maybe in terms of different care centers or patient background, which -- from the strong data?

Dean Li - *Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories*

Yes. So why don't I give Joerg a brief chance to talk about the excitement of that pooled analysis that was discussed, and then I'll have Jannie talk about how easy that might impact the uptake.

Joerg Koglin - *Merck & Co Inc - Senior Vice President, Head - General & Specialty Medicine, Global Clinical Development*

So when you look at our clinical development program, we had a number of readouts -- very positive readouts in the New England Journal. You see us starting from a prevalent population in STELLAR, expanding to really advanced patients to understand is there a mortality benefit that was at ZENITH, expanding into patients that were just recently diagnosed also advanced patients to understand how early should you use the drug. So that's the data set that we have right now.

I think, Dean, in the prepared remarks, talked about the new LDL -- the new WINREVAIR label that we've gotten. This is going to be the first indication that includes a reduction of death and the need for lung transplantation in the indication statement. And I think that speaks to the strength and the uniqueness of WINREVAIR achieving something that you don't see with other PH drugs at this point of time.

Jannie Oosthuizen - *Merck & Co Inc - President - Human Health U.S.*

Yeah. And I'll just add, whenever you strengthen the label like that, it really is useful. And it also continues to expand the type of patients being treated on starting to answer questions that maybe previously we didn't answer in full, for instance, in connective tissue disease. So that really does help to continue to expand the treated population.

In the US, we obviously have the HYPERION data set pretty much in the STELLA label, but that is an expansion for the label outside of the US as well.

And then to your point, the hard endpoints really, I think, continues to build into the efficacy profile of this product but further increases the confidence in the use of WINREVAIR. And we do see positions increasingly starting to use it in patients not on injectable prostacyclins in that deal, deal treated population is now sitting at about 25%, and we expect that to continue to increase over time.

Dean Li - *Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories*

I'll just make one comment. As we're talking about the LDL cholesterol and the silent cardiovascular epidemic, there is a general standardized way to think about guidelines, whether it's in Europe or whether it's in the US. I don't believe the same thing has been done for PAH, but I do believe this data will force the field to reconsider and to come up with very hard guidelines similar to what you see with LDL.

So I think this is really important data more broadly to the field. It will trigger the need to come up with very clear guidelines when you have a 56% reduction in lung transplantation and death and 51% reduction in mortality. And I believe the field understands it, and they will work with speed to get that done.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Any other questions here in the room? Daina?

Daina Graybosch - *Leerink Partners LLC - Analyst*

I have another one on the study. You had this correction in the CORALreef Lipids study, this is Daina from Leerink Partners, it's sort of awkward to have to state the effect twice. Is there anything beyond the awkwardness from that, that's a regulatory challenge? Or does it suggest anything beyond those five patients? Maybe you can help us better understand what happened.

Joerg Koglin - *Merck & Co Inc - Senior Vice President, Head - General & Specialty Medicine, Global Clinical Development*

So in principle, when you try to understand how effective is the drug, of course, you look at your LDL lowering across your entire program. That's actually how labels are written for lipid-lowering therapies. You don't see one LDL reduction. You see the LDL reduction across studies.

And so what I think we were trying to describe is we have this consistency in LDL reduction across studies. And we have this consistency between LDL reduction and ApoB reduction and non-HDL reduction those other parameters are also somehow linked with each other, specifically to the Lipids study.

So we had data handling rules in the ASCP that resulted in 5 out of almost 3,000 patients having these baseline values that were biologically impossible. And following the advice of our statistic -- Scientific Advisory Board, we performed a post-hoc reanalysis.

The idea, really, was we want to understand what's the true effect size, what's the best estimate of the two effects size. And so in the reanalysis, we just corrected these extreme outliers. And we are presenting both at the New England Journal paper. In the end, we'll describe in more detail precisely what was done, will be, I think, a very transparent decision. I think the presenter already did a very nice job in links that out in the field that I think didn't cause any questions in the scientific community.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Great. Any other questions in the room? Ivy, any other questions online?

Operator

Steve Scala, TD Cowen.

Steve Scala - *Cowen and Company LLC - Analyst*

Thank you, Can you provide some perspective on the enlicitide launch curve? Lipitor sold billions by the third year. Should we expect at least that for the Merck drug?

And secondly, is Merck working on decreasing the fasting duration, whether it be through additional studies of the existing formulation or perhaps a different formulation? Thank you.

Dean Li - *Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories*

I'll let Jannie take a stab at the commercial, and I can answer the other one.

Jannie Oosthuizen - *Merck & Co Inc - President - Human Health U.S.*

Yeah. So yes, Steve, thanks for the question. Just given the strength of the data, we do believe that there will be meaningful adoption from the beginning. Having said that, we are cognizant that there's a few factors that could affect the trajectory upfront, which would be just how quickly can we increase the awareness? How quickly can we create a sense of urgency to more aggressively treat what is the rate of insurance coverage that we can bring about?

And then also just how quickly will the guidelines move, right, in relation to setting some real goals. And obviously, some of those will help the others. So in terms of the trajectory, those are the things that we're taking into account in terms of how we think about the trajectory in the first few years.

In terms of where we think we're going to go in terms of peak, we have said that we believe this is a multibillion-dollar opportunity. We feel very confident about that. I think the data this week further builds into that confidence, and I think that's where we have good alignment on the long-term outlook with analysts in terms of the full potential of enlicitide.

Dean Li - *Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories*

Yeah. In terms of what you asked in relationship to the need to take this or the recommendation, I shouldn't say the need, the recommendation to take this in the morning along the lines that Joerg suggested, we're very comfortable with that. Clearly, other sort of descriptive studies might create a better understanding of what the leeway is in relationship to that. I would also emphasize that your last question, I think, related to is are we thinking of reformulating or something like that? The answer is no.

With 97% compliance rate and the results that we have consistently, I think that we're extremely comfortable that this is the most potent oral lipid-lowering cholesterol medicine that there is. And so we would not want to do something that disturbs that.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Great. Thank you, Steve. Next question, please.

Operator

(Operator Instructions) Courtney Breen, Bernstein.

Courtney Breen - *Sanford C Bernstein & Co LLC - Equity Analyst*

One more question from our side. And just another question on adherence from a slightly different angle. Can you -- you've obviously shared with us the adherence for enlicitide in the study. Can you give us any details around the adherence to the statins and other background therapies that patients were being prescribed? How adherent were they to those medications?

That'll be useful to kind of be able to contextualize that, recognizing we've got some more data on how they are taken in the real world and how representative this patient population is for what we're seeing in the real world today.

Joerg Koglin - *Merck & Co Inc - Senior Vice President, Head - General & Specialty Medicine, Global Clinical Development*

Yeah. No, thanks for that question. And I think the implication or the implied need to have these studies in patients where the background therapy is, a, optimized; and, b, stable before they get randomized. We fully buy into this.

We had in the 52-week studies, very stable background therapies. You also see that when you look at the stability of the LDL levels in the placebo group. I think that is an essential feature of a study that really then is able to test the true effect size of a new intervention placebo-controlled, and we feel very comfortable with the cleanness of our study results in that respect.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Great. Ivy, any further questions online?

Operator

I am showing no other questions in queue

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Okay. Anything further here in the room? Great.

Thank you all very much. Dean, any closing comments?

Dean Li - *Merck & Co Inc - Executive Vice President, President - Merck Research Laboratories*

Yeah. I would just emphasize that enlicitide, as we have discussed over the years, and many of you have had discussions with me in many different forms, was designed to deliver PCSK9 antibody-like efficacy. And in an easy-to-use pill with a compliance rate of greater than 97% that has the ability, the potential to be distributed at a global scale.

I also think, at this meeting, the importance of being antibody-like in design and efficacy really came to the forefront. It was highlighted by other data that was presented in relationship to the monoclonal antibodies, and I will sort of emphasize in that study, they were able to achieve, in general, a 55% reduction in LDL. They were able to drop people's LDL to around 45, not 70, not 90, not 55, but 45. They had important effects in both those patient populations appropriate patient populations in primary and in secondary prevention, and they led to CVOTs or cardiovascular outcomes or reductions of 20%-plus.

And so this is an important opportunity for Merck, but we also understand that the ability to impact the leading cause of death globally, heart attack and stroke, is profound. And we are excited by the data that we have shown and we are excited by the movement of the field to adopt even more aggressive LDL-cholesterol-lowering guidelines so that we can address the silent and deadly cardiovascular epidemic.

Peter Dannenbaum - *Merck & Co Inc - Senior Vice President, Investor Relations*

Great. Thank you all very much for your attention here tonight and appreciate your interest in Merck. Have a good night. Thanks.