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EDITED TRANSCRIPT

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

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OVERVIEW:

Company Summary

LSEG DATA & ANALYTICS

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PRESENTATION

Operator

(audio in progress) AIDS Conference. (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, Senior Vice President, Investor Relations. Sir, you may begin.

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

Thank you, Amanda. Good morning, everyone, and thank you for joining us for Merck's HIV investor event following the 26th International AIDS Conference that took place in Rio de Janeiro, Brazil last week.

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 and the 2025 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 this morning. Merck & Company, 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 posted to the Investor Relations section of our company's website.

Joining me today are Dr. Eliav Barr, Senior Vice President and Chief Medical Officer; Dr. Liz Rhee, Vice President of Clinical Research for Infectious Diseases; and Brian Foard, Executive Vice President and President, Specialty, Pharma, and Infectious Diseases Business Unit.

Now moving to the agenda. Eliav will begin with an overview of the HIV landscape and our strategy. Liz will then discuss the data that was presented at AIDS 2026, and Brian will finish by discussing the commercial opportunity associated with our portfolio before we then move to Q&A. During Q&A, we will be joined by Greg Szabo, Head of our Global HIV franchise.

With that, let me turn it over to Eliav.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

Thank you, Peter. Good morning, everyone, and thank you for joining us today. We are meeting at an exciting time for our HIV development program. At AIDS 2026, we presented important updates across several programs that have the potential to improve outcomes for individuals living with or at risk of HIV infection.

Most notably, we shared positive Phase 3 results from the ISLEND-1 and ISLEND-2 studies, evaluating once weekly islatravir/lenacapavir, while continuing to advance our broader efforts in both treatment and prevention.

Now, before discussing our strategy and the data presented at the AIDS conference, I wanted to step back and frame how we think about HIV today. For more than four decades, Merck has remained committed to HIV research innovation. Over that period, the HIV epidemic has transformed from a uniformly fatal disease into a chronic, manageable condition for many people around the world. At the same time, we are far from ending the damage caused by this epidemic.

Despite the availability of active antiretroviral regimens and prophylaxis options, we are far from meeting the 2030 goals public health authorities have set some years ago. Progress has slowed for many reasons. The most important of which are the known limitations of current HIV treatment and prevention regimens and the evolving nature of the epidemic.

Now, putting a real dent into the HIV epidemic will require a diverse set of highly efficacious treatment and prevention strategies that reduce the burden on people and practitioners and fit seamlessly into the fabric of the communities impacted by HIV.

Now, many of the medical tools needed to further reduce the impact of the HIV epidemic are already within reach in our pipeline. We have focused on developing simple, easy-to-use pills that can be highly effective oral treatment and prevention regimens.

Now, we've made tremendous progress over the past year in our clinical development program. We now have a new approved daily treatment option, positive Phase 3 data supporting a potentially first, once-weekly oral treatment regimen, continued advancement of another weekly oral program to provide more choice, and ongoing Phase 3 development of a monthly oral PrEP pill.

Today, we're excited to share with you our innovative weekly oral approach to treatment and monthly approach to prevention.

With that, let me turn it over to Liz.

Liz Rhee - *Merck & Co Inc - Vice President, Clinical Research, Infectious Disease*

Thank you, Eliav. Good morning, everyone. I'm so pleased to be here this morning to share with you the data we presented at AIDS 2026 across both of our weekly oral treatment programs.

I'll begin with the Phase 3 results for islatravir/lenacapavir and then discuss the Phase 2 data for islatravir/ulonivirine and the path forward into Phase 3. This slide highlights how dramatically HIV treatment has evolved over the past decades. It has progressed from the early days, when complex regimens required as many as 16 pills per day, or more than 5,800 pills per year, to the modern single tablet regimens that are taken daily.

Today, we are evaluating the potential for once-weekly oral treatment, reducing the floor for pill burden from 365 tablets per year to just 52. The data we presented at AIDS on our two weekly oral treatment programs that are given weekly support that next step in HIV treatment evolution.

We'll start with ISLEND-1, which was a global Phase 3 double-blinded study evaluating. Islatravir/lenacapavir, once-weekly two-drug combination given orally, against the daily three-drug treatment of B/F/TAF path studied in virologically suppressed adults.

In this trial, a total of 607 participants were randomized one-to-one to each treatment group. The primary endpoint was HIV RNA greater than or equal to 50 copies per milliliter at week 48 by the FDA snapshot analysis.

Secondary endpoints included rates of viral suppression, CD4 cell count changes, and treatment discontinuations. Results in ISLEND-1 for islatravir/lenacapavir showed that non-inferior efficacy was achieved against the comparator, the B/F/TAF.

The regimen demonstrated efficacy as well in terms of rates of viral suppression, which were above 90% through week 48. And importantly, there was no treatment emergent resistance to either islatravir/lenacapavir in this trial.

These strong efficacy results support the potential for islatravir/lenacapavir as the first complete once-weekly oral treatment regimen for HIV. In ISLEND-2, the second Phase 3 trial, we also evaluated islatravir/lenacapavir, but in this study, the design was open-label, and the comparator was a variety of daily oral treatment regimens. In this study, we enrolled 626 participants who were randomized to these two regimens.

Similar to ISLEND-2, islatravir/lenacapavir also demonstrated non-inferior efficacy. Rates of viral suppression as well in this study remained high at approximately 95%. Importantly, in ISLEND-2, because of the open-label study design. We had the opportunity to examine participant satisfaction with weekly oral treatment.

Participants reported being more satisfied with islatravir/lenacapavir than with their standard of care therapies that they had come in on, and as well found islatravir/lenacapavir to be less of a burden compared with daily orals. We were very satisfied, and we were very pleased to see these satisfaction rates.

In addition, safety across ISLEND-1 and ISLEND-2 were consistent. Islatravir/lenacapavir was well tolerated, with the safety profile comparable to bictegravir, FTC/TAF, and standard of care regimens. There were no clinically meaningful changes in lymphocytes, CD4 counts, or body weight that were observed. And there were no participants discontinued due to declines in CD4 or absolute lymphocyte counts.

Taken together, these data support the potential for islatravir/lenacapavir to become the first once weekly oral single tablet regimen for the treatment of HIV. Across both Phase 3 studies, we observed high rates of viral suppression, no resistance signals and safety and tolerability comparable with the control arms. We look forward to submitting islatravir/lenacapavir to global regulatory authorities and working to bring this innovative weekly option to appropriate people living with HIV as quickly as possible.

I'll now turn to our wholly owned investigational once-weekly oral treatment regimen containing islatravir and ulonivirine. As we've discussed in the past, the once-weekly two-drug combination of islatravir and ulonivirine has the potential to be the smallest weekly pill approved, with no loading dose and a favorable DDI profile. In addition, this is being evaluated not just in virologically suppressed, but also in treatment-naive participants.

At AIDS 2026, we presented data from the Phase 2B trial of islatravir and ulonivirine with week 24 results demonstrating that the combination maintained viral suppression and demonstrated efficacy comparable to continuing daily bictegravir, FTC/TAF . There were no participants on the islatravir/ulonivirine group with an HIV RNA greater than or equal to 50 copies per ml. And viral suppression rates were high at over 94% of participants remaining suppressed. Importantly, there were no treatment emergent resistance cases detected.

In this trial, islatravir/ulonivirine was generally well tolerated. There were no new safety concerns identified. In addition, the adverse event profile was comparable to cabotegravir FCC path, and we observed no meaningful effect on lymphocyte counts or CD4 counts.

Based on these results, we plan to advance islatravir/ulonivirine into a comprehensive Phase 3 program. The SYMPHORIA studies will evaluate this combination in both virologically suppressed adults, switching from daily therapy and in adults with HIV without prior treatment experience.

The Phase 3 trials in virologically suppressed adults, SYMPHORIA number 1 and SYMPHORIA number 2, are anticipated to open in the first half of 2027. SYMPHORIA number 3, the study in treatment naive participants, is a phase two/three trial. The Phase 2 component has been completely enrolled, and we anticipate results in the first half of 2027.

With that, I'll turn it over to Brian.

Brian Foard - *Merck & Co Inc - Executive Vice President, Specialty, Pharma & Infectious Diseases*

Thank you so much, Liz, and good morning to everyone. I'd like to first start off by saying that it is particularly exciting to join a company with such a rich history over four decades and enduring commitment to HIV. I'm energized by the science, the innovation, and the possibility of helping provide new options for HIV prevention and treatment.

Now, as you heard from Eliav, continued progress against the HIV epidemic will require a diverse set of prevention and treatment strategies. The HIV landscape is also continuing to evolve, people with HIV are aging. Roughly one-third of people living with HIV have comorbidities today, and the need to manage multiple different therapies for comorbidities is likely to increase.

While the existing antiretroviral medicines are generally safe and effective, certain classes also can impact renal, bone, and other areas of health differently, further highlighting the need for multiple treatment options with different mechanisms.

And for the majority of people living with HIV who choose daily oral treatment options, despite the important progress that has been made, the daily pill burden remains. Daily dosing can contribute to treatment fatigue and stress, as well as concerns about inadvertent HIV status disclosure. In prevention, opportunity remains to reach more people who could benefit from HIV PrEP.

Starting and remaining on PrEP can be complex, and many people who could benefit from prevention remain unreached. We are advancing a series of potential options designed to address these evolving needs. IDVYNSO, our newly approved once-daily oral treatment, marks the beginning of a broader portfolio strategy.

IDVYNSO is the first and only non-InSTI, tenofovir-free, once-daily, complete two-drug regimen to demonstrate non-inferior efficacy in a head-to-head Phase 3 trial versus three-drug regimen B/F/TAF. IDVYNSO provides people living with HIV an important new option when looking for switch therapy.

The key drivers of switch include tolerability, desire for simplification from multiple tablet regimens to two-drug single tablet regimens, comorbidities, and drug-drug interaction considerations. We're pleased with the launch progress so far, including the early access announcements, and look forward to access ramping up over time.

Beyond IDVYNSO, we are preparing to bring forward weekly oral treatment options and looking ahead to our entry into PrEP, where we are aiming to launch the first monthly tablet. I will address each of these opportunities in turn.

We are particularly excited about the potential for ISL/LEN to be the first once-weekly oral treatment option. The need for additional treatment options remains clear as many people living with HIV continue to experience challenges related to daily dosing fatigue, stigma, and the practical constraints of injectable therapies. Weekly oral therapy offers a less frequent dosing approach that aligns with preferences frequently expressed by people living with HIV.

In collaboration with Gilead, we look forward to sharing the positive results from ISL/LEN-1 and ISL/LEN-2 with regulatory authorities with the goal of bringing ISL/LEN to adults living with virologically suppressed HIV as quickly as possible.

One of the strengths of this opportunity is that it combines what we believe is a highly differentiated product profile with the capabilities of two global organizations with a shared commitment to advancing innovation for people living with HIV.

From a launch perspective, planning is already well underway. The collaboration structure allows both organizations to prepare for commercialization while coordinating around a shared global strategy. For the long-acting oral program, Gilead will lead commercialization in the United States and Merck will lead outside of the US.

Finally, I'd like to briefly touch on Alimatravir, our investigational monthly oral prep. This differentiated approach offers the potential for discrete, monthly dosing and a rapid onset of protection predicted within 1 hour. Alimatravir is a molecule developed specifically for prevention. The EXPrESSIVE-10 and EXPrESSIVE-11 trials are anticipated to read out in 2027.

Recently, we announced initial plans intended to support rapid, broad, and sustainable access to Alimatravir in low and middle-income countries should it ultimately be approved. Those plans include voluntary licensing agreements covering more than 129 countries, support for regional manufacturing capabilities, and investments intended to facilitate timely access following approval. We believe innovation has the greatest impact when it reaches the people who need it most, and this announcement reflects our long-standing commitment to HIV in global access.

Now, stepping back, we believe the combination of IDVYNSO, ISL/LEN, ISL/ULO, and Alimatravir creates a meaningful long-term opportunity. We see an opportunity of greater than $5 billion on a non-risk adjusted basis by the mid-2030s.

These programs reflect a long-term commitment to advancing HIV science and a vision for a future in which prevention and treatment are increasingly simple, accessible, and fit seamlessly into the fabric of the communities impacted by HIV.

And with that, I'll hand the call back over to Peter.

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

Thank you, Brian. Amanda, we're now ready to begin the question-and-answer portion of the call.

Before we get started, I'd like to request that today's questions remain focused on our HIV treatment and prevention programs.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions)

Trung Huynh, RBC.

Trung Huynh - *RBC Capital Markets Inc - Analyst*

Morning, guys. Thanks for having us on. So just two questions from our side.

First, the ISLEND-2 CD4 data that showed continually gradual decline of the ISL/LEN arm versus Biktarvy over 48 weeks, even though both arms ended at equivalent levels. ISLEND-1 1 and the ISO/ULO Phase 2b, they were both modestly better than Biktarvy on this metric, which helps contextualize, but how are you interpreting the ISLEND-2 curve divergence? Is that a baseline imbalanced artifact, the class signal you're monitoring or something that you believe will fully resolve at 96 weeks? And how does FDA engage with this in the context of labeling discussions?

And then second question, just can you walk us through the planned ISL/ULU SYMPHORIA Phase 3 program in the treatment experience patients, specifically design, enrollment timeline, any expected readout? And relatedly, what does the 48-week secondary endpoints and treatment naive Phase 2/3 data need to show for you to be confident in an NDA path towards that 2030 approval target? Thank you.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

Thanks. Thanks for the questions. This is Eliav Barr, and I'll moderate, but I'll take the first one, and then Liz can take the second one.

With respect to the CD4 counts in ISLEND-2, there was a small statistical difference in change in baseline CD4 T-cell count at the week 48 time point, but we didn't consider it to be clinically meaningful for a variety of reasons.

First, as you noted, none of this was seen in ISLEND-1 nor in the Phase 2 ISL/ULO studies. There was a baseline imbalance, as you also noted. The CD4 T-cell count was higher in the ISL/LEN group compared to standard of care at baseline, and the changes were greater in those -- the changes that we observed in terms of CD4 counts were greater in those with the highest baseline counts. So, we think that it's probably a regression to the mean.

And we looked at a variety of different other factors in the studies, including the percent changes in baseline CD4 T-cell counts and discontinuations and other metrics that both Gilead and Merck together assessed from the perspective of changes in CD4 counts. None of those were statistically significant.

And so, bottom line is that we don't see this as being at all clinically meaningful. We don't anticipate this to be a problem with this drug or any islatravir containing regimen going forward.

And in terms of the SYMPHORIA trials, let me turn it over to Liz.

Liz Rhee - *Merck & Co Inc - Vice President, Clinical Research, Infectious Disease*

Sure, thanks, Eliav. So for the very logically suppressed indication, we're planning two studies as I indicated earlier, SYMPHORIA-1 and SYMPHORIA-2, both of these studies in terms of primary endpoints would follow FDA guidance with the primary endpoint being those with viral load greater than or equal to 50 analyzed by the FDA snapshot. We would also be looking carefully at safety, of course, in these studies.

And I think with SYMPHORIA number 1, which is an open-label study, we would have opportunity as well here to collect PRO or patient-reported outcomes, such as satisfaction as we had done in other weekly trials.

At this point, we are anticipating starting the studies in the first half of next year. The details of the secondary endpoints and timelines of the trials, we don't really have ready to share at this point in time, but we will share them in the future when they are ready. We are in the process of sharing our plans and discussing with the FDA.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

But just to make to be clear, I mean, I think SYMPHORIA studies are going to be very important, addition on the Q-week regimen. Just to remind everyone, we'll have both treatment experience and treatment-naive patients.

This is something we heard loud and clear at the HIV meetings. A lot of interest in starting people right on Q- week to really help them in that period of time when they're still grappling with the fact that they're HIV positive. So, we're really looking forward to starting those studies and we'll let you know about the timelines when we're more set with them.

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

Great. Thanks, Trung.

Next question, please, Amanda.

Operator

Mohit Bansal, Wells Fargo.

Mohit Bansal - *Wells Fargo Securities LLC - Analyst*

Great. Thank you very much for taking my question, and thank you for doing this. So my question is regarding some feedback we get from both experts, as well as Gilead is also talking a little bit about this, that integrase inhibitors are considered the gold standard of treatment in HIV as of now.

I mean, if you look at the guidelines, there are like four integrase inhibitor combos there. But your two-drug combo does not include integrase inhibitors just yet. How do you think about -- like, one, you agree with that. Number two, how do you think about the positioning of your islatravir relatively-based combinations? Or is there a subpopulation out there that could actually benefit from these combinations rather than this being a frontline agent? Thank you.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

Thanks so much for that question. First of all, as we were the discoverers of the Intergrase class, but I think that it's important to have options for patients. These options are very -- this is a very long-lasting disease. It requires many different options.

I'll turn it over to Liz to talk a little bit about what we've heard and what we're thinking about in terms of the InSTI free regimens.

Liz Rhee - *Merck & Co Inc - Vice President, Clinical Research, Infectious Disease*

Right, so the feedback we've heard is that there is a need for options for patients that are regimens that don't contain integrase inhibitors. Remember, this is a chronic infection. People are aging now with HIV, meaning that they have carried this diagnosis sometimes for decades, and one type of regimen is not going to fit all.

So, one size does not fit all. In addition, as people living with HIV age and deal with comorbidities, there's particular concern on effects, for example, on cardiometabolic factors, on weight that can lead to people needing to switch due to tolerability issues as well drug-drug interactions as people are taking more medicines for their comorbidities. So, Eliav, to your point, we hear loud and clear from providers and

also patients themselves, people living with HIV, that they want more options and that integrase is not going to solve every problem for them.

Mohit Bansal - *Wells Fargo Securities LLC - Analyst*

Great.

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

Thanks, Mohit.

Next question, please, Amanda.

Operator

Evan Segerman, BMO Capital Markets.

Unidentified Participant

Hi, [Malcolm off] and on for Evan. Thanks for taking our question. So you had framed a $5 billion non-risk-adjusted opportunity in the mid-2030s from new and potential HIV launches. I know that this reflects Merck's share of collaboration revenues. Can you help us think about the relative contribution of treatment versus PrEP within that $5 billion target? Thanks.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

Thanks for the question. I'll ask Brian and Greg to address.

Brian Foard - *Merck & Co Inc - Executive Vice President, Specialty, Pharma & Infectious Diseases*

Yeah, thank you so much, Eliav. And I think it's a really great question. And just as we're talking about today, think about it overall, first and foremost we're talking about four potential therapies. One is approved in the marketplace today with IDVYNSO and then three additional potential options for those living with HIV or looking for PrEP.

And so we framed it first and foremost in the treatment category. The treatment category today in 2025 is about $26 billion. We're expecting that to continue to grow to more like $32 billion by the mid-2030s. We're also expecting the PrEP market space today, which is a much smaller market space, it's about $4 billion today. We expect that to more than double over time. And we see this as a significant and meaningful reason for us to be in this space with these potential therapies.

But maybe, Greg, if you want to give a little bit more details to it.

Gregg Szabo - *Merck & Co Inc - Senior Vice President, Integrated Global HIV Franchise*

Thank you, Brian. I would really start by mentioning the very positive reception that we had at the Congress last week for our data and for our portfolio. We had a strong positive reaction across scientific leaders, prescribers, and advocates, and it really gives us a growing confidence in our potential to achieve that greater than $5 billion revenue by the mid-2030s.

I think as Brian laid out, we've got several options, and each of these programs is well differentiated and I think brings significant value to the space. In talking about the treatment market, which is the larger market, we do see evolution today, and we expect it to continue into the future towards two-drug regimens and also towards long-acting regimens.

Ultimately, we expect long-acting regimens to represent the solid majority of patients by the mid-2030s, and we feel the two weekly orals will have a strong place within that segment. Each of these assets, including Alimatravir in the PrEP space will be contributors to that overall $5 billion number. And I think Alimatravir just has such an exciting profile with rapid onset, once-monthly discrete oral dosing, and we believe that also will be an important option within the PrEP space.

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

Great. Thanks, [Evan].

Next question, please, Amanda.

Operator

Alex Hammond, Wolfe Research.

Alexandria Hammond - *Wolfe Research LLC - Equity Analyst*

Thanks for taking the question. Can you kind of walk us through how we think about Alimatravir in the context of a PrEP market that's actively organizing around injectables? Who the target patient population is, how you're thinking about that window before YEZ, apretude,, establish those deep prescriber and infrastructure relationships, what the access and pricing strategy might also look like in both the high-income and high-burden markets. Thank you.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

Thanks for that question. Let me start by saying that for the PrEP market, what we've heard very loud and clear is the need to have regimens that are seamlessly integrated into communities that require minimal medical intervention that enable patients to have access in various locations that don't require the need for advanced care.

And with all of that in mind, we think that an oral monthly would be very useful indeed. In fact, if I had to say, what was just a wow moment for everyone at the AIDS meeting was Alimatravir. We could not get away from anyone who wanted to say something about Alimatravir, to think about Alimatravir as part of their treatment regimens and so on.

Maybe I'll turn it over to Greg to talk a little bit about his impressions.

Gregg Szabo - *Merck & Co Inc - Senior Vice President, Integrated Global HIV Franchise*

Thanks, Eliav. I would start by saying that despite the availability of a number of highly effective PrEP alternatives today, either daily orals or injectables, we still see many new infections, and we still see that a relatively small percentage of people who can benefit from PrEP are actually taking it regularly. Certainly less than half the people in the United States and less than one in five globally.

And there can be a number of reasons for this. Some of them are just low perception of risk on the part of the patient or low awareness of PrEP. But there's also a number that are potentially mediated by the drug profile itself. And these include things like concerns about side effects or tolerability, the stigma that's associated with using PrEP, and also suboptimal ease of implementation and accessibility within the

healthcare system. So we feel very confident in an oral once-monthly pill. We believe this is something that's easy to access, in that it doesn't require HCP administration.

The fast onset of action, that was something that got a lot of favorable feedback at the conference last week. Current options often take days to be effective. We believe that Alimatravir can be effective within an hour. It also has a favorable DDI profile, which can be really important within this population.

And with regards to stigma, this is something that can be very discreetly taken or stored to really protect the user's privacy and avoid stigma. So ultimately, we feel like this opens up new models of implementation to increase the number of people using PrEP, and we also feel it has a very strong value proposition relative to all the other options that will be available.

Brian Foard - *Merck & Co Inc - Executive Vice President, Specialty, Pharma & Infectious Diseases*

Maybe just a couple of extra points here. While it's too early to really specifically speak about the access strategy as it relates to that, we do think that it does have a compelling value proposition and key differentiation, which should assist in gaining access. We're also too, and I want to make this point because I think it's an important one,

We're encouraged by the SCOTUS ruling for the USPSTF that was important for individuals to access PrEP with no out-of-pocket cost and has implications for all preventative services and medicines. And so, the environment is set up for innovation. And so we're excited about potentially bringing that innovation.

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

Great. Thanks, Alex.

Next question, please, Amanda.

Operator

Geoff Meacham, Citibank.

Geoffrey Meacham - *Citi Infrastructure Investments LLC - Analyst*

Hey, guys. Thanks for the question. Another one on the weekly oral. Just want to get some perspective on the PK/PD. Do you have residual drug extending beyond a week? I'm just thinking about real-world compliance and the risk of resistance.

And then commercially, would you view this as a switch opportunity at the onset or is it more upstream to perhaps newly diagnosed patients? Thank you.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

So, let me ask Liz to talk a little bit about PK/PD and the forgiveness that's already in our Q-week regimens, and then I'll ask Brian and Greg to talk about the commercial potential. Liz.

Liz Rhee - *Merck & Co Inc - Vice President, Clinical Research, Infectious Disease*

Right. So, for both of the oral weekly regimens, islatravir/lenacapavir, as well as islatravir/ulonivirine, the doses were selected to enable a window for forgiveness of about seven days. And this is to take into account the fact that people may forget to take their dose on a certain day, may need a window to catch up essentially.

So that week of forgiveness means that you forget your dose on a Monday, you have a week to get back on. And then if there are -- if that window is exceeded for each of these programs, we have thought really carefully about how people would need to then restart the regimen. So, this has been factored into the development program in the Phase 3 studies.

So, from that perspective, we feel that there will be very clear instructions for participants on what to do if they do miss a dose and, outside of that forgiveness window.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

And indeed, in the Phase 3 trials, compliance was extraordinarily high and a lot of satisfaction around the use of QW instead of QD.

But maybe I'll ask Brian and Greg to talk about the other piece.

Brian Foard - *Merck & Co Inc - Executive Vice President, Specialty, Pharma & Infectious Diseases*

Maybe just at a really high level, and then I'll pass over to Greg for a bit more details. Now we know, again, in the treatment space, as I mentioned before, this is one of the biggest areas today, and we anticipate it will continue to grow. And just as Liz nicely said, we believe it's because individuals like options, and this is really important to continue to bring options. I know you didn't necessarily specify which weekly option, but it's exciting to be bringing two, to be quite frank.

And so maybe Greg can give a bit more details about the two opportunities as we see it.

Gregg Szabo - *Merck & Co Inc - Senior Vice President, Integrated Global HIV Franchise*

Yeah, thanks, Brian. And I think you're right. I mean, options are important. Obviously, if you look at the daily market, there's been continued innovation there that ultimately has led to more and more satisfaction for patients as time has developed, and we think the same thing can happen with long-acting therapies as well.

If I start with ISL/LEN, again, I think there was a great reaction at the Congress last week. This has the potential to be the first weekly oral regimen to market. There's really strong patient interest and it's highly differentiated, and I want to double down a bit on the patient interest because I think this is something that is really important from the perspective of the long-acting oral regimen.

It has the potential to address pill fatigue. This is an important issue for people living with HIV and also the potential to address, what can be injection fatigue. I mean, this is designed ultimately for people who want more freedom that they can get with less frequent dosing, but not be tied to a physician visit for administration. So, obviously we're excited about ISL/LEN because it brings together two highly potent agents that have the potential to maintain the viral suppression and do it with reduced dosing frequency.

But then if we move to ISL/ULO, this is also a highly effective program based on our Phase 2 data so far, effective with a small two-drug tablet. This has the potential to be the first weekly regimen that will address treatment naive patients.

As Eliav mentioned earlier, this could be an important opportunity to really start people, especially when they're undergoing reaction to being diagnosed with HIV. Also, importantly, there's no loading dose associated with ISL/ULO. As I mentioned, the small pill, and it has a

favorable DDI profile. So we believe that the unmet needs and the desire to switch to easy oral dosing for a once-weekly will persist beyond the launch of islatravir/lenacapavir and we see ISL/ULO continuing to expand that market category. And over time, we feel the biggest opportunity is really moving people from daily to weekly, supported by a portfolio of differentiated options.

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

Great. Thank you, Jeff.

Next question, please.

Operator

Vamil Divan, Guggenheim Securities.

Vamil Divan - *Guggenheim Securities LLC - Equity Analyst*

Great. Thanks for hosting this and taking my question. So maybe two follow-ups on one just on the comments you were just making around islatravir/lenacapavir, ISL/ULO. So, I appreciate some of what you said there on the benefits that ULO may provide in terms of no loading dose, smaller pill, favorable DDIs. What about the other way around? If both of them are available, what would be the benefits of ISL/LEN other than maybe getting to the market first?

And then the second, you spoke previously around the $5 billion commercial opportunity and the sort of breakdown between PrEP versus treatment. I'm curious if you can give any sort of similar breakdown on how you see the US versus the ex-US contribution to that, that's greater than $5 billion number? Thank you.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

Thanks so much. It's Eliav. Let me take that first, and then we can talk about the commercial elements.

So, it's exciting to have islatravir/lenacapavir as the first drug because lenacapavir's safety profile and efficacy profile are well known and understood. They're part of a lot of lenacapavir is part of a lot of regiments, and so we have. Here a new class of drug that has a strong and well-defined efficacy safety profile. And people are aware of the drug-drug interactions that one needs to keep in mind. So, islatravir/lenacapavir, I think, will be an excellent first option and a continued option over the course of the years along with islatravir/ulonivirine.

So, if I could switch to Greg.

Gregg Szabo - *Merck & Co Inc - Senior Vice President, Integrated Global HIV Franchise*

Thanks, Eliav. I would just say that this product, these products are highly differentiated, and I think they're going to have a big impact in that regard outside the US as well as in the US. We're not specifically breaking down the opportunity across geographies at this point in time, but I would say one could imagine something similar to the breakdown in the current market for HIV.

Brian Foard - *Merck & Co Inc - Executive Vice President, Specialty, Pharma & Infectious Diseases*

One last point that I'd make about that, too, is we get this question commonly about these two assets. I think one is important. The first asset actually comes with the power of two organizations that have been in this space for a long time. But we think about that space, the long-acting is really where the growth is going to be in the future.

And so we believe that marketplace is going to be largely dominated by the long-acting therapies. And so while we don't-- We're excited about bringing two therapies. We're not necessarily thinking about one versus the other. We think the space is going to have options, and we think a lot of the growth is going to be there for the longer-acting treatment versus PrEP.

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

Yeah. Good. Thank you, Vamil.

Next question, please.

Operator

Chris Schott, JP Morgan.

Christopher Schott - *JPMorgan Chase & Co - Analyst*

Great, thanks so much. Just coming back to the role of your initial weekly, the slash of ISL/LEN, can you just elaborate a little bit more in terms of the role that can play in the treatment experience market, specifically what percent of the market do you think this can address and when you think about switches, how quickly you can ramp as we think about that commercial opportunity?

And then my second question is, given some of your peers are pursuing injectables in both PrEP and treatment. Is this an area Merck is looking to explore, as you just mentioned, markets bifurcating lots of options? Is there an opportunity to take these assets into longer treatment regimens? Thank you.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

So let me take the second first, and then I'll turn it over to Brian and Greg. Of course, we're looking at all different options, and we have a robust discovery pipeline. The past few years at Merck, we've really focused on simplification.

And if you think about LIPFENDRA, for example, as a simplification option compared with injectables, and then you apply that to the HIV space, it's the reason why we spent a lot of time thinking about easy-to-administer, long-acting orals that will ultimately make it just much less complicated to get patients their medicines with reasonable access.

So that's where we are right now. But of course, we're looking at all manner of opportunities to provide both treatment and prevention. We'll look at that in our discovery pipeline, and we'll be able to share some of that as the drugs progress into later development.

So Brian, Greg?

Brian Foard - *Merck & Co Inc - Executive Vice President, Specialty, Pharma & Infectious Diseases*

So maybe I'll start, and then Greg, if you want to add anything additional to it. I think first and foremost, the market today, the treatment market today is largely daily therapies. I mean, so we believe the longer-acting therapies are going to play an important part, as I just mentioned a moment ago.

And number two, as you look at today from a switch standpoint, about one in five people living with HIV switch annually for a variety of reasons, tolerability, long-term toxicities concerns, comorbidities, as was mentioned before, and desires for simpler regimens. And so we believe, again, for a variety of reasons, it will create a significant opportunity there.

But I don't know, Greg, if there's any additional points you want to make?

Gregg Szabo - *Merck & Co Inc - Senior Vice President, Integrated Global HIV Franchise*

Yeah, I would just reinforce, again, that we do see current evolution in the market, both within and away from, I guess, the daily class, so within the daily class towards two drug regimens and then towards two-drug long-acting regimens, we do expect that to continue.

And as mentioned earlier, we really expect the long-acting regimens to ultimately represent the solid majority of people within the market. Within that, we see a solid place for the Q-weeklies. We could see that ultimately getting to about overall about one-third of the overall treatment market, and I would just reiterate the strong patient preference and I think that will also help with the initial ramp is -- there is a strong patient driven aspect to these long-acting oral therapies.

There are people that want to get away from that daily pill and want to also may not be right for injectable treatment. So we do feel that progress will be substantial in this space.

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

Great. Thanks, Chris.

Next question, please.

Operator

Daina Graybosch, Leerink Partners.

Daina Graybosch - *Leerink Partners LLC - Analyst*

Hi. Thanks for the question. Two on a Alimatravir, trying to say that correctly. I wonder if you could talk about weekly, monthly PrEP versus a weekly oral PrEP, why monthly might be better or differentiated from weekly?

And then the second question, you talked about the hours onset. Is that something you can measure as an outcome and will you measure it in any of your registration trials so that gets on label? And does that matter for that differentiation to really get out there and be used by clinicians in the community?

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

Thanks. I will ask Liz to comment on the clinical trials program. In terms of a weekly PrEP versus monthly, the ideal for people who are in a prevention mode, right, this is not infected individuals is to have as little as possible need to do anything, really to get protected. So, just as much as, as little as you don't want to go somewhere to get an injection, you want to just get it and be done with it. So, I think that the longer the interval on the oral, the better in that circumstance.

The other piece of that is with regard to the second question that I'll turn over to Liz to talk about is, I don't want to think about it and plan ahead because it's Saturday night, et cetera. So being able to have your PrEP available and effective within an hour is consistent with what life is really like.

And Liz, you want to talk a little bit about the PK?

Liz Rhee - *Merck & Co Inc - Vice President, Clinical Research, Infectious Disease*

Right. So, actually, at CROI earlier this year, we presented PK data for Alimatravir and justification for the 11-milligram monthly dose that was selected. And as part of the dose selection process, we look carefully at the PK and at the onset, and when we expect drug levels to be above the threshold that we expect to be efficacious.

So, the 11-milligram dose has this baked in where you'd expect levels to be protective within one hour. There's no need for a loading dose. There's no need for a higher dose to start with. I think the dosing regimen itself is quite simple because of these PK attributes.

In terms of the label, I mean, the PK section of the label will include all of this data. We are collecting PK data in the Phase 3 program, and we'll be able to report that out.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

And I would add that there's been a lot of interest in a PEP study, post-exposure prophylaxis program, and we are taking that under advisement.

Maybe I'll turn it over to Greg for the commercial side.

Gregg Szabo - *Merck & Co Inc - Senior Vice President, Integrated Global HIV Franchise*

Yeah, and maybe just one last comment that I would make that, one of the key things for PrEP is avoiding the stigma associated with taking PrEP and having a longer option, such as a monthly and an oral option, where you're not having to have frequent trips to the physician to have that administered. This can be very helpful.

So a monthly versus a weekly, for example, just gives you less opportunities from being observed, taking the product, it gives less opportunities for somebody finding stored products. So it allows for a lot more discretion that can really help to protect the user's privacy. And we think this will ultimately be something that's very important within the community.

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

Great. Thank you, Daina.

Next question, please.

Operator

Carter Gould, Cantor Fitzgerald.

Carter Gould - *Cantor Fitzgerald LP - Analyst*

Great. Good morning. Thank you for hosting. I want to come back to Alimatravir. As you think about the bar for efficacy here, I recognize the studies are against B/F/TAF, but the cross-trial comparisons are pretty straightforward, and PURPOSE 1 and PURPOSE 2 set a pretty high numerical bar there. In light of all your commentary around the differentiating features, does Merck sort of address this with potentially some more leniency on efficacy in terms of the bar they might be held to, or from a clinical and regulatory perspective, is it going to be critical they match that sort of very high 90s sort of bar we saw on PURPOSE 1 and PURPOSE 2. Thank you.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

Yeah, the standard that is applied for all of the PrEP drugs are the same in terms of regulatory agencies. And so, our expectation is that this will need to have the same kind of efficacy that would meet those statistical criteria.

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

Great. Thank you, Carter.

Next question, please.

Operator

Jason Gerberry, Bank of America.

Jason Gerberry - *Bofa Merrill Lynch Asset Holdings Inc - Analyst*

Hey, guys. Good morning. Thanks for taking my questions. Just two follow-ups. You mentioned potentially the ability to get one-third share in the treatment market with Islatravir/ulonivirine. What is your assumption regarding ability to take share from injectables? Do you view the injectable space as sort of a separate segment that's harder to claw away share? And is the assumption mainly that it's an oral switch.

And then as a follow-up, any updates? I know last time you did this call about a year ago, you talked about your injectable options being early stage, but when do you think we could be in a position to potentially get an update on the efforts Merck has with this injectable offering? Thanks.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

So, I'll take the second first. We're still working on a variety of injectable options. You see that there's a lot out there, so we don't want to have just something that would be “me too” it would have to be differentiating, and we're working on that.

In terms of the commercial elements, Brian, Greg.

Brian Foard - *Merck & Co Inc - Executive Vice President, Specialty, Pharma & Infectious Diseases*

Yeah, I'll first start off by saying one of the things that we reiterated a bit earlier is that we feel like in the treatment marketplace, you're going to see the marketplace continue to move to these longer-acting therapies, the weekly therapies, and we're really excited about that.

Today, it's largely daily therapies if you think about where the market is today. So we see the marketplace going to continue to grow, and we think it's going to be growing primarily because of these longer acting therapies.

But Greg, maybe a bit more specifics.

Gregg Szabo - *Merck & Co Inc - Senior Vice President, Integrated Global HIV Franchise*

Yeah, I just want to address. I think what we had mentioned earlier around one-third was for Q-weekly options, not specifically for ISL/LEN. So I do just want to correct that comment that was made.

And I think your other question was, do we see it as primarily coming from dailies versus injectables? I think the value proposition is there for either. But as Brian has mentioned, the market still today and expected to be next year is still dominated by dailies. So I think the pool in which you're operating is likely to be much higher on the daily side.

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

Great. Thank you, Jason.

Next question, please.

Operator

Michael Yee, UBS.

Michael Yee - *UBS AG - Analyst*

Great. Thanks. Maybe two questions here. On the weekly treatment option with Gilead, can you just talk a little bit about the economics there and how you think about a profit share there, given that the partner already has wholly owned rights on the standard of care and complications of a partnership there in that context and how that works.

And then a second question on the monthly PrEP, which sounds very exciting. Can you talk about the window and margin of error there for retreatment and compliance there? I know you said fast onset of action, so perhaps there's definitely room just because of the fast onset, but how that works there with the monthly pill and the PK if you miss a dose. Thank you.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

Thanks so much. Liz, could you comment on the forgiveness of the Q-monthly, and then I'll ask Brian and Greg to talk about the economics?

Liz Rhee - *Merck & Co Inc - Vice President, Clinical Research, Infectious Disease*

Yeah, thanks, Eliav. And actually, this was also addressed in the data we presented at CROI earlier this year that I'd mentioned before about Alimatravir. So, the 11-milligram dose allows for approximately a week of forgiveness in case a dose is missed.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

Thanks. And Brian, Greg?

Brian Foard - *Merck & Co Inc - Executive Vice President, Specialty, Pharma & Infectious Diseases*

Yeah, so across the programs that we have with Gilead, Gilead and Merck will share global development and commercialization costs 60/40, respectively. And then for the long-acting rules, as we said, Gilead will lead commercialization in the US, Merck will lead commercialization ex-US, and Merck and Gilead will share global product revenues 50/50 up to around $2 billion or up to $2 billion, and then 65% Gilead, 35% Merck thereafter.

Gregg Szabo - *Merck & Co Inc - Senior Vice President, Integrated Global HIV Franchise*

Perhaps I can just add to that, we've had a very productive partnership with Gilead and I would start with what is the most important point, which is that working together, Merck and Gilead is allowing us to provide a new and important option for people living with HIV. In fact, this is the only way or the way that we could get to the market the fastest with something that will be highly desired by the community.

And so ultimately, we've worked well so far. Certainly, in developing the launch strategy, we're beginning to move into execution. We've established appropriate governance for all the key decisions. We believe it's working well, and I think both companies are firmly committed to establishing the oral weekly category. And as a lend, as we've noted, has the strong potential to be the first option.

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

Great. Thanks, Michael.

Amanda, I know it's a busy morning for most, so we'll take time for one more question, please.

Operator

Luise Chen, Scotiabank.

Luise Chen - *Scotiabank - Analyst*

Hi. Thanks for taking my question here. I wanted to ask you if you think what you have, have what you need for a full product offering to HIV patients in both your commercial and pipeline products, or are there other areas that you think will be important for you to be involved in? Thank you.

Eliav Barr - *Merck & Co Inc - Senior Vice President, Head of Global Clinical Development & Chief Medical Officer*

So maybe I'll start with the future. Look, I think everyone is looking for new therapeutic classes. This is a disease that people have to grapple with today for 50, up to 50 years. And so, there are always going to be important enhancements that will need to be made. There's a lot of desire for functional cure.

We're working on a lot of those elements, and I think we've got a very unique set of discovery assets and also capabilities, given our interest in immuno-oncology and immunology in general to think about how we might address that, but these are our long-term plans.

I'll turn it over to Brian and to Greg to talk about the commercial element.

Brian Foard - *Merck & Co Inc - Executive Vice President, Specialty, Pharma & Infectious Diseases*

I think it's a fantastic question. And I'll pass to Greg here in just a minute. I think the key thing for us to do as we've continued to do for many years now is to continue to collaborate with the community and make sure that we understand exactly what it is that they need. And so I think from that, we'll continue to work tirelessly, I think, to develop innovative options for the community.

Greg, anything else?

Gregg Szabo - *Merck & Co Inc - Senior Vice President, Integrated Global HIV Franchise*

I would maybe just say that we already have, I think, a very clearly defined and well-sequenced portfolio strategy. Each of these assets is really designed to address distinct unmet needs. Each of these assets has meaningful scientific differentiation, and we're putting around that. We've undertaken extensive internal and external benchmarking to make sure that we have the resources, the capabilities, and the investment levels that are aligned with the competitive dynamics of the field to make sure that we can be confident in our ability to allow us to compete and we're confident that we can invest at that level.

So I think this begins with IDVYNSO. We're already out there in the marketplace across medical affairs, market access, commercial function, actively engaging with stakeholders, leveraging our longstanding relationships. And so far, the progress has been good and the reception has been very positive.

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

Excellent. Well, thank you, Luise, and thank you all for your interest and time this morning. Please reach out to the IR team for any immediate follow-ups, and we look forward to speaking with you tomorrow. Thank you.

Operator

Disconnect at this time.
