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EDITED TRANSCRIPT

MRK.N - Merck & Co Inc to Hold Investor Event to Highlight Advancing Research Pipeline for HIV Treatment and Prevention

EVENT DATE/TIME: JULY 17, 2025 / 1:00PM GMT

OVERVIEW:

Company Summary

REFINITIV

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PRESENTATION

Operator

Thank you for standing by. Welcome to the Merck & Company Incorporated, Rahway, New Jersey, USA, HIV 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, Senior Vice President, Investor Relations. Sir, you may begin.

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

Thank you, Shirley. Good morning, everyone. Welcome to Merck's HIV Investor event coinciding with the 13th International AIDS Society Conference on HIV Science.

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 this morning. Merck & Company Incorporated, Rahway, New Jersey, USA, undertakes no obligation to publicly update any forward-looking statements.

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

Speaking on today's call will be Dr. Eliav Barr, Senior Vice President, Head of Global Clinical Development, and Chief Medical Officer; Dr. Liz Rhee, Vice President, Clinical Research, Infectious Disease; and Chirfi Guindo, Chief Marketing Officer, Human Health. The full biographies of the speakers can be found in the appendix of the accompanying slide presentation.

Now moving to the agenda. Eliav will start our prepared remarks with a strategy overview. Liz will then provide a research update across our broad HIV pipeline, and Chirfi will discuss the commercial opportunity. Eliav will then wrap up with closing remarks before we turn to Q&A.

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 - Merck Research Laboratories*

Thank you, Peter, and good morning, everyone. Thank you for joining us in today's event in conjunction with the International AIDS Society meeting. Today, we'll provide an in-depth review of our HIV treatment and prevention pipeline as well as the opportunity that stands before us to help more people at risk for or living with HIV infection.

Our commitment to HIV started at the very beginning of the AIDS epidemic. And over the years, we've been responsible for creation of the prototype of each of the potent antiretrovirals that are designated as anchors of HIV treatment regimens.

Now I joined Merck in 1995. At that time, Merck had just announced the results of the CRIXIVAN Phase 3 program that led to the licensure of this proteus inhibitor anchor medicine within weeks of submission. The company had also discovered the first NNRTI, efavirenz, a drug that became the anchor medicine in Atripla, the first single-tablet regimen for HIV treatment.

After these successes, we continued to innovate. We discovered the integrase strand transfer inhibitor, or INSTI, class of anchor medicines; and we launched Isentress, which is the prototype for this class. Iterations on Isentress' profile led to development of INSTIs that have become the most common anchors in HIV therapy regimens today. We've continued our innovation by ensuring availability of drugs for pediatrics, even down to newborns.

More recently, our goal has been to find new types of antiretrovirals with high barriers to resistance and potency to help enable reductions in the burden of HIV treatment and prevention regimens. With the in licensing of islatravir from Yamasa, we introduced a new class of anchor medicine, the nucleoside reverse transcriptase translocation inhibitor, NRTTI. Doravirine/islatravir is a first investigational regimen in the NRTTI era.

Now Merck remains active in the field of HIV research because collectively, the HIV treatment and prevention community has yet to reach full control and prevention of HIV as defined by the UN AIDS 2030 goals. There still remains significant unmet need globally in HIV, with currently approximately 40 million people living with HIV.

An estimated 1.3 million people were infected with HIV in 2023, which equates to about 3,500 new infections per day. For these individuals, it has proven difficult to remove the stigma associated with HIV. We intend to be part of the solution for the continued unmet need in HIV treatment and prevention worldwide.

So how are we going to do that? We aspire to be the first -- to be first in class and best in class with our NRTTIs, which we hope will serve in important roles in both treatment and PrEP for prevention.

NRTTIs inhibit HIV reverse transcriptase through immediate and delayed chain termination after incorporation into spiro DNA. These agents also block reverse transcriptase translocation, preventing nucleotide incorporation.

NRTTIs are potent and long-acting molecules, as exemplified by our candidate medicine for PrEP, which is being studied in a Phase 3 trial at 11 milligrams once monthly. Because of this, NRTTIs may be appropriate for weekly, monthly, and potentially even longer interval regimens. A longer dosing interval has the potential to reduce treatment failure due to non-compliance, to offer additional treatment options, and to reduce stigma.

Our clinical trials have shown that at the appropriate doses, NRTTIs have had favorable efficacy, safety, and drug-drug interaction profiles, features especially important in older individuals and those people with comorbidities. Finally, our regimens are InSTI free, reserving this important class of therapies for later if needed.

Now our current inline portfolio includes the original Isentress as well as PIFELTRO, or doravirine; and DELSTRIGO, which is a fixed dose combination of doravirine, TDF, and 3TC. Doravirine is an important part of the current portfolio, but it's also in our current investigational two-drug islatravir-based regimen.

It is an NNRTI with favorable efficacy and safety profile. In the near term, we will leverage our experience with Doravirine to create a single-tablet regimen with islatravir, our leading NRTTI candidate. Now, Liz will review the data for this regimen. It's been filed in the US, and a PDUFA date has been set for April 28, 2026.

We've also invested heavily in our once-weekly treatment regimens, which can reduce the burden of adherence to 1/7 compared with daily regimens, an advantage for individuals with busy or complicated lives.

The first of these investigational weekly treatment regimens will combine islatravir with lenacapavir, and this is part of our ongoing collaboration with Gilead. This regimen leverages the potency of islatravir and the proven track record of lenacapavir to create a two-drug regimen.

Our long-term expertise in NNRTIs has enabled us to discover several candidates with different pharmacologic profiles. One of these is ulonivirine, which we are studying in combination with islatravir is a weekly single-tablet regimen. The islatraviric duo has the potential to be the smallest tablet approved, and one with a favorable DDI profile.

Control of HIV transmission requires multiple PrEP options. We're very excited about the potential of MK-8527, which is being studied as a once-monthly oral PrEP pill. It's a very small tablet that can be used easily and in a discreet manner, and we think it's going to be very important globally.

We also have intensive research efforts to look at new therapies, not only longer term, longer acting, longer half-life medicines within the classes we've talked about already, but also new classes of medicine.

We've been at the forefront of developing anchor medicines in HIV with features to enable different attacks on the HIV virus. We believe this -- those opportunities also exist in our preclinical and early clinical pipelines.

As we move forward to the next period of future innovation in HIV, we'll be considering our ability to develop long-acting formulations which include assets in the family of NRTTIs and also in the family of NNRTIs. These leverage our expertise in those classes of drugs. We also have collaborations with Gilead and a variety of options in both treatment and PrEP under development.

We're also thinking hard about how we will leverage our expertise to bring forward either cure or long-term control or reset approaches. One of these approaches of interest is the RT-TACK mechanism of action. These are NNRTIs that have the additional feature of selectively killing HIV-infected cells. We're currently evaluating candidate medicines in early development.

So with that, I'd like to turn the virtual podium over to Liz, who's going to be telling us more about the current pipeline, focusing on the results we presented recently at CROI as well as at IAS this week. Liz?

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

Thank you, Eliav. I am very excited today to be here with you to share more about our expansive HIV pipeline, which has continued to make great progress.

Today, we'll be highlighting the four programs that are currently in late stage development in our HIV pipeline. These programs are anchored on our NRTTI molecules and are leveraging the properties of this class. Each program has generated data that we think is really exciting and support the progression of these programs.

We have three programs in development for treatment that are anchored by islatravir, including a once-daily oral treatment program with doravirine and islatravir, which has recently filed the initial NDA in the US based on data in adult participants who are virologically stable. The PDUFA date for this filing is set for April in 2026. In addition, we have filed an application for doravirine/islatravir in Japan.

Then we have our first weekly oral treatment with islatravir in combination with lenacapavir, which we are developing in partnership with Gilead and which is in Phase 3 development. We have a once-monthly oral PrEP option with a new investigational NRTTI, MK 8527, which is on the cusp of starting Phase 3. Finally, we have our wholly internal, oral, weekly treatment regimen candidate where islatravir is being combined with our new investigational NNRTI, ulonivirine, which has recently started Phase 2.

With these four programs, we have the potential for four NDAs to be filed over the next few years. This is truly exciting for us as we see that each of these products can be a potentially important option for people living with HIV or people who are at risk of acquiring HIV.

The NDA for deriving islatravir is currently under review by the FDA, and the basis for this filing was two pivotal studies in virologically suppressed adults who have no history of treatment failure. Importantly, in this program, this is the first set of Phase 3 studies where we were able to demonstrate that a two-drug regimen that does not contain an integrase inhibitor was not inferior to a three-drug regimen containing an integrase inhibitor.

The two Phase 3 trials, Protocol 051 and Protocol 052, were conducted in virologically stable participants. In each trial, they were randomized to either continue on their baseline treatment or switch to doravirine/islatravir.

In Protocol 051, the baseline treatment was background antiretroviral therapy, which included different kinds of two- and three-drug regimens. And in Protocol 052, the comparator was bictegravir/FTC/TAF. In both trials, we were able to demonstrate strong efficacy results.

In both trials, doravirine/islatravir was not inferior to the comparator, as demonstrated by the primary endpoint results at week 48 based on people having RNA levels above 50 copies per mL. This is on the left of each of the figures.

As you can see in the figures, the second set of bars on the right showed that there were high rates of virologic suppression greater than 90% in both trials. Importantly, there was no treatment of emergent resistance to either doravirine or islatravir that was observed in either study. And the tolerability and safety profiles were comparable in each of these trials to the comparator.

Also important to note is that we saw that total lymphocyte and CD4 count changes over the course of these studies were similar between doravirine/islatravir and the comparator regimens. These are very promising results because this is the first two-drug regimen that does not contain an integrase inhibitor that's demonstrated comparable efficacy with a three-drug regimen containing an integrase inhibitor.

Our filing in the US was accepted for an indication in virologically suppressed adults. We have another study, Protocol 053, being conducted in treatment-naive adults which has completed enrollment. And we expect that the week 48 data will read out by the end of this year and will be presented next year at a scientific meeting. We expect these data to support the initial application in the EU and to support a US label expansion as well.

In addition to a once-daily regimen, including islatravir, we are also developing two once-weekly, two-rug oral treatment regimens, both containing islatravir. And we think that each of these will be an important option for patients who desire a weekly oral regimen as a way to shift away from

daily treatment. We believe that once-weekly oral regimens will help to address challenges around pill fatigue that people living with HIV often grapple with.

Islatravir/lenacapavir, which we're developing with Gilead, our partner on this program, is currently Phase 3 and recently completed enrollment for those studies. This combination is being studied in virologically suppressed adults and will include a loading dose strategy followed by a single tablet administered once weekly. We are excited that this has the potential to be the first weekly oral treatment regimen to market and the first complete long-acting oral treatment regimen for HIV.

The islatravir/ulonivirine program has recently started Phase 2 and is currently being evaluated in adults who are virologically stable. But we also have plans to study this in adults who are treatment naive. This regimen is differentiated from islatravir/lenacapavir by the inclusion of ulonivirine, which is an investigational and NNRTI.

It's being studied at a dose of 200 milligrams in combination with islatravir, which we think will have the potential for a more simplified regimen as a single tablet that has the potential to be smaller than the islatravir/lenacapavir tablet without requiring a loading dose. And we also believe, importantly, that this has the potential to have a favorable safety and DDI profile.

For the islatravir/lenacapavir program, we've conducted a Phase 2 study to evaluate this combination and presented these data last year at CROI and at IDWeek. What's shown on the slide are the week 48 results that were presented at IDWeek.

In this trial, as you can see, where the comparator was bictegravir/FTC/TAF, islatravir/lenacapavir resulted in virologic suppression at high rates that were similar to what we've seen in the comparator group. Importantly, there were no participants that were discontinued due to decreases in CD4, T cell, or lymphocyte counts; and the overall lymphocyte and CD4 counts were similar across treatment groups.

These are the data that gave us confidence to move this program into Phase 3. And this program, we're calling the ISLEND program. This was initiated at the end of last year and an enrollment recently completed.

ISLEND-1 and ISLEND-2 are being conducted in adults who are virologically suppressed. And in ISLEND-1, the comparator is bictegravir/FTC/TAF. This is a blinded -- double-blinded randomized control trial.

ISLEND-2, in contrast, is an open-label randomized trial. And here, the comparator is baseline antiretroviral therapy, which can include different two- and three-drug regimens. Both of these trials are expected to read out the 48 week results in mid 2026, and we look forward to seeing these results.

Ulonivirine, or MK-8507. This is our novel investigational NNRTI, and we are moving this forward in development in combination with islatravir as part of our wholly internal, Merck oral weekly treatment regimen.

This week, we presented data from this program at IAS. Ulonivirine is a potent NNRTI. This was demonstrated in a Phase 1b proof-of-concept study where we saw excellent virologic activity.

We did conduct a prior Phase 2b study where we dose range ulonivirine in combination with a higher dose of islatravir. And this study, whilst stopped early, did provide helpful supporting data for the combination and for the selection of the ulonivirine dose.

As shown on the slide, the predicted ulonivirine exposures with a 200 once-weekly dose met the PK threshold to cover wild type and common NNRTI variants. We've also generated data to demonstrate that there's no clinically meaningful drug-drug interaction between islatravir and ulonivirine and that repeat dosing of ulonivirine has no adverse effect on total lymphocyte counts and CD4 counts.

The Phase 2 study of the combination is currently enrolling, and we look forward to seeing the results next year for week 24 primary endpoint.

So in addition to creating meaningful options for treatment, we believe it's really important as well to provide meaningful options for HIV PrEP. We're very excited that we have the opportunity with MK-8527 and that we've made progress in advancing this program.

The concept of a once-monthly oral pill to prevent HIV infection has many potential benefits for people who are at high risk for HIV. MK-8527 is being uniquely developed only for PrEP, and we believe it can have a potential very important impact on global public health.

Based on the pharmacokinetic profile of this molecule, we anticipate a fast onset of protection so that within an hour of taking the first dose of MK-8527, people would be able to have a month of protection from HIV. There would also be no need for a loading dose.

In addition with the discretion that's allowed with a small once monthly oral pill, we believe this will be easy to use and address concerns around stigma that are associated with taking a pill for PrEP every day. And this will also, we believe, offer different ways for implementation that may be more convenient for people compared to an injection that patients would have to go to a physician's office to receive.

Importantly, based on the data seen so far, MK-8527 has the potential to provide favorable efficacy, safety, and DDI profile for those people who could benefit from using PAP.

This week at IAS, we've presented Phase 2 data for MK-8527, and these are the results that supported advancing this program to Phase 3. MK-8527 is an NRTTI with the same mechanism of action as islatravir. It is also highly potent and has excellent resistance in vitro.

The Phase 2 study results informed our selection of a dose for Phase 3 trials, which will be starting imminently. As you can see in the top figure, which shows the study schema, we conducted a Phase 2 dose ranging study of MK-8527 compared to a placebo where we looked at three different doses of MK-8527.

The study was conducted in people who are at low risk for HIV infection and evaluated safety, tolerability, and pharmacokinetics. As you can see from the concentration over time figure, the pharmacokinetic results support monthly dosing of MK-8527 for PrEP.

Based on the modeling that's been conducted from these data, we selected a dose of 11 milligrams to advance into the Phase 3 program. Importantly, all three doses were well tolerated and demonstrated the safety profile that was comparable across the different doses of MK-8527 and to the placebo group.

So we are moving forward to initiate the Phase 3 EXPrESSIVE program for MK-8527 PrEP. This program is comprised of two Phase 3 trials, EXPrESSIVE-10 and EXPrESSIVE-11. EXPrESSIVE-10 is being conducted in adolescent girls and young women at greater likelihood of HIV exposure, and EXPrESSIVE-11 is being conducted in populations at greater risk of HIV exposure, which includes men who have sex with men and transgender individuals.

Both of these trials are large studies evaluating MK-8527 once monthly against the daily oral comparator FTC/TDF. Of note, EXPrESSIVE-10 will include not only older adolescents, meaning 16 to 17 years old. But also, women who become pregnant while on the trial may opt to stay on the study. So we anticipate data in pregnancy and lactation in this trial.

EXPrESSIVE-10 is being conducted in partnership with the Gates Foundation, and this is a collaboration that both the Gates Foundation and we are very excited about. We do see the great potential here to bring forward, a meaningful option for people around the world, as well as an opportunity to impact the global epidemic in areas where there's still very high rates of infections such as sub-Saharan Africa.

EXPrESSIVE-11 is slated to start any day now, and we anticipate the first participant will be involved in early August. And this study will be conducted globally. So we look forward to the initiation of the Phase 3 program and sharing the progress with you in the future.

With that, I will turn this call over to Chirfi.

Chirfi Guindo - *Merck & Co Inc - Chief Marketing Officer - Human Health*

Thank you, Liz. Good morning, everyone. As we mentioned before, Merck has a long and rich legacy in HIV. We have a track record dating back to the early 2000s of working in partnership with governments and global partners, such as the Gates Foundation, to enable broad, sustainable global access to our HIV innovations.

I'm proud to have been part of several of these important access initiatives when I led global marketing for HIV at our company and before that, when I served as Managing Director for Merck in South Africa. It is humbling to now be in a position to potentially bring forward four very important options for both treatment and PrEP in the near future.

HIV is a large market that is anticipated to continue to grow rapidly, primarily driven by demand for PrEP. The treatment market is also expected to continue to grow to approximately $25 billion by the mid-2030s.

As you heard from Eliav earlier in the presentation, high unmet needs remain in HIV. Up to one in every five people living with HIV switch their treatment regimens annually due to tolerability, resistance, or the desire for simpler regimens.

On the PrEP side, a substantial opportunity exists to bring new options into the market, including a monthly oral option like MK-8527. This is particularly exciting for people who are seeking flexibility and the discretion that comes with having a monthly pill that can protect against HIV.

The HIV landscape -- next slide. The HIV landscape is continuing to evolve, and the needs of the community are becoming more and more clear. We have done a lot of work in market research, interacting with patients, advocacy groups, providers, and other members of the community.

Four main insights have emerged from those interactions. First and foremost, people with HIV are aging. Currently, half of people living with HIV in the US are 50 or older. Roughly one-third of people living with HIV have comorbidities. It is therefore important to bring forward suitable options for these individuals.

The second insight is on the growing need for simplification and two-drug regimens in particular. People on treatment are wanting less drugs while enabling viral control and the efficacy that these regimens provide.

The third insight is the need for additional options and choice because adherence challenges continue, with many people living with HIV missing doses on their existing treatments.

Finally, stigma continues to be a challenge. As Eli have noted, almost half of adults have discriminatory attitudes towards people living with HIV. It is important to be able to bring forward options that allow for discrete dosing and potentially have minimal interaction with the healthcare system.

Approximately one-third of people, when asked, would prefer long acting oral options for both treatment as well as for PrEP. This is precisely what we will offer as we continue to develop our exciting pipeline.

On the treatment side, we have DOR-ISL as a potential daily oral regimen; ISO-LEN, in collaboration with Gilead, as a potential first oral weekly regimen; and ISL-ULO as a wholly owned potential weekly oral regimen.

For these options -- these options provide virologically suppressed people living with HIV with a simpler two-drug regimen that do not contain an InSTI. This can be particularly meaningful for people who are getting older and for whom drug-drug interactions, cardiometabolic toxicities, and other tolerability issues may be a concern.

Our new treatment options may be able to offer choices for both switch as well as treatment-naive populations of people living with HIV. Importantly, they can reduce pill burden with weekly dosing for ISL-LEN and ISL-ULO.

On the PrEP side, we're aiming to launch the first and only monthly tablet for HIV prevention with MK-8527, our investigational NRTTI that has been specifically developed for PrEP and PrEP only. This is important because there will be less concern about the potential for resistance when thinking about use of the same molecule for treatment and for PrEP.

MK-8527 has the potential to enable fast onset of protection within one hour of intake with no loading dose needed. It would provide discreet, monthly, oral dosing to meet the preferences of many people seeking long-acting protection who do not want injections.

We expect this program will be meaningful for public health on a global basis, and we fully recognize the responsibility our company has to work with partners to address public health needs, both in high-income countries as well as in low- and middle-income countries. We feel we are well positioned to drive important progress for people impacted by HIV around the world.

Earlier this year, we laid out the components of our expansive, late-stage pipeline that comprise a potential revenue opportunity of over $50 billion by the mid-2030s, putting MFN aside. With that, we see an opportunity of greater than $5 billion for our late-stage HIV portfolio, which consists of four impactful new product launches anticipated over the next few years, the first of which is DOR-ISL for daily oral treatment.

Last week, the FDA accepted for review the NDA of DOR-ISL and set a PDUFA date of April 28, 2026. This would be the first regimen containing an NRTTI to be approved by the FDA. It would also be the first complete two-drug regimen that does not contain an InSTI.

Subsequently, we have a potential first long-acting oral treatment to be approved with ISL-LEN in partnership with Gilead, which is currently in Phase 3 and has primary completion dates next year. Next, we have our potential once-monthly oral PrEP, MK-8527, which will begin in Phase 3 imminently.

Finally, we have ISL-ULO which combined islatravir with our investigational, next-generation, long-acting NNRTI, ulonivirine, with a high barrier to resistance. ISL-ULO, which is fully owned by Merck and currently in Phase 2, has the potential to be the smallest pill approved for one-weekly treatments, which also does not require loading.

This greater than $5 billion opportunity on a non-risk adjusted basis underlines our confidence in this pipeline of HIV treatment and prevention options. Our excitement to bring forward these innovations is mashed by the enthusiasm of the community, as we heard this very week at IAS.

It identifies our important presence in HIV since day one. We're eager to leverage our commercial engine and our global footprint to bring forward these great new options for people impacted by HIV around the world.

And with that, I turned the call back to Eliav.

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

Thank you, Chirfi. From all that has been shared, it should be evident that we are highly interested in continuing to contribute to HIV treatment and prevention. We're confident in our ability to play an important role with these programs we've laid out.

We are pioneering potentially novel options, including with an NRTTI anchor medicine that has a unique mechanism of action, high potency, high barrier to resistance, favorable DDI profile, and the capability for longer-acting impacts in treatment and prevention regimens.

We anticipate four new approvals in the near term, and we are working with speed to ensure that we can get these important medicines to people globally. We continue to work with the community to ensure that HIV treatment and prevention remains a top priority for public health officials.

We want to make sure that people are not defined by their HIV, firstly, by preventing infection; and secondly, by bringing forward regimens that enable people to control their HIV without having to think about it often.

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

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

Thank you, Eliav. Shirley, we're ready for Q&A. Before we get started, two things, please. First, Kathryn Hayward, Senior Vice President, US Pharma, will be available for questions. And secondly, if I could request that questioners, please limit the subject matter today to our HIV program.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Trang Nguyen, UBS.

Trang Nguyen - *UBS AG - Analyst*

We've just got two on 8527. So I guess first, what makes you confident that 8527 doesn't have the lymphocyte lowering issues when used at higher doses for the monthly combos?

And then secondly, and perhaps linked to the first question, but is there a roadmap for injections for longer durations for this product, like a four or six months or even resuming the implant development for 12 months which you previously had for islatravir? Or can you not push that dose higher because of those lymphocyte lowering issues?

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

Right. I'll take that. This is Eliav. We have had an extensive de-rising program for MK-8527 that followed the same path that led to the successful derisking of MK-8527 -- I'm sorry, MK-8591 or islatravir. We have the right models and the right clinical data that have given us that confidence.

And equally, the data that we've presented today -- or this week at IAS and also reviewed extensively with regulatory authorities has convinced them that we are on the right track here with a drug that has enormous potential. So we're very excited about that.

With respect to your second question, we're exploring a variety of different injectable options. That work is in earlier stages of development, and we're confident that we'll be able to bring forward medicines that will allow for a whole variety of different durations of therapy and hopefully, as long as possible.

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

Next question, please, Shirley.

Operator

Mohit Bansal, Wells Fargo.

Mohit Bansal - *Wells Fargo Securities LLC - Analyst*

Just a couple of questions. One is that it does seem like markets might shift to injectables if -- in longer term, especially for the PrEP market. What does your market research suggest which makes you more confident around the monthly oral? Yes, it is monthly.

And then number two, with the islatravir-ULO combo, you are combining two NRTTIs. So is there any potential for added toxicity given that they are two similar mechanisms and one of them did cause, at higher doses, lymphotic issues?

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

Yeah. Let me start by -- the second with a correction. The islatravir-ULO are two -- actually, two different mechanisms of action. Islatravir -- I know that the letters are very similar, but they're completely -- they're different mechanisms of action.

Islatravir is an NRTTI, and ulonivirine is an NNRTI. There is natural confusion, but they're different. So we don't expect any -- and we've actually derisked both molecules pretty well, including a long-duration dosing of ulonivirine monotherapy just to make sure it has absolutely no lymphocyte effects. So that combination. I think, will be a very exciting one.

With respect to the monthly, I'm going to turn that to Chirfi to answer.

Chirfi Guindo - *Merck & Co Inc - Chief Marketing Officer - Human Health*

Yeah. No, thank you for the question, Mohit. So I think it's important to highlight that despite the availability of daily options for PrEP, the availability of injectables, still, 1.3 million people get infected on an annual basis. So clearly, more is needed to protect individuals who want to be -- want to avoid HIV infection around the world.

So we believe -- when we did the market research, we presented options to these individuals. About a third of them have signaled preference for a monthly oral option to protect themselves. And the reason for that is really the fact that it would be more convenient for them. It would give them the option of having a potent, rapid protection within an hour.

In the case of MK-8527, sorry, they could take this medicine in the comfort of their home. You could think about telemedicine in this context, where individuals would not need to necessarily go to the doctor to get their injection.

So we believe that this oral monthly PrEP option would actually expand access and facilitate access to many individuals in the United States and around the world. So we're excited about this opportunity, frankly. You should have been at IAS. You would have heard the community super enthusiastic about this monthly oral option.

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

Next question, please, Shirley.

Operator

Evan Seigerman, BMO Capital Markets.

Evan Seigerman - *BMO Capital Markets (US) - Analyst*

Malcolm Hoffman on for Evan. Thinking about MK-8527 again, can you talk about how Merck may be able to capture a greater opportunity in the lower-risk patients not exposed to HIV? Also, I know this is not the majority of the market opportunity in this patient population, but could you maybe contextualize how you think about the opportunity for these patients?

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

Chirfi, why don't you take that?

Chirfi Guindo - *Merck & Co Inc - Chief Marketing Officer - Human Health*

Yeah. So for us, I mean, the opportunity is so huge in the people who are at risk, as I mentioned, 1.3 million who are getting infected on an annual basis. So our studies were done specifically in those populations. And so this is really the opportunity that we're going to go after in the coming periods.

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

Next question, please, Shirley.

Operator

Asad Haider, Goldman Sachs.

Asad Haider - *Goldman Sachs Group Inc - Analyst*

Great. Two quick ones. First, for PrEP. Can you maybe talk about how you're positioned and what market share you think is possible versus generic daily orals -- Gilead's DESCOVY will also be generic around the time you launch -- and also against Gilead's lenacapavir, where there will likely be the early injection formulation when you launch as well?

And then second, on treatment. How do you think about how much share you could build from Biktarvy with the Gilead-partnered weekly oral? And how might that compete with Gilead's wholly owned weekly oral if both make it to market, recognizing of course with the latter is currently on a clinical hold?

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

Just -- this is Eliav. I'll just make a couple of general comments. I think it's really important in the PrEP space to have options that enable people to have discreet and low compliant -- low-compliance burden options.

When we talked to folks around the -- in both high- and middle- and low-income countries, the idea of having a monthly pill, discreet, at home telemedicine, or not having to go to a healthcare center to get an injection, is a real home run winner for them. I think it's a very important one.

And in terms of the treatment, again, they -- there'll be a lot of options needed for treatment. We have -- with our Q weekly, we have the power of working together with Gilead. We'll have our own wholly owned drug that will have some very unique properties and a broader label.

In terms of looking at the opportunities, I'll turn it over to Chirfi more contextualization.

Chirfi Guindo - *Merck & Co Inc - Chief Marketing Officer - Human Health*

Yeah. So I would go back to what I said about PrEP to start with. And Eliav summarized it nicely in terms of what the community is wanting, the options that the community is seeking for protection.

I think the advantage of MK-8527 really is the fact that it is a small pill. It works very fast. Within an hour of intake, you get a full protection for a whole month. And you even have forgiveness up to seven days beyond that. And you can take it with the discretion that Eliav talked about.

And you don't have to go to the doctor and get a needle injection and so on and so forth. So we believe that many, many individuals will choose this option. And market research suggested about a third of people would opt for this for their protection if it were available.

And then on the treatment side, again, I agree with what Eliav said. We believe that our weekly options are going to be well positioned, and we will have a meaningful share for both ISL-LEN when approved as well as ISL-ULO when approved. These are very good options that provide differentiated benefits for patients going forward.

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

Next question, please, Shirley.

Operator

Luisa Hector, Berenberg.

Luisa Hector - *Berenberg Capital Markets LLC - Analyst*

On MK-8527, I wonder if you could comment on the amount of data you have on drug-drug interactions, including perhaps recreational drug use?

And then secondly, on your sales ambitions by therapy area. They do tend to arrive in $5 billion increments. So given the amount of data that you have in-house in HIV, could you comment on whether you're over $5 billion sales potential has increased towards $10 billion? And if not, why not?

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

Great. Well, maybe we'll start with the DDI question. And I'll ask Liz to comment on that.

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

Yeah. Thank you, Eliav. So MK-8527's potential for drug-drug interactions is low. And this is based on the preclinical profiling that's been done for this compound as well as the Phase 1 dedicated studies that we've conducted. So we do think that overall, the potential for meaningful DDI is low with this compound.

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

And I'd just add to that that these -- the NRTTIs are the metabolism, such that it has -- that the drug-drug interaction potential is really quite minor. Obviously, we can't do direct drug-drug interaction studies in people with recreational drugs.

But we -- but based on our understanding of the metabolism of those drugs, we don't anticipate any drug-drug interactions there necessarily. Of course, there's a lot of impurities in these drugs, and we don't really know what might happen unfortunately on an individual basis.

When we -- let's talk about the commercial side.

Chirfi Guindo - *Merck & Co Inc - Chief Marketing Officer - Human Health*

Yeah. I don't want to give -- our confidence continues to be reinforced with respect to our HIV pipeline based on the data, obviously. One thing I would give to you is that we believe that DOR-ISL, which will be the first half of the gate, is likely to be the preferred switch option for many individuals who are going to be switched from their existing regimen which usually contains an InSTI, right?

And so DOR-ISL being the first in a new class of NRTTIs, which provides robust virocontrol, high barrier to resistance, and the convenience and the tolerability and the DDI benefits that we've talked about, we believe that -- importantly, that does not include an InSTI. We believe that DOR-ISL would actually be the preferred switched option for those individuals.

And just as we mentioned earlier, one in five patients treated with the HIV regimen will be switched on an annual basis. So this gives you an indication of how we are thinking about the opportunity for the first out of the gate. But similarly, we are equally excited about the weekly options going forward.

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

And Luisa, it's Peter. So when we're asked about what's underappreciated at Merck, one of the subjects that we typically lead with is HIV. So when we look at consensus estimates, there's not a lot in models for HIV pipeline and portfolio. And that's one of the reasons why we did this call today.

We're very confident in the $5 billion-plus opportunity that we've spoken about, and we're not going to update that today. But we look forward to continuing to see progress across this program. And hopefully, today's event will help you understand why we're so confident.

Next question, please, Shirley.

Operator

Courtney Breen, Bernstein.

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

This is Courtney. I just wanted to dig a little bit into the PrEP opportunity specifically. And one of the pieces that you've pointed out has been the convenience and the ability to kind of dose a monthly oral at home.

What we've learned with labeling update recently for Yeztugo , the lenacapavir asset from Gilead, is that another key component that requires doctor visits is actually testing to ensure that the patient doesn't have HIV. And so for the injectables today, for Yeztugo with the longer dosing interval, of every six months.

That's a six-month requirement. Whereas for Descovy, which is the daily oral, it's a three-month environment for HIV testing to ensure that that patient hasn't contracted the disease. Can you give us some context as to what we should expect for the monthly oral? Would this be a requirement for an HIV test every month, every three months, or something even longer than that?

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

So it's Eliav, I'll turn it over to Liz in a second, but I'd just say we can't anticipate labeling. Obviously, that's something that we'll discuss with FDA. I'd point out that HIV testing can be done rather anonymously and also not necessarily through a visit to a hospital center.

In terms of how we are doing it in the clinical front, I'll turn it to Liz for comments.

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

Yeah. Thanks, Eliav. In the trials, we are testing for HIV status monthly actually in this trial. But this is not necessarily what we expect the position to be when we bring this product forward for regulatory submission. I mean, I think that every three-month frequency that's associated with the daily options is something that we think is probably more realistic.

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

Right. And although, again, we can't speculate on what FDA or other agencies would say. But considering the standard of care in the field, the ability to get HIV testing again, without having to visit a hospital center, is relatively well established.

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

And I'll just add. The reason why we're checking HIV status monthly is to understand if we do see any infections when they happen. So this is really to enable us to collect need to really fully characterize any infections that do occur in the treatment when participants are in treatment in this trial.

So to answer a scientific question, this is not what we expect in terms of how we would be used in the real world, how testing would be used.

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

Next question, please, Shirley.

Operator

Geoff Meacham, Citibank.

Geoff Meacham - *Citi - Analyst*

I just have two. The first is in the treatment setting, I was curious how you guys think about resistance, especially as you develop doublets in HIV from what is three- or four-drug combos today. And then how would you compare the resistance of ISL or ULO versus, say, an integrase or a capsid?

And then a second question, more of a commercial one PrEP. It's been mostly a US-based market. But what do you think is a tipping point for Europe or Asia more broadly adopting PrEP commercially?

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

Right. So with the first one on resistance, let me turn it over to Liz.

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

Yeah. Thank you. So I think when you think about resistance in the context of multidrug HIV regimens, the number of compounds is not really what's driving the emergence of resistance. And if you think about this historically, we went from three-drug regimens being standard to now, more recently, two-drug regimens showing really excellent efficacy.

And so what's really key, I think, based on the last 20 years that we've learned, is that you need to have at least one agent with the really strong barrier to resistance to protect the regimen. And I think this is often what's behind the concept of an anchor agent in an HIV treatment regimen.

So with islatravir, one of the features that we -- that got us really excited about this molecule is the potency. So you need to make sure you've got adequate potency and levels with the doses that you pick. And then also, the resistance profile. Meaning that islatravir, if you tested in vitro, really takes a while to get resistance-associated mutations detected.

And the one that we do see is M184B, which is a fairly -- a relatively less problematic patient. So this is why it's important when we're looking at our data in our Phase 3 doravirine/islatravir trials that we saw no emergence of resistance to either islatravir or doravirine.

And this is why the concept of doravirine anchoring our treatment regimen is one that we've been talking about. Because we see this molecule as really bringing the potency and barrier to resistance that you need for a drug to anchor a regimen, whether it's a two-drug regimen or a three-drug regimen.

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

Right. And I just would add that this is why we've chosen these two drug classes together there. They're actually quite complementary.

One of the interesting things for islatravir is that it actually -- some mutations that occur, the older medicines actually potentiate the effect of islatravir. And so that is an interesting biological plus that we see. In addition to that, I think that we've shown in our studies, which is actually the most important thing, the lack of emergency resistant.

And I'll turn it over to Chirfi to talk about the commercial elements.

Chirfi Guindo - *Merck & Co Inc - Chief Marketing Officer - Human Health*

Yeah. So for PrEP outside of the US, you're quite right that today, the PrEP market is disproportionately a US market. And so there are many reasons for that outside of the US. And I'm leaving aside the low-income countries in sub-Saharan Africa and so forth, where there's actually quite a bit of PrEP use in the daily form and then going forward in the long acting as well.

So if you look at other high-income countries, there's still a lack of perception of risk by many individuals, low awareness of PrEP and concerns for side effects and the stigma associated with daily use of PrEP. And I think that by having Merck coming back with our global footprint, our commercial engine, we believe that we will actually have a -- make a meaningful difference in helping to develop the PrEP market in these other high-income countries.

We have done this in other therapeutic areas. We know how to reach consumers in many of those markets, we've done that. And we believe that that engine would help enhance the level of awareness. And the once-monthly oral option will help address many of those barriers that I just talked about.

And finally, in terms of implementation, right? To have an option where you're actually not -- you're not relying on going to the clinic, right, with all the challenges of having a nurse in the clinic in many of those countries, I think the monthly oral option will really help develop PrEP in those high-income countries outside of the U.S.

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

Next question, please, Shirley.

Operator

Vamil Divan, Guggenheim.

Vamil Divan - *Guggenheim Securities LLC - Equity Analyst*

So maybe one clinical one and one commercial. One just on the ISL-ULO combination. Can you talk about how that would differentiate from ISL-LEN? I think both will be weekly oral. Then obviously, you only own one and the other one shared with Gilead. But just curious, from a clinical side, how you expect to differentiate there.

And then maybe just in terms of -- on the commercial side, again, going back to the $5 billion HIV pipeline potential that you've highlighted. Maybe can you break that down further as you think about the US versus ex US or treatment versus PrEP? Just kind of a little bit more of a sense of where the $5 billion or $5 billion plus will be coming from.

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

Let me take the clinical ones. So islatravir/ulonivirine, I think, will be -- so for both of these are very nice, are terrific. The islatravir and ulonivirine will be a very small tablet and a very favorable DDI profile of drug that will also have a treatment-naive indication.

So you'll have a set of attributes that I think will be very important for some people, which is not to take away from the islatravir/lenacapavir which will have the potency of islatravir and the proven track record of lenacapavir. So I think that these are going to be complementary drugs that will have very, very important uptake in different segments of the population.

On the commercial side, I'll turn it to Chirfi.

Chirfi Guindo - *Merck & Co Inc - Chief Marketing Officer - Human Health*

Yeah, we're not breaking down the $5 billion opportunity. We're equally excited about all four of these major innovations. And we see opportunity, meaningful opportunity for each one of them. And cumulatively, we believe there will be greater than $5 billion.

And as I mentioned earlier, we do have significant opportunity outside of the US as well based on our engine and our capabilities in those high countries outside of the US.

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

Next question, please, Shirley.

Operator

Terence Flynn, Morgan Stanley.

Terence Flynn - *Morgan Stanley - Analyst*

Great. Two for me. I guess on 8527, I noticed that you're taking the 11 mg dose forward, but it looks like 12 mgs was studied. Not a significant difference there, but just wondering why that decision was made.

And then on MK-8239 plus Len, I know you highlighted it early on. You didn't talk too much about it, but maybe just talk about the target profile there and timing of when we might see the Phase 1 data.

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

So I'll take the first one, and I'll ask Liz to talk about 8239. The -- we chose the 11-milligram dose because we have a very strict modeling program that looks at all the different factors that are necessary for patients to -- for individuals, I'm sorry, this is PrEP, individuals to have control.

We -- it could have been even lower dose. We had no issues with the 12-milligram dose either. But we went through a pretty rigorous algorithmic approach and chose the 11 milligram because it was a sweet spot for all the different attributes we wanted to get.

It shows there's no issues for them going to 12 or anything like that. There was just -- is really just from a modeling point of view. Maybe you can tell us a little bit, Liz, about the earlier development compounds.

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

Yeah. So MK-85 -- sorry, MK-8239, which we are developing in collaboration with Gilead -- so this is a molecule that's part of our partnership -- is in Phase 1. The Phase 1 work is ongoing. So at this point, I don't have a time yet when we can share results from that study.

But the intention here is this is an islatravir prodrug that we think could be suitable for -- as a long-acting injectable to be included as part of potentially a long-acting complete treatment regimen that's injectable. So that's the general concept behind the program, but it remains quite still early in development.

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

We're continuing to do our dosing, and we're working through to make sure that the studies are done appropriately and with a sufficient rigor that regulatory authorities in both companies will feel comfortable to advance forward. And I look forward to presenting those data in due course.

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

Next question, please,

Operator

Daina Graybosch, Leerink Partners.

Daina Graybosch - *Leerink Partners LLC - Analyst*

I wonder if you could talk about payers for a moment from your market research and other attributes that have value, both for your treatment and PrEP around stigma and DDI, which resonate across treatment and PrEP most with the payers.

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

Kathryn, maybe you'd like to address that the.

Chirfi Guindo - *Merck & Co Inc - Chief Marketing Officer - Human Health*

The US-specific question, yes.

Kathryn Hayward - *Merck & Co Inc - Senior Vice President - US Pharma*

Sure. I mean, I can provide a perspective from a US payer standpoint related to some of the attributes. I think one thing that's really important and that is recognized by payers within the US market is that effective treatment and PrEP requires individualization and optimization of treatment based on people's individual needs.

And I think the importance of retaining choice and access to treatments will continue to be critical ultimately to achieve favorable clinical outcomes. Obviously, improved adherence, the ability to actually take and stay on treatment is an important attribute for payers. Clinical efficacy and the ability to actually address unmet needs within our population of people living with HIV is also critically important as well.

Chirfi Guindo - *Merck & Co Inc - Chief Marketing Officer - Human Health*

No, what I would add is, as people get older on their meds and get older with their HIV, obviously, you have to worry about co-morbid conditions. You have to worry about drug-drug interactions. And those are attributes that are also important. And this is where our portfolio overall anchored on the NRTTI class really is well differentiated and we believe that we will be well positioned for early payer access.

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

Next question, please, Shirley.

Operator

Richard Wagner, Bank of America.

Richard Wagner III - *Bofa Merrill Lynch Asset Holdings Inc - Analyst*

Richard Wagner from Bank of America on for Tim Anderson. During the presentation, Merck cited market research indicating a one-third preference for monthly oral regimen for PrEP. What can you say about the market demand for a once-weekly regimen?

I believe the target was described in the presentation as individuals with busier, complicated lives. And I wanted to get a better understanding of that.

And then related, clearly, it seems to me that Merck is confident that there would be adherence advantages for once weekly and once monthly compared to once daily. It's easier for me to see that for the once monthly, but I would like to hear your thoughts on potential adherence advantages for once weekly orals.

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

Let me turn back to Chirfi.

Chirfi Guindo - *Merck & Co Inc - Chief Marketing Officer - Human Health*

Yeah. Just to clarify the insights from the research, Richard. So we put in front of individuals who are patients and nonpatients, right? Options for treatment as well as for PrEP. And about a third of those individuals on either category, right, those who have HIV and those who are at risk of contracting HIV, they opted for one-third long-acting orals.

So on the treatment side, this was a weekly treatment. On the PrEP side, it was a monthly PrEP. Just to clarify, why presented on the slide earlier.

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

Right. And I think that in terms of adherence, the idea here is, certainly, once daily is complicated. Once weekly allows you to say, ready for the work week. I'm going to start or on the one day I'm at home and not traveling or other kind of lifestyle issues.

It certainly is great to have 1/7 of the burden of a daily tablet. So I think that would be very useful. Obviously, we'll be monitoring this in the real world. But I think from the point of view of reducing the burden of adherence and HIV --

And remember, you have to take these drugs every day like very, very fastidiously. It's not like cholesterol where if you missed a couple of days here and there, it's not a big deal. It's a big deal here. So having a once-weekly approach, I think, would be really life-changing for patients.

Chirfi Guindo - *Merck & Co Inc - Chief Marketing Officer - Human Health*

If I add one more point, Eliav, the left inside that we got from patients -- these are patients people who are living with HIV -- is that on the daily regimens, you're reminded every day that you have HIV in your body, right?

So to have the option of taking your pill, a small pill, maybe every Sunday or maybe whatever fits your lifestyle has an emotional benefit in addition to the convenience benefit as well for these individuals. So you're not really stressed out every day in case you happen to miss a pill or something.

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

Next question, please, Shirley.

Operator

Steve Scala, TD Securities.

Unidentified Participant

This is Chris on for Steve. We have two on MK-8527. First, are the Phase 3 trials sufficiently powered to show statistically superior efficacy to Truvada? And is that the birth for success? And second, do you expect commercial launch for this asset before late 2028?

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

I'll ask Liz to talk about the Phase 3.

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

Yeah. So for the EXPrESSIVE trials, EXPrESSIVE-10, which is the study that's being conducted in women, that study is designed and powered to be a superiority trial. That is the primary hypothesis of the study.

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

And then on the commercial side?

Chirfi Guindo - *Merck & Co Inc - Chief Marketing Officer - Human Health*

So we are not providing a specific date for launch. I mean, obviously, we have to -- we are ready to go into Phase 3, very excited about that. And then we'll just have to wait. We will obviously look forward to getting this to the finish line as quickly as possible so we can bring it to people who want to be protected with this once-monthly oral.

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

Yeah, I'll add. I mean, these are event-driven trials, these Phase 3 studies. So we have estimates of how long it will take to complete these studies that are reflected in the posting, but it's possible it could take a little bit longer or less time even.

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

Next question, please, Shirley.

Operator

Alex Hammond, Wolfe Research.

Alexandria Hammond - *Wolfe Research LLC - Equity Analyst*

So on MK-8527, in the Phase 2, we saw one SAE of spontaneous abortion at six weeks of gestation considered related to drug. I know you mentioned in the EXPrESSIVE-10 trial that there'll generation and pregnancy and lactation patients. So can you walk us through the risk benefit of treatment here?

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

Thanks. I'll turn that over to Liz.

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

Yeah. So the decision to allow women in EXPrESSIVE-10 who become pregnant to stay on MK-8527 if they choose to do so is based on the overall data from the program, which includes not just the clinical trial data, but also the non-clinical safety assessment in terms of safety to the embryo toxicity and juvenile safety as well. And overall, the data is very clean and supported the approach that we have -- we are taking with use in pregnancy.

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

These studies have been vetted through the regulatory authorities, and we look forward to getting the results. And we're confident that we'll be able to get the proper safety profile. It's a very important patient population to help with prevention of HIV infection.

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

Next question, please.

Operator

Umer Raffat, Evercore.

Umer Raffat - *Evercore Inc - Equity Analyst*

Thank you for all your transparency on the intracellular triphosphate exposures. And that's really where my question was as well. At the 6 mg dose, it looks like by month -- by the end of month one, the PBMC triphosphate levels are almost basically at that efficacy threshold of 03 picomolars.

And I'm curious, what percentage of the patients that drove that mean we're already below that threshold? And less so focused on the 6 mg dose and more so really asking about the 12 mg dose, what percentage of patients?

I realize mean is above, but what percentage of patients are below the threshold? And secondly, since Chirfi is on and I'm dying to ask him a question, Chirfi, in your view, what percentage of the market by the time you guys launch will be on orals, meaning not on an every four to every six-month long-acting injection?

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

So Umer, thank you. Let me take the first one. When we do our modeling work to look at the doses that we chose to go into Phase 3 studies, they -- as you know, neatness means there's people below, people above.

The 6-milligram dose was good, but we wanted to make sure that it would be covering all different weights, all different potential metabolic profiles and various circumstances, along with a little bit of forgiveness as well.

And when you add all of that together, and you -- we did through both our safety and efficacy modeling-- the 11-milligram dose got us to the point where we were able to have high confidence that the vast, vast, vast majority was well above the bottom threshold for what we anticipated to be efficacy.

So in that regard, the 6-milligram dose was pretty good, but we wanted to be able to not just go for mean but also take the lower growth in the distribution of variability and make sure that that lower 5% were able to get above. And that's why we chose 11.

12 was just nearby, but it was -- 11 was just good enough for that. And you always want a little -- whatever dose, you want the minimal best effective dose even if it's a scooch lower than the highest dose we've tested. Chirfi?

Chirfi Guindo - *Merck & Co Inc - Chief Marketing Officer - Human Health*

Yeah. So Umer, I assume your question is in regards to PrEP, correct?

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

I think he's --

Chirfi Guindo - *Merck & Co Inc - Chief Marketing Officer - Human Health*

All right. So assuming it's in regards to PrEP. So what we do know is that you have a number -- many, many individuals have needle phobia. That's the first consideration, the first insight that I wanted to highlight and reinforce; and the implementation challenges, having to go to a clinic, having to have a nurse inject these meds, and so forth.

So we anticipate that by the time we come to market with MK-8527, there will still be a significant number of people at risk of HIV infection who would be either on Truvada daily, right, daily PrEP; or who would want to be on an oral long-acting option. So the opportunity will be meaningful when we do come to market.

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

Shirley, any further questions?

Operator

At this time, I'm showing no further questions.

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

Okay, great. So I want to thank you all for your interest and time this morning. Appreciate you being with us. And please reach out to the IR team if you have any follow-up questions. And we look forward to connecting with you all soon. Thank you so much.

Operator

Thank you. And this does conclude today's conference. We thank you for your participation. At this time, you may disconnect your lines.