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US Biopharmaceuticals

Notable Quotes, Replay, and Full Transcript from our KOL call on HIV and CROI 2024

Industry Overview

Expert call on CROI 2024 updates and HIV

We hosted a call with Dr. Jihad Slim to discuss updates from CROI 2024 and the evolving HIV treatment and prevention landscape (see our call takeaways). A transcript of the call is available in the body of this report with key quotes below (call replay here).

There's a place in the HIV paradigm for long-acting orals

"I do think that it's easier to have to, I mean, because a lot of the problem with the pill is the stigma related to HIV people don't like to carry antiretroviral drugs and have [people] find their drugs or patients see that they have HIV. So, I sort of get it. In some cases, the idea of long-acting order is that you don't have to tell your status or anybody discovering it without you wanting them to know. So that fits I guess 20%, 25% of patients."

Thoughts on GS-1720

"So, [GS-1720] is definitely more tempting than islatravir combination. Because integrase are a better class theoretically than the NRTTI which we don't know a lot about. So, in that sense in theory the perception is that it would be a better combination. But the truth though is that islatravir and lenacapavir so far is not looking bad either."

6-month lenacapavir treatment still needs a partner...

"I think [bNAbs] is the one that is currently being studied the most...The bNAbs are very safe and have a very interesting mechanism of action. But it's not clear to me that we understand them well until we know better how to get the real sensitivity and how to understand the virological failure...They're still pretty experimental at this point so more than two years to be in the mainstream."

...though positive feedback on Sunlenca bodes well

"Again, so far, it's too early to tell but safety seems fine. Genetic barrier seems low but even when there is resistance, looks like the virus has to pay by lowering its fitness in order to become resistant. So, it is definitely an interesting drug. There's no question that lenacapavir has it all and I think the toxicity is overplayed."

The evolving at-risk and HIV patient population mix

"...The issue is that women don't seem to see themselves at risk for HIV even though they are one of the growing populations of new HIV infection. So, in New Jersey they represent 25% to 30% of new HIV infection. And in the south...on the increase as well."

Convenience of lenacapavir PrEP could be game-changing

"I think taking a pill every day when you're young, healthy, and very sexually active is probably difficult to do. And two months is too much it's just six times a year when you're pretty busy. Twice a year is totally doable where you get your STD screen again depending on how sexually active you are..."

HIV cure elusive, HIV vaccine may be nearer

"And until we have a clear measurement or a real measurement on the reservoir, I think the cure is going to be very elusive... But I happen to think that we have a better chance with the vaccine than with the cure at this point from everything I've seen..."

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Abbreviations:
CROI: Conference on Retroviruses and Opportunistic Infections
PrEP: pre-exposure prophylaxis
HIV: human immunodeficiency virus
KOL: key opinion leader
MOA: mechanism of action
CD40: cluster of differentiation
PK: pharmacokinetic
NRTTI: nucleoside analogue reverse transcriptase translocation inhibitor
STD: sexually transmitted disease
FDA: Food and Drug Administration
IAS: International AIDS Conference
AIDS: acquired immunodeficiency syndrome

Refer to important disclosures on page 12 to 14.

Call Transcript

Operator: Please standby. This call is not for Media Representatives or BofA Securities, Investment Bankers, or Commercial Bankers, including Corporate and Commercial FX. All such individuals are instructed to disconnect now. A replay will be available for BofA Securities, Investment Bankers, and Commercial Bankers, including Corporate and Commercial FX. The replay is not available to the media.

Good day, and welcome to the Expert call on HIV and CROI 2024 updates. Today's call is being recorded. I'd now like to turn the call over to Geoff Meacham, Senior Biopharma Analyst at Bank of America. Please go ahead, sir.

Geoff Meacham: Okay, great. Thank you, operator. Thanks everyone for joining us. My name's Geoff Meacham. I'm the Senior Biopharma Analyst here at BofA. My team is on the phone as well. We have Susan Chor, Charlie Yang, Alexandra Hammond, and John Joy. And we're thrilled today to have with us Dr. Jihad Slim, who is an Infectious Disease Specialist and Chief of Infectious Disease at St. Michael's Medical Center in Newark. Also, he's been a principal investigator for a lot of different HIV trials in the treatment setting is affiliated as well with Newark Beth Israel Medical Center. Dr. Slim, thanks a lot for joining us.

Dr. Jihad Slim: My pleasure.

Geoff Meacham: We're going to talk a little bit about CROI today and the latest and greatest from that meeting and maybe what it means to the paradigm. But for the listeners give us a perspective on maybe on your background on the types of patients that you treat and things that you've been affiliated with in development over the years in the HIV setting?

Dr. Jihad Slim: So, as you said, Geoff, I work in Newark. I'm the Chief of Infectious Disease at St. Michael's. I started my infectious disease training in 1985 in Newark and I've been there since. Most of my academic work has been in HIV and hepatitis C. But I do also a lot of antibiotics and infectious disease. I have a big infectious disease practice mainly based in Newark mainly in Ryan White-funded clinics. So mostly black underinsured, and Medicaid.

Since it's been such a long time that I'm doing it. I'm mainly working with the state to try to help end the epidemic for HIV and hepatitis C as well. And I do go to CROI mainly to see what's new in HIV and what's going on my current investigators I currently have the long-acting PrEP in our clinical trial unit. We have lenacapavir at every six months PrEP. And we have bictegravir, lenacapavir and we have few bNAbs trials ongoing as well.

Geoff Meacham: That's helpful. And before we get into some of the data just set us up with what would you say are the unmet needs in the treatment setting? What are the types of things that patients are coming into asking for? I'm assuming that long-acting with GSK is becoming a little bit more of a common practice. But I want to get a sense for how you think the paradigm kind of what's the biggest trend overall?

Dr. Jihad Slim: So the idea of having every HIV patients diagnosed and treated and being undetectable to decrease treatment as prophylaxis while we're still working on the PrEP are key. The most unmet needs where I work are mainly related to issues that are not being addressed at those meetings. It's more the psychosocial issues that prevent people from getting diagnosed and treated which is the biggest problem we face in Newark and in New Jersey for that matter. And I think in most areas in the US people who are not getting diagnosed and not getting into treatment is really the problem. People who are in treatment, on the other hand are looking for simplification and more tolerable, more toxic, and better drug regimens that they could live with. So these are two separate things.

Geoff Meacham: Let's talk about the treatment setting first and then we can get into PrEP as well for most of the call. Tell me in your current practice when you look at the cabotegravir regimens what's been the reception thus far in the commercial setting? And what do you think is needed to make that competitive? Is it moving to every four months, you know, from every two months? Is that reasonable? Are patients responding to this long-interval type of injection therapy?

Dr. Jihad Slim: So the patients are happy with every two months injections. As you may or may not know the one month still have some indications to a certain degree. Some HIV treaters still believe that once a month, and difficult to treat patients who start out maybe, which doesn't fit exactly the indication of the drug. May need at least in the beginning to be on every month then every two months.

The long-acting cabotegravir for four or six months still need to find a partner. So the rilpivirine may not be the partner that will go with it for that long. There isn't that much work I think right now even though at some point Jensen before they got out of the HIV, they were talking about four months rilpivirine. But we didn't see anything in this meeting regarding the four months. Four months Cabotegravir on the other hand seems to be feasible even up to six months. But it has to find the right partner which at this point looks like it may be the bNAbs. But that study is also enrolling very slowly.

Geoff Meacham: And maybe compare and contrast, Dr. Slim the enthusiasm versus between say lenacapavir and cabotegravir. I know same issue with Gilead lenacapavir needs a partner drug to get to potentially every six months in the treatment setting. If one company were to accomplish every six months, would you say that has a bias to being Gilead over GSK or what's your view on that?

Dr. Jihad Slim: Well, I think they're both at the same level at this point with the six months. And four months may be more achievable. But the truth is that I think both companies at this point are at the same level. They're in their stage of looking for a true partner. The bnAbs are very interesting. The problem with the bNAbs there's still a lot of testing that needs to be adjusted in order to get to where you need to be. And not everybody is a good candidate for them. The test for the sensitivity of the bNAbs is difficult to do and is difficult to interpret. And the virological failures on be bNAbs are difficult to interpret. So we still have a lot to learn on the bNABs before they are in real practice. But we're getting there. It's getting better but this meeting clearly shows that we still have some ways to go before the bNAbs has become standard of care.

Geoff Meacham: Is there a mechanism that you would say is ideally suited for combining with lenacapavir in the treatment setting? Or is it really just a pretty high bar from every six-month treatment frequency?

Dr. Jihad Slim: No, I'm pretty sure that we will get to every six months treatment at some point. I just don't think it's going to be next year. But the six months is going to be mostly for direct observed therapy. I think that the issue with where we're going with HIV is that Darunavir is going to be generic or is already generic, I'm sorry, is already generic Darunavir. That dolutegravir is going to be generic in 2027. So by the time that every six months treatment is happening, very good well-tolerated drugs are going to be generic.

So it's not going to be for everybody to be on the every six months. It's going to be few people who are getting direct observed therapy or clearly cannot take pills or have some kind of great insurance. I don't know we'll have to figure out what's going to happen. But I think that the good generic drug is getting into the picture are going to muddy the future a little bit of those long-acting drugs. Even though definitely they're going to happen because there is a need for them. But it's not clear who's going to be receiving them and who's going to pay for them.

Geoff Meacham: Well, let me ask you just on that point if you were to say GSK or Gilead comes up with probably a two-drug combo that is every six months long-acting injectable. What do you think kind of the steady state like penetration rates would be? Would that be half of patients in the treatment setting would eventually go on a long-acting injectable if it's every six months? Do you think it's like two-thirds? I wasn't sure what other modalities people prefer.

Dr. Jihad Slim: Yeah, I honestly think so. So the epidemic currently the 1.2 million people living with HIV at least a million of them know they have it and they're living with it. And they're on a single tablet regimen that they are tolerating pretty well with very little toxicity and are sort of used to taking the one pill once a day. So that they're tolerating fine. And there will be obviously the one pill once a week and maybe the one pill once a month that will be available if they don't like to take too many pills or a pill every day. So the injectable is not going to be for that many people. Honestly, I think it's going to be more for the direct observed therapy for people with bad mental health that you need to go to their site to inject them every six months to keep them undetectable so that they don't get sick and they don't transmit the virus. It might turn out to be for some, again, elite people who really cannot take pills but I don't see it 50%. I see it 20%.

Geoff Meacham: Okay. That makes sense. And the bNAbs would you say that looks to so far to be the most viable to pair up with a drug like lenacapavir or are there other [inaudible]?

Dr. Jihad Slim: I think this is the one that is the currently being studied the most. But I do have my doubts of where it's going to lead. It is a very safe drug. The bNAbs are very safe and have a very interesting mechanism of action. But it's not clear to me that we understand them well until we know better how to get the real sensitivity and how to understand the virological failure. And have enough people on them so that we could understand more about them. They're still pretty experimental at this point so more than two years to be in the mainstream. And in two years there'll be such good generic that I just wonder how this is going to pan out.

Geoff Meacham: And let me ask you on lenacapavir itself maybe talk through your use of I guess Sunlenca the branded in very treatment refractory populations. Has the commercial experience been good so far? I want to get a sense for maybe real-world safety and tolerability. Some people like GSK has highlighted all the tolerability of the bn toxicities. But I'm not sure if that really is [inaudible].

Dr. Jihad Slim: Unfortunately, New Jersey happened to be one of the worst state for acquiring the drug. It's been very difficult to get it. I only have three patients on it and my three patients are tolerating it very well. So tolerability is not an issue. But I know people in New Jersey have very difficult time getting it because it needs to go only through the CVS specialty pharmacy. And it's been very difficult to obtain. So also, of my patients who needed it couldn't really get it.

So that is an issue with Gilead distribution and the CVS specialty that eventually is going to get better obviously. No, I think the drug is a very good drug. Again, so far, it's too early to tell but safety seems fine. Genetic barrier seems low but even when there is resistance, looks like the virus has to pay by lowering its fitness in order to become resistant. So, it is definitely an interesting drug. There's no question that lenacapavir has it all and I think the toxicity is overplayed by these.

Geoff Meacham: So, the nodules in the skin issues are not really that big a deal in your experience?

Dr. Jihad Slim: In my experience, it's not. I've heard some HIV treaters saying that their patients suffered some bad nodules for a long period of time. But it's the same people who keep repeating the same story. I speak to hundreds of them literally and there are two or three who seems to be always complaining about those same patients getting

the nodules. So, it must have been impressive for them. But the vast majority have patients on lenacapavir with no issue.

Geoff Meacham: Okay. That makes sense. I want to ask you; you mentioned the long-acting if every six months I guess from a Wall Street perspective like a lot of investors are focused on that being sort of the pinnacle. But we've had less of emphasis on longer acting weekly orals, weekly formulations of lenacapavir. But Gilead talks a lot about that. What are your thoughts on sort of a longer-acting oral either every once a month or once a week. Do you think that finds its place [inaudible]?

Dr. Jihad Slim: I do think that it's easier to have to, I mean, because a lot of the problem with the pill is the stigma related to HIV people don't like to carry antiretroviral drugs and have patients find their drugs or patients see that they have HIV. So, I sort of get it. In some cases, the idea of long-acting order is that you don't have to tell your status or anybody discovering it without you wanting them to know.

So that fits I guess 20%, 25% of patients. I think as the society get better theoretically and the stigma goes away it may become less important. But it is amenable for direct observed therapy. That's really what we like as infectious disease doctors. We've done it for tuberculosis. We could do it for HIV if we had less often to give the pills than the daily because it's impossible to do 365 days a year. But if you had to do it only 50 times a year or even 12 times a year that's doable. You could call them make sure you see them taking their pill and you know that they're undetectable and fine. It is tempting and I think useful drugs in our armamentarium especially for such a public health disease that has the public health implications.

Geoff Meacham: That's helpful. I want to ask [inaudible].

Dr. Jihad Slim: [Inaudible] until the vaccine takes over. So, again, at CROI there was some hope again around the vaccine finding the right immunogenic vaccines which could theoretically start happening in five years down the road. So, if that happens then obviously that's going to change the landscape.

Geoff Meacham: Yeah, on that perspective when you think about the adoption of PrEP have you seen fewer new patients coming into the treatment paradigm because you're preventing infection from PrEP. Or has it been pretty consistent each year the number of new patients that come into your practice for treatment?

Dr. Jihad Slim: Yeah, so again, I'm in New Jersey so the whole Northeast and the West actually have a decreased the new HIV. It's not clear if it's because we have more people undetectable and more people on PrEP or we think that that's the reason why. Most of the epidemic right now has moved down south with more women. So even though the absolute number of new HIV every year is slightly shrinking. But the huge changes that is that most of it has moved from northeast and west to the south. So I'm seeing less new patients with HIV.

Geoff Meacham: Okay. That makes sense but not just because of demographics and not necessarily because of PrEP though?

Dr. Jihad Slim: No, possibly. In New Jersey, we don't have a great uptake in PrEP. But we're between New York and Philadelphia where there's been a good uptake of PrEP. And so, it is possible that PrEP had some effect. Most of the new HIV patients we see are actually the immigrants that came in most of them knowing that they had HIV back in their countries and now are here to continue their treatment. But in my sense, we see less HIV than we used to currently.

Geoff Meacham: And let me ask you on other mechanisms. Do you have a view of Merck's islatravir I know it's had a bit of a stop-start in a few years ago in development. But what's your view of that drug in and of itself? And then maybe the viability when you combine it with lenacapavir?

Dr. Jihad Slim: So, yeah. Again, we are doing the once-a-week switch study to Islatravir. Well, so there is a Doravirine, Islatravir by Merck and there is a Lenacapavir Islatravir with Gilead. Well, no, doravirine islatraviris is daily actually. Lenacapavir Islatravir is weekly and we're doing both studies. And my take is that it's going to stay. It's going to always be tented by that decrease in CD4 count. But because it's going to be the first one pill once a week with what so far looks like a good safety it didn't decrease the CD4 count compared to bictegravir. So I think it will have some pickup. But Merck has their patent of Islatravir another NRTTI that hopefully if it turns out to be safer is also long-acting and it's going to be more a weekly or possibly monthly pill. So that's going to take over I think Islatravir. Islatravir may have a small uptake initially because it's the one that is the most advanced in the studies right now. But I think, as soon as, other drugs get into the long-acting pills it'll probably go away.

Geoff Meacham: Can we talk a little bit about the integrase GS-1720 the weekly oral integrase? Talk about that one in and of itself and maybe your opinion of the data from CROI and then maybe viability of that combination right together with Lenacapavir?

Dr. Jihad Slim: So, it's definitely more tempting than islatravir combination. Because integrase are a better class theoretically than the NRTTI which we don't know a lot about. So, in that sense in theory the perception is that it would be a better combination. But the truth though is that islatravir and lenacapavir so far is not looking bad either. And there are all those combinations that they're working on for oral long-acting that at the end it's not clear to me which one is going to win.

The problem with all of them to me is going to have to be the genetic barrier. So integrase and this particular integration seems to have a good genetic barrier so that's going to be a plus for the future. But I, yeah, it's unclear where we're heading with them. There's going to be few competing once-weekly or once monthly pills that are going to be interesting. And I think what will win would be the one with the highest genetic barrier and mainly the genetic barrier is going to be the key.

Geoff Meacham: Would you say in the treatment setting are there concerns that you have or maybe some of your colleagues on resistance or breakthrough from Lenacapavir? The data have been very good. But as we start to get into some long-acting either integrase or capsid or whatever the modality are there worries on seeing new variants?

Dr. Jihad Slim: Well, we're not seeing that much resistance yet but it's clear that lenacapavir, cabotegravir don't have the same genetic barrier then dolutegravir and bictegravir or boosted darunavir for that matter. So that's been the issue. This is where I think ViiV is working on the third-generation integrase with a higher genetic barrier. Because as you do know at that meeting, they showed all the resistance not a lot. But still resistance to dolutegravir is starting to happen in the world especially in Africa and in all the places where it's been used without a good guidance on resistance testing because they can't afford the resistance testing. So, people who have failed prior regimens and then getting on dolutegravir are failing.

CABENUVA also get their small share of failure. So, the integrase resistance hasn't shown yet that it's increasing. But clearly is going to be the one that will increase because that's what we're using most of right now. We mainly use integrase inhibitor drugs not protease inhibitors or NRTTI anymore. So that resistance is going to increase hence I think the need for a third generation that will overcome that resistance and the logical use of drugs that don't fail [inaudible].

Geoff Meacham: And let's just talk about the CROI meeting. Beyond what we've talked about so far what would you say, you know, in the treatment setting in particular is there anything any other new drug [inaudible] that you thought you did well?

Dr. Jihad Slim: Yeah, the maturation inhibitor could turn out to be interesting as well. Again, potentially long-acting and a new class. So that is the only thing we didn't talk about. And there isn't too much to talk about to be honest with you other than they seem interesting. And we'll see what happen and the unboosted PI from Gilead also the once a week. So these are in the treatment arena what's going to come what is in development that seems interesting but too early to tell.

Geoff Meacham: Let's switch gears to the PrEP setting. Talk a little bit about maybe your experience with PrEP. And I know it's mostly patient who doesn't have HIV typically doesn't go see HIV specialists so PrEP is more for let's say a primary care type of audience. But maybe just give us some background for your experience, and in using these drugs for PrEP and maybe walk us through your experience going from Truvada to Descovy and then what we will eventually get with Lenacapavir?

Dr. Jihad Slim: So the PrEP obviously started with Truvada. Truvada's problem is again the kidney and the bone mineral density and the potential anorexia or the nausea that prevents the weight gain. And so even though it's generic, and it's fine for young, healthy sexually active people. The issue is that aptitude had two studies showing superiority because people forget to take their pills and they get their injections every two months even though every two months is not very practical.

But it seems that for cisgender women it is the drug of choice at least it would be the drug of choice because Descovy is not approved in cisgender women. And Truvada definitely will cause decrease in bone mineral density. And it's not liked. And at this point, it's much easier for women to go. The issue is that women don't seem to see themselves at risk for HIV even though they are one of the growing population of new HIV infection. So , in New Jersey they represent 25% to 30% of new HIV infection. And in the south, they're definitely on the increase as well.

So moving on to lenacapavir it looks like every six months PrEP would be desirable. The problem with it is the fact that the study is going very slowly and as of now I'm not sure when we expect it to be approved. There wasn't much at CROI regarding lenacapavir PrEP. I don't think there was anything or I haven't seen it if there was. So, we'll wait for maybe IAS or see what's going on there. I just know that it is slowly enrolling and I'm not sure how close it is for FDA approval. But once every six months PrEP is available. It's going to be so much more practical.

The problem is how do you recruit more people into PrEP? It has not been very easy in New Jersey. I could tell you that there's been pick up everywhere, but we are still in my understanding nationwide we're still at 30%, [not] where we need to be. We're only at 30%. So 70% of people who could benefit from PrEP are not receiving PrEP. So more to come on how do you implement it more and how do you keep people on it longer? But as I said, I think in our area new HIV is on the decline. It's going to mainly be more in the south where this will need to be implemented where most of the current HIV infections are happening and a lot in women.

Geoff Meacham: Do you think that the patients, Dr. Slim, that don't have an ideal experience on Descovy, for example, for PrEP, do you think a longer acting like Lenacapavir is that going to grow the PrEP market in a pretty material way?

Dr. Jihad Slim: I think taking a pill every day when you're young, healthy, and very sexually active is probably difficult to do. And two months is too much it's just six times a year when you're pretty busy. Twice a year is totally doable where you get your STD screen again depending on how sexually active you are you could get your STD screen at home rather than have to come for your syphilis and gonorrhea testing and stuff. So, you could do those at home. But come get your injection hopefully in a more convenient place too. Maybe it doesn't have to be the office either but even if it's the office twice a year I don't think would be such a big burden as six times a year. And the daily pill is

clearly not, as good as, the injections. The caveat is that some people just don't like needles. So there will still be some people who want to take something oral whether it's daily, or weekly or monthly.

Geoff Meacham: And the last question on PrEP and then I'll hand over to Susan from the team to talk through the cures and that made a bit of a splash at CROI. Just talk about kind of the challenges of development and PrEP. I know Gilead had to go to I think Africa and definitely outside the US and outside of Europe for the bulk of the studies. Are these easy studies to run? They should be. But I wasn't sure there's a lot of ethics with putting somebody at risk who may be sexually active but not on an active drug.

Dr. Jihad Slim: Well, the Gilead active drug is Truvada. There is an active drug. There is a placebo in PrEP anymore. The same thing with Apretude when they did all their study for cisgender women in Africa, it was the Truvada versus Apretude. There was no placebo.

Geoff Meacham: Yeah. Well, that's right. Yeah. But I think I would say suboptimal.

Dr. Jihad Slim: What's clear though is that it's difficult to enroll people who are at the highest risk of infection. And so, in the US you're right it's been difficult to enroll for PrEP because those who are getting infected don't want to be close in areas where they will enter into clinical trials. That's the problem. The clear example are women especially black women not perceiving that they are at risk for HIV because. And they are the one who has one of the most growing number of people getting infected. But they're not aware that they are at risk. They don't perceive themselves at risk. So, there is a lot of education that needs to be done. And a lot of investigation of where are the new infection? Who's getting infected? And how do you get them into taking PrEP so that they don't get infected? That's still not done deal [inaudible].

Geoff Meacham: I think the idea is that the data could come possibly by the end of this year and maybe lenacapavir long-acting PrEP could be commercially available. I don't know end of sometime next year or early the following. So, it's close but it's not sort of imminent in terms of availability. But I agree with you that it could have a lot more commercial viability compared to first or second-generation PrEP.

Dr. Jihad Slim: Yeah, I agree.

Geoff Meacham: I know one of the themes at the meeting was also cures. And I know over the years there's been some talk about this with regard to using zinc finger compounds and using cell therapy. But Susan, I have to you to go over a couple of questions on the curative approaches and some of the data coming out of CROI to ask Dr. Slim. Susan, are you on mute?

Susan Chor: Yes. Apologies for that. So the first question I wanted to cover is just to talk through the different mechanisms for HIV cure. And if you had any opinions on which mechanisms seems the most interesting, most effective just what was widely received at CROI?

Dr. Jihad Slim: So, the hope that there will be a cure is clearly important and interesting. The problem with the cure is that if you can't really measure the reservoir adequately you can never be sure that there is a cure even though it could be a virtual cure. But currently, the only way we could say that somebody is cured is that if they never have a virus load that's detected before they die. So you have to keep checking it.

And until we have a clear measurement or a real measurement on the reservoir, I think the cure is going to be very elusive. But it is very interesting that you could make somebody undetectable for a while before the virus comes back and that you're required to treat them. But I happen to think that we have a better chance with the vaccine than with the cure at this point from everything I've seen other than obviously the bone marrow transplant with a delta 32 marrow other than those kind of cure. The current

approach to our cure the induction and the treatment and the monoclonal antibodies seem to decrease the reservoir. But then the reservoir is so wide it seems and has a lot of barriers that it's only a matter of time before the virus comes back probably. That's my view. But that's my personal view. It's not very optimistic.

Susan Chor: So following up on the vaccine what are your thoughts about the AELXI-002 HTI trial that Gilead has?

Dr. Jihad Slim: I know nothing about it. Susan, I'm sorry. I know nothing about it. I just know from the feelings I got at the meeting is that we are getting close to understanding the immunogenicity of the vaccines and will potentially be able to have a viable vaccine in the not very distant future. But I've been in HIV since 1985 so I know all the issues we've had with vaccines. And I decided that I'm not going to spend my time following until something really interesting happened. And at this CROI meeting I got the feeling that something interesting is happening but I don't know the details I wouldn't be able to tell you.

Susan Chor: With that, we're coming up on 15 minutes at the top of the hour. Going to pass it back to Geoff maybe to start up Q&A.

Geoff Meacham: Sure. Yeah. We have a couple more and some email questions as well. But operator if you want to read out the instructions for asking a question let's go ahead and do that.

Operator: Absolutely. If you would like to ask a question, please signal by pressing star one on your telephone keypad. If you are using a speakerphone, please make sure your mute function is turned off to allow the signal to reach our equipment. A voice prompt on the phone line will indicate when your line is open. Please state your name before posing your question. Again, press star one to ask a question. We'll pause for just a moment to allow everyone the opportunity to signal for questions.

Geoff Meacham: We're waiting. Dr. Slim, just to follow up on Susan's question, on the cure. Do you think is there more momentum towards research for cures of the bulk of the investment dollars really in your sense going towards longer acting kind of better combinations that are in the treatment setting?

Dr. Jihad Slim: Yeah, I think definitely the money is going to be more in the longer-acting treatment than in the cure. The cure is going to always be interesting and elusive and academically very interesting. But as I said, since we cannot measure the reservoir, we have no good way of measuring the reservoir. And every time we think that we got it, it seems like we don't have it. So, it's more like a virtual cure waiting meaning somebody that has an undetectable virus load without taking antiretroviral therapy. But you don't know when the virus is going to come back. So that's how we currently address it. Until we have new tools or different PCR or nuclear something that could tell us that clearly there are no more virus, I think we're just going to be stuck with the theory that somebody is cured.

Geoff Meacham: We have a couple email questions, but operator any questions from the phone?

Operator: We currently have no questions from the phones. Again, star one if you'd like to ask a question.

Geoff Meacham: Okay. We'll go back to you one more time operator. But Dr. Slim, the other question that we get quite a bit an email question is, in your view what's the greatest challenge to PrEP uptake? Is it pricing reimbursement kind of access? It's just that uptake has stalled I think maybe in the 30% range and I wasn't sure where the upper end of it you think it could be?

Dr. Jihad Slim: It's education delivery sigma but it starts with education. It starts with a society that accepts that it's good to have sex and it's good to have a healthy sex when

we are still living in a society where sex is a taboo. It's really tough for people to want to come and get their PrEP. it's not that much the cost. And again, also the every two months is not convenient. The everyday pill is not convenient. But if you have an every six months and you have a society that accept that it's good to have sex but you have to have it in a healthier way then I think there will be a good uptake of PrEP.

Geoff Meacham: On the competitive front I know others have looked to try to encroach some of that market with respect to Gilead's leadership position. From GSK or others have you seen any alternatives in PrEP that you think could be more competitive. Or is it more following Lenacapavir and its progression assuming that's going to be a pretty broad standard of care going forward?

Dr. Jihad Slim: Well, so the vaginal ring is interesting. And I don't know why vaginal rings never seem to pick up in cisgender women. They didn't pick up much in birth control and they probably would not pick up much in PrEP as well. But they are interesting too. I mean as a different mode and maybe once-a-week pill would be more palatable. Not everybody is going to want injections and not everybody's going to come to the office for those. It should be more STD testing at home or in a more convenient way. And this is where one needs to talk to young sexually active people to see what is the most convenient for them to get done. And I haven't seen those interviews. But I'm sure Gilead and ViiV are probably doing them. I just haven't read what do people prefer for their PrEP so that they could participate more.

Geoff Meacham: For sure I think this is a big focus for Gilead but really, it's about lifecycle management moving towards long-acting. I think most folks agree with you that that could be pretty broadly commercially available. Do you expect conversion? So that's the other part of the question. And this email question that we got is talk about PrEP from converting the patients that are on Truvada or Descovy for PrEP. Is there likely to be a shift to Lenacapavir and would you expect there to be kind of access issues on that front? We always talk about PrEP in terms of new patients but there is a lifecycle management also to be played out here.

Dr. Jihad Slim: Yeah, no, when Apretude came out we had a lot of people that were on Truvada that switched to Apretude. Descovy not as much to be honest. But yeah, no, I expect that once you have every six months people who don't mind a needle every six months would be fine. So most people who didn't want Apretude were those who don't like needles. There are people who don't want needles. And we're worried about the fact that the long half-life would be too long and they're not sure where they're going to be. And so, it has its own issues. But I think there will be clearly more people on the oral that will go to every six months, more people on the two months that will go to every six months. Once it's available I think people are going to switch to it.

Geoff Meacham: Operator, any questions from the phone? If not, I have one more and then we can wrap up.

Operator: We have no questions from the phones.

Geoff Meacham: Yeah, just a question just back to the curative approaches. Gilead is a company that has obviously biologics and small molecules. But they also have cell and gene therapy. I wasn't sure if you thought that approach using a curative intent therapy. You do have curative approaches that have been successful in hematology and oncology [inaudible].

Dr. Jihad Slim: If anything, that may be the way to go. I'm more open. The problem again is the barrier. The blood-brain barrier and the barrier to all the reservoirs that are in difficult areas for medicine to penetrate but cells could clearly go after them. Yeah, no, you're right. There is an interesting approach. We're not there yet. But, yeah, it's interesting.

Geoff Meacham: Yeah. Okay.

Dr. Jihad Slim: Perfect. All right, Geoff.

Geoff Meacham: Well, it's fantastic. Thank you, Dr. Slim. Really appreciate the time very helpful conversation. And you have a great day.

Dr. Jihad Slim: You're welcome. My pleasure. Take care. Bye.

Geoff Meacham: All right. Take care. Bye bye.

Operator: This concludes today's call. Thank you for your participation, you may now disconnect.

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