MoonLake Immunotherapeutics R&D Day

Sunday, 10th March 2024

Introduction

Matthias Bodenstedt

Chief Financial Officer, MoonLake Immunotherapeutics

Welcome remarks

Good morning, everyone. Good afternoon for those that dial in through the webcast. It's my pleasure to welcome you to MoonLake Immunotherapeutics R&D Day today here out of San Diego. It is my pleasure to welcome here as well two of my colleagues, our CEO and Co-founder, Jorge Santos da Silva, our CSO and Co-founder, Professor Kristian Reich. We are also joined here by two of the leading KOLs, Professor Ken Gordon and Professor Joseph Merola, who are joining us here to reflect on us with the data on the opportunity of sonelokimab in HS and in psoriatic arthritis.

Agenda

We have a very busy agenda today. You see it here on the screen, so we'll have three main sections. On the one hand, we will present the psoriatic arthritis 24 weeks' data so we have a whole section dedicated to psoriatic arthritis, one of our lead indications for sonelokimab. Then we have a whole section dedicated to the opportunity in hidradenitis suppurativa. Couple of important and relevant updates also on that front. Then in the third main section, we will talk a little bit about the new frontiers for sonelokimab at MoonLake, including the announcement of new indications that we will going to pursue for this asset.

Housekeeping

Before we get there, a couple of housekeeping rules. Here you see the disclaimer on forward-looking statements, so please acknowledge the disclaimer. You will also have the opportunity to submit questions through the Q&A function in the webcast. Here in the room towards the end, we will have time for a couple of questions, so then please raise your hand. The presentation will also be available as a replay on our IR website, and if you have any technical issues dialing in, please also use the Q&A function. For any other requests, you see the email addresses here on the screen.

Now, before we get started with the content, maybe I hand over to Jorge to provide a little intro. For those of you that are less familiar with MoonLake, less familiar with sonelokimab, just a very quick summary on MoonLake and on the asset sonelokimab.

Objectives of MoonLake

Jorge Santos da Silva

CEO and Co-founder, MoonLake Immunotherapeutics

MoonLake

Background and Objectives

Thank you, Mathias. Good morning to all of you joining us here in the room. Good morning. Good afternoon, good evening to the many of you that are joining us through our webcast. Just

a couple of comments here up front for those that are less familiar with the story and the objectives of MoonLake. MoonLake is a biotech company, a clinical stage biotech company that was founded in 2021 in Switzerland on the back of a license agreement with Merck. That's the German Merck that gave us access to a very exciting new technology in biologics, the Nanobody technology, but more importantly, gave us a full worldwide rights to a molecule that we are very excited about called sonelokimab and the reason why we are excited about this molecule is that in our minds represents a new technology for patients that suffer from inflammation and immunology related diseases, and also addresses an MOA that we think is very important and new and that is the IL-17A and IL-17F inhibition.

I'll come to a few more details on that but we believe this molecule is a true game-changer when it comes to inflammation and gives us the opportunity to treat many, many patients and obviously, access a very important commercial opportunity. After we founded in 2021, we went public in 2022, then we started running some very robust phase 2 trials that we are going to be talking about today and through those strong data readouts, we were able to raise significant amounts of money. By now, we have raised north of 700 million.

MIRA trial

We, as I said, are a clinical phase company. We have run three large phase 2B studies. Obviously, not very usual for a small young biotech. You have heard about our MIRA trial, a very large trial in hidradenitis suppurativa. We will come to that today. As you know, we are having this session here directly from AAD. We will have Professor Brian Kirby presenting late breaker on that MIRA trial this afternoon in the conference.

ARGO trial

We also ran a large phase 2B called ARGO in psoriatic arthritis. We are very happy to share with you the 24-week data today and we also built on a very robust, large trial in psoriasis where we treated more than 300 patients, and of course, all these designs, as you know from MoonLake, very robust designs, pivotal like designs, always using an active reference arm to compare ourselves to standards of care.

HS and PSA

As we go into 2024 into this new phase of the company, we really have three indications that are ready for phase 3. We will talk today about HS and about PSA, and we expect the product to be in market in 2027. In HS and PSA alone, we see a very significant opportunity for sonelokimab in our minds north of $5 billion.

Nanobodies

Very quick word on why the Nanobodies are so exciting. What are Nanobodies? Nanobodies are essentially the variable region as you see here in blue of heavy chain only antibodies. Here to the left of the page, you see the traditional very large monoclonal antibody. What we love about these Nanobodies is that they are very small entities, as you can see here, but they retain all the great characteristics that we like about monoclonal antibodies. That is the high specificity and the high affinity for targets. What is also very cool is that they are small and we are able to muti-merise them. We are able to bind some of these things together to create molecules that can do very interesting things.

Sonelokimab technology

In the case of sonelokimab, which is depicted here to the right, we have two domains and with these two epitopes, we combine two different targets in IL-17A and IL-17F, and we even have a third domain that allows us to buy albumin, not only to stabilise the molecule in terms of half-life, but as a targeting mechanism to sites of inflammation, which are rich in albumin. And obviously, binding two different molecules in different epitopes, being targeted by a third domain is all things that a monoclonal antibody cannot do. Even when we do all of these things, the molecule is 40 kD, so it is much smaller than a monoclonal antibody, and that allows us to penetrate tissues better.

The molecule is very convenient, is administered through subcutaneous administration. The maintenance dose is a monthly dose. It is one ml and an injection that takes three seconds, so obviously, from a patient perspective, very exciting. That is the technology which we think is very differentiating of our molecule versus, any other molecule in these pathways. As I mentioned, the pathway itself is also very interesting. The role of IL-17 in inflammation is well known. The inflammation is driven by two types of cytokines IL-17A and IL-17F. These As and Fs form dimers as you see there with a little bolts on top on the right and it is these three dimers that signal through different confirmations of receptors of IL-17.

Now, what is interesting is you have molecules like Cosentyx or like Taltz, what we call the traditional IL-17A inhibitors. They really can only inhibit the A homodimer and to a certain extent can affect the signalling through the heterodimer of A and F, but only our molecule, the Nanobody sonelokimab and another molecule called bimekizumab, a traditional large monoclonal antibody are actually able to inhibit all three dimers. What is different in our molecule, as I said, is that we are a Nanobody, so we have all those characteristics that a molecule bimekizumab does not have. And when it comes to the affinity to bind these three dimers, the profile is very different. We can bind all three dimers with very similar, very high affinity. That is very different from what bimekizumab can do. That is the technology. That is the way that we are pursuing and we think that the clinical data so far is nothing less than exciting.

Clinical data

As you can see here, we are talking about HS, PSA, PSO and other indications very clear from the data, our own data and the data of bimekizumab, that IL-17A and F is the leading MOA in these indications when it comes to safety and the benefit risk ratio. And as you can see here to the right, all our clinical data suggests that we are numerically above even bimekizumab. When it comes to HS, as you know, we ran a very large study. Professor Ken Gordon will talk about it. We will talk about it. This was the first ever trial to use high score 75 as a primary endpoint. We have shown the largest deltas. We have shown depth of response, effect on tunnels so not only we have the leading MOA, but we believe that we have the leading dataset.

When it comes to PSA, again, a large trial in this case also placebo controlled with Humira. Again, a disease where IL-17A and F has shown to create the best responses and we believe that we really changed the game here, especially when it comes to composite scores in PSA. Professor Joe Merola will discuss this as will Kristian, as he presents the final data set from ARGO and the same story in psoriasis.

There are also a lot of other indications where IL-17A and F really plays a role and where we have an opportunity to win, like we are pushing for in HS and PSA, and today we'll be telling you a little bit about what those other indications are that we are going to go for. Fantastic technology, very novel, a great MOA already very, very robust clinical data so this is where we stand today as we move to tell you about the full ARGO data set, about the opportunity in HS and about the new indications.

Psoriatic arthritis

Matthias Bodenstedt

Chief Financial Officer, MoonLake Immunotherapeutics

Thank you, Jorge. Now that we introduced a little bit the company and the asset for those that were less familiar with it, let us dive right in into psoriatic arthritis. Clearly, everyone is excited about seeing our 24 weeks' data. Maybe before we get there, Professor Merola, you can provide a little bit of an introduction to psoriatic arthritis, the disease. What are the unmet needs? What are the challenges that clinicians and patients are currently experiencing in this disease?

Psoriatic arthritis

Joseph F. Merola, MD, MMSc

Chair of Dermatology, Professor of Dermatology, Medicine and Rheumatology, UT Southwestern Medical Center

Introduction

Perfect. Hello, all. I am delighted to be sharing despite my voice, a little bit about PSA. I get the professorial role, first of all, of talking a little bit about disease state, talking about how we are measuring it today, a little bit how we should be measuring it and then we will talk a little bit about unmet need as was mentioned, including burden of disease currently among our patients, and a little bit of a refresher on the data where we are currently before my colleague gets the exciting role of presenting what you're all here to hear about. I will dive right in. These are my disclosures.

Understanding the disease

I think this is really a key slide to understanding the disease. The fact that PSA is a multi-domain disease is incredibly important to our ability to treat the disease meaningfully in our patients. Just to orient you for a moment on the left-hand side of the slide here, I will just put this here, we have really the key domains of disease. What are they? Skin disease, psoriasis, and there are sub-bullets below that, of course. Joint disease, peripheral arthritis, you see there in the more extreme variant where you have damage. Axial or spine disease, and what is called enthesitis inflammation of tendon insertion points. A common manifestation nail disease and dactylitis or the so-called sausage digit. You can see there a swollen digit. That is actually one of my patients from my own clinic. And then you've seen traditional measures that seek to try to understand the activity of disease using measures typically borrowed from RA, for example, such as the ACR, to look at peripheral joints, PASI, of course, for skin and a variety of other

outcome measures to look at each of those other individual domains. Hold that thought, we will come back to it.

Patient reported outcome measures

We then have patient reported outcome measures, so what are those? Classical ones to look at functions such as hack, pain vast looking at patient pain, very important one and then disease severity, including overarching disease severity, such as patient globals.

Minimal Disease Activity (MDA)

What I want to introduce here is the MDA to begin with. So, being a multi-domain disease, the MDA is unique for two reasons. Number one, it is not just borrowed from rheumatoid arthritis, but is in fact a psoriatic arthritis specific outcome measure that really looks across the breadth of these domains of disease that we just covered. Not only that, but it is a very stringent and high bar of efficacy in that it really represents minimal disease activity across multiple domains. It is a high bar, and we'll talk about what those have looked like in recent studies, but a lot of our systemic therapies, we are typically looking for 25-30% or so achievement of MDA at primary endpoints in general. It is five out of seven of the domains that are listed there just below it.

ACR plus PASI response

Another interesting composite is the ACR plus PASI response. Most typically, ACR50 plus PASI 100. We'll even introduce a concept of ACR70 plus PASI 100, which I like very much. ACR50 plus PASI 100 was introduced in some of our combination trials in the past where we are looking at both skin and joint impact in head-to-head studies. For example, historically ixekizumab and others. It is also a high bar. It is an important bar in that we are looking at both joint response and skin response, all the things that matter to patients across those domains.

What does unmet need look like currently?

What does unmet need look like currently? PSA is quite common. As psoriasis is common, PSA is common, so there estimates, as you can see, are 1.5 million Americans thought to be living with PSA. We typically quote, but there are variants around this, about a third of patients with psoriasis who go on to progress to develop psoriatic arthritis. You will see slightly lower and higher numbers around that incidence, and about 50% of patients already have musculoskeletal symptoms at psoriasis diagnosis. I can tell you how many achy patients I have in clinic with psoriasis. I absolutely believe that number. There is even some data we don't have time to cover today, where you treat patients with psoriasis with absolutely no psoriatic arthritis, and they feel better, they feel less achy. There is a lot of psoriatic arthritis in these patients underscored by some of the next data.

This is the PREPARE study, very frequently quoted in our literature that PSA is often underdiagnosed and undertreated. This is just per chance. These three numbers, independent numbers all happen to be 41%. That is just by chance, but we frequently put that 41% of patients have undiagnosed psoriatic arthritis. 41% of patients who have a diagnosis of psoriatic arthritis are not on biologics and this is nice because it is new data that was presented at this meeting, in fact. Among a survey of US patients with psoriasis, 41% already had joint symptoms, but in most cases had not discussed treating their symptoms with their doctor. Again, it is common, it is absolutely underdiagnosed and certainly undertreated except in my clinic, of course.

Symptom burden of psoriatic arthritis leads to substantial work impairment

The symptom burden of psoriatic arthritis leads to substantial work impairment, and this is important because we can immediately get our head around the obvious, which are skin symptoms, itch, skin pain, joint symptoms, joint pain, functional impairment. But there is so much more to this disease we know from a very deep body of literature that talks about mental health comorbidities, anxiety, depression. Fatigue has been well worked out in psoriatic arthritis. Itis a key domain as it is in rheumatoid arthritis, for example, which is bidirectional with disturbed sleep. All of that plus functional impairment really leads to work impairment. And you can see here that it's not at all uncommon that patients are having presenteeism, absenteeism on metrics for work impairment. And the comorbidities we mentioned are not uncommon. A third of patients, quarter of patients with anxiety, depression, impact on physical activity, physical function. And I think really it makes sense here that we need to intervene not only for patients, but for a broader society on these terms.

This is a slide I like very much, in particular, because we publish this data, which is you ask an academic to speak, this is what happens. You have the skin responses on the Y-axis, joint responses on the X-axis. Essentially, the take home point at very high level is patients want to be here in the red. They want to optimise their quality of life, which means getting their skin as clear as possible, getting their joints as clear as possible across all of those domains that we talked about. It is quite a simple concept from that to that end. We also know that multi-domain psoriatic arthritis leads to more pronounced quality of life impairment along with greater risk of flare, more work impairment, higher rates of comorbidities, including mental health comorbidities, worse overall quality of life. And so, looking at endpoints that are composites of this, I hope I have made the case, are particularly important and relevant.

Last, I think one of our last points about unmet need is this, and this is really important. About three-quarters of patients do not achieve minimal disease activity, MDA, within six months of even biologic initiation; and that is across many trials, and so obviously, a very big unmet need at a high bar fair, but a bar that is very, very clinically meaningful to patients. And we have hit a little bit this treatment ceiling. We have certainly hit the treatment ceiling in ACR endpoints. I think the MDA even further underscores the treatment ceiling that we have hit when we know how clinically meaningful MDA is to patients in terms of function, quality of life, etc.

How do we best treat across the domains of disease

I also love this slide. I would not say why. The top line is really a nice summary of a complex topic, which is how do we best treat across the domains of disease. Where you see the green check marks, that is some of our highest efficacy by MOA in that domain. The yellow is efficacy but a bit lower; and in some cases, such as the psoriasis column, we have much head-to-head data supporting those relative amounts that are listed. You can see the green check marks, peripheral arthritis for IL-17, peripheral arthritis, psoriasis, axial enthesitis, dactylitis nails; and radio inhibition of radiographic progression, which really means lack of erosion, lack of functional impairment over time with drugs that have a check mark.

Can we optimise IL-17 inhibition

Let us take a little bit of a data dive now just to set the stage and then we will get to the exciting moment. Can we optimise IL-17 inhibition? This comes a little bit back to the introduction that

we had. The question of what is the value of IL-17F inhibition over just IL-17A inhibition, for example, in a very objective I would think disease like psoriasis, for example.

Here we have plaque psoriasis data looking at PASI 100 complete clear skin in the BE RADIANT trial, which was a head-to-head comparing bimekizumab IL-17A/F inhibition to sonelokimab IL-17A inhibition only. The data speaks for itself, showing improved statistically significantly better results both at the primary endpoint and week 48 when we inhibit both A and F. And this is looking at now psoriatic arthritis. This is really impactful data from bimekizumab, again, I think highlighting these points about the value of inhibiting both A and F in psoriatic arthritis. What do we see here? A primary endpoint of ACR50 I remind folks, if you are looking back in history, ACR 20 used to be the endpoint, primary endpoint, we have shifted to ACR50. It is more like the PASI 90 equivalent of joint efficacy at higher bar, more clinically meaningful.

What do we see here? We see essentially bimekizumab, in this case, behaving as well as our gold standard and best-to-date treatment in psoriatic arthritis, which was adalimumab; but we see a consistent message of much higher efficacy across other domains, including skin as shown here with the PASI 90 data where there is a clearly improved benefit here of skin treatment with the IL-17A/F inhibition referenced certainly over placebo. But pay attention and this is a highlight moment to the MDA. It is the first time we are seeing MDA data and what we see here, again, is now looking a snapshot across the entirety of psoriatic arthritis domains, 45% achieving minimal disease activity. That is a fairly high bar. In fact, one of the highest bars we have seen to date in this arena.

Why do I get excited about structure? This was presented as well and just the high level here that as an antibody that we have this concept that Nanobodies are able to penetrate difficult-to-reach tissues and directly target sites of inflammation. I am hopeful that that will continue to translate into our ability to break that ceiling that I mentioned earlier because we have not really, to be honest, broken that ceiling of MDA or ACR 20, 50, 70 in recent years. We have a couple of recent commentaries about how the ceiling is, let us say, rheumatologists are jealous of what dermatologists have been able to do in the skin.

Let us just refresh a little bit on sonelokimab here. This is sonelokimab achieving high levels of response in joints. This is in the ARGO programme, the phase 2 programme for psoriatic arthritis. Very standard entry criteria, very standard design for psoriatic arthritis. These are typical patients I would see in clinic, for example, with psoriatic arthritis. And this is now looking at IL-17A/F inhibition with a Nanobody. Primary endpoint of ACR50 in joints. You can see slight numerical difference here between sonelokimab and adalimumab reference. 46%, meeting ACR50, but again, as expected pretty remarkable skin endpoint with regard to 77% PASI 90 as early as week 12. We see skin, we see joints, very impactful data.

But this is where I want to really spend the moment, so MDA. Again, I and my colleagues in the little realm of psoriatic arthritis really feel strongly about this endpoint because it is a high bar and it is across all the domains we shared, and we see that 44% MDA response here, but with a slope that is increasing and I think really something to keep an eye on. The ACR50, PASI 100 data. Again, this is that composite we talked about earlier. And here we see a higher threshold than what we normally see ACR70, PASI 100. Almost a third of patients reaching completely clear skin and the highest bar from a psoriatic arthritis standpoint that is really quite hard to achieve ACR70 number.

Conclusion

In summary, and I know we are short on time, I will just say there absolutely remains an unmet need across multiple domains of disease. I want to highlight that with one sentence, which is that we quite literally have a list and have had a list of patients in clinic who have cycled through multiple therapies who are waiting for the next therapy to come along because they have tried multiple, multiple things and need to get onto another therapies to really get their disease under control. We talked about MDA, a high bar, really PSA specific across the domains of disease, and we talked about the value of IL-17A and F inhibition in psoriatic disease.

With that, I will turn it over to my colleague.

PSA Trial

Kristian Reich, MdD, PhD

Chief Scientific Officer and Co-founder, MoonLake Immunotherapeutics

24-week data from the PSA trial

Thank you. Let us turn up the heat, although I am not so sure that this is healthy in this room. The heat is quite high enough, already. Very warm welcome also from my side, and absolute pleasure to take you through what is a new data set, the 24-week data from the PSA trial. Let me maybe just quickly start by picking up some points, Joe, that you made and as you know, I have been also seeing and treating these patients for many, many years. I think it is essential to understand that you will never have a happy PSA patient if you just make the musculoskeletal disease better. There is a reason why psoriatic disease, psoriatic arthritis is called psoriatic arthritis because 80% of the patients have skin lesions.

You have heard that there are other relevant domains, but I think we agree you need to make skin and musculoskeletal outcomes better to start with; and ultimately, we also want to improve enthesitis and some other important domains, including nails. It is one of these little clinical observations. You think nail disease is a little thing. For many of my patients, it is the main thing because you cannot hide your hands. Everyone will look at you, it is painful. You cannot really functionally, optimally use your hand. Even nail disease is one of those domains where you need to win if you really want to manage PSA well.

Relevance of the IL-17 pathway

I am also excited as an immunologist that we get more insight into the relevance of the IL-17 pathway. You may say, yeah, IL-17, we have heard this for years, but the truth is that as we move along, we get more insight. What is this pathway really doing? I think one of the highlights is really to add IL-17 F to the story. Look at old reviews three, four years ago. You only see IL-17A. Now there is no review that ignores IL-17F and even putting this pathway on top of other pathways like IL-1 beta or IL-23. I think this pathway is becoming the dominant driver of a growing number of diseases, including PSA. And this is just a snapshot from a publication where with a very simple technique, IL-17A on top and F containing cells have been stained in an inflamed joint. You can just look at this and you see, wow, there is a high abundance of IL-17F. And as we move along, we actually begin to understand what this IL-17F is driving.

Just some pictures. This is what we talk about when we talk about nail disease. You will understand how relevant this is. This is how many of our patients look like that not only have

arthritis, but that is also have skin disease. The prevalence is high, as high as Crohn's disease. Just to give you a feel, you heard about the unmet needs. So we will need to go back and critically analyse our data, specifically with regard to the effects on multi-domains. At the same time in the same patient. We think that we really need to elevate the standard of care. You talked about this ACR 20, 50, 70 paradigm. Let us see if we can finally develop a drug that goes beyond this existing paradigm.

Study design

This is the study design. Again, our focus today on Part B. Just to remind you, in Part A, we tested three doses of sonelokimab, the 120 that we know is the optimal dose in psoriasis with induction, the 60 milligram with induction. We know from 17 inhibitors that sometimes half the dose that's already doing a good job in psoriasis is enough to do a good job in PSA. Of course, we wanted to test this then just to understand, do we need the induction. As a scientist probably would say yes, because patients come in with very high target levels. You need to give a lot of drug at the beginning to bring the target levels down. Once they are down, you need less drug to keep the disease under control. That is exactly what we test in these arms. This arm, no induction.

Maybe to say this upfront, it worked, but it did not reach statistical significant at the primary endpoint. This is not a dosing scheme that we intend to therefore move forward into phase 3. I will mainly focus on the 60 and 120 with induction. MoonLake study, so we have an active reference arm. This is particularly important in PSA, why? Placebo is not placebo in PSA, you have to allow background concomitant DMARD use. In our study, 70% of the patients were on background methotrexate. Some patients were on additional oral corticosteroids. Of course, you are going to see a response. And the later your study is the more patients are on background drugs. So real relevant comparison is to adalimumab. And also, and I will talk about this if you want to do a cross-study comparisons, try to find a study that has the same reference arm, and only this allows you to make meaningful comparisons.

The second part, patients continued on sonelokimab 120, continued on sonelokimab 60. You see there is a small group of patients that were crossed over to another drug or another dose. These were patients that did not even achieve a 20% improvement of tender and swollen joint, so a low hurdle. This is a low number of patients, hard to scientifically sound analyse. The only data that I will show you, just to give you a little feel, is this subgroup here. So patients that did not even achieve any response to adalimumab were crossed over to sun sonelokimab just to get a feel is non-response to Ada a predictor of response or non-response to SLK.

Joe already said it. Otherwise, this is all absolutely standard of care. All data that I will show you is NRI. There continues to be this confusion around statistical analysis. This is the most conservative way of looking at this. Every missing data point is imputed as a non-responder and the way we handle these patients here that go to another drug or another dose, we imputed them with the last bed value that they had before they crossed over, so I think that this is the most conservative way to analyse this data.

Why is the dropout rate important?

Why is the dropout rate important? Because it is a nice integrated view on the safety and the tolerability of your drug. We have been seeing dropout rates 10%, 15%, 20%, not with SLK. This is the third study after psoriasis, after HS where we see dropout rates in the single-digit

percentage range. I will share some safety data with you but this is a, again, study with a very clean safety profile, and I think this is also reflected in the low dropout rate. This by the way, also means whatever readout you do, you will get very valid results.

This is a build, allow me to click on this already. You see here ACR50, you see ACR70. Professor Merola shared with you the week 12 data. Of course, the hope, the idea was that this drug will not have hit the ceiling at week 12. It is hard to have optimal musculoskeletal outcomes, and this is exactly what you see. Between week 12 and week 24, you see a more than double-digit further percentage of patients reaching ACR50, and you see the same with ACR70. Yes, we have a very fast onset of response. You see separation ACR50 by week four. Clearly, a lot of separation by week eight, takes a little bit longer as expected for ACR70 to get there, but the week 24 numbers here clearly are higher than the week 12 data that we have seen.

The placebo crossover

You look at the placebo crossover; I always look at placebo crossover as an internal control. Were you just lucky in what you saw in Part A, or do you replicate your Part A findings in the placebo crossovers? I think we can all agree the placebo crossovers very nicely validate the findings we had in Part A.

Paradigm

The paradigm, Joe that you talked about. We are not even showing this year. ACR20 was above 80% at week 24. So, we had the 60, 40, 20 paradigm, ACR20, 50, 70. With this drug sonelokimab, we have an 80, 60, 40 paradigm. And I think this is really telling you that we make another big step in treating these patients in an optimal way.

Adalimumab reference arm

Yes, we had the adalimumab equally sized adalimumab active reference arm in our study. This was not meant to do a proper head-to-head comparison. But of course, we are always asked for how does this, your data compare to ada, the gold standard to bimekizumab, the IL-F inhibiting antibody. What you can see here is that, first of all, looking at the other reference arm in our own study, sonelokimab does come out on top at week 24. And this is a new finding, I think. Other drugs could not show this coming out on top of adalimumab.

Bimekizumab reference arm

The other thing you can see here is – and this is not a cross-study comparison. There is always scientific limitations to this, but this is the study where bimekizumab used the same design. So this is the other reference arm in our study. This is the other reference arm in their study. So if you want to make a comparison, compare us to Ada, this is the delta; compare bimekizumab to Ada in their study, this is the delta. I think you begin to get this feeling that already at this musculoskeletal outcomes, we seem to be the gold medal drug.

We knew we would have a great drug on skin. We have our phase 2 psoriasis results, and yes, boy, we do. You see here 80% plus PASI 90, you see 70% plus PASI 100. And let me pause here for a moment. We are here at AAD in San Diego. Yesterday, we went to the late breakers. There is this oral 23 inhibitor and this was viewed as the best oral data ever shown was 40% PASI 100. With drugs like sonelokimab, you get 20% more patients to PASI 100 and that is also true for the psoriasis component in patients with PSA. We do not show you the Ada arm here, but the delta to Ada is 20% plus for this PASI outcomes and even if you look at

bimekizumab, again, cross-study comparisons limitations, but these numbers again seem to be the gold medal numbers shown for skin manifestations in PSA so far.

Patients that achieve both ACR50 and PASI 100

Now, Joe talked about the relevance of making the same patient better across multiple domains. Let us measure us by our own standards. Let us really look at patients that achieve both ACR50 and PASI 90. Let us look at patients that achieve both ACR50 and PASI 100. The first thing you will see is that for these high level of response, yes, indeed, you need to give the drug a little bit more time. You see that the delta between week 12 and week 24 is even bigger than some of the deltas I showed you before. Number one.

Number two, forget about Ada. It was a great drug. It was one of the great first biologics that we got in our hands to treat PSA, but really if we now compare to adalimumab in our study, you see 20% plus delta on ACR50 and PASI 90. An interesting phenomenon here. We had an 11% delta at week 12. This delta to Ada increased to almost 20% at week 24. And again, allow me to peak at the optimal results where bimekizumab the same endpoint, ACR50 plus PASI 100 had 7% delta to Ada at week 16, but only there was no further improvement. It stayed flat and at week 24, there was a 6%. Again, these are not formal comparisons, but you walk away with the feeling that is the best data that we have seen so far.

We do have a real interest at MoonLake to not develop MeToo drugs. We really have the intention, we did this in HS. I will come back to this to look at higher goals than have been shown before. So here is something that I am not aware that any other PSA trial has reported. This is ACR70 plus PASI 100. So the highest level of musculoskeletal improvement and in the same patients' skin clearance, and I think the number speak for itself. That is one out of two. That is one out of two patients getting to this high level of response. Look at the delta to Ada, that is almost 30% difference at week 24. If I would look at this in my patients, in my practice, I think the decision to prescribe a drug is very clear.

Professor Merola talked about MDA, the multi-domain per excellence outcome. You need to not only win on all these domains but look at the levels that you need to win; so less than one tender joint, less or equal one swollen joint PASI, absolute PASI one or below, you need to win on enthesitis and on the three most important patient-reported outcomes. These are the numbers. And if I would pick two slides to show it to you, I would pick ACR70 plus PASI 100, and I would pick this one, because this is where the rubber hits the road. You see here, there'd be optimal data, good data for bimekizumab, but not really separating from Ada at week 24. This is the difference, and you can say, is it 60 plus? Is it 58? It is more than 15% above what we had with Ada and I think this is again, indicating that, especially when it comes to this high levels of response, this is where sonelokimab scores.

MoonLake has this tendency to always overwhelm you with multiple outcomes because we think this adds to the validity and not just picking three outcomes and hiding aid. I am not sure we have made the best experience with this all the time. But I talked about nail diseases and I showed you this picture, and it is actually, PSA is linked to nail disease. PSA patients have more nail disease than psoriasis patients. Let us focus here on the middle, this is nail clearance. Patients that have nail disease at baseline, but that at week 24 no longer have nail disease, and we focus here on the fingernails because this is what matters most for patients. And Ada is a great drug in nail psoriasis. Again, we were very excited to see that with sonelokimab, you

see more than 10 percentage points delta to Ada when it comes to patients achieving full nail clearance after half a year.

And besides this is a very complicated clinical readout. I am not trying to make fun here out of rheumatologists, but you know how it is done. You press on the point and the patient says ouch, oh, one for enthesitis. I think we need to really be better in the future to quantify this. We saw some variation in the amount of enthesitis. This leads enthesitis index actually goes from zero to six, and I see study data where the baseline value is one point something. So we saw in our active arms more than three point something through actually a lot of enthesitis. And in order to best look at this, we here show you patients that actually have a lot of enthesitis at baseline, so two or more, and that made a lot of improvement. So, when became better by two or more scales at week 24, I am not sure this absolute number is telling me a lot. Yeah, it is a high number. This number is telling me something. That is the beauty of having an internal adalimumab control arm because again, Ada is a good drug in enthesitis, but sonelokimab appears to be a better drug. But clearly, we need to do better studies, Ada outcomes, we will talk about this, look at this in much larger studies to confirm.

Crossover groups

I promised you that I would not go into the details of these small crossover groups. I said I would show you one, and again, take this with a grain of caution. I am talking here about seven patients. Please, let us not over-interpret. But what you can see is that those patients that at week 12 not even had 20% improvement of tender and swollen joints to Ada, so really primary non-responders to Ada. When they were switched to sonelokimab 120, we saw an MDA response that was similar to the MDA response we saw in Part A in patients exposed for 12 weeks to the drug from baseline. Again, nothing to over-interpret, but we think at least there is no evidence that non-response to Ada means that you will be a non-responder to sonelokimab, quite the opposite. And of course, we will explore this in much more detail. We will dedicate a whole phase 3 study to specifically look at TNF inadequate responders.

Difficult to treat subgroups

One important, and this is going to be a complicated slide, and you see there will be many builds, but one important question that you may ask is, Kristian, you showed us 60 and 120; and for many outcomes, the 60 was already great, but for some, the 120 seemed to be better. Now why is that? I think it's absolutely expected for a 17 inhibitor.

Let is look at so-called more recalcitrant. Let is look at difficult-to-treat subgroups, and these are well established. One difficult-to-treat subgroup are patients that actually have a lot of skin that have a PASI above 10. And you see here, ACR70 on the left, you see PASI 100 on the right. Let us look at these high levels of response that are introduced, and you see that indeed, in the overall patient population, 60 is doing great. 60 and 120, very similar, but you see that in patients that have a lot of skin, you see the value of the 120 kicking in, both from musculoskeletal and skin outcomes.

Patients with high inflammatory load defined by a high CRP at baseline

Let me show you a second example. Let us look at patients that have a high inflammatory load defined by a high CRP at baseline, and you begin to see a similar pattern in the overall patient population. Very similar, but in those that with high CRP, more inflammation at baseline, you see the value of the 120. We analyse this data in a lot more detail. You would see a similar

pattern for patients with high DAPSA. You would see a similar pattern for patients with nail disease and we do think that this is all reflecting a higher inflammatory burden.

What does MoonLake plan to do? Surprise, surprise. We want to take forward the 60 and the 120. We hope to get both doses ultimately in the label. You start with 60. If you belong to a recalcitrant patient subgroup, if you do not achieve this optimal response, you have the chance to go to 120.

Safety profile

Safety profile. Long story short, this is the third study now we have exposed more than 700 patients where we continue to see what I think is a very favourable benefit risk profile. I have to say that in a patient population where 70% are on methotrexate, many are on corticosteroids. We were surprised that even the candida cases are very, very low, a lot less compared to what we saw in HS. We continue to see no IBD. There was a diarrhea, but there was a diarrhea in adalimumab. No liver signal. Sonelokimab has no topic with injection site reactions and you can again see this here. So a nice confirmation in a third large phase 2 study for a really good benefit risk profile.

This is more for the specialists. But it is important that you know that antibodies have struggled to, for example, get good levels in HS and we still don't understand why; do these patients metabolise antibodies more? Why is it that Cosentyx, Ada they all need to double the dose compared to psoriasis to see meaningful responses in HS, not with sonelokimab? Joe and Jorge talked a little bit about the unique molecular characteristics. Maybe this adds in here that, again, this is the third study where our PK modelling very nicely predicted what we actually ended up seeing in our trial.

What does this mean? You see here, the dotted line, this is the blood level where we know our tissue concentration will be able to deliver optimal, and I am saying optimal, anti-inflammatory response in patients that come in with high target levels. You see that the 60 and the 120 easily jump over this. You also see that other crossover patients and patients going to the every four-week dosing remain on top of or around this very high level of response, so we leave nothing on the table. Again, we are very certain that we see the optimal doses reflected here.

Anti-drug antibody drugs

With all antibodies and with all Nanobodies, there is always the question, what about anti-drug antibodies? And do you see them? Do they do anything? Again, like in psoriasis and like in HS, we show you here on the left-hand side the drug levels in patients with or without anti-drug antibodies. You see Ada positive patients in red. You see patients without Ada in blue and you would agree with me that there's no impact whatsoever on drug levels, and therefore it's not surprising and you see ACR50 response here, that there is also no impact on the clinical response. I can share with you, there is also no impact on safety. So we continue to think that there is no clinically relevant immunogenicity with sonelokimab.

What does it all mean? We are planning our interactions with the regulatory authorities as we speak. We see a very clear path towards a meaningful phase 3 programme in PSA. I talked about the fact that we will have one phase 3 in TNF inadequate responders. I think for most US colleagues, that is the data they want to see. We will also look at radiographic progression, which is an important outcome in patients that are bio-naive. Based on this phase 2 data that we shared with you, we are very confident that we have a clear path towards phase 3.

I am a scientist, I am an immunologist, but I learnt to also look at markets and market size. I shared with you that PSA is as big as Crohn's disease. And even if you look at conservative estimates for market size, you see numbers here around 10 billion in 2035. When we analyse this, we are convinced that this is an underestimation. Why? Because the impact of the 17 inhibitors coming in, which are all predicted to be responsible for the biggest growth up to 2030, they are not even adequately reflected in here. So, we think that a $15 billion size is still a conservative estimate for a PSA.

Number two, the share that the IL-17A and F inhibitors will have within this 17 inhibitor class really bimekizumab 20% of 17 inhibitors, and sonelokimab, of course, not even addressed with this data, again. We think this is an underestimation here and we are very convinced that the 17A and 17F inhibitors will play a much bigger role.

PsA – ARGO Results Confirm SLK as the Potential Leader in PsA

So, to summarise quickly, we are very excited, maybe a little tired, but very excited. And just to reflect on some numbers here. I think 60% MDA. Joe, you have seen this data before, we spoke to colleagues, I think this is exciting. I will, again, talk about the 50% of patients, one out of two, that reach ACR70 and PASI100. So we want to win on these multi-domain outcomes and I think we do. Yes, we have a fast onset of response, but probably not unexpected. We had very good data at week 12, but we feel that the week 24 data is absolutely compelling.

I talked about the 60mg and the 120mg, why both doses make sense to be moved forward into phase 3. And we talked about the very favourable safety profile. We think we are differentiated in the outcomes that matter for patients, we think we have data that helps us to clearly structure our path forward into phase III. And in addition to the Derm indications, that means that we continue to be very excited about our Rheum indications as well. Thank you very much.

Q&A

Matthias Bodenstedt: Thank you, Kristian. Before we move to HS, we received a couple of questions, but maybe before we get there, Professor Merola, you have probably seen hundreds of data sets on psoriatic arthritis. You were one of the first that we shared this data with, you just heard Kristian presenting it again. Maybe you can share your reflections. When you look at the data, you talked earlier about the treatment ceiling, what are your thoughts on the sonelokimab 24 weeks' ARGO data?

Professor Joseph F. Merola: Yeah, I am happy to weigh in. So I can tell you I have sat through many data presentations, as you might imagine, and we have had, historically, the hope that we would start to break the ceiling. Kristian already mentioned the ACR20/50/70 rule, 60/40/20 and such that we are almost taught in training. I remember a recent drug, I will not call anyone out, where we were hoping for and expecting to break that ceiling again, whether it be through MDA or other outcomes, and it was disappointing. I truly and honestly can say the MDA data here, I agree with Kristian, is the highest we have seen, period. It is

really, really very exciting, and I like the use of composites in thinking through the skin and joint endpoints for patients. So I am quite excited about what we are seeing.

Matthias Bodenstedt: Thank you. Maybe, Kristian, one for you. One question here is at what time point would you expect the impact on PsA outcomes to begin to plateau, given that we have seen, now, the increase week 12 to week 24? It still looks like it is increasing, where is the limit?

Professor Kristian Reich: Yeah. I do not know, right? The pattern that we see is the higher the outcome the longer it takes, and that makes a lot of sense. You saw that for PASI week 12 is great, right? Week 16 will probably be optimal. You saw that for ACR70 week 24, is this the ceiling? Are we going to see more? Could well be. I think, also when I look at this combined endpoint ACR70 plus PASI100, the MDA, I am not sure that we have hit the ceiling yet. Clearly, in phase 3, Matthias, week 16 will be the primary endpoint. There is an ethical limit to the amount of time you can do placebo-controlled trials, but we will generate the data and we will see, and I would not be surprised if some of these outcomes even are seen in more patients as we move along.

Matthias Bodenstedt: Thank you. There is one more question here on the phase 3. Anything you are planning to do in phase 3 to minimise the risk of high placebo response, as seen at week 12 on ACR50?

Professor Kristian Reich: Yeah. It is so interesting, right? You talk to a rheumatologist, it is non-issue because they know that placebo is not placebo. Of course, Matthias, in a phase 2, and this still is a phase 2 with 40 patients in each arm, we know that this whole placebo response was driven by seven patients. Six happened to be on a high dose of methotrexate, two were on additional oral corticosteroids, so obviously there was a propensity in the small subgroup of placebo patients for a response.

Our phase 3 programme will include 1,200 patients. So, I think, just by the size, it is very unlikely that we are going to see this kind of impact again. It is just the fact that you cannot do these studies without concomitant demands because that is the clinical reality, and this is why I think, Matthias, the validity of this data for me stems from the other comparison. That is rock solid and that is the reason why we had it.

Professor Joseph F. Merola: If I may, I will just build on that to say being a dermatologist and a rheumatologist, yeah, with psoriasis studies, we are used to seeing, Ken, minimal placebo rates, right, quite low placebo rates. Placebo rates of 20s and 30s and 40s in rheumatology are standard fare in RA, PsA, etc. I even look at enthesitis placebo rates of 50% plus in some cases. I had not even noticed it until the question, frankly, but I think it is something we have become accustomed to. There is a couple of interesting commentaries on why even placebo rates have increased in PsA studies over the years, and RA studies, that are pretty interesting. No small part background therapy. There may be a little bit, even some thoughts that [inaudible] disease. Patient populations that are going in the studies have changed over the years.

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Matthias Bodenstedt: Great, thank you. I have a couple of other questions here. Maybe I keep them for the end so that we get to speak, also, about HS, which is clearly another very important indication for MoonLake, for sonelokimab. You have seen the MIRA 12 weeks' data, MIRA 24 weeks' data. This afternoon, Professor Brian Kirby will present the late breaker at the AAD congress at 14.00, so please join us there as well.

HS – Franchise Building Indication

Matthias Bodenstedt

CFO, MoonLake Immunotherapeutics

Before we get into the details of the data set and also the regulatory feedback that we have received, both from FDA and EMA, to talk about the next steps, Professor Ken Gordon. Maybe similar to what we have had for psoriatic arthritis, a little bit of an overview of the HS disease, the unmet needs, the challenges in treating HS. Where is the opportunity for a company like MoonLake with sonelokimab?

HS – A Devastating Disease

Professor Kenneth B. Gordon

Chair of Dermatology, Medical College of Wisconsin

Thank you very much. I am very pleased to be here today. I want to say that if there is any disease where there is an unmet need and desperate need for more medications out there it is in HS. Hidradenitis suppurativa is one of the most disabling diseases. It is a disease that causes consternation in almost every dermatology office. That is why you are seeing such a development of speciality areas of HS in academic institutions like mine, simply because people in the community do not have good weapons to treat it. And so it is being sent to speciality areas, speciality clinics, so we can try to deal, at some level, with these patients who are suffering horribly.

Disclosures

So, to say HS is a devastating disease is, I think, one of the great understatements of our time. Here are my conflicts of interest.

Hidradenitis suppurativa – A Challenge and an Opportunity

This patient that we see here in this picture, dermatologists are oftentimes accused of showing pictures just to make sure everyone else in the audience feels uncomfortable, and it is the worst of the worst to ruin everyone's breakfast.

This is a very typical patient we see with HS. And think about that for a second. You see draining tunnels, you see abscesses, you see ulceration, you see scarring. The sensation that you see in looking at this is complicated by, also, other sensations. This is a disease that odour is involved in, this is a disease that pain is involved in; all of those things come into play with hidradenitis suppurativa, so it is one of the most intolerable diseases that we see. It is progressive, it gets worse over time and the tissue destruction is irreversible. Thus we need to be able to modify the disease over time. Now, I hesitate to use the word disease modification, but the treatment of HS in the short term is, 'Let us improve symptoms, let us improve signs.' In the end, the ultimate problem that we are trying to face is how we do prevent this? How do we keep patients from getting there? That is where the delay in treatment and lack of diagnosis appropriately is so critical in our patients.

We talk about estimating market sizes, things of that sort. Underdiagnosis in this case, I think in HS, in rampant, but not only does it lead to changes in marketing and things like that, it has

significant patient impact because it delays our ability to make a difference in helping keep these patients' lives on track and are impacted by the disease.

So, current underdiagnosis is a significant issue for patient care. The other issue is patient treatment. Delayed treatment, insufficient treatment also can lead to ongoing worsening of disease. We need to have this therapeutic development that gets people to a position where they feel comfortable and they feel appropriate in treating patients not only who have disease like we show in the picture here, but in the milder disease or in the more moderate disease, that will lead to this eventually. And, if we can do that, we will make a bigger difference in patient lives.

HS is Characterised by a Profound Burden for Patients and Society

Symptoms

So, its profound effect on patients and society. Again, I want to point out that the symptoms are multiple sensory: odour; depression; all the comorbid states, but pain.

Hospitalisations

These patients are in pain. And, if you look at our patient population, the biggest reason for patients admitted to the hospital is people who are in pain, intractable pain, people who are put on opioids, which are not particularly effective, and they say, 'How are you going to treat my pain?' The answer that we give the patient is, 'We need to treat your HS to treat the pain; and if we do not have the tools to do that, we are doing that insufficiently.' Thirty per cent of patients with HS are hospitalised in greater than one occasion over three years. Think about that number, that is a huge number of hospitalisations. If you can block some of those hospitalisations, or shorten the hospitalisations, you are making a major impact on the healthcare community. Six days in hospital costing $33,000, it is a pretty typical hospitalisation. Our goal is to try to change that. If you do just shorten that by a couple of days and do an integ

ral, do the area under the curve, imagine the amount of money saved to the healthcare system by just treating these patients appropriately.

Work and employment burden

The work and employment burden, I think, is quite significant as well. There is significant time lost from work for these patients that both have absenteeism and presenteeism. I also have made the joke somewhat facetiously, but not really, that this is the one disease that I know of where the work productivity of the patient and the work productivity of the person working next to them is inhibited. The odour, the ability to put up with the some of the elements that are in that milieu of that patient really can affect people around them; it affects their families, it affects people who work with them. Now, that is not proven, that is my statement in general, but I think if you talk to people and talk to patients and say, 'How is this bothering your work?', which is a standard question we ask in the clinic, the patients will say, 'Well, no one wants to be in conferences with me.' It is a very significant outcome.

Chronic Inflammation in HS Progresses to Irreversible Tissue Destruction

Here is a design we put in together in thinking about disease that I think is really critical for people to understand when thinking about how we go about treating. There is a disease onset, it can happen early, it can happen late, and there is this early disease concept that is filled with nodules and then leading to abscesses. Sometimes the disease will stop there, but oftentimes,

and I think more often than not, it will continue to progress; and that is when you get scarring, that is when you get tunnel formation. These tunnels with draining, basically, pus coming out of them and leading on to scarring and permanent damage.

Some people have said that HS is a surgical disease. I would argue that HS is only a surgical disease when our medical therapy fails. Surgical therapy for HS is a statement of failure of treating the patient sufficiently. And if we think about surgery being failure, then I think that it demonstrates how early and how aggressively we should be treating these patients to try to prevent the other sequelae, not only to the patient, but to their family, their work colleagues and to the healthcare system, moving forward.

The other thing I want to point about this, and when we look at HS studies that I think is something that is underestimated. The worsening of HS is not linear. It is one of those things that goes up and down; it will be waxing and waning over time, both naturally and in patients under therapy. Getting someone treated and having no flares anytime in the future to date has not been particularly successful. Hopefully, we will change that over time. What we had to say is when we look at our tests and we look at high score 50 at 12 weeks, or 16 weeks or 24 weeks, we are looking at one point in time.

So I think other outcomes are necessary to understand, just like Joe talked about; looking at the MDA, looking at the totality of disease, looking at the frequency of flares, looking at the frequency of hospitalisations. All of those things over time, while they might not be able to be seen in a phase 2 or phase 3 trial, I think are going to be very important looking at over time for the benefit of understanding the natural history of the disease.

Can we Treat HS More Effectively in the 'Window of Opportunity'?

So, do we have a window of opportunity? I believe so. It is an early disease, so people who are just beginning to progress, how can we make them better? Remember, lifelong disease, not something we are going to be able to treat for one-time point and then make it better and stop progression over time, so we need better therapies. Efficacy is the key; getting patients better is what is going to prevent moving on to these other worsening outcomes. Shorter time to treatment, getting the diagnosis quickly. But I want to emphasise particularly in the right. We have two treatments right now approved from HS, one more than last year at this time. So we have got 100% increase, right? Psoriasis, we have 12 biologics at this point. And we are very proud of that. But what that allows us to do with all those biologics is say, 'Here is a patient that is treated insufficiently, we have somewhere to go.'

In HS at the moment, we really do not. In HS, and we will talk some more over the course of day, and there is data at this meeting that really suggests that the ability to maintain patients with therapy and keep them from going into that progression over time is extremely limited. So what we need to do is not only have things. Number one, we need things that are effective. We need more therapies because we are going to need to use them over time to maintain patients over time. Finally, we need things that can be maintained over time. One treatment over time is better than 10 treatments over time, and I think that is really critical for us to understand.

Current Therapy with Adalimumab Has High Discontinuation Rates

Median drug survival

So, current therapy with adalimumab and high discontinuation rates. I think this is something that those of us who had really, really high hopes for adalimumab a number of years ago have met this problem and it has become a very, very disabling problem for not only our patients, but for docs. This is why we see all these patients going to specialty care. The median survival is less than a year in a lifelong disease and a third of patients discontinue in six months. What have we really accomplished for the long-term benefit of those patients in those six months or in that year? Relatively limited amount. Clearly, we have improved symptoms, we have made people a little better for a short period of time. There is value to that, but the value is limited by not being to control it over time.

Patient groups with the highest burden of drug discontinuation

The patient groups with the highest burden of drug discontinuation are those groups who are generally underserved. I want to point out the ones on the right and the most recent surgical patients, they are the folks that we need to have better treatment. We want to prevent you the second surgery, prevent ongoing difficulties.

Finally, the second to last are the younger adults, lifelong disease. I would actually suggest that they are some of the least-aggressively treated patients because people are concerned about what happens when we treat younger patients. My argument would be these are the patients we need to treat most aggressively, that we can make the most difference for.

What do we Need from an Effective Therapy in HS?

Sustained efficacy is key for both derms and patients

So here is something that I feel very, very strongly about. What do we need for an effective therapy for HS? Everything comes down to efficacy; if the drug does not work and does not work over time, you are not going to be able to block the other sequalae. Our goal is, of course, alleviation of symptoms in the short term. That patient who is hospitalised, we want to prevent the hospitalisation, we want to keep the patient out of tertiary healthcare, we want to keep them in the office and doing well and in the clinic, and that is where we need to decrease symptoms. The symptoms are not only just pain, they are also odour, they are also the impact of scarring over time.

Again, hospitalisations. Decreasing not only hospitalisations, but emergency department visits. We do not know how many patients we get consulted on from our emergency department on a weekly basis saying, 'We have a patient with a bunch of cysts. Can you come in and lance them and drain them?' Then we come in and say, 'This patient does not need surgical intervention. They have hidradenitis suppurativa and they need to be put on medical therapy,' and it gives us an indication. It might not be clear to people who are not in the clinical arena that there are lots of patients who come in and see us for the first time in what we think is an inappropriate environment in the emergency department, saying, 'You got it wrong.' It happens every week.

Finally, the work and employment burden. If you are an employer and you have a patient with bad HS you want something that works for that patient, not only because it is going to make that patient better and you want your employees to feel well, but because it is going to make a big change in the work environment.

Established safety profile

Finally, safety. Obviously, safety is critical. Risk of adverse events, we do not want to do that. It is very interesting, when we started with adalimumab and thinking about these patients who have open areas and things that we would consider to be a risk for infection risk, and we started treating with high-dose adalimumab in HS patients, what we found is there is really no increased risk of infection. So even though these patients look bad, we have been very, very lucky in being able to treat patients with, actually, a very good safety record. I think that, as we go into drugs that have a more traditional advantage over anti-TNFs in safety in the treatment of, for example, psoriasis, or psoriatic arthritis or rheumatoid arthritis, I think that safety profile that we feel comfortable with in HS will get even better, and we feel very comfortable, when we have a good safety record, of being able to treat those patients with earlier disease, in preventing the bad outcomes in the future.

Treatment Goals Have Not Been Advanced in Eight Years

Adalimumab FDA HS approval 2015

So our treatment goals obviously are improving patients' outcomes not only in the short term, but in the long term. Where have we gone since adalimumab was approved almost a decade ago now? So, in the PIONEER trials we were able to show improvement in placebo to adalimumab. What is interesting to me is the discussion of the placebo arm we heard before in PsA. It happens in HS as well, and I have a sense that it is the volatility of the disease; that up and down, waxing and waning really does impact the outcomes of the disease.

In dermatology, we have been spoiled by psoriasis over the years, right? We have 3% PASI90 placebo control rates, it is great. Kristian and Joe and I have loved that in the development of our careers, but that is not real clinical trials, right? HS is more typical of what we see. So you will see placebo control rates, though they do vary quite a bit, and that is why I think we have to emphasise, and looking at our clinical trials, the treatment effect, effect minus placebo, as well as making sure we look at the placebo arm and say, 'What is really going on in the clinical trial? Are the sites the best sites that can do these examinations?'

So I think we have to be just very careful in looking at the data in the clinical trials, and that is why clinical trials and doing the best clinical trial you can in HS is of such critical importance versus doing psoriasis trials where we have been spoiled; you can pretty much figure things out pretty quickly and easily. It is a little bit harder in HS, and so the quality of trials really does make a difference.

Secukinumab FDA HS approval 2023

The secukinumab changed, we have had approved in the last year. Looking at the high score 50, you begin to see high placebo rates and rates that are better, an improvement, but still not where we want to see. If you are seeing a treatment effect of 15%, it is not where we want to be in treating our patients.

So I think all of these factors are very clear. Not only do we not have enough drugs, we do not have a level of efficacy that is really going to keep our patients at a significant rate, in a predicable rate, from having ongoing difficulties with the disease.

Can Targeting IL-17A + IL-17F Advance Treatment Goals in HS?

Is IL-17A and F an improvement over IL-17A alone? I want to say there are lots of theoretical reasons. There is quite a bit of IL-17F that you will see in FF heterodimers, we believe, in legions of hidradenitis suppurativa. So I think there is no question there is a theoretical benefit, but, really, where do you see the data? It is in the clinical trials. If you look at the bimekizumab trials, you do begin to see effects that are quite significant in comparison to placebo. You will see 18-19%, up to 20% differences in the high score 50. When you go up to high score 75, you actually begin to see the effects of patients that really differentiate medications. You see that Q2 bimekizumab, at 15% over placebo or 20% over placebo, really begin to shine. So I believe that targeting both A and F does make quite a significant difference.

I want to add something about changes in the high score goal that we have. Remember that patient we saw, that picture we saw initially of the patient with HS, making that patient 50% better is great. There is improvement – there is improvement in pain, there is improvement of symptoms – but that is not enough for that patient. If you think about, objectively, having 50% of that disease, a really bad disease, what do you have? You have really bad disease.

So I think from both a clinical trials aspect and from a clinical aspect, setting our goals higher is what we should be doing. I think that it is generally accepted amongst the community of folks treating HS at a high level today that we need higher goals so we can a) get better differentiation in studies, but even more so, we can understand, to get the patient to the goal they want to be at. We need to have those numbers to tell them, 'This is the likelihood you are going to get there.'

Elevated IL-17A + IL-17F in HS – Rationale for Targeting Both Cytokines

Both IL-17A and IL-17F are elevated in HS lesions, including inflammatory nodules and draining tunnels

So here is the rationale for having both IL-17 and F. You can see differences in both tunnels and in nodules. There is some thought that nodules and tunnels have slightly different physiologies and that there is a difference in potential responses of different drugs. So I think that is something that is very much in its infancy right now, this was published just this year. So this is a science in its infancy, but I want you to hold a view of this space, looking at drugs that improve tunnels, which is not really measured very well in any of our scoring scales. IHS4, they say, is a little bit better, but I think it is insufficient.

I think looking at tunnels individually is actually what we want to do, looking at nodules and inflammatory nodules and at abscesses, which is part of the high score, they might be different. So, again, this space is new. It is not something that has been developed, but it is something,

I think, over the next three or four years we might want to look at, and I actually think this, potentially, because of the impact of IL-17F in tunnels, might be a place where blockade of both A and F is of particular importance.

Can Nanobodies improve outcomes in HS?

Can nanobodies improve outcomes of HS? We have seen pictures of scarring. We have seen pictures of places where you do not have ulceration, oftentimes means having poor blood flow. So does the small molecule give an advantage? We do not know 100%. There is some data from animal models that suggest that nanobodies can get into smaller spaces. I do not want to say that is the equivalence, but at least this gives us some sense that there is a potential advantage, especially a disease that is scarred and has irregular blood flow, like HS.

High levels of response were seen with sonelokimab in the MIRA trial

What about the MIRA trial? Now I want everyone to be there at two o'clock today for Dr Kirby's presentation. I will actually be chairing that session, so I will be sure to ask Dr Kirby any question that any one of the audience wants me to ask him.

He is now very scared, and I am feeling in danger on the walk over to the convention centre later this afternoon.

But here is the week 12 data from the phase II trial. You can see scores and responses that are, comparison to placebo, higher than you will see in other disease states and in other treatment areas. And I want to particularly emphasise the HiSCR75 numbers, which was the primary endpoint, first trial that had a primary endpoint of what I think is the most clinically meaningful endpoint we have seen so far.

And looking at the 120 milligram dose, you see almost a 30% difference. That is extraordinarily significant. I also want to point out on the right, and this is something that I personally requested that we show, is to look at the pain outcomes. That is a big difference. Looking at an NRS of 50, that is showing real significant differences in pain. That is what is getting people to the hospital. That is what patients complain about. That is the thing that is going to allow people to go back to work.

Imaging lesions beneath the skin shows a different effect on tunnels

I want to point out some ultrasound images and I love ultrasound. In looking at it, I think it looks cool. It is a very difficult process and it is something that we have to figure out how to fit into clinical research. But in the meantime, you can see tunnels shrinking with treatment sonelokimab.

Incredibly important idea, can you get these tunnels to shrink, get less outflow, will improve some of the elements we talked about including things like odour. Complete resolution at 40% is a very, very significant number. Does that mean they're gone forever? The answer is probably not in the short term. In the long term, I have no idea.

I am hopeful that if you could shut these things down and keep them from draining over time, they might close, but I cannot prove that. And that is something that studies with ultrasound are going to be things that really drive us to understand over time.

After MIRA: what I would like to see in a Phase 3 programme

So what do I see in a phase III programme that I think needs to be done? There are lots of new phase II and phase III programmes. I have to credit MoonLake, and I will always give credit to my colleague, Dr Reich, for many years that it is really hard to do a good phase II trial in HS. There is a lot of incentive to get it done quickly and to get the patients enrolled as fast as possible.

I think this is a disease that calls out for active comparator in trials. Because we do not have that anchor, it is extraordinarily different to have understanding of what the results really mean because of that placebo arm. But endpoint select.

So the MIRA phase II trial was probably in my mind as good if not better than any other phase II trial we have seen in HS over time. And so I give credit where credit is due.

For phase III, what I look for, endpoint selection I think is really important. The HiSCR75, as I said, is I think that, that should be the minimum what we are looking for. Getting complete clearance of draining tunnels is great. I would love to see that. And that is again, another extremely high bar.

Maintenance of response is going to be very, very important. Remember, this is a lifelong disease and people need to be able to maintain response to prevent. You can delay response for a year, but in someone's lifetime, that might not be so significant. If you delay it, worsening for a great or long period of time, that is important.

Baseline patient severity is really important in how we judge outcomes. It has been clearly shown over time that patients with more severe disease tend to be more difficult to treat in our outcome measures. So I think you have to have significant baseline disease.

Optimal dosing, it is incredibly important. Obviously, a simple protocol. HS trials are hard for study sites. And so when we do them, we do not have too much fluctuation in what we do. Patients moving around too much in those studies makes it difficult to analyse the data. And finally, sufficient number of patients, obviously regulators like it, but with high placebo rates and patients fluctuating disease, that becomes even more important.

But I think really for me, the endpoint selection is the critical thing. Getting patients to a level that is going to make a difference for them and being able to silence a little bit of that fluctuation is incredibly important.

So now I am going to spread on to Dr Reich.

SLK differentiation & Phase 3 programme

Kristian Reich

Co-founder & CSO, MoonLake

Recap: Setting a new bar in HS for primary endpoints

Thank you, Ken. Thank you very much. You are here in San Diego at the AAD. We attended the HS Foundation reception yesterday. There were several hundred people in the room. The room was filled with excitement. You go to the late-breakers, you see one, two, three, four studies on HS presented.

Why do I stress this so much? If you look back in ten years, this is the moment where HS became psoriasis. This is the starting point. This is where I think we all feel this. This is where we were in psoriasis 20 years ago. And as Ken said, this is so, so, so needed.

So for us, we have really a strong interest in ultimately creating a therapy that will make HS better, right? Better than with other therapies. So for us, this is great. Of course, I am biased. What is also great for me as a CSO of MoonLake is that I look at all those studies, I think they are still the best. Whatever comes out and whatever has been shown here, we think we still have better numbers.

So, Ken, you showed it here, 30% delta to placebo, HiSCR75, that was the primary endpoint. You see the primary endpoint from some other studies as they were analysed and presented. I remind you, and I am just reflecting on the reality here, that Cosentyx, the second drug that just came in, got approved with a delta to placebo, HiSCR50 of 11-12%. We had almost 40%. Just to give you a little feel for how powerful the effects of sonelokimab in HS were.

HS: Response with SLK increases through week 24, with monthly dose

A little bit similar to PsA, and Professor Kirby will talk about this, of course, week 12, again, is not where the drug hits the ceiling. When you look at especially the high levels of response, and let us even go beyond HiSCR75, you see we add another 10% here just going from week 12 to week 24, we have 60% HiSCR75 here.

But when you turn up the heat a little bit more, again, you need to wait a little bit longer for patients to get there. I think the numbers to memorise is 40% HiSCR90 and 30% a solid HiSCR100 at week 24.

Now the limitation of the HiSCR is that it does not quantify draining tunnels. And we can talk about it. We now have clear evidence the tunnel is the inflammatory powerhouse in HS.

If you measure cytokines as high as in and around tunnels. So that is the real driver of the inflammation. It is also, I think, the most burdensome phenotype of HS for patients, because this is where the odour and a lot of the pain is coming from.

HS: SLK allows patients & physicians to aim for inflammatory remission

So let us look at scores that also quantify tunnels. We can talk about IHS4 and the usefulness of the weighing factor, but let me jump to this bar here on the right side.

IHS4-100 means patients that have no nodule, no abscess and no draining tunnel. That is IHS4-100, right? So take away the weighing factors. It is just zero of any of the inflammatory phenotypes. We get one out of four patients to this, what we call inflammatory remission at week 24. And this is not là pour la[?]. You heard Professor Gordon saying it is the non-treated inflammation that progresses to the irreversible tissue destruction.

So this is a disease where really every percentage point more on reduction of inflammatory lesions, we think matter when we think about the course of the disease and we will surely continue to look into this.

HS: The results are staggering and confirm SLK as the potential leader

So just to summarise, and we talked about this 80, 60, 40 as the new rule in PsA and 60% plus MDA. So what are the numbers to memorise here? 60% HiSCR75, 40% HiSCR90, 30%

HiSCR100. And one out of four patients achieving, and I use this word again, inflammatory remission.

Of course these patients are not in complete remission. They still have scars and tunnels, but they are inflammatory remission, and we explained why this is so important.

I will not walk you through some patient reported outcomes, but the one number, and Eva Cullen, our Senior Director of Medical Affairs who is in the room, she did this analysis and said, "Let us look at patients that themselves say, I no longer have any symptom of the disease or only minimal". So I am clear or almost clear, and this is 40% of the patients.

So I think we begin to see numbers that we feel really will move what we can do with this devastating disease.

We have clearly shown that 120 milligram, the dose interestingly that was the best dose in psoriasis is also the best dose in HS. And we saw data, and I am not going through the details here where we clearly separate from adalimumab, also when it comes to this long-term response, the stability of the response. We saw a crazy stability of our response. In the one-year psoriasis trial, we have all evidence to believe that we will see the stability of response in HS, and this is where adalimumab struggles. It is an okay drug, but the long-term control of the disease, I think, this is where the drug really struggles.

Already talked about the favourable safety profile in PsA, we saw a very favourable safety profile in HS.

HS: Very positive FDA & EMA EoP2 meeting, HS highly de-risked

Now, as the Chief Scientific Officer of a small company, you know what you feel when you go to the FDA, or to the EMA, right? You think you will be beaten up. You come with your phase III protocol and you have asked your nine questions and you sit there shaking and we were all in Bethesda before Christmas. I have to say we were so pleased to see that both the FDA and the EMA gave us a goal for all the key design elements that we asked for.

We always said that we think we will get something for doing our phase II study pivotal-like, and I think the answer that we got reflects that this may really indeed be the case. This was a 234 well-done pivotal-like phase II. We only have to do 800 patients in phase III. You can see what other companies had to do in phase III.

We will use the same protocol for these 800 patients. We will divide this likely up into two studies that we now call VELA I, VELA II. You know we love these star names being MoonLake. So here is another star name, VELA I, VELA II.

Both agencies agreed with us that we have identified the dose with the optimal benefit risk in HS. And ultimately, that is the goal of your phase II. If a company shows me this two, three doses in phase III, I would be critical to say you have not done your phase II homework. So we have one dose here, that is the 120 milligram with induction, will be a straight shoot out versus placebo, placebo patients cross-over, we treat for one year and then there is a chance for patients to continue in a two-year open label extension.

I have been doing clinical trials all my life. This is the simplest phase III you can think of. I think this is great for patients, this is great for physicians. And of course our primary input will be HiSCR75, right, and I will come back to this. But we will move it to week 16 to give the drug a little bit more time to really work.

One little element here, we have seen companies recently struggle to see safety events popping up in their study that might or might not be the intrinsic comorbidity of the disease that you treat. And of course, if you want to protect yourself against seeing some numerical imbalances, your placebo arm has to have a healthy size. So we will not do some four to one or five to one randomisation. We will do two to one, right, to make it attractive for patients, but to avoid this risk that suddenly you see a rare event overrepresented in your small placebo, and then you have a problem explaining what is really going on.

HS: VELA builds on the success of MIRA

So again, we are here at the AAD. We get a lot of, I think, extremely positive feedback from sites that are interested. We are really happy that we can now start VELA I and VELA II. We think that this drug really deserves to be developed and brought to the patients as quickly as possible.

HS: Pivotal-like MIRA design is replicated in Ph3, in contrast to other trials

Allow me to come back to this pivotal-like design for one other important question that we always get. And this question is, yes, your phase II is good, but you will be compressed in phase III. Everybody is compressed in HS, going from phase II to phase III. We do not think so. You will be compressed if your phase II is a single-centre non-controlled POC study, where you do crazy things that you would never do in a pivotal-like trial.

I am using some rhetorical language here, but this is the other thing that we get from our pivotal-like phase II. We get a protection against being compressed going from phase II to phase III because our phase III study will be a replication of our phase II. You see here all the important study design elements in our phase II, and everything that is green means we will have the same study design element in phase III.

So basically, we change very, very little. We move from phase II, from week 12 to week 16. We do some other mild adaptations in the statistical readout. But basically, our phase III is our phase II. So we do not see any reason why we should have a high risk of being compressed.

And just to point this out, even bimekizumab, their phase II was a POC study. They even used a loading dose that they never used in phase III, and they did not identify their best dose in phase II. So they had to take several dosing into phase III. This is all very different. This is not something that we think we are going to face.

So we are very enthusiastic about the great feedback. We continue to be excited about the data and we think we have a very high chance to replicate this great data in phase III.

HS is the Next large Indication in Derm

Jorge Santos da Silva

Founder & CEO, MoonLake

Recap: The HS market is expected to growth to >10bn USD by 2035

Great. So let me take over here for a few minutes to talk about another big question that always gets asked around HS. Is HS big enough? Can you really build a business on HS? Can somebody build a franchise on HS?

And we set out to find a strong fact base to make this conversation fact-based and not just idea or opinion based.

You have seen this picture from our side before. This has been our early estimations of what the market could be. We felt that there was a number missing out there on what can this market really become. You know that our perspective is that the market is about $2 billion in sales right now, and we will prove it with you with facts that this is the case. But we also know that this market is mostly driven today by Humira.

You heard from Professor Gordon, you heard from many other people. This is probably a misleading number of market size because there is so much limited durability, so few patients benefit from adalimumab to start with, and then the majority of them drop off within a year. So all the sales that you see here are dynamic sales. There are sales that created new every year. It is probably not a good indication of the market size.

And we believe based on some estimations that again we will detail further today, that this market can really go in the United States well above the $10 billion mark. One of the critical drivers to start with is of course that we will see what we saw in psoriasis back in the day, what we now start to see in AD and in many other indications that you finally start to have different therapeutical alternatives.

So these poor guys can sit in their practice and have a solution to present to patients. You have Cosentyx just recently approved. We are eagerly awaiting the first signs of commercial performance. You know that in 2025, bimekizumab is expected to launch in HS. This brings the IL-17 A&F MoA with a traditional monoclonal antibody that Ken already mentioned.

In 2027, we come into the market with the results that you have already seen of the MIRA trial, that again you will see again today detailed in the afternoon in the late-breaker we come in 2027, and obviously there is other products that are coming in like the JAK inhibitors, obviously these are more late-line therapies.

And obviously, the relevant element here, and you saw the numbers, is that we are really bringing the best of both worlds with this unique MoA, which is IL-17 A&F, but also the characteristics of sonelokimab as a particular molecule. And so you see this leading HiSCR75 responses. 75 is great. We even want to go higher than that, the effect on tunnels, which is very unique to our molecule of a very interesting drug to potentially use in the clinic because of the speed and depth of response and how you can disease control over time, plus all the other excellent profile elements that we have started to build with SLK.

So a market that is growing also because there are several options and obviously an option here that really seems to be stepping over the shoulders of others.

Market: Large market size is substantiated by real-world data

So to factualise some of that, and I do not know if factualise is a real word, but well, let us assume it is. Okay, thank you. We went and said, okay, let us look at the real world. Let us look at the real facts out there. What we did to do so is we used claims in the United States, so unique US patient claims. We have a very large database that covers about seven to eight years of longitudinal data, so it is very significant and covers about 75% of American life. So quite a good coverage.

And we immediately use a very, very stringent filter. In this big pool of patients, let us find the patients that are bona fide HS patients, patients that have received an HS code and have been treated for that disease.

What do we find? We find an absolutely staggering number. If you look at claims today, cumulative of the last few years, there are two million Americans that are diagnosed and treated for HS, right? So this does not even include the people that are diagnosed and not treated. This does not include the people that are undiagnosed, which I think, Ken, you would agree is probably the larger majority. But bona fide patients today two million Americans, and I remind you that this is a chronic disease. There is unfortunately no cure.

So if you were a patient in 2016, believe me, you are also a patient in 2024. So this number alone would make it a very large market by any means. It is also something that despite all the challenges, people are recognising more and more. So we have a very healthy rate of increase of the number of diagnosis of about 200,000, 250,000 patients a year. It confirms that there is a lot of potential out there and that we can bring a lot more of these patients into the clinic.

If you look at biologics, of course, the picture is very disappointing. So we have 40,000 patients being treated with adalimumab, for example, in 2023. The total number of patients that is treated with biologics is a little bit higher, about 30% of about 60,000 patients are treated with other biologics, which again tells you there is probably unmet need that these patients are bumping around and not getting the treatments that medically avoid all the dramatic long-term consequences that Professor Gordon has talked about.

And last but not least, we do see that the biologics are getting some uptake. They are being more and more used as all these patients come into the market and get diagnosed, but obviously this is starting as you can immediately calculate, from 60,000 over to a million patients, this comes from an extremely low base.

Market: Claims alone show ~2M HS patients – not incl. undiagnosed

I want to deep dive on a couple of these numbers to really drive some points home. What you see here is two million patients diagnosed today, so they are in the claims. We know that they are there. They are being treated in some healthcare setting. If we simply would assume that the market behaves as it has in the last eight years, just the historical diagnosis progression, we would get to about three million patients by the time we plan to launch. If you continue this, what we consider is a very conservative assumption of just continuing to diagnose these patients, we believe that we get to about five million Americans when we come to peak sales.

What this also means is that we have always this discussion, what is the real prevalence of this disease in the real world, wild numbers out there. I think in the last years, you see that, and Professor Gordon talked about it, we are sort of netting out at this 2% of prevalence, but this is again an estimate. But we can already show you that we find 1%. 1% is already in our claims, right? So it is very likely, and these are just the diagnosed and treated. It is not a big shot of mind to imagine that indeed the real prevalence is 2%, maybe even a little bit bigger. But certainly there is already a base here to create a very large therapeutical area.

Market: HS patient face challenging journey – even years after Dx

Putting some numbers to the drama that Professor Gordon talked about, and again, this tells you about the huge opportunity there is for biologics. Here what we do is we take patients in a given year and we see what happened to them as they go into years two and three, and the picture is horrible, right?

Majority of patients get treated with antibiotics, steroids, opioids, etc. This is the same in year one. Things do not really improve. Two year, too, a lot of patients. Here, our numbers match so, that is good. About a third of the patients end up in the ER for one or multiple visits in the first year. Things do not improve. As time goes by, significant percentage of patients get surgery. Things do not get any better over time.

And obviously you see that, there is about 3% of patients that are being treated with biologics and that number dramatically decreased in year two or three. And then of course if you look at the Sankey diagrams and you follow all these individual patients, it is a very sad story of patients just moving around from therapies, from sites of care, all over the place, but without a real solution. So lots of patients that really need a medical treatment that delivers on all the dimensions we talked before.

Market: Adalimumab with limited duration of response in real world

Adalilumab is not it. I think we have heard this from Professor Gordon. I think we also see this in the claims in the real world. Here on the left, we show you PIONEER data, right? So this is the famous picture from PIONEER that took all the patients that responded at week 12, the primary endpoints. I remind you that 50% of patients responded.

And then you track those patients over time and you see that even those patients that responded very quickly lose response to the drug to a point where the placebo actually performs exactly like the drug. So really not something that provides a durable treatment and obviously has other limitations in terms of efficacy.

If you actually look at the claims data, you see the story in numbers that we have been talking about. The median time that patients stay on adalimumab is 11 months. So obviously this is not going to be a solution for a chronic disease like this one. And so often times we say, well, this is probably a US problem, access is complicated. Probably not, because if we look at data from different registries in Europe, you see exactly the same picture, right?

Market: Growth and unmet need expected to remain high

So lots of patients, lots of need. Clearly, adalimumab is not a solution, but it also starts telling you the story that patients' cycle every year on adalimumab. So again, this story that the market size probably requires a little bit more analysis. This shows you the progression of the

biological therapy over time in all the patients until 2023. We do not still have full data for 2023, but it already tells you a good picture.

As I said, 3% of patients being treated. This is dramatically lower than anything else that you see in immunology, in dermatology, in rheumatology. We probably should be seeing about 15% or more. Of course, for the physicians here, 15% penetration is still a disgrace, but clearly, we need to get to 15% and then we worry about the next step, but obviously a lot of potential here.

Market: Humira accounts for most of current $2bn+ biologics market

What we are showing you here is again a double click on these biological sales so that you understand what we mean by dynamic market. Here is the 2023 data that is available. You see the number of patients that are treated. You already see that it is not just Humira, there is a lot of other biologics that are being used and on which patients jump back and forth.

Considering the fill rates that are available, the net price that we know of, you see that about $1.6 billion of these sales in 2023 belong to Humira. The total is about $2 billion. But what you can already see is, of course, you have about $0.5 billion sales here in other biologics that are being used. So obviously a lot of use. But you also see that, of course, because the patients fall off Humira towards the end of the year, these are new sales every year. So please do not look at the Humira sales as a proxy for the size of the market. It is incorrect.

Market: PsO shows clinical differentiation wins over time-to-market

One of the other things that I think are very important, what will happen now that, as Professor Gordon mentioned, we have all these new drugs coming in. Maybe the next one takes the market and then that is it. Nobody else can do much. I do not think that is the story that you see in dermatology. And here we are bringing you back the psoriasis example, this complicated chart, but I will use it to illustrate a couple of points.

You see here in the dark blue, that is Humira launched in 2005, had a very slow uptake, but as you see, took a big market position up to about a third of the market as the market grew. Then in 2015, you have Cosentyx being launched, that is the lighter blue. You see that it also build its position and grew the market to about 15% of the market.

And then in 2019, you have the incoming IL-23s, which obviously are great skin drugs, and you see them creating their own market. So I think this tells you a story of, there are a lot of patients here. There is a lot of potential, and if you continue introducing MoAs, and therapeutical solutions that really create a delta, there is ample opportunity to take market share and to continue growing the market, especially a market that we know is so depressed like HS.

So this concept of like, well, you only come in 2027, there is no way you can make sales. That would be true if the drug was not a very, very good drug. So this is another important point that for us is important to outline.

Market: The HS market might be even larger than $10bn in 2035

So we stick with our idea that just based on the prevalence that we see, just based on very humble biological adoption in the next, whatever, 12 years, 11 years, we really can get to $10 billion relatively easy, probably the market is much bigger than that if you really consider that we are not even seeing under-diagnosed patients or non-diagnosed patients in these claims

and considering that if we get to any biological penetration that is anywhere similar to any other of these indications we get to a market that is extremely sizable, right?

So if anything, we believe that we are being somewhat humble in our predictions for the market, but now there is clear evidence, we can find every patient in the United States, you know what the dynamics of the market are and you really see the potential for molecules like us and others.

Targeting: Achieving SLK blockbuster status in concentrated landscape

I want to just highlight a few other elements that I think are relevant from a market perspective. Oftentimes we are asked, well, but could MoonLake do this? Could MoonLake go out there and commercialise it? It is interesting. It is a very particular distribution of patients when you look at HS. You see here the hotspots, they tend to be in large urban sites. There is a number of reasons for that.

What happens in the West is a bit different from what happens in the East, but in general these patients are very concentrated. So it is not one of these disease-like psoriasis in which you have to cover the whole market, if you will, but whereas you can see also here in the left, it is a very steep curve in terms of the healthcare organisations that are seeing half of the patients or 70% of the patients.

So whether it is us, whether it is anybody else trying to push into HS, and we know that there is a couple of companies now pushing hard here, this is going to be a very particular market when it comes to targeting very different from some of the other dermatology indications.

Competition: Bimzelx above expectations – SLK is further differentiated

Another element from news from the market that I think is important, I think you have seen this, the penetration of bimekizumab, bimzelx in psoriasis as the first entry market for an IL-17 A&F drug has been incredible. I think a lot of people were surprised, we were not. We knew that the market was desperate and very interested in using IL-17 A&F because of the clinical data that you have in psoriasis, but this really illustrates the point, once again, that if you bring a proper drug that really changes therapy that provides new opportunities, the market will take it, even in a competitive place like psoriasis.

HS: SLK is most convenient

And obviously, if you try to create a parallel to sonelokimab, it is very obvious that versus bimekizumab, versus any of the other competitors, we are sitting on a data set that is extremely strong that probably will allow us to clearly differentiate when we come to the market, both in HS and in PsA. So I think this bodes very well in terms of how we will be perceived by the dermatologist, by the rheumatologist when we come for HS and PsA.

Recap: HS provides a sizable market with high unmet need

So just as a quick summary of this particular section of the market, sizable under-diagnosed market, I will continue insisting on this number. There are two million patients that are diagnosed in this country. This market is very, very large and needs to be addressed for all the reasons we heard. The biologics are there, they are growing, but there is a lot to be done. There is a lot of value that we can add by adding MoAs and therapeutical solutions that solve the problems that Professor Gordon mentioned, but also in PsA that Professor Merola mentioned.

You see that these patients are cycling all over the place. We need to balance and stabilise and control the disease with drugs that act strongly over time. And obviously, this will lead to very

interesting conversations also with payers, etc., because obviously there is a big patient burden and a big health system burden, a big societal burden that we can manage here if we can control these patients.

And as I mentioned, I think when it comes to SLK, we really have a true opportunity to hear we last, we work for much longer than adalimumab does. As Kristian mentioned, even on a primary endpoint like HiSCR50, we deliver a lot more response than current options.

And when it comes to bimekizumab, our IL-17 A&F monoclonal competitor, I think you see that no matter how many scores you look at, we are always consistently above that drug. So this is a very, very large market and I think we are well positioned to be the leaders. And I hope this starts to bring some facts to the table and it is inescapable that this is a very large market. I hope this starts to help with that conversation.

Maybe I stop here, Matthias.

Q&A

Matthias Bodenstedt: Yes, thank you, Jorge. Maybe in the interest of time, one question that we can take here. We received one specifically for you, Professor Gordon. The MoonLake team seems very confident of being able to replicate the MIRA phase II results, in their phase III programme. Do you think that the results will be replicated, or is there a reason to believe that the data would compress in phase III?

Kenneth Gordon: So it is a great question.

Jorge Santos da Silva: Do you want the crystal ball?

Kenneth Gordon: Well, but that is really it. So when you look at that question, what are you thinking about? You are thinking about what is the likelihood of having reproduction versus compression of the results. I am not sure I am familiar with it. The results are not quite as good in phase III.

I think when you look at the phase II to phase III transition in development of many drugs, as I think Kristian pointed out, there are changes in the protocols. There are changes in how you go about the trial, the different entry criteria, things of that sort. The way to try to best protect against that is to have your phase II trial be as similar to a phase III trial as you possibly can.

And so when I gave credit to MoonLake for doing a phase III like phase II, there is a reason for that, because the likelihood of it being predictable goes up. Is it 100%? No. But I think if you think in a normal trial that maybe it is two thirds predictable, you might go up to 90% predictable. Those are numbers completely, I picked out of the thin air, right? But what you are doing is protecting against that by having your phase II be as good a trial as possible.

Obviously in phase III, selection of sites, other things going on in the world that can change enrolment, all of that can change the outcomes in phase II, phase III. But I think that if you look at the MIRA trial, it is done the best job you possibly can to protect against compression that we have seen in HS.

Is it perfect? I hope so. I would love to see it. I mean, we have even seen some trials programmes get better in phase III, right? It happens. And it has happened in psoriasis a number of times. We are very hopeful, at least I am hopeful from a personal standpoint, that

it will get better, not because I have any vested interest in it, but because I want my patients to have good outcomes.

And so, I think that you can never guarantee anything, but MoonLake has set itself up for as much success as you can possibly get, and I think that is what your goal is. So I am feeling pretty good about it, but I would never go up and say I guarantee it by any stretch.

Matthias Bodenstedt: Not quite the guarantee, but thank you for the answer. I think in the interest of time, we will park other HS questions for the very end, and maybe speak a little briefly about the next frontier for MoonLake for sonelokimab. We have seen the PsA data. We have seen the HS data. We have seen the positive regulatory feedback. Jorge, what is next for sonelokimab?

New Indications New Frontiers for SLK and MLTX

Jorge Santos da Silva

Founder & CEO, MoonLake

SLK is a unique molecule: Nanobody that targets IL-17 A&F

Yes, so let us look at the new indication. I think we are good on time here. Obviously, we are getting to our last significant update of today's R&D day, which are the new indications.

As you know, we have been focusing quite a lot in all our communications, certainly today on HS as our main indication in dermatology and PsA as main indication in rheumatology. But obviously we are always very excited about our MoA, not only because we are only one of two molecules that can actually do this type of inhibition with all the great characteristics that we have already talked about of it being an antibody, but also because in our minds, the pathway, the IL-17 A&F pathway is something that is a little bit of a crux in a lot of signalling that happens in many of the inflammatory diseases.

Key MoA: IL-17A & F is at the crux of many inflammation pathways

So you see there is a lot of upstream pathways that signal through IL-17 A&F and many of them have been tried and some failed. In a lot of these indications, IL-23 failed in HS, C5 failed in HS. There is several of these that failed. We believe that if you go too much upstream, there is too much redundancy that can be compensated and we believe the same happens when you go too much downstream. IL-36, etc. being a great example.

So being a crux, we believe that there is, of course, a lot more potential to capture this pretty fundamental basic element of signalling to harness the inhibition to address many other diseases.

Many diseases involve IL-17 A&F as a key pathway, beyond HS and PsA

If many of you are familiar with this picture, as always, we try to put as much information as we can in one single piece of paper. But you remember this story. You see here a little bit the various indications that we see immediately as potential because there is information that IL-17 is involved, that IL-17 A&F is involved, that the inflammation is sitting very deep in tissues where our nanobody can reach.

And we have listed this out before. We divide them into different groups. We have this thing that we call the MoonLake Core indications. These are where the evidence is the strongest, where we ourselves already have some evidence that indeed we can become a winning therapeutical solution. In blue, of course, you see the indications that we have already have very large phase II data for. There is a few others that we have not pursued yet.

And then, of course, there is horizons with other indications, and there is a lot of ideas and options in dermatology. There is a lot of ideas in rheumatology. There is also a lot of other opportunities in many other tissues. And the opportunity from a market perspective is very, very large.

MLTX will expand its portfolio of SLK indications in Derm & Rheum

Now, for a company like ours, we have to choose very wisely, right? We are not a very large pharma company that can throw money at 20 trials at the same time and see what happens. We have to be very judicious as to how we use our cash position and our knowledge to really make a difference in additional indications. So that is really what we took into consideration when we thought, what are we going to be doing next.

We considered, okay, there is the HS phase III, there is the PsA phase III. These will all read out in 2025 and 2026, as we already mentioned publicly. This is, of course, a big effort for a company like MoonLake to scale up and go after these indications. So what are the strengths that we can build on to choose the next indications for us?

So one critical criteria is let us build where we already have leadership. So let us really double down on dermatology and double down on rheumatology because obviously we have the sites, we have the connections with the scientific and the clinical network out there. We also have built our own organisation with people that know a lot about dermatology and rheumatology, so it makes sense to go after these TAs rather than completely new ones.

Again, let us look at particular diseases, in particular sites of inflammation, where our nanobody can really make a difference.

How the new indications drive value for MLTX

And in what I would proudly call MoonLake style, let us go for indications, designs, where we can make a difference, where we can make an innovation, where we can change something. Be it the composite scores in PsA, be it the HiSCR75 and the inflammatory remission in HS, let us try to make it different rather than the me too stuff, as Kristian mentioned.

And so there are four programmes that we will be initiating in short order. Two of them in dermatology. And do not worry, I will go through a little bit more detail. We will introduce a completely new indication to our programme, palmo-plantar pustulosis. Again, I will share a little bit more detail, but this for us is one of the next HS, no drugs approved, horrendous disease, a huge disease burden and unmet need. So we are going to start a project in a trial on PPP, as we call it.

And in Derm, we will strengthen HS. And we will do so by running a clinical trial in parallel with our adult trial in adolescent HS. I remind you that no drug has created data, clinical data, in juvenile HS patients. And as we heard, this is probably the time where we really need to start treating the disease to avoid all the problems that happen after that. And of course, as you can imagine, this will reinforce our position as the partner in HS when it comes to dermatology.

On the Rheum side, a little bit the same play. We will introduce a new indication, and that is axial spondyloarthritis. So that continues to build our position in the seronegative spondyloarthritis, which of course includes PsA, and now axSpA, we will do radiographic and non-radiographic, and we will add another supportive phase II in PsA to bring imaging to match with clinical outcomes, and I will go through that detail. Again, this is to strengthen our presence in the current indication so that we can lead PsA together with rheumatologists. So that is a little bit the picture.

How the new indications drive value for MLTX

PPP

Allow me a couple of minutes to go through some of the thinking and some of the details that are associated with these indications. As I mentioned, PPP, I will no longer say palmo-plantar pustulosis, let us just go PPP, it reduces time.

As I said, it is also a priority for derms. It is one of those diseases where you are sitting there in the office going like, what do I do? Huge unmet needs, very high prevalence. So we think something that, of course, others have already shown. Bimekizumab as a case series, showing that IL-17 A&F is really probably the first MoA that can really make a change for these patients.

And always, giving a little wink to the psoriasis side. Of course, a lot of these psoriasis patients have palmo-planter involvement. And this is another opportunity for us to stay close to the psoriasis patients as we are with PsA. And as I said, strong clinical evidence that A&F will probably make a huge difference here.

PPP: Elevating position as the leading innovator for Derm

For PPP, I just want to mention a few things. Again, I want to insist on the fact that no approved therapy. The usual people that have failed have already failed, so this is something where there is a big need. And it is really a chronic inflammation. I want you to remember that these patients, which is about 0.3% prevalence, really lead very difficult lives. It is the palms of the hands, the bottoms of your feet. You cannot walk, you cannot grab anything. It is painful.

As you can see from the pictures, this is not something that you want to suffer from, obviously. And as we build our phase III, you will see as we announce the details that we are introducing again higher and I think quite ambitious outcomes in terms of what we are going to be reading in this phase II. And we believe the design that we have will allow us then to move into phase III in a disease that again has zero options.

How the new indications drive value for MLTX

Juv HS

Juvenile HS as I mentioned, typically drugs are approved in HS. And then, of course, you have PedCO and PIP and you have to do some work in adolescence, but everybody just postpones this to observation studies in the market. You see the effect that we have on tunnels. You see the needs, Professor Gordon talked about it, to treat these diseases early so that you avoid these irreversible lesions. And we are so good in the tunnels.

And we thought, let us turn the argument around. Let us not wait for the market to address these patients. Let us commit to a trial where we really have the opportunity to control the irreversible damage and provide a solution to when the disease has its actual onset. So this will run in parallel with our adult trial and the idea is that we will have both results by the time we

get to market and again be a true partner in HS but also the first company that has clinical data in adolescence.

A couple of very interesting elements about our Rheum programmes, and obviously suffice to say that on the Juvenile HS, we will continue having the primary end point very high at the HiSCR75, etc., etc.

How the new indications drive value for MLTX

axSpA

In axSpA, as I mentioned, both radiographic and non-radiographic, as you know, there are some limitations that you also see in PsA with the current standards of care. Together with PsA, this allows us to continue trying to lead in seronegative spondyloarthritis, which is obviously a market basically the size of RA. And we already know, and here again, we are following the coattails of others. We already know from some of the bimekizumab cases that A&F works.

And obviously you are talking about very deep tissues, very difficult to reach tissues, so we believe that our drug will have a key advantage here.

axSpA: Broadening leadership in Rheum by elevating care in axSpA

I think you are all familiar with axSpA, again, very large disease. I mean the prevalence is extremely high. What I would really like to call your attention to is the innovative design that we are going to be running here.

So we are going to be measuring all your traditional clinical outcomes, what I would call subjective outcomes, like ASAS, etc., but we will be complementing these rheumatology trials with an innovative imaging set where we do MRI and PET so that we can really go into the tissue and see exactly which joints, by how much is our drug able to impact in terms of inflammation.

So not as Kristian would say the press and say ouch, but the press and say ouch, and then I actually look into your joint and say, here is sonelokimab is maybe making a difference or not, right? And we believe that this is the first time that this type of imaging technology is used together with clinical outcomes in a phase II setting.

And as you can already see, this is a way for us to start creating data that nobody else has. So rather than competing just on ASAS40 me versus you, it is that plus the showing that in the real tissue we can make a difference.

How the new indications drive value for MLTX

PsA

And PSA is going to follow the same logic. This is a supporting phase II to our phase III programme. Again, here it is about doubling down on these indications and it is using this innovative imaging. It is again MRI with a slightly different modified PET strategy that will again allow us to confirm the clinical measures that we show in phase II for PsA but bring in the imaging to show that we are really acting deep in the tissue and really resolving the inflammation on particular joints, be it in the fingers, be it in any other joints.

So again, us innovating here to bring the subjective clinical outcomes together with objective measures, which we think will contribute greatly, and I hope you agree, Joe, that this will

hopefully help in getting a bit more precise when we are treating these patients in the real world.

New indications provide sizeable opportunity in multi-bn markets

You will see this in the document that is now already available at our webpage, the document you are seeing. This is a bit of a summary. We are talking about all diseases with very high prevalence. We are talking about very high markets. And we are talking about largely empty spaces, especially when it comes to some of the new indications that we are following. So we are very excited to add that to the mix.

New indications further enrich the potential catalyst calendar in 2024-25

Again, I am not going to go through the detail here. This will be available for your careful perusal. We believe we will bring about 200, maybe a bit more patients into these new indications. And as you can see, the time that it takes for us to get to the primary endpoint of HS next year and to PsA primary endpoint end of next year beginning of 2026, you will start seeing news from all these trials as we go through 2024 and 2025.

Potential new indications could further build out SLK's potential

Obviously, what we are trying to achieve here is increase the value that we are capturing with sonelokimab as a drug. We have told you before that we believe that we have about $5 billion in sales or so that we predict with HS and PsA. But we believe that adding these additional indications in Derm and Rheum will allow us to continue building on the value of this asset so that we really make it the very large asset that we believe that it is.

Taking a step back: Overview of R&D programmes at MLTX

This also starts to build the picture of what we are doing from an R&D perspective at MoonLake. We now have bona fide, let me call it, BLA-enabling programmes, the phase III in HS, the phase III in PsA, and now phase III in Juvenile HS.

We are filling the pipeline with what comes next. So we have the phase III enabling studies as we call them, PPP, axSpA, and the new supporting PsA study. And we never really have time to go into this, but obviously, rest assured that we do a lot of work in terms of biomarkers, we do a lot of work in penetration, and we do a lot of work in testing in human models' potentials to expand the use of sonelokimab.

But this really enriches the programme and the set of catalysts that we have over the next years.

Maybe I stop there, Matthias.

Moving Forward

Matthias Bodenstedt

CFO, MoonLake

SLK combines properties like no other asset

Thank you, Jorge. Maybe briefly, a couple of minutes now in the last section, some strategic considerations and a brief update also on the financials of MoonLake before we then open up for Q&A.

So maybe to summarise, what do we believe do we have with sonelokimab? I think on the one hand, a very, very promising, I would say leading MoA. We have seen the data from bimekizumab. We have seen our data now in multiple indications, where we would argue this is really the leading MoA, and this is a differentiated MoA that has shown the highest efficacy outcomes across multiple indications, but not only the highest outcomes, but also durable outcomes.

Just yesterday we saw a presentation on IL-17 A&F inhibition with four-year data, which was, I have to say, very, very impressive to see the durability, something that we have seen it now for the TNF inhibitors in HS. You do not see this with other MoAs. So really high efficacy, durable efficacy, but then also very favourable safety profiles.

IL-17s are a very safe MoA, and I think from all the over 700 patients that we have now exposed to sonelokimab, we do not see any difference. We do not see any signals that would be worrisome. We do not see any cancer, any cardiovascular events, any deaths. We do not see any signal for SIB. We do not see any signal for any liver problems. So really a favourable safety profile that we observed with sonelokimab.

And then ultimately, I mean, there is only two assets that share the same way. There is bimekizumab, the traditional antibody, and then there is sonelokimab, the innovative nanobody that also binds to albumin, further helping the tissue penetration, getting the drug to the sites of inflammation.

But even beyond this MoA, we do believe we have a differentiated molecule in the MoA. We have shown you the data, the efficacy data. Not only do we aim for higher outcomes, we use HiSCR75 as a primary endpoint. We look at IHS4-100 full clearance. We look at these very high, like ACR70, PASI100, that no one has ever shown before, and we get to outcomes that we have not seen in any other clinical studies before.

So clearly elevated performance that we bring to the table, higher goals we talked about it, higher primary endpoints than that other companies are going for. And then ultimately also, we did not speak about it now, but a very convenient posology. Sonelokimab is in maintenance, one injection, 1 ml, once a month with an autoinjector, takes a couple of seconds. So a very convenient pathology that also we believe will further help us differentiate in the market versus other treatments.

Strategic path forward remains unchanged

Now, how do we take it forward? And I think this page is a page that many of you have seen. Some people say, well, the MoonLake guys, why did they show it? But we do not mince words. We see it still continuing. There is two possible paths for MoonLake. There is one, the current owner scenario. There is the other one, the better owner scenario.

We could not be in a better position than that we are in right now. We have very, very strong clinical data from the ARGO study, from the MIRA study. We have very supportive feedback from the regulators, from the FDA, from the EMA, clear path ahead. We know exactly what we need to do. We do have the team and we do have the money. So we could not be in a better spot to drive this forward. And this is what we are doing.

On the other hand, nothing has changed on this one. It is also no secret that I&I is in a very attractive space for pharma companies. They are looking for assets and there is not a lot of assets like sonelokimab that are as de-risked as sonelokimab is and that it addresses multiple billion dollars across very large indications. So no real change here. The strategic path forward remains really unchanged.

Operating from a position of strength: over $500m in cash on the B/S

Now a brief update on the finances. Here you see that was, I think, filed yesterday, a week ago in our 10-K. You see it there. We are in a very, very strong financial position. In the end of the third quarter, we had close to $500 million on the balance sheet. We continue to operate in a very focused way. We are a single asset company, focused on the development of sonelokimab. So in the fourth quarter, a cash burn of approximately $16 million, which actually half of that is prepayments for the manufacturing runs for 2025. Now getting ready for the commercial supply with the launch expected in 2027.

We have also utilised in the fourth quarter and at the beginning of the first quarter a little bit the at-the-market facility that we have to top up the balance sheet, to really drive forward and double down on the development of sonelokimab. Jorge presented the additional four programmes that we are running now, but now we are in a very, very strong financial position with funds that are able, or allow us to run the full phase III programme in HS, the full phase III programme in psoriatic arthritis, to do the additional indication work that Jorge presented, submit for regulatory approval, and also covering all the other base stand, really runway until the end of 2026, well beyond the next clinical read, so putting us into a very strong financial position to drive forward the development of sonelokimab.

Focus on strengthening the story of SLK as leader in Type 3 diseases

This is the last page that I want to leave you with. It is like, where do we see now sonelokimab fitting in the world of I&I? And if we look at I&I indications, we see broadly three types of inflammation.

Type one or type two is the one where you see dupilumab, where you see the atopic dermatitis, allergic asthma. This is where dupilumab is currently the market leader. Then you see the other type one inflammation. This is one where people talk about the TL1-alphas. We believe for us this is really the type three inflammation where you have HS, where you have PsA, where you have PPP, where you have a lot of other indications. That is where we believe IL-17 A&F is the leading MoA, and if you can then deliver it with a nanobody like sonelokimab, you are in a very strong position to really unlock the potential in many, many large indications in I&I.

With that, opening it up for Q&A. I do have quite a few questions here online, but maybe starting in the room, whether there is any immediate questions.

Q&A

Matthias Bodenstedt: Maybe I repeat the question and then Kristian you want to address it. The question asked here from the audience is, what if one of our phase III studies in HS fails? If we fail to meet the primary endpoint, would we still have a chance to get approval?

Kristian Reich: Yes, I mean, I do not want to preempt what the FDA and the EMA ultimately say, but you have seen, for example, in Cosentyx that not in all studies, all arms met the primary endpoint, right? Is Cosentyx approved? It is. So I think in the end, it will be down to the real data.

I have to say why I struggle to answer this in this way, I need 50 patients to show statistical significance to placebo, right? I mean, the size of the study is completely driven by safety. So if you ask me, is there a real risk that we are not going to show statistical superiority to placebo in HiSCR75 in one of the studies, you should never say no, but the risk is very, very, very, very low. So we would need to see how far are we away. Is it still better, just not reaching statistical significance? Does the safety look good?

Clearly, the 234 patients that we have in phase II will be integrated part of what we submit, what regulatory authorities look at. So we are very confident that this phase III has a good chance to come out positive.

Matthias Bodenstedt: I repeat the question again. So I think, do we see a difference in the PsA study and the ARGO study between biologic-naïve and biologic experienced patients?

Kristian Reich: Not really. I showed you this one, I mean we will test it. The biggest thing I think for prescribers is TNF inadequate responders because they are still used as the first line biologic by many. Although, I have to say my colleagues have been switching to 17 inhibitors because of the better response in the skin. And that will be interesting. Will we work in Cosentyx failures, right?

I think even there we have a strong chance to win. From all the evidence that we have, no problem with TNF inadequate responders. I would see from them mechanism of action, no problem in 23 in the inadequate responders because these are really different and only partially overlapping MoAs. And as I said, even in 17A non-responders, I think we still have a chance to work.

Matthias Bodenstedt: Thank you. So the question is, on the one hand, the expected impact on prescribing behaviour stemming from the fact that sonelokimab is the only trial aiming for HiSCR75? And the other question, what is the impact of Humira biosimilars, adalimumab biosimilars?

Kenneth Gordon: Okay, so first of all, I think we can go back to the experience in psoriasis, and looking at our modification of our endpoint over time. If you remember, I am old enough, most of the people in the room are not old enough to remember when PASI50 was an endpoint that we were looking at and it was considered to be a good response.

What happens as the metrics get better, right? We get better responses is that everyone is held to the same standard, right? We are now asking Amgen for apremilast, PASI90 response. They are not all that anxious to show us that. But the point is it differentiates medications because it does make a difference to patients.

And so if you are concerned about getting patients to the point, especially in this disease where the outcomes of not controlling the inflammation is so significant, as we get to higher standards, and eventually it might be to the inflammatory index of zero as the goal. Physicians are going to have to respond to that in terms of this is going to be the goal we treat or else we are under-treating our patients and exposing them to permanent damage, which we do not want.

So I highly espouse higher endpoints. I would not mind a HiSCR90 as an endpoint to look at too. Obviously not as many patients will get there, but it better differentiates medications and it is getting the patients to where I can say this is the level I want you to be at as best as possible. So I think it is actually only positive.

Adalilumab is almost very interesting. And this disease state, I think you have to differentiate between initial treatment and what patients are going to eventually be on. So with adalilumab biosimilars, I think there is no question for cost savings that people are going to be pushed to using adalilumab biosimilars initially, right? That said, we have already seen the data of how many patients persist on that to a year, to six months, even short periods of time. You have got 50% response rate at a HiSCR50 to begin with.

And then you look at a third of those patients are gone within six months. Well over 50% are gone within a year. And if you just go further out than that, these patients drop off very quickly.

So while I think you might have initial requirements, it might be a point of entry to systemic therapy, but I think for very few, that will be the point where patients end up. And so I think from whatever impact they might have, it might be transient. And occasionally, if you can get a patient who does well and maintained on an adalilumab biosimilar, I have no issue with healthcare costs, I am all for it.

But the problem is going to be, are we going to be able to sustain them? And I think so, I think not. Over time, the data suggests not. And I think it is incredibly critical to think of how we treat patients, not only as what is going to be the first thing we choose, but what is going to be the lifetime of the patient and how we treat them?

Matthias Bodenstedt: So again, two questions there. I think Kristian, the first one for you, on the whether we can share more details on the upcoming or now proposed PsA phase III design. What will we propose to the regulators in our interface to meeting?

Kristian Reich: Let me put it this way. As much as we offer innovation, we want to take the minimum risk to get to approval. And we will probably not invent the real new. Once again, for the prescriber, it is very important to have a solid study in TNF and as a quick responders. So that is clear, that box is ticked.

I think it remains important to show effect on radiographic progression, right? It gets more and more complicated, but in order to do so, you need to do this in biologic-naive patients, because otherwise, you have no arm to compare to how you can protect against radiographic progression. So that will be the likely scenario.

If you look at the size, we probably talk about 1,100, 1,200 patients, but be assured that when it comes to the details, when we look at the composite endpoints, for example, what are our key secondary endpoints, we will bring all of this back that we showed you today.

So I think using the path to get to an approval, but do it in a way that all the innovation is not lost.

Jorge Santos da Silva: Yes. Let me add to that. I mean, you saw, Serge, the additional supporting trial without jeopardising the main trial, the main phase III, so that it can be accepted by regulators. And important, Serge, that we can compare to all those other biologics, right? Because we have some really, really high response. We need to be able to compare ourselves, number one, make sure that the regulator accepts that it is comfortable with it, that we are testing the right patients and it is ethical.

But also our supportive phase II, with all the innovative imaging, that is where we want to bring something else that nobody else is bringing. So it is not through the phase III. It is actually through different actions that we bring the innovation.

And I will take you to the second question, which I will play back for those on the webcast, with, Serge was asking, with the data from bimekizumab, will you now go after psoriasis? The answer is no. As much as we like it, as much as that data gets us excited, as much as we know the result from our phase IIb, it is just too big of a bullet for us to bite. These are very large studies.

For us, it would be a choice between doing psoriasis or doing other indications, right. So we believe that we can unlock a lot more value through the other indications. It is a bit of a shame, yes, but it is locked value that we have within MoonLake. There was one more question here.

Matthias Bodenstedt: Yes, maybe repeating the question. I think the question is, there is a lot of approved drugs out in psoriatic arthritis. And the consensus so far is none of them is really standing out or like, we do not see recent innovation that is really able to move things. What is our view, and Professor Merola's view, on the ability to really differentiate for sonelokimab also versus bimekizumab?

Joseph Merola: So I will answer first very basically, which is, again, just to look back at that domain chart, the very clear little green and yellow check box that we showed, which is just reminded that while there are several MoAs, right, the big ones here we are talking about from biologic standpoint, being IL-17A/IL-17 AF, we'll come back to that, 23 TNF historically.

The 23 inhibitors, while I think we have made cases reasonable for probably more mild moderate disease, I really do believe it is, and we have the only head-to-head data that IL-17 inhibition really has been equivalent to our gold standard in PsA.

We have the radiographic progression piece, we have the axial or spine piece, so it really checks all the boxes, but we have the elevation in skin. So I think it is not true that there is sort of all the platform is even. I mean, I think in many respects, one could make a case that IL-17 inhibition really checks all the boxes in the psoriatic disease standpoint.

Second part of your question, though, I think this concept that we have not been able to break the ceiling of up, I think when we saw bimekizumab data come out, at first, we were hopeful that that was going to be our break the ceiling moment, and it is phenomenal data in the skin, clearly better than TNF inhibition, but it is TNF-like effect in terms of many of the PsA domains of disease.

I was quite excited to be able to see this MDA and other composite data that really has, and frankly, HiSCR50 and 70 itself data that really is moving the bar higher. So I do believe we are seeing something in phase II. I hope that we will see something similar in phase III. I am also hoping that there is something mechanistic here, and I love that they are committing to some of the imaging studies that we have been asking for, for a long time, because we really want to have a look at whether we are having impacted sites of inflammation that are not immediately accessible.

There are entheses peripherally, there are spinal entheses, there is the entire spinal compartment, the SI joints, there are areas here that we may have impact in a very different way, and we have not even gotten into uveitis and other areas that may be relevant. So it is a great question. I do believe I am seeing something a little bit stand apart.

Matthias Bodenstedt: Thank you. Maybe time for one more question.

Matthias Bodenstedt: So patent protection as it stands is until May 2032 for the compound. On the other hand, we actively work on patent extensions. We just filed two new patents last year, so that could potentially bring us to 2043. I think what matters most or what we have for sure as a guarantee is like the regulatory exclusivity.

So in the US, after launch, we get 12 years of marketing exclusivity. That means you heard us saying talking about a launch date of 2027 for sure until 2039 we should be protected from any biosimilar competition.

Another question would be there has never been any biosimilar for nanobodies so also something to be seen, but certainly until 2039-2040 we should be completely fine with the potential opportunity to even go beyond with the new patents that we have filed.

Looking at the time, I think we are at the end of the session. There is a few more questions that we received online that we will address afterwards. I hope this was helpful for everyone. I hope you enjoyed the presentation of the 24 weeks data, the presentation of the regulatory feedback, design of the HS study, the new indications, the perspectives and reflections from our two KOLs here, Professor Ken Gordon, Professor Joe Merola.

Thank you for joining us here during a very busy week or weekend for you here at AAD. And for all of you, please join us this afternoon at 14.00 at the late-breaking session where Professor Brian Kirby will present the 24-week data of our HS MIRA study. We hope to see you all there. And thank you for joining. Have a good day.