[Drew Kasper] 09:00:36
Good morning and welcome to the new technology add on payment or in tap town hall meeting for fiscal year 2027.

[Drew Kasper] 09:00:40
I'm your host Drew Casper with a division of new technology. In the Center for Medicare's technology coding and pricing group.

[Drew Kasper] 09:00:49
Thank you all for being here with us today. We're excited to be hearing from and interacting with all of you today in today's event.

[Drew Kasper] 09:00:58
For we begin, I'd like to cover some basics for the meeting.

[Drew Kasper] 09:01:03
Anyone doesn't already have the agenda.

[Drew Kasper] 09:01:08
You can find that on our web page through a simple internet search for CMS NTAP. That should take you there very easily or you'll find the webpage address in the chat.

[Drew Kasper] 09:01:22
Where you can download the agenda from our download section of the web page.

[Drew Kasper] 09:01:28
In the event we experience any major technical issues with the webinar, you can reach out via email to the new tech mailbox which is NTAP or ntap@cms.hhs.gov.

[Drew Kasper] 09:01:42
And we will do our best to keep you apprised of what's happening. In the interest of data volume and bandwidth, With such a large group of people the standard for today will be to not activate your video unless you're presenting or speaking.

[Drew Kasper] 09:01:57
Presenters are welcome to activate your camera during your presentations, of course.

[Drew Kasper] 09:02:03
10 days may submit their questions about each presentation using the Q&A feature at the bottom of your screen.

[Drew Kasper] 09:02:10
Or by using the raised hand Zoom function. If you raise your hand, we can enable you to unmute yourself during the Q&A sessions.

[Drew Kasper] 09:02:20
For public attendees who are only dialed in by telephone, You'll need to email your questions to the CMS NTAP.

[Drew Kasper] 09:02:29
Email box. NTAP at CMS. I'll be monitoring that mailbox throughout the session.

[Drew Kasper] 09:02:37
Questions for presenters should pertain to the substantial clinical improvement of the technologies that are presented today. We sometimes refer to substantial clinical improvement as SCI.

[Drew Kasper] 09:02:49
So that you'd be familiar with that acronym. As a reminder, there are 3 main criteria for new technology.

[Drew Kasper] 09:02:56
Out on payment eligibility. Cost, and substantial clinical improvement over existing services or technologies. We're here today to talk about the substantial clinical improvement criterion for fiscal year.

[Drew Kasper] 09:03:10
2027 and tap applicants specifically. For CMS consideration in the IPPS proposed rule, public comments must be submitted to CMS in writing.

[Drew Kasper] 09:03:22
Via the email box. That I had mentioned earlier, ntap@cms.hhs.gov with the subject line.

[Drew Kasper] 09:03:30
Town hall comment followed by the technology name. All comments must be received by 5 PM. Eastern Standard Time on Monday, December, 15, th 25.

[Drew Kasper] 09:03:42
Even if you raise a verbal comment during the town hall today during the Q&A. Segments after each technology presentation you must send the written comment to ensure consideration in the proposed rule.

[Drew Kasper] 09:03:53
You'll see this announcement about submitting comments at the bottom of the agenda as well. As a heads up for fiscal year, 2027 and tap applicants and presenters.

[Drew Kasper] 09:04:05
CMS is issuing more SEI related questions using RFIs or requests for information earlier in our process this year.

[Drew Kasper] 09:04:13
That reason you may not hear as many questions from CMS today as you may have experienced in town halls from prior years.

[Drew Kasper] 09:04:20
Those RFIs capture our questions and your answers in the NTAP application in the Mira system.

[Drew Kasper] 09:04:26
So we won't be repeating those questions here today. We are as curious as ever about your technologies, but we do have that parallel process happening to answer a lot of our SEI related questions.

[Drew Kasper] 09:04:40
Well, now move on to fiscal year, 2027 and tap applicant presenters. I'd like to remind the presenters that we've allotted exactly 10Â min for each presentation today, after which we'll have questions from the public.

[Drew Kasper] 09:04:54
And then from CMS with responses from presenters. CMS will advance the slides for each presentation.

[Drew Kasper] 09:05:01
Presenter should indicate when to advance to the next slide. You can do that by simply saying, next slide.

[Drew Kasper] 09:05:10
Okay, and with that we will. Now here from presenters for the Coventry technology, you may now unmute and introduce yourself.

["Greg Mattingly] 09:05:22
Good morning, Drew. Good morning, everyone. This is Greg Mattingly. I'm an associate clinical professor at the Washington University School of Medicine.

[Drew Kasper] 09:05:22
Okay

["Greg Mattingly] 09:05:31
President of the Midwest research group in St. Louis, Missouri, and co chair for the US psychic, Chichondras.

["Greg Mattingly] 09:05:37
It's my honor to be here with you this morning and get things started and probably most importantly for this topic not only am IA professor and I've done a lot of research in this field.

["Greg Mattingly] 09:05:46
I have a family member living with schizophrenia. I am here today on behalf of Bristol Meyers Squib and it's my pleasure to talk about my disclosures if we go to the next slide.

["Greg Mattingly] 09:05:58
I've been a researcher for the past 35 years doing clinical trials, looking at advancements in treatment of all mental health conditions, everything from autism to Alzheimer's, and once again with a special place in my heart because of our family member with schizophrenia.

["Greg Mattingly] 09:06:11
Let's go to our next slide.

["Greg Mattingly] 09:06:16
Our agenda today, I'm going to talk a little bit about schizophrenia.

["Greg Mattingly] 09:06:21
Why are we here today? Because schizophrenia quite often winds up in a hospital setting. More place to make the biggest difference in someone's life.

["Greg Mattingly] 09:06:29
And we know that outcomes of schizophrenia have been very dire throughout the years. Today we're going to overview a new treatment molecule, cobenphy, which is a novel way to treat schizophrenia instead of modulating dopamine receptors, which is what every other schizophrenia treatment has done.

["Greg Mattingly] 09:06:46
We are changing the release of dopamine in the synapse through an entirely different mechanism. And my belief, and I think the scientific literature, that represents a substantial clinical improvement for our patients and for our health care system.

["Greg Mattingly] 09:06:59
Let's go to our next slide.

["Greg Mattingly] 09:07:04
So let's talk a little bit about Copenfi. Cobenfi is FDA approved for schizophrenian adults.

["Greg Mattingly] 09:07:12
It combines 2 different compounds. Zenomaline, which crosses into the brain and stimulates m 1 and M 4 muscarinic receptors.

["Greg Mattingly] 09:07:20

Those muskerinic receptors then modulate presynaptic release of dopamine.

["Greg Mattingly] 09:07:27
The reason the brain's getting ill, the reason people are getting They're getting delusional.

["Greg Mattingly] 09:07:30
Is their brain is releasing too much dopamine in certain pathways? Up until now, we've just had to block the receptors, but we couldn't change the release of dopamine.

["Greg Mattingly] 09:07:39
This pathway is changing presynaptic release. And in addition to zenomoline, we're combining a compound called trophium.

["Greg Mattingly] 09:07:48
Trosbium is a muskrenic antagonist that stays in the periphery.

["Greg Mattingly] 09:07:50
It has very little CNS penetration and it's there to help minimize the side effects of zenomally.

["Greg Mattingly] 09:07:58
So we're letting xenomally get into the brain, stimulate inborn in 4 receptors.

["Greg Mattingly] 09:08:02
We're letting zenomaline and trouse beams stay in the periphery where they can help to neutralize each other's actions, helping to minimize muskerinic side effects.

["Greg Mattingly] 09:08:10
When we take a look at this, what does this mean for our country? What does this mean as far as innovation?

["Greg Mattingly] 09:08:16
What does this mean as far as significant clinical improvement? The FDA did something they've never done before.

["Greg Mattingly] 09:08:22
They said, we're going to call this medicine not an anti-psychotic. We're going to call it a muscleinic medication for the treatment of individuals with schizophrenia.

["Greg Mattingly] 09:08:31
This is the 1st and only. Schizophrenia treatment that does not carry an antipsychotic label.

["Greg Mattingly] 09:08:38
That alone shows that the FDA thought that this was novel, was different, and was a significant clinical advance in our care of patients with schizophrenia.

["Greg Mattingly] 09:08:47
The FDA in this label also did something else novel. Cobenfee does not have the historic boxed warnings of every other schizophrenia medication.

["Greg Mattingly] 09:08:55
So Cobenfi does not have the box warnings about waking in metabolics.

["Greg Mattingly] 09:09:00
It does not have the box warnings about tardy discunnesia and movement disorder side effects.

["Greg Mattingly] 09:09:05

It does not have box warnings around suicidality that many of our medications carry because it's novel and represents a significant clinical improvement for our patients in those fashions.

["Greg Mattingly] 09:09:16
Let's go to our next slide.

["Greg Mattingly] 09:09:21
Let's talk a little bit about schizophrenia. I know many of you out there may come from various healthcare backgrounds.

["Greg Mattingly] 09:09:28
This may be statistics, it may be science, it may be health care economics or health care equity. I come to us from a engineering background originally.

["Greg Mattingly] 09:09:37
I went to medical school. I was lucky enough to get a Fulbright scholarship. 1st in my family to go to college and then go to medical school.

["Greg Mattingly] 09:09:42
I've been working in the mental health field and the brain science field for the past 35 years.

["Greg Mattingly] 09:09:48
And what we know is around the world schizophrenia affects about 1% of the population. We know that schizophrenia does not discriminate.

["Greg Mattingly] 09:09:55
You can being a single working mom, a single working dad, you can be a physician, a doctor, a lawyer, a researcher, and someone in your family can have a 1st psychotic break.

["Greg Mattingly] 09:10:05
We know that part of the neurobiology of schizophrenia involves inappropriate synaptic pruning in neural pathways that usually occurs in those late teens and early twentys.

["Greg Mattingly] 09:10:16
We know that certain pathways are pruned back when they shouldn't be, and then all of a sudden the brain starts releasing too much dopamine.

["Greg Mattingly] 09:10:23
We know the synapse gets flooded with dopamine, that causes hallucinations, agitation, paranoia, misperceptions.

["Greg Mattingly] 09:10:30
And historically the way we've treated this is by blocking dopamine throughout the brain.

["Greg Mattingly] 09:10:34
We're blocking pathways that have too much dopamine, but unfortunately we're also blocking pathways that don't have enough dopamine.

["Greg Mattingly] 09:10:42
So we improve positive symptoms, but we do very little for negative symptoms such as social withdrawal, isolation.

["Greg Mattingly] 09:10:48
We do very little for things like insight, which is why our cities around America are populated by a homeless population that has high levels of schizophrenia because they have very little insight in the fact that they're ill.

["Greg Mattingly] 09:11:00

We know that that target of blocking dopamine does very little to improve cognitive symptoms of schizophrenia and in this digital world you have to be able to process information and keep up.

["Greg Mattingly] 09:11:08
Let's go to our next slide.

["Greg Mattingly] 09:11:12
So when we talk about what are some of the needs for new treatment, I think anyone who lives in America can just walk down the street in a major city and look for the need for new treatments.

["Greg Mattingly] 09:11:22
We see that most patients with schizophrenia wind up in the hospital multiple times. We see that most people with schizophrenia tend to have transient housing.

["Greg Mattingly] 09:11:31
We see that most people with schizophrenia have difficulty maintaining significant relationships and 75% of patients are going to stop their medications within 18 months.

["Greg Mattingly] 09:11:39
Either because of lack of significant improvement or because of significant side effects, weight gain, metabolics, sedation.

["Greg Mattingly] 09:11:48
Let's go on up to our next slide.

["Greg Mattingly] 09:11:53
With Cobenfi, we offer an entirely different approach to treating schizophrenia. No longer are we hitting dopamine receptors either as an antagonist or partial agonists.

["Greg Mattingly] 09:12:04
I've been part of those studies. I've done research going back to a pain, olanzapine, rasperidone.

["Greg Mattingly] 09:12:09
I've been in all of the partial agonist studies. Those compounds all help symptoms. They reduce symptoms by blocking and modulate dopamine receptors, but they're doing very little to affect why the brain is getting ill.

["Greg Mattingly] 09:12:23
Copenfi has no direct effect on dopamine receptors. Instead, we're hitting muskeric receptors that control dopamine presynaptic release.

["Greg Mattingly] 09:12:32
The very mechanism about why the brain is getting ill and why the brain is staying ill. So we're decreasing presynaptic release of dopamine by targeting tube receptors that have high localization in the central nervous system.

["Greg Mattingly] 09:12:45
The m. 1 receptor, which tends to be in top-down areas, the prefrontal cortex, the M.

["Greg Mattingly] 09:12:50
4 receptor, which tends to be in bottom-up receptors. The brain stem, the associative stratum, all to modulate and bring back dopamine release to a more normal level.

["Greg Mattingly] 09:13:00
If we go to our next slide.

["Greg Mattingly] 09:13:04
Let's talk about the clinical trial design. And I think this is one of the reasons why Cobinfi is an ideal medicine to start in a hospital setting.

["Greg Mattingly] 09:13:13
If we take a look at Kobenfi, we start with a lower dose, mainly that get used to GI side effects.

["Greg Mattingly] 09:13:19
We do that for 2 days. And then after 3 days.

[Catherine Bernstein] 09:13:20
3. Meeting.

["Greg Mattingly] 09:13:23
After 3 days we go to the 100 milligram dose. The 100 milligram dose is a therapeutic dose and by the end of a week we can go to 125 milligram BID dose which is the maximum dose.

["Greg Mattingly] 09:13:34
We know the average hospitalization for schizophrenia last between somewhere between 7 to 14 days. So that gives us time to get this met.

["Greg Mattingly] 09:13:42
It started and get to optimal dose. Let's go to our next slide, please.

["Greg Mattingly] 09:13:49
What did we see? We saw significant symptomatic improvement. Dramatic symptomatic improvement across all 3 trials with Kobenfee with no negative trials.

["Greg Mattingly] 09:13:58
Let's go to our next slide.

["Greg Mattingly] 09:14:02
If we take a look at positive symptoms, hallucination, agitation, paranoia, we see some improvement.

["Greg Mattingly] 09:14:08
If we go to our next slide.

["Greg Mattingly] 09:14:13
Taking a look at safety. Here's where we really see the medicine stand apart not only we see high significant improvement We see safety where we're not seeing weight gain, metabolic issues, and other side effects.

["Greg Mattingly] 09:14:23
Next slide.

["Greg Mattingly] 09:14:27
Negative symptoms also improve significantly in 2 of the 3 trials in numerically and 3 out of 3 trials with Cobenfee and 3 out of 3 trials with Cobenfi, a very hard target when it comes to schizophrenia treatment.

["Greg Mattingly] 09:14:41
Side effect profile what we see here is the side effects are those related to the muskrinic system, primarily GI in origin.

["Greg Mattingly] 09:14:50
If we go to the next slide.

["Greg Mattingly] 09:14:54
When we take a look at long-term data, we did long-term study. I was a part of this study looking at long-term benefit, long-term improvement.

["Greg Mattingly] 09:15:02
Let's take a look at the next slide.

["Greg Mattingly] 09:15:07
We see with long-term improvement we see reduction in overall global severity of illness. Next slide.

["Greg Mattingly] 09:15:17
This is where we're going to talk about some of our new data. Let's take what?

[Catherine Bernstein] 09:15:19
Have 1Â min.

["Greg Mattingly] 09:15:21
Let's take a look at long-term outcomes for patients in a comparison in the year before and the year after Coben fee.

["Greg Mattingly] 09:15:28
Go to the next slide.

["Greg Mattingly] 09:15:32
In this study, we found that people on Cobenphy in the year after they started it had very good compliance, something that's been very difficult with schizophrenia.

["Greg Mattingly] 09:15:41
The majority of people stayed with the medicine over time. And I think even more importantly, we saw a reduction in the need for other psychiatric medicines.

["Greg Mattingly] 09:15:50
A 22% reduction in use of long acting injectable medicines, a 26% reduction in other antipsychotics, a 13% reduction in mood stabilizers and a 16% reduction in anticolonergics in this real-world outpatient setting with one year of COBEN fee.

["Greg Mattingly] 09:16:05
Next slide.

["Greg Mattingly] 09:16:08
That leads us to a network meta-analysis of 58 studies. They were all were done over 4 to 6 weeks in inpatient settings with various psychotics so we could take a look at how does

[Catherine Bernstein] 09:16:19
Can you hear me? Has it spied?

[Drew Kasper] 09:16:26
Sorry to bring things to. An abrupt ending. If you wanted to just finish your sentence here before we move on to the QA.

["Greg Mattingly] 09:16:35
Yes, I would just say in this network meta-analysis we found that Cobenfi had significant better improvement in reduction in symptoms and significant better improvement in weight gain as compared to traditional medicines, including novel antipsychotics and the partial agonists.

[Drew Kasper] 09:16:54

Thank you for your presentation. And just as a reminder to all presenters, we do keep it tightly to 10Â min just to be equitable across the board.

[Drew Kasper] 09:17:04
So again, thanks for your presentation. And as a reminder for all attendees, you may submit your questions using the Q&A feature at the bottom of the screen.

[Drew Kasper] 09:17:13
And, the raise hand feature is the other option. If you just raise your hand in zoom, we will enable you to unmute yourself and then you can ask the question verbally.

[Drew Kasper] 09:17:25
Those who are dialed in by telephone. You'll need to email your question to the CMS New Tech or in-tap email box, which again is ntap@cms.hhsgov.

[Drew Kasper] 09:17:39
Just wanted to give that reminder in case any of you missed that at the intro. Are there any questions now from the public?

[Drew Kasper] 09:17:57
You don't have any questions coming in through the Q&A?

[Drew Kasper] 09:18:11
I don't see any raised hands from attendees.

[Drew Kasper] 09:18:19
Or from panelists. Okay, and in the QA we now have A question.

[Drew Kasper] 09:18:29
Do you have the reimbursement for the new codes of C, 16 0 7? And 0 9 0 8 t.

["Greg Mattingly] 09:18:41
I do not have any reimbursement codes here with me today, no.

[Drew Kasper] 09:18:48
That question was from Tracey Gatiris. If there is.

[Drew Kasper] 09:18:57
Any secondary layer you wanna ask, feel free to enter another question into the Q&A. Thanks.

[Drew Kasper] 09:19:18
And there are no other questions coming into the QA yet.

[Adina Hersko] 09:19:24
Hello.

[Drew Kasper] 09:19:28
You don't have raised hands.

[Adina Hersko] 09:19:31
Hi have a question, Drew.

[Drew Kasper] 09:19:31
And have a question. Go ahead, Edina.

[Adina Hersko] 09:19:35
Hi Greg, thanks for your presentation. Just a question on what you mentioned previously about Coventeen not being an antipsychotic.

[Adina Hersko] 09:19:44
Can you talk a little bit more about that? I did notice, some communications from FDA where it was referred to as an antipsychotic.

[Adina Hersko] 09:19:53
So just looking to clarify.

["Greg Mattingly] 09:19:53
Yeah, I mean, it's a great question. So the FDA in their package label did not label his name as psychotic.

["Greg Mattingly] 09:20:00
So you don't see it anywhere in the FDA label as a nanoscotic and nowhere do they mention the boxed warnings about being an anti psychotic.

["Greg Mattingly] 09:20:06
I think that what represented 2 things. Once again, first, st certainly a novel mechanism, a very different safety profile, whereas we saw and they met analysis, lower levels of weight gain, lower levels of metabolic issues and a very low level of any type of movement disorder.

["Greg Mattingly] 09:20:21
And I think once again, just an entirely different approach to modulating schizophrenia symptoms. We're not hitting dopamine receptors.

["Greg Mattingly] 09:20:28
We're changing dopamine release. So I think this was kind of historic by the FDA to break away from every other treatment for schizophrenia in the package insert has been called and anesthetic.

[Adina Hersko] 09:20:37
Welcome.

["Greg Mattingly] 09:20:38
And has carried those boxed warnings that come with being labeled a nano psychotic.

[Adina Hersko] 09:20:43
Thank you. Yeah, in FDA's press releases, it does call it an anti-psychotics.

[Adina Hersko] 09:20:49
Just wondering about that discrepancy.

["Greg Mattingly] 09:20:49
Yeah, I think because it's for schizophrenia but in the package insert it's not called an antipsychotic.

["Greg Mattingly] 09:20:55
So if you look at the label, nowhere in it does it mention it, is nano psychotic.

[Adina Hersko] 09:21:01
Thank you.

[Drew Kasper] 09:21:09

Do you have any other questions from CMS?

[Drew Kasper] 09:21:26
Let's take a last call from CMS for the public if questions. Have come up since the initial solicitation.

[Adina Hersko] 09:21:37
You have a question in the Q&A.

[Adina Hersko] 09:21:43
Because how quickly did the drug take effect?

[Drew Kasper] 09:21:44
Okay.

["Greg Mattingly] 09:21:47
Yeah, so these were inpatient trials and within one to 2 weeks we saw it improve symptoms significantly.

[Drew Kasper] 09:22:00
Great. Thank you. Sophia, you have a hand up. Do you have a question?

[Sophia Chan] 09:22:06
Yeah, thank you so much, Greg, for the presentation. You mentioned about compliance and that there was excellent compliance.

[Sophia Chan] 09:22:17
Across the patient population for the drug. I'm wondering. If part of the clinical trial. Include case management that follow up with individual patients and sure they have access and sure.

[Sophia Chan] 09:22:32
They use a drug according to the right regimen

["Greg Mattingly] 09:22:38
That, yeah, that, no, that's an excellent question. So the study that I talked about, which was a real world open level study, it's a real-world open level study, it's kind of a mirror image study that I talked about, which was a real-world open level study.

[Sophia Chan] 09:22:38
Or

["Greg Mattingly] 09:22:48
It's kind of a mirror image study of the year before Kobenfee and the year after Gobenfi looking at compliance levels.

["Greg Mattingly] 09:22:52
It did find very good compliance. You know, typically within a year of starting a medicine, 75% have stopped.

["Greg Mattingly] 09:22:57
In this case, we saw that it was something like 79% were still on their medicine. But they did have some wrap around support services.

["Greg Mattingly] 09:23:03
You could call in and ask a nurse for questions about your medicine. If I forget it in the morning, can I still go ahead and take it in the evening?

["Greg Mattingly] 09:23:11

Those types of things. So they do have a wrap around support system trying to improve compliance. And I think it also, you know, people vote with their feet.

["Greg Mattingly] 09:23:17
People vote with their beat based on how do I feel efficacy. Do I feel like I'm feeling better?

["Greg Mattingly] 09:23:23
Also, how do I feel as far as side effects? Am I gaining weight? Am I having movement disorders?

["Greg Mattingly] 09:23:28
Am I sleepy all the time? Benefits your rights, some of the wraparound services, the improvement and symptoms that we saw, but then also not having the side effects that caused many patients to stop their medicine, waking, sedation, metabolic issues, things of that nature.

[Sophia Chan] 09:23:43
Do you have some at least some qualitative? Evidence that because of the sense of efficacy, patients are willing to be compliant even without any nudging.

["Greg Mattingly] 09:23:59
They, they do. So, if you look at these studies, not everybody was in those wrap around services, they could opt in or opt-out.

[Sophia Chan] 09:24:05
Okay.

["Greg Mattingly] 09:24:06
And this, not everybody was in those wrap around services, they could opt in or opt out. And this air image study wasn't looking at just people who were in the opt-in group.

[Sophia Chan] 09:24:11
I see. Thank you.

["Greg Mattingly] 09:24:12
Welcome. That's a great question.

["Greg Mattingly] 09:24:18
I'll follow up to your question. One of the reasons I'm passionate about this whole project and this topic.

["Greg Mattingly] 09:24:24
Is my family member, you know, for a decade or more, was taken from our family, was too ill.

["Greg Mattingly] 09:24:29
To get care and realize they needed care. So when you look at these novel treatments that make a difference, that's some of the questions that I tend to ask myself, so thank you.

[Drew Kasper] 09:24:45
We'll take a last call for questions.

[Drew Kasper] 09:24:55
Okay. Thank you very much for your presentation.

["Greg Mattingly] 09:24:59
Thank you to everyone for your, evaluation. I appreciate you.

[Drew Kasper] 09:25:06
Okay, and so we will now hear from presenters for the rapidly. Technology, you can go ahead and unmute yourself and activate your camera now.

[Drew Kasper] 09:25:19
Thanks.

[Jason Katz] 09:25:20
Great. I hope you can hear me. I hope everyone can hear me. My name is Jason Cats.

[Jason Katz] 09:25:28
I'm at Advanced Heart failure transplant and critical care cardiologist and a professor of medicine.

[Jason Katz] 09:25:34
And then why you Grossman School of Medicine. I also serve as the associate chief of cardiology at Bellevue Hospital.

[Jason Katz] 09:25:42
I am really privileged and pleased to have the opportunity to discuss with you today. Our and tap application for wrap a book or landial law for the short-term reduction of ventricular rates in adult patients with super ventricular tacic cardias.

[Jason Katz] 09:25:58
Including the very common atral arithmetic as atrophibrillation and atro flutter.

[Jason Katz] 09:26:05
Next slide, please.

[Jason Katz] 09:26:08
Here you can see my disclosures. Next slide.

[Jason Katz] 09:26:14
Well, as an advanced hard failure and transplant cardiologist and in particular as a critical care cardiologist operating in a numerous intensive care unit settings.

[Jason Katz] 09:26:25
I know very well and I'm sure you do as well the super ventricular tech cardias are really common.

[Jason Katz] 09:26:31
They're very commonly encountered in the care of heterogeneous ill patients across the continuum.

[Jason Katz] 09:26:36
With Hral fibrillation in particular being the most common arrhythmia scene. And these sick patient populations.

[Jason Katz] 09:26:44
And although to be sure, atral fibrillation can be seen in a myriad of patients.

[Jason Katz] 09:26:50
You know, this shows some of the common clinical settings in which we, see these superbent chicletecha cardias in particular, post operatively after cardiac surgery is a common setting for atral fibrillation.

[Jason Katz] 09:27:04
Among patients with chronic failure, those presenting with complications of chronic heart failure with acute on chronic heart failure.

[Jason Katz] 09:27:11

And then those hospitalized with critical illnesses including sepsis. Next slide, please.

[Jason Katz] 09:27:20
Can consensus guidelines currently recommend a variety of pharmacotherapies or cardio version to achieve either rate control or rhythm control for patients who have acute atral fibrillation.

[Jason Katz] 09:27:33
But unfortunately, the currently available tools, whether they be pharmacologic or electrical, may be contraindicated among most of the typical patients we see in our heterogeneous ICU settings.

[Jason Katz] 09:27:46
Particularly those who have concomitant hypotension. Or impaired underlying cardiac function. And as an example, looking at the 2023 atral fibrillation consensus guidelines.

[Jason Katz] 09:27:59
There was a class one recommendation for beta blockers or calcium channel blockers, but only those who have relatively preserved.

[Jason Katz] 09:28:07
Party at contract tile function with ejection fractions of at least 40%. And due to their negative ionotropic properties.

[Jason Katz] 09:28:15
And they're untoward impact on vastular tone and the progression of hypotension beta blockers like Ezmol.

[Jason Katz] 09:28:24
Or calcium channel blockers like Deltai ism may be contraindicated. Or even harmful in most of the patients we see in our ICUs.

[Jason Katz] 09:28:35
For those with an ejection fraction less than 40%, the only potentially available agents considered somewhat safe would be amioderone or dejoxin.

[Jason Katz] 09:28:44
And, however, however is not FDA approved for the acute treatment of atral fibrillation.

[Jason Katz] 09:28:50
It also has a number of well known potential toxicities. And it's classically a rhythm controlled drug so it may lead to cardio virgin even when cardio version is not the goal or perhaps contraindicated which is especially troublesome.

[Jason Katz] 09:29:05
And patients who have a high risk for cardioambolic phenomena and subsequent stroke and when that has not adequately been addressed.

[Jason Katz] 09:29:12
Rhythm control strategies may not be ideal. Did Jockson is the other agent, but a very weak agent.

[Jason Katz] 09:29:19
We've known this for a long time. Data would suggest that and practice within the ICU setting, in the setting of high ageneric states.

[Jason Katz] 09:29:26
Leads us to conclude that the Jackson does a relatively poor job of rate control, atrol fibrillation patients with critical illness.

[Jason Katz] 09:29:35
And it also requires dose adjustments in patients with renal dysfunction. And has a very long half-life.

[Jason Katz] 09:29:41
Next slide. As a result, there exist a gap. There is a gap in available and effective rate control therapies for these high risk and common patient subgroups.

[Jason Katz] 09:29:54
And rapidly for the 1st time has the potential to really address this gap. Then as a result received FDA approval in November of 2024.

[Jason Katz] 09:30:03
Or the short-term reduction of ventricular rates in adults with SDT, including atral fibrillation and atral flutter.

[Jason Katz] 09:30:11
On this slide, you can see some of the clinical evidence underscoring the real potential value of rapidly in this particular therapeutic space that of the ICU.

[Jason Katz] 09:30:21
Additionally, wrap a blix rapid onset of action. I tradeability and ultra short half-life allows for very precise control.

[Jason Katz] 09:30:29
And efficacy evaluation. And the high risk very rapidly evolving ICU environment, an environment in which patients are quite susceptible to adverse events that associate with any pharmacotherapies, which again are often magnetized, magnified given their critically ill state.

[Jason Katz] 09:30:47
Next slide, please.

[Jason Katz] 09:30:51
On this slide, you'll see information about wrap ups, pharmacokinetics and mechanism of action.

[Jason Katz] 09:30:57
As mentioned, Rapa Blick offers a heart rate control option. For patients with acute atral fibrillation and additional comorbidities, including the very common comorbidity of chronic heart failure and dorenal impairment.

[Jason Katz] 09:31:11
It's very low beta to blocking action with a ratio of beta one activity to beta 2 blocking activity of 255 to one.

[Jason Katz] 09:31:21
Provides very effective heartbreak control with minimal effects. On systemic vascular tone and resistance. Blood pressure or bronchial tone.

[Jason Katz] 09:31:30
And so this enables this use in patients that are susceptible. To cardiac decomposition and those in particular who have impaired cardiac contractility.

[Jason Katz] 09:31:41
In fact, as you can see in table one here, wrap-up book is the only beta blocker now with an FDA recognized dosing regimen that is specific to these common patients with impaired underlying cardiac function.

[Jason Katz] 09:31:53
Next slide, please.

[Jason Katz] 09:31:57
Rapa Blix Ultra Beta one selected mechanism action permits treatment of different high risk populations that have historically not been well managed by other beta blockers in the ICU.

[Jason Katz] 09:32:09
Next slide, please.

[Jason Katz] 09:32:12
On this slide you'll see a summary of a study actually published this year. This was a prospective randomized open label study comparing landial law.

[Jason Katz] 09:32:21
With Ezmol and post operative ICU patients with underlying cardiac dysfunction after vascular surgery.

[Jason Katz] 09:32:28
And here the investigators found that land deal all produced a more rapid and more substantial reduction in heart rate compared to esmolo.

[Catherine Bernstein] 09:32:33
3Â min.

[Jason Katz] 09:32:35
Importantly, it also achieved heart rate control without leading to hypbo tension. As Malol, as you can see on the other hand, was associated with much higher rates of hypotension.

[Jason Katz] 09:32:46
Next slide, please.

[Jason Katz] 09:32:48
In this study by Kafaro and colleagues leveraging a systematic review and meta-analysis.

[Jason Katz] 09:32:54
Of landial all compared to sailing control and analysis including In this case, 9 randomized control trials.

[Jason Katz] 09:33:01
The author's found that rapidly reduced the incidence of atral fibrillation and importantly hospital length of stay.

[Jason Katz] 09:33:07
For the primary endpoint they found that the landala group had a significant reduction in post-operative atral fibrillation compared to control.

[Jason Katz] 09:33:14
As it depicted in the forwards plot you can see here. And for the secondary outcome of length of stay landial all again resulted in a significant reduction in overall hospital length of stay.

[Jason Katz] 09:33:24
From 15 to 12 days. Next slide please.

[Jason Katz] 09:33:29
And finally, here we show a study by C and others from 2023. This a retrospective observational study.

[Jason Katz] 09:33:35
Comparing Landala and Esmol over a six-year period in 438 patients.

[Jason Katz] 09:33:40
For this particular study heart rate control was the primary outcome, all secondary outcomes included specific hemodynamic variables, hospital and ICU length of stay.

[Jason Katz] 09:33:50
But the primary endpoint in a propensity score matched analysis, the authors observed and reported that Landia law provided superior heart rate control.

[Jason Katz] 09:33:59
And critically ill patients with tacacardia compared to esmolo. With regards to the secondary outcomes.

[Jason Katz] 09:34:04
The study found that compared to as small again, land alone, a lot of greater proportion of patients. To remain unstable vasopressor dosages without the need for escalating these phasoactive medications.

[Jason Katz] 09:34:18
And this occurred in the 1st 24Â h. It was also associated with a significant reduction in hospital length of stay.

[Jason Katz] 09:34:25
And post I see a mortality. Next slide, please.

[Jason Katz] 09:34:30
So in conclusion, I hope I've effectively summarized some of the key evidence and there's of course more.

[Catherine Bernstein] 09:34:34
1Â min remaining.

[Jason Katz] 09:34:35
And outcomes favoring landalal over other therapies in the care of critically ill patients, particularly those with no viable alternative.

[Jason Katz] 09:34:43
Including patients with advanced real dysfunction and a paired LV dysfunction. Landia has been available in Japan and the European Union for a number of years where clinicians and patients have been able to use it to fill this important treatment gap to control heart rate.

[Jason Katz] 09:34:58
Thanks to its ultra selected beta one blockade rapidly can combine speed control efficacy. Importantly safety to enhance clinical care over other standard of care treatments.

[Jason Katz] 09:35:11
Thank you so much for your time. And I'm I would love to take any questions. That you might have.

[Drew Kasper] 09:35:22
Great. Thanks for your presentation. Are there any questions from the public?

[Drew Kasper] 09:35:30
So you can ask your questions via the QA or the raised hand feature. In your Zoom ribbon.

[Drew Kasper] 09:35:42
Don't have any questions in the QA yet.

[Drew Kasper] 09:35:52
How don't have raised hands at this time. I'm going to check the intat mailbox just in case.

[Drew Kasper] 09:36:00
Anyone has joined just by phone they would have to send their questions to the and tap mailbox.

[Drew Kasper] 09:36:09
We do not have questions there. Okay, so we'll open it up to questions from CMS.

[Drew Kasper] 09:36:29
As I mentioned early on with the RFI process being more prolific. At this point in the process that has been in the past, we've got that parallel process going on asking a lot of SCI questions.

[Drew Kasper] 09:36:43
But we'll take a last call here from the public or CMS. Any questions? I'm wrap a blick.

[Drew Kasper] 09:36:56
Okay, there are no open questions in the Q&A.

[Drew Kasper] 09:37:02
There are no Raise hands.

[Drew Kasper] 09:37:08
And no new questions in the entire mailbox. Alright then. Thanks again for your presentation very much.

[Jason Katz] 09:37:19
Thanks so much, and team.

[Drew Kasper] 09:37:23
We will now hear from presenters or gamma fans. You may now unmute and introduce yourself.

[Drew Kasper] 09:37:32
And activate your camera if you wish.

[Lynes Torres Cartularo] 09:37:35
Great. Hello, my name is Lenez Cartelero and I'm the Associate Medical Director for the Immunology Franchise here at Soby North America.

[Lynes Torres Cartularo] 09:37:46
On behalf of my colleagues at Sobe, thank you for inviting us to describe how Gamma Fant and anti-interferring gamma monoclonal antibody provides substantial clinical improvement for patients with HMAS instills disease.

[Lynes Torres Cartularo] 09:38:02
Next slide, please.

[Lynes Torres Cartularo] 09:38:05
Let's talk a little bit about HH. In the fag acidic lymphohistocytosis, macrophage activation syndrome, Quite a mouthful of a term here, but it's it's really a broad term used to describe a systemic hyperinflammatory syndrome that can occur as a complication of rheumatological conditions of which

[Lynes Torres Cartularo] 09:38:27
still disease is actually the most common. So for the purposes of this presentation, the term stills the disease encompasses both adult onset stills disease and juvenile atopathic arthritis, both of which are rare themselves.

[Lynes Torres Cartularo] 09:38:43
Prevalence estimates suggest that up to a quarter of still disease patients develop HHH. MS.

[Lynes Torres Cartularo] 09:38:51
And honestly with moreality rates as high as 56% HHH S. Is one of the most serious and potentially life-threatening complications a still disease patient could face.

[Lynes Torres Cartularo] 09:39:04
Standard care relies heavily on high dose steroid regimens, but only 14% of patients are successfully managed on steroids.

[Lynes Torres Cartularo] 09:39:13
Which really illustrates a high on met need. The FDA approval of and the POW MAP for HHMS and SILIL disease earlier this year brought the 1st approved therapy for these patients is and it's the only treatment option that targets the the recognized pathogenic over production.

[Lynes Torres Cartularo] 09:39:32
Of interfering gamma. Next slide, please.

[Lynes Torres Cartularo] 09:39:37
So where does interfering gamma fit in the pathology of this syndrome? In HH.

[Lynes Torres Cartularo] 09:39:45
HMAS access interfering gamma stimulates macrophages to secrete a bolus of inflammatory cytokines triggering an uncontrolled feedback loop that leads then to systemic hyperinflation.

[Lynes Torres Cartularo] 09:39:58
Map binds both free and receptor bound interfering gamma and was FDA approved, as I mentioned earlier, in June of this year for the treatment of HHM.

[Lynes Torres Cartularo] 09:40:11
And was FDA approved, as I've mentioned earlier, in June of this year for the treatment of HHMAS in known or within an adequate response for intolerance to corticoids or with recurrent.

[Lynes Torres Cartularo] 09:40:18
Next slide, please.

[Lynes Torres Cartularo] 09:40:21
The approval of and the PM. Was largely based on the pooled outcomes of 2 open label single arm studies.

[Lynes Torres Cartularo] 09:40:30
These studies enrolled HH. MS instills patients who had had an inadequate response despite being treated for 3 or more days with high dose steroids.

[Lynes Torres Cartularo] 09:40:41
The design of both studies centered on a 4 week interventional phase during which enrolled patients received an initial 6 meg per cake IV infusion of Empty Map, followed by 3 meg per cake infusions roughly every 3 days.

[Lynes Torres Cartularo] 09:40:56
Patients were monitored through week 8 when they were assessed for response per the primary endpoint and that's what's depicted in the wheel on the right hand side of slide.

[Lynes Torres Cartularo] 09:41:05
In the absence of prior HH. MS and S. Disease clinical trials from which to base.

[Lynes Torres Cartularo] 09:41:12

A clinical remission, a novel yet rigorous definition of complete response was developed in close consultation with HHMS experts.

[Lynes Torres Cartularo] 09:41:20
For a patient to achieve complete response or CR, they must have achieved normalization or near normalization of 7 disease relevant laboratory parameters and have achieved a low MAS clinical activity score as assessed by the investigator.

[Lynes Torres Cartularo] 09:41:37
Next slide.

[Lynes Torres Cartularo] 09:41:40
A total of 39 patients enrolled in these 2 international clinical studies. And this end may seem small, but it's simply reflective of the rarity of H.

[Lynes Torres Cartularo] 09:41:54
H. Just under a quarter of the patients were 17 years of age older. And these patients started the study obviously receiving steroids and on average that was about 9.7 mix per per day.

[Lynes Torres Cartularo] 09:42:09
35% of these patients grappled with a history of MS and many were deemed as having a high burden of MS clinical activity, averaging 6.5 on a VAS scale.

[Lynes Torres Cartularo] 09:42:21
Next slide, please.

[Lynes Torres Cartularo] 09:42:25
So, 21 out of the 39 patients were able to achieve a complete response. At week 8, which meant they were able to fulfill.

[Lynes Torres Cartularo] 09:42:34
All 8 laboratory and clinical components of the primary and point that I described earlier. Next slide, please.

[Lynes Torres Cartularo] 09:42:44
There are a number of secondary. And points that help. Further illustrate the the substantial clinical improvement granted by gamma fan treatment and I'll touch on just a few of them today.

[Lynes Torres Cartularo] 09:42:56
In addition to the 21 patients that achieved our rigorous complete response criteria, they were an additional 8 patients that achieved a partial response.

[Lynes Torres Cartularo] 09:43:05
What amounts to a 76% overall response rate? It's also worth building that overall response. Was observed as early as day 5, you know, just speaking to and the Pine Maps rapid onset.

[Lynes Torres Cartularo] 09:43:19
Because much of the the the recognition and management of HHH HMS in clinical practice is based more so on the clinical presentation.

[Lynes Torres Cartularo] 09:43:31
The treating physicians assessment of response is very insightful. As such, 82% of patients were deemed by the investigator as achieving clinical MAS resolution, meaning they reached a VAS score of one or 0 at week 8.

[Lynes Torres Cartularo] 09:43:50
Next slide, please.

[Lynes Torres Cartularo] 09:43:53
An important aspect of an appointment treatment efficacy is the potential to taper steroid reliance, mitigating their well-documented, well described side effects.

[Lynes Torres Cartularo] 09:44:07
Treatment with M the pie map enabled. Rapid taper of steroids. With a 70% reduction in mean daily dose by week 2.

[Lynes Torres Cartularo] 09:44:15
By week 8, the mean daily dose dropped by 92%. To 0 point 8 makes per per day.

[Lynes Torres Cartularo] 09:44:22
Despite their being HL. GMAS mortality rates as high as 56% in the medical literature.

[Lynes Torres Cartularo] 09:44:28
94.9% of the patients treated with ammipine that were alive at week 8. Next slide, please.

[Lynes Torres Cartularo] 09:44:37
Adverse events were reported in 36 patients, the majority of which of which were mild. Infections were reported in 22 patients.

[Lynes Torres Cartularo] 09:44:47
And these infections were predominantly of viral origin and resolved spontaneously or with standard treatment.

[Lynes Torres Cartularo] 09:44:53
Serious adverse events were reported in 12 patients. The most common of which was pneumonia.

[Lynes Torres Cartularo] 09:45:00
And the Pimab was with was withdrawn in one patient who developed pneumonia.

[Catherine Bernstein] 09:45:01
3Â min remaining.

[Lynes Torres Cartularo] 09:45:08
And it was reported that the patient recovered from the case of pneumonia after 14 days, thankfully.

[Lynes Torres Cartularo] 09:45:14
Fatal adverse events occurred in 2 patients. But overall, in the time I've demonstrated an acceptable safety profile in line with its established safety profile.

[Lynes Torres Cartularo] 09:45:24
And was well tolerated. Next slide, please. So to summarize, HHMAS is one of the most serious and potentially life-threatening complications.

[Lynes Torres Cartularo] 09:45:38
A still disease patient could face. It's driven by an excess of interfering gamma that subsequently triggers systemic hyperinflation.

[Lynes Torres Cartularo] 09:45:48
And in practice, this hyperinflammation is typically managed with hydro steroids. But most patients do not achieve an adequate response.

[Lynes Torres Cartularo] 09:45:57
That's in 2 pooled clinical trials of patients. Who had an inadequate response to Sarah's just over half of patients who

were treated with them the Pali Map and anti-interfering gamma monoclonal antibody achieve a complete response that weekend.

[Lynes Torres Cartularo] 09:46:12
82.1% were deemed by the investigator as achieving clinical MES resolution. And the Pine Mab enabled a rapid and meaningful reduction in steroid dosing in these patients.

[Lynes Torres Cartularo] 09:46:25
And 94.9% of patients treated with Mapimat were alive at week 8. And the Pine Map was well tolerated with viral infection as the most common AE.

[Lynes Torres Cartularo] 09:46:35
And with that, I'd like to thank you for your time and I'll take questions.

[Drew Kasper] 09:46:45
Thank you for your presentation.

[Drew Kasper] 09:46:49
Where are the folks that have joined? After the initial. How's keeping? I'm just going to periodically restate for attendees.

[Drew Kasper] 09:47:00
Public attendees, you can submit your questions using the Q&A feature at the bottom of the screen or you can use the raise hand feature in zoom and we will enable you to unmute yourself and ask your questions verbally.

[Drew Kasper] 09:47:13
Those who are dialed in by telephone, you'd need to email your question to the CMS new tech email box, which is ntap@cms.hs.

[Drew Kasper] 09:47:26
That said, are there any questions from the public?

[Drew Kasper] 09:47:38
Hey, we have no open questions in the Q&A yet.

[Drew Kasper] 09:47:48
We don't have any raised hands. So we'll move on to open it up to C and M have questions.

[Drew Kasper] 09:48:05
Okay, and we will take another call from anyone. Or CMS

[Drew Kasper] 09:48:22
There are no raised hands.

[Drew Kasper] 09:48:27
No new questions in the Q&A.

[Drew Kasper] 09:48:31
And no new questions in the and tap mailbox. Okay. So with that, again, thank you very much for your presentation.

[Lynes Torres Cartularo] 09:48:41
Thank you. Thank you for your time.

[Drew Kasper] 09:48:44

Okay, and now we'll move into a break next.

[Drew Kasper] 09:48:50
And we'll be back at 1015. Kicking it back off with Narsup the Map.

[Drew Kasper] 09:48:56
See you all at 1015. Thanks.

[Drew Kasper] 10:15:18
Okay, welcome back everyone.

[Drew Kasper] 10:15:22
Hmm.

[Drew Kasper] 10:15:26
Right, so we will now hear from. Presenters for an diplomat. You may now unmute and introduce yourself.

["Miguel-Angel Perales] 10:15:37
Good morning, my name is Miguel Palace. I'm the chief of the Adult Bomo Transport Service at Memorial S.

["Miguel-Angel Perales] 10:15:42
Kettering Cancer Center in New York. Thank you for giving me the opportunity to present this morning.

["Miguel-Angel Perales] 10:15:47
But I'm going to be discussing today is the use of no supplement for the treatment of hematopiotic stem cell transplant associated apathy or Now, the next slide, please.

["Miguel-Angel Perales] 10:16:02
These are my disclosures. Next slide.

["Miguel-Angel Perales] 10:16:07
So what I hope to show you this morning is the benefit of NASA. This is a drug that offers substantial pinnacle benefit in patients with TTMA.

["Miguel-Angel Perales] 10:16:18
For whom there's currently no FDA approved treatment. TTM is a life-threatening complication of transplant.

["Miguel-Angel Perales] 10:16:26
It's marked by endosystem injury, complement activations from the cyberpenia, micro vascular fumbai and hemolidic anemia.

["Miguel-Angel Perales] 10:16:33
And there is currently no FDA approved treatment for TTMA. That's a. Mab is a antibody which is a 1st in class selective inhibitor of mass 2, which is the affected enzyme of the electing pathway of complement.

["Miguel-Angel Perales] 10:16:48
And importantly, what I'm going to share with you today is data from the clinical program at the supplement which consists of a pivotal trial as well as an expanded access program.

["Miguel-Angel Perales] 10:16:58
And what I will show you is that the complete response in laboratory markers and importantly also an organism function was demonstrated in 63% of adult patients with high risk TTMA.

["Miguel-Angel Perales] 10:17:11

We also observed the 3 to fourfold improvement and survival compared to well-matched external control.

["Miguel-Angel Perales] 10:17:17
And the one year overall survivor, the Costa del and pediatric patients was 54% in treatment naive patients and over 50% in patients who had failed other treatments or discontinued other treatments typically used in these patients.

["Miguel-Angel Perales] 10:17:33
That block complement and also the drug called the febrile. And in over 700 patients.

["Miguel-Angel Perales] 10:17:41
Who have been treated across multiple indications. There have been no safety signals. And so I think given this evidence.

["Miguel-Angel Perales] 10:17:51
And and the hopeful approval of this drug we believe that NTAP will enable a doubt TTMA patients the need of treatment to access the benefits.

["Miguel-Angel Perales] 10:18:00
Next slide. So transplant is a potential curative patients with patients with either high risk or advanced malignancies and TTMA is often a lethal complication of that treatment unfortunately.

["Miguel-Angel Perales] 10:18:14
It results from microvasca and the seed of dysfunction and complement activation, which results in endocilial injury and activation of the lectin pathway of complement.

["Miguel-Angel Perales] 10:18:23
And this leads to information that's from us for motion formation resulting in organ dysfunctional failure.

["Miguel-Angel Perales] 10:18:29
A number of etiological factors have been identified. Including patient factors as well as factors related to the treatments, the use of mimoblady regiments, carcinogeno inhibitors for GDHT prophylaxis or MT.

["Miguel-Angel Perales] 10:18:45
Inhibitors or GDP profiles. As well as 1st transplant complications such as infections and graphs as host disease.

["Miguel-Angel Perales] 10:18:52
And there were currently no treatments approved by the FTA or other regulatory bodies for TTMA.

["Miguel-Angel Perales] 10:18:58
Next slide.

["Miguel-Angel Perales] 10:19:01
So in addition to the complications that we see in terms of platelets and anaemia as well as the renal dysfunction.

["Miguel-Angel Perales] 10:19:11
This is really a multi organ. Disorder which you can include, complications of the g, the lungs, the CNS and skin.

["Miguel-Angel Perales] 10:19:19
And so that has a significant burden in terms of mobility and mortality leads to extended hospitalizations as well as ICU, states for patients.

["Miguel-Angel Perales] 10:19:28
And Next slide.

["Miguel-Angel Perales] 10:19:32
And we estimate that about 1,100 patients will be potentially at risk for TM, TTMA and fiscal year, 2,027.

["Miguel-Angel Perales] 10:19:43
And this is the right from an estimated incidence of TTMA and transport patients of about 39%.

["Miguel-Angel Perales] 10:19:50
We currently do, 23,000 transplants in the US and annual basis, of which a little bit less than half about 10,000 now allergenic transplants.

["Miguel-Angel Perales] 10:20:00
And 20, 2,800 of those are performed in patients over the age of 65. So given the 39% incidents that yields about 1,100 Medicare eligible beneficiaries who would be addressed for TTMA in fiscal year 2,027.

["Miguel-Angel Perales] 10:20:16
Next slide.

["Miguel-Angel Perales] 10:20:20
So as I mentioned, our supremab is a drug that blocks the mass to enzyme, which is the effector in time of electing pathway.

["Miguel-Angel Perales] 10:20:27
This pathway is activated by indiocedial intravene. And this occurs during transplant and often triggers to ETMA.

["Miguel-Angel Perales] 10:20:35
Now, sub the members of human IGG 4 antibody, it inhibits mass 2, which is the effector enzyme of the lectin pathway as also an activate of the calculation cascade.

["Miguel-Angel Perales] 10:20:46
So you really have this duality of effects which probably explains a large part the benefit of the drug.

["Miguel-Angel Perales] 10:20:51
And importantly, it's designed to also leave the infection fighting classical passway and alternative pathway fully intact.

["Miguel-Angel Perales] 10:21:00
Next slide.

["Miguel-Angel Perales] 10:21:03
Now, the supplement, as I mentioned, is a unique drug in the space for TTMA, but there are a number of other drugs.

["Miguel-Angel Perales] 10:21:11
Which have been used off label. Most of these are inhibitors of complement and are listed here.

["Miguel-Angel Perales] 10:21:19
And the fibrotide which is approved for sinusoidal syndrome, a post transplant has also been used, though the mechanism of action is unclear.

["Miguel-Angel Perales] 10:21:29
And then some people have also tried, retaxed some, although I have not used that in my practice.

["Miguel-Angel Perales] 10:21:34
But importantly, that are currently no FDA approved drugs for this indication. Next slide. So as I mentioned, I'm gonna share with you pinnacle data from 2 populations primarily, the pivotal trial and then the access as well as a comparison with registry data.

["Miguel-Angel Perales] 10:21:54
So this was a pivotal trial. It was published in JCO in 2,022.

["Miguel-Angel Perales] 10:21:59
It was an open label, single on multi-center pivotal trial in which all patients who were treated in BET criteria for high risk TTMA.

["Miguel-Angel Perales] 10:22:08
You can see on the right the key eligibility criteria, patients were over the age of 18, they had a diagnosis of TTMA that was defined by anaemia as well as thrombicyidopina and real dysfunction and no alternative explanation.

["Miguel-Angel Perales] 10:22:25
And we excluded patients from this trial who had exposure to a collusion map, which is a complement inhibitor.

["Miguel-Angel Perales] 10:22:31
As well as other causes potentially. For that presentation the primary endpoint importantly is a co-primist but it looks at both efficacy in terms of improvement of planning count and LDH as well as improvement critical status.

[Catherine Bernstein] 10:22:47
3,

["Miguel-Angel Perales] 10:22:49
And at least one organ of freedom from transfusion and also looked at safety and tolerability. Secondary employees looked at survival.

["Miguel-Angel Perales] 10:22:56
Next slide. And this is the bottom line. We saw a 61% complete response rate in this high risk.

["Miguel-Angel Perales] 10:23:05
A patient population and a 68% 100 day survival. Next slide.

["Miguel-Angel Perales] 10:23:13
In terms of, and safety, there really is no safety concern. No patients discontinued the drug due to adverse events.

["Miguel-Angel Perales] 10:23:22
6 patients died to the trial and these were not attributed to complications of Nasoptera.

["Miguel-Angel Perales] 10:23:25
Next slide.

["Miguel-Angel Perales] 10:23:28
This is the expanded access, program, which was started in 2,017 in 10 countries.

["Miguel-Angel Perales] 10:23:35
And basically it includes data from 2,017 through 2,023. And this is broadly, inclusion criteria, basically patients with a diagnosis of TTMA.

["Miguel-Angel Perales] 10:23:46
Next slide.

["Miguel-Angel Perales] 10:23:50
And what we did is compare this data to a published cohort where we had access to the primary data from a Japanese registry and what we demonstrated on shown on this forest plot is a 3 to four-fold improvement in survival compared to

a well matched control treated with best supportive care.

["Miguel-Angel Perales] 10:24:07
And we did a series of sensitivities analysis to support these findings. Next slide.

["Miguel-Angel Perales] 10:24:16
We also demonstrated greater than a 50% one year overall survival in both pediatric and adult patients with TTMA.

["Miguel-Angel Perales] 10:24:23
And we've looked here. As you can see in this table, one year survival in patients who were treatment naive.

["Miguel-Angel Perales] 10:24:30
You can see the range there. 54% for all patients. And then in the lower part of the table, we looked at patients who had failed or stopped other drugs that have been used and you can see here greater than 50% overall survival.

["Miguel-Angel Perales] 10:24:44
Next slide.

[Catherine Bernstein] 10:24:45
1Â min remaining.

["Miguel-Angel Perales] 10:24:48
So we also serve as threefold improvement and survival with SUP to MAV and the EAP versus the external control treated with best supportive care.

["Miguel-Angel Perales] 10:24:57
Next slide. I think this figure really speaks for itself and patients with high risk TMA with organ dysfunction, not supplements, have significantly improved survival versus the well match control.

["Miguel-Angel Perales] 10:25:12
And they were looking at the one year overall survival between the 2 chords. Next slide.

["Miguel-Angel Perales] 10:25:19
So as I showed you, 3 data sets essentially the pivotal trial with a complete response rate of 61% through the forefold improvement in OS versus the well-matched external control, expanded access program and treatment naive patients a 1-year overall survival at 52% in adults and a salvage survey greater than 50% versus a historical, historical data of less than 20%.

["Miguel-Angel Perales] 10:25:43
And the 3 4th improvement in OSPS is now supplement. When we combine the 2 cohorts versus the well-match control.

["Miguel-Angel Perales] 10:25:53
We see again this 3 to 4, the improvement in overall survival. And the full-fold improvement in OS in patients is open this function.

["Miguel-Angel Perales] 10:26:00
And the drug has been well tolerated across the different patient populations. Next slide. Same conclusion, they'll sub the map of a substantial clinical improvement over existing off label therapies for TTMA.

["Miguel-Angel Perales] 10:26:15
And, the supplement addresses a significant unmet medical need and then tap will enable a doubt TTMA patients in need of treatment, access to Thank you for your attention.

[Drew Kasper] 10:26:29

Thank you for your presentation.

[Drew Kasper] 10:26:32
As a reminder, I know we had some new folks join us as public attendees. All attendees may submit their questions.

[Drew Kasper] 10:26:40
Using the Q&A feature at the bottom of your screen. Or you can use the raise hand feature in Zoom.

[Drew Kasper] 10:26:47
And we will enable you to unmute yourself and ask your questions verbally. If you are only dialed in by telephone, then you'd need to email those questions to us at NTAP at CMS.

[Drew Kasper] 10:27:03
And with that, are there any questions from the public?

[Drew Kasper] 10:27:08
That would include other presenters. Well.

[Drew Kasper] 10:27:15
We don't have any questions in the and tap mailbox. In the Q&A. Does not have any new questions at this time.

[Drew Kasper] 10:27:25
I don't see any raised hands. The public is welcome to continue to ask questions if they arise, but let's open it up now to see MS as well.

[Drew Kasper] 10:27:34
Do we have questions from CMS?

[Drew Kasper] 10:27:53
We'll ask call for any questions from CMS or the public.

[Drew Kasper] 10:28:01
We don't have any raised hands. No, no questions in the Q&A. Or in the internet mailbox.

[Drew Kasper] 10:28:09
Okay, so with that, thank you very much for your presentation.

["Miguel-Angel Perales] 10:28:14
Thank you very much.

[Drew Kasper] 10:28:17
And we will now hear from the presenters for Waskira. You may now unmute.

[Drew Kasper] 10:28:24
Turn your camera on if you wish. And introduce yourself. Thanks.

["Dr. Francesca FERRUA MD] 10:28:30
Good morning. I'm Dr. Francesco Ferwa from Sara Fella Scientific Institute in Milan, Italy.

["Dr. Francesca FERRUA MD] 10:28:36
On behalf of Teleton Foundation, the applicant, today I'm going to present you the clinical efficacy and safety of Oskira or DD.

["Dr. Francesca FERRUA MD] 10:28:45

Totem cell and autonomous a metropolitan stem cell based Nentivirrogen therapy indicated for the treatment of viscottologic syndrome.

["Dr. Francesca FERRUA MD] 10:28:54
Next slide please.

["Dr. Francesca FERRUA MD] 10:28:56
Viscontolic syndrome is a rare x-linked life-threatening import matter of immunity and plateal disorder.

["Dr. Francesca FERRUA MD] 10:29:05
WAS is characterized by chromositopinia and consequent bleeding events, recurrent and severe infections, ex, an increased risk of immunities regulation and malignancies.

["Dr. Francesca FERRUA MD] 10:29:13
Without a curative intervention, the risk to develop disease related complication is lifelong and media survival is poor.

["Dr. Francesca FERRUA MD] 10:29:21
Next slide.

["Dr. Francesca FERRUA MD] 10:29:23
Was is caused by lots of function mutation in the worst gene resulting in reduced or absent was protein expression.

["Dr. Francesca FERRUA MD] 10:29:30
This causes multiple cellular defects in platelets and leukocytes. Next slide.

["Dr. Francesca FERRUA MD] 10:29:37
WASS can be cured with supportive treatments, mainly aimed at preventing or treating disease related complications.

["Dr. Francesca FERRUA MD] 10:29:44
Alternating metropolitan and cell transplantation can be curative but this is ampered by limited donor availability and potential complications such as GVHD, rejection and aluminum complications.

["Dr. Francesca FERRUA MD] 10:29:55
In particular, age above 5 years remain a risk factor for overall survival. Next slide.

["Dr. Francesca FERRUA MD] 10:30:02
Indeed, curative therapeutic approaches for wars offer limited, limited alternatives driving the need for new therapies.

["Dr. Francesca FERRUA MD] 10:30:10
For this reason, exleval antiviral, a metropolitan synthetic in therapy has been extensively studies and alternative treatment options in the past years.

["Dr. Francesca FERRUA MD] 10:30:18
Next slide.

["Dr. Francesca FERRUA MD] 10:30:21
Was Kira or atto BT, D. Genootetem cell, is a gene therapy product, composed of autologous C.

["Dr. Francesca FERRUA MD] 10:30:28
34 positive, a metropolitan and progenitor cells trust to sleep with self-activated cell antiviral vector encoding human was CDNA under the control of the reconstituted promoter from the endogenous locus.

["Dr. Francesca FERRUA MD] 10:30:40
Waskira, barely addresses the genetic defect underlying water through plenty of urging transfer. Waskira is

intravenously fused after a single dose of in 20 monoclonal antibody retoxima, reduced intensity conditioning with semi-alablative weight base and pk, adjusted, bussolphin and fluid.

["Dr. Francesca FERRUA MD] 10:30:58
Was Kyra has recently received a positive opinion by the Committee for Medicine by the Committee for Medicine and Products for Human Use of the European Medicinal Products for Human Use of the European Medicine Agency and Products for Human Use of the European Medicine Agency, for human use of the European Medicine Agency, we recommend that the granting of a smart to contain authorization for the treatment of those patients aged 6 months and holder

["Dr. Francesca FERRUA MD] 10:31:14
for whom a transfer disapricate and lacking a suitable HL. Match related donor.

["Dr. Francesca FERRUA MD] 10:31:21
Furthermore, yesterday the US Food and Drug Administration also approved Was Kira with the same indication.

["Dr. Francesca FERRUA MD] 10:31:26
Was Kira? Sorry, next slide please.

["Dr. Francesca FERRUA MD] 10:31:32
Was Kira is indeed a personalized living drug with no risk of GVHD and or rejection being an autonomous procedure.

["Dr. Francesca FERRUA MD] 10:31:40
The drug product is produced under GMP through a complex process and intensive QC testing is performed for its release.

["Dr. Francesca FERRUA MD] 10:31:47
Next slide.

["Dr. Francesca FERRUA MD] 10:31:50
Was Kira clinical developmental program included data from 2 clinical studies and one expanded access program. These data have been integrated to access its clinical efficacy and safety in a combined analysis for regulatory purposes.

["Dr. Francesca FERRUA MD] 10:32:05
Next slide.

["Dr. Francesca FERRUA MD] 10:32:06
The primary focus and points for this integrated analysis were overall survival, rate of severe infections from 6 to 18 months of postogen therapy and rate of moderate and severe bleeding events in the 12 months before gene therapy as compared to the 12 months.

["Dr. Francesca FERRUA MD] 10:32:22
Prior to the. These endpoints are clinically relevant as severe walls is life-threatening and tromboseitopinia, often associated with the chorus of leading events recurrent infections and XEMA are the main symptoms of WASS.

["Dr. Francesca FERRUA MD] 10:32:36
The valuation of these endpoints aimed to demonstrate improvement of what's disease in treated subjects.

["Dr. Francesca FERRUA MD] 10:32:41
Clinical efficacy data were supported by an extensive data set on biological correlates of efficacy, including markers of engravement, postppression, immunological function and platelet specific parameters.

["Dr. Francesca FERRUA MD] 10:32:53
Next slide, please.

["Dr. Francesca FERRUA MD] 10:32:56
17 patients receive the fresh formulation of Asquira while 10 patients receive the cryo preserved one.

["Dr. Francesca FERRUA MD] 10:33:04
HSBC source for drop product manufacturing consisted in Mombasa for 5 patients mobilized peripheral blood for 21 or both in one patient.

["Dr. Francesca FERRUA MD] 10:33:13
AGA treatment range between one and 35 years with a median of 2.6 years. Medium followup in surviving patient was 5.7 years.

["Dr. Francesca FERRUA MD] 10:33:21
This court of patients written with Volkira is representative of the heterogeneity of Wasp brought to this spectrum, including patients with zoo zis scores of different severeities.

["Dr. Francesca FERRUA MD] 10:33:32
Next slide.

["Dr. Francesca FERRUA MD] 10:33:34
Or some just treated with whiskira are currently alive and well. Except one EAP subject who die early after gen therapy due to the duration of a prerequisite neurological condition.

["Dr. Francesca FERRUA MD] 10:33:44
This event was not considered related to what was cure by the treating physician, but the role of conditioning regiment could not be ruled out.

["Dr. Francesca FERRUA MD] 10:33:52
To date, there have been no reports of treatment related adverse events or suspected unexpected series of best reactions.

["Dr. Francesca FERRUA MD] 10:33:59
Wasquira was well tolerated with no engravement failure and no evidence of insertion and mutagenesis abnormal clonal proliferation, replication competent lentivirus and no size of minogenicity.

["Dr. Francesca FERRUA MD] 10:34:11
Next slide.

["Dr. Francesca FERRUA MD] 10:34:13
Overall, the adverse events recorded following treatment with Waskira are consistent with those expected inverse patients undergoing metological reconstitution after reducing density conditioning and are not indicative for specific risk related to the drug product.

["Dr. Francesca FERRUA MD] 10:34:27
Most series adverse events occur in the 1st 6 months of follow-up after treatment and most have been infections mainly device related.

["Dr. Francesca FERRUA MD] 10:34:35
None of the treated patients required any secondary procedures after gene therapy. Next slide.

["Dr. Francesca FERRUA MD] 10:34:42
Durable and robust multi-linear engravement of the gene corrected cells was confirmed over time up to the latest follow-up time points.

["Dr. Francesca FERRUA MD] 10:34:50

Gencoretic cells were detected in all tested, omaro and peripheral blood lineages with agile levels of transduction in info cells as suspected by their selective advantage.

["Dr. Francesca FERRUA MD] 10:35:00
Next slide.

["Dr. Francesca FERRUA MD] 10:35:02
Sustaining graphment of genetically corrected HSPCs led to stable restoration of oscillation in lymphocytes, monocytes and platelets, which resulted in a ameliorated immune cell function and platelet scant.

["Dr. Francesca FERRUA MD] 10:35:15
Next slide. Focusing now on the clinical benefits of obscure treatment is important to note that after the 1st 6 months of follow-up thanks to immun function reconstitution, the analyzed rate of severe infections by personnel of observation dramatically dropped in the 6 to 18 months for lower period after gene therapy as compared to 10 months before gene therapy.

["Dr. Francesca FERRUA MD] 10:35:39
Not worth the rate of severe infection remained extremely low throughout the follow-up. Next slide. The reduction in severe infections is evident also from this graph on the right where the grey horizontal bars represent the time of observation of each individual patient from birth up to up to the less available follow-up.

[Catherine Bernstein] 10:35:54
I have 3Â min remaining.

["Dr. Francesca FERRUA MD] 10:35:59
Dark squares representing severe infections are almost absent after the 56 month postgen therapy in the majority of patients.

["Dr. Francesca FERRUA MD] 10:36:06
Next slide.

["Dr. Francesca FERRUA MD] 10:36:09
As further clinical benefit after treatment with WASCAR, patients were able to stop supportive treatments.

["Dr. Francesca FERRUA MD] 10:36:16
In particular, most valuable subjects stopped immunoglobin in replacement therapy and sustained antimicrobials at a medium of 11 and 14 months after gene therapy respectively.

["Dr. Francesca FERRUA MD] 10:36:26
Next slide.

["Dr. Francesca FERRUA MD] 10:36:28
Let little count increase as compared to baseline after treatment with whiskira and normal mean platelet volume was absurd in most patients during follow-up.

["Dr. Francesca FERRUA MD] 10:36:38
Moreover, also pleated function and morphology improved after gene therapy. Next slide.

["Dr. Francesca FERRUA MD] 10:36:44
Thanks to this combined amelioration of platelet number and function, all available subjects reach Platter Transfusion Independence after gene therapy at a million of 49 days after treatment.

["Dr. Francesca FERRUA MD] 10:36:57
And both the rate and severity of reading events decrease already in the 1st 12 months of the treatment which was Kira

as compared to the 12 months before gene therapy.

["Dr. Francesca FERRUA MD] 10:37:07
This reduction was even more pronounced in the following years up to the list its available time points. Next slide.

["Dr. Francesca FERRUA MD] 10:37:14
In line with these in the majority of patients the difference in the incidence of moderate and severe bleeding events before and after gen therapy is evident also from describe to on the left with only rare meeting events and few patients during follow-up despite the cessation of sustained plate and infusions in our patients.

["Dr. Francesca FERRUA MD] 10:37:32
Next slide.

["Dr. Francesca FERRUA MD] 10:37:34
Further to these results, X, also resolved in all treated patients and in, dysregulation improved in most patient postogen therapy.

["Dr. Francesca FERRUA MD] 10:37:43
Freedom from supported treatments impacted positively on the quality of life of patients and their families by reducing their medical needs and time spent in hospital.

["Dr. Francesca FERRUA MD] 10:37:52
Indeed, after gen therapy, hospitalisation rate declined. And quality of life improved in our patients. Next slide.

[Catherine Bernstein] 10:37:54
You have 1Â min remaining.

["Dr. Francesca FERRUA MD] 10:38:01
Overall, this integrated safety and the frequency analysis, I like the outstanding clinical efficacy was Kira together with the absence of any adverse events related to the drug product.

["Dr. Francesca FERRUA MD] 10:38:10
These life-changing results have been obtained thanks to the robust and sustaining graphment of genetically modified metropolitics themselves after a single infusion of Askira following a reduce intensity conditioning regimen.

["Dr. Francesca FERRUA MD] 10:38:24
Outcome was similar across different ages. This is characteristic was mutation and DP formulation. With up to 13 years follower who scare demonstrates a favorable benefit risk profile with sustained long-term significant clinical benefit.

["Dr. Francesca FERRUA MD] 10:38:39
Thank you.

[Drew Kasper] 10:38:43
Thank you for your presentation. Are there any questions from the public?

[Drew Kasper] 10:38:50
And this can include other applicants, other presenters as well.

[Drew Kasper] 10:38:56
If there are questions, please use the QA feature or raise your hand.

[Drew Kasper] 10:39:01
May also use the n-tamp@cms.hhs.org mailbox.

[Drew Kasper] 10:39:07
If you're on telephone only.

[Drew Kasper] 10:39:13
Can we don't have new questions in the QA at this time? We do have.

[Drew Kasper] 10:39:23
Question from CMS and I don't see any other questions from the public yet, so let's open it up.

[Drew Kasper] 10:39:29
To CMS. Go ahead, Kelsey.

[Kelcy Kelly] 10:39:34
Oh yes, thank you for your presentation. I saw there were kind of different trials for the different formulations and I know you mentioned that the outcomes weren't different.

[Kelcy Kelly] 10:39:45
Were there any safety differences for the fresh versus the cryopreserved formulations?

["Dr. Francesca FERRUA MD] 10:39:52
Thank you. For this question. No, there were no differences also on the safety side. So the results were comparable both on the Ficas and safety side in patients receiving either the fresh or the cry present formulation.

[Kelcy Kelly] 10:40:08
Okay, thank you. And just one other question. Is there a reason for it looks like a lot of the to see is kind of after 6 months.

[Kelcy Kelly] 10:40:21
Is there a reason for that or could you provide a little more insight into those results?

["Dr. Francesca FERRUA MD] 10:40:27
Thank you for this question. Yes, indeed the 1st 6 months are the minimum time for a matter both in methodological and immunological time for a both a metallological and immunological reconstitution, both a metallological and immunological reconstitution after reduced intensity conditioning.

["Dr. Francesca FERRUA MD] 10:40:42
And immunological reconstitution after reduced intensity condition after reduced intensity conditioning. So it's the time required by the new system.

["Dr. Francesca FERRUA MD] 10:40:45
So it's the time required by the new system to start functioning. So it's the time required by the new system to start functioning again in particular, corrected the T cells.

["Dr. Francesca FERRUA MD] 10:40:49
And start needed to time to maturate in the time so they start to coming out in the peripheral blood at least after 3 to 6 months after infusion of gene corrected the metropolitan.

["Dr. Francesca FERRUA MD] 10:41:04
So in this 6 months patients are more vulnerable to infections. But then after the immune, vulnerable to infections, but then after the immune, new reconstitution completes.

["Dr. Francesca FERRUA MD] 10:41:14
And then after the immune, new reconstitution completes, this does not happen anymore and also in terms of, new reconstitution, new reconstitution, completes, this does not happen anymore.

["Dr. Francesca FERRUA MD] 10:41:20
And also in terms of, the platelets, this does not happen anymore. And also in terms of the platelets, this does not happen anymore.

["Dr. Francesca FERRUA MD] 10:41:22
And also in terms of, the platelets, a metallurgical constitution is faster, but there is, time necessary to for them to start to function properly and And so these kind of time required to the, ematological system start to work again, with the corrected stem cells producing gene corrected the metropolitan cells both in terms of leukocytes and

["Dr. Francesca FERRUA MD] 10:41:51
platelets.

[Kelcy Kelly] 10:41:52
Okay, thank you.

[Drew Kasper] 10:42:03
Do we have questions from CMS or the public?

[Drew Kasper] 10:42:15
New questions in the Q&A or the and tech mailbox and I don't see any raised hands.

[Drew Kasper] 10:42:21
At this point in time.

[Drew Kasper] 10:42:24
Okay, so with that last call. Thank you very much for your presentation.

["Dr. Francesca FERRUA MD] 10:42:30
Thank you.

[Drew Kasper] 10:42:33
Okay. Well now hear from the presenters for a zoo skin. You may now unmute and you're welcome to turn your camera and introduce yourself.

["Sarah Abdelwahab] 10:42:45
Thank you. So much. Good morning, everyone. My name is Dr.

["Sarah Abdelwahab] 10:42:50
Sarah Dolahab. I'm an MD who works for, Abeona therapeutics as their executive medical director and today I'm honored to be standing before you presenting on Ziviskin or Pradoagine Zamy Carousel.

["Sarah Abdelwahab] 10:43:05
Full the sculpture. I do work for Abeona Therapeutics. Next line, please.

["Sarah Abdelwahab] 10:43:10
So, Zeibuskin as an autologous cell based gene therapy that is indicated for both adult and pediatric patients with recessive distrophic epidermal and I'll call it our from now on.

["Sarah Abdelwahab] 10:43:23
Ziviscan targets the underlying cause of arta bones by genetically correcting the patient's own skin or own skin cells to allow for functional .

["Sarah Abdelwahab] 10:43:34

One to be in the cellular sheets that are provided to the patient. Next slide, please.

["Sarah Abdelwahab] 10:43:43
Part of is an ultra rare genetic disorder that is estimated to be in less than 1,500 patients.

["Sarah Abdelwahab] 10:43:50
Within the US. This is a very debilitative connective to Zoom disorder where it's caused by an absence of a functional pull 7 a 1 gene and this gene encodes for collagen 7 which creates anchoring fibr.

["Sarah Abdelwahab] 10:44:06
And you can think of it as the Velcro that keeps the skin layers intact and together so that keeps the epidermis and the dermis connected to each other.

["Sarah Abdelwahab] 10:44:15
So in this horrific order what ends up happening is any mechanical friction or we're hearing forces things like this can just allow this to slip off and you get these wounds all over the body.

["Sarah Abdelwahab] 10:44:25
In these patients, on average greater than 30% of their body surface area is affected. As you can see from some of the pictures that we have with people who are living with And these chronic ones can remain remain open for years on end, which causes a bunch of sequela that makes it very very difficult for the patients.

["Sarah Abdelwahab] 10:44:49
So one, there's a huge burden on in terms of, you know, the amount of bandaging and hours that they have to.

["Sarah Abdelwahab] 10:44:53
You know, like look after these wounds daily, the patients themselves as well as their caregivers.

["Sarah Abdelwahab] 10:45:00
And then subsequently, there's also the risk of infection and the higher risk of squamous cell carcinoma in these chronic foods, which unfortunately becomes one of the highest rates of the reasons for mortality in this patient population.

["Sarah Abdelwahab] 10:45:17
So there's obviously severe local economic and humanistic burden on these patients. As you can see from, you know, how just horrifying this condition can be next slide, please.

["Sarah Abdelwahab] 10:45:31
So like I mentioned before, Zeibuskin is an autologous cell based gene therapy that targets the underlying cause of these wounds.

["Sarah Abdelwahab] 10:45:40
It starts with skin biases that we get from the patients, which are then sent over to our manufacturing.

["Sarah Abdelwahab] 10:45:45
Facility in Cleveland where cells are extracted, they are isolated, and transduced with the corrected or correct 7 e 1 gene, they're then expanded and matured.

["Sarah Abdelwahab] 10:45:57
To become up to 12 credit card sized cellular sheets that are then put onto the patient in a qualified treatment center.

["Sarah Abdelwahab] 10:46:06
Next slide, please.

["Sarah Abdelwahab] 10:46:10

So this is applied in a surgical procedure. They are sutured onto prepared moon beds of these patients and this is not under general or other appropriate anesthesia and it's then followed by a 5 to 10 day post.

["Sarah Abdelwahab] 10:46:23
Surgical recovery and immobilization in the hospital to really allow for that. Immobilization and for the take of the corrected, you know, like jet genetic component of the cellular shapes, the take on and allow for that food healing to occur.

["Sarah Abdelwahab] 10:46:39
Next slide, please.

["Sarah Abdelwahab] 10:46:42
So, the, the substantial chronicle improvement criteria for MCAP. For 2 reasons so one it offers a treatment option for a patient population that's unresponsive or ineligible.

["Sarah Abdelwahab] 10:46:59
For currently available treatment. And secondly, the use of status can significantly improves clinical outcomes relative to already existing technologies that are available for this patient population.

["Sarah Abdelwahab] 10:47:11
Next slide, please.

["Sarah Abdelwahab] 10:47:14
Specifically for criteria on one, the current standard of care for these patients is supportive and won't care and we kind of discussed how that.

["Sarah Abdelwahab] 10:47:24
It's, you know, expensive and very long, bandaging, regimens that are in these patients.

["Sarah Abdelwahab] 10:47:31
And this is obviously extremely painful and labor intensive and just. Emotionally and and and and physically driven some on patients as well as their caregivers.

["Sarah Abdelwahab] 10:47:43
These chronic bones pose a high risk of developing squinous cell carcinoma and the only other 2 therapies that are proved for we're not studied specifically in these large product bones, nor did they specifically address, you know, the relief of pain and itch that these patients often have.

["Sarah Abdelwahab] 10:48:02
So, is a single surgical application on these wounds. It's intended to be a single-time application on these wounds.

["Sarah Abdelwahab] 10:48:10
It's intended to be a single-time application on wounds that are treated that instantly covers and allows for that wound healing to occur.

["Sarah Abdelwahab] 10:48:14
Covering up to 495Â cm square of body surface area on these patients and specifically like I said studied in pain and itch.

["Sarah Abdelwahab] 10:48:27
Just for full transparency, obviously there have been no head to head clinical studies as of yet comparing all these 3 therapies.

["Sarah Abdelwahab] 10:48:33

Next slide, please.

["Sarah Abdelwahab] 10:48:37
The other criterion that we need is that, can significantly improve clinical outcomes compared to existing technology. But is currently on the market for Arctic.

["Sarah Abdelwahab] 10:48:47
So in our vital phase 3 study, which allowed us to gain, the approval for Zeva's can in this patient population.

["Sarah Abdelwahab] 10:48:58
It was an interpretation control trial that was conducted at both Stanford and And these patients had some of their booms, you know, on their bodies.

["Sarah Abdelwahab] 10:49:06
Somewhere, the control arm, which was bandaging and some were put under Zetaskin. We had to meet 2 co-primary endpoints.

["Sarah Abdelwahab] 10:49:14
One was 50% or greater wound hailing and 2 was pain reduction and both of these were at that 6 month mark that had to be met.

["Sarah Abdelwahab] 10:49:23
Next slide, please.

["Sarah Abdelwahab] 10:49:26
These, these wounds and in the chronicle trial had to be open for at least 6 months.

["Sarah Abdelwahab] 10:49:32
And, but in some cases they were open for up to 21 years of never having been closed as these wounds before they were involved in the clinical trial.

["Sarah Abdelwahab] 10:49:43
Next slide.

["Sarah Abdelwahab] 10:49:46
So, Ziva's can approved wound healing in as early as 6 weeks and across all time points in this phase 3 clinical trial.

["Sarah Abdelwahab] 10:49:55
Next slide, please.

["Sarah Abdelwahab] 10:49:58
The coal primary endpoint of 50% of greater wound healing was met in our vital study. And and 81% of the ones that were treated have 50% or greater versus 16% of control.

[Catherine Bernstein] 10:50:09
You have 3Â min remaining.

["Sarah Abdelwahab] 10:50:14
And this is an example of that. Next slide, please.

["Sarah Abdelwahab] 10:50:20
For 75% or a percent of greater room healing 65% of ozivus skin trade and bones achieved that versus just 7% of control wounds and here's a picture of a thigh that shows that 75% or greater wound healing.

["Sarah Abdelwahab] 10:50:35
Next slide.

["Sarah Abdelwahab] 10:50:39
Month 6, again, 16% of zigzags and traded bones had complete wound healing versus none of the control ones and this is an example of that we did have very very rigorous criteria for complete wound healing so things that would that people perceive as complete volatility with wound healing normally may not have been met but we definitely hit that you know that that 50% are greater as well

["Sarah Abdelwahab] 10:51:06
as the 75% are greater in a ton and a majority of the wounds that were treated with zebra skin and definitely more substantial than the control ones.

["Sarah Abdelwahab] 10:51:13
Next slide, please. This is just another example of, 75% or greater, wound healing, which is the upper wound that you see, and, and complete wound healing in one of our Chronicle trial.

["Sarah Abdelwahab] 10:51:27
Next slide, please. We also had to the other co primary endpoint was a change in pain and we did show a reduction in pain as compared to the control.

["Sarah Abdelwahab] 10:51:40
At point. And we also saw a reduction in itch, which was an exploratory and point and not one of the cold primary imports, but we did see a reduction in both or change in both as compared to the control ones in in our state.

["Sarah Abdelwahab] 10:51:55
Next slide. Just going back to this idea of a single-time application of 3 patients that were biopsyed with zebra skin.

["Sarah Abdelwahab] 10:52:05
2 patients were positive for college and 7 or ink 5 roles at that two-year mark. So.

[Catherine Bernstein] 10:52:09
Have 1Â min. I mean.

["Sarah Abdelwahab] 10:52:10
This really is intended to be, you know, long term treatment. Next slide, please.

["Sarah Abdelwahab] 10:52:17
And just another example of a 5 year follow-up where you know patients from day 0 to year 5 they still have that long term healing in Yeah, next slide.

["Sarah Abdelwahab] 10:52:31
Very favorable PPP profile with no Oscar. The cell carcinoma or no replication prompted to retrovirus.

["Sarah Abdelwahab] 10:52:38
So again, really, really significant, you know, study here and really significant safety profile. Next slide.

["Sarah Abdelwahab] 10:52:47
So in conclusion, Zeuskin allows for substantial clinical improvement with patients, for art compared to other approved therapies.

["Sarah Abdelwahab] 10:52:55
It is the only therapy that was specifically, you know, looking to target chronic bones and study in chronic bones and addressing chronic bones and studying in chronic bones and addressing both pain and itch.

["Sarah Abdelwahab] 10:53:08
And I think that's it.

["Sarah Abdelwahab] 10:53:13
Thank you so much.

[Drew Kasper] 10:53:19
Thank you very much for your presentation. Are there any questions from the public?

[Drew Kasper] 10:53:30
Taking questions down from the public in the Q&A function at the bottom. Of your Zoom screen. Or through the raise hand feature.

[Drew Kasper] 10:53:40
We can enable you to unmute and ask your question verbally.

[Drew Kasper] 10:53:49
Have no raised hands or new questions in the Q&A.

[Drew Kasper] 10:53:55
Or in the and tap mailbox. So with that we'll open it up to questions from CMS as well.

[Drew Kasper] 10:54:01
Do we have any questions from CMS?

[James Rollins] 10:54:06
This is Jim Rollins, CMS. My question is you've mentioned wound healing.

[James Rollins] 10:54:11
How do you define wound healing?

["Sarah Abdelwahab] 10:54:14
Absolutely. So, in the clinical trial, like I said, that wound healing had to be 50% or greater than wound healing.

["Sarah Abdelwahab] 10:54:22
So at least 50% of that area was, was, you know, closer looking to normal skin as much as possible.

["Sarah Abdelwahab] 10:54:31
There's no, no necrotic tissue, there's no opening of that.

[James Rollins] 10:54:37
Do you define wound healing as re-epithelialization?

["Sarah Abdelwahab] 10:54:41
Yes. We don't. Yep.

[James Rollins] 10:54:45
So if a biopsy was done on one of these areas which were healed, it would It would duplicate skin by that I mean it would show an epidermis, dermis as well as the other components under the dermis.

["Sarah Abdelwahab] 10:55:00
So just full transparency, we did not specifically take biopsies to show that, but that is presumably, that was not specifically studied, but yes, we did show the epithelialization at least, to the naked eye.

["Sarah Abdelwahab] 10:55:16
And as you could see in some of our pictures. Yeah, it was presumably done. So what we did look at biopsy for in early phase trials was specifically that college in 7 in in in.

["Sarah Abdelwahab] 10:55:27
C.

[James Rollins] 10:55:28
And once the wound healing occurred, there was no recurrence of our deb.

["Sarah Abdelwahab] 10:55:34
So again, we specifically looked at it at the two-year mark and we specifically looked at. at the two-year mark with biopsies at a molecular level, we did show that collagen 7 or ink fibrils were in these patients at that 2 year mark so The idea is that this is intended to be genetic correction with integration of the corrected.

["Sarah Abdelwahab] 10:56:01
Pole 7 a 1 gene for a 1-time application. On the wounds that actually end up end up healing.

["Sarah Abdelwahab] 10:56:07
Now as it pertains to whether art have actually recurred or not that's not something that was studied long term in terms of the biopsies themselves.

["Sarah Abdelwahab] 10:56:16
One of the reasons being was as you can imagine if you've had your had an open room for 21 years you have this therapy put on you and then you say hey We want to get biopsies from this treated area that is looking pretty good every single like year or every 6 months.

["Sarah Abdelwahab] 10:56:33
Lot of patients weren't really fans of that because they were just so relieved that you know they did.

["Sarah Abdelwahab] 10:56:40
Have skin that looked you know a lot better than it was so that wasn't studied beyond that 2 year mark but but we do have long-term follow-up with patients where we see that the skin is doing a lot better.

["Sarah Abdelwahab] 10:56:54
And if, and there is that, closure of these rooms as compared to prior.

[James Rollins] 10:57:01
Yeah, I do understand that, but I still think that Long-term studies should include biopsies to confirm.

[James Rollins] 10:57:09
That the structural abnormality which is corrected persists as opposed to just relying on the general appearance of the skin.

["Sarah Abdelwahab] 10:57:22
Yeah, so I mean, it that was done, like I said, in early phase trials and just due to ethical reasons, it was not continued because, patients did not opt.

["Sarah Abdelwahab] 10:57:34
For having their, you know, treated areas continue to be biopsy in long term.

[James Rollins] 10:57:44
And you have no intentions of.

[James Rollins] 10:57:47
I guess for ethical reasons. Not to

[James Rollins] 10:57:53
Follow these patients. Long term. I think you said the the longest that you follow patients was for 5 years

["Sarah Abdelwahab] 10:58:00
So the longest that we've followed patients is actually, 8 years, which, that patient still showed intact skin, from a, from a physician like, inspection and we're actually following these patients for up to 15 years.

["Sarah Abdelwahab] 10:58:19
Post, So there are there are plans for long term follow-up that is definitely planned. Currently just as it pertains to the molecular correction of it and biopsy these patients there are not currently plans to do that, but there are.

["Sarah Abdelwahab] 10:58:35
Plans to continue to follow these patients for up to 15 years should the patients choose.

[James Rollins] 10:58:43
Thank you.

[Drew Kasper] 10:58:49
And the Dina, did you have a question?

[Adina Hersko] 10:58:51
Yes, thank you. And thank you for your presentation. I have a question. slide number this is, but you were talking about how Ziviskin is, was used for a median body surface area of.

[Drew Kasper] 10:58:53
For your

[Adina Hersko] 10:59:08
200Â cm, so some of these look like less than 200Â cm, right?

[Adina Hersko] 10:59:14
So I was wondering if there any of these patients were also kind of looked at for some of these other therapies, for example.

[Adina Hersko] 10:59:22
One wound with like having gel on it versus using the zealous skin. In the smaller wounds and have those compared to each other.

["Sarah Abdelwahab] 10:59:30
Got it. Yeah, so excellent question. So 1st of all, Ziva skin is, allows for coverage of up to 495Â cm squared so not 200Â cm squared and you're absolutely right some of these patients did have less coverage than that.

["Sarah Abdelwahab] 10:59:46
One of the reasons being was that sometimes it wasn't a really large surface area that was, that was treated, but rather separate discreet ones over their body.

["Sarah Abdelwahab] 10:59:55
In the chronicle trial patients, we're not allowed to have other therapyies as well as CVS can directly so that was not something that that we specifically studied and thus far there have been no head-to-head steps.

["Sarah Abdelwahab] 11:00:09
With that said, we are, we as the differentiator from the other occurred therapies on the market.

["Sarah Abdelwahab] 11:00:16
We specifically, you know, can apply up to 495Â cm squared on body surface area and we specifically studied for pain and itch, which other therapies, their proof therapies on the market have not.

[Adina Hersko] 11:00:33
So in terms of efficacy for wounds under 200. Centimeters squared. There is no comparison.

[Adina Hersko] 11:00:40
You're not able to kind of match those differences to see.

["Sarah Abdelwahab] 11:00:44
So if you're asking, has there been head to head trials between those ones?

[Adina Hersko] 11:00:48
No, not, to head trials, but perhaps a match comparison of some type.

["Sarah Abdelwahab] 11:00:54
Not that I'm aware of, but, we'd be happy to, you know, delve that back into that further in, in a comment letter.

["Sarah Abdelwahab] 11:01:04
If we find anything.

[Adina Hersko] 11:01:05
Thank you.

[James Rollins] 11:01:08
This is Jim again with another question. It seems like most of the slides looked at lesions on the back.

[James Rollins] 11:01:15
David Skin is it also effective on limbs as well as feet and hands?

["Sarah Abdelwahab] 11:01:23
Excellent question. So, actually, we did have a variety of, different, an atomic areas that were done.

["Sarah Abdelwahab] 11:01:34
It was not just specifically not on back. There was a couple of arms on there. some legs as well, specifically on the feet.

["Sarah Abdelwahab] 11:01:42
It was not done in the chronical trials nor on the hands up, but there is nothing to preclude, it from being used on these areas.

["Sarah Abdelwahab] 11:01:51
But it was not just studied on, you know, the back it was study on different areas of the body.

["Sarah Abdelwahab] 11:01:58
Including the trunk, the extremities. And the trunk and extremities.

[James Rollins] 11:02:02
And other than pain and itch, you did not, there were no other outcomes that you were exploring.

["Sarah Abdelwahab] 11:02:09

We had other exploratory outcomes for sure, including the, you know, timing of bandaging.

["Sarah Abdelwahab] 11:02:16
What does that like on all of these other aspects. It was. Specifically for our code primary endpoints.

["Sarah Abdelwahab] 11:02:25
For our co primary endpoints, just looked at, wound healing as well as, pain specifically.

["Sarah Abdelwahab] 11:02:32
But we did have, other exploratory endpoints as well.

[James Rollins] 11:02:39
Thank you.

[Drew Kasper] 11:02:49
Do we have any other questions from CMS or the public?

[James Rollins] 11:02:57
This is Jim again one more time. Wound healing, you said.

[Drew Kasper] 11:02:59
Yeah.

[James Rollins] 11:03:04
And I ask you a question about re epithelialization and you said yes, but before you said I guess the re-establishment of the collagen fibers and that's at a molecular level that is what you were looking at to confirm healing.

["Sarah Abdelwahab] 11:03:21
So in early phase trials, so, so for example, for, our, wound hailing criteria and again, we'd be happy to specifically tell you what they were for 50, 75 and, and complete one feeling for complete wound feeling.

["Sarah Abdelwahab] 11:03:36
For example, it was complete reapithelialization of the entire woman bed with no cresting, no, kind of fibratic tissues, no opening of anything like that.

["Sarah Abdelwahab] 11:03:47
So that was specifically our criteria to, to look at what that looks like on, on a patient level for the vital study.

["Sarah Abdelwahab] 11:03:55
In early phase trials, we also looked at the molecular component of it as well, but, but that was not done in our vital state.

[James Rollins] 11:04:05
Okay, thank you.

["Sarah Abdelwahab] 11:04:09
And, just, just so we can kind of like, you know, think about this. I think it's, it's also really important to understand how small this patient population is.

["Sarah Abdelwahab] 11:04:19
So less than 1,500 patients population is so less than 1,500 patients across the US. So this is an ultra rare genetic disorder.

["Sarah Abdelwahab] 11:04:25

So that's just another thing to kind of think about.

[Drew Kasper] 11:04:40
You are last call for questions from CMS or the public.

[Drew Kasper] 11:04:53
See any raised hands? No new questions in the Q&A and no new questions submitted to the and tap mailbox.

[Drew Kasper] 11:05:02
So with that. Thank you. Very much for your presentation.

[Drew Kasper] 11:05:11
And we will now hear from presenters for. Ka's a gene. Lanparovic, you can Now unmute.

[Drew Kasper] 11:05:22
And introduce yourself and you're welcome to. Activate your camera. Thank you.

[Robert Crozier] 11:05:28
Great. Thank you very much, True. Good morning, everyone. I'm Robert Crowger, Senior Medical Director at And as Pharma and today I'll be telling you about Klimiza Gene Lanparvic.

[Robert Crozier] 11:05:39
An investigational gene therapy for the treatment of mucopolysaccharide doses type 2 or MPS 2.

[Robert Crozier] 11:05:47
And just to note on the side there that this, therapy is currently under evaluation with FDA.

[Robert Crozier] 11:05:53
Next slide, please.

[Robert Crozier] 11:05:56
MPS 2 is also known as Hunter syndrome. It's a lysosomal storage disorder caused by mutations in the IDS gene that encodes for the ITS enzyme or I.

[Robert Crozier] 11:06:12
It's an X length recessive disorder, so typically affects males, of which about 40 are born each year in the United States.

[Robert Crozier] 11:06:20
It's a progressive disease with a wide spectrum of clinical symptoms. Therefore, impacting nearly every tissue and organ in the body.

[Robert Crozier] 11:06:30
And some of those initial symptoms are listed in the next bullet. Next slide, please.

[Robert Crozier] 11:06:39
The currently. There's only one currently approved. A treatment for MPS 2 and that's an enzyme replacement therapy.

[Robert Crozier] 11:06:51
I do so face. And it's administered as a once weekly IV infusion. And while it's effective at reducing urinary gags and liver and spleen volumes, which are impacted in this disease, not crossed the blood brain barrier to address the CNS symptoms that are seen in neuronopathic patients.

[Robert Crozier] 11:07:13
So there are 2 types of patients. There are attenuated patients. Whose symptoms are largely restricted to the periphery

and they are neuronopathic patients, which is the more severe type.

[Robert Crozier] 11:07:24
And they have both peripheral as well as central nervous system. Impacts. And so this is the unmet need and the substantial clinical.

[Robert Crozier] 11:07:39
Improvement that we hope that, and, and, PARVEY, will fill.

[Robert Crozier] 11:07:39
Next slide, please.

[Robert Crozier] 11:07:42
This is an overview of the campsite study, which is a phase 1, 2, 3 study.

[Robert Crozier] 11:07:49
It was 2 parts. Part one was a phase one to dose escalation. Part 2 is to phase through your pivotal portion.

[Robert Crozier] 11:07:57
Turning to the right most part of this slide. Each trial enrolled 13 participants. So 26 total.

[Robert Crozier] 11:08:06
Their age 4 months to less than 5 years and had the Nerone pathic or severe form of NPS 2 and they may be receiving standard of care.

[Robert Crozier] 11:08:18
ERT. The primary endpoint for part one was safety. There were hosted secondary and exploratory endpoints, 2 of which I'll be discussing are d 2 s 6 levels in the cerebral spinal fluid.

[Robert Crozier] 11:08:33
D 2 s 6 is a disacrite component of heparin sulfate, which is a glycosum monoglycan.

[Robert Crozier] 11:08:42
That is toxically accumulated in the CNS. And I'll also be talking about neurodevelopmental function, as assessed by the daily scale of infinite, toddler development.

[Robert Crozier] 11:08:57
The primary point for part 2 is a responder analysis. Which is a proportion of patients with c 2 s.

[Robert Crozier] 11:09:05
D 2 s 6 levels. Hello, maximum attenuated level, 16, and I'll explain that in a minute.

[Robert Crozier] 11:09:11
As well as, again, a host of other secondary endpoints that I'll be focusing on the B.

[Robert Crozier] 11:09:18
Part 1 2, the part one study is complete. Part 2 is ongoing. And the highest does from part one was carried forward for part 2.

[Robert Crozier] 11:09:29
And all participants were encouraged to enter a long-term follow up. For 5 years post initial dosing.

[Robert Crozier] 11:09:38
Next slide.

[Robert Crozier] 11:09:43
So Clemens, a gene lamp parvivc as an AAV. 19 therapy.

[Robert Crozier] 11:09:49
The entire full length, human IDS gene is, provided and there are 2 roots of administration.

[Robert Crozier] 11:09:58
One is through this into the Sisterna Magna as shown on the left. Worth through intro and tricially as shown on the right.

[Robert Crozier] 11:10:06
And then a, regimen is required. Next slide, please.

[Robert Crozier] 11:10:15
So here we're looking at data from part one, the dose escalation study and we're looking at median concentration.

[Robert Crozier] 11:10:23
CSF, Heper and Sophie, d 2 s 6 levels. So 1st they wanted to direct your attention to this 3 bars on the right.

[Robert Crozier] 11:10:32
On the left, sorry, we're looking at severe attenuated and normative levels of d 2 s 6 and the 1st point I wish to make is that d 2 s 6 levels can differentiate between the severe type as shown as the highest bar.

[Robert Crozier] 11:10:48
From the attenuated type, which is the middle second bar. And then normative is at the bottom.

[Robert Crozier] 11:10:54
The second point is that dotted line, which is the maximum attenuated level at a hundred nanograms per ml.

[Robert Crozier] 11:11:02
And this will be important for the responder analysis. What we're looking to drive d 2 s 6 levels below that 100 nanograms per ml level.

[Robert Crozier] 11:11:13
Turning to the right, you can see the dose response for, of the 3 levels.

[Robert Crozier] 11:11:19
Doses over the 2 year time period. And next slide, please.

[Robert Crozier] 11:11:27
As mentioned, the Bailey scale was used to measure neurodevelopmental change. Participants were Pars into 2 groups based on their baseline cognitive function.

[Robert Crozier] 11:11:40
Either they were within minus 2 standard deviations. Of the normative mean or they were outside of that minus 2 standard deviations of the normative mean.

[Robert Crozier] 11:11:52
And the expected treatment responses are shown on the right. They were either, expected to gain skills.

[Robert Crozier] 11:11:59
Or show stabilization. Next slide, please.

[Robert Crozier] 11:12:06
And that's just what we've seen in the part one, those escalation study. So turning to the left hand side.

[Robert Crozier] 11:12:14
The open symbols are the Predose or baseline responses. And the angled thin black line is the normative mean.

[Robert Crozier] 11:12:24
The light ray is one standard deviation in the dark rays, 2 standard deviations. So you can see a baseline they all fell within that cone.

[Robert Crozier] 11:12:34
And 4 of the 5 participants continue to. Gain skills and maintain their cognitive function.

[Robert Crozier] 11:12:43
Turning to the right hand side. You can see that at baseline these participants were outside of the minus 2 standard deviations of the normative mean and 6 of 7 of them.

[Robert Crozier] 11:12:55
Achieve stabilization and some should perhaps a small bit of improvement. Next. Okay, next slide please.

[Catherine Bernstein] 11:13:01
You have 3. Beginning.

[Robert Crozier] 11:13:06
This is part 2 data. Again, this is a portion of the. Participants who achieved, d 2 s 6 levels below that maximum attenuated level.

[Robert Crozier] 11:13:16
9 it's 13 achieve this. That was that SIG. At week, 16, at week 24 is 10 of 13.

[Robert Crozier] 11:13:24
By one year it was maintained at 8 out of 11 2 participants They were not able to obtain samples from them.

[Robert Crozier] 11:13:34
On the bottom row is the percent medium reduction. And you can see that that was stable over one year at greater than 80%.

[Robert Crozier] 11:13:42
Next slide, please.

[Robert Crozier] 11:13:45
Shown on this slide or the B. SET data for, the, the 5 different sub-scales.

[Robert Crozier] 11:13:52
Including cognitive, finding gross motor, and receptive and expressive language. Again, the participants.

[Robert Crozier] 11:13:59
And this is the part 2 data. Dependal study data they were. Carson same way they were either within minus 2 standard deviations that's the middle column.

[Robert Crozier] 11:14:11
Were less than minus 2 standard deviations. And you can see in the middle column that they continue to.

[Robert Crozier] 11:14:19

I show improvements, whereas on the rightmost column. They shed stabilization across. These different subscales.

[Robert Crozier] 11:14:28
Next slide, please.

[Robert Crozier] 11:14:32
Sean, this slide is the safety data. 3 week point of 4 for part one. Looking at the overall.

[Robert Crozier] 11:14:40
There were 6 adverse serious adverse events. None of it, none of them were considered related to Clement's as Jane Lampard.

[Robert Crozier] 11:14:48
You can also see the different. AEs. Related to treatment. Procedure related AEs and I mean a suppression related AEs.

[Robert Crozier] 11:14:58
Most were mild to moderate. And, next slide, please.

[Catherine Bernstein] 11:15:00
You have one minute.

[Robert Crozier] 11:15:05
Shown on this slide is the safety data for part 2. The pivotal dose, 5 essays, one was considered related to, therapy.

[Robert Crozier] 11:15:16
It was an asymptomatic elevation in transaminations. You can see the other AEs listed here.

[Robert Crozier] 11:15:23
Again, most for mild to moderate. There was one death that was considered unrelated. To therapy.

[Robert Crozier] 11:15:31
Next slide please.

[Robert Crozier] 11:15:34
So I've covered most of this. The only new point is the 4th bullet, which is the anticipated.

[Robert Crozier] 11:15:43
Is February 8th of 2026. Thank you.

[Drew Kasper] 11:15:52
And thank you for your presentation.

[Drew Kasper] 11:15:56
With that, we will now open it up to questions from our comments from the public.

[Drew Kasper] 11:16:03
As a reminder, that would be through the QA function or through the raised hand feature and we can enable you to unmute and ask your question verbally.

[Drew Kasper] 11:16:12
And if you're on the phone, you'd have to email that to our. Email box@andtapatcms.hhs.

[Drew Kasper] 11:16:19
Gov. Are there any questions from the public?

[Drew Kasper] 11:16:25
We have no open questions in the QA.

[Drew Kasper] 11:16:30
And no raised hands at this time. So if that will move on, but we have a.

[Drew Kasper] 11:16:36
That will move on to, questions from CNN, CMS. You want to kick us off, Edina?

[Adina Hersko] 11:16:43
Thank you. And thank you for your presentation. Can you clarify the relevance of this treatment for Medicare patients?

[Robert Crozier] 11:16:55
I'm not sure I follow the question.

[Adina Hersko] 11:16:57
Looks like in the studies you were mostly looking at very, very young children. So, you know, and that is for Medicare patients, so I'm just wondering.

[Robert Crozier] 11:17:08
Oh, okay.

[Adina Hersko] 11:17:08
Which patients would be relevant for, yeah, But.

[Robert Crozier] 11:17:12
So, I'm certainly not the expert on this, but I was told that about 20 to 30% of the eligible population would, fit into that category.

[Adina Hersko] 11:17:26
Based on age or disability or some other example.

[Robert Crozier] 11:17:29
It's based on a disability.

[Adina Hersko] 11:17:34
Okay.

[Robert Crozier] 11:17:34
It's a very, it's a very, That's detrimental disease.

[Robert Crozier] 11:17:41
As I mentioned, it affects nearly every organ and tissue in the body. And. So I think disability would be the most likely reason.

[Adina Hersko] 11:17:55
Thank you.

[Drew Kasper] 11:18:08
Open it up questions from CMS for the public.

[Drew Kasper] 11:18:23
That's call for questions.

[Drew Kasper] 11:18:27
There are no new questions in the Q&A. There are currently no raised hands. And no new questions in the and tap.

[Drew Kasper] 11:18:37
Mailbox? So with that, thank you very much for your presentation.

[Robert Crozier] 11:18:43
Thank you, Tree.

[Drew Kasper] 11:18:43
And. We will now move on to a lunch break. And I am going to stick around for those who are presenting after lunch.

[Drew Kasper] 11:18:56
We could do a mic and camera check. For everyone else, we'll see you back here at noon.

[Drew Kasper] 11:19:07
I am not for backup. I saw you. Out there in attendance, do you want to go ahead and unmute and do a Mike and camera check to prepare for after the lunch break.

["Susan Prockop] 11:19:22
Your thing. Can you hear me okay?

[Drew Kasper] 11:19:26
Okay. Yeah, we've got visual and I hear you loud and clear. Thanks.

["Susan Prockop] 11:19:31
Okay. Perfect. And I'm correct that you guide the slides and I just say next slide when I'm, to the next slide.

[Drew Kasper] 11:19:41
Exactly, yeah.

["Susan Prockop] 11:19:42
Okay, perfect.

[Drew Kasper] 11:19:45
And we do have a hard stop at 10Â min. So, We will, we will give a 3Â min warning and a 1Â min warning along the way.

["Susan Prockop] 11:19:54
Okay.

[Drew Kasper] 11:19:58
Thanks. And do we have, Dr. Yes. With orca T.

[Drew Kasper] 11:20:09
There's a look like, So I'll check back in. Right before we return and, and see.

[Drew Kasper] 11:20:20
Yes, the folks from Marketee would like to do a mic and camera check. See you all back here at 12 p.

[Drew Kasper] 11:20:27
M. Eastern time.

["J. Scott McClellan] 11:38:43
Hello, Drew.

["J. Scott McClellan] 11:38:47
This is Scott McClellan calling from orca bio.

["J. Scott McClellan] 11:38:52
Let's open to do a quick mic check.

[Lily Yuan] 11:38:53
Okay. Hi, Dr. McClellan. I can hear you.

["J. Scott McClellan] 11:38:57
Okay, great. Thank you. I'll go back on.

[Drew Kasper] 11:38:59
I can as well, if you want to do a camera check, you're welcome to do that as well.

[Drew Kasper] 11:39:04
Most folks are using their, yeah, there you are. Excellent.

["J. Scott McClellan] 11:39:07
Alright, okay sounds good. I can't see myself but I'll, that's fine.

[Drew Kasper] 11:39:14
We can see you. You've got a, looks like a black backdrop there.

[Drew Kasper] 11:39:19
Or maybe that's the way it's set up.

["J. Scott McClellan] 11:39:20
Yeah, just kinda dark in this room, but yes.

[Drew Kasper] 11:39:23
Oh, okay. That works. Alright, great. Well, we'll look forward to, getting things kicked off at noon.

["J. Scott McClellan] 11:39:26
Perfect.

["J. Scott McClellan] 11:39:31
Sounds good. I'll be standing by.

[Drew Kasper] 11:39:33
Thanks for checking in.

["J. Scott McClellan] 11:39:35
Thank you.

[Drew Kasper] 12:00:17
And welcome back from our lunch break, everyone.

[Drew Kasper] 12:00:29
Yeah. Well now hear from presenters. For orca Tee technology you may now unmute and activate your camera introduce yourself.

["J. Scott McClellan] 12:00:43
Alright, good afternoon, this is Scott McCullough. Thank you for having me today.

["J. Scott McClellan] 12:00:54
Drew, would you like me to go ahead and get started?

[Drew Kasper] 12:00:57
Yeah, thanks for being with us ship. You can go ahead and, get started with your presentation. Thanks.

["J. Scott McClellan] 12:01:04
Alright, thank you. Well, I appreciate the opportunity today to discuss Orca Tee. Orcotees and allergenic stem cell and T cell immunotherapy, which is in development for the treatment of hemologic malignancies.

["J. Scott McClellan] 12:01:15
Next slide, please.

["J. Scott McClellan] 12:01:20
Allogenic aquatic stem cell transplant is a curative strategy for patients with high risk in the logic malignancies such as acute leukemia, acute myeloid leukemia and myelodysplastic syndrome.

["J. Scott McClellan] 12:01:32
Indeed, for many patients, it is the only available curable period of therapy. Conventional sources of hematopoitic cell product contain T cell subsets that mediate positive effects including graph versus leukemia and graph versus infection in facts in the patient.

["J. Scott McClellan] 12:01:50
But they also lead to undesirable side effects, including graph 1st disease, which can cause significant morbidity.

["J. Scott McClellan] 12:01:59
And even treatment related mortality. Which is related to the underlying transplant. To help prevent this, physicians use multi-agent prophylaxis.

["J. Scott McClellan] 12:02:11
Including drugs such as ticholomus and methatrexate. But despite this, GVHD remains a leading treatment related complication in Alo HTT.

["J. Scott McClellan] 12:02:20
This potential for treatment related mortality limits the widespread use of particularly in older patients who may be considered too frail for this therapy.

["J. Scott McClellan] 12:02:32
Next slide, please.

["J. Scott McClellan] 12:02:35
Orca has taken a approach to this. To try to prevent these undesirable side effects while still preserving the beneficial effects of transplant.

["J. Scott McClellan] 12:02:45
This figure contrasts a standard allo transplant with orchids approach, which we call work T.

["J. Scott McClellan] 12:02:52
On the left, when a patient undergoes a transplant, they typically receive and uncontrolled mix of many different cell types.

["J. Scott McClellan] 12:03:00
We know that many of these cell types are beneficial and in fact necessary to achieve the goals of the transplant.

["J. Scott McClellan] 12:03:07
But many of them also cause unwanted side effects. In contrast, orca T on the right.

["J. Scott McClellan] 12:03:14
Consists of a defined population of cells. Specifically, orca T is comprised of 3 cell populations.

["J. Scott McClellan] 12:03:22
I'm atquatic stem cells or HSCs. These are given to the patient to reconstitute their blood and immune systems.

["J. Scott McClellan] 12:03:31
Regulatory T cells are T-rags. These cells. Part used to prevent graph versus host disease in the patient.

["J. Scott McClellan] 12:03:39
And conventional T cells or Tcons. These cells are there to. Bridge immune reconstitution.

["J. Scott McClellan] 12:03:47
Killing leukemia cells and providing infection control for the patient. Next slide, please.

["J. Scott McClellan] 12:03:56
At Orkabi, we wanted to test the hypothesis that orca T could result in better outcomes in patients undergoing alloy transplant.

["J. Scott McClellan] 12:04:04
That in we designed the precision T study which is depicted here. We enrolled 187 patients on this study and these patients were randomized one to one to receive either orcity.

["J. Scott McClellan] 12:04:16
Or a standard of care allergenic graph, which is our control arm. These are patients that had AML, MDS, Al, or mixed phenotype acute leukemia who were otherwise undergoing a all transplant.

["J. Scott McClellan] 12:04:30
Patients were aged 18 to 65. The figure on the right that depicts the treatment for these patients.

["J. Scott McClellan] 12:04:38
Patients are randomized to the orca T arm, received orca T in 3 different infusions.

["J. Scott McClellan] 12:04:47
So on day 0, they received HSC and T regs. And then on day plus 2.

["J. Scott McClellan] 12:04:51
Of their transplant, they receive. The conventional T cells. Following that, they received single agent to chromos to prevent graffiti.

["J. Scott McClellan] 12:05:00
Of note they don't receive any other immunosuppression post transplant. In contrast, patients randomized to the control arm.

["J. Scott McClellan] 12:05:10
Receive an unmanipulated allograph. Plus to chromos and methatrexate to prevent graphher.

["J. Scott McClellan] 12:05:16
Sose disease. I should note that this approach has been standard of care in the transplant field.

["J. Scott McClellan] 12:05:21
For many years now. Primary import of this study was survival free of moderate to severe chronic DHC.

["J. Scott McClellan] 12:05:28
But of course we looked at other endpoints too, including overall survival. GBH, GVHD and relapse free survival or GRFS and chronic DVHD itself.

["J. Scott McClellan] 12:05:40
Next slide, please. This is the demographics of the patients enrolled on the precision T trial.

["J. Scott McClellan] 12:05:48
You'll know that the patients were well-balanced across both arms. Of note the median age of patients on the study was 44 years old.

["J. Scott McClellan] 12:05:57
But we do have a significant number of patients who are older than 55 enrolled on the study.

["J. Scott McClellan] 12:06:02
So more than a quarter of the patients fell into that age demographic. The study was well balanced across the underlying diseases as shown in the bottom left here.

["J. Scott McClellan] 12:06:13
And I would also note that this study include allographs derived from HLA match sibling donors and HLA match unrelated donors.

["J. Scott McClellan] 12:06:23
Approximately 50% in each of those categories. Next paragraph.

["J. Scott McClellan] 12:06:30
So these are the top line results of the precision T study. On the left is a Kaplan Meyer plot that depicts the primary endpoint of the study, survival free of moderate to severe chronic DVHD.

["J. Scott McClellan] 12:06:42
So one year after transplant. 78% of patients on the orchid T arm were alive and didn't have chronic DVD.

["J. Scott McClellan] 12:06:51
In contrast, only 38% of patients on the control arm were alive without chronic. This was the primary endpoint of the study and analysis of this showed that the pot the trial had met his primary endpoint with orca T.

["J. Scott McClellan] 12:07:06
Being significantly improved with regards to the primary endpoint.

["J. Scott McClellan] 12:07:13
On the right, we, depict a pre-planned subgroup analysis. So the paid we looked at patients via We looked at different characteristics for the patients that were enrolled on the trial.

["J. Scott McClellan] 12:07:26
And, the outcome or outcomes here are depicted with a diamond. If the diamond is is situated to the left of the dotted line, that means that in that subgroup of patients the outcome favored orca Tee relative control arm.

[Catherine Bernstein] 12:07:44

3Â min remaining.

["J. Scott McClellan] 12:07:44
The black bars. Sorry. Okay, the, you can see that all subgroups, in all group subgroups analyzed orca Tee was favored this was true of patients both below 55 and 55 or older Next slide, please.

["J. Scott McClellan] 12:08:09
This slide is looking at the safety and tolerability of Orcity. On the left you can see chronic GHT.

["J. Scott McClellan] 12:08:16
This was significantly reduced in patients they got orca Tee relative to standard care. Also on the right in the table.

["J. Scott McClellan] 12:08:22
We looked at outcomes including non-relapse mortality. In other words, death that occurred from toxicity of the procedure.

["J. Scott McClellan] 12:08:29
Only 3% of orcati patients succumb to this. Versus 13% of patients on the control arm.

["J. Scott McClellan] 12:08:38
I've discussed already chronic DVD, but I would note that patients on the or TRM also had a decrease incidence of acute GHD and that's depicted in the middle section.

["J. Scott McClellan] 12:08:49
And finally, I would, just point out the percentage of patients that had to be rehospitalized, in other words, go back into the hospital after initial discharge.

["J. Scott McClellan] 12:08:59
Due to an adverse event was 27% in the orca T arm versus 46%. On the control arm.

["J. Scott McClellan] 12:09:08
Next slide, please. This is a depiction of overall survival. At one year, 94% of market T patients were alive versus 83% of patients on the control arm.

["J. Scott McClellan] 12:09:22
This is not yet statistically significant, but I would point out that this is an interim analysis and we do plan to retest this when the last patient has reached the two-year mark.

["J. Scott McClellan] 12:09:33
Next slide.

["J. Scott McClellan] 12:09:36
Outside of the precision T. Terri, we also have looked at Orca T in other patient populations.

["J. Scott McClellan] 12:09:43
Most notably, we have looked at orca T in combination with reduced intensity conditioning.

["J. Scott McClellan] 12:09:49
Which is appropriate for older patients. We've treated patients up to 74 years in this context.

[Catherine Bernstein] 12:09:55
You have 1Â min.

["J. Scott McClellan] 12:09:57

And I would point out that we recently published Data to suggest that Orca T is well tolerated and efficacious in this older population as well.

["J. Scott McClellan] 12:10:10
When we compare this to patients who received post transplant cycle fossilmide, which is an alternative DVHD prophylaxis.

["J. Scott McClellan] 12:10:18
Strategy OS rates were higher with worker T than with the compar. Next paragraph. In summary, Orcity, the 1st and only precision engineered allergenic T cell, in immunotherapy, leverages high purity regulatory T cells to prevent grappers.

["J. Scott McClellan] 12:10:35
Sose disease. Or could he significantly improve survival free of chronic GVHC in patients compared to standard of care, manipulated alligraphs.

["J. Scott McClellan] 12:10:44
Orca T demonstrated significant improvement in chronic DVD rates. Grfs, any trend towards improved overall survival.

["J. Scott McClellan] 12:10:54
Patients on the work of TRM experience fewer serious treatment emergent adverse events and other unwanted side effects.

["J. Scott McClellan] 12:11:02
So orcati overall had a favorable benefit risk profile for patients with high risk, haemologic malignancies.

["J. Scott McClellan] 12:11:08
We're candidates for all transplant and who are at risk for severe toxicities and mortality with Sandra appear.

["J. Scott McClellan] 12:11:15
I'm manipulated allographed, including Medicare H. Patients. Finally, the FDA has granted Orcity a priority review with a PEDU for target date of Hey.

["J. Scott McClellan] 12:11:28
Thank you for your attention.

[Drew Kasper] 12:11:31
And thank you for your presentation. We'll now take questions from the public. And as a reminder, you can enter your questions in the Q&A that you'll see.

[Drew Kasper] 12:11:44
And in the Zoom toolbar. Usually at the bottom of the screen. Or you can raise a hand and then we can know that you have a question.

[Ron Kline] 12:11:51
Yeah.

[Drew Kasper] 12:11:52
We will then enable you to unmute yourself and ask that question. So with our 1st inquiry for questions from the public.

[Drew Kasper] 12:12:03
Not seeing any raised hands from the public. Yeah. And no open questions in the Q&A. But, if you do have questions that come up, don't hesitate to raise a hand or enter them.

[Drew Kasper] 12:12:19
While we move on to questions from CMS and Dr. Klein, would you like to kick us off?

[Ron Kline] 12:12:25
Yes, hi. Good morning. I should say good afternoon for those on the East Coast. As Dr.

[Ron Kline] 12:12:29
Ron Klein, I'm the chief medical officer for the quality measurement and value based incentives group.

[Ron Kline] 12:12:35
I'm also a pediatric oncologist and transplanter. I guess my question to you is in in in the data that I review that you submit and I didn't review some the last couple of things.

[Ron Kline] 12:12:46
I never saw a relapse related mortality. Measurement. And I did note that in your phase 3 study, there was, no difference in survival, but decreased.

[Ron Kline] 12:12:59
Treatment related mortality, which would imply that the relapse related mortality was higher, higher. So I guess my question is, you know, obviously this in this, in this group, in this group of patients where, you know, graphic leukemia effect is very important.

[Ron Kline] 12:13:12
I'm just wondering what your relapse related mortality is. Compared to controls, so compared to standard treatment.

["J. Scott McClellan] 12:13:19
Absolutely. So I 1st of all, I would point out our, as you've alluded to, our relapse free survival for both arms was 76% and one year and they work a T arm and 74% in the control arm.

["J. Scott McClellan] 12:13:32
And then if the question is how many patients actually died from relapse related causes. As of our data cut off, for patients in the orca T arm and 3 in the control arm had died.

["J. Scott McClellan] 12:13:47
And that will be coming out in, in a print publication very soon.

[Ron Kline] 12:13:53
Okay, thank you.

[Drew Kasper] 12:14:04
And Sophia?

[Sophia Chan] 12:14:07
Thank you so much, Dr. McClellan for your, presentation.

[Sophia Chan] 12:14:12
Could you remind me on slide 136? Differences between the result of the control arm and the orca T arms.

[Sophia Chan] 12:14:23
Are they statistically significant?

["J. Scott McClellan] 12:14:26
Yes, but I should point out that this is it was not a randomized trial. This is a retrospective comparison to registry data, specifically CIB, MTR registry data.

["J. Scott McClellan] 12:14:38
So it is a cross trial comparison. But with that analysis, yes, it was statistically significant.

[Sophia Chan] 12:14:46
Okay, thank you.

[Drew Kasper] 12:15:00
Are there any other questions from CMS or the public?

[Drew Kasper] 12:15:12
Raised hands, no new questions in the Q&A.

[Drew Kasper] 12:15:17
And no.

[Sophia Chan] 12:15:18
Actually, I have one more question, Drew. Dr. McClellan. Could you, could you let

[Drew Kasper] 12:15:22
That's again.

[Sophia Chan] 12:15:27
Give us an idea of How the assignment. Was conducted. Were the patients assigned to either arms? Kind of.

[Sophia Chan] 12:15:45
Consecutively.

["J. Scott McClellan] 12:15:47
Yes, so we, so they're randomly assigned to each arm. We, did stratify based on 2 variables.

["J. Scott McClellan] 12:15:57
One is the the DRI risk score, which is a a metric which measures the risk of the patient's relapse effectively.

["J. Scott McClellan] 12:16:04
And also whether the patient had a related or unrelated donor.

[Sophia Chan] 12:16:09
Okay, thank you.

["J. Scott McClellan] 12:16:11
Yeah, but assignment was random ultimately.

[Sophia Chan] 12:16:16
Thank you.

["J. Scott McClellan] 12:16:19
Welcome.

[Drew Kasper] 12:16:28
Okay, and.

[Drew Kasper] 12:16:31
In case questions are still formulating, I get the impression. That we're gonna digesting some some Q&A here.

[Drew Kasper] 12:16:41
So I'm just gonna provide a reminder for the public that If you have a question, you can use the QA feature at the bottom of your screen.

[Drew Kasper] 12:16:51
Or the raised hand feature and We would be happy to enable you to unmute your mic if you use that raise hand feature.

[Drew Kasper] 12:17:03
So with that, I'm gonna make a last call for questions from CMS or the public.

[Drew Kasper] 12:17:14
And I don't see any raised hands.

[Drew Kasper] 12:17:20
There are no new questions in the QA. And there are no new questions in the NTAP mailbox, which is of course how the public would submit questions if they are on telephone only and don't have access to the Zoom features.

[Drew Kasper] 12:17:38
That being said, it looks like. We have no more questions at this time, so thank you again very much for your presentation.

["J. Scott McClellan] 12:17:46
Thank you for your attention.

[Drew Kasper] 12:17:48
We will now hear from presenters for. The tabsell technology, you may now unmute.

[Drew Kasper] 12:17:56
And introduce yourself, you're welcome to turn on your camera as well. And start your presentation.

["Susan Prockop] 12:18:04
Thank you. Fine, Susan Prokop and the program director or. Clinical and transitional research at Boston Children's Santa Barbara in pediatric transplant.

["Susan Prockop] 12:18:17
And I appreciate the opportunity to speak to you today about treatment with T for patients with Epstein. Virus-driven post transplant, prolifer, disease, or, Next slide, please.

["Susan Prockop] 12:18:31
These are my disclosures relevant to this presentation is by consultancy for it's hard about therapeutics and PR.

["Susan Prockop] 12:18:38
Next slide.

["Susan Prockop] 12:18:40
Host transplant, one propeller for disease or PTLT is a particularly needful complication.

["Susan Prockop] 12:18:46
That's a metaphoric and cellar organ transplant. The majority of cases of PTO, DR, Epstein bar virus driven.

["Susan Prockop] 12:18:53
Resulting from newly acquired or reactivated EVD virus. Inacting d lymphocytes.

["Susan Prockop] 12:18:59
Emerges as a result of impaired, EBB directed immunity And these immune compromise transplant recipients.

["Susan Prockop] 12:19:08
Next slide.

["Susan Prockop] 12:19:11
There are currently no approved therapies for treatment of VPVPTLD. 1st line therapy includes CD.

["Susan Prockop] 12:19:19
20 targeting monoclonal antibody therapy such as peroxima. The reduction of immune suppression, which is an approach that can increase the risk for graph versus host disease and haemodic transplant recipients or organ rejection in solid organ transplant recipients.

["Susan Prockop] 12:19:34
And most some patients are treated with multi-aging chemotherapy. There's a significant risk of treatment related mortality and morebidity in these medically fragile patients.

["Susan Prockop] 12:19:45
Oh, for those patients whose disease fails to respond to 1st line therapy, prognosis is very poor.

["Susan Prockop] 12:19:52
In a retrospective. And now, he's the median overall survival in recipients of hematopetic transplant was just point 7 months.

["Susan Prockop] 12:20:03
And in recipients of salivore again transplant just 4.1 months. So this demonstrates a high I met need.

["Susan Prockop] 12:20:10
And if approved, TABLELUCL would be the 1st FDA proof therapeutic agent for patients with relapsed or refractory, VPTLD, emerging after aematopredic or solid organ transplant.

["Susan Prockop] 12:20:22
Next slide, please. Tubalic the cells generated from normal healthy EBP 0 positive donors.

["Susan Prockop] 12:20:29
These cells are separated from a lekophoresis and transformed with a laboratory strain of the virus.

["Susan Prockop] 12:20:35
And these transformed B cells are co-cultured with T cells separated from the same recipe.

["Susan Prockop] 12:20:41
With this serial stimulation, T. Sells recognizing EBB are sensitized and expanded.

["Susan Prockop] 12:20:47
And the tease a lot is then fully characterized and frozen for potential immediate off-the-shelf use.

["Susan Prockop] 12:20:53
Next slide, please. Tabaloocha is not genetically modified. It is an allogenic off the shelf, ebb specificspecific t.

["Susan Prockop] 12:21:03
Cell, immunotherapy. It's administered without lympho depletion.

["Susan Prockop] 12:21:06

And can be administered either in the inpatient or outpatient setting requiring just 2Â h of post infusion monitoring.

["Susan Prockop] 12:21:14
The product targets, the infected cells through the native T cell receptor. That recognizes EBB epitopes presented on the surface of the infected cell in an HLA specific manner.

["Susan Prockop] 12:21:27
That's treatment lines are characterized for the HLA allele through which they recognize. And then selected for individual patients.

["Susan Prockop] 12:21:38
Based on HLA typing of the patient's EBV disease. Next slide, please.

["Susan Prockop] 12:21:43
The efficacy and safety of T is being studied in the allele trial, an ongoing global phase 3 pivotal study in patients with relapse 4 pivotal study in patients with relapse for factory EVPTLT.

["Susan Prockop] 12:21:54
This trial is open to recipients of the matter product transplant with the DVPTLD that's failed to respond to.

["Susan Prockop] 12:22:00
And 2 cohorts of recipients of solidar can transplant those with EBB PTLD that failed to respond to And those with, with, with, VPTLD that failed to respond to rutxomv and chemotherapy.

["Susan Prockop] 12:22:14
Treatment is administered in 35 day cycles, but dosing of Tableau Masala days 1 8 and 15.

["Susan Prockop] 12:22:20
And response assessment around day 35 with the primary study and point of objective response rate. Patients can receive multiple cycles of treatment until they meet end of treatment criteria with subsequent cycles being administered either from the same donor those with initial response to treatment.

["Susan Prockop] 12:22:40
Or potentially from a different. A lot that recognizes EBV through a different HLA. And that would be for those not responding to the initial cycle of T cells.

["Susan Prockop] 12:22:52
Next slide, please. Here we are presenting data from 75 subjects treated on the allele trial with a data cut of October 9, th 2023.

["Susan Prockop] 12:23:03
The meeting age of this population was 44.4 years. It spans from less than 3 years of age to 81 years of age.

["Susan Prockop] 12:23:11
18 of these patients had any performance for greater than or equal to 2. 56 head extranodal disease.

["Susan Prockop] 12:23:20
63 of these patients had either intermediate or high PTLD prognostic risk.

["Susan Prockop] 12:23:26
Risk index and the majority had histology consistent with diffuse large piece of lymphoma. Next slide, please.

["Susan Prockop] 12:23:35
Here you can see the objective response rate of 50% and 51% respectively in the HTT and SOT recipients.

["Susan Prockop] 12:23:43
With a complete response achieved in 28% of patients and a partial response in 22.7%.

["Susan Prockop] 12:23:50
With a median time to response of 1.1 months. Next slide, please. Most importantly, those recipients who responded to therapy experience improved survival with one year overall survival of 78.7% in responding patients.

["Susan Prockop] 12:24:09
If you're compared to just 28.2% in non responding recipients. Would that median follow up of 17.4 months for responders and 2.5 months for non responders the median duration of survival is not yet established in responding cohorts.

["Susan Prockop] 12:24:26
And is 3.7 months in the non responders. To survive on non responders alliance with that demonstrated in the historical cohorts I previously referenced.

["Susan Prockop] 12:24:38
Next slide, please. In terms of toxicity, 47 of these 75 medically complex patients had treatment emergent adverse events.

["Susan Prockop] 12:24:50
6 of which were attributed to treatment. None of the fatal events were related to treatment. Importantly, this therapy is not associated with toxic cities commonly seen after genetically modified CT cell therapy.

["Susan Prockop] 12:25:05
So we saw no 2 more player. Sorry to kind of release syndrome, or, or cell associated neurologic toxicity.

["Susan Prockop] 12:25:14
And there was no case of Tabaloo, the cell related graph versus host disease or organ rejection reported.

["Susan Prockop] 12:25:22
Next slide, please.

[Catherine Bernstein] 12:25:24
You have 3Â min remaining.

["Susan Prockop] 12:25:27
I don't need that much. In summary, Tabaluca is a non genetically modified allogenic off-the-shelf EV specific.

["Susan Prockop] 12:25:37
If approved, Tabaa will be the 1st and only FDA production for treatment relapsed or refactory, EBB associated PTLD emerging after her metropolitan or solid working transplant.

["Susan Prockop] 12:25:51
The clinical evidence, amented by real-world post-marketing evidence in the EU and UK, established a cell is a transformative off-the-shelf therapy.

["Susan Prockop] 12:26:03
For this disease where survival is otherwise measured in weeks to months. And has demonstrated a clearly meaningful efficacy with rapid.

["Susan Prockop] 12:26:14
Yeah, anti tumor activity. A clear survival benefit. And a favorable tolerability profile with low rates of immune adverse

events.

["Susan Prockop] 12:26:24
Tabaloo, asel will address an urgent unmet medical need for this population of credibly ill immune compromised patients.

["Susan Prockop] 12:26:33
With treatment refractory or relapse disease. Thank you for your attention and I'm happy to take any questions.

[Drew Kasper] 12:26:42
Thank you very much for your presentation. And now we will open up to questions from the public first.st Do we have any questions from the public?

[Drew Kasper] 12:27:01
And. There are no open questions in the Q&A. There are no new questions in the NTAP mailbox.

[Drew Kasper] 12:27:11
And there are no raised hands from the public. So with that, we'll move on to questions from CMS, but, those of you in the public, you can still submit your questions.

[Drew Kasper] 12:27:22
Will. Open it up to questions from everyone after the questions from CMS. At a raised hand here.

[Drew Kasper] 12:27:35
Dr. Klein, you want to start us off with CMS questions? Yeah.

[Ron Kline] 12:27:38
Yeah, hi, good afternoon. Just I just trying to understand a little better how your technology works.

[Ron Kline] 12:27:45
Do you do class one in class 2 HLA typing? And if, you only do class one, have you found any correlation between the efficacy of the therapy and how close you're able to match the class one.

["Susan Prockop] 12:27:59
It's a great question. So, we do do so high resolution typing is done at 10 allele.

["Susan Prockop] 12:28:08
So class one and plus 2. The product selection for individual patients requires a class one as the restricting allele meaning the class one.

[Ron Kline] 12:28:17
You

["Susan Prockop] 12:28:21
Sells recognize EBB through. And at least 2 alleles matching overall, but both both the donor Tsa lines and the recipients are typed at high resolution.

[Ron Kline] 12:28:36
So you're able so 3 8 3 class one HLA. You're able to find products for, you know, that match all 3, you know, that match all 3.

[Ron Kline] 12:28:49
And, and if not, Does your I guess my question is your efficacy correlate with how well you're able to.

[Ron Kline] 12:28:53
Match at class one.

["Susan Prockop] 12:28:54
Right, so, so, so the matching algorithm does not require more than one class one, And at least in.

["Susan Prockop] 12:29:06
Most of the published experience to date in, patients have, have had, a median of 2 matched alleles.

["Susan Prockop] 12:29:15
And. This data set to the extent it's been looked at and in our historical single center data, there was no difference in efficacy.

["Susan Prockop] 12:29:27
When patients received lines that happen to be matched at more.

[Ron Kline] 12:29:32
Thank you so much.

[Drew Kasper] 12:29:47
Okay, let's open it up then. Questions from? CMS or the public?

[Drew Kasper] 12:30:02
As the last call for questions from CMS or the public. See any raised hands at this time.

[Drew Kasper] 12:30:13
There are no new questions in the Q&A. Then no new questions in the antenna mailbox.

[Drew Kasper] 12:30:23
Okay, so with that, thank you very much for your presentation.

["Susan Prockop] 12:30:28
Thanks so much. Have a great day everybody.

[Drew Kasper] 12:30:31
He was well as a reminder for CMS's consideration in the IPPS proposed rule public comments must be submitted to CMS in writing via email to ntap@cms.hs.

[Drew Kasper] 12:30:47
Gov with the subject line. Town hall comments and then please enter the technology name that you're commenting upon.

[Drew Kasper] 12:30:54
All comments must be received by 5 PM. Eastern Standard Time on Monday, December 15, th 2025.

[Drew Kasper] 12:31:02
Even if you raise a verbal comment during the town hall today, you must send the written comment to ensure consideration in the proposed rule.

[Drew Kasper] 12:31:10
We'd also appreciate any feedback on the town hall. Whether it's about what you think worked well or what didn't work well or how we might improve the process.

[Drew Kasper] 12:31:20

We welcome any input that you have about the town hall. Any feedback can be sent to us via email at You Guest it and tap at CMS.

[Drew Kasper] 12:31:29
With the subject line down hall. Thank you all, our presenters, panelists and attendees on the call on the webinar today.

[Drew Kasper] 12:31:38
We appreciate all the time and preparation you've put into today's presentations. And And our questions from the public as well.

[Drew Kasper] 12:31:46
This concludes our days events. Happy holidays to you all. Take care everybody.

[Allison Pompey] 12:31:57
Things drew