OncoSec Medical Incorporated (ONCS)
Medical Key Opinion Leader Symposium
April 5, 2019

Daniel J. O'Connor, President, Director & Chief Executive Officer

Welcome to OncoSec's Breakfast KOL Symposium. I really appreciate everybody getting up early and making the way to New York City to be here with us, also appreciate everybody who's webcasting and listening in on the webcast. We're proud of our company and we're really excited to show you the information that we've gotten in these presentations as well as what the future holds for our company. And so I just want to make sure I touch upon this during the presentation. We may be making some forward-looking statements. So if you have a moment, please read this line.

Okay, here is today's agenda. And before I really go through the agenda in detail, I just say a couple of words about where we are as a company and where we see our future. So as I said, we are very proud of what has been done at the company to date and we're really excited about what we've been seeing with respect to our data, not only in our melanoma program, but some early signals that we're seeing in our breast program. So with respect to our melanoma program and I think we're really shifting the company's focus from looking for that signal and making sure that we're seeing what we hope to see in this study, which we have seen, as you know, you've seen our data with about a fifth or 20% of the patients read out on KEYNOTE-695, which is our melanoma combination study.

We've seen exactly what we wanted to see, which is patients are developing meaningful responses in the group of patients who are – have exhausted or have no available treatment option to them, so an extremely difficult patient population to treat, coming onto this study with progressive disease and seeing that disease halted in its tracks and then seeing a reversal of that disease and then seeing that reversal maintain. And that's what we've seen in the first 20 patients we were able to look at. So a very deep, meaningful, durable responses just what we hope to say. So, as we look forward, we see no reason why we wouldn't continue to see that level of responses in our dataset and so that has shifted the company's focus to preparing to file for regulatory approval, a word about that.

We're Fast Track designated in the United States. We also recently received the ATMP designation in Europe. The Fast Track designation opens up an accelerated approval for our company. When we applied for Fast Track and before we received it, we asked the agency to look at the protocol we're doing today to make sure that it was sufficient to garner and accelerated review. And in that context received feedback around not only what type of patient had to be enrolled in the study in terms of checkpoint failure, but also the level of rigor around response. And Dr. Daud will cover a little bit of that in his presentation, but that point around how the definitive nature of checkpoint failures really should not be overlooked on our data. It's one of the things that make these dataset

unique. I think it's first of its kind data. So as you listen to the presentation this morning, I ask you to listen carefully to that point around our data.

There are a lot of companies that have reported data and checkpoint failures in this setting. I think the challenge is understanding how that definition was interpreted, how responses were defined, how those failures were defined and noting inconsistencies in those responses. These data that we have count and our goal is to make the study – from the outset was to make the study interpretable and we think we've done that. We now think we've seen level responses that put us in a very good bonafide position for an accelerated review request and we've also now positioned the company on the same footing in Europe with the ATMP designation. So why is TAVO important is really the title of Dr. Adil Daud's presentation. For those of you, who don't know Dr. Daud, I think it's probably impossible to pick up a publication in the melanoma setting without seeing Dr. Daud's referenced or listed as an author if not the first or last author, which are the dominant all ship positions.

He is a force of nature in moving forward important cancer treatments for his patient population in melanoma. But more than that, Dr. Daud has been a champion and really I should say champion is probably not the right word, but it's been kind of clairvoyant in knowing that IL-12 was going to play an important role probably a decade ago, but that IL-12 will play an important role in cancer immunotherapies. So he had the foresight to see that this cytokine could provoke a very strong pro-inflammatory response and then started to figure out a way to deploy it and he'll discuss that with us this morning, but I think it's really unique that you have not only one of the top leading oncologist in melanoma with us this morning, but also the gentlemen who really piece this altogether many years ago and really positioned the company to be in the place it is today.

And so also today – sorry, I'll go back to the agenda a little bit more up here. Go back. We have Dr. Kim Lyerly. And Dr. Lyerly is joining us from Duke. He and the company are going to be working on HER2 and IL-12 in a preclinical study that he is a strong believer in IL-12 as well and you'll hear that from him. But he also wants to take the approach of using IL-12 with a vaccine. So combining it with a HER2 antigen approach and deploying IL-12 in that fashion, so we're going to be starting to work with him and again we have the benefit of him discussing that with us. And I'll introduce him a little bit more in a moment.

Following that, we'll have Bob Ashworth. Bob is present in the room today. And I'm not going to introduce all of our team that's present in the room, but I will say a word about Bob. Bob has a long successful career in developing drugs in across many different types of indications, especially in oncology and underlying successful and he's got 13 drugs successfully approved to his name. So we're extremely fortunate to have him here. He's going to discuss really what I said at the beginning, which is where our focus is today, getting ready to file this drug for drug approval. We've seen the response that we hope to see. We see no reason why we wouldn't see continue responses, so we're positioned the company for a drug evaluation and a hopefully successful event and Bob will take us through that portion of our company.

After Bob, our Chief Scientific Officer, Chris Twitty, PhD, immunologist, who did his PhD with Dr. Bernie Fox, who many of you I'm sure know. And Chris is going to talk about not only the product candidate that we recently provide data on an AACR, but also our new initiatives to get inside the body and treat deep visceral lesions. So when you think about our technology, sometimes people misjudge it. They think, okay, these guys are really only hitting surface lesions and therefore there's a limitation on what they can do. I guess in a way today that's slightly true. I'd caveat that by saying surface lesions meets 5% of all cancers and there's a very long list of cancers we could treat. And I would probably eventually say before we ever got to all of them, a decade would go by, but we've gone beyond that.

We've used our ability and research that we've learned using preclinical work, we've miniaturized our applicator and we can now do something I don't think anybody can do, which is get inside the body for deep visceral lesions, lesions like pancreatic cancer or liver cancer. There's a tremendous interest around our company in that. We published a white paper on that. It's just actually got published this morning. We'll be putting on the press release soon about that. So Chris will be taking a moment to educate us on that. So, or again, I really appreciate everybody coming to the city this morning and being present for our presentation.

I'm now going to ask Dr. Adil Daud to take the podium and tell us why we should be considering TAVO. Thank you.

<<Dr. Adil Daud, Principal Investigator and Co-Director of Melanoma Research, University of California San Francisco School of Medicine>>

Thank you everybody. I know this is early for many of you. So, let me go through the beginning and start right here. Let me just tell you guys – just a few words about myself. I'm a medical oncologist. I trained right here in New York City at Sloan-Kettering. I worked with Alan Houghton and Jedd Wolchok. This is in the late 1990s. One of the things I took away from my oncology training was the importance of new drugs. Back in those days, it's kind of hard to remember now, but patients with breast cancer were getting high-dose chemotherapy. We would see patients in our clinics taking the wheelchair in because back in those days, the idea was that some drug is okay, more drugs got to be better and so people would give high doses of Taxol. It was actually hard to get out of your wheelchair if you have that much Taxol because of the peripheral neuropathy that Taxol cause.

And somebody had made the observation that HER2 expression on breast cancer cells was an adverse prognostic factor. And we saw patients with high HER2 levels have their disease progress, brain metastases and stuff like that. And then Herceptin was introduced. And we just saw that major difference in from something that was adverse factor turn into something that was a good – I mean it's hard to say that HER2 expression is good, but it's almost become like a positive aspect now in breast cancer. When you see somebody who has HER2 expression because we know there's a treatment for it. And so

that lesson stayed with me that a good treatment and effective treatment can make a huge difference. And so I finished my oncology fellowship in 2000 and then I was at Memorial for a year in the Phase I department and then moved to Moffitt Cancer Center in Tampa in 2001 and I established a high-dose IL-2 program there. That was a big deal in the early 2000s.

And I remember treating lots of patients with interferon and high-dose IL-2. And I know that people know in this room know what high-dose IL-2 is all about. There is all those immediate toxicities that you go through the ARDS, the hypotension, the fact that you have to give people fluids and stuff. Well, what sometimes people don't recognize is that the delayed toxicity, the neuropsychiatric toxicity that can happen from using high dose cytokines like interferon alpha. Once you had a year of interferon, I have this patient [indiscernible] (12:00) this morning, I have this patient, a 35-year-old pharmacist, who after a year of interferon told me that she couldn't count pills anymore. I had a patient who was a colleague of ours at the VA in Tampa, who's a cardiologist, he told me he couldn't interpret EKGs anymore because – it's just couldn't keep that train of thoughts straight.

I had patients who are – I had this guy who was a tax preparer, who couldn't even do his own taxes because, the 1090 or whatever form it is, can never remember what exactly what it was to do for your taxes, but whatever form it is, couldn't fill the form out because he couldn't – his brain got scrambled. And so, it's that delayed toxicity that's an important thing to remember. And when I heard about interleukin-12, one of my colleagues at Moffitt talked to me about interleukin-12. He had been doing experiments in mice and basically using this B16 model, which many of you know is not a very immunogenic model. It's a model in which PD-1 doesn't work well, CTLA-4 doesn't work well, you've got to use a vaccine even to make CTLA-4 work. And when you have PD-1 or CTLA-4 work in the B16 model, you're not talking cures, you're talking delaying tumor progression by a few days. And so what Rich told me is that he had been doing experiments in B16 and IL-12 if you did it this way, three treatments over the course of a week, you eliminated tumors.

And so I had a lot of skepticism back in those days, because, I think, I went 10 years, or maybe it was about six years, I had done 10 clinical trials with zero percent response, I remember sending a letter to Clinical Cancer Research, I did a trial that 45 patients no responses. I said that that was a positive trail because that was my spin. I said, well, nobody responded. But one patient had delayed disease progression for nine months and that counted for something. And actually the editor of CCR agreed and he said okay, fine, we'll count that as a real, meaningful thing.

So this is the early 2000s. And so I was skeptical when Rich told me about interleukin-12. But the more I learned about it and the more I treated patients, I kind of let my skepticism drop. I think one thing important for you all to remember about IL-12 is that it's a clinical signaling intermediary between our innate immune system and the adaptive immune system. So a lot of times the way our immune system recognizes something is a myth about like a tumor, or infection is through IL-12. A lot of innate immune cells like

macrophages, neutrophils, DCs, dendritic cells basically signal to the adaptive immune system is through IL-12.

And then the other important thing about IL-12 that back in those days made me sit and take notice, was the fact that there's a positive feedback loop between IL-12, and gamma. And so the more IL-12, DCs and adaptive and the innate immune cells produce, the adaptive immune cell pays that back by producing interferon gamma, which then causes more IL-12 production which then causes more gamma production. That's important because remember, a lot of gene therapies where they will fail is the fact that if you have limited efficacy getting into a tissue, you need a positive feedback loop, otherwise you're just going to get extinction of that signal. If there's a lot of negative feedback in a signaling pathway, if you have 10% or 15% efficacy getting into a tissue, you're going to – that signal is just going to die out because of the negative feedback aspect of it.

So this is a picture we took back in 2004, I want to say, when we did the first animal studies with IL-12. And this is Rich Heller's lab. This is Rich Heller who had the idea initially and electroporation is very simple. You basically put a plasmid directly into a tumor lesion and then you use an electric field to open pores in the plasma membrane like you can see over there and then basically the plasma membrane temporarily permeabilizes, the plasma gets in and then it re-seals itself. The idea isn't that you're killing cells, idea isn't that you're destroying tumor, idea is that you're just temporarily creating pores and putting in plasmid.

So I was in this state of skepticism. Imagine the state of mind of somebody who has done a lots amounts of negative Phase I trials and then I come across this patient we call him patient number nine, this was in the first Phase I trial of Interleukin-12, and this is in 2006. We have this guy who had liked I want to say about 100 lesions on the front of his right chest, and on the back of his right chest, and that pretreatment tells you – those are the pictures from the – this is his black and that's is his front. And when we applied to the FDA, to do this clinical trial, they were concerned about the possibility of plasmid integration into the genome so we could only do one single treatment.

So this guy had no other accompanying treatment just one single treatment. So he had day one, five and eight, and of all the hundreds of tumors he had, we were only allowed to treat four of them. And that's where those tickers are from that's two, three and four and there was another tumor that was treated at that time. And then you can see that his back had a lot of these pigmented melanoma in transit and metastatic lesions. And at first, it didn't seem like it did much to him even. And six months later when we saw the lesions, the only thing we could tell is that lesions had flattened out and fading a little bit. And what was interesting is if you looked at his back there was some redness developing around the lesions.

And then, finally, about a year later, I started talking to him and he was like, hey, you know, these seems to have kind of going away. And I actually biopsied a whole bunch of them. I'll show the pathology in a second. But you could see that his – the lesions on his back started disappearing as well and by this time it was two years after treatment. So no

accompanying treatment, just one single cycle of Interleukin-12 in four of these lesions. So sometimes when journal editors ask me like hey how do you know that it's not direct effect and how do you know it's not ablative that's, I remember this patient.

And then there was another patient who has very similar story, this is patient number 14. This is a lady who had a bunch of metastatic lesions on her leg, and you could see those lesions, and you could see that she had had lymph node dissections, you could see how pale that leg is and how swollen it is because when you do lymph node dissection and lymph perfusion that she had done back in those days, you could see that a lot of times you'll have lymphedema and so the color of your skin kind of has that pallor to it.

And so you could see again, the same thing we treated four of those lesions, so not all of them just four of them. And then by more than year and a half later, you could see that the lesion started regressing. And I don't know if you guys can see it from there, but there's this kind of this whiteness de-pigmentation around some of the non-treated lesions. So again, that has stayed with me the fact that you do not need to treat every single lesion, you just need to get the immune reaction going, that's all you're doing with IL-12. You're creating this in situ vaccine.

So these are pathology from those two patients and you could see that like that patient nine, you could see to start off with he had a pretty viable looking tumor. And you could see that by 18 months into the treatment, all you see here is just some pigment in macrophages, so leaving that kind of tattoo appearance on the skin. And you can see that patient 10 has some robust CD4 and CD8 infiltration by day-22.

So the message that I want to share with you guys is the fact that you don't – with an effective immune treatment you don't really need to treat every single lesion, every single time, you just need to get the immune system working. So we then – yes.

<<Unidentified Analyst>>

[Question Inaudible]

<<Dr. Adil Daud, Principal Investigator and Co-Director of Melanoma Research, University of California San Francisco School of Medicine>>

Yes and that's a great question. Thank you. It's confusing sometimes to you that abscopal effect, like for instance, if you were doing the IL-12 plus PD-1, I'd hesitate to call that abscopal, but only because you are using a systemic treatment at the time. You know how abscopal is that. So this is – but in this situation yes, definitely, this is before any of the checkpoints. So yes, I can say with total confidence that that was abscopal.

So we do this Phase II trial, which we are about getting ready to publish in 2011 to 2014. And in this trial, we treated 51 patients, there's 48 patients in this particular slide. And we looked at different cycles, and different schedules of treatment. Day one, five and eight, which was basically the treatments cycle that we'd used in the Phase I trial derived from

the animal experiments, from the mouse experiments. But you guys all know mouse tumors have a very different growth trajectory, compared to human tumors and so we thought maybe weekly might be a better idea or some other schedule might be better.

And what we – the bottom line was that we do think that day one, five and eight works better even in human beings. Now I have to say that we haven't exhaustively explored all kinds of different doses and schedules and certainly not in combination. So I don't know if you can say – I think we could say that of the three treatment schedules we tested, day one, five and eight is the best of all those schedules. And you could see that again, it's not just treated lesions, it's untreated lesions that respond. So that to me is the biggest. We know that IL-12 electroporation will work 60% to 80% of the time in treated lesions, and that doesn't impress me. It's the fact that you can get responses in untreated lesion that's what's so impressive clinically about this treatment.

So what fast forward now back to 2015 and we have PD-1 approved, we have CTLA-4 approved, the big question now in our field – and then still today is what happens to patients who don't respond to PD-1? What happens to tumors that are cold? What is going on with them? What do we know about them? Look, the bottom line is that cold tumors don't have a lot of what we call exhausted T cells.

And we showed that in our publication and that was published in JCI in 2016. Mike Rosenblum, who is a colleague of mine at UCSF is an immunologist and he basically showed that if you had a lot of these partially exhausted T cells and tumors, you would have a response to PD-1. If you didn't have these cells, you wouldn't have response to PD-1. And that's our JCI paper basically showing that if your exhausted T cell number fell below 20% like all these little red bars, basically, you would not have a response to monotherapy PD-1 treatment. You might have response to PD-1, but not monotherapy PD-1. And so we thought what if you take those patients, the ones who wouldn't respond and then treat them with TAVO or IL-12, combined with PD-1. What would happen? So like the cold to hot transformation idea.

And this is data that I am going to share with you in a second. And so in this trial, we had 23 patients evaluable for treatment and here is the result. And here is the schedule of treatment. Patients were given TAVO every six weeks. So every other time you got TAVO and then you got pembro that was the PD-1 drug that we used every three weeks. And you could see that this is the partially exhausted CTLA-4 number and then that's the response data and you can see how many of those patients have complete responses. 43% of patients had some response and most of them were actually complete responses. And if you look in that little histogram thing at the end, you can see that partially exhausted CTL number in those with those little yellow boxes and the responses by RECIST and by clinical assessments right next to it, so you could see that like for instance, this patient here had 22% partially exhausted CTL have complete response. This patient had less than 1% partially exhausted CTL. So it's a very cold tumor and still had a response. And this here is the CFS and OS just showing that how prolonged some of these responses have been.

So I just wanted to share with you some clinical data from this trial from the cold to hot trial, and I deliberately picked a patient who did not have a good response just to give you guys a flavor of what's going on. So this is a patient who had extensive tumors over his left leg, and he had progressed on ipi and progressed on nivo, and his medical oncologist had decided to give him pembro after failure of nivo which we don't do typically, it's just kind of like Coke and Pepsi, there isn't a huge difference between pembro and nivo, so giving somebody doesn't – you could argue it doesn't make a lot of sense, but he had progressed on both of them and he had extensive disease in his left leg.

And so he was this guy here, who had a pseudo-progression to start off and then had a response and you could see that lesions on his leg and so over time and again, it's the kind of the both the delayed nature of the responses and the long lasting responses that you can both see there, that it actually took a couple of years to get rid of all of the lesions, and it's an immunologic kind of reaction and takes a while for that to happen and it's also durable. He's still in response as far as we know today. And that's the last slide there is a photomicrograph taken 23 months of treatment of one of these lesions here just showing that basically what you have is just a healing scar. You don't have any active tumor left.

So when we analyzed the data and this is a lot of the work that Chris has done to kind of illustrate the responses and look immunologically at the tumors. I just wanted to share a couple of highlights with you over here. If you look at IL-12 monotherapy, that's the top panel here, and combination therapy that's the bottom panel here, the couple of things to look at is the fact that in monotherapy, you have a lot of increased PD-L1 expression following treatment like you could see right over here.

When you do a combination therapy, you see even more PD-L1 expression, and that makes – made us think that there is a rationale for the combination with checkpoint inhibitor therapy because you even though you're getting immune cells infiltrating these tumors, you are getting adaptive resistance building up and so that's why the checkpoint inhibitor is so effective in combination with IL-12 because otherwise that once you get adaptive resistance that shuts down the immune response and so you're just going to get a limited amount of bang and you're going to get not as durable responses.

And then another interesting panel to look at is panel D, where you look at this, this basically shows you proliferating exhausted cells. If you guys are familiar with the work of John Wherry at Penn, he has basically shown that it's proliferation in these partially exhausted T cells that can predict the response. So what you can see there is that if you look at the monotherapy, you're not getting as much proliferation in these exhausted T cells in systematic circulations post treatment. When you look at the combination, there is a statistically significant increase in proliferating T cells. And that is in his recent study that was just published in nature medicine, actually after we did this work already. What they have shown is that in patients who are getting neoadjuvant treatment PD-1, one way to predict response is proliferation in these exhausted T cells. So you could see that same kind of effect when you do the TAVO plus PD-1 combination.

So we further analyze data from our – from that combinations the cold versus hot paper. And basically if you look at that at volcano plot here that just shows the increase in transcript, immune transcripts this monotherapy versus combination therapy. If you could just see at a glance how much of a change there is when you do a combination of TAVO with PD-1 versus monotherapy.

And we've looked at ways different measures of immune activation, including antigen presentation, right here and a lot of these genes are thought to be critical for antigen presentation, which will make sense because that's what IL-12 does, it kind of juices up dendritic cell function and innate immune signaling. And not surprisingly you also see increases in adaptive resistance in genes like PD-1, TIGIT, TRAIL and SOX1 which again, kind of, goes along with activation in the immune system. Once you get activation, there is a pathway that tries to shut it down with adaptive resistance and that's why you're getting that adaptive resistance increase.

So can we tell you guys today what the differences between somebody who will respond to the TAVO plus PD-1 combination versus somebody who won't respond to? Well, we have some clues, but we don't have definitive answers yet. So here is two patients, one who had progressive disease and one who had a complete response. And you could see that in both cases, the treated tumor, so if you compare this to this, that's three and four in that other panel, you could see that both the complete responder and the person with progressive disease had tremendous amount of immune infiltration.

So that was not the difference. The difference appears to be how much immune infiltration you have without macro – TAMs, and M2 macrophages and Tregs coming in. So in some cases, you have immune infiltration and that's productive. In some cases, you have immune infiltration and then the tumor tries to shut it down via macrophages and via Tregs, which are known immune regulatory pathway. So I think some of our work now is trying to figure out how to counteract those suppressive pathways.

So people have used our trial samples to show other interesting findings and this is a paper that was just published recently through a collaboration between Chris Twitty, and between Mikael Pittet, who is an immunologist at Harvard. And basically what they did is they looked at our pre and post samples to try to figure out what was going on. And their hypothesis is that PD-1 effect, just PD-1 monotherapy effect relies critically on IL-12 production in the tumor. So basically that's that theory, that you need to have not just T cell activation, but you have to have T cell activation leading to licensing of dendritic cells in the tumor microenvironment through IL-12 for PD-1 to work.

So our study was very useful for them and basically what they were able to show is that if you look at all of these little green, these are IL-12 producing dendritic cells after PD-1 treatment. And so it now make sense that IL-12 would turn cold tumors to hot because of the fact that even for PD-1 to work, you need IL-12 production in DCs. So if you're – if you have an IL-12 deficit so to speak, you're making that up by exogenous IL-12 administration that make sense that you'd turn a cold tumor to hot if you guys are with me here.

So with that, I'm going to turn to our clinical development program, and our flagship program I would say is the KEYNOTE-695, and just a couple of things I want to highlight about KEYNOTE-695. The one important thing is that this is something that we have mutually agreed to with FDA and that is the definition of what types of patients come in. I know many of you go to meetings in AACR and SITC and ASCO and people talk about checkpoint progressors, or checkpoint non-responders. There is checkpoint non-responders and then there is other checkpoint non-responders and I just want to highlight the rigor of the patients that are being enrolled here.

So these are patients who have to have progressed on PD-1. So you can't have a couple of doses of PD-1, had a response, stop PD-1 and then the tumor starts growing and then you give your drug with PD-1 and [indiscernible] (0:36:26) so that's not the kind of patient we're talking about. We are talking about patients who have had resist progression on PD-1 treatment and then go on our trial where they have PD-1 plus TAVO, and then have a resist response, so it's just a different kind of population. And the published data is not super robust I would say in this population, but most – the most significant publication, in which I'm a co-author as a matter of fact, is suggested there is about 6% response rate, 6% to 9% response rate for PD-1 in this population. So people who have actually had resist progression on PD-1. And we're – just to set the stage for KEYNOTE-695 study.

So currently the clinical options that I often use in this population is patients who are ipi, nivo, combo and the response rate is around 14% in this population with relatively low duration of response in a high toxicology profile as you all know. And then, chemo, this is also sometimes used in this population, DTIC 10% to 15% response rate with low duration. Our study is sized at roughly 100 patients so that we would have a 95% conference in devoted to detect a 17% or greater response, so that's just a size of the study.

So what we've seen so far and what's been publicly disclosed has been pretty encouraging. And I'm going to share with you just a snippet of the data. These are patients with extensive progressive disease and we've seen responses both in treated and in untreated lesions on them. And the duration of response is consistent with an immunologic response, not an ablative response to treatments.

And then our safety profile continues to be excellent. One of the impressive things about TAVO treatment is that, remember I told you that cytokine treatment is toxic and systematic cytokine treatment is pretty toxic. What is interesting about TAVO is that patients can have TAVO treatment and basically 30 minutes later go back to work. There isn’t any nausea, there is no systemic side effects to speak of that can be some grade 1 lesion pain or lesion discomfort, some bleeding, some local redness and irritation, but that is pretty much it in terms of side effect profile. So you could imagine that it’s combinable. So this study is about 40% enrolled at this point and we’re on track to complete enrollment by year-end.

So this is a patient who was treated at Roswell Park and he is 81-year-old male with Stage 4b melanoma, and basically has a medical history of squamous and basal cell carcinoma which happens a lot patients with melanoma. Patient who had knee replacement, type 2 diabetes, sinus bradycardia, also had GERD and constipation. And this is his time like. So 2017, October is when he was diagnosed with melanoma. He had a lesion below his left ear and then had wide excision done in December 2017, had a recurrence following that treated with nivolumab, 240 milligrams for 6 cycles, had disease progression by May of 2018 and that is pretreatment scanned there. You can see that he has some mediastinal lymph nodes right here.

You can see that lung lesion and then he had several lesions on the left side of his face including one just below his ear. And you can see that's marked with a sticker one. And this just shows the evolution of his treatment. And so you could see at baseline, he has that mediastinal lymph node, he has the lung lesion, he has another lung lesion and several skin lesions. And so one of the interesting things about him is that he have response, he started to have a response in his mediastinal lymph node, his lung lesion and his other lung lesion, but lesion one, which was actually one of the electroporated lesion apparently seem to progress and increase in size. You could see how much increase in size has been within the first 12 weeks, and so we were talking to the investigator and asking him hey, what's going on and that to me that was surprising just seeing the sequence of events.

And then 24 weeks later that lesion, the whole thing basically just pops off the guy's face and you could see that what's left there is, kind of, a scar and he has near complete response in terms of his mediastinal lymph nodes and in terms of his lung lesions. So this is before – we obviously these lesions, the lung lesions and the chest lesions have not been treated with TAVO, they are deep inside, so it's not something that we could even access, but just kind of illustrates the type of response that we are seeing in this trial and illustrates both the immune nature of the response – just the delayed response and what we think is a delayed – it's also a prolonged duration of response.

<<Unidentified Company Speaker>>

[Inaudible] (42:26)

<<Dr. Adil Daud, Principal Investigator and Co-Director of Melanoma Research, University of California San Francisco School of Medicine>>

What is often a clue is the fact that patients who have this kind of delayed response initially stop developing new lesions, that's been my experience. So like if you take – like the guy with the 100 lesions on his chest the one thing I realized within the first few weeks of treatment actually was that before he came on the study, he was as you can imagine popping up with new lesions every time I saw him, right. And so that's what was very interesting about the patient that was treated at Roswell Park, is that – the lesions that were visible that weren't even treated, were responding.

And the one out of four lesions that was treated on his face seemed to be apparently progressing. So just that – and that's been my experience a lot of time in patients who have "pseudo-progression" on immunotherapy array, they're seem to feel better, numbers getting better, but then you look at the scan and you think that this increase in the size of lesion and then if you do buy see and you see that a lot of that have a lot of lymphocyte and filtration. So it's a long winded answer.

But so just to give you a highlight on another trial that's ongoing, that's the KEYNOTE-890, which is a breast cancer trial combining TAVO plus KEYTRUDA, and patients with breast cancer. And again, these seem – without going too far into details about patients, so these are patients who have visceral disease, who have also have skin disease. And also have accessible treatable lesions. And we've just seem some amazing responses in this trial and will be presenting these in – as the year goes on.

So with that, I'm going to end, and hopefully, you guys are not all completely asleep by this time, and that's…

<<Daniel J. O'Connor, President, Director & Chief Executive Officer>>

Thank you, thank you very much. I'm just going to give a round of applause to Dr. Algazi. Thank you. I should have mentioned that the offset Dr. Algazi is actually the U.S. Lead Principal Investigator on this study. He is treating patients that UCSF. Our next speaker again, is such a luminary probably does not need any type of introduction because I think so many already know this gentleman. But, he is Kim Lyerly, is at Duke, he is deeply involved in immunology, he is a leading surgical oncologist at Duke, and his vastly idea along with our CSO, that you can potentially combine IL-12 with an antigen presenter such as HER2, and get responses in breast cancer.

Our goal, and as you just heard from Dr. Algazi – excuse me, Dr. Daud, is to continue to progress in the breast cancer setting triple negative as many of you know is an extremely difficult subtype of breast cancer to treat, immunotherapy is notoriously be poorly there, those tumors are considered cold if not ice cold. And so our opportunity here is to expand that not only with reversing resistance to checkpoint in TNBC, but also adding IL-12 alongside of an antigen presenter in the vaccine like approach.

So with that, I will ask Dr. Lyerly to explain to us the work he is pursuing and also discuss with us IL-12. Dr. Lyerly?

<<Herbert Kim Lyerly, Duke Department of Surgery>>

Okay. Are we okay now?

<<Daniel J. O'Connor, President, Director & Chief Executive Officer>>

Yeah, thank you.

<<Herbert Kim Lyerly, Duke Department of Surgery>>

Okay. Thanks, everyone for joining. My work with IL-12 started about 20, 25 years ago. As you guys know, the Nobel Prize is never awarded to anyone after their death, except for a single exception and I was from the very groundbreaking work of Ralph Steinman at the Rockefeller and the identification of the dendritic cell, the critical cell necessary for transferring antigens and stimulating antigen specific T cells again, the basis for cancer immunotherapy.

And we have found 20 years ago that the key cytokine for activated and fully matured dendritic cells was IL-12 production and in fact, you can identify those dendritic cells that were most effective in stimulating the immune system was IL-12. Unfortunately, at that time, IL-12, which had generated enormous amounts of enthusiasm as an anti-cancer cytokine suffered from systemic toxicities that seems to preclude its use without finding a technical solution to exquisite delivery and I think this is one of the opportunities afforded by the OncoSec technology.

I am exploring our work in the breast cancer immunotherapy with OncoSec, and one of the reasons we are doing that is because we have independently developed a set of data that demonstrates that IL-12 in the setting of a local delivery in a variety of breast cancer models, stimulates a profound anti-breast cancer immune response and leaves the systemic immunity and really therapeutic opportunities that go beyond just simply treating end-stage cancer, but potentially being a foundational therapeutic in the treatment of early-stage disease.

Imagine if you will that if you had the opportunity to deliver IL-12, stimulate systemic antitumor immunity that would provide lifetime benefit to you, would you not include that in your initial treatment regime. So rather than simply thinking about the treatment of end-stage cancers, we begun to explore the potential of IL-12 delivery and really developing systemic antitumor immunity to prevent recurrences and attach these cancers and again this is ongoing work with one of the reasons we were excited about the potential for the OncoSec technical solution.

In addition, work that we had done with a variety of cancer vaccine studies that demonstrated that a very profound and well accepted strategy is a prime boosting technique in vaccine, and that is we use a DNA-based vaccine, then we come back and we used our viral-based vaccine as a boosting mechanism. And this consistently across all platforms, across all diseases led to the best immune response. For example, all of the HIV investigators at the National Institutes of Health are profoundly interested in this type of prime boosting for the next generation AIDS type vaccine.

One of the challenges of course is that if you have a viral vector, is that you get neutralizing antibodies through viruses and so they are not affected and repeated dosing. One of the things that we had found was a priming with DNA-plasmid followed by a boosting rather than using a virus actually using an IL-12 construct, recapitulated the boost effect of the virus. And so as you can imagine, this made a lot of sense to us,

because of the nature of IL-12 in stimulating antigen responses. But we think this is a quite profound opportunity because we can then enable prime boosting vaccines on an ongoing basis. And that doesn't really limit our capabilities of delivering, repeated dosing or different types of vaccines and so forth.

Finally, I would say that, we have independently experienced a variety of IL-12 delivery mechanisms or variety of other cytokine delivery mechanisms that have included viruses and those types of strategies for direct gene transfer. And we would say that, although the viruses are attractive and look very promising in the laboratory animals, they are profoundly affected by antiviral immune responses. And this is one of the reasons why oncolytic viruses, although very attractive and seeming to have a lot of promises, I think we'll eventually be limited because repeated dosing is quite intimidated by the immune response against the viral components themselves.

The idea of using a plasma delivery system and generating an IL-12 sort of supported microenvironment, as you heard earlier. But without the complication of the viral antigen or the viral delivery system really seems to be quite attractive and we've found it independently and in comparison to the viral vectors, quite an exciting opportunity. So we're very excited about the upcoming collaborative research that we're planning. We think there are variety of opportunities, in addition to melanoma and heard about them in triple negative breast cancer, but not only in the setting of a potential treatment of late-stage disease, but the potentially being expanded into the adjuvants or potentially primary treatment of some of these solid tumors in which the immune system seems to be such a central component of the long term control of disease.

<<Daniel J. O'Connor, President, Director & Chief Executive Officer>>

One question. With respect to electroporation, you mentioned the viral vector developing neutralizing antibodies and that'd be potentially being a rate limiter for that technology. How do you feel about electroporation plasmid base technology, what’s your point of view?

<<Herbert Kim Lyerly, Duke Department of Surgery>>

Well. We had done a lot of work early, again, 20-25 years ago in the gene therapy. And in fact, we were the first group to do mRNA gene transfer in cell therapy sort of in the world. So we tried a variety of strategies including liposomes, exosomes, subcellular vesicles, et cetera. Consistently, not only in our hands, but across variety of other people's hands, electroporation that always comes out to be quite an attractive and effective opportunity. And when I look at data, on published data, grant applications and so forth, typically the ones that really get high quality gene transfer are people doing electroporation and so forth. So I do think, it has been kind of the goal standard and I think ex vivo definitely viruses were great, because you don't need to worry about neutralizing antibodies or adaptive immunity, any of the CAR T cells are generated using lentiviral vectors and so forth, again, very attractive. But in vivo, electroporation really seems to be the sort of industry standard.

<<Daniel J. O'Connor, President, Director & Chief Executive Officer>>

Great. Dr. Lyerly, thank you so much for presenting here this morning. Really, appreciate your time. And we're looking forward to getting going on that preclinical program with you. Thank you again.

<<Herbert Kim Lyerly, Duke Department of Surgery>>

Great.

<<Daniel J. O'Connor, President, Director & Chief Executive Officer>>

You Bet. Okay. With that I'm going to turn the program over to our Senior Vice President and Head of Regulatory Affairs. And as I said, our focus for the company now on is moving into two zones, one enrolling our study. And secondly, preparing ourselves for regulatory filing, Bob, you bet.

<<Robert W. Ashworth, Vice President, Regulatory, Quality and CMC>>

Good morning, we don't usually get the opportunity in regulatory affairs to have a prime spot in KOL Day. So thank you for the invitation. But I hope, it's going to educate you a little bit on what we're doing. Thank you very much, Adil for that very compelling presentation. As you can see, the data that continues to evolve and mature from KEYNOTE-695 has really reaffirmed our commitment to make this product available to patients as quickly as possible.

And there's a quote that is often used from Lewis Carroll's Alice in Wonderland. And that's, "If you don't know where you're going, any road will take you there". The more I think appealing quote is from 20th century philosopher Yogi Berra. He said, when you don't know where you're going, you'll wind up some place. Well, I hope over the next couple of minutes that you'll understand that OncoSec knows where it's going, has a plan to get there. And more importantly, it has executed on that plan. So let's talk a little bit about the plan.

We always get questions about regulatory strategy. Regulatory strategy sounds like some core investing game plan. It really – it isn't proprietary to a company. And there are certain key elements that are I think useful across the board regardless of whatever company you're following or whatever company that – we as pharmaceutical professionals that are employed in. And there are a number of components and I'll just generally top line review them for you. So let's demystify regulatory strategy. What is it? It's really composed of a number of very important components that have to come together to make this thing work.

The first is knowledge of the rules of engagement. How do you interact with a regulator, whether it's in the U.S., or in Europe, or in Australia, or Japan, right? And that's the

primary foundation to all of this. And that generally is geographically specific, right? And then there's a next component, which is understanding the regulatory requirements in those areas and one of the things that I think our regulatory group brings to a company isn't compiling and submitting documents to FDA, right? It's the internal console that provides the company a direction about what is required to get a specific product approved. It's very, very important, because you don't use regulators as consultants. And so that knowledge of regulatory requirements is really product specific.

And I think the third thing that's very important here, is the execution of carefully orchestrated activity that lead to a timely submission. In this case, we're talking about the goal of an accelerated approval. So let's try to, from a top line, understand how the U.S. views our products and how the EU views our product. And then from that basic understanding, we can derive a certain program of activities that get us to the point we want to be, right?

So another question, we often get is, how does the device factor into this? This, no question, is a much more complicated than traditional drug development. It's much more complicated because there's really two issues. We have a groundbreaking therapy, which is TAVO, but we also have a device. A device that provides the means by which the plasmid enters the cell, and electroporation has been around long time, but there are no commercial electroporation for human use. All right, so the device in itself is groundbreaking. And there's a lot of information about it. And I think at this point, the regulators are very, very interested in what we've done.

So in the U.S., we've got it an easy situation. We deal with one agency and we have a device and a drug, but the agency makes it a little bit more easy for us to deal with them because they've decided that it's reviewed by one center at FDA and that center is based on the mechanism of action of the combined product, which is primarily the biologic. So many of the questions, we get are, is the device a standalone? How is it regulated? No, it's regulated by one center. It's biologics. It doesn't have an independent investigational device exemption application. We're not applying for it as an approved standalone product. The product will be cross-labeled. Cross labeled for use with TAVO. So that makes our life a little bit easier.

Now what are some of the things that we've done to seed FDA's interest in collaboration with us? Well, the first thing that I think the company approached the FDA on was a very important expedited designation known as fast track. And the fast track, I will tell you, really relates to not only the drug, but the program. And I can't emphasize that enough. These talked a little bit about interactions with the agency. In order to get a fast track designation, you need to be able to demonstrate that you will achieve results that will serve to support the conclusion that this drug meets an unmet medical need.

And so concurrently with the discussion about the mechanism of action is a very important discussion about the clinical aspects of the development. And it's in that context that I think we arrived at the current study, right, which is designed to demonstrate an objective tumor response in patients who have no alternative therapies.

And I think that was clearly pointed out early, but I want to emphasize that, that is clearly the linchpin of our strategy as we move forward that initial conversation with the agency, talking about the design of the study and its potential use, data, of course, being the unknown, right? That will lead to an accelerated approval.

Now when you have an expedited program, the [indiscernible] (62:44) is on the company to worry about what happens with all of the other activities. We are clearly focused here on the clinical data, which is clearly the linchpin of the whole submission, but there's a heck of a lot of other moving parts here, right? So when I talk about the pathway, think about four trains leaving on four separate tracks at different times and hoping to arrive at the same destination at the same time. And to do that, you have to be thinking years in advance about where you're going. And so what are the four tracks we're talking about? We're talking about obviously the clinical data, we're talking about the nonclinical program, we're talking about the manufacturer and supply of the drug and we're talking about the device.

And I can tell you that with respect to the drug and will reaffirm today that we have a commercially viable process to produce the drug at a reputable manufacturer. And we're now just focused on process validation. So, this is our way of advancing that very important second track. Okay? Moving, making sure that the presumption that you can just go to the shelf and pull the drug off is really a reality, right? Sometimes we – people aren't focused on that. The other thing is the nonclinical program, which is pretty much complete. We have a few minor things to add, but obviously as time goes on, the nonclinical evaluation and the pharmacologic basis for all of this becomes less important, because we've got the validated model, the human model, the clinical results.

And the last, I'll mention is the device. Now the devices for most people a black box, it's a generator that generates a certain voltage that applies the electric field on the surface of the skin. But I can tell you, we're focused on making sure that we meet all the requirements that FDA requires for it to be a standalone device, although it's be a review by one particular group. So, Fast Track was important, because it sets the stage for us in the U.S., and I'll talk a little bit more about the ATMP in the context of EU. So, in the EU, it's a little bit more complicated. Nothing is spontaneous. You must plan way in advance to get to go in where you want to be at a certain time. And the device and the drug are considered separate entities that have to be advanced by actions on the part of the sponsor and stimulated by the sponsor.

So, the device has to comply with certain directives regarding health, safety and environmental issues. And there's something known as a CE Mark, which is Conformity European, it basically says that we comply with all the directives and we're proceeding to get – get that in place before the device would be manufactured and made commercially available. And the ATMP classification, which Dan referred to earlier, really is akin to this Fast Track. So, it's an advanced therapy medicinal products, what it allows the company to do right is to avail itself of conversations with the agency early and often, so that we can move this product as quickly as possible. And it gives us the opportunity to

actually have a preliminary discussion on the other components, right of the application, namely the preclinical and quality.

So, I want to again reaffirm that we are in a position to make good on our objective and that's to make this product available as quickly as possible, not only in the U.S., but in Europe as well. And this is just a summary of what we are intending. As you know, we've already got some foundational activities in place, but our intent really is to – at the end of this year, began talking to the FDA about the actual submission and our plans for submitting the application with a submission following early in 2020 and hopefully, with an approval late 2020, early 2021. The EU is a little bit further behind only because administratively things take a little longer and we have to kind of separate the activities. So, we're on track again for some meetings in early 2020 and then a filing about six months after the U.S. filing.

I will say that one of the key components that was already addressed in Europe is a meeting with the German biologics group that was last year was primarily a quality meeting. We intend to seek scientific advice from the Swedish medicinal products agency, later this quarter. The focus on that meeting is really going to be about conditional approval in the U.S. So, I mean, no mistake about it. We're focused on completing the clinical study, but there are a lot of things going on behind the scenes and we're making sure that they're all going to come together at the same time to make this product available to patients as soon as possible. Thank you.

<<Daniel J. O'Connor, President, Director & Chief Executive Officer>>

Okay. So, I can make sure those four trains lead to the exact same time and getting the exact same place at the same time. Bob, we – I thought it was important to take a few moments to describe an extremely important part of drug development, getting our drug approved. And it's not just – people tend to focus exclusively on data and those kinds of things. I think, as I said, now, we like what we see in our data. We expect it to continue. There's no guarantee there. But we see no reason why we wouldn't see the same response the board have been seeing, continuing to manifest. So, the focus now is on those activities. And again, I felt it was really important for you to hear that that work and those activities are on track and from my point of view in very good hands.

Our next speaker is Dr. Chris Twitty. We really appreciate everybody hanging in with us in a – sorry, I give Chris the last speaking spot. But the two points that, I'd ask you to listen to for Chris is that what he calls the plastic nature of our technology and our ability to get inside the body to hard to access lesions, what we call deep visceral lesions with the development of what we call the VLA, that Visceral Lesion Applicator. Chris?

<<Christopher G. Twitty, Chief Scientific Officer>>

All right. So, I'd like to thank doctors, Daud and Lyerly for sharing their insights into IL-12 and particularly how the TAVO platform can drive those critical immunological pathways that lead to some really striking clinical data that Dr. Adil touched on. And

when you couple that with the deep regulatory experience and leadership that Dr. Ashworth brings to the table, it becomes clear that that TAVO is positioned nicely in the near future. So, where does that leave the program? What's the next step? Where do we go from here? Well, it's with some excitement that I share with you the next step, that's the next generation of OncoSec's TAVO platform. And really, the focus is going to be on treating visceral lesions. There's really three components that I'm going to touch on.

Some of which have been shared just last week at AACR. So, those three components are – it's not simply just miniaturizing the applicator, which we have done. There's a lot of engineering that went into that and it's not just advancing the generator to create a more efficient electroporation. But it's really the therapeutic as well. So, all three componenets have been simultaneously coordinated in their evolution and again, have coalesced into what we're calling spark. So, I'll touch on these three components, focusing in on the generator, APOLLO. This has been years of advancement and effectively, we've changed the electroporation parameters, so that we're delivering a lower voltage with a longer pulse width, I'll touch on some of the data that that illustrates how much better this is compared to what's already working fantastic in the clinic, it's a significant improvement however.

Also, I'd like talk about the foundational IL-12 or TAVO itself. So, the plasmid currently in the clinic is working very well. We've enhanced it and are calling it TAVO plus. And from that foundation, we've now inserted some new immunological elements, which we've coded for in the plasmid which synergize to drive even deeper and more robust immunological responses. And when you finally put this with the new applicator, you can see that we are really positioning ourselves to get into that visceral setting.

So, the two pieces that are critical in terms of the immunological side are the incorporation in CXCL9 and this is coming in with IL-12 as you can see – as you can see here, as the bicistronic platform that codes for both subunits (p35 and p40) of IL-12 similar to what's currently known as TAVO that was also put on the CXCL9 with it. So, this is creates or it augments the chemokine gradient allowing T-cells - encouraging them to get into the tumor. So, this was touching a little bit on what Dr. Daud discussed, we know that TAVO inflames the tumor. If we can encourage more of those CD8 get in there, we're going to be inflaming it the right way.

Used in sequence, we're also creating the TAVO plus anti-CD3 below as you can see here, and this is actually, a membrane anchored anti-CD3 a very strong polyclonal T-cell stimulator. The rationale here is that we've noticed and it's been recently published, it's no secret that a lot of the cells in the tumor that are actually bystanders or they can – as Dr. Daud discussed, they can be partially exhausted. So, we can encourage activity in a large frequency of T-cells that might be otherwise be non-tumor reactive, exhausted or are agnostic to the tumor antigens. We can drive not only a better tumor microenvironment, we also can get enhanced killing. So, put that together with our new applicator and you can see that spark really has a bright future.

So, okay, just some details here. So, this is the current – I apologize, there's a lot of the names and acronyms and I'll try to just give you a quick overview on the key components. This is TAVO here. And TAVO again, is very similar to the TAVO plus, a key difference being the IRES versus the P2A skip motif which allows both to produce a functional P70 IL-12, heterodimer. But it's much more efficient with the P2A. The other element here is the APOLLO. This has been years of development and is a fantastic generato. Thr experiment I just want to highlight here, and I'll move quickly but essentially it really highlights the power. So this is the B16 melanoma model that Dr. Daud, referenced, and it's not the easiest tumor model. We've done this also in different models. But here again just highlighting with B16. Looking at this is two tumor model that allows us to address the abscopal response. So the treated tumor is interesting but really I want you to focus on in the red box on the nontreated contralateral tumor.

What you can see in tumor growth is retarded here and that there is actually a significant difference when you look at the tumor retardation, the limited growth with specifically, the high-voltage current clinical applicator versus APOLLO you can see there is an advantage just using electroporator. But when you take that new APOLLO, the new electroporator and you compare either TAVO or TAVO plus, you can see that TAVO plus has an additional significant benefit. You can see that as well in the survival curve. So TAVO plus alone is probably be enough for us to say "hey, we're good, this is a real improvement". But to meaningfully get into the visceral arena, but we didn't stop there, we continued.

And we asked ourselves, what else can we do to perturb and/or enhance our therapy? So, TAVO plus, it's foundational and we're keeping that as a baseline. And if we look at the tumor immunity cycle, you can see there's lots of areas that we can intervene and arguably TAVO might work across a lot of these areas. But likely focusing in on antigen presentation and finance, like IL-12 has its dominant role. We want to introduce, as I said, a chemokine that can help trafficking and the other component being TAVO anti-CD3 to help recognition and drive the killing of the T-cell sort of balancing a more holistic therapy across the tumor immunity cycle, that's the rationale.

In terms of a more simplified model…We can see that some we're playing with sequencing in addition to how we actually roll out these therapeutics, but you can see that, the TAVO plus-CXC at top can create that chemokine grading in conjunction with IL-12 helping to drive the right type of inflammation. And then importantly with the TAVO anti-CD3 you're driving that robust activation and killing with the anti-CD3 to polyclonal stimulator.

So this last, you can here on the right, I'll just touch on, this is a very interesting day. This was shown that ACR. The point of this was really comparing TAVO plus as our backgrounds which is already a significant enhancement. I want you to keep that in mind as we look at first the level IL-12. So we're using sort of a more of a physiological level, not the super level on the far right that you can see with a 100 micrograms, which is more like a positive control with saturating amounts IL-12. When you're in the – and this is again, on the left, 10 microgram of plasmid or a more physiological level of IL-12 which

leveled with spark. You can see they're basically the same level. We wanted to tease out the potential synergy when you add in these other elements.

And so when you look at the below at the actual tumor volumes, you can see that even though the levels IL-12 are very similar between the 10 microgram, you can see on the light blue bar versus the orange spark bar, there is a significant difference suggesting synergy. So we've shown this other models and we're continuing to develop, again, the sequencing and how it's going to roll out, but it's very exciting. We're very, very encouraged by this data and what it means in terms of giving us power to really perturb the difficult to treat visceral lesions.

So the last element here, I wanted to just highlight is the actual applicator itself as Dan call this VLA, visceral lesion applicator. And so these are two examples of that – that we're going to be rolling out soon. This is more of a trochar based example that we could use maybe to treat a liver lesion. So, this is a miniaturized to 1.9 millimeter at the distal end. The actual electroporation needles are down to two, and they're miniaturized. So it's a really ingenious system that, that tucks into this port. And when it deploys, it spreads out, as you can see on the right there, to about three millimeters and there is a colocalization with the needle. So the ergonomic handheld which we ran by different physicians, who are very comfortable with this, and allows them to get that colocalization and placement right into the areas that they need to get into.

And so, if we think about more of a sort of a laparoscopic or endoscopic version of it. Again, this plays well with standard, sort of a laparoscopic or endoscopic systems that we can fit into the port readily giving us a GI access, for example, if we wanted to get into this lesions type. Again this is more of an ultrasound guided application and you can see with the same elements at play. The colocalization and the electroporation that would ensue. So it's really simple yet I think an exquisite development that we've done, lot engineering has gone into it. And again, it gets us back to this idea of using our powerful platform to perturb and drives the tumor immunity cycle in a way that I think, OncoSec is uniquely positioned for.

So with that, I'm going to back to give it back to Dan. Thanks for your time.

<<Daniel J. O'Connor, President, Director & Chief Executive Officer>>

So that really finished up our speaker program. I'd just like to show you what we have developed. Our prototypes are coming up with Keir LoIacono who runs our business development program. Keir is also a patent attorney, and handles our intellectual property. So it's not just an idea. We've distilled that idea to prototypes. The prototypes are available here for you to see. So I encourage you to come up and take a look, but I think, what I really like to leave you with the final thought of ask yourself what technologies can actually interact with the immune system the way that OncoSec is able to do.

We know as drug developers, communication with the immune system is one of the prime features, how we are doing that? Adenoviruses, bacteria, monoclonal antibodies, the list goes on, all endeavors to try to communicate with the immune response. That's what this is about. This system goes directly into the cells that are in the tumor, as Chris just described. But it doesn't stop there. We have the versatility, the add-ins CXCL9, a membrane-bound CD3, CTLA-4 avoiding the systemic toxicity of that. So as a final thought, you can see the potential that we have with this technology.

And our focus is to make sure that we not only get done the four station simultaneously, that we execute on a program to get our drug to patients in melanoma, hopefully breast cancer under new occasions with our existing version of TAVO as soon as possible. But at the same time make sure that we're following carefully with what is an incredibly, I think, profound idea, which is getting inside to a pancreatic lesion or a liver lesion, and deploying that immunologically relevant genes that need to be there that are missing. I don't think there's anybody that it's in development that can do what we say we think we can do.

So again, I really appreciate everybody being here. We appreciate your time, and I'd encourage you to come up and take a look the BLA. I'm sorry, Ted.

<<Ted Tenthoff, Analyst, Piper Jaffray>>

Thank you very much. It's helpful to see that just where you are now with melanoma Dr. Daud all the work that you're doing, but also where you're going. I had two, actually really simple questions but I want to make sure I understand this correctly. So when the plasmid is administered, it doesn't actually integrate or is it sort of just like it's a little plasmid inside the cell that is kicking off protein.

And then the second question is, so for CD3 that a) and I apologize is a really basic. Are you calling it an anti-CD3 and if so, how is it an anti-CD3, that's working is, it actually anti-CD3 antibody that is binding the T-cell or because the term anti kind of to me sort of indicates that this may be blocking CD3 interaction. Thank you.

<<Daniel J. O'Connor, President, Director & Chief Executive Officer>>

Great questions, Ted. Connor if you don't mind, you can add the Mike or Chris on that one. Thank you. Connor has got the mic with the handle he got there. He might just bring in the mic, that’s great.

<<Unidentified Participant>>

Those are great questions Ted. So, to answer the anti-CD3 question first. So it's a single chain variable fragment, so not a truly antibody. But it's essentially same in it. It's actually not a blocking antibody, it actually is agonistic so it binds to the CD3 on the T-cells, which agnostic to the TCR pat-MHC interactions., so irrespective of the pat-MHC drive that signal as if it that were signaling through the T-cell directly. So a potent

activator and that's the anti-CD3. And then the other question was, it is episomal. So it does not integrate. It's transient, but I think immunologically relevant timeframes if you think about the sort of the duration of expression.

<<Daniel J. O'Connor, President, Director & Chief Executive Officer>>

Ted that answered your question?

<<Ted Tenthoff, Analyst, Piper Jaffray>>

Excellent. Thank you. If I can open it up to the floor, if there any other questions, Mikael?

Q&A

<Q>: So two questions, maybe first for Dr. Daud. In your presentation I noticed that even looking at some of the volcano plots of monotherapy versus combination with PD-L1s. The CD8 T-cell is actually didn't show very large enhancement when looking at the CD8 T-cells accounts. So maybe you can postulate as far as – do you need a new generation similar to what Chris had just described in order to see that greater kind of immunological activity. And the second question is for Bob. As you kind of think about filing for accelerated approval, regulators tend to also want to see what your confirmatory study might look like and have that be designed. And maybe you can just kind of give some thoughts in terms of what a confirmatory study melanoma might look like for that setting. Thanks.

<A – Adil Daud>: Thanks for those questions. Mikael maybe a deal first if you don't mind responding.

<A – Mikael Pittet>: So yes, that's a great question. Definitely an eagle eyed reviewer. With total CD8 cells that do not show a difference, but if you notice somewhere buried in there was these proliferating exhausted T-cell. So what we think is that a lot of the CD8T-cells that are present in tumors are bystanders. And so, yes that is true. And you're not seeing a difference in them, but exhausted, those are the guys, who are chronically activated. And so at Ki-67, saying that, I don't know if you've noticed that, but somewhere in there was a proliferating PD-1, so these are exhausted T-cells that are in systemic circulation you're seeing a significant increase when you're doing combination treatment. So that's it, so we do think that the checkpoint is additive or synergistic; however, you want to look at that. And I think that without the checkpoint, you are activating a lot of adaptive resistance. And I think there's something to be said for combining that with – even with some of the newer, the exciting new drugs that Chris was talking about. I didn't think you're probably going to have to combine it with a checkpoint inhibitor.

<A – Daniel J. O'Connor>: Thanks, Adil. Bob, if you can answer that second question about it.

<A – Robert W. Ashworth>: Sure.

<A – Daniel J. O'Connor>: Thank you.

<A – Robert W. Ashworth>: This is something we've already given quite a bit of thought to and just to put it in context. So, the basis for an accelerated approval that FDA is using an endpoint that's easier to measure than overall survival, why it gets you there quicker, right? And FDA is willing to give companies a pass on the gold standard of approval, which is overall survival, if they demonstrate that there is a benefit on tumor response. So, as you've heard what the endpoint is, objective tumor response, and we have a clinically meaningful range we are looking for.

Now, once the FDA gives an approval accelerated or full, it becomes an ethical and logistic impossibility to repeat that study in the same population, right? People are not going to be in a randomized trial when there's an approved therapy. So, you're already forced to consider a different population for your confirmatory study, which would be an overall survival study. And that confirmatory study will be an actually in a population that's a bit earlier where catching people that are flowing off the table. Let's try to prevent that in the outset. So, you take pembro eligible patients as first-line therapy and you randomize them to treat them with pembro plus pembro and IL-12 or TAVO and then you demonstrate that TAVO as an incremental benefit over that response in the first-line therapy. So, that's the study that we're going to propose and there's already been some discussions with FDA around it, but the devil is always in the details.

<A – Daniel J. O'Connor>: Thank you, Bob. Kellie, did you have anything you wanted to add to that?

<A – Kellie Malloy Foerter>: Yes. Sure. I think right now we're expanding our footprint into Europe, so that we have a nice launching pad for that larger confirmatory study.

<A – Daniel J. O'Connor>: Great, thanks. And that was Kellie Malloy Foerter, who has joined the company at several months ago, joined to us from a company known as Syneos Health just as Kellie's background is year 25 in drug development, 28; sort of shorts are there three years. But Kellie started as a CRA and Monitor at Besselaar Associates many years ago, some of you may remember G. H. Besselaar Associates and left us after not many years in drug development working for Pfizer and many other, which is very significant companies on very significant programs. And it was fortunate that Kellie looked at our company and decided that she wouldn't be part of as working the other side of the equation, not the CRO side per se, but the drug developer side. So, really, fortunate to have Kellie, whose initial mandate to the company was to drive quality into our program and that's what we've been doing since. So, I appreciate that. I think, Jason, you had a question. Thanks.

<Q – Jason McCarthy>: Two questions. One on the regulatory side, can you tell us historically how many patients in a single-arm study have led to approvals? And then a

more broad question going back to the cytokine landscape in particular, it's been active, it's at the Nektar in particular has an IL-2 combo with nivo that's in Phase 3 in front line or first line metastatic melanoma, very similar. So, how do you see the space shifting towards cytokines and how could that positively impact OncoSec?

<A – Daniel J. O'Connor>: Yeah. Two great questions, Jason. Thanks for that. So, I'll take a crack at the first part of the question and maybe ask Bob to augment. And so – and now I forgot what the first question was. Sorry about that. Give me that one again. Sorry. You remember it.

<Q – Jason McCarthy>: Size of the trial.

<A – Daniel J. O'Connor>: Size of trial. Yeah. So, I think the question Jason was how many previous single-arm accelerated approval studies and generally speaking, how are those study sites? One of the great things we have going for us is, I think one of the best drug development companies in the world, our partner in this study, Merck. Merck is with the FDA probably every day of the week as it probably – one of the best points of view in terms of what the requirements are in the moment and what the agency is going to be looking for in terms of sample size. I think when you serve it as single-arm studies; you see generally 70 to 100 patients are the sample size that are used for accelerated approval.

I think, that can vary a bit, but I think as a rule of thumb, that's essentially the sample size. But we initially started at 50 in our study and that was purposefully organized to make sure that we saw some results and when we started to see those results coming in. We sized up to 80 and our partner Merck advised us to go to 100 based upon their experience. So that's really the landscape in terms of how we got to that point. Bob, did you want to add to that?

<A – Robert W. Ashworth>: I'll just say that in general, the size of the trials is, is really a function of the magnitude of effect you're looking for. And so it isn't just sticking your thumb in the air and waiting for which way the wind blows. So, Dan is correct. On an average, it's about 100. There are some that go less if the magnitude of effect is greater. But at the end, it's based on very simple statistics and it has to do with sample size as a function of confidence interval. So, if you're looking for a large treatment effect, you can study fewer people. If you're looking for a smaller treatment effect, you expand it, so that you get a statistical competence, which is the precision around that measurement. Okay? That's basically what it is. The other thing that drives sample size is the desire for FDA to have safety data. Let's not underestimate that. We haven't talked much about safety here, but I will tell you that it's remarkably well-tolerated and safe. This is not a product, where one is concerned with patients developing really extreme adverse events and then just continuing dying, because of it.

<A – Daniel J. O'Connor>: So yes, it's about 100. And before we get to the next question is just like to amplify the last point Bob just made. He's absolutely right. We all focus on efficacy and obviously that's the most important element. But when you go for an

accelerated approval, you're already in its subjective, standard, you're at a lower standard and you're looking at single-arm studies, obviously, not going to have a p-value, where you can define benefit over control. So, other things come into the equation. One of those things is safety. And you heard Dr. Daud described, the initial use of IL-12 was not the right use and that the right use of putting it back into tumor on plasmids. We don't see side effects associated with IL-12. So, we don't see side effects associated with IL-12. That's not a small sample size as 180 patients.

So that I think will – I think I'm optimistic that that point will carry weight when this package is hopefully evaluated by the agencies that we'll be looking at it in Europe and the United States. And I think that, again, knowing that the standard is not a controlled study standard. The other element that comes into play is the area that Chris has developed and we implemented in this study, which is a biomarker program and the biomarker program, and the data that we've developed so far attracted very nicely with our responses. And so that I think is another important feature as we developed the dataset and the evidence that we'll be asking the FDA to consider and the EMA to consider or the CHE, the committee and events therapeutics consider our efficacy and data package.

It will be three elements. It'll be the safety – excuse me, the efficacy, the safety, and then the immunological correlative data, which we think is strong in our program that makes the program stand out. It's an investment in our program to have to do that. It's an investment in our laboratory there, Chris is running. But I think at the end of the day, it's going to prove itself to be very worthwhile investment. The second part of your question, Jason, was landscaped vis-à-vis Nektar and kind of competing companies that are in the space. I think before I asked Chris to respond to that question, I'll make a note. The deals that were done last year when the cytokines. I think the light bulb is burning brightly that cytokines are the way to capture that patient population that's not getting a benefit from checkpoint therapy.

It's not that the checkpoints not blocking the receptor that it's intended to blog, PD-1, CTLA-4 et cetera. It's that the patient's biology of the tumor is not situated to respond. IL-12 changes that, IL-2 plays a role. IL-10 plays a role, that's in a Nektar and ALMA. So Chris, I don't know if you want to go ahead and answer the rest of my questions?

<A – Christopher G. Twitty>: Yes. A couple of other points to add. So, I think generally rising tide lifts all boats. And I do, I'm encouraged by any cytokine company and Nektar is one of the leaders. So, for good and bad word, we're tethered to them to a certain extent. But if you reflect on sort of the ESMO updates from CheckMate-057, I believe, there wasn't – there was – there's a little bit of wiggle room there and I think it's sort of forced Nektar to really go to that confirmatory study, because the differential and their combination compared to nivo alone. We'll see where that lands. I think if we think about the mechanism of action in a way that our therapy works, I think it's, in my opinion it's a little bit better than IL-2. I do think IL-12 differentiates itself a little bit in that way.

So, if you think back to adult study, where we purposely enrolled patients, who are unlikely to respond and saw nearly a 50% response rate, I think that bodes well for coming back to Bob's confirmatory study. I think we'll compare well and frankly we will beat them likely to the punch anyway in terms of timeline. So, I'm not worried about it. I'm actually encouraged to see Nektar doing well. So, I'm not sure if that addressed it exactly that.

<A – Daniel J. O'Connor>: Does that answer your question, Jason? Great. Thank you. We have another question in the back. Thanks, Cornie.

<Q>: Hey, guys. Thanks. I'm just kind of figuring up of Jason's question here about the competition from other set of kinds of, I was curious, I ask something about other IL-12 purchaser that are out there in the clinical development. It seems like one of the key differentiators for TIVO and in this approach to local IL-12 delivery with the plasmid that you have persistent IL-12 expression well beyond what we see with other plasmid approaches, where you should expression diminished fairly rapidly due to turnover of transfected cells. We have to read those as often as weekly. And so, if you can tell us, wondering if you guys could dig into a bit why you believe this essentially more durable change that you're seeing with your approach, exists relative to others. Is it something about the particular variant of the junior using, which shells you're driving uptake into with electroporation?

<A – Daniel J. O'Connor>: Yes, that's a good question. And so we can just go straight to those other datasets, where there's plasmid based technologies. Okay, great. Chris, you want to sort of detail that?

<A – Christopher G. Twitty>: That's a great question. So, there's – we definitely have, particularly when I touched on before that is an advanced plasmid. Our electroporator also is, I think is strong, the duration that we see is notable without seeing the data in front of me, I can't really comment. But we've seen in Merkel cell for example, looking out eight weeks, we can see a significant increase in that – at least two fold or more expression in IL-12.

Preclinically, we can see it out – the other footprint out from single cycle more than a week. So with IL-12, a little bit goes a long way. So, immunologically the footprint is there in a meaningful way with our current cycle. So, what's that always better? I think the question is really the quality of the type of the immune response that we generate with our platform. A part of that might be the little bit of antigen release that we can generate with our applicator, all coming coalescing into really a potent therapeutic. So, I can't comment much more than that in terms of head-to-head comparison of other IL-12 based electroporation, but I do know that our kinetics and expression are working well, and I like what I see in terms of the biomarker program et cetera.

<A>: Yes. And those other programs may not be EP derived, they may be plasmid based, they're not EP based. And Chris, I think you just touched upon that a little bit as we do reversible EP, which means necrotic, we're not killing the cells, we're keeping this cell

alive intentionally. We want the cells alive, so that they will be capable to be transfected except the plasmid and deliver IL-12 in the microenvironment, in the tumor and then get that as a deal described that gamma feedforward loop going, so that you see the whole body effect. But Chris, from your point of view, do you think that EP itself in the way we use it could play a role in enhancing IL-12?

<A – Christopher G. Twitty>: Yes. All right. And just for the – what were you noted, so, an antiviral based, we know that there's companies out there pursuing delivering IL-12 through antiviral, and Kyle touched on – sorry Dr. Lyerly touched on a little bit the idea of a neutralizing antibody, you can maybe get one, maybe two administrations of fat before you're effectively limiting your efficacy of that type of platform. We can have repeated dosing here in a way that's sustainable.

So, you touched also on the energy and release aspect of it. We know that electroporation by itself doesn't necessarily have an effect, we see that preclinically very evident that way. But there likely is a bit of antigen release as we quote for a plasmid doesn't have IL-12. We can see there's a small benefit in the primary tumor. It doesn't translate into the contralateral tumor, but likely there's something being initiated there. So, more immunogenic model you can actually see a slight benefit and we couple out IL-12 and you can imagine that gets amplified and sequelae that happens is that – we touched on that a little bit, but certainly, there's a few facets of electroporation that I don't think are advantageous over other platforms.

<A>: Okay. Thanks, Chris. Are there other questions in back?

<Q>: Hi. This is Jennifer with Baird. I just had two quick questions. One was a more general question about first-line melanoma patients. Do you know what the percentage of patients that get a PD-1 plus CTL-4 versus the patients, who get a PD-1 followed by CTL-4 – CTLA-4 after they progress? And then the second question was regarding the trial that you're writing in melanoma. I think you said that you were expecting or your power for a 17% response rate. Was that 17% above standard of care or 17% absolute?

<A>: Yeah. So, we'll start with the last question first and Adil, if I could ask you respond to the first question. You want to do that first, right? Yes. Maybe, well before you do that, just in terms of the 17%. So, our target is 20% and as Bob described, we're powered for 95% compensatable, which would be detected as low as 17%. Another way of saying that is if we see 17% and above, we're filing, and so open label study, obviously no p-value. So, we put a target of 20%, 17% would still exist with 95% competence.

What does that mean clinically? And this is one of the point, Dr. Daud was teasing out during his presentation when he talked about, relating to your question of that, the ipi/nivo combo 14% in a retrospective study and then more chemotherapy giving maybe 15% with no – with very little duration in a belly of associated difficulties for the patient. So, when we think about 17% or 20% or 22%, we ask ourselves the question, is that relevant to a clinician? Adil and his colleagues, are they going to want to use this technology?

And what holes can we poke in that? And I think, you see – just yesterday at AACR, you saw Syndex did report result with an HVAC1 and it makes our point about our study design being important that was in IRI's standpoint, which was not acceptable as we interact with the FDA, they said, it must be research responders. So that's another – right off the bat, that's a differentiator from that data. But that was – I think a 19% response rate. And so – and Syndex is now moving forward with that and that what does that tell you? That tells you that they respond to these response rates in this patient population that is devoid of options got disease that's spreading that are coming onto this study and is not an easy patient population to treat.

I was in Australia a couple of weeks ago interacting, Kellie and I were in Australia interacting with one of our key investigators there, one of the predominant KOLs in Australia. For those of you don't know, Australia is unfortunately a place where a lot of melanoma exists. I think it's one of every five people get melanoma in lifetime and Australia. So it's a very significant health issue in Australia and the KOL there when I said, how do you feel about a 20% response rate in this patient population? You said, are you kidding me? I would be high fiving at 15% in this patient population.

So that I thought was important information for me to have because I think that's going to echo the type of answers we will hear from the clinicians who will be gathered at a table to discuss the results of our study once completed. Because certainly, we expect that there will be a review by an advisory panel or something akin to that. And they will be asking the question, what do you think about this data? Is it convincing? Importantly, is it clinically relevant? Should your patient can access to it in an accelerated basis. And again, I think that the – when I look at a 17% response rate and listened to the clinicians like Dr. Daud, Dr. Algazi and many others, I hear repeatedly, getting a 17% response rate and anything in that with duration is important to them and would be clinically relevant. I would really appreciate that question. I feel, can you rephrase your first part of your question?

<Q>: Yeah, so just in general, off the first line of melanoma patient that you see or you know – do you know what percentage about them get combo CTLA, PD-1 treatment as opposed to PD-1 followed by CTLA-4?

<A>: [Inaudible] as you see a fast approach we follow, is that somebody has a hot tumor, we'll give them a single agent pembro or nivo. If they've got colder tumors, we will give them combination treatment. That's what everybody does. But we do have our in-house assay that might Rosenblum runs that can differentiate. If you – some people use PD-L1 testing, which I think is also reasonable. If it's – if it's negative, go with a combo, if it's positive, go with single agent, some people just flip a coin or if it's Tuesday they're doing something and Monday they're doing something else.

So I think is also, there isn't compelling evidence as you know that statistically the survival benefit of combination treatment is very small, response rates you're talking 50% to 55% versus 30% to 35% for single agent. So there's a response rate difference,

but the survival benefit I think in the most recent update five years, it does appear to be statistically severe, but it's a small difference like less than 5% difference. You're getting in terms of side effects, you're increasing grade III toxicities from like say 15% to 55%.

So you're paying for your responses basically with combination treatment. I think one of the things we think is going to be exciting going forward. So, I mean, we are talking about cold and really cold and really cold tumors being, but there's no great reason why you couldn't do this upfront. It's just, I mean, I think the regulatory stuff, but then there's also the clinical use and that might actually be an upfront setting and we are thinking of doing unlike a neoadjuvant study, that kind of stuff just showing that it could be useful upfront.

<<Daniel J. O'Connor, President, Director & Chief Executive Officer>>

That's great. I'm going to just conclude the Q&A at this point. The team is here, you see the team on the slide. We're here to answer any questions you may have. Just one parting thought, Dr. Daud is not affiliated with the company, he is a principal investigator, as I said the lead principal investigator in our KEYNOTE-695 study. His colleague Dr. Alain Algazi is now serving as an advisor to the company. And Dr. Algazi has been a very significant help to the company, I know if he's listening, we want to convey our appreciation thanks to him.

Lastly, I'd like to thank our clinicians and our patients who participate in our study. Thank you very much for coming today. Appreciate it.