Below is an unedited transcript from the B. Riley FBR Infectious Disease Summit Part III with Agenus, Inc. Excision BioTherapeutics, and Pluristem Therapeutics hosted by Mayank Mamtani held on Tuesday, July 21, 2020, at 3:00PM ET. B. Riley FBR makes no representations about the accuracy of third-party content nor of the transcription itself. It is provided to you on a confidential basis for your organization's internal use only. Reproduction, retransmission, or any use of the content is strictly prohibited.

B. Riley FBR

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3:00 p.m. ET

MAMTANI: Good afternoon, everyone. We're on to our last panel of the day pursuing approaches for infectious diseases.

We have the pleasure to have on this panel with us Agenus, Excision Biotherapeutics and Pluristem Therapeutics. We also have the opportunity to have Dr. Manuel Hidalgo on the call. He's the Chief of the Hematology and Medical Oncology Division at Weill Cornell Presbyterian Hospital.

Quickly introducing our panelist, from Agenus, we have Dr. Jennifer Buell, the President and Chief Operating Officer of Agenus and has been with the organization since 2013. She has extensive experience working on new adjuvant vaccine platforms as well immuno-modulating antibodies and cell therapies and obviously, we'll touch on the cell therapy aspect today.

From Excision Therapeutics, an exciting privately held biotech company in San Francisco. We have the CEO, Daniel Dornbusch, Mr. Dornbusch has worked in the world of biotechnology for 20 years for large and small biotech companies with roles as diversified as clinical development, CFO, marketing and product development. He recently served as Founder and CEO of Acteris.

Additionally, we also have Dr. Racheli Ofir, the Vice President of Research at Pluristem Therapeutics. Dr. Ofir is responsible for leading projects involving characterization of the PLX platform, which is the placenta derived cell product candidate, including evaluating the biological activity of the cells in vitro, and then he will lead on applying this platform to the COVID application.

And last but not least and we'll get started with Dr. Hidalgo here, whose team focuses on hematology, oncology and bone marrow transplant patients. There was a pretty high surge of COVID patients at the start of the pendemic which has become more manageable.

Dr. Hidalgo, could you speak about platforms that can be useful in patients with cancer and COVID-19.

So whichever platform you'd like to talk about, vaccine or cell therapy, just curious to learn because you are seeing much COVID-19 in your hospital right now in real time.

MANUEL HIDALGO: Yes, thank you and good afternoon. A few months ago, we had a major pandemic, major influx of patients affected with COVID to our hospitals across the entire New York City. I am a medical oncologist. I am the Chief of Hematology and Oncology at the Weill Cornell Medicine and the NYP, the New York Presbyterian, but since late March, basically all our hospitals became sort of a COVID unit.

So, we have been actively working to combat this disease from different angles and that is not only of interest to the infectious diseases specialist with that have been working mostly with antiviral and virus directed agents, but it's also a disease which has made significant impact in a pulmonary and critical care medicine and really has affected the entire way the hospitals work and manage.

Fortunately, lately the number of cases has decreased, as you said substantially and now, I think we have a little more time to try to understand what is going on with this virus.

Now, my interest is that this is a very peculiar disease in the sense that you get an infection, in the pulmonary system, the lungs appear to be initially impacted as the major organ. But we have learned that it can affect multiple other organs. We are very interested in mitigating this disease due to the cytokine release syndrome or cytokines release process which is very fundamental in the pathology of this disease. And also, I am the Chief of Hematology and we have been interested in understanding the significant pro-thrombotic and thrombotic complications that patients develop.

So in particular because of the pro-inflammatory or inflammatory process of the virus infecting the lung, eventually we're learning that patients who will recover from this process, they are left with significant pulmonary fibrosis, which is also of interest for cancer researchers because lately we're working very actively on anti-fibrotic agents to facilitate the delivery of chemotherapy and to boost the immune system in cancer.

So even in a different disease we became interested for these reasons: thrombosis, the immune system and the fibrotic process.

With regards to the immune system, we've been working with a reagent, with Agenus' iNKT cell therapy, which is a therapeutic approach that we think may have an important role in this disease both in the acute phase that we will study in this new trial but we are also interested in how these cell therapy strategies are able to help patients as they recovered in the pulmonary function.

So AgenT-797 is an iNKT cell therapy product. We're about to launch a study in patients with moderate to severe COVID-19 disease. We know that those patients have functionally impaired and reduced number of innate and adaptive immune cells. This disease, as I said, is characterized by very acute inflammation in the pulmonary system, in the lungs, and in pre-clinical models that there are some similarities to the SARS CoV-2 infection. There is an increase in the frequency of iNKT cells reduce the viral shedding and prevent inflammation driven lung injury.

In preclinical models of tumor inflammation, iNKT cells promote a viral clearance by an immune mediated mechanism. We think it has the potential to control acute inflammation and limit tissue damage in the acute process. So, this is also an allogeneic approach which is expected to have limited toxicity and thus it can be administered without the complexity of other cell therapies and can be rapidly produced.

And these allogeneic approaches are off the shelf, you can just manufacture to treat many patients, actually probably more than a thousand patients in a single manufacture run. So the IND submitted, the protocol is pending final review at the IRB; the field is changing so rapidly that you write a protocol today and then we need to change many things tomorrow because corticosteroids now or dexamethasone is recommended when this was approved. So there are things are changing, but we are about to get started.

And as I said, we're very excited to use this product, both for the acute phase, but I think it will be important to see how patients that receive it and recovered how they're left with it with respect to the pulmonary function will be improved, because they will be less, likely with less fibrosis.

So these are the three comments and now we can take questions or discussion. Do you want to add anything?

MAMTANI: That's super helpful, Dr. Hidalgo. And I would like to ask Jen to talk about the program. So, Jen, as you talk about the iNKT cells approach, it would also be helpful as Dr. Hidalgo pointed out the lung inflammation part, but also the long-term immunity part, the durability of response that obviously from the vaccine priority, that's something we're watching out for.

And then also as due to the introduction of the company, we'd love to hear the broader pipeline that you're working on. So Jen?

JENNIFER BUELL: Sure. Thanks very much, Dr. Hidalgo and Mayank. That was a great introduction. I'm with Agenus and Agenus has been advancing immune therapies for ~26 years, born out of cancer immunology and vaccine biology and now a company with an extensive pipeline of checkpoint antibodies, cell therapy, adjuvants, and vaccines designed to activate immune response to cancers and resolve infections.

Dr. Hidalgo covered the relationship between infectious disease and cancer very eloquently. We are leveraging the immune system to fight cancer; with the most recent developments and approval of PD-1 and CTLA-4 and the profound efficacy that we're seeing with those agents and other immune-modulating molecules and cell-therapies, the reality of unleashing the immune system to fight cancer and infectious disease, like COVID-19 – has moved to the forefront which is quite exciting.

And Mayank, as you mentioned, we've been advancing therapeutic modalities for these diseaes for some time. We have leveraged our neoantigen cancer vaccine program to explore the immunization against viruses, like HSV-2 and co-administering it with an immune boosting adjuvant, QS-21 for viral elimination.

In our clincal trials with infectious disease, we saw profound reductions in viral load as well as very specific CD4 and CD8 responses. We illuminated disease specific responses by the vaccine; we have seen the same with cancer. We saw really profound anticancer benefits for patients, and immune responses to disease specific antigens, CD4, CD8 immune responses that not only were systemically evaluated, but also upon recurrence were able to interrogate the tumor and use the trafficking of those cells to the side of a tumor.

As we've continued to advance our pipeline, we have check point antibodies, both mono specific and multi specific antibodies. We validated IO agents advancing to BLA (anti-CTLA-4 and anti-PD-1) and first or best in class novel agents, such as an F_C engineered anti-CTLA-4 which is showing pronounced benefit for patients in the clinic.

We can leverage these platforms and apply them in infectious diseases as well as in cancer. We're doing that with the iNKT cell platform that Dr. Hidalgo just mentioned a few moments ago. iNKTs are relatively rare immune cells, they're called invariant NKT cells, which are specialized cells with T and NK cell properties. What we have already seen from preceeding technology is that iNKT cells demonstrate low to no graft versus host disease. We can administer them without any genetic manipulation – we can do so at speed and limited cost. As Manuel mentioned, we can manufacture cells from one patient to generate product for more than 1000 patients. In their unmodified format, they present a potential significant benefit to patients.

These cells specifically tumor targets CD_{1D}, these receptors are common in a number of different tumors, such as myelomas, hematologic cancers, as well as solid tumors, hepatocellular carcinoma, thymoma, and others. *And so we have been on a fast track to deliver iNKT cells to patients with solid tumors with the ultimate goal of demonstrating safety and then initiating combination studies with our portfolio of check point modulating antibodies to truly induce long-term durable curative responses for patients with cancer.*

When the pandemic hit, we started interrogating the value of these cells for patients with COVID-19. Patients with mild to severe COVID-19 have functionally impaired and reduced numbers of innate and adaptive immune cells. In data generated over the past six months. The infections characterized by lung hyper-inflammation, and in preclinical models that resemble similarities to the SARS and MERS, these NKT cells reduce viral shedding and have prevented inflammation driven lung injury.

We believe that iNKT cells actually promote viral clearance and stimulate a secondary antiviral immune response. And they also appear to control the inflammation IL1 and IL6, they appear to reduce or dampen a hyper-immune response that we're observing, particularly in the lung tissue which could be really quite beneficial.

Now we are FDA cleared to test the iNKT cells in their unmodified forms on patients with cancer as well as patients with COVID. The trial for patients with COVID will start first once it is clear at NYP. As Dr. Hidalgo said, we have had to make a few changes to accommodate new treatment regimens that were just recently approved and in that – and it's back with the IRB, so we're anticipating clearance imminently for this. The allogeneic approach that we've been able to generate is scalable. So we can take a healthy donor and generate enough cells for over a thousand patients. And that's just without any process development work. Thus, we are getting prepared to treat many patients.

We are looking forward to announcing first in man and getting some more information on the cells' persistence. Their ability to particularly convert patients who are more severely ill to remove them from ventilation and return them to health. So we're excited about it and I'm delighted to be partnered with Douglas's team at Cornell, it's an incredible group there. So thank you for the opportunity to talk about this program.

MAMTANI: Yes, no. I do have follow-up, Jen. Maybe a quick one and then I want to move to Racheli and talk about PLX platform. But quickly, your clinical trial is mostly the site with Dr. Hidalgo is or you're obviously moving as the pandemic kind of moves south, is that something that you are actively working on right now as you try to help more patients that could benefit…

BUELL: That's right. We are going to be expanding it. So we – we're starting with Dr. Hidalgo's site for a few reason, not the least of which is that's one of our sites for our cancer program, we are able to really quickly activate and the team there understood the technology very well, are very familiar with it because of our chance of collaboration.

So we – so that was our – the first priority, particularly given some of the sensitivities of this virus, and at the time when we submitted the protocol to the FDA, Manuel – Dr. Hidalgo's site was actually the most severely hit. They had a huge number of patients they were managing. So that was our first.

We are now in the process of expanding the trial to a number of other sites and nearby, we will be – we're working on a protocol to quickly activate in regions of greatest need.

So there's only a handful of centers that are looking for – that will be treating these patients and are looking for some support. So, yes, we will be expanding it and we're – but we're starting it at Cornell.

MAMTANI: Got it. Got it. And I'll come back to you with a couple of more questions I have. But Racheli, why don't we now talk about the PLX platform a little bit and I think the similar framework because you are – obviously ahead with your ARDS application there and sites already in Israel and US, maybe Europe also, I could be wrong there.

But seems like you're furthest ahead of the company that we have here, and you already have some interesting clinical data, I think seven or eight patients that you already had. So why don't you Racheli talk about the platform, the specific ARDS application that you have with the PLX PAD platform and then – and then we can take questions on the – on the clinical side.

RACHELI OFIR: Great. So thank you very much for inviting me and it's fascinating to hear the work of my other colleagues here. So I'm from Israel, from Pluristem, we're a clinical stage cell therapy company working on regenerative medicine and we have several allogeneic placenta derived cell products, all of our products are placenta derived.

We are into a phase 3 clinical trial with our similar products, one for critical limb ischemia, which is associated with diabetes complications and the other for muscle regeneration. So since we're already in phase 3, we have favorable safety profile and efficacy data from hundreds of patients with our placenta derived cells and we also have our unique manufacturing facility where we can produce a large number of cells in a bio-reactor three dimensional setting enables not only large scale manufacturing but also a very high level of control over the process.

And so as I said, the cells are from the placenta they are allogeneic, and we've been working on these few indications and during the process I've learned quite a lot on the mechanism of action, the mobility capabilities and also pro-regenerative and using antigens and other forms of regeneration.

And as the COVID pandemic started, we – very, quite fast became clear that a large part of the morbidity in these patients is due to the hyper-inflammation as my colleagues here stated and the cytokine storm. And this made us realize that all of the work that we've done studying the immunomodulatory effects of cells which were very relevant also for the other indications that we're working on is also maybe also very relevant for this pandemic.

And this includes very briefly inhibition of proliferation of T cells and optimization of the creation of anti-inflammatory cytokines and down regulation of pro-inflammatory cytokines such as CMSI, gamma I17, et cetera, also effect on the switching M1 macrophages to M2, the anti-inflammatory form inducing up regulation of regulatory T cells and, et cetera, in terms of immune modulation, and therefore as you said, we indeed approached both the Israeli regulator and the FDA.

We started with the – in the compassionate use program in the US and Israel, we have treated several patients, they, so far we've published the data on eight of these patients showing very nice survival data, 87 percent of the patients will survive, they were on invasive mechanical ventilation and we're, of course, following the other patients.

What we really need to do here, and this is clear to everybody that you have to have a controlled clinical trial, compassionate treatment, provide enough solid data, and we have a cleared IND in the US and we're expecting to have clear in Europe and we – in the next few days now. And we're activating sites who started in the East Coast but also moving to other hot spots of the pandemic in California, Texas, Arizona, Florida, the centers are moving so we are moving with them with opening the study.

The clinical trial is controlled randomized double-blind study, 140 patients with three doses and we're hoping to finish recruitment and the – and the 28-follow-up period by the end of the year. Hopefully the patients will not jump in, but if they are, then we're already there to treat them. I think…

MAMTANI: And it seems like – that's a very helpful overview. It seems like this study is a pretty large enough study, I think 140 patients and the endpoint being 28-day ventilator free primary endpoint. So is this potentially in some way a registration study, you think? And then I also – the follow-up here is like how long do you have to go from a safety standpoint, because some of these endpoints are quicker, but then it is cell therapy at the end of the day.

OFIR: Yes. So as you said, indeed we targeted a relatively large population and so in the case that we have the robust data, efficacy data, then it is expected to support registration, of course, this depends on the data.

As for the safety, we are obliged for 52-week safety. Follow-up, nevertheless, since we do have a very solid safety data on patients receiving these cells in other indications, so we are quite a positive in thinking that if the efficacy data is strong enough, it could lead to registration.

MAMTANI: Got it. Got it. And then I'll come back with a couple of specific questions I have on the study. But moving on maybe Daniel, I feel like you're taking on the – probably the biggest challenge longer term of trying to cure something that has not – like something we have not – we have tried but not really kind of given up more lately.

So why don't we talk about your platform, the CRISPR-Cas9 platform that you have and seems like you have obviously been at this for a little while and you have interesting preclinical data that is supporting your IND filing. So why don't you talk to us about that and then – and we can learn how longer term a platform that could be curative to infectious disease, we can learn about that from you.

DANIEL DORNBUSCH: Sure. My pleasure. Thank you very much Mayank and thanks for the B. Riley team, Andrew Smith, Matt Feinberg, and Jason Buttles, you've got a great team. We take a bit of a different approach here at Excision.

Excision is a private company here in the San Francisco Bay Area using CRISPR editors to cure viral infectious diseases. So we take the in vivo gene therapeutic approach and are doing something just a little bit different. Certainly our lead program as Mayank mentioned is an HIV, would be a one-time administration cure for HIV.

We are the first, I guess, and only still company to be able to achieve functional cures in HIV in animals with a therapeutic. We published that in Nature last year, we're currently about to – we now have finalized our preclinical package along two different primate studies, IND in process, we'll be submitting our IND later this year for clinical trials next year.

So what we're doing is we've applied new breakthroughs in CRISPR biology to therapeutic treatment. So what we do is by administering currently using AAV9 to administer CRISPR, we've been able to remove HIV genomes from animals, we now have a pipeline that includes Hepatitis B, Herpes virus, as well as JT

virus, we've got its PML. And now relevant to the – to the discussion, we're using the same approach in a slightly different way for COVID-19 and SARS CoV-2 to be specific.

So what we do is in most of these with the exception of SARS CoV-2, we go, and we actually remove the HIV genomes from animals to create functional cures. The – while this has been tried for many years, you can take a look at a litany of different approaches using gene editing technologies for viruses, everything to-date before our had failed and so let's take HIV as an example, whether it's thick fingers meganucleases, there's been no shortage of gene therapeutics applied but they've all failed because of essentially the viral escape mechanism, viruses especially retroviruses are very good at evolving around limited base edits to their genes.

What we do which is a different approach and we submitted patents back in the 2013 timeframe, have now issued patents, if – and the contract is to actually essentially chop up viral genomes. So rather than making a single cut using the traditional approaches, we use multiple guides to make multiple cuts into a viral genome, thereby removing thousands of base pairs and not leaving anything of the virus behind to replicate. Essentially a simple concept that took the company several years to prove that it works, but we do a couple of things that are – that are different in that approach.

The first is in the targeting and cutting, we only target nonhuman viral genomes with our pipeline which minimizes our chance of off target effects. Second is we're not replacing genes as most companies do. All we're doing is returning the human genome to its native state, something – the way it should be there in the first place. These are the primary reasons that we haven't seen any off-target effects and we've seen incredible safety in our preclinical studies in multiple species. And the last duration of efficacy, we can now – we're looking for very quick turnarounds, this is not for the lifetime of patients in terms of activity of our therapeutics.

We're looking to go in, remove the virus, and be done. So this has implications to certainly shorter preclinical and clinical trials, monitoring patients to show that we can reduce viral loads enough for the immune system to come, take over and essentially defeat the virus and in the case of HIV, have patients come off of their antiretroviral therapies ideally for the rest of their lives.

MAMTANI: That's fascinating and a helpful overview. Maybe Daniel, a couple of things, if you could address specifically about this concept of vital rebounding and then also how – like you are able to cut off these large sections of viral DNA.
Like – so just maybe about the platform if you could be more specific how longer term you could – you're so confident you can have that doable effect.

And then also on the preclinical toxicology work, could you maybe give us more details on the different species that you tested on and how long has that exposure been and, again, we can follow up on the Nature paper that you mentioned but just at a high level would be helpful.

DORNBUSCH: Yes, my pleasure. We used, as I mentioned, multiple guides with CRISPR to make more than one cut. For example, in our ABT-101 program for HIV, we're using two guides; for JC virus, we're using three guides; for herpes simplex, we actually use four guides, and all of these are in our analysis development the most efficient way to cut and deactivate the viruses in *in vivo* systems.

So, for HIV, for example, we took humanized mice, inoculated them with HIV, put them on antiretroviral therapies and so as you would imagine, the HIV level, the RNA goes to zero, undetectable. We then dosed these animals with CRISPR and have them – we, actually, took them off of antiretrovirals three weeks before we dosed them with our therapeutic.

And just under half of the animals, we saw no rebound, meaning the animals did not bounce back and show HIV. Every other experiment to date in animals when they had been removed from antiretroviral therapy, just like in humans, except for the Berlin patient, of course, a special case, their titers came back and the HIV rebounded.

What we're doing in the case of at least HIV is reducing the viral loads to the point that the immune system can take over. And what we saw in the animals that did not rebound that their CD4 counts came back up to almost normal levels.

And that's we think is the critical component in order to achieve a lasting, we call it functional cure, meaning, HIV does not rebound. We now can show – we haven't published it yet, but we will show soon, we have the data in our long-term primate studies that the same thing happens in primates, that the CD4 counts go right back up to normal levels where the antiretroviral treated animals only don't. So, that's the case for HIV.

JCV is a bit different. Deactivating the JC virus, at least our clinical investigators that we've been speaking with for a potential clinical trial here coming in the next couple of years, that this approach – if you know the PML market – everything has failed to cure or prevent PML. This approach, our clinical investigators think this could actually be a true way to defeat that indication.

Herpes simplex, we'll be working on a topical or subQ administration for CRISPR. There's some really good data currently that that kind of approach could work for a gene therapeutic.

And lastly, our COVID-19 approach is slightly different. Rather than approach the virus directly like most other or maybe all other companies are doing, ours is a little bit longer term. We're actually looking to deactivate the receptor and co-receptor, whether one or both is essential, we'll know.

But, exactly, the idea would be it would be a one-time administration and a treatment as well as preventative for SARS-CoV-2 or whatever mutation comes down if there's another pandemic in future years, that this would essentially be used for or useful for any corona or even norovirus.

MAMTANI: Got it. Hey, actually, that is really a nice segue to bring back Dr. Hidalgo. In previous panels, Dr. Hidalgo, we discussed about how to be better prepared and think more pan-coronavirus not just SARS-CoV-2.

And also, specific to the program that you're involved with, agent-797 it's a two-part question. Just broadly how to think about longer term when you think about

pan-coronavirus approaches and then specifically with active clinical trials you are enrolled with, as Jen mentioned, there are things that are changing standard of care with regard to dexamethasone coming out of left field.

So, just kind of how do you think about some of these changes that have to made in real time, some of these real time trials that are consideration which I'm sure that JD is also thinking about. So, maybe Dr. Hidalgo, it would be really helpful to hear from you just the longer term and the real world on the scene application today.

Are you on, Dr. Hidalgo? Dr. Hidalgo, can you hear us?

OPERATOR: This is the operator. It looks like Dr. Hidalgo may have disconnected instead of unmuting his line.

MAMTANI: Oh, OK. So, maybe, Jen, I think you can take the second part of that question and then we can have him comment on the first part when he's back. Jen?

BUELL: Maybe just for the two parts, what was the second part that you wanted me to highlight?

MAMTANI: Yes. The second part was like a lot of the protocols just need to be changed in real time. I think you also mentioned your entity with steroids now taking center stage. So, just talk to how you're thinking about your trial execution, and also, I think it would be a good point to highlight about the like the correlates of both viral protection and also immunity that you're looking out for when the study kind of gets to that endpoint.

BUELL: Well, I think it's a matter of the dynamics of the landscape right now and I think flexibility and agility is going to be really important. I think being really measured about what you can actually get out of an early trial in such a dynamic landscape. New treatments are coming in all the time and physicians are working aggressively in real time with patients based on – and sometimes customizing therapies based on comorbidities or other issues that they're trying to manage.

So, we have – one way you can mitigate against some of the dynamics here is through a really robust pre-clinical plan. We had that data due to our longstanding work in this area.
HIDALGO: Hi. I'm back.

BUELL: Oh, hi, Dr. Hidalgo, you're back.

HIDALGO: Sorry. I was just going to – yes, I know you were asking a question.

MAMTANI: Go ahead.

HIDALGO: But I got cut in the middle of it so...

MAMTANI: So, Jen is taking the second part of the question maybe, we can have you address the first part. Go ahead, Jen.

BUELL: But I think that part of testing in a pandemic is that you just have to be ready for almost anything. I mean, there were depleting agents that were being discussed. And so, we've generated some data across a lot of different approaches that help us to understand what the impacts might be to our therapy and what we can interpret from the data that we're generating, and we'll have to stay quite flexible to observe other changes as well.

MAMTANI: And quickly, Jen, the correlates that you – from the study that we should be looking out for, like should we expect for a strong antiviral response in a short period of time that we are looking at here?

BUELL: Well, with COVID, the antibody responses, the T cell responses, natural killer responses, are all important and we would expect some of the durability and memory responses.

MAMTANI: OK.

BUELL: We also think that we might have some myeloid modulation with these cells. They've got some important MDSC capabilities. So, we'll get information and persistence, on homing where the cells are going, and we'll certainly get information on pro-inflammatory cytokines and the impacts of these cells on dampening those cytokines.

MAMTANI: Great. And, Dr. Hidalgo, maybe since we have you back, could you also just provide your perspective on this study that obviously you're part of? But also, the bigger question I had for you was as we think about preparedness towards the next pandemic and a lot of conversation in previous panels was about pan-coronavirus, how can we kind of be prepared for that next pandemic. So, can you talk about that bigger consideration as you're learning from what we are going through today but...

HIDALGO: Yes, sure. I think that being prepared is a multi-pronged approach. Certainly at the hospital level, we need to be prepared in terms of more equipment, more ICU beds, more respirators, having the ability to deploy teams in a faster manner, cohorting patients, everything that has to do with treating the patients aggressively and rapidly and also all the public health policies and recommendations.

MAMTANI: Of course. Yes.

HIDALGO: I don't want to talk about that.

MAMTANI: Yes.

HIDALGO: In terms of medicines, of course, it will be ideal to have a vaccine, right, because if we have a vaccine and we are able to vaccinate the population, that will be fantastic. We still need to know how preventive or protective I should say antibodies are. And if there's going to be a time where we'll reach herd immunity across some communities, that will be – that will be important because the problem is not so much to have cases, it's to have cases all of them at the same time. So, anything that we can do to spread, to flatten the curve will be very important.

But going back to our product and the agent we are trying to develop, I think that there may be opportunity for cell therapies that stick around for a while and can create really longstanding immunity that administration of one of those treatments early on in the course of the disease before the patients become with the need of being intubated or even hospitalized could be another approach to test.

So, I think there's a role for treatment strategies that can be sort of effective and long-lasting. And that will be as important as having a vaccine.

MAMTANI: Right. Right. And we covered the vaccine part of this at length, and as you know there are several approaches and a lot of data to sift through that we are learning in real time, but that's great.

Racheli, maybe scale of some of these approaches, I'm glad all of this is allogenic. I feel like, Racheli, maybe there is something you can talk about your approach that really can obviously in the clinical trial setting be helpful for the number of patients you are trying to treat. But also like wherever like this pandemic or the next pandemic takes us, I feel like you have the placenta-based things that you – so, could you talk to that maybe Racheli and this would be good, helpful approach for any cell therapy.

Again, they're not comparable by any means but just your learnings would be useful if you can share that, Racheli.

OFIR: So, we've been very interested in the immunogenicity of these cells, of course. A lot of the stromal cells, mesenchymal cells, mesenchymal like cells, they have low immunogenicity. Nevertheless, the immune system is not blind to them. We know there is an interaction and part of our mechanism of action is by interacting with the immune system.

And we were very interested in our clinical trials to see if there is any immunogenicity, any antibodies or any other form of immunogenicity developed following the administration of our cells, and especially since we have some of the indications when we did the repeated administrations of the cells. And since we have cells from several placentas, we can check if the immunogenicity is stronger following repeated administrations of cells that are from the same HLA typing.

And the findings are a little bit not completely clear. What we can see, there is no memory T cells against the cells. In some cases where the patients, usually when they were pre-sensitized maybe because of pregnancy, maybe because of biological treatment, maybe because of blood transfusion, we can see some development of antibodies following repeated administrations of the same HLA.

Nevertheless, some patients got repeated administrations of the same placenta without development of antibodies. The majority of the patients did not develop antibodies against cell therapy, and the ones that did were usually the ones that already had anti-human HLA antibodies to begin with.

The effect was never clinical. We never saw any clinical effect of the – because of the allo-transplantation, but if we want to maximize the efficacy of the cells and elongate the persistence as much as possible then we want to avoid such allo-antibody development. So, it's good to know that it is a rare event, but it does happen sometimes.

MAMTANI: OK. That's great. I think we're almost at time – sorry to cut you off, Racheli. We're almost at time and I know people have hard stop.

But, quickly, just a question, Jen, I had on – could you, Jen comment on the QS-21 adjuvant and the thinking there on how that could be applied to the vaccine potential there. Could you maybe just give an update on specifically – I know that's part of the Shingrix program with GSK, any update there would – I got this question over email – so, if you can address anything, that would be great.

BUELL: Of course. Of course. QS-21 is near and dear to me. Just by way of background, it's an immune-boosting adjuvant. It's generally manufactured from Chilean soap bark tree. And we're funded by the Bill & Melinda Gates Foundation in a partnership to generate a sustainable supply and that work is undergoing. We have preliminary evidence that we have identified the path to have a sustainable source which is very exciting.

That particular adjuvant is currently licensed to GSK for the Shingrix vaccine for shingles and it generates over 90 percent immunity. And most importantly, it generates that immunity and gets stronger over time which is unlike competing shingles vaccines and it benefits the elderly. It's very effective in elders and elders, on earlier vaccines that were less effective waned over time, their efficacy waned over time so that as people got older, their immunity was less.

And with QS-21, we see a more pronounced response over time which is very, very valuable. We are developing this product for use in a number of other vaccines in oncology but now also in infectious diseases actually including COVID and we've got a number of business development discussions underway to allow, enable access to QS-21.

The government has requested that vaccines for COVID meet about 50 percent efficacy but many of the world health experts have said that you need to exceed 70 percent to actually eliminate this pandemic, which is something we all want to do. With QS-21, we may be able to do that.

So, Shingrix is the most successful vaccine, the most efficacious vaccine with the responses that we've observed to date. And we know that that's in large part due to QS-21 and data have been generated to demonstrate the value of QS-21.

There is a need to increase the efficacy of the vaccines that currently are under study and QS-21 could be a way to do that. So, we currently have in supply the general material and the production method that we've always used and that has been used for the QS-21 and Shingrix and we're in the process of actually scaling that with the eternal sustainable supply which is actively underway right now.

MAMTANI: OK. Great. And we all do, I guess learn on that as you advance in the scaling and all the development efforts.

I really appreciate everyone's spending this time with us. This was I think real – I learned a lot personally and really excited about the fascinating work you all are doing in your respective companies.

So, again – and then especially, Dr. Hidalgo, I appreciate you joining us and giving us a clear view of how you're seeing things with patients on the field, and most importantly, thank you to our audience, too, having stayed with us for the past three and a half hours. Thanks again and back to you, operator.

OPERATOR: And that does conclude today's conference call. We appreciate your participation. You may disconnect your lines at this time and have a great day.