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Q3 2018 Adaptimmune Therapeutics PLC Earnings Call

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PRESENTATION

Operator

Good day, ladies and gentlemen, and welcome to the Third Quarter 2018 Adaptimmune Earnings Conference Call. (Operator Instructions) As a reminder, this conference call is been recorded.

I now like to introduce you host for today's conference, Ms. Juli Miller. Ma'am, you may begin.

Juli P. Miller *Adaptimmune Therapeutics plc - Director of IR*

Good morning, and welcome to Adaptimmune's conference call to discuss our third quarter 2018 financial results and other business updates. We issued a press release earlier this morning, and I would ask you to please review the full text of our forward-looking statements. As a reminder, we anticipate making projections during this call, and actual results could differ materially due to a number of factors.

James Noble, our Chief Executive Officer; Rafael Amado, our President of R&D; and Adrian Rawcliffe, our Chief Financial Officer are with me for the prepared portion of this call. And other members of our management team will be available for Q&A.

With that, I'll turn the call over to James Noble. James?

James Julian Noble *Adaptimmune Therapeutics plc - CEO & Director*

Thank you, Juli. Good morning, everyone, and thank you for joining us. After my brief remarks, I will turn the call over to Rafael for a clinical update and then to Adrian for a financial summary. Then, I will give a few closing remarks and open the call out for Q&A.

We have completed the third dose escalation cohort of our MAGE-A4 basket study and our MAGE-A10 triple tumor study. The Safety Review Committee agreed yesterday that the more intense preconditioning regimen and higher cell doses are tolerable and agreed that the studies can now move into the expansion phase. This allows us to use doses of up to 10 billion cells without a stagger between patients.

Our MAGE-A10 and MAGE-A4 studies are first-in-man dose escalation studies, and a critical aspect of these first 3 cohorts was to discharge any safety concerns such as off-target toxicity or dose-related safety concerns. We have only dosed 3 patients in the third cohort of the MAGE-A4 basket study and 4 patients in the third cohort of the MAGE-A10 triple tumor study at target doses of 5 billion cells. And we need to accumulate an adequate amount of clinical assessment in a broader range of solid tumor indications and a larger number of patients to draw any meaningful conclusions. Therefore, we plan to report data on these patients at the same time, as some expansion phase data, by no later than our first quarter financial results in May 2019.

I also want to update our progress with our AFP study. It is worth noting that AFP is not a cancer-testis antigen, like MAGE-A10 and

MAGE-A4, and it is highly expressed in a subset of hepatocellular carcinomas. AFP itself is actually used as a diagnostic biomarker for this malignancy. To date, we are very pleased with our progress dosing patients in the first cohort of our AFP study, and we anticipate that we will escalate Cohort 2 early next year.

With that, I will turn the call over to Rafael for a clinical update. Rafael?

Rafael Amado ***Adaptimmune Therapeutics plc - President of Research & Development***

Thank you, James. I will briefly summarize the current status of our clinical programs. As James said, we have been progressing through our studies with MAGE-A10 and MAGE-A4 and AFP. We have completed the transition of our NY-ESO program to GSK, which has enabled more focus on our wholly-owned assets.

We have treated 9 patients in total with MAGE-A4, 3 patients in each of the 3 dose cohorts, 7 of whom were women with rare encounter. In MAGE-A10, we have treated 8 patients in Cohort 1, 3 patients in Cohort 2 and 4 patients in Cohort 3. Eight of these patients have lung cancer and were treated in Cohorts 1 and 2 of the MAGE-A10 lung cancer study.

Assessments for the patients in the third cohort are in progress. The Safety Review Committee met yesterday and reviewed data from 7 patients dosed in the third cohort of our MAGE-A4 basket study and MAGE-A10 triple tumor study. And they agreed that these studies can now move into the expansion phase.

At ESMO, we presented data on the first 2 cohorts for MAGE-A4 and MAGE-A10. As expected, the 100 million cell dose was subtherapeutic, with no antitumor effect and poor expansion and persistence. Although, a dose of 1 billion cells could potentially be associated with antitumor activity, we did not observe any responses per RECIST criteria in this MAGE-A4 and MAGE-A10 cohorts. This could be due to a number of variables, such as type of tumor, pretreatment history, conditioning regimen, degree of antigen expression, to small number of patients and importantly cell dose.

It is worth noting that we only saw responses above 1 billion cells with NY-ESO and that the median dose among responders in Cohort 1 of synovial carcinoma was 5.1 billion cells with a range of 2.2 billion to 8.3 billion.

We have data indicating that the intensity of the preconditioning regimen as well as cell dose are critical for SPEAR T-cell expansion, both infusion and for responses. Specifically, we have observed that certain gamma-chain cytokines such as IL-7 and IL-15, which correlate with T-cell expansion, are significantly higher in the peripheral blood of patients who received more fludarabine than those who have less intense preconditioning. And we will present this NY-ESO data at SITC later this week.

In addition, the NY-ESO sarcoma trial shows a relationship between lymphodepletion dose intensity, T-cell expansion, response rate and response duration. Based on this data, we added an extra day of fludarabine to the third dose cohort and the expansion phases of this study.

Focusing specifically on data from the second cohort, in which patients received the target dose of 1 billion cells, we only have data from 3 lung cancer patients from MAGE-A10 and 3 patients with ovarian cancer from MAGE-A4. We saw expansion of our transduced cells at peak levels of approximately 20,000 vector copies per microgram of DNA in MAGE-A10 patients.

In MAGE-A4 patients, the expansion was slightly higher with 1 patient reaching levels of around 100,000 copies in whom some evidence of transient antitumor activity was observed.

Following our recent presentations at ESMO from Cohorts 1 and 2 of these studies, there have been comments about adverse events, with speculation that there may be a correlation between neurotoxicity, cytokine release syndrome and cell dose. I want to clarify that to date, the most frequent adverse events and treatment-related adverse events, irrespective of those, were consistent with those typically experienced by patients with advanced malignancies undergoing cytotoxic chemotherapy or other cancer immunotherapies, including low frequency of cytokine release syndrome and low-grade encephalopathy. All events resolved after treatment, and we have not seen any concerning correlation between cell dose level and CRS, encephalopathy or other side effects even in the third dose cohort, in which

patients received target doses of up to 6 billion cells with more intense preconditioning.

The third cohort of these studies were designed to include a minimum of 3 patients with a predetermined lag between dosing. We have dosed 3 patients in the third cohort of the MAGE-A4 basket study and 4 in the third cohort of the MAGE-A10 triple tumor study, and we did not see any dose-limiting toxicities.

As we move into the expansion phase for these 2 studies, we no longer have a predetermined lag, and we will be able to gain information more quickly from those patients with a higher preconditioning than the regimen we use for the first 2 cohorts.

Further, to be able to make meaningful clinical evaluations of the potential of this therapy, it is important to evaluate a greater diversity of cancer types than we had in the first 2 cohorts. And there are eligible patients across a broader range of indications for the expansion phases of these studies, including indications in which T-cell therapy has been shown to be affected, such as melanoma and sarcoma.

As we accumulate clinical data across a broader range of cancer types, we will report them for the third cohort of these studies as well as for the patients in the expansion phases.

We remain optimistic that with better expansion and trafficking of SPEAR T-cells to the tumor with higher cell doses and more intense preconditioning, we may see patient benefit.

Now I would like to turn the call over to Adrian.

Adrian Rawcliffe ***Adaptimmune Therapeutics plc - CFO***

Thanks, Rafael. This past quarter, we completed the transition of the NY-ESO program to GSK. In financial terms, we have received payments of approximately $150 million from GSK since 2014, including the $26 million received in Q3 as a result of the transition. We may also receive subsequent development and sales milestones and royalties based on successful development of the NY-ESO program.

Lastly, on NY-ESO, there will be an update of the MRCLS data and the translational data in synovial sarcoma, which will both be presented at SITC. The abstracts were published today, and details of these data are included in our press release and in our 10-Q, which will be available later today.

Also in the quarter, we announced the closing of the registered direct offering of our ADSs, with net proceeds of approximately $100 million, which extends our cash runway to late 2020.

And with that, I'll turn the call back over to James.

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

Thanks, Ad. In considering the data presented to date, I want to emphasize that we've only dosed 3 patients in each of the second cohorts of the MAGE-A4 and MAGE-A10 studies, which is not a sufficient number to draw conclusions, particularly given the limited number of tumor indications represented in these early cohorts.

It's also important, as we look back at 2018, that we acknowledge other progress we have made. First, we've seen no evidence of off-target toxicity to date. We are now in the expansion phase of the MAGE-A4 study and MAGE-A10 triple tumor study and can dose without a predetermined stagger. We anticipate moving into the expansion phase of the MAGE-A10 lung study in early 2019 and dose escalating to the second cohort of the AFP study in early 2019.

We've added more centers for our MAGE-A10, MAGE-A4 and AFP studies. We have evolving translational data that enables better understanding of our products and how to improve them, some of which will be presented in 1 of the 2 posters at the upcoming SITC meeting at SITC.

We are routinely manufacturing cell doses of 5 billion or more transduced cells at our Navy Yard facility, and we are progressing with our

Catapult facility in the U.K. for vector manufacture. We are prepared for the next steps of the company and funded to see our ongoing studies to the next phases of development. We are actively investigating our therapies to determine the best next steps, and we remain optimistic.

With that, I would like to open the call up for questions. Operator?

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Our first question comes from the line of Jonathan Chang of Leerink Partners.

Wei Ji Chang ***Leerink Partners LLC, Research Division - Director of Biotechnology & Senior Research Analyst***

First question, you've guided to providing a clinical update by no later than your 1Q earnings call in May. How should investors be thinking about potential updates between now and May? And how are you thinking about your overall strategy in terms of data disclosure?

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

So thanks. That's obviously a key question. Essentially, we've been looking forward at the runway, if you like, of the patients and the number of patients who will be dosed and the time of the data will come from. Essentially, if you take a single patient, you have to remember that if they're dosed today, we wouldn't take the first scan until 4 or 6 weeks depending on the trial. And then, to get a confirmed response, it's a further 4 weeks after that. So even if you dose someone today, it takes 2.5 months to get a response. So what we've been emphasizing in the press release is that we think that it's the most sensible thing to get a reasonable number of patients. And bear in mind, we're only just getting out of the staggered dose 3 cohort across indications. I think it's unfortunate and just -- its just the way these things happened that we ended up with purely ovarian patients in the second cohort -- and actually, the first and second cohorts of MAGE-A4, and I think it's important for us to test it. So where we have material data before then, we will be telling investors, and, of course, we'll be attending JP Morgan. But I'm trying to guide the fact that when I look at the runway, the -- we will have a decent number of patients with a decent interval after they have been dosed by that of the latest. And that's what I'm trying to guide to. Obviously, if we have something very material before them, we'll have to -- we'll be discussing it earlier and we will be at JP Morgan.

Wei Ji Chang ***Leerink Partners LLC, Research Division - Director of Biotechnology & Senior Research Analyst***

Got it. Second question. Now that the Safety Review Committee has recommended moving into the expansion phases of the MAGE-A10 triple tumor and A4 basket studies, can you talk about the overall lessons learned in terms of the safety of your platform? And you mentioned this earlier, but I love to get any additional color, have you seen any correlation between safety signals and the higher dose levels?

Rafael Amado ***Adaptimmune Therapeutics plc - President of Research & Development***

Yes. I think overall, there's been sort of 3 areas where the toxicities are focused on. One is this chemotherapy side effects, mostly myelosuppression, which in the first 2 cohorts was quite mild and then we've actually added a day of fludarabine, and so far have been resulted in worsening neutropenia or febrile neutropenia or infections, but patients do get myelosuppression. The other is immune-mediated responses. So we have seen, as we said at ESMO, low-grade encephalopathy, which is now picked up more readily because they are very thorough assessments that most tertiary care centers do looking for clues of mental status changes, disorientation, et cetera. And the patients are querying like 3x a day. So it's easier for this diagnosis to emerge. So -- but the highest grade has been Grade II and resolved with tocilizumab. And the third area is disease related. So some of the patients, unfortunately because of the stagger, they have advanced cancer and they may have symptoms related to their disease or eventually disease progression. I think the most important feature for us is that we haven't seen a dose-related sort of increase in toxicity either one of the 3 that I mentioned. And clearly, no evidence of cross-reactivity, which is, obviously, the toxicity that one worries about in this field. And so we are pretty happy actually moving into the expansion phase, knowing that now that there's a shorter lag, patients won't have to wait that long and patients would be fitter with other more diversed set of tumors. And knowing that the tolerability, that's an entailed cross-reactivity, which would have been very worrisome for these programs.

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

Yes. I think in terms of platform, I think we have described before how -- that we have a very comprehensive preclinical testing program. And I'd say that what MAGE-A10 and MAGE-A4 have shown really is what we saw preclinically, we've seen clinally, so that's obviously very encouraging. But every product is its own product. So you have to make sure you do it diligently for every new product as you did in the past. But when -- I think one thing we've also learned that is that while the 100 million cell dose is, obviously, a nice starting point, because of the very limited expansion, we don't really think you get a definitive answer as to whether the toxicity is at that level. So I think the lowest level probably doesn't show very much. And that's why we, as a company, are so pleased that we've got through the 1 billion and the 5 billion cell dose because at that level you certainly would pick up any cross-reactivity. So I've been encouraged by both the preclinical sort of platform and the fact that the doses even where we have seen reasonable expansion, we're not seeing cross-reactivity, which is definitely the most concerning toxicity you could hope not to see, and we haven't seen it.

Wei Ji Chang ***Leerink Partners LLC, Research Division - Director of Biotechnology & Senior Research Analyst***

Got it. And just one last question, if I may. Can you talk about reasons for confidence in the ability to approve upon the durability of the responses in stable diseases that you saw so far?

Rafael Amado ***Adaptimmune Therapeutics plc - President of Research & Development***

I think the lessons that we have are from NY-ESO, and the durability has been variable. We have been learning from our tissue collection and serum markers, such as persistence, cytokines, the type of cells that persists, what's in the tumor ability to traffic into the tumor. We have a nice summary of all those data as we mentioned during the prepared remarks at SITC. We think, obviously, that persistence is important, that trafficking to the tumor bed is important, that the degree of conditioning is important, and that there's a minimum threshold of cells that's required for activity to be seen. And so I think if -- in the right patient, with the right conditions, the responses can be quite durable. And we have had patients in the synovial sarcoma program that have enjoyed very long remissions. And then, patients that have had remissions and then minimum increase in a single lesion, which they had irradiated or resected, and the patient has remained with functionally controlled disease without any therapy. So I think this treatment has the potential to control disease long-term. But obviously, with this wholly-owned programs, we need more experience. And I think we're now well poised to start testing them.

Operator

Our next question comes from the line of Marc Frahm of Cowen and Company.

Marc Alan Frahm ***Cowen and Company, LLC, Research Division - VP***

It's, I guess, for James and Rafael. James, in your prepared remarks, you mentioned you kind of difference of AFP relative to the other targets you've tested not being a cancer-testis antigen. If you just think back now you know more that you've learned about MAGE-A4, MAGE-A10, are there any kind of material differences when you look at them as a target versus NY-ESO as a target?

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

So between MAGE-A4 and MAGE-A10 on the one side and NY-ESO on the other...

Rafael Amado ***Adaptimmune Therapeutics plc - President of Research & Development***

AFP.

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

And AFP on the other. So AFP is obviously not a cancer-testis antigen. And the reason that we were, I think, rightly cautious about the trial is that it's expressed on some healthy liver progenitor cells. So far so good on that. So I don't think we see differences between MAGE-A4, MAGE-A10 and NY-ESO in terms of sort of characterization; obviously, there are in terms of populations of patients and different percentages of patients. But actually, I think, generally speaking, NY-ESO is a more heterogeneously expressed antigen than the other 2 and MAGE-A4 -- as it happens that MAGE-A4, MAGE-A10 in vitro killing is slightly superior. But I think that -- I don't think they are fundamentally different. I mean, none of the 3 has any known purpose in terms of the -- any function. So they're just flags, they are just targets for different T-cell receptors.

Rafael Amado ***Adaptimmune Therapeutics plc - President of Research & Development***

Yes. I would just add that alpha-fetoprotein is -- when it's expressed, it's expressed at really high levels. So the cell is not only expressive, but secretes this protein, and the peptide is very well characterized. We know it's real and it's been described before. It's the same peptide that TCR mimic from Eureka is targeting. The secretion of the protein allows us to diagnose patients and select patients, which is very useful in a clinical program. And it has the potential to actually be picked up by antigen-presenting cells and amplified in immune response. But more importantly, it's expressed in most of the tumor cells. And as you now, cancer-testis antigens sometimes have heterogeneous expression. The other thing that's interesting about this is that it's in hepatocellular carcinoma, and the liver is one of the first-class organs where these cells go. And so the homing and the trafficking, which is important for the success of these therapies is almost guaranteed in this disease. So obviously, we're cautious because of the toxicity, but we're pleased that we have not seen at least in the low doses any normal liver injury. And so far, AFP appears to be presented and seems to be immunogenic. So we're pretty hopeful about this program as we move forward.

Marc Alan Frahm ***Cowen and Company, LLC, Research Division - VP***

Okay. And then you mentioned, you're having premanufactured cells for some patients. And I think even in the ESMO presentation disclosed the number of patients who are awaiting therapy. Now that you've cleared the mandated safety windows, how fast do you think you can actually manage from a clinical trial infrastructure position and from a corporate risk perspective to ask how many patients do you think you can dose kind of on a monthly basis across the MAGE trials?

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

The manufacturing capacity is around 2 patients a week in the Navy Yard facility and another 2 patients a week in the HCATS, Hitachi, which is the old PCT in Allendale, New Jersey. So that's the sort of overall capacity. But that doesn't mean you dose that many patients. So that's the sort of maximum capacity we run at, at the moment. What happens is though that many patients we've made cells for, who are actually not ready to receive the cells, so these are patients who are either going through some other form of treatment from their doctor or they're are not progressing. So obviously, we have to get through that list. So there's quite a --- there's a backlog of those, if you like, to address. And then, as I say, the most as sort of -- the most of one could hope for is to go to 2 a week or week to the 2 sites. But it is very important to think about the dynamics of all of these programs. What actually happens in practice is if you see some encouraging data, let's say a response in a particular indication, you'll suddenly find you get enormous number of patients suddenly put in for screening in that indication, and you can see that in the MRCLS stage -- MRCLS cohorts and the previous synovial sarcoma cohorts. What then happens is it goes a bit slowly until you see something, and then you get a -- you'll get a rush of patients. So it will be indication -- that would be indication-specific, I think, that certainly was in sarcoma before and multiple myeloma. We did the trial and the same thing happened. We started getting responses. We started getting quicker treatment. So we -- and that's why I say, I think we should have a decent number of patients to report on by the 3, 4, 5 months away.

Marc Alan Frahm ***Cowen and Company, LLC, Research Division - VP***

Okay. And then, I guess, you mentioned the 7 out of 9 ovarian cancer patients in MAGE-A4 and the lung cancer patients in MAGE-A10. Have you now dosed anybody from these tumor types like synovial and MRCLS, where we kind of know T-cells can work?

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

We've dosed 1 synovial sarcoma patient in Cohort 3. We have not dosed an MRCLS patient.

Operator

Our next question comes from the line of Robyn Karnauskas of Citi.

Robyn Karnauskas ***Citigroup Inc, Research Division - Director and Senior Analyst***

So just want to ask quickly about the AFP -- about AFP. So couple of questions. So what are your thoughts about the competitive landscape? What are your thoughts about repeat dosing, whether you think that's necessary? And then expand that into like thoughts about what we're starting to see about good data coming after out of repeat dosing for solid tumors? And how you think that will inform your decision when you develop plans going forward?

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

So I'll start off, then Rafael will give the things. We have repeat dosed a number of patients in the sarcoma studies in the past. It was up to the clinician involved actually. And interestingly, one of the partial responders in the MRCLS study on repeat dosing became a complete response -- synovial sarcoma Cohort 4, it was, sorry, became a complete response after being a partial response, who has then relapsed. And on second dose, we used to take the view that there was only if at any point, if the T-cells -- if the transduced T-cells had disappeared for some reason and the tumor was still there and still antigen positive, so that's why we didn't dose very many people. In the first cohort of synovial sarcoma, I think we redosed 2 or 3 patients. It proved that the cells could be kept because they were actually kept 18 months, I think, at least. You can keep them, and they're still perfectly viable when you put them back into the patient 18 months later. But we didn't see much effect. But then in the fourth cohort, we did see this one PR relapse go to a complete response. So I think that the data are going to merge. On AFP, we think the competitive landscape, we think, is immensely encouraging with the Eureka data, to be honest, because they are targeting exactly the same HLA, despite being a far eastern study. It's actually HLA-A2. So it is the same peptide and the same HLA that program and they did get responses. Now I'll let her Rafael complete it. Go ahead, Rafael?

Rafael Amado ***Adaptimmune Therapeutics plc - President of Research & Development***

I mean, it is the field that's changing pretty fast after a lot of many years without effective therapy. So of course, sorafenib and regorafenib are available. There's -- the checkpoint inhibitors are approved as single agent for persistent disease in the U.S. And there are some lung trials, as you know, that are going to redefine, I think, the treatment of this disease. So the fact that it is an immunogenic tumor, I think was a revelation, which is welcomed by the field. I think as James mentioned, the fact that the peptide appears to be presented by the encouraging data from Eureka. The question that we have is, if we have activity in hepatocellular carcinoma, what would be the place in therapy of this product? Because these patients can decline pretty fast. But I think that is something that we'll have to think through and design the trials in the best possible way. But there's definitely lot of room for improvement in this disease. And I agree with the repeat dosing. And I mean, fortunately, for these patients, we had a question as to whether or not we would be able to manufacture. The manufacturing for patients with liver cancer has been extremely successful. So we, obviously, cannot give most of the cells we make because we're still dose escalating, but it is a perfect setting in which to test repeat dosing as we gain more clinical data.

Robyn Karnauskas ***Citigroup Inc, Research Division - Director and Senior Analyst***

So when would you start doing repeat dosing, given that you've -- given the data that you know from the competitive landscape? How might you start incorporating that for AFP? And what about your thoughts on safety profile? Do you think you could have a similar safety profile?

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

I think, the -- I mean, the repeat dosing probably would come into play, I think, in 2 ways. One is, we are modifying the protocol to 3 patients that have received subtherapeutic doses during dose escalation. So the patients that are still able to be treated will get higher doses as we clear the subsequent cohorts. And then, during the third cohort and the expansion phase, I think we will want to see what the activity is with single agent at the top doses, which can be up to 10 billion. And then, if we saw responses depending on the durability and depending on what we see in the tumor, if there's been trafficking, the antigen is still there and there's no evidence that antigen presentation machinery has any deficit, then we would test repeat dosing. So I think we have a little way to go before we make that change in general. But as I said in the dose escalation, we will change the protocol to 3 patients at low doses, now that we know that is safer, at least, in the initial cohort. In terms of how we think about safety, our main concern was cross-reactivity with AFP expressed in normal liver. We biopsy all patients normal -- the normal liver of all patients, or the non-tumor liver rather, to rule out AFP expression. Of course, that doesn't guarantee that there won't be cross-reactivity, but as I said so far we haven't seen. And what we expect is the normal sort of immune reactions that we see with this adoptive T-cell therapy in other diseases. We started with lower dose conditioning. We are now increasing the conditioning to chemotherapy, it's also well tolerated. And the patients in this trial have to have good liver function. So overall, we're constantly optimistic that this will be tested fully, and hopefully we'll see some benefit as we go into higher doses.

Operator

Our next question comes from the line of Peter Lawson of SunTrust Robinson Humphrey.

Peter Richard Lawson ***SunTrust Robinson Humphrey, Inc., Research Division - Director***

Just as we think about trying to drive deeper responses in A4 and A10, what do you think gates that? Is it preconditioning? Is it is trafficking to the tumor bed? Or is it just hitting the right tumor type?

Rafael Amado ***Adaptimmune Therapeutics plc - President of Research & Development***

I think the -- I mean, trafficking is absolutely required. And we are -- we have shown trafficking in sarcoma. And we have -- in some patients upon relapse, we have seen that the tumors are no longer inflamed. And we are working on how to overcome that. But obviously, the cells need to get to the tumor. There are, obviously, other factors. As I mentioned before, the antigen has to be present. The antigen-presenting machinery has to be functional. There's a lot of resistance mechanisms that have emerged from the checkpoint field, some of which may overlap with cell therapies, such as loss of heterozygosity for the HLA in question or mutations in gamma interferon signaling and TAP proteins, et cetera, beta 2M. Those are fortunately rare, and we haven't actually seen that in the relapse patients in sarcoma, but conceivably that would be an issue. And the patients that we're treating have for the most part already seen checkpoint inhibitors, if they are of a disease where checkpoint inhibitors are approved. And so cell dose and conditioning are variable, so we can control. And then as we learn more about what mediates trafficking and persistence, then we could modify some parameters to optimize those factors. But we're starting in the monotherapy studies with maximizing doses, which for TCR seems to be critical and maximizing lymphodepletion, which allows for T-cells to expand and proliferate and traffic and kill. So those are some of the factors. There are a lot of other factors that we're exploring. But these are some of the ones that are readily modifiable in the clinic that we're testing.

Peter Richard Lawson ***SunTrust Robinson Humphrey, Inc., Research Division - Director***

And then James, would you press release the first response you've seen in A4 or A10? Or would you wait for really a larger cohort to kind of discuss that data?

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

Well, I think we've talked about how to difficult it is. We -- I'd much rather do a larger pool of data, but we are obliged, obviously, to put out material data. And also, I think I've mentioned before on these calls, the difficulty we generally have is that both clinicians and patients, there's nothing to stop them going on social media, which they have done in the past. So obviously, if they do that, then we have to. I just think the reasons I'm so keen on more indications in more patients, if you actually think about a 50% response rate, well, that means if you dose 10 patients, 5 respond, it doesn't mean that the first 5 respond, it means 5 of the 10 respond. With the first 3 dose -- I mean, if you take Cohort 3 of the synovial sarcoma study with NY-ESO, what actually -- the one without fludarabine, what happened is the first 4 didn't respond. The first 5 -- the fifth one got an 80% response. Now had the fifth patient come in first, we would have thought cracky, without fludarabine, you got an 80% response rate, an 80% reduction in the tumor. And then we had the reality of seeing one by one no more responses without fludarabine. In other words, I think these terribly small patient numbers can deceive. That's why I'm keen there. But responses are material. And if we have to report material things or if they leak, in particular, obviously, we'll have to talk to people. It's just that nothing has worked in a solid tumor in every patient so far as I am aware. I'm looking at Rafael here. I don't think anybody has had a 100 response -- 100% response rate in anything. And therefore, the fact that you don't get responses in the first 2 or 3 patients doesn't really tell you. You have to dose more patients. That's really what I'm trying to say. But it's something we watch daily, don't worry.

Peter Richard Lawson ***SunTrust Robinson Humphrey, Inc., Research Division - Director***

Got you. Okay. And then just a final question. What's the longest duration you've had a patient on higher dose for the MAGE-A10 and A4?

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

Well, it must be a couple of months. But it's simply -- I'll just -- we'll get back because there was stagger of 2 weeks between and then we -- and then a 30-day period for the safety -- before the Safety Review Committee. So it must be 30 days plus 3x 2 of those. It must be a couple of months, but I don't have days on hand.

Operator

Our next question comes from the line of Michael Schmidt of Guggenheim.

Michael Werner Schmidt ***Guggenheim Securities, LLC, Research Division - Senior Analyst & Senior MD***

I had a couple. The first one is on the efficacy side. How confident are you that the 5 billion cell dose is a high enough dose to achieve potentially RECIST responses and that you don't have to go higher at this point? And then, secondly, you did speak about looking at a greater diversity of cancer types in these expansion cohorts. And I was just wondering to sort of following up on what you've said earlier that, I guess, what are factors or other potential factors besides target expression that could determine whether a patient is -- could be responsive? And what insights do you have whether there are -- some of those factors are more noticeable in certain types of cancers than others, for example, when thinking about the synovial sarcoma data, which obviously looked very compelling compared to data that sort of emerge from other tumor types?

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

So I'll let Raphael answer it in general. But that's why we pointed out to people 7 of the first 9 MAGE-A4 patients to be in ovarian cancer. This is not like running a cohort of 9 synovial sarcoma patients or MRCLS patients or indeed multiple myeloma, where we saw responses in the context of autologous stem cell transplant. I mean, previous data in -- and just to give you a comparison, you may recall that we actually did have an ovarian arm in NY-ESO study. And that wasn't -- were the ones which GSK has decided to take forward, and you could see why? Because the response rate there was very -- wasn't very impressive. So I think it maybe disease specific. And I think that's why we're very keen on trying more of these different diseases. Now some diseases, we now, have responded whether in our trials or other peoples trials to targeted therapies. So that's why, for example, there'd been no melanoma patient so far. And we know at NY-ESO in the hands of Dr. Rosenberg at the NCI that he had a 55% response rate in the melanoma trial admittedly with different preconditioning and different use of retrovirus, et cetera. But nevertheless, it could be responsive. We didn't have any of those patients. We had no synovial sarcoma patients, as I said, in the first 2 cohorts. But I just -- I think we need to give the cells a proper chance is what we're really saying, by giving them across different tumors and that's what we're saying, so a better test of whether they're actually going to become functional. I'll left Rafael answer the other half of it.

Rafael Amado ***Adaptimmune Therapeutics plc - President of Research & Development***

I think the 5 billion comes from, obviously, the sarcoma clinical trials, where we know that, that was the median dose for responder. So we know that can be a therapeutic cell dose. Of course, there's been trials where people have given many more cells and there is a group that doses up to 100 billion cells and gives IL-2 and so on. So it's not like the dose response curve for this technology has been very well defined. But we know 5 billion can be active. Whereas, we also know that doses below a 1 billion, we've never seen responses. So we are testing higher doses, so in the expansion we can go up to 10 billion. And we believe, again, that if what we saw with NY-ESO is recapitulated with MAGE-A4 and MAGE-A10, we will see activity. In terms of the tumor type, I think in the field people believe that as long as the antigen is relevant, you can see responses in any tumor. And the surgery branch that shown that by cloning the right TCR in a patient with cholangiocarcinoma, there's been really very long responses. The same has been seen in melanoma and very recently in breast cancer. So I don't think this is necessarily tumor-specific, provided that you have active cells, that the antigen is relevant and it is properly presented in the context of MHC and that the cells can traffic to the site of the tumor. Of course, there are indications where patients, as I said before, may have a deficits in antigen presentation that cross react with cell therapy. And those have been described with checkpoint inhibitors And so patients have received checkpoint inhibitors, particularly if they responded for a long time and then they relapse, their cells, their constructs may bear some of those alterations. But in general, we think that we can exclude a particular tumor type at least at present. And that's why we included so many tumors in our study. And in the expansion phase, it's a much larger diversity of indications than during the dose escalation phase.

Operator

And our next question comes from the line of Ren Benjamin of Raymond James.

Reni John Benjamin ***Raymond James & Associates, Inc., Research Division - Senior Biotechnology Analyst***

I guess maybe just starting off with the manufacturing of the cells. Can you talk to us a little bit about the sort of the mean dose per production running in Cohort 3? I know that you have this range of 1.2 billion to 10 billion cells. And what the target dose is? And what I'm getting at is when you start these expansion studies, don't you want to be focused on only those patients that are getting, let's stay, above 5 billion cells? And I think somewhere in the press release, you mentioned how you're at a capacity where over 50% of your runs can get over, I think, it is 5 billion. So can you help us maybe just triangulate how confident you are that these next expansion studies will be at the doses that you want to be evaluating?

Rafael Amado ***Adaptimmune Therapeutics plc - President of Research & Development***

Yes. That's a great question. I mean, I can tell you that in the patients that we've treated in the third cohorts have all received doses in the upper bound of the range. And so we have a number of patients that receive 5 billion, and the upper bound was actually 6 billion and some patients have gotten 6 billion. We've had a patient where we had fewer cells, and we did another run because the patient could wait. And we were in the stagger phase, and we combined to be able to give something closer to 5 billion. So this runs that we are manufacturing largely, most of them pretty successful. And when we can, we dose towards the upper bound of what's allowed.

Reni John Benjamin ***Raymond James & Associates, Inc., Research Division - Senior Biotechnology Analyst***

Got it. Okay. That makes a lot of sense. And just for setting expectations regarding the data update in the first quarter of 2019, when I'm thinking about the number of patients worth of data we should possibly see, obviously, I come with 7 for Cohort 3. And then, is it fair to say that roughly another 7 or so from the expansion cohort seems reasonable? Or should expectations be somewhere around 10 patients worth of data at these high doses?

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

Well, it'll be obviously more than 7. It's very difficult to be precise. I mean, patients come into these studies and dropout of the studies. I mean, so they are actually -- I mean, in all cancer studies that I have been in, people didn't dropout the day before. Obviously, they're not obliged to do any of these things. It will be a number greater than 7. I actually -- I don't know where it will be myself. So it would be misleading to give you a number, but I hope that it'll be a decent number, above 7.

Reni John Benjamin ***Raymond James & Associates, Inc., Research Division - Senior Biotechnology Analyst***

Yes. No problem. And just one final question for me. And it goes back to this idea of persistence, and I think an answer, Rafael, to which you provided before, regarding all these different aspects between trafficking and the lymphodepletion regimen, everything adding up to how you can make these cells more persistent. But we've talked about, I guess, a couple of times during this conference call the use of checkpoints, in general, in oncology and then, I think, in particular, in combination with cell therapies. And it seems that, that would be the ideal sort of place to go. I know that we've talked about -- sorry, you guys have talked about this in the past. Can you just remind us kind of where we are with those kinds of programs? And what next-generation programs could look like to improve upon persistence?

Rafael Amado ***Adaptimmune Therapeutics plc - President of Research & Development***

Yes. I mean, clearly, we're looking at the monotherapy activity right now. But thinking about how to make the therapy better, one is with new generations of vectors, which they are actually through safety assessments, and we have plans to bring them into the clinic once we've characterized the benefit-risk of this products as monotherapy. But we're very keen on trying to explore them, and we'll announce exactly when they go at the right time. It is really top of mind for us in R&D. And the second is combination trials. We started one, as you know, with NY-ESO in multiple myeloma, and then that was passed on in flight, if you will, to GSK, multiple myeloma and there are not being an indication where checkpoint inhibitors will be registered. So we now have an opportunity with the diversity of indications that we have to focus on indications where checkpoint inhibitors are standard of care and try to build upon that with cell therapy. There is a lot of enthusiasm for that concept among investigators and among the potential partners that we've talked too. And I think we'll say more about that once the discussions progress.

Operator

Our next question comes from the line of Jim Birchenough of Wells Fargo Securities.

Nicholas M. Abbott ***Wells Fargo Securities, LLC, Research Division - Associate Analyst***

It's Nick on for Jim. It is very early here on the West Coast, so I apologize if I missed this, but -- so for dose level 2, you're allowed to leapfrog, I believe, A10 triple due to safety in the lung. So is there reciprocity for dose level 3 in lung? Or do you need to complete both triple and lung at dose level 3?

Rafael Amado ***Adaptimmune Therapeutics plc - President of Research & Development***

Yes, great question. We actually didn't discuss that with the Safety Review Committee. I think potentially one could have decided to sort of graduate, if you will, that non-small cell lung cancer study into the expansion. But we had patients that are ready to be treated, and we couldn't have done it without amending the protocol. And we just didn't think we had enough time to go to the amendment, the IRB

and so on before these patients were ready to go. So because the cell doses aren't that different, the maximum is 6 in the third cohort and 10 in the expansion. That's really the only difference in addition to the stagger. We've decided to just proceed with a third cohort. But in theory, it's something that we could have done. It's just -- in practicality, it wouldn't have made that much difference. So we're going to complete Cohort 3 in lung cancer and then continue with expansion.

Nicholas M. Abbott ***Wells Fargo Securities, LLC, Research Division - Associate Analyst***

Okay. Great. And then just to clarify on the A10 triple, you dosed 4 patients, so 1 patient, obviously, did not get through the whole DLT period, is that correct?

Rafael Amado ***Adaptimmune Therapeutics plc - President of Research & Development***

That's right. One patient hadn't. The protocol allowed a minimum of 3 for evaluation of DLT. And so that patient had gone through the acute phase of hospitalization, where most of the side effects tend to be seen. And what's discussed during the SRC review and as I said before -- as we said before, the SRC endorsed proceeding with expansion.

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

I mean, the reality is that's the -- Rafael just mentioned, the acute phase, I think it's very important. In general, if you don't see something in the first week or 2, you're not going to see issues coming out in later stage. So that's not the pattern in the cohorts. I mean, sometimes you see things but not very often. But as you, obviously, do, you expect to see things like CRS come along in a few days within the first week or 2.

Nicholas M. Abbott ***Wells Fargo Securities, LLC, Research Division - Associate Analyst***

Okay. And then a follow-up from me. So can you -- I know it's early, but can you comment on peak expansion, whether you're routinely hitting your 100k threshold?

Rafael Amado ***Adaptimmune Therapeutics plc - President of Research & Development***

So far in the third cohort, the expansion levels are around that number. So we've seen actually quite a faithful dose response, if you will, in terms of peak expansion. So we're pretty pleased with those numbers. Of course, we don't have long-term persistence. And we would like to look at the area under the curve to see how long cells persist at that high level. But the data that we have so far is encouraging and that sort of recapitulates the expansion that we were seeing in sarcoma.

Nicholas M. Abbott ***Wells Fargo Securities, LLC, Research Division - Associate Analyst***

Right, it's very encouraging. We'll look forward to next update.

Operator

Our next question comes from the line of Ying Huang with Bank of America Merrill Lynch.

Alec Warren Stranahan ***BofA Merrill Lynch, Research Division - Research Analyst***

This is Alec, on for Ying. Just a couple from me. On the A4 and A10 studies, it was nice to see the interim data from the first 2 cohorts at ESMO. Now that you have a few patients dosed in Cohort 3 from both studies, could you maybe give us a sense, other than safety, how these patients are doing? And whether you have any emerging favoritism between the 2 programs based on data to date?

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

We can't update on that because that would just be -- as we said, we're going to try and update on when we got reasonable amount of patients. I think the only preference between MAGE-A4 and MAGE-A10, which I think we've mentioned times -- many times before is that MAGE-A4 is expressed in many more cancers and at a higher percentage of those cancers. So instead of commercial terms, it's much more important. But we can't give any updates on the third cohort today above from saying that it went through the safety truly.

Alec Warren Stranahan ***BofA Merrill Lynch, Research Division - Research Analyst***

Okay. And along the same lines, how has the real-world expression of the antigen levels sort of compare to your expectations?

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

So that is a really excellent question. And I think -- we learn as we go along. I think with -- as you know, with some -- with some NY-ESO programs, we got much higher expression we expected finally enough in sarcoma and I think in multiple myeloma, both higher than the database figures. The normal database people start with is TCGA. And that's what we sort of start with. There was some very difficult low percentages that did not correspond to the database. And that was, for example, in the ovarian cancer with NY-ESO, it was actually much lower than reported, and so is adenocarcinoma of the lung. So there were some which you get surprised, and some which you don't. I think MAGE-A10 is relatively low expressed compared to MAGE-A4. I think MAGE-A4 bears out the TCGA database in most respects. Obviously, you've to go individually by disease, but in most of them where we had actual tumor samples, it reflects the database much more closely I'd say than NY-ESO ever did.

Rafael Amado ***Adaptimmune Therapeutics plc - President of Research & Development***

Yes. I mean, I would just add we've validated expression with tumor banks at MD Anderson or with -- we collaborate with that group through our alliance. And we've seen hundreds of samples of multiple tumor types that are included in our studies, and then contract that with what we are seeing. We've screened many patients already in the trials. And so we now are pretty precise with our predictions, which is excellent because it allows us to size the study correctly and get the right number of centers, et cetera. In MAGE-A4, finally, MAGE-A4 patients have not really been a problem actually. And those -- there it's expressed in enough malignancies at the right level that there is a healthy runway.

Alec Warren Stranahan ***BofA Merrill Lynch, Research Division - Research Analyst***

Great. And last one for me more of a modeling based question. So now that you have the proceeds from the $100 million raise, how do you sort of see capital allocation over the next 6 to 12 months?

Adrian Rawcliffe ***Adaptimmune Therapeutics plc - CFO***

So obviously, the advantage of transferring NY-ESO to GSK is that essentially all of that capital is allocated to a wholly-owned platform. And the guidance we've given is that, that plus the receipts from GSK, plus the amounts that were previously in the bank, and the cash balance at the end of Q3 is $238 million. That balance will see us through to the end to late 2020 with running the business that we have, which is now almost entirely a wholly-owned platform.

Operator

And I am showing no further questions at this time. I would now like to turn the call back over to Mr. James Noble for closing remarks.

James Julian Noble ***Adaptimmune Therapeutics plc - CEO & Director***

So thanks everybody for joining us this morning. I feel that we are at a pivotal stage in the company. It's a very exciting time to have got through the safety cohorts and now have most of the things lined up. We have centers lined up, have patients who've enrolled in the trials. We've got through the dose expansion -- we've got through the dose escalation, and we're now -- dose expansion. And we should be able to provide data over the coming months, both of MAGE-A10 and MAGE-A4. With that the -- we're making good progress, and we hope to get through to the second dose level early in 2019. So I see very exciting times ahead of us. And I look forward to giving you further updates in due course. Thank you very much.

Operator

Ladies and gentlemen, thank you for participating in today's conference. This concludes today's program. You may all disconnect. Everyone, have a great day.