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ADAP - Q2 2018 Adaptimmune Therapeutics PLC Earnings Call

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PRESENTATION

Operator

Good day, ladies and gentlemen, and welcome to the Q2 2018 Adaptimmune Earnings Conference Call. (Operator Instructions) As a reminder, this call is being recorded.

I will now turn the call over to Juli Miller. You may begin.

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

Good morning, and welcome to Adaptimmune's conference call to discuss our second 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 there. As a brief reminder, we anticipate making projections during this call and actual results could differ materially due to a number of factors, including those outlined in our latest filings with the SEC.

James Noble, our Chief Executive Officer is with me for the prepared portion of this call and our management team are available for Q&A.

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

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

Thank you, Juli. Good morning, everyone, and thank you for joining us. Today's call will be brief and the 2 main messages are that: First, we are on track to deliver response data for MAGE-A10 and MAGE-A4 later this year, with both programs having a strong patient runway in place. We'll also be sharing initial safety data for AFP later this year; secondly, we completed the transition of the NY-ESO program to GSK in July, and we are now dedicating all of our clinical, manufacturing and regulatory resources to our wholly-owned assets.

We remain confident that 2018 will be a transformational year for us and this conviction is reinforced by the positive momentum across trials with our wholly-owned assets. We set out milestones at the beginning of this year, and we have consistently hit those milestones. First, we announced

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in January that the safety review committee recommended dose escalation to 1 billion transduced cells in the MAGE-A10 triple tumor study in bladder, melanoma and head and neck cancers. Secondly, we announced dose escalation to 1 billion cells in the non-small cell lung cancer study with MAGE-A10 during our last quarterly call. Thirdly, we announced at ASCO in June that we have dose escalated to 1 billion cells in the MAGE-A4 basket study, and we added synovial sarcoma and MRCLS as additional indications. Fourthly, we announced last month that the safety review committee recommended dose escalation to the third cohort in both MAGE-A10 studies and these patients will receive a dose of up to 6 billion cells. Finally, as all 3 patients in the second cohort have been dosed, the safety review committee for the MAGE-A4 basket study will meet shortly to review dose escalation to cohort 3 for MAGE-A4.

In addition, we are please to share that we recently had a poster accepted by ESMO to present MAGE-A4 data and this Congress will take place in October in Munich, Germany. Thus far, we have delivered against our projected 2018 milestones and this keeps us on track to deliver response data through our MAGE-A10 and MAGE-A4 SPEAR T-cells later this year as projected. We have a strong runway of eligible patients identified for our studies.

In addition, once we pass the third cohort, we'll be able to dose patients without a predetermined stagger phase, which will allow us to gather even more clinical momentum.

As we recently announced, the transition of the NY-ESO program to GSK was completed, and we'd like to take a moment to reflect back on this very successful development endeavor. 99 patients were enrolled and treated with NY-ESO SPEAR T-cells across several indications, including synovial sarcoma, MRCLS, non-small cell lung cancer, melanoma, multiple myeloma including the combination study with KEYTRUDA and ovarian cancer prior to the completion of the transition. We completed enrollment in the synovial sarcoma, non-small cell lung cancer and MRCLS trials prior to transition, and we have seen favorable benefit risk data in these indications.

In March of this year, we announced responses in a second solid tumor, MRCLS. As a reminder, we have seen complete responses in both multiple myeloma and synovial sarcoma, and multiple confirmed responses in our MRCLS. The NY-ESO program has taught us many lessons that we are applying to our ongoing studies with our wholly-owned assets, including: First, that there is a threshold dose that we think is required to see responses based on data from Cohort 1 of the synovial sarcoma program, where patients who received fewer than 1 billion cells showed suboptimal expansion; secondly, that expansion of SPEAR T-cells correlates with the responses. The profile of expansion in the 100 million dose cohorts of MAGE-A10 and MAGE-A4 looks similar to patients receiving the lower doses in the NY-ESO program, this further strengthens our hypothesis that cell dose matters; thirdly, based on data from Cohort 1 and 4 of the synovial sarcoma program in which patients received 4 days against 3 days of fludarabine respectively. We have determined that an extra day of fludarabine is important for optimal expansion and response. Therefore, as far as the third cohorts and beyond are concern, we've incorporated this extra day of fludarabine into our ongoing studies.

In financial terms, we have received payments of $123 million from GSK since 2014, which with the $27 million that we will receive in the third quarter as a result of the recent transition of NY-ESO, brings the total to $150 million receivable. We will also receive subsequent development and sales milestones and royalties based on successful development of the NY-ESO program.

Future presentations of NY-ESO data are now the responsibility of GSK, but we can say that abstracts have been submitted to the upcoming International Immunotherapy Conference, CRI, at the end of September in New York City and also to FITC, which will take place in November in Washington, D.C.

With the completion of the NY-ESO transition, we can now dedicate all of our clinical manufacturing and regulatory resources to MAGE-A10, MAGE-A4 and AFP. To deliver more effectively on this clinical focus, we have announced this morning that Rafael Amado, our Chief Medical Officer, has assumed a new role as President of Research and Development, effective from the 1st of August. This brings together the clinical and research teams under a single leadership, which will allow better alignment and integration of all parts of R&D from target identification and selection to regulatory filings, enabling the delivery of our key priorities. Under Rafael's leadership, we are actively planning for registration trials.

With NY-ESO transitioned to GSK, coupled with this integration of our clinical and R&D teams, we are positioned to pivot rapidly and prosecute any response signal we see, whether indication or target specific. With more than $129 million in total liquidity, which, of course, excludes the $27 million payment from GSK as a result of the transition, we are funded to deliver data from our wholly-owned pipeline and through to early 2020.

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We are confident that we will achieve our goal to be first to market with SPEAR T-cell therapies in solid tumors. With that, I'd like to open the call up for questions. Operator?

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Our first question comes from Robyn Karnauskas from Citi.

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

I was just trying -- in terms of how data this year, I'm just trying to seek through -- you said that you're in the last cohort where you have to go very slowly, when you start to dose up higher than that, how many patients are you going to do? I think I remember you saying in the last call sometimes you may not be able to make 10 million cells for all patients. So just trying to understand how [many patients] from other cohorts can I get?

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

I'll let Rafael answer in detail. But just to take the manufacturing, the billions of cells. So the second cohort, which we've just been doing is of 1 billion cells, where we just told you today that we've [recruited] all 3 MAGE-A4 patients. That's been regularly achieved. We often achieve more than 5 billion cells, and we normally actually achieve somewhere between 2 billion and 3 billion, I'll say is the most common area of production for manufacturing. So we can dose escalate. We don't intend to dose escalate to keep up -- there are only 3 dose escalations with the 100 million dose, the billion, and the next one, which is essentially 5 billion, although the technical range is 1.2 billion to 6 billion. In terms of the stagger, I'll let Rafael take that point.

Rafael Amado - *Adaptimmune Therapeutics plc - Chief Medical Officer*

Yes, Robyn. So the stagger at the moment is potentially 7 days of observation and 7 additional days for the conditioning. So it turns out to be 14 days between dosing for patients. We will continue with that in cohort 3. And then after cohort 3 is finished, there'll be no stagger, so we will be able to dose patients as they come. And we have been making products for patients that are awaiting treatment. So we anticipate that many of these patients will be able to be treated as soon as cohort 3 has cleared. Now in terms of the cell dose, we're making 2 changes in cohort 3, one is obviously the cell dose going up to 6 billion, and the other is, we're increasing the dose intensity of fludarabine. Once cohort 3 has cleared, there will not be any further dose escalation. The only modification we'd make to the product goal is that, if a patient has more cells available, we will infuse as many cells are available up to a maximum of 10 billion. And I think that will allow us to characterize the dose response curve in the upper range of cell dosing.

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

Got it. So basically -- so -- okay after 6 billion, so for that cohort of 6 billion, what happens if you can't make 6 billion cells for that patient, it's like only 2 billion to 3 billion, do you count them in the cohort? Or do you just have to keep enrolling until you hit a certain number of patients that are at 6 billion and when you go above that, [you're just going to make as much and] put it in, what percent of people do you think you can [successfully] make for 10 billion versus a fixed [percent] of patients can get fixed. I was just curious like how [far will this yield] to manufacturing be [tied] dose is?

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Rafael Amado - *Adaptimmune Therapeutics plc - Chief Medical Officer*

Yes, so cohort 3 is a range of 1.2 billion to 6 billion. So any patients that receive cells within that range is evaluable for that cohort. If a patient gets more than 6, we will not infuse more until that dose escalation has completed. In terms of how many patients we're able to manufacture that -- at levels of 10 billion in the -- Navy Yard manufacturing facility we are I would say about 6 billion in probably about half the patients. If not, 60%-or-so. So I think that gives us an opportunity to look at those higher doses.

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

Yes, and in fact, it is a bit of a moving target that how many people get 10 billion cells. I'd say that almost nobody when we were only at PCT a year ago and before we made certain improvements to the manufacture, almost nobody at 10 billion cells coming out of the manufacture, but now 5 billion is common and sometimes it's more.

Operator

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

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

James, just thinking about GSK, do you get any sense of what we're going to see in the data that they're going to release? And do you also get any sense of how frequently they could potentially release data, is there -- do you think a desire to kind of validate the platform and make sure there is a kind of a constant data flow around the NY-ESO?

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

Yes, so as I said, I think there'll be 2 updates this year, 1 in September and 1 in November. I think that if they -- if we see a response that -- I think that they're going to focus on starting some larger trials. I think -- but I think there is going to be a natural tension in GSK between a major pharma, which wouldn't normally comment on small trials, and the fact is that the clear excitement they had at their R&D update whenever it was last week or a week before when they clearly featured cell therapies, so I think there'll be a tension. I think if we see responses in lung cancer in particular, I think that will be known. And I also think that from our own experience, just to be clear, it's extremely difficult to keep responses out of social media, because both doctors and patients tend to go on to social media if anything happens. So I think one way or another there will be things, but it is entirely up to GSK, apart from including the actual presentations of those 2 conferences. So I think, we just have to watch and see with you.

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

Great, thank you. I really appreciated. And then the change in title for Rafael, the role is, does that kind of signal increased efficiency or was there any worries about control issues going from the R&D stage to the clinical stage?

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

No, actually, it is a real feedback loop in cell therapy which is incredibly important and that feedback loop is, okay, let's have a look at the patient data, the translational data, what's going on inside the patients? What type of cells survive? What type of cells appear to be doing the -- giving the responses? It is an amazing feedback loop back into research all the time, and it's very important -- and in fact it goes all the way back to what type of targets you want, it's an incredibly integrated thing. I mean, essentially the company can make T-cell receptors, not quite at will, but generally speaking, if we find a target and we find the peptide, we can make the T-cells receptors. So it's incredibly important to integrate it all right from the first stage. And one thing that I'd say, for example, in the selection of second-generation, we're very excited about some of the second-generation programs, which one you pick and which one you put into the clinic is obviously very important. So it's really a function of the fact that it has to be

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Client Id: 77

seemless all the way from target identification to regulatory from all the way through. And of course -- and to be honest, actually Rafael had the same role within GSK actually. So it's really, I think it's just an emphasis. I think in cell therapy, in particular, that, that feedback circle is incredibly important to keep us as 1 unit.

Operator

Our next question comes from Ren Benjamin of Raymond James.

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

Maybe just a couple of questions. I guess starting off, I believe at ASCO, you guys had mentioned in the MRCLS results that there was unconfirmed PR and there was somebody else who is awaiting efficacy assessment. Could you just give us an update by chance on kind of where everyone stands? And I know we looked at overall response rate data, but can you give us a sense as to how the durability has been with that study?

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

So we can't really comment on durability because, obviously, a lot of the patients were dosed very recently. I mean, we have -- the first patient who had a response actually was fairly durable over quite a number of months, but actually many of the patients were dosed earlier this year or in the last 3, 4 months. So we don't really have durability. In terms of response rates, we ended up with responses on the first 8 patients, and of those, 4 confirmed and 1 was unconfirmed. And that's where we ended up. So the -- and that's what will be updated later this year in -- which 1 is that being updated at (inaudible).

Rafael Amado - *Adaptimmune Therapeutics plc - Chief Medical Officer*

It's at (inaudible), yes, so we treated the last 2 patients recently, and we don't have response outcomes for those, so we hope to be able to report on the entire 10 patient cohort at (inaudible). But that's where we are with the first 8.

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

Got it, okay. And one of the other things that came out on the last call, and I'd love to kind of probe a little bit more is this idea of retreatment of these patients and kind of -- I believe per your protocol, you can retreat if a response is seen. Can you talk a little bit about what your experience has been up to date and how you plan on thinking about retreating these patients and potentially extending responses and durations of response going forward?

Rafael Amado - *Adaptimmune Therapeutics plc - Chief Medical Officer*

So I mean, the retreatment experience has been variable. And early on we really didn't see responses in patients upon retreatment. But we were also dosing at low levels. Recently, probably because of the transition to GSK, a lot of patients and physicians requested reinfusions actually upon progression, so we manufactured a number of products for patients for reinfusion, and we ended up dosing some and then transferring product to GSK for reinfusion that they will do. And out of the last 5 patients that we infused, 3 of them responded and 1 of them actually had commented in the past actually had a complete response. And we -- so that may be a function of the fact that we're now, as James was saying before, able to manufacture higher cell doses. Having said that, we've also -- we also can say that the response rate upon reinfusion is lower than it is initially and that we have seen patients that the tumor expresses the antigen and we've reinfused and haven't responded. But we found interesting in that, at least in some patients they made the right benefit again, and hopefully, the last reinfusions have not taken place a long time ago. But hopefully they will be durable. So there is benefit to be derived from reinfusion.

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

And when, I guess, just as a follow-up to that Rafael, when you're thinking about, or I'm thinking about, the preconditioning regimen, is that something that kind of happens again when you're reinfusing or do you just automatically reinfuse once you've lost the response?

Rafael Amado - *Adaptimmune Therapeutics plc - Chief Medical Officer*

Yes, so we condition everybody. And actually, we are looking at the data in detail because the type of condition they receive depended on what cohort they have been enrolled to begin with and what kind of response they've had the first time around. So some patients that were treated under Cohort 4 ended up being reinfused with conditioning for akin to Cohort 1. And so, we'll just have to look at the entirety of the redosing experience. But definitely they all require conditioning prior to infusion.

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

Got it.

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

It certainly looks more interesting and hopeful than -- for redosing than when we first redosed patients some time ago in Cohort 1 where we didn't see a lot. As Rafael said, of the last 5, we redosed 3 -- we had 3 responses, 2 partial and 1 complete. What we don't have is any durability data on that because they're quite recent.

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

Got it. And then final one for me with the manufacturing. I believe in the press release you mentioned about expanding manufacturing. I know we've talked in the past about shortening manufacturing time. And so, is -- does 1 kind of come before the other, are you expanding really to account for the number of clinical trials that you anticipate will be started? Or is it more just the current trials and the number of patients you think will be coming in?

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

So we're expanding, because when we look at our patient recruitment plans for the next 18 months, then we need to have more than 10 slots. So we've got 10 slots essentially, which is basically 2 a week at each of PTT, which is now called [Hitachi] and our own Navy Yard. What we didn't want to do is to leap in with a huge expansion until we knew that Navy Yard was functioning well, and it is functioning extremely well, very efficiently. And what we want to do is to push up the capacity. It takes quite a long time to build up capacity because it involves training lots of people, some [miss] out, but mainly training people. And what we -- when we look at the patients, particularly I think the number of patients who express MAGE-A4, if we get any form of signal with that target, there are lots and lots of patients out there and we need to be able to go beyond 20 a month in terms of slots available to us during the next year. So it's all part of pivotal planning to registration trial. You've obviously got to have more patients available at once. Just to remind you what Rafael said earlier, when we finish the third cohort, at that point, there is no stagger between patients assuming everything goes well in the third cohort so it's all safe. So once you finish that third cohort, essentially if patient turns up, you need to be as ready as possible to manufacture the cells, rather than say, well actually because of the stagger, you can't be dosed for 6 weeks anyway, or whatever the current situation is. So it's a combination -- it's a combination of all those factors. Along side that is the efficiency of trying to get the process better and shorter. But that's completely -- that's completely different thing that involves reducing release testing, it involves better logistics, it involves manufacturing changes, all of that is going on, we have a very big team, what we call process development doing that. That's in parallel to that, but it's in addition to the expansion of what's going on at the moment.

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Operator

Our next question comes from Jonathan Chang of Leerink Partners.

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

First question. Can you talk about how you're thinking about efficacy and safety benchmarks and the amount of data that you want to see before making go/no-go decisions for the next stages of clinical development, whether indication or target specific?

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

So we've also had a rule of thumb, which we've talked about in the past. And that's, if you have 10 patients at a relevant dose with the right preconditioning, and there's not some sort of freakish explanation about there's some problem with the patient for example, then you need to see at least 2 or 3 reasonably durable responses to think that you have a product. I think the -- and I think that holds true. Cell therapy won't succeed commercially if only 1 in 20 patients responds and if the response is only for 2 or 3 months. So that's been the rough benchmark. Of course, the comment about indication or antigen specificity is the fact that these are multiple cancer trials. So I think, there are 9 cancers in the MAGE-A4 trials. So in the event that you got fantastic responses in 3 different tumors, you might consider doing antigens -- anybody presenting their antigen with those 3 tumors might come into the thing rather than saying this particular subject. I think the one exception to all of that, I think, is synovial sarcoma where I think if we begin seeing responses, we will be extremely confident that it would be worth going straight into a pivotal trial with sarcoma, because all the data we've had with NY-ESO.

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

Great, that's helpful. Second question, can you help set expectations ahead of the MAGE-A10 and A4 data in the second half, in terms of just patient numbers, dose levels and how to follow-up, et cetera?

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

So there are 3 patients at each dose level in each cohort. So that means that, the 1 billion to 6 billion cells, if we take the 1 billion cells for MAGE-A4, for example, as I mentioned in the call, we have dosed all 3 patients. So that means that the safety review committee can meet fairly shortly. We have to wait 30 days after the last patient is dosed before the safety review committee. We then go up to 1 -- assuming the safety review committee says it's okay, we go up to the 1.2 billion to 6 billion cells as Rafael mentioned earlier. And then we hope to start dosing those patients very shortly, again we still got the stagger. So there should be a reasonable number of patients by the end of the year, but it's very difficult to give you exact numbers. But we won't be dosing more people at 1 billion cells only at MAGE-A4. Once you get to 3 at a particular dose and the safety review committee approves the dose escalation, then we'll stop in that cohort and just go up to the next dose. So you'll get data on the 3 patients at the 1 billion cell dose, and then however many we can get dosed at the next level up.

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

Okay, great. And then just one last one from me. With regards to the announcement a couple of weeks ago that MAGE-A10 was advancing to the third dosing cohorts, can you talk about whether there is enough time at that point to assess efficacy?

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

So not really, because you get -- what is -- the way you do it is you -- the safety review committee meets essentially 30 days after the last patient has been dosed. And you wouldn't have the first scan back on the last patient for then. And then -- the difference between an unconfirmed response

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Client Id: 77

and a confirmed response is that you then have to have another scan 30 days after that. So you wouldn't have data at the safety review committee. It is only a safety check, it's not dealing with responses and that's just the function of the time. The same is true of MAGE-A4, when the safety review committee meets, which it will do shortly, they won't have any -- we won't have response data. We'll just have the safety data. And that's all the committee is there for; it's just simply a panel of doctors obviously who assess whether it's suitable to go up a dose. It's not looking at responses at all.

Operator

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

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

Now that NY-ESO has transitioned, and James in the past you've mentioned that takes up a significant amount of kind of corporate effort. So one just from a modeling perspective, should we expect a step down in the spending or is that capacity going to be immediately taken up by kind of the existing programs? And then also does that free up some space to either put in a new target in the next several months into the clinic or is that even not the priority and the priority would be getting the generation 2 version of the cell in?

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

So the answer is that, it dovetails perfectly as we hoped it would, in that as GSK has transitioned and therefore freed up all the staff, we've got lots of work on our own programs because we are actively expanding in several directions. So, for example, adding European sites, which is a very complex -- a very complex procedure. We are looking at a second generation to go into the clinic next year, and we are also looking at another target to go into the clinic next year. And on top of that, of course, as I mentioned, we're having to do all the planning for a pivotal study. And the pivotal study -- the pivotal study, of course, irrespective of which program it is, whether it's MAGE-A10 or MAGE-A4 and what [it is] and takes a huge amount of planning. So actually it's evolved perfectly that the team on the transition has just switched over to (inaudible) there is a priority -- we're actually also looking at other HLAs for the existing programs as well, particularly the MAGE-A4 program obviously. So the pipeline is very full, so we expect to -- we're planning for a pivotal study, we're obviously planning further pilot studies with these. We're looking at combination studies, other HLAs, another program -- another target for next year and maybe a second generation as well. So that's what they're doing. And it's incredibly complicated, and also Europe. So it's a whole stack of things, but we're delighted that we have all the resources at our disposal now.

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

Okay, great. And then just following up on some of your earlier comments. And it sounds like you have a backlog of manufactured cells of some patients just waiting for the dose levels to be cleared. Should we -- once the dose level 3 is cleared, should we expect a bolus of patients really to get infused? Or is there also kind of maybe a researching from your risk mitigations/clinical operations capacity, that's just going to kind of spread those patients out?

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

So we will obviously offer all patients the cells, assuming everything's gone well by then, and we're out of a stagger. We obviously go through patient-by-patient and determine whether they are ready to get the cells, because many of them, the reason they haven't had the cells, not just because of the stagger, but because, let's say, they're going through 1 more round of chemotherapy or the medic wants to do 1 more -- the doctor wants to do 1 more treatment of something else. So what's happened is, we've made the cell, so as soon as that's free, then we'll be able to treat them. And obviously, we can amend the protocols at the time, but essentially we have a list of people, well obviously we don't have who they are, the individual patients. We have a list of patients for whom cells have been made, and then we would go -- once we're free of the stagger, every single patients' doctor will be contacted and see where they want to go, whether they're ready.

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

Okay. And then one last one. On AFP, in the past you've mentioned -- and maybe about a year ago, you mentioned there was -- you're finding people with antigen expression was not really the issue. The issue was finding people with antigen expression and sufficient remaining liver functions that can meet your enrollment criteria. But it seems like you've, in recent quarters moved up the timing of safety data and presumably then ultimately efficacy data from the trial. Have you changed the enrollment criteria, or maybe if you haven't yet, is that something that you're able to do once you start clearing kind of safety cohorts?

Rafael Amado - *Adaptimmune Therapeutics plc - Chief Medical Officer*

Yes, hi. I'll address that. So you're right. We've been thinking about this study and particularly, since we've begun to actually dose, we were very cautious initially, obviously because there is some AFP expression in the normal liver. And so we wanted to make sure that, that we could ensure the safety of the TCR. Obviously, we're in early days, but we're growing more confident, if you will. And so one of the things that we've decided to do is to allow patients to come into the study, they have very high circulating alpha-fetoprotein levels. During the past, the criteria was only based on immunohistochemistry. And now, it's either expression by [IHC] in the tumor or high levels of circular AFP. So that's increased the pool of patients available for enrollment. And the second thing we've done is expand the study in -- particularly in Europe, where we have a lot of excellent sites that have participated in the development of products in the past like (inaudible). And so we're a bit more optimistic that the study, the pace of recruitment will increase.

Operator

Our next question comes from Soumit Roy of JonesTrading.

Soumit Roy - *JonesTrading Institutional Services, LLC, Research Division - Research Analyst*

Maybe this question is for Rafael. Just want to get a sense from you like on the quality and the subtype of P-cells you're seeing in these MAGE-A10, MAGE-A4 trials compared to NY-ESO trials because these patients are going to be very different from the synovial sarcoma patients. They're I-O treated, possibly higher tumor mutation burden. Do you think the T-cell type is going to dictate how much it's going to expand and what memory type it's going to form? And also, how confident you are or what's your thinking to see efficacy data from 1 billion dose versus cohort 3, where you think it's more -- you are more confident to see efficacy from much higher like 2, 3, 5 billion dose level?

Rafael Amado - *Adaptimmune Therapeutics plc - Chief Medical Officer*

Yes, that's a great question. So obviously, we have an experience that the starting product material variability can affect the eventual cell dose that comes during the production. And so it's taken the process development team some time to understand what are the key variables that lead to successful cell activation and expansion and a suitable dose. But we're pleased to say that we've been able to manufacture successfully across a very wide range of tumor types at the moment from obviously, sarcoma to melanoma to multiple myeloma to patients with head and neck, ovarian cancer, obviously lung. So all these tumor types are very obviously diverse, and as you know, the pretreatment of the patients is very different, and so it's been really great to see that the process optimization is paying off. In terms of the final product, they go through release criteria before they are administered. And in a large subset of patients, we also look at potency, so the ability of these cells to create [interferum] when exposed to targets. And also cell killing. And we haven't done this in every patient, but in large number of samples we've seen that the cells are actually active. In terms of cell dose, I think, there's probably a critical threshold of dose that's required for these cells to travel to the tumor deposits and to penetrate the matrix of the tumor and encounter antigen. And low doses of cells may not be sufficient. Having said that, in MRCLS with NY-ESO we've seen responses at a just above 1 billion and also in doses between 1 and 2 billion in synovial sarcoma, we've seen responses. So we are obviously not ruling out that we may see some positive data in these patients that we're treating currently in Cohort 2. And obviously, the chances can only go up in cohort 3, and we're in the middle of that at the moment for MAGE-A10 and very soon we're going to be in the middle of that for MAGE-A4. So we are at a phase in our development of these 2 programs where we are really doing the 2 tests of the efficacy of these products.

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Soumit Roy - *JonesTrading Institutional Services, LLC, Research Division - Research Analyst*

That was really helpful. And I just have one last question. What percent of the screened patients are getting enrolled for the MAGE-A10 and MAGE-A4 trials, do they match up with the academically published papers, or is it different in the real world as you're enrolling patients? And do you see there needs to be a cutoff for high expresses versus low expresses of A4 and A10? Just want to get a sense of how you're looking at it?

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

So on the patient numbers, we haven't actually given out screening data. I think we were surprised, and I think we've told people that before that the adeno lung cancer both for NY-ESO and the MAGE-A10 actually are much lower than the published data. I'd say on MAGE-A4, it's halfway between -- we're very encouraged by how many people present the antigen and how closely it sticks to the data. MAGE-A4 is pretty prevalent across the tumor types that we have been looking at and has been very encouraging. I don't think that data are far out in the public domain of the TCJ, which is the main database for the MAGE-A4. Sometimes you get much higher expression in the database. An example of that would be synovial sarcoma and multiple myeloma with NY-ESO, both of which were higher than the databases, in the real world. I think MAGE-A4 pretty much reflects the real world. MAGE-A10 has been a bit rarer, certainly in lung than we expected.

Rafael Amado - *Adaptimmune Therapeutics plc - Chief Medical Officer*

I guess, what I would add is, we have a great partnership with MD Anderson Cancer Center, and as part of the alliance, we're now routinely testing expression with the very assay that we use to select patients, which is important, because prevalence there is depending on what assay you're using to screen. And so, we're doing it -- we've done it for MAGE-A10 and MAGE-A4, and we're doing it for the future TCR, so we plan to bring into the clinic. So we know exactly what the prevalence should be in the real world. And these tumor banks are 100s and 100s of samples. So we get a lot of precision on the prevalent.

Operator

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

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

It's Nick in for Jim this morning. The first question relates to the use of checkpoint inhibitors and in the trials that -- so you have several tumors where checkpoint inhibitors could be used and I believe the protocols allow for that. But as you think about moving forward, how would you plan on integrating checkpoint inhibitor use in those tumors where checkpoint inhibitors are approved? And I have a follow-on.

Rafael Amado - *Adaptimmune Therapeutics plc - Chief Medical Officer*

Yes. Initially our goal is to characterize the single agent activity of this products. Because we do need to establish a baseline against which to optimize this therapy. You are right, many of the tumor types we're including in our studies, are indications for PD-1 Class inhibitor. And the majority of patients that we're enrolling have been exposed to PD-1s. So they're PD-1 failures in the primary assistance, or acquire assistance. And in some of the indications like lung cancer, these products have been moved earlier and earlier in line for therapies. So many patients are getting PD-1s in front line. So there is an opportunity to explore the PD-1 failure pool of patients, which is becoming a very prevalent clinical entity, where there is beginning to be the regulatory space in terms of the definition of PD-1 failure where products potentially could be developed. And there is also a preclinical rationale to combine them and to potentially restore sensitivity to PD-1 in patients that progressed. So, I guess, with this in mind, our first goal is to see where the single agent activity is. And as Jim has alluded to, we are planning for a combination trial. We started 1 with NY-ESO and that's been transferred to GSK, that is in multiple myeloma. We treated a few patients prior to the transfer and GSK will report on that. But that's been very helpful for us to try to characterize the combine ability of our technology with PD-1 inhibitors. And we're now in discussions with

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potential partners about doing combination studies with adopted T-cell therapy, which is SPEAR T-cell and PD-1 inhibitors, particularly in non-small cell lung cancer. But we have to complete the dose escalation with the TCR long before we initiate those trials.

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

And my follow-up is, since last question was about expression of these antigens across the various tumors. What you see tumors that express both 4 and 10, and since you are now safety established, or will have safety established for both products, what do you think about a combination approach?

Rafael Amado - *Adaptimmune Therapeutics plc - Chief Medical Officer*

We think -- definitely thinking about the possibility of combining both and again this will be something that we will consider once we have established the safety of both. In terms of expression, you're right, the majority of patients that are A10 positive are also A4 positive. There are a lot more A4 positives than A10 patients. So A10 patients could potentially in a trial written that way to receive both products in either sequentially or concomitantly. And we're actively thinking about what is the best way to test that. Whether that starts next year or subsequently, I think, we just need to see whether that fits within the priorities because as you've heard, we have second generations to test, we have combinations to test and we have the new products that are coming in against new targets to test. So -- and we're preparing for pivotal trial. So we'll have to make sure that we (inaudible), but it is something that we are thinking about and could potentially execute with other partners in the future.

Operator

(Operator Instructions) Our next question comes from Ying Huang of Bank of America Merrill Lynch.

Jenny M. Leeds - *BofA Merrill Lynch, Research Division - Research Analyst*

It's Jenny on for Ying. The first is just a clarification. In the 8K where you talked about the SRC up dosing. You mentioned that 8 patients received a 100 million cells in both of the studies, and then you talked about 3 patients who received 1 billion cells in the second cohort of the lung cancer study. Just wondering if the second cohort of the MAGE-A10 basket study was actually dosed and you have the data. I know that the SRC didn't use that data in order to up dose to the third Cohort. But just wanted to get some clarification there?

Rafael Amado - *Adaptimmune Therapeutics plc - Chief Medical Officer*

Well, I'll give it a try. I'm not sure, I fully understood the question. But we have dosing A10 all the way through Cohort 2. And that was -- we're actively dosing in cohort 3 in non-small cell lung cancer. We dosed a total of 8 patients about at 100 million cells between the 2 trials, the triple tumor and the lung cancer study. And then 3 patients at a 1 billion cells in the non-small cell lung cancer. And based on the safety the SRC recommended dose escalation in both trials. So we are currently are going into the third cohort, which is 1.2 billion to 6 billion in both studies. And so that's where we are with A10.

Jenny M. Leeds - *BofA Merrill Lynch, Research Division - Research Analyst*

Right. So I guess the question is, was Cohort 2 of the basket trial ever dosed? Because you said 3 patients in the lung cancer trial were dosed with 1 billion.

Rafael Amado - *Adaptimmune Therapeutics plc - Chief Medical Officer*

So that is based on the safety of the lung cancer study, the SRC recommended that we bypass that cohort, so we've moved on to 5 billion.

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Jenny M. Leeds - *BofA Merrill Lynch, Research Division - Research Analyst*

Okay. Yes, that's what I thought. Just want to clarify. And then just in terms of the data that we could be expecting to the response rates, would that be more likely a PR or you want to present the full data at a medical meeting? And when you think about what's considered mature, I know we have to see multiple scans, just trying to think there how many scans per patient would you want before you would present that data as mature?

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

So the difficulties I alluded to earlier about the fact that these are obviously open-label studies. And obviously, the patients and their own doctors know whether they've had a response or not, it's actually -- and because unfortunately in cell therapy even 1 or 2 responses are clearly material. We can't do what we'd like to do, which is to wait for a medical conference and [submit] data months in advance, all that. So I think, the model you should be looking at is the model we used for the MRCLS data earlier this year, where at a -- I think it was a quarterly presentation, we talked about the data in rough terms to get the sort of materiality of that out, because we had a lot of responses. And then we follow that up with an oral presentation at ASCO, and that's actually the model going forward. So in terms of the responses, we're not going to go patient-by-patient, we'd like to have 2 or 3. But -- so we would like to present confirmed responses, which basically means 2 scans, 30 days apart. And I think, the only reason we wouldn't do that is if we were trying to give a general update across the program. So if we're commenting on all 3 patients, we might give an unconfirmed response as well, which would mean that we have 1 scan but not the second 4 weeks apart. So we will -- we will -- so essentially, we'll put out either a press release or do it in an earnings call of the sort of broad outlines of response data. And then we follow it up at a medical conference as soon as we can thereafter.

Operator

There are no further questions. I'd like to turn the call back over to James Noble for any closing remarks.

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

Great. Well, thanks everybody for listening and really excellent questions as usual. We really are at a very exciting moment where we can put all our resources into our own programs. We've got a great runway of patients lined up for both MAGE-A10 and MAGE-A4. So I am very confident that we will come up with a lot of data before the end of this year, and I look forward to presenting that as and when we get the responses. So thank you very much.

Operator

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

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