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ADAP - Q1 2018 Adaptimmune Therapeutics PLC Earnings Call

EVENT DATE/TIME: MAY 09, 2018 / 12:00PM GMT

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PRESENTATION

Operator

Good day, ladies and gentlemen, and welcome to the Adaptimmune Q1 2018 Earnings Call and Business Update. (Operator Instructions) As a reminder, this call is being recorded.

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

Juli P. Miller

Good morning, and welcome to Adaptimmune's conference call to discuss our first quarter 2018 financial results and other business updates. We issued a press release earlier this morning, and I would ask you to please refer to 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. Helen Tayton-Martin, our Chief Business Officer; Adrian Rawcliffe, our Chief Financial Officer; Rafael Amado, our Chief Medical Officer; Gwen Binder, our Chief Technology Officer; and Bill Bertrand our Chief Operating Officer will be available for Q&A after the prepared portion.

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

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

Thank you, Julie. Good morning, everyone and thank you for joining us. Today's call will be brief and the 2 messages are the first 2018 is off to a great start for Adaptimmune and secondly we are on track to deliver data from our wholly-owned SPEAR T-cells throughout 2018. Earlier this year,

we observed responses in a second solid tumor with NY-ESO in myxoid/round cell liposarcoma, or MRCLS and one of our investigators will present the first chemical report in an oral presentation at ASCO in June. These data in MRCLS strengthen our conviction that we have a pipeline capable of treating solid tumors. We will also be presenting updated safety data from our ongoing MAGE-A10 studies in a poster at ASCO. Based on the first quarter, we remained confident that 2018 will be a transformational year for us. And this conviction is reinforced by the positive clinical momentum across trials with our wholly-owned assets. We announced in January this year 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. And today we are pleased to announce that the safety review committee has also recommended dose escalation to 1 billion transduced cells in the MAGE-A10 non-small cell lung cancer study and we are now dosing in this cohort. This keeps us on track to deliver response date of MAGE-A10 SPEAR T-cells later this year. Our MAGE-A4 basket study across 7 solid tumor indications, including bladder, melanoma, head and neck, ovarian, non-small cell lung, esophageal and gastric cancers, is also dosing patients and we remain on track to deliver initial safety data from this study in the second quarter of 2018, with response data anticipated later in 2018. I would also like to mention the preclinical data from MAGE-A4 and MAGE-A10 SPEAR T-cells recently presented at AACR. We had 2 posters summarizing the discovery process and extensive preclinical validation work performed by Adaptimmune to characterize the specificity, affinity and potency of these SPEAR T-cells. There is also news from our next-generation program. Recently, Adaptimmune was granted a U.S. patent covering one of our approaches to help our SPEAR T-cells overcome resistance to immunosuppressive elements in the tumor microenvironment and this enhancement is likely to be used in some of our upcoming clinical trials. Our proprietary preclinical development and validation program for our SPEAR T-cells is unique and one of the many reasons that we believe we have the industry-leading pipeline of TCRs to address solid tumors. We generate TCRs that have the right level of specificity, affinity and overall avidity for cancer cells expressing specific targets while minimizing the risk of off-target toxicity. Our proprietary preclinical methods combined with our compelling foundational clinical data with NY-ESO and synovial sarcoma and results in a second solid tumor MRCLS make us very optimistic for the remainder of 2018.

To summarize, anticipated data readouts for 2018 include: first, additional safety and initial response data from the MAGE-A10 pilot studies; secondly, initial safety data from the MAGE-A4 basket study to support dose escalation to 1 billion cells; thirdly, initial response data from the MAGE-A4 basket study as well as additional response data from the MAGE-A10 studies throughout the second half of 2018; and lastly, we anticipate initial safety data to support dose escalation in our AFP study in hepatocellular carcinoma later in 2018, with response readouts in 2019. As we have stated before, our focus on MAGE-A4, MAGE-A10 and AFP has been greater since GSK exercised its option over our NY-ESO program and we plan to complete the transition later this year. Until then, we are continuing to execute on the studies in MRCLS, synovial sarcoma, non-small cell lung cancer and the multiple myeloma combination study with Merck's PD-1 inhibitor KEYTRUDA or pembrolizumab.

Turning to manufacturing, we continue to make great progress to becoming a fully integrated cell therapy company. We are routinely manufacturing SPEAR T-cells at our Philadelphia Navy Yard facility and have received regulatory clearance to manufacture SPEAR T-cells for all 3 of our wholly-owned clinical programs. We announced in January of this year that we executed an agreement with Cell and Gene Therapy Catapult in the U.K. to provide our own dedicated manufacturing space to secure vector supply for the medium term. And I am pleased to say our vector manufacturing site is now officially open. We also on the manufacturing side had a U.S. patent granted covering a WPRE-free vector system that will further optimize the vector system use in manufacture of our SPEAR T-cells.

To conclude, we have demonstrated compelling results in synovial sarcoma and additional responses in a second solid tumor MRCLS. These data combined with the encouraging initial safety in our MAGE-A10 pilot studies the first we got are the wholly-owned assets along with our unmatched proprietary preclinical development methods reaffirm the potential of our SPEAR T-cell platform in solid tumors. Further, I'll strive towards becoming a fully integrated cell therapy company will put us in the best position to conduct future pivotal studies to support approval and ultimately deliver products and value for our patients and investors. In 2018, we are on track to deliver data from our wholly-owned pipeline in up to 8 different solid tumor sites. With more than $161 million in total liquidity, we are funded to deliver these data and through to early 2020. We are confident that we will achieve our goal with the first to market with an engineer TCR T-cell therapy in solid tumors.

With that, I'd like to open up the call for questions.

QUESTIONS AND ANSWERS

Operator

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

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

First can you help set investor expectations ahead of the NY-ESO myxoid/round cell liposarcoma data coming up at ASCO? How many more patients' worth of data can we expect to see versus what you've already disclosed?

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

So it's very difficult to be precise about things and we dare not to comment on individual patient numbers. It would be a handful of patients and obviously the more recently they have been treated the less data we have on them if you like. So there'll be an update on the patients who we've already given the data out on and -- but essentially we're embargoed from giving you the exact numbers at this point.

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

Got it. And second question, as you dose patients at the 1 billion cell dose with MAGE-A10. Can you talk about the implications of the safety data that's been generated at the 100 million cell dose?

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

I'll let Rafael Amado, our CMO take that one.

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

I think there are different ways to answer that question. I think if there is a clear cut cross reactivity, it is possible to see that with handful of millions of cells so I think a 100 million cells is reassuring with regards to major cross reactivity. I think obviously the more -- the higher the cell dose the more sort of confident we can be that at least an obvious cross reactivity either on target or off target is not present. So we were pretty pleased to see absence of cross reactivity in the first Cohort, but I think the definitive proof will come as we start treating as we are now patients that are 1 billion cells.

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

Just a reminder, that 1 billion cells is really the reason that 1 billion cells they think is important is that approximately the level of cells with NY-ESO that led to major cell expansion within the patients and there is a correlation between expansion in vivo and the response rate so that's obviously we hope it will work in the same way as it did with NY-ESO.

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

Okay. That's helpful. And then just one last one for me. Can you talk about the manufacturing turnaround time at the 1 billion cell dose?

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

Yes. I'll ask Ad Rawcliffe, he runs manufacturing tool (inaudible).

Adrian Rawcliffe - *Adaptimmune Therapeutics plc - CFO*

Certainly. So there's essentially no difference between the manufacturing time at the 1 billion cell dose or 5 billion cells, which is the target dose for the top Cohort in our pilot studies and the 100 million cells we -- as we've discussed before we're operating on around about 30 to 35 days from start to finish for the manufacturing process and release itself.

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

Yes, the actual manufacturing itself is around 10 to 12 days whether it's 100 million cells or 1 billion. We routinely -- when we say we've had routine success at the Navy Yard, we mean we've had routine success of achieving at least 1 billion cell -- transduced cells out of the run because that's essentially the lowest level for the highest dose, it's the mid dose and it's also the lowest level permitted at a highest dose. So that's only the most successful runs, but it doesn't take any longer. We just have a lot of cells left over for the people in the 100 million Cohort.

Operator

Our next question comes from Tony Butler of Guggenheim Securities.

Charles Anthony Butler - *Guggenheim Securities, LLC, Research Division - MD & Senior Equity Analyst*

I have 3 questions, if I may. James, when -- as you're handing off NY-ESO to GSK. Question is are you -- could you characterize that as being in the eight inning? Or you're closer to the fourth inning if you will as it relates to (inaudible) at Adaptimmune they are actually spending more time on that hand off or less time? That's number 1. Number 2 is, you alluded to 1 billion cell dose that was now a non-small cell lung cancer according to the Data Safety Monitoring Board. What is that they're specifically looking at that says that is successful and you can now dose up? Is it simply a duration of time plus toxicity or is there another parameter? And then finally, is there a goal even beyond 1 billion to look at 5 billion, or 2.5 billion or some other number greater than 1 billion?

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

I'll answer questions 1 and 3. As for the eighth inning, I didn't play American football. That was a joke. Remember that. So the answer on the GSK is that it's a multiple modular transition. There are programs that had to be -- there are written up programs and reports. Those mostly are finished. There are trials that are ongoing where you have to agree, which patients we will dose before it gets handed over that's more or less agreed, it's planned 1 or 2 patients discussing that and then as a multiple database transfers agreements that they have to set up, a lot of that is done, it's absolutely going well. Folks say we are right at the cusp of deciding whether we can hand it over. The most difficult thing to hand over, as you probably realize, is manufacturing because it's not something that GSK has done before. It is a very big company, but it hasn't actually got in-house vector manufacturer or in-house cell manufacturing. So I think we're in the sort of penultimate round, if it was a boxing match. I don't know what innings that would be in baseball. Helen, do you want to add anything to that?

Helen Katrina Tayton-Martin - *Adaptimmune Therapeutics plc - Co-Founder and Chief Business Officer*

No, I think that, that's pretty much spot on, I would say when you are in the eighth innings, but it's not done till it's done. Manufacturing is a challenge.

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

Yes. So -- and we still work very constructive with the GSK teams, so I don't think there's any -- this year it's just the timing issue. It does take quite a long time to set these things up. And I'll answer your third question is on the number of cells, all of the trials are set up to go 100 million, 1 billion, and then 5 billion that's the intended number of cells with minor variations, but essentially that is the program. But it was -- the reason that 1 billion, we think is significant is that, that's the sort of threshold level with NY-ESO. So we have the same threshold with MAGE-A10 and MAGE-A4. You wouldn't expect to see responses below that, but you might get them above that, that would be the hope. And I'll let Rafael answer the middle question.

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

Yes, Tony, so the question was essentially how do they adjudicate whether or not to dose escalate. So we made this decision based on recommendation from a safety review committee, which essentially is data monitoring committee for safety and is composed of 3 individuals with expertise in Cell and Gene Therapy, external to the company and external to the trial that is they're not investigators as well as safety physicians from inside the company. There is a charger that sort of stipulates what they look at, but essentially they have focus on dose limiting toxicities whether any have been declared in which case there are rules for expansion of the Cohort or safety event that don't need criteria for DLT, but they could become concerning so they are essentially evaluated and discussed. And so in general, those escalation follow the protocol rules and if there are no DLTs, then after 3 patients, we move on to the next dose. If there are DLTs, will follow the rules, we just essentially add an additional 3 patients. You may recall that's what happened with the non-small cell lung cancer MAGE-A10 study. So that's essentially the process that we follow and just to conclude that DLT window is 30 days so we have to wait 30 days from the dose infusion and we space out patients about 30 days apart. So every Cohort takes 30 days in between patients.

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

And that's the other significance of going up in the dose by the way, is that window reduces so we don't have to wait so long in between the patients.

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

And just to add to what James said in regards to your third question, the third dose Cohort is 5 billion, but every Cohort has a window of sales so the upper bound of the cell dose in the third Cohort has been increased to 10 billion. So we can dose up to that with a target of 5 billion.

Operator

Our next question comes from Robyn Karnauskas of Citi.

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

Just so you mentioned that the window gets shorter as you dose up. So is it shorter than 30 days? Can you elaborate a little bit on that? And then as far as when do you think that you might want to present this data in the second half of the year? Do we expect a press release or a presentation? And then, lastly, what plans are underway? Did you have any discussions as you were going through getting a manufacturing process approved about may be reducing Q2 time to reduce the 35 -- or 30 to 35 days from start to finish?

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

I'll answer the first question. So after the first Cohort, the decisions on accrual between patients are made, if there are no DLTs during the -day observation period. So in essence, we need 7 days for lymphodepletion so we make the decision to lymphodeplete 7 days after the previous patient

has been dose provided that there are no DLTs, which means that in between patients, we have to wait a total of 2 weeks, 7 days for observation and then 7 days of -- to lymphodeplete the subsequent patient. So that assumes they have not been any DLTs in the previous Cohort. If there are DLTs in the previous Cohort, and we do dose escalate, we still maintain a wide space in between patients.

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

In terms of when we actually announced data, I mean, obviously these are all open-label studies and equally obvious is that they're very price-sensitive whether we do or don't get responses and we're acutely conscious of that. I think it's very unlikely that we will therefore be able to hold off announcing data until conferences. And obviously, what we prefer to do and I think what we will end up doing is what we have done with the MRCLS data, which is giving an outline sketch of response data at some form of earnings release or press release and then following it up as soon as we can with the presentation at a medical conference that give more objective obviously. It's not us who will be speaking and on top of that there will be far more data. I don't think it's really possible to just cling onto data, I mean, there are patients and doctors out there who actually go on social media as we've already discovered about various things. So I think it's about to happen as we get a few patients, we wouldn't on single patients, but once we get a few patients then I think we will put in the next either quarterly or put out a press release and then follow it up with the medical conference. And I'll let Adrian talk about the manufacturing timetable.

Adrian Rawcliffe - *Adaptimmune Therapeutics plc - CFO*

Certainly. And so the -- yes, we are working on shortening the release time. The critical step, the largest critical step on that is sterility testing commonly takes 14 days. Obviously, they're are ways of shortening that and we are working on introducing rapid sterility, which would take a week of that timeframe, take 7 days of that timeframe. The theoretical minimum of the current process is similar to that the Novartis has that is sort of in the 22, 23 days and obviously as we push towards commercialization, that would be a more acceptable target for us.

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

And just one follow. So does that mean like within the next 3 months it sounds like we get that data from 1 or 2 patients? Or would you wait to release in it from all 3 patients in a Cohort completed your billion dollar -- sorry, billion cell Cohort -- sorry about that. Tell me -- give me the price? And then secondly is how short do you think over time you can get the turnaround time? You said for commercial 22 to 23 days? Do you think you actually could go beyond that over time or is that sort of the peak?

Adrian Rawcliffe - *Adaptimmune Therapeutics plc - CFO*

I'll take that second question. So with our current process, which has a 12- to 14-day manufacturing time, and using rapid sterility of 7 days, lets say that obviously gives you a theoretical minimum. You -- one can go beyond that, but that's sort of where we're targeting with the existing process, alternative processes could reduce it below that, but that's not where we are at the moment.

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

So I think it's very difficult to answer other question. What I do know is that and we have a large number of patients sitting, waiting for treatment across the MAGE-A4 and MAGE-A10 programs and therefore as long as nothing goes wrong with those patients, we will have data on a significant number of patients over the next few months, it's very (inaudible) that patients do dropout, number 1, for any number of reasons and say it's actually quite difficult to predict exact timelines ourselves, but I think we do have a very good pipeline for (inaudible). We have very good number of patients awaiting treatment and so it's really -- what's relevant is actually more to that gap between patients and actually finding them now both MAGE-A10 and MAGE-A4.

Operator

Our next question comes from Peter Lawson of SunTrust Robinson.

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

Just on the transition of NY-ESO over to GSK. Is there any way of quantifying the number of FTEs that have kind of been freed up in the transaction?

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

Well, we have obviously internal data on all of that. I would say that I don't know if I want to give you an exact number, but I think NY-ESO, by the end of last year was using at least half of the clinical regulatory resources of the U.S. office overall. So it's making a very significant difference in terms of recruiting patients, being able to amend protocols, deal with the FDA, recruit -- add additional sites and the general maintenance, the clinical trials. So I'd say it's probably -- we would have had to add -- it's partly a function that we would have to add enormous numbers of people and to get the same -- if we get the same resources then it's actually free up at least half of the resource -- I am sitting at the Navy Yard, seeing at least half the resources here were being used on the NY-ESO program. So they're all now being freed up to work in our own stuff.

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

Great. And then on the vector manufacturing in the U.K. When you're going to start using that in clinical trial work?

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

Yes, so as you probably know when you setup a new manufacturing facility you do something called an engineering run, those are set for early in the second half of this year and it depends how this goes when we can actually get to GMP runs. I should say that we have -- because I know vector manufacture is a key topic in the industry. We have a lot of slots booked at a lot of different places other than Catapult as well to make sure that we are covered for all emergencies, both companies and academic institutions in the USA. The reason that the Catapult is so important to us is that if in an ideal world, that is where you would make vector for a pivotal trial because it's best to make vector in a single location under your own control and that's what we would like to do. If possible, that's what we would do, but I would hope they will be up and running completely by the end of this year around the end of the year.

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

Great and then for both A10 and A4 when you release efficacy data, sounds like it's going to be 3, 4 patients, there won't be single patients when you get it to first PR or DPR, et cetera?

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

I would hope that the MRCLS is the sort of perfect model really that when we have dosed enough patients to see whether and sort of convincing ourselves and they have -- that we had a reasonable time that we can actually release something and as I say immediately then try and get into the next sort of high-ranked conference for a presentation where obviously more detail given and the patients (inaudible) dose for longer and as I said earlier, there maybe another 1 or 2 patients in the data at ASCO from the original. It is very difficult to be more precise than that and actually ASCO doesn't think as given too much detail away before ASCO has them.

Operator

Our next question comes from Ren Benjamin of Raymond James.

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

I guess, maybe just starting off as we move from 100 million cells to 1 billion do you see any additional -- or when you're doing the work do you see any correlation between expression levels of antigens? And potentially AEs trying to get a sense of the higher levels of antigen expression leads to more potentially AEs.

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

So, it's Rafael. I think it is a really good assumption. It's difficult for us to make that correlation right now because of the sample size. But all I can say is that when patients coming to the study with bulky disease and high expression levels, we obviously are very tuned into the potential for toxicity, but I cannot say that right now we are seeing appreciable differences based on antigen. May be in the future, as we treat more patients, that would be the case. But so far, the numbers don't (inaudible) out.

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

Got it. And, I guess, just switching gears kind of back to the Philadelphia Navy Yard. Can you talk a little bit about what the current manufacturing capacity is and what if potentially could be as you get closer to commercialization?

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

Yes, so right now the capacity -- we also still retain our contract with (inaudible) Hitachi which used to be PCT by the way and that capacity is roughly 8 to 10 patients a month and we expect to be that level at the Navy Yard within a short period from now. So it will quite adequately deal with the pilot studies. So that's okay. The Navy Yard is actually designed to get much bigger initially it can go to around 300 patients a year and then 3x that we build out the second half of it. So it's a modular building so what we physically build out we can get up if you put in more equipment and obviously took on some more people, we get up to around 300 patients a year if you go beyond the second half you can triple that and actually we have an option on the land next door to this building to put another one up if needed it. So it's a modular approach to -- which will follow the trials basically. We have success, we will obviously go to the board and ask for permission to build the other half of the building and then we'll be quite well advanced.

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

Right. Okay. And then just sticking with manufacturing. Can you talk a little bit about the next generation approach and is that already being worked on at the Philadelphia Navy Yard or is that still kind of very early in development and maybe just some thoughts as to when you think that next-generation approach could get to the clinic?

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

So we have a very substantial process development team actually in the U.K. and the second team here in the Navy Yard looking at everything from vector all the way through to cell manufacturing. So you can do a lot of incremental things on both vector and cell manufacturing, which we're doing. So things change all the time and in fact one of the biggest advantages, I would say, I would hate to be in a position without my facility because I think one of the biggest advantage having your own facility is that you can implement incremental changes very, very quickly and effectively, you can see in real-time what needs to be changed and change it, which is incredibly helpful. So the version 2 in the vector side is what it's designed to be used in the Catapult and in fact we have 1 commercial supplier of vector other than the Catapult where all they tried to develop that and that has been developed in-house. On the cell manufacturers, it's a continuous process as Ad mentioned, the next step is to get a sterility testing done from 2 weeks to 1 week, which automatically we just chop a week off the manufacturing time, but there are a lot of other things that

we are doing in terms of a whole loads of things internally to do that. So it's a bit of a how long is a piece of string, I don't think we'll ever give up process development in cell manufacturing for the next at least 10 years.

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

Got it. And then just one final one for me. I think you mentioned James from the prepared remarks about combination with checkpoint inhibitors. Can you talk a little bit more about how you guys are viewing that program? Will it be patients who have already been treated with checkpoint inhibitors and now you're trying to potentially desensitize them? Do they need to be naive and, I guess, I'm really interested also in hearing yours and Rafael's thoughts on the idea of genetically deleting PD-1 from these T-cells. What the -- what do you think in terms of the advantages and disadvantages of that strategy? I think one of your patents is the next-generation that tackles the immunosuppressive microenvironment.

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

Yes, so just to be clear, what we are doing now, we are running a multiple myeloma study, which is a randomized 28 patients study half of whom will get our cells alone and the other half will get our cells and then 4 weeks later they get KEYTRUDA or pembrolizumab. So that is a trial ingoing, that's one of the trails that we did carry on recruiting and when GSK takes over the program, they will just finish up that trial, so we call that inflight. We are the company extremely interested in running combination studies with our own programs once we have understood both the responsive and the safety profile of our own programs. I'm a great believer in not altering 8 variables at once. You don't really know what is happening. So what we're trying to do is if we get a response, but it's not deep or durable enough we'll be very keen to do combination studies. I'll let Rafael take over from there.

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

Yes. So I think we are learning a lot actually on how to operationalize the combination of PD-1 and SPEAR T-cells from multiple myeloma study. That study is going pretty well. We have an interim safety path to look at potential toxicity of the combination and then it will continue on to accrue. It will be obviously transferred to GSK into Cohort after the transition takes effect. But it's been a very good learning experience for us as we prepare for potential combinations with our own proprietary pipeline and I can say those discussions are already ongoing with the right companies. With regards to whether doing genetic editing for PD-1 or any other checkpoint receptors (inaudible), obviously, there are groups doing that externally. We have the opinion that it's probably best to use a pharmaceutical first to sort of be able to titrate potential toxicities, remove the product if the tolerability is not there, but then once we establish benefit risks then consider whether that is something that could be incorporate into a second generation program. That's true particularly for things like PD-1 receptors or all the checkpoint receptors where the potential toxicity is there. With regards to other ways to interdict tumor microenvironment to affect a bit of spreading, et cetera, those are part of our second-generation strategies, which we are by definition building them into our constructs together with the parental TCR.

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

I think we're quite nervous about introducing immediately into a new trial -- into a new product, a PD-1 knockout into the cell because it causes (inaudible) reversible so we must clean as Rafael said on the pharmaceutical combination because obviously you can titrate the dose and the pharmaceutical product itself has a known toxicity and obviously PK profile, et cetera. I'll let Gwen comment a little on the second-generation program on the tumor microenvironment program because that is not PD-1.

Gwendolyn Binder-Scholl - *Adaptimmune Therapeutics plc - CTO*

Yes sure. Thanks James, I would also add to the PD-1 discussion that by using PD blockade to stomach, where your not just affecting the SPEAR T-cells, but also the other T-cells in the body to maybe rejuvenate some endogenous immune responses against other tumor antigen, just as neoantigen, and other [camps]to test these antigens that might be expressed so there could be advantages to the combination that maybe preferred over engineering in a PD-1 knockout. And in particular with ourselves, we don't see a massive upregulation of PD-1 as well so it might

not actually be effective in all of ourselves. Instead we've refocused on 4 approaches, second generation approaches all of which are going through preclinical testing right now for -- so that we're able to select one or more to go into our MAGE-A4 programs next year. And they are meant to address 3 areas. The first, there is 2 programs that are meant to address the immunosuppressive effects of the tumor microenvironment, and actually the phosphodiesterase patent that was just issued is one of those 2 approaches. The other approach we previously publicly disclosed, it's the expression of the dominant negative TGF-beta receptor. The -- a second approach is to have inducible expression of cytokine with the T-cells to help promote expansion of those T-cells in vivo. And the third approach is to express a gene that helps to improve the function of the CD4 component of our SPEAR T product and that's important because the CD4 T-cell helped to (inaudible) the toxic T-cells components of product will actually help to drive antigen spreading in the patients and also can mediate direct antitumor toxicity so overall that would improve potency of the product.

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

Just as a quick follow-up on the multiple myeloma study. Because I totally forgotten about that. Can you just give us an update as to -- it seems like from Rafael's comments that you've already treated patients with KEYTRUDA and so there is some learnings from that. And I think you mentioned an interim look maybe I heard that wrong. But can you give us an up -- status update on what's happening with that strategy and when we might see some results?

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

So the study is designed so that after 3 patients have been treated with the combination of KEYTRUDA and SPEAR T-cells, there'll be a pause to look at safety and because it's a randomized trial that will be approximately after 6 patients have been enrolled. We are enrolling in the pre-interim analysis phase of the study and we have -- and the screening has been quite good and there has been quite a bit of a excitement around that trial. We anticipate that the trial will be transferred to GSK obviously upon transition and whether or not the interim analysis will be done under our oversight or GSK's oversight obviously depends on when that translation takes place.

Operator

Our next question comes from Eric Schmidt of Cowen and Company.

Eric Thomas Schmidt - *Cowen and Company, LLC, Research Division - MD and Senior Research Analyst*

It was a little unclear to me from the prior discussion whether or not you actually dosed a patient at 1 billion cells with the A10 in the triple tumor trial. May be Rafael could clarify.

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

So I think that the payment was made in the prepared remarks is that we are dosing at 1 billion cell.

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

Yes.

Eric Thomas Schmidt - *Cowen and Company, LLC, Research Division - MD and Senior Research Analyst*

Okay. And then in terms of the ASCO poster on MAGE-A10, the safety update. I know we saw 8 patients earlier in the year. Roughly how many more should we expect there?

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

I think the poster will cover those 8 patients actually and there'll be much more detailed examination of what happen and what didn't happen with them.

Eric Thomas Schmidt - *Cowen and Company, LLC, Research Division - MD and Senior Research Analyst*

And when should we start thinking about sort of the next generation of SPEARS, say a new IND candidate, when might that be disclosed?

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

So as Gwen said, we're going to do preclinical testing. I think the -- there are multiple -- they're actually some which are -- at least 1 for MAGE-A10, which is clinically ready and there are severals MAGE-A4, which will be clinically ready, i.e. ready for an IND sometimes this year, but actually what's much more likely to determine the timing and filing an IND is, which one do we need and why? In other words based on the data from the initial pilot studies from MAGE-A4, we wouldn't just launch an IND with a new second-generation candidate if we're doing really well particularly. If the evidence for the A relapse is X, then -- and we got something to do with X, then we would obviously launch that one as soon as we could, but could be next year, but it certainly won't be this year, but we really need to get much more data on generation 1 before we select the generation 2 because it may be appropriate to continue generation 1 in the given disease and generation 2 in something else. So it's a bit of a complicated matrix, but the programs themselves will be ready to go into the clinic sometime next year if we so choose.

Eric Thomas Schmidt - *Cowen and Company, LLC, Research Division - MD and Senior Research Analyst*

That all makes sens, James. Are there other late stage preclinical programs that are looking at different antigen targets?

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

Yes, yes, and again, we would -- our target would be to have one of those ready for the clinic next year and one the year after.

Operator

Our next question comes from Jim Birchenough of Wells Fargo.

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

It's Nick in for Jim, this morning. Thanks for a lot of details and not dropping the ball there James. Well done on the sports question. So in terms of transitioning to 5 billion cells. It sounds like, if everything is ticking along well, and it's approximately 2 weeks between patients so within a quarter, would -- should we be expecting the transition to 5 billion from 1 billion?

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

As I said earlier, it's very difficult to be precise. So go to 5 billion, you have to have 3 patients with the gap. You then have to have a safety review committee, you have to have no DLTs because you have a DLT, you have to expand the Cohort and also some Cohorts recruit much more quickly than others. So it's very difficult, but I -- if things go well, we will definitely be in the 5 billion later this year with both MAGE-A4 and MAGE-A10. It is -- I'm not being difficult it's just -- it is very difficult to be precise about that.

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

Right. So, I guess, I'm not -- if you have patients waiting in queue to get cells what -- where the delay is?

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

Well patients, as I mentioned earlier, patients do drop out or their doctors can decide they are not well enough or they can simply pull out of a study. Any patient can pull out of a study. The doctor can turn around and say, well actually I advise you to have something else first, et cetera. They're whole host of reasons why patients dropout. They may not feel well. They may have -- they make -- have some other -- may contract pneumonia or something. These patients are obviously a lot of them are very unwell and therefore there are a number of reasons why people drop out and if you have someone drop out, the next person won't immediately be ready. They won't (inaudible) to be manufactured. Their doctor maybe waiting for them to washout from chemotherapy or something, in other words the next patient who we'd scheduled for a month away maybe not be able to be brought forward. So that's why it's at a practical level, it's extremely difficult to get the timing exactly right. I'm not trying to obfuscate but all I could say is that we get a better lineup of patients than we've ever had before.

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

Okay. Have you -- if had the situation where you've manufactured products but then lost the patient between the decision to manufacture and administrator?

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

Yes, well, actually we on a number of occasions, we know the patient won't be ready so we categorize patients into those who could take the product immediately if the product is available. But as you know, number of patients who we know are going to go off and have some other treatment. So we often manufactured sort of prospectively for patients because as I said, we got a certain number of slots so we use those manufacturing slots and sometimes those patients go on something else and do very well or do very badly and never become available. So there any number of reasons. We do occasionally lose patients because they progressed too much during the manufacturing, but I wouldn't say that's the largest cause of loss of patients by any means.

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

Okay. And then in terms of these newer generation of cells -- sorry SPEAR products, such as the (inaudible) TGF-beta that you previously described. Would you have to start from scratch with a product like that or would be able to say start it at 1 billion cells or does it depend on the characteristics of the cell?

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

That's a very good question. I think, I let Rafael answer that.

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

Yes. So we are rethinking our approach to what doses to start with, with SPEAR T-cells whether the first or second generation based on our current experience. Our hope and obviously this is without having had the proper regulatory discussions is that we could start if we have cleared the top dose in the program that uses the parental TCR then we can start with at least 1 billion cells and that will likely be our proposal going forward. Based on the fact that the parental TCR host has already -- we've already been able to exclude cross reactivity and also if the secondary gene is not

thought to add any further toxicity and we're completing the preclinical safety assessment in all this strategies that Gwen just outlined earlier in the call. So the answer is, yes that we would try to start with the higher cell dose than we do with branded TCRs.

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

Okay. That seems a very reasonable strategy. And then maybe just last one for me, there (inaudible) lot of questions answered. Can you sort of give us an update on where you are with Universal Cells and also the Bellicum collaboration?

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

So I mean (inaudible) continues to make good progress. It's still a long way from the clinic. I don't think we really can update you on anything very significant. It's a long term, it's a complex and quite a long-term project. I am delighted to say that that takeover by (inaudible) has made no difference at all to the extent to which Universal Cells wants to indulge and collaborate with us. So I think that's going very well. And I don't think we have anything on the Bellicum front to say. We know we've done some preclinical work and we'll probably be -- I think we aim to say much more at the end of the year.

Operator

Our next question comes from Ying Huang of Bank of America.

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

This is Jenny on for Huang. I just wanted to ask about the competitive landscape now that you were talking more about Kite 71A with MAGE-A3, MAGE-A6, just wondering how you guys differentiate and definitely what indications you think A4 and A10 have in advantage over A3, A6 and then also with your relatively clean safety profile, have you guys thought about dosing patients in outpatient rather than the hospital setting?

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

So on the competitive situation, I think it's inevitable to -- given the interest in achieving data in solid tumors, that there'll be a lot of people trying to get into the space. The CAR-T has got wonderful data in hematological tumors and 2 approvals and more to come obviously in these (inaudible) data. There's no question that in hematological tumors, it has been fantastic data. It's very difficult for us to comment on competitive programs until you get a sort of data set as significant and using the same set of patients. We're very careful on the -- and ways the programs do 4 different cohorts with very specific entry criteria. You can actually look at them and they're each a reasonable size, 10, 12 patients. You can actually look at the response rates. It's very difficult to find data for other companies, which have gone through 40 or 50 patients like that and given stratified data on response rate and safety. So that's the first thing. In terms of capacity of this, I can't remember the HLAs the MAGE-A3, MAGE-A6, but it's not A2, I think it is (inaudible) A4 from memory. So it's a different HLA type. The way these cancer tested antigens work, is that they tend to be present on 20% or 30% of many other tumors. Now MAGE-A4 we consider to be our sort of prized project because it happens to be on a higher percentage in quite a lot of tumors and that's why we're in 7 different tumors because it's highly presented. So MAGE-A3 or MAGE-A6, it would depend on exactly the way individual patients overlapped. I didn't have that in my head at the moment because it so -- it won't be the same patients who present MAGE-A3 and MAGE-A6 and the (inaudible) A4 as are A2, A1 represent MAGE-A4. So I think it's very difficult. I think that -- first of all I think we need to see quite significant bodies. We're very conscious, we're not arrogant. We know that other people come here with data. As it happens, we do think that the affinity maturation is the key to getting responses. It certainly the key in preclinical programs that we run. And I'll let Rafael talk about whether we think that these are going to be outpatient programs.

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

Well, I think on the second question, it's premature to really make a prediction on that. Certainly, we're not at a point we're able to say that this could be given as an outpatient. I know that in the CAR space, everything has been sort of very prescribed with predetermined centers that are qualified to administer these products, but that there's already efforts out there to make this more community setting based if the safety and tolerability of the CAR warranted. I think in the TCR space were update earlier than in the CAR space, we'll be able to say that. But certainly, our goal will be to make this available to as many patients as possible and to the extent that training physicians and understanding the safety and tolerability allows us to streamline the process. We will work to do that as we commercialize the product. But right now, it's difficult to say much more than that.

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 and Director*

Well, thank you everyone for the questions. They were certainly covered a wide range of things today. And I think really represent the stage the company is at. This is a really, really exciting moment for us getting through the safety cohorts and then getting towards the response data and programs that we own ourselves. At the same time, as retaining our emphasis on innovation, which is why we talked about the 2 new patterns today at the same time as making sure that people have really understood the progress we've been making on manufacturing both in facilities and people, but also in innovation and the manufacturing side. So this is as I said we had a really outstanding first quarter moving everything forward. And I am very excited about the rest of the year. 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.
