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Q4 2018 Adaptimmune Therapeutics PLC Earnings Call

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PRESENTATION

Operator

Good day, ladies and gentlemen, and welcome to the Adaptimmune Therapeutics conference call. (Operator Instructions)

I would now like to introduce your host for today's conference, 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 fourth quarter and full year 2018 financial results and other business updates. We issued a press release earlier this morning, and I would ask you to please review the full text of our forward-looking statements. As a reminder, we anticipate making projections during this call, and actual results could differ materially due to a number of factors.

In addition, I would like to make you aware of an update to our SPEAR T-cell nomenclature. From here forward, we will refer to our SPEAR T-cell's with a prefix, ADP for our company name, followed by a reference to the HLA-type specific for the SPEAR T-cell, which is currently A2 for all of our trials and then a reference to the target antigen.

So MAGE-A10 is now ADP-A2M10, MAGE-A4 is ADP-A2M4 and AFP is ADP-A2AFP. This is also outlined on our website for reference.

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

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

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

Thank you, Juli. Good morning, everyone, and thank you for joining us. We came a very long way during 2018. We started the year with trials in our partnered NY-ESO program and 2 studies with our wholly-owned SPEAR T-cells targeting MAGE-A10. We had not treated any patients in our other 2 wholly owned programs targeting MAGE-A4 or AFP.

In January last year, we had just announced our first successful manufacture of patient product at our Navy Yard facility and that we have finalized an agreement to open a dedicated vector manufacturing plant in the U.K. By the end of 2018, we had transitioned the NY-ESO program to GSK, allowing us to focus on our 3 wholly-owned programs.

Our trials with our SPEAR T-cell targeting MAGE-A10, MAGE-A4 and AFP all cleared major safety milestones and progressed throughout 2018. In addition, we are routinely manufacturing patient product at target doses at our Navy Yard facility for multiple solid tumors, and we expect to have our first vector production in the U.K. in 2019.

In our trials with ADP-A2M10 and ADP-A2M4, we saw no evidence of off-target toxicity or alloreactivity in the first 3 dose cohorts, which enabled us to progress into the expansion phase, treating patients with up to 10 billion cells. We are currently enrolling and dosing in the expansion phase of all 3 studies. As previously indicated, we are accumulating data and plan to give a full clinical update at our next quarterly call in May of this year.

We also cleared the first dose cohort in our ADP-A2AFP study and are currently dosing in the second cohort with target doses of 1 billion cells. Later today, you will find an abstract that will be available online for the upcoming AACR conference, where we will provide a safety update on the first 2 patients of this study. We plan to provide further updates throughout the year.

Our trials have progressed as planned, and we have continued to add new clinical sites. We are working with more than 20 active clinical sites at leading cancer centers in the USA, Canada and in the EU. We have also increased our focus on our translational research to understand fully our SPEAR T-cell. To that end, there were several key pieces of translational data published last year, which we believe are critical to the conduct of our trials. First, data from Cohorts 1 and 4 of our partnered NY-ESO study in synovial sarcoma indicated that a more intense preconditioning regimen could be beneficial.

Second, upon further investigation of the cytokine profile from the peripheral blood of these patients, we found that there were higher levels of cytokines that promote T-cell growth and expansion in the Cohort 1 patients who received more intense preconditioning compared to the Cohort 4 patients. These data prompted us to increase the intensity of preconditioning in our current trials. We have learned a great deal from our translational research to date and it will continue to inform our current and future trials. We have been working for some time on ways to improve how our T-cells confined and destroy cancer cells as part of our next-generation programs. We have already shared data for 2 initial next-generation approaches, namely phosphodiesterase and TGF-beta.

As you will see in another AACR abstract coming out later today, we will share initial data for another next-generation SPEAR T-cell, in which we have added a CD8 alpha homodimer that will be expressed along with our engineered TCR targeting MAGE-A4. The addition of the CD8 element is believed to increase TCR binding ability and promote CD4 T-cell responses post-infusion, thereby, broadening the immune response against our tumor targets.

We also made good progress with our off-the-shelf program in 2018. In addition, we have been actively exploring potential collaborations with partners, which have technologies that could enhance the activity of our SPEAR T-cells. This is an exciting area and one in which we feel we are well positioned to lead the way and advancing not only our knowledge of TCR therapy but also the way in which TCRs are employed to fight cancers.

Turning to manufacturing. Capacity at our Navy Yard facility is now at 10 patients per month and scalable to 30 patients without significant additional capital expenditure. We also have capacity for 10 patients per month at our CMO HCATS, formerly PCT. In addition, we have implemented rapid sterility testing at our Navy Yard facility to better deliver SPEAR T-cell to patients.

With respect to vector, we are well positioned with our own vector manufacturing coming online as well as production in place at a third-party vendor. The vendor has already manufactured vector for ADP-A2M10, ADP-A2M4, ADP-A2AFP and next-generation SPEAR T-cells, and we anticipate vector production using our proprietary suspension process at our dedicated facility in 2019.

We remain funded to late 2020 and are well positioned to complete our trials and to initiate the next stage of development. We continue to examine data in trials with an eye to the future, so that we can utilize our therapies in the most effective way for patients.

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

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) And our first question comes from Jonathan Chang with SVB Leerink.

Wei Ji Chang ***SVB Leerink LLC, Research Division - MD of Emerging Oncology & Senior Research Analyst***

First question, based on the NY-ESO experience, would you expect responses from the MAGE-A4 and MAGE-A10 studies to be achieved in the first 2 scans?

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

Rafael, do you want to call it?

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

I'm not sure I heard the question. Are you saying the first 2 scans?

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

Yes. The question, Rafael, just to repeat, it wasn't quite clear. Was the -- based on the NY-ESO experience, would you expect to see responses when you have had 2 scans in patients?

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

Yes, it's a good question. In general, in sarcoma, responders have responded perhaps within the first 2 scans. Many patients of the first scan were underway to responding but didn't achieve the 30% threshold from RECIST. So these are not fulminant responses where you see large decreases in tumor size right away. So perhaps you start with a percentage and then eventually it crosses the threshold, whether it's at the second scan or the third, that varies patient by patient. I think the patients that took the longest to respond took 6 months, and occasionally, there's been patients that have responded at the first scan. But I would say that by the second scan, the majority of patients that were to respond have responded. Now those are unconfirmed responses, so as you know, one needs another scan at least 28 days later to confirm that response.

Wei Ji Chang ***SVB Leerink LLC, Research Division - MD of Emerging Oncology & Senior Research Analyst***

Got it. Second question, can you talk about reasons for confidence in why responses could be achieved at the current high dose being evaluated in those studies with the optimized High Flu regimen?

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

Well, we...

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

Go ahead.

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

I will just say a couple of comments and then pass it on to you, James. I think nobody knows what the best conditioning regimen is, but choosing those 2 drugs, High Flu, both in terms of clinical outcomes, measured by response and durability and also by biomarkers such as cytokines that promote T-cell expansion with higher doses of fludarabine are better, and that's -- I think been shown in our NY-ESO studies and then we've been able to replicate that in our mixed trials as well. We're now looking at the role of cyclophosphamide and whether higher doses of cyclophosphamide, such as dose employed in Cohort 1 also contribute to higher peak expansions. And so I think conditioning is definitely important. And higher doses of cells, we know what the minimum dose is. We haven't characterized the dose response curve at the upper limit of some numbers because, frankly, we weren't -- we didn't make 10 billion or 15 billion cells in the past. Now routinely, we're able to make high number of cells in our facility and so we're planning to see whether there is a dose-response relationship at the upper range of the dosing curve. So I think a higher-dose question is still to be answered. The floor, I think, is 1 billion cells. We rarely see anything below 1 billion.

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

Yes, so just to add, the concept of dose-driving studies wasn't always in any of the protocols in either our or actually any of the other players, and so the -- if you -- as you get back to the NY-ESO cohorts, we effectively dosed the patients with the number of cells that we had produced as of the previous manufacturing systems, and in fact, from memory, in Cohort 1, they range from about 300 million cells to 14 billion, and in fact, the range was based on at least 10% transduced cells anywhere between 1 billion and 10 billion cells, and in fact,

one patient got 14 billion. So there was no dose-response information coming out of the original studies because none of them were designed that way, but we are seeing, as Rafael said, that you see nothing when you dose patients with below 1 billion cells because you don't get any decent persistence or expansion in vivo. So we think, obviously, it's that threshold effect.

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

Yes. I mean, I would also add that when this product was tested at the NCI, they gave a medium of 50 billion cells. This was some time ago. They used IL-2. It was separate to viral vector. It was a different manufacturing process. So there are all the caveats about whether the T-cells were the same. The TCR was the same TCR, but the T-cells may have been different. But in that institution, they routinely administer many for higher doses. So I think no one really knows in the TCR co what the optimal high dose is, and as I said before, we're attempting to characterize it now because this is really the right time to do it during the dose-finding studies.

Wei Ji Chang ***SVB Leerink LLC, Research Division - MD of Emerging Oncology & Senior Research Analyst***

Okay, got it. That's helpful. Just one last question from me. Will investors get a sense of durability of responses achieved in the May update?

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

I think that's very difficult to expect just because the way the expansion and third cohort really started very -- towards the end of last year and actually then what happens, you have to understand there's quite a long period for, first of all, the patients have to [be -- freeze] then they have to -- the cells that you manufactured and then the first scan doesn't take place for either 4 weeks or 6 weeks depending on the protocol and obviously, the second scan, therefore, doesn't take place for another 4 weeks after that. So the first scan just gives you unconfirmed response data. The second one gives you confirmed, but I don't think we'll have any meaningful durability data in there, I don't think the timetable works for that.

Operator

And our next question comes from Peter Lawson with SunTrust Robinson.

Minh Vong ***SunTrust Robinson Humphrey, Inc., Research Division - Associate***

This is Minh on for Peter. I guess a few questions on the expansion cohort. This seems to us that there are 2 advantages in the expansion phase, in one [year] the lack of staggering. But also there's an increase of our upper range for the target dose to 10 billion from 6 billion. I guess, can you talk a little bit about the progress you've made in manufacturing that may take advantage of using the increased upper limit because it seems to us that mostly manufacturing driving it, not so much patient characteristics, but also if you can comment on whether certain patients may be excluded from being able to take in high dosage as well.

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

Yes, I'll make a general comment and that's I think if you'd asked us 2 years ago whether we would regularly produce 5 billion cells, we'd have said no way, but actually we have made a lot of progress, but I'll ask Ad to comment specifically. Ad Rawcliffe, our CFO, since he's in charge of manufacturing.

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

Yes, so I think you're right to characterize, as Rafael spoke to the confidence in the top end of that dose range has been established by the performance of the manufacturing organization over the past 18 months or so. And key to that is, obviously, the setting up of our own cell manufacturing site and the development of that up to its current capacity of sort of 10 patient slots per month at the moment. And we are routinely getting cell doses out or transduced cells that are around 10 billion cells and in some cases, even higher. So it seemed logical to be able to give all of those cells to patients, and we've not so far characterized patients who would not be eligible for the top end of that dose different to the -- this sort of 6 billion threshold on the third cohort either. But that's all a function of the number of transduced cells that we get out, which in turn, relies on the vector efficiency and things like that. So it's a number of improvements across the entire manufacturing process that's led us to this point.

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

Yes, I would point out something that's been remarked on before, and that's the biggest variable autologous T-cell therapy is of course the starting material. And I think there is an incredible advantage of having your own manufacturing facility. So for example, we can

actually normally tell within the first week of manufacturing a particular patient, whether we're going to get enough cells at the end of the manufacture. So the end of sort of 4 days or so, we actually know whether we're going to have a success, and if we're not looking very successful, then we can just initiate a second run for the same patient out of the same apheresis and make it up. So the patient will never know that there was a -- the manufacturing was difficult, and I think all of those things are part of the learning of the -- that really justifies the investment in having your own facility. In fact, I would go so far as to say that not having your own manufacturing is more or less catastrophic for an autologous T-cell company right now because the technology is still evolving and the only way you can control that evolution is to have the process under your own house, under your own roof.

Minh Vong ***SunTrust Robinson Humphrey, Inc., Research Division - Associate***

I see. Great. So I guess, right now -- I guess, from MAGE-A4, I guess, you have 3 patients in progress for the expansion. Do you happen to have sort of how many patients you may see in the May update from the expansion? And then also, I guess, given all these variables in play, what would you say on, I guess, of all the patients you would probably treat, like how many of them may receive up to 10 billion cell dose?

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

Yes, so we're not giving individual patient numbers out. But anybody in the expansion phase is eligible to get 10 billion. So some will, some won't.

Minh Vong ***SunTrust Robinson Humphrey, Inc., Research Division - Associate***

Okay, great. I guess, one final question for Rafael. How are you thinking about integrating? Since now that you have kind of combined your roles in as clinical and R&D. Can you give us a little bit more color about your plans on integrating the two? And changes that may be made flowing from the clinic to -- or R&D to clinic?

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

Yes, that's a great question. I think in oncology, it's a comparative advantage to have R&D integrated because as you know, approvals can be attained with very early phase trials, and so you want to have that cross-pollination of people that understand how to develop drugs, how to write labels, and how to understand a med need and regulatory guidance, et cetera. Those people working with the scientist very early on in how they select the targets and how they use surrogate markers for PKPD relationships, and eventually, how to design the trial. And so our discovery group now is really exclusively focused on activities that have line of sight to making medicines and all the activities that support that, not just obviously, the discovery of the product but also characterization and improvement and translational sciences that will tell us how our products are functioning in vivo. And so likewise, the discovery group is also now better informed of what's happening in the clinic and so when we are designing improvements, such as some of the ones that James described in the second generation, they're going to be tailored to whatever deficits we are observing in patient tissue with regards to the potency of the T-cells, their ability to traffic to the tumor site to kill cancer cells, to persist, et cetera. So it's that start cross talk, I think, that's going to be really necessary from the choice of the target to the choice of the disease to characterization in patients, back to improvement of the TCR and T-cell product. And so it's sort of a 3-legged stool, if you will, aside from research and development, manufacturing is an intricate part of what we do because it's really the T-cell that is the effect of cell that causes cancer killing and they're also very well integrated within our discovery and development group. So that's been really the emphasis as in fact to cover is to really unify these 3 groups and remove anything that was strenuous to being able to get a drug in the market. So I know this is sort of a high-level answer, but it's -- I think those are the fundamentals of our R&D organization at the moment.

Operator

And our next question comes from Peter Lawson with SunTrust.

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

Just a couple of follow-ups. Just as we think beyond May, the potential updates there, how should we be thinking about the timing of other data for the year and potential venues for data?

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

Yes, so when we say we're going to give a full update in May, we're going to give details on responses of any, obviously, across the programs. We're also going to give an update of what we intend to do with the programs, first and second generation, in other words, what further trials we will be setting up, which trials will be looking to start and will also, at that time, give details of where we can present. As you know, one of the issues with presenting with these very small patient numbers is the very long lead times for the conferences, that's sometimes difficult unless you have a late breaking abstract. So -- but at the May meeting, we intend to give a sort of complete overview of where we are today, and where we're going from today and if we can, we'll give the conference information out at that time. As you've seen today, we've just put a couple of the abstracts in the AACR, which will be published online later today, and one on the CD8, one on the AFP safety profile. And we'll also be following it up. So we do intend to give quite a full May update, not just saying what has happened in the trials, but also what we plan in future, which programs going to go forward, in what respect, and then what type of trials, and we'll also try to give a better indication of where we expect to present data.

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

Got you. And -- more, the data you have so far and also how the competitive landscapes are changing. Do you think it's kind of pointing more towards combination therapies versus monotherapy?

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

I think we're interested in both actually. And I think we remain interested in both. We've always, as you know, with the NY-ESO program, we ran a combination that obviously it's now gone to GSK. We ran a combination study with KEYTRUDA on multiple myeloma, and they -- that was an initial study which we handed over to them. And actually it's more important to look at the effect of a monotherapy and then to see if there is a role for a rationale, a scientific rationale for adding a combination to that. So rather than start off with it, I think, we'll always start with a monotherapy, if you like, and maybe first generation, maybe second generation and then add a combination study to that if it's appropriate in the context of that disease. We didn't run a -- as you have noticed, we didn't run a combination study in sarcoma because it wouldn't have been appropriate in that instance. So I think where there is a role, whether it's a disease which might help, we will -- we're just as keen as ever, but we'll start with monotherapy and then move to combination trials when there is a disease where it looks as though the combination will be beneficial.

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

And then just a couple of questions for Adrian. Just around any pointers on expense spend for 2019? And how we should be thinking about the cap rates of revenue line item going forwards?

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

Yes, so I think the guidance that we've given produces a fairly logical and rational outcome as to what the cash burn will be for 2019 and 2020, and that at the end of last year, we closed with $205 million of total liquidity. And that we've said it takes us to late 2020. So without -- we're not going to give guidance on an expense line basis or indeed in total, but I think that gives you a fairly clear runway as to what that is likely to look like within realms of materiality, certainly. On the revenue line, I think the large payments that we've had relating to the GSK contract, I think have largely happened in the short term, one is in 2018 and 2017 as well, and the GSK contract is now in a phase where as we've talked about before, they're able to nominate additional targets, but we do -- we complete the work through to a preclinical stage, and we don't take that into the clinic, and so that will carry on and we anticipate getting revenue from that, but not to the same magnitude obviously, as the option fees, or indeed future development milestones that might be associated with any of the programs.

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

Got you. And the other income expense line item, I didn't catch that, was there anything -- was there a one-timer in that?

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

The other income and expense line largely relates to the exchange rate gains and losses on the portfolio of investments that we hold as part of our total liquidity balance. So we hold those and the balance sheet of our U.K. subsidiary when converted back into dollars. So there is not actually a -- is not a real expense gain or loss but it is an accounting expense gain or loss.

Operator

And our next question comes from Michael Schmidt with Guggenheim Securities.

Kelsey Beatrice Goodwin ***Guggenheim Securities, LLC, Research Division - Associate***

This is actually Kelsey on for Michael. Two quick questions. First on your last earnings call, you had mentioned that the A10 enrollment was accruing mostly nonsmall cell kind of across both studies. And then the A4 was mostly ovarian. Has there been a focus on further diversifying these? Or should we be expecting mostly read through to those two? And then secondly, how will the May data update inform potential next development steps kind of what are the clinical hurdles?

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

Rafael, do you want to answer that one -- these two?

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

Sure. So for MAGE-A10, there are 2 trials, one is exclusively long, and obviously that one is enrolling all histologies of lung cancer, squamous and adeno mostly, and that's in the expansion phase as was mentioned before. And then there is a triple tumor one, which is enrolling bladder, head and neck and melanoma, and I'll have to look at the numbers, but I think it's been pretty diversified in terms of the histologies for those 3 tumor types. So we haven't really suffered from a clustering of a particular tumor type in the triple tumor. In MAGE-A4, we did, initially in the dose expansion, have mostly ovarian cancer patients and that was just a function of the fact that we have had a NY-ESO study in ovarian cancer. So we had a lot of patients that we knew already were accelerate to positive and the investigators were very keen to see whether they would qualify for a MAGE-A4 study, and so therefore, we got a bolus of patients that came through, and because we were trying to characterize the safety and tolerability, then the histology wasn't as critical. Since then, we've made efforts to expand the range of tumors. But having said that, there are 9 tumor types in that MAGE-A4 study. So it's really very difficult to have a very good representation of each one of the tumor types, and we won't have that by May because, obviously, by May, this study wouldn't have finished. But we have made a lot of progress in enrolling patients with other diseases, including bladder, head and neck, some melanomas and gastric and others. And recently, I think we announced in the not too distant past that we added sarcoma to that trial and so we went ahead and added a number of centers that are sarcoma center, with which we have been working with in the past in NY-ESO. And so we have a runway of patients with synovial sarcoma, and we're also trying to recruit MRCLS patients, and we've been successful in finding those patients, some of them have been treated already, some are being treated now and there are some to be treated that hopefully will have some results to talk about during the May call. So I would say won't be a full diversity in MAGE-A4 but there will be representation from a number of tumors, and in order to accomplish that, we've come to disease-specific sites as well. In the past, we were mostly in phase I sites, where we would get whatever gets referred to the phase I unit and now we are able to go to disease-specific sites to get the specific tumors that we would like to get, to have enough diversity. And in terms of what would emerge from that, I think we would need to characterize the signal well enough before we're launching 2 large trials or registration trials, and I think that's something that we will know when see it. So if see responses, we will continue to enroll in that particular histology to try to characterize the benefit risk and then make decisions on where to invest our resources for Phase II/III registration studies, and we hope to be able to make those decisions this year.

Operator

And our next question comes from Marc Frahm with Cowen and Company.

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

James, just to clarify an earlier comment when you kind of described the agenda for the May update, you just said programs. Is it still just going to be just the MAGE programs or should we expect that kind of fulsome update on AFP as well at that time?

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

I wills say, whatever is going to happen on AFP, but as we've repeatedly said it's a much slower study to recruit. We are recruiting patients at the 1 billion level. So we're still not at the 5 billion level. We haven't got there. It is slower to recruit, and we have been adding centers recently just trying to speed that up. So we'll tell you whatever we've got I think is the answer at May, but it's going to be -- there will be far more MAGE-A10 and MAGE-A4 patients to comment on than there would be for AFP.

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

Okay. Great. And then you're now kind of [a menu] different generation 2 -- or next generation kind of constructs that you've disclosed or are about to disclose at AACR. Could you talk about which one you think you're going to file the IND on and what the -- maybe what the level of data is supporting that, that's the right choice for the first one?

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

Yes, we're not disclosing today which one we are picking for the IND. We've now disclosed the details on 4 different programs actually. So one was Phosphate [S] arrays, then the TGF-beta, which we've talked about before. This week we actually had a published patent on IL-7, which is the third; and the fourth one is the CD8 program. And for competitive reasons, really, we're not going to tell people where we're going exactly, but in general, they're going to enhance the effect of the T-cells in man, but we will be telling people at the May meeting, when we're going to file an IND and for what. I mean, it won't come as a great surprise, it will be to do with MAGE-A4, because it is clear from all of our studies that MAGE-A4 has a much higher presentation than MAGE-A10 or in fact, NY-ESO of that matter, in patients. There was many more patients who expressed MAGE-A4 or NY-ESO, even more so than the literature suggest. So it will to do with MAGE-A4, but we will update the timing of an IND, and which one we have selected for IND at the May meeting.

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

Okay, great. And then the last one is just, you mentioned through 2018, the kind of progress and manufacturing and that now you have in-house the ability to do 10 -- roughly 10 patients per month and there's the flexibility to expand out. Are there plans in 2019 to expand beyond that or do you think the 10 capacity is the right place for you for the near-term future?

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

Yes, obviously, the more successful the trials are, the more we need capacity. It's very easy for us to get to 30 a month, in terms of capital expenditure in this Navy Yard Facility. We've actually built a quite a lot of numbers of suites and essentially you just equip the suites more effectively and so to get to 30 a month here, and don't forget we have 10 a month at PCT or HCATS as it's now called. So to get to there is relatively simple and doesn't involve much expenditure. To go above that 30 plus 10 would involve a serious fit-out of the other half of the building. We've got an empty half of the building, which is for the next stage. So we've got the facilities in place in order to expand. To get to 30 as I say is a relatively insignificant amount of capital expenditure, though you have to hire people but to go beyond that 30 requires significant expenditure.

Operator

And our next question comes from Ren Benjamin from Raymond James.

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

James, in the past we've talked about the response rate of somewhere in the 30% range when it came to go/no-go decision. I kind of wanted to get a sense from you now, kind of, based on all the data that you've seen so far, is that still the bogey that we're looking at and going forward, if that isn't met let's say for one indication, does that -- it doesn't seem like there's any more tinkering per se that we can do. Maybe you can go above 10 billion cells? I'm not too sure what else could be done. If you can kind of talk about what else could be done if the response rates are below 30%? And has that bogey changed at all, that will be great.

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

I think the cell therapy is a complex procedure for patients, and I think if one projects forward having something on the market, it wouldn't be fair to the patients and I don't you would expect clinicians and payers to favor something without a reasonable response rate. And that's really where the 3 and 10 came from is that, if you have a sort of 1 in 20 patients responding, I just don't see autologous cell therapy really cutting the mustard. So that's where that came from. I think in general, so that's -- I don't think that has changed very much, but I don't agree with the second half of your question or sentiment that there isn't much more you can do. Yes, you can put up the doses. Rafael mentioned earlier that the NCI has dosed up to more than 50 billion cells but actually that's exactly the tinkering that you do, I think to use your word, is that's what the second generation is about. So they do have different characteristics. They are designed to address the issues of the tumor micro environment or epitope spreading, et cetera, which are the things that may make the cells less effective or in the case of the CD8 program, which we just -- you'll see the poster later today for AACR, that's really to make CD4 cells active as CD8 cells, if you like, and that could induce a whole series of different things. So I think we are, as I've said many times before,

we are on the foothills of exploring a very complicated technology. I'm at personally, fantastically pleased that we can dose large numbers of cells, apparently safely, without serious -- any cross activity or other activity. So I think that the thing -- and the last bit of that, there are 2 other bits I would add on to that, and that's -- one is the combinations, which I mentioned earlier, may be appropriate. And I also think that it is astounding how many technologies there are out there to enhance the performance of cells and cell therapy, and we have been looking very keenly at -- have actually signed a few proof of concept deals with technology companies. And so I think there are a lot of things as you can do, whether it's characterizing the cells that you put back into people. Whether it's enhancing the activation of the cells in the patient, whether it's combinations, whether it's increasing the ability to traffic to the tumor or to deal with the tumor microenvironment. I think there are many different routes to go, and I think Rafael put his finger on it earlier in response to that question about coordinating research with development. He said essentially that is what the research engine is doing now, it is making better medicines by taking account of the data we are getting back from -- the translational data we're getting back patients to looking at both the characterization of the cells and the response data to see how you can enhance them. So I think there are only about 50 more years of development to go, but it's still quite a lot. There are lots of things you can do and it isn't just about increasing the cell dose. So quite a long answer, but it is a very complicated thing, it's something we pay a lot more attention to.

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

Yes, that make sense. And just switching gears to manufacturing, I think you mentioned that the first vector production using the suspension process would be in-house in 2019. I'm kind of curious, I mean, I understand the importance of bringing the cell manufacturing part in-house. I was pretty much under the assumption that vector production was pretty standard and so I'm curious why bring it in-house and what are the advantages kind of there versus just contract manufacturing.

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

So actually that is a very good question. There actually are a lot of advantages. First of all, the ability to get the titers that you need to make cost-effective vector, that is certainly an art, which is continuing to improve, so there's absolutely massive improvement still to be made in terms of how you actually make vectors. The whole movement away from adherent processes to suspension processes is inherently much more efficient. And we -- there is -- it's just not a fixed -- if you know exactly what vector you want, there are people out there, and you know exactly the process, there are people out there who can do it. If you want to improve that process and you want continuously to make it more efficient and have certain characteristics, which we do, then actually bringing it in-house has been fantastic. So effectively, we have a process development team, which addresses obviously, the cell manufacturing. We have a second team which actually looks at nothing but improving the vector and it has had some -- vector costs can be absolutely astronomical and cell therapy is going to have to come down in price at some point. And if you use the vector cost of 3 years ago where sometimes you can spend $100,000 a patient, you cannot make things at $100,000 of the vector because there are obviously lots of other things. Now it's radically below that already so before you write that down, and get concerned about that, but it's got to come down to a few thousand dollars for patient at most and it will do and that's really why you have it in-house.

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

Okay. And so just a follow-up, the game plan is not just to, for lack of a better word, tinker with the process to make the best vector production and then out-license it back to a third party. It really would all be in-house even at the commercial stage?

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

So I think we have a dual-source supply at the moment. We have a commercial vector, supplier that as James pointed out to supply our vector for our current trials. And we have our in-house capacity. And that's similar to what we would do for -- that's similar to what we're doing for cell therapy. Whether or not you then sublicense our process out to a third-party or you have 2 different vector production processes running in parallel, including for different trials, I think very much depends on the characteristics of the process and the plan and the development plan and the regulatory plan for those at the time. But that's absolutely an option. I think what James was referring to is that it's very difficult, like cell therapy, it is very difficult to end up with a well -- an advanced cost-effective process if you are entirely reliant on third parties for that supply.

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

Got it. And then one final...

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

By the way, I think in time it will become commoditized, I agree, because you can have, unlike cell manufacturing, you can actually have inventory and it will become commoditized, but I promise you it's nowhere near that at the moment, whatever people say out there and there are also issues we haven't mentioned to do with obtaining slots exactly when you want them. I mean, for example, a program is suddenly becoming more successful then you need more vector suddenly. We can switch obviously, in-house, at the drop of a hat. Whereas third parties tend to be a bit more complicated if they haven't got slots. So I think it will, unlike the cell manufacturing, it will become commoditized, but it's nowhere near that yet.

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

Okay. Got it. And then just one final from me. You mentioned the good progress that you made with off-the-shelf product. So can you provide a little bit more color regarding that and when do you think an off-the-shelf product could be in the clinic?

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

Rafael, that's probably one for you. I doubt we are commenting on the timetable, but Rafael, do you want to comment about the progress on the off-the-shelf?

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

Sure. So there are 2 aspects to making off-the-shelfs from induced pluripotent stem cells. One is the genetic editing aspect. So what modifications do we want to make to the cell genome to make the cell essentially invisible to the host immune systems to prevent graft versus hosts disease but also to carry the therapeutic TCR so there a number of editings that can be done. One can do multiple editings to knock out class 1 and class 2 and including HLAE to avoid NK cell susceptibility, and knock out the indigenous TCR. So there's still a menu of editing steps, but the minimum that one would have to do is to move the indigenous TCR, because otherwise the cells will cause RGVH. And so the timeline will very much depend on the amount of editing that we choose to do and this is done in partnership with Universal Cells, which is a company now, a subsidiary of Astellas. And we're working very closely with them. And they have all the expertise on AAV gene editing and we're supplementing that in-house, but it is likely that we would go initially to the clinic with minimally edited line, and we started to have regulatory discussions around that on the choices of cell line and on the editing steps and how, obviously, the process would look like. So in addition to the editing, the other pillar of being able to do this is to differentiate stem cells into T-cells that are functional and that is something that we have done in-house, and we are very happy with the progress. We have made tremendous progress in differentiating these cells into CD34 positive cells which are hematopoietic progenitors and then from there going into double positive and single positive T-cells that express TCRs to numbers that could be used for therapy, so hundreds of billions of cells. And then we are also showing the functionality of these cells and all this work will be presented at the American Society of Gene Therapy, I think, for the first time. So again as James said, we're not necessarily guiding on the timing of it, but we are working pretty hard on being able to put our first TCR into the system as soon as possible.

Operator

And our next question comes from Soumit Roy from Jones Trading.

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

I just have 2 questions. First is, you guys are in a unique position to look at the effect of TCR, T-cells in quite a variety of solid tumors from lung to bladder to melanoma to several others. Curious, if you are seeing -- and all these patients, these indications have different patient characteristics in different tumor stroma, different mutational burden. Are you seeing any difference or marked difference between T-cell proliferation, expansion between -- among these patient groups and you compare it back to synovial sarcoma? And the second question is, what kind of immunological data you're collecting, or we could expect to see to make some kind of thoughts around durability like, are we looking at epitope spreading, memory cell formation, number of [9] memory cells. So what kind of immunological data could we expect to see long before the durability data really comes out a year from now?

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

Rafael, that's probably one for you.

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

Yes, so I think the first question was whether there were differences in expansion among histologies. I think it's too early to be able to answer the question. Clearly, the differences in expansion are more to do with the initial cell dose than any other parameter that we've been able to analyze to date. There is anecdotal evidence that there is higher expansion in patients that have higher target expression but we'll take a look at everything we have and see whether we can make those correlations within a significance to make conclusions. I think the difficulty with expansion is that it is difficult to know what is really through expansion that's due to homeostatic sort of resetting the T-cell numbers versus antigen-driven expansion, and I think those parameters probably play more of a role in the expansion together with the cell dose and the antigen expression than the type of tumor itself. But by and large, given a similar dose, we're not seeing stark differences between different histologies, including sarcomas. So that's just kind of a general statement. And I think in terms of the immunological data that we're collecting, well first of all, we're looking at the makeup of the product that we are given. So obviously what the phenotype? Most of the cells are obviously CD3, but how much of them CD4 versus CD8? How many of have the TCR, we measure that by [decimeter]. How many of them are terminally differentiated cells versus stem cell memory cells? And so we try to characterize what's in the apheresis, what's in the manufactured product, and then periodically, what survived in peripheral blood and when available, in tumor in patients and we do that -- unfortunately, we had to stop doing that when the patient -- if the patient progresses, because we stop collecting this data, persistence data, but as long as we have samples, we continue to look at this, and we've shown in the past and this has been published in ways. So experienced that patient that persist the longest and have long responses tend to have a persistence that's characterized by stem cell memory type phenotype. So to do these correlations you need very long follow-ups, which obviously, we don't yet have. But I think being able to identify those cells early on because you see expansion and then there is a decline and then a resetting. If you can identify those stem cell memory T-cells that carry the TCR in the 1% or 2% of the cells that persist, we believe that, that's a good predictor that there may be immunological memory that has developed, but all of this will need to be verified in these new tumor types that we're treating with our new products.

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

Got it. I mean, Is there is reason why you wouldn't try to look into a later stage, like a May update or even second half this year update, the epitope spreading or how much effective T-cells versus memory T-cell forming later on versus the -- in the apheresis product, if there is a not -- don't you think that will give a better look into durability of the response, a little earlier look or it doesn't really not matter that way?

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

So as I said before, the patients that remain without progression will continue to be followed and obviously, we'll continue to characterize again the makeup of the T-cells, and we expect that there would be a shift from MRAS or effector cells to stem cell phenotype. That's at least what we've seen and what we're beginning to see in the few patients that we've been able to follow for the longest time, and we'll continue to do that. I think epitope spreading is not an easy thing to discern, but it is, I think, you can make some inferences about epitope spreading by doing T-cell clonality, which we have published on in our multiple myeloma study and shown that we see emergence of clones that do not carry the TCR that were not there prior to T-cell infusions suggesting that, that there are some T-cells that are clonal, that are reacting to epitopes other than NY-ESO, and we will definitely do that in the current studies. In fact, we think that to have durable responses, we studied testis antigens one has to expect epitope spreading, because not all the cells express these kind of testis antigens and therefore, if there is no epitope spreading, it's likely that there will be a survival advantage of antigen negative cells and you'll get resistance. And so we collect the samples, and we will analyze T-cell clonality at different time points, looking exactly for what you said and it's just too early to do based on where we are with these trials.

Operator

And our next was income from Jim [Bertinel] with Wells Fargo.

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

Nick on for Jim this morning. James, just to clarify, as far as the Navy Yard expansion, I've heard you say a couple times now that you can expand to 30 per month without significant investment. The press release says 100 per month without significant investment, I believe.

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

I hope it doesn't. The draft I've got in front of me says 30. I guess that was a mistake. It shouldn't be.

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

It says scalable to 100 patients per month without significant capital expenditures when fully integrated.

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

Yes, good spot. It is 30 patients a month without significant capital expenditure. It's 100 patients a month within the facility but that will cost a few tens of millions. Well spotted.

I'll employ you as a proofreader in the future but you're right. That should say 30. We'll correct that.

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

And then the other thing that sort of jumped off the page at me was really that the target dose for the expansion is 1 billion with up to 10 billion. But dose Level 3 was I think 5 billion or 6 billion. So why is that -- why -- and I heard you say that some patients are hard to make the cells. So is this really just to give you a flexibility so it takes a long time to get these patients and then if they don't get the 5 billion you have to say I'm sorry, whereas you don't really know yet whether 1 billion is good enough?

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

Yes, the system is designed, actually, the 10 billion is designed so we don't throw away cells. If we've made 7.2 billion, let's take it as an example. The 10 billion just means we give them all 7.2 billion. It seems a bit ridiculous to give them 5 billion, or actually it was technically 5 billion or it could have been 6 billion an then not give them the rest, so it was really to give us flexibility. We don't get 10 billion, I think I'm right, I'm looking at [Ed] here, we don't get 10 billion every time, we do get it frequently. So it's just a method of -- in a protocol of course, you have to specify what the dose is and if you just specify something lower, you can't then just give them the extra cells even though they are just sitting there, so it's really to give us that flexibility, so if we produce anywhere between 5 billion and 10 billion, they will get that number of cells, the ones that are available.

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

My question is really why is the target 1 billion for the expansion, not 5?

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

The target is 5. We're allowed to give as low as 1.2 billion. The target is 5 for the expansion. AFP is currently 1 billion cells, it's the MAGEs are the high -- AFP is only -- we can only give 1 billion because the second dose of the dose rising but for the MAGEs the target is 5 billion, We can give 1.2 up to 10.

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

Yes, just again the press release says target of 1 billion but doses up to 10 on the third bullet.

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

That's AFP on MageA10, I've got 5 billion, and MageA4...

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

For the treatment patients, the expansion phase is M10, M4 with target doses of 1 billion cells with doses up to 10 billion cells.

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

I've lost you.

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

It's 5 billion.

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

It's 5 billion. It's 5 billion. We are going employ you as a proofreader.

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

Yes. Okay. So maybe I'll ask a question not based on what I read in the press release and that is, just can you remind us of the number of patients that are going into each of the expansion phases? Pre-trial.

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

Rafael, you want to comment?

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

Yes, they vary by trial but essentially, there are between 10 to 20 patients, inclusive of the third dose, so however many patients we put on the last dose, which has a target of 5 billion, we would add that to the patients in the expansion to treat between 10 and 20 patients and that varies by study.

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

That's fine. So really I'm just wondering when you get to May, just how much -- I think you've said that the trials won't be completed, so will you be able to define concrete next steps for initiating potential registration-enabling trial, or is it more, well we think we need to move to Gen 2 or a combination approach to get to the efficacy levels that we want to see.

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

So that's exactly what we're going to do, talking about in May, this is the data, these are number of patients. It could be anything from, we'll need to dose more patients to know the answer to that to we're now going to move forward with the registration trial or we need to move to Gen 2. That's exactly what we're going to talk about at that May release.

Operator

(Operator Instructions) And our next question comes from getting Ring Huang with Bank of America Merrill Lynch.

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

This is Alec on for Ying. I had a couple of clarification questions on your cash burn guidance. So on manufacturing, the 10 patients per months is a slight increase from the roughly 8 at both the Navy Yard and HCAT you mentioned previously. Is this due to a capacity expansion or better efficiencies with your current capacity? And is the up to 30 patient expansion included in your 2020 cash guidance? In terms of the vector manufacturing plant, what does this look like sort of in a physical manifestation? And how much are you budgeting towards that? Is buildout of this baked into the 2020 guidance as well?

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

If I just start with a comment on the vector plant and then I'll add the others in detail. We are incredibly lucky in the vector plant. It's a dedicated facility, but the capital expenditure was actually borne largely by the U.K. government which decided for whatever reason it will build a large building actually on GSK land at Stevenage in the U.K. out of taxpayers money to host various companies activities' either for cell manufacture or for vector and that's actually where the vector production has taken place. It's our staff but it's their facility, so we were very lucky in that respect. Just to clarify that. So it's dedicated to us, but we didn't have to build the thing, I'm pleased to say.

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

Great. So taking your first question, the throughput of the Navy Yard facility at the moment is roughly 2 patients per week. So that is how you get to in a short month depending on timing you end up with sort of 8 patients; in a slightly longer month you end up with 9 or 10 patients. And 10 patients is sort of the capacity that we're thinking about. So those numbers are actually about the same. The infrastructure is in place to be able to go to 30. The key thing to have in mind is the number of people that we would employ to do that and we will do that in accordance with the demands of the clinical trials that we've got ongoing. But it should be noted that between 10 patients at Navy Yard and the month at Navy Yard and roughly the same at HCATS, we do have the capacity to service the pilot trials out of the existing capacity and in some cases, the move into pivotal trials as well. So we are not commenting in detail on how much is in the cash flow for both the vector requirements, we have a choice of either going externally or internally and at the moment, those costs are in there on the trials-we-expect-to-complete basis as opposed to as James pointed out, the need for significant CapEx.

Operator

This concludes our Q&A session for today's conference. I would now turn the call back over to James Noble for closing remarks. Sir, you may proceed.

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

Thanks again everyone for joining us this morning and giving us some very interesting questions. And our commitment to our patients remains strong, and we will continue to work diligently to realize the potential of our SPEAR T-cell therapies to treat cancer patients with few other options, and we look forward to giving a more general update in May. Thank you very much.

Operator

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