Adaptimmune Therapeutics plc (Q1 2021 Earnings)

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Corporate Speakers:

- Juli Miller; Adaptimmune Therapeutics plc; Senior Director of IR
- Adrian Rawcliffe; Adaptimmune Therapeutics plc; CEO, Principal Accounting Officer & Director
- Karen Miller; Adaptimmune Therapeutics plc; SVP of Pipeline Research
- Elliot Norry; Adaptimmune Therapeutics plc; Chief Medical Officer
- Helen Tayton-Martin; Adaptimmune Therapeutics plc; Co-Founder & Chief Business Officer
- John Lunger; Adaptimmune Therapeutics plc; Chief Patient Supply Officer

Participants:

- Marc Frahm; Cowen and Company, LLC; Director
- Nicholas Abbott; Wells Fargo Securities, LLC; Director & Associate Analyst
- Kelsey Goodwin; Guggenheim Securities, LLC; Associate
- Tony Butler; ROTH Capital Partners, LLC; MD, Senior Equity Analyst & Head of Biotechnology Research
- Jonathan Chang; SVB Leerink LLC; MD of Emerging Oncology & Senior Research Analyst
- Mara Goldstein; Mizuho Securities USA LLC; MD of Equity Research Department

PRESENTATION

Operator: Ladies and gentlemen, thank you for standing back, and welcome to the Q1 2021 Adaptimmune Earnings conference call. (Operator Instructions) Please be advised that today's conference is being recorded. (Operator Instructions)

I would now like to hand the conference over to your speaker for today, Juli Miller. You may begin.

Juli Miller: Good morning. And welcome to Adaptimmune conference call to discuss our first quarter 2021 financial results and business updates. I would ask you to please review the full text of our forward-looking statements from this morning's press release. We anticipate making projections during this call and actual results could differ materially due to several factors, including those outlined in our latest filings with the SEC.

Adrian Rawcliffe, our Chief Executive Officer; and Karen Miller, our SVP of Pipeline Research, are with me for the prepared portion of this call. Other members of our management team will be available for Q&A.

With that, I'll turn the call over to Adrian Rawcliffe. Ad?

Adrian Rawcliffe: Thank you, Juli, and thank you, everyone, for joining us. Keying off this year's conference season, May will be a busy month for us. We will present our first preclinical data from our mesothelin targeted HLA independent TCR, or HiT, at ASGCT on May 11. And Dr. Karen Miller is here to talk more about this platform and the potential of our deep preclinical pipeline. Abstracts came out last week, and data will be updated in the poster. Then on May 19, ASCO abstracts will be out, and we will issue a full press release with an update of our initial data from our SPEARHEAD-1 trial with afamitresgene autoleucel, or afami-cel, for people with synovial sarcoma, or MRCLS.

Data from SPEARHEAD-1 will form the basis of our first BLA filing later next year. We completed enrollment in the 45-patient registrational cohort of SPEARHEAD-1 last year in about 12 months, and we recently treated the last of these patients. At the time of data cutoff for the abstract, which was in early February, 32 patients had received afami-cel. The oral presentation at ASCO include initial data on these and additional patients, but not all of the 45 patients in the registrational cohort, and we will issue a press release on May 19 summarizing these results. We plan to update these data later in the year at CTOS. And at that point, the vast majority of patients should have at least 6 months follow-up.

We are incredibly motivated to bring afami-cel to market. When you compare the Phase 1 data with afami-cel to what can be achieved with available treatment options, this product clearly has the potential to change the lives of people living with synovial sarcoma.

Moving on to our next-generation SPEAR T-cell targeting MAGE-A4 and our program targeting AFP. 2021 is off to a good start. In Q1 2021, as the pressures of COVID lifted, we've been able to enroll and treat more patients in Q1 in our SURPASS and AFP trials than we did throughout the whole of 2020. And I believe this recruitment will continue, and I'm optimistic that we'll be able to present meaningful updates from both trials later in the year.

We continue to treat patients in this past trial, focusing on indications where we have seen signs of efficacy with our MAGE-A4 targeted products, namely lung, head and neck, gastroesophageal and bladder cancer. Given the increased enrollment we've seen during Q1, we aim to share a robust data update in the fall with the aim of identifying further indications to take into late phase.

We also plan to present updated data from our Phase 1 ADP-A2AFP trial for people with liver cancer at ILCA in September. We're planning to identify the next steps for this program also based on these data. One of our key commitments since I became CEO has been speed and quality of execution. With these upcoming data updates, this is what we're doing.

Financially, we're again confirmed, we're funded into 2023 and equipped to deliver on our ambitions. And our critical component of realizing these ambitions relies on developing cell therapies that are both curative, meaning people don't die from their

cancers; and mainstream, reaching a large number of people with cancer. We have a deep preclinical pipeline that I believe will move us meaningfully towards these goals.

To talk more about the exciting data emerging from our HiT platform, I'll turn it over to Dr. Karen Miller, who leads our pipeline research team. Karen?

Karen Miller: Thanks, Ad. Next week, at ASGCT, we're going to present preclinical data from our HLA independent TCR or HiT platform. These are proof-of-concept data from the first HiT candidate targeting mesothelin, which is now being codeveloped with Astellas. And we're really excited about HiT as this platform enables us to target solid and hematological cancers without the need to select patients based on HLA type. And the work we've done with this first candidate establishes a preclinical testing strategy to evaluate HiT against additional targets.

I'd like to take a few minutes to put HiT in perspective though, and explain why we think there is such a tremendous opportunity here. First of all, the HiT platform leverages our vast experience in TCR engineering and affinity optimization. It opens a whole new range of targets for us that don't depend on HLA, and have to date been targeted by CARs or other cell therapies that use antibody moieties to engage with antigen. There are many options for cell therapies to target cancer, and each comes with distinct advantages and disadvantages.

To date, Adaptimmune is focused on T cell receptor or TCR therapies, for which we have proprietary technology enabling us to engineer TCRs to target cancer antigens presented by HLA. TCRs have the advantage of giving us access to basically any protein processed by a cancer cell, which is important when targeting solid tumors as they often lack unique cell surface antigens. And we've seen success in the clinic with our TCR therapies. And as Ad has laid out, further meaningful data updates are found throughout the year.

However, a limitation of our current therapies is that they are restricted to certain HLA types. There's also been great success with CAR-T cell therapies that use an antibody to target large cell surface proteins, which are broadly expressed in hematological malignancies. However, CAR-T cell therapies come with some well-publicized challenges. These include the need for engineered intracellular signaling domains to mimic what the TCR does naturally. That can result in tonic signaling, potentially leading to toxicities.

Furthermore, the CARs need a relatively large amount of antigen or target, which is not a limitation in multi hematological malignancies, but does limit the number of solid tumor indications available. More recently, there have been next-generation advancements, but attempt to overcome the limitation of CAR-T cell therapies. One of which includes coupling antibody moieties to TCRs, and these are known as TRuCs. The TRcCs have the distinct advantage of using the TCR's native signaling machinery.

One potential drawback, however, that will not be able to come by this approach, is that antibodies have been shown to be neutralized by soluble protein. And this is especially

important because there are many cancer targets such as mesothelin, that are both cell surface bound and secreted of soluble proteins.

At ASGCT next week, we will demonstrate that we have developed a TCR that can recognize and kill target cancer cells expressing mesothelin, independent of HLA. I can't discuss the full data update as it's under embargo until May 11, but I can say that these data are very exciting. We demonstrate that our HiT candidate is effective at killing tumor cells expressing mesothelin, both in vitro and in vivo. We also show that our HiT targeting mesothelin has advantages in our experimental system over a comparative TRuC construct that we developed in-house.

Now beyond HiTs, we are working to expand our cell therapy capabilities with new targets, new modalities, broad HLAs and our allogeneic platform. All of these are designed to make our arsenal against cancer better and accessible to more people. This deep preclinical pipeline supports our ambition to bring 5 new products to the clinic by 2025. And I'm truly pleased with the rapid progress we have made with our first HiT program, and I look forward to further updates on this and the rest of the pipeline.

And with that, I'd like to turn it over to the operator for the Q&A.

QUESTIONS AND ANSWERS

Operator: (Operator Instructions) Our first question comes from the line of Marc Frahm with Cowen and Company.

Marc Frahm: Congrats on all the progress. Maybe Ad or someone else on the line may also want to chime in. Just the fall update for SURPASS, do you kind of expect -- given the enrollment increase you've seen recently, do you expect that update to kind of mark the transition of that program from the basket signal finding approach into kind of an exclusively tumor-specific development program? Or do you think it still won't be quite able to fully determine the range of tumor types that justify advancement?

Adrian Rawcliffe: That's a innovative way of trying to ask how many patients have we dosed and what indications are they in. You ought to be congratulated for that. And we've avoided giving that type of information because it's not been useful. I think, though, that, that's one of the options. I think we want to understand the breadth of indications where we see activity for this treatment. And therefore, what the consequential development program will be. And you pointed out a couple of potential outcomes, and those are within the spectrum that we're considering, and we'll have more information in the fall.

Marc Frahm: Okay. Fair enough. I tried. And then maybe on the comments on the HiT program that's going to be lit as you see. Thanks for that kind of overview and kind of contrast from your approach versus the traditional CAR approach, but there's also a competitor out there, particularly for mesothelin, who kind of already has like a hybrid approach already. Can you maybe speak to the differences between that andhow you guys are going about it?

Adrian Rawcliffe: Yes. Absolutely. I presume you're referring to the TRuC constructs, the TCR² isproducing. And I'll ask Karen to comment on the difference between that and our approach.

Karen Miller: Sure. So for our preclinical evaluation, our intent was to test how our mesothelin HiT performed in vitro and in vivo. We wanted to do this relative to a valid comparator, and for this we've chosen. And these are filled in TRuC as were the emerging positive clinical data from TCR Square to TRuC that's currently in the clinic. And so for our experiments there, we synthesize the mesothelin TRuC from publicly available sequence. And then obviously used our own vector and cell manufacturing process to test it alongside the HiT in vitro and in vivo. And this is the data that we're going to share with you on the 11th of May.

In terms of the differences between the TRuC and our HiT. Our HiT is a natural TCR that binds in the normal way for a TCR and has normal TCR signaling. Whereas the TRuC, I'm sure you're aware, has an antibody moiety tagged to each epsilon chain of the CD3 part of the TCR. And this has a higher affinity interaction than a standard TCR. And so the kind of advantages that we see here are that the TRuC will actually bind to soluble cleaved forms of the target antigen like mesothelin.

And this acts as a sync for things like both CAR-Ts and TRuCs, and it effects their ability to migrate to the tumor and inhibit their function. So because of HiT cells having a lower affinity for antigen, which is in the natural range for TCR and it has high functional lividity, our HiT T cells are not inhibited in the same way.

Operator: Our next question comes from the line of Nick Abbott with Wells Fargo.

Nicholas Abbott: First question on SPEARHEAD-1, we noticed that a second synovial sarcoma cohort has been added to the trial, and the trial size increased from 45 to 90 patients. So can you talk about the second cohort? And what the differences are perhaps for the first cohort?

Adrian Rawcliffe: Certainly. I'll ask Elliot to comment on that. Elliot?

Elliot Norry: Thanks for the question. Really, Cohort 2 was opened to strengthen the efficacy and safety database that we'll have and will aid in subgroup analysis of the patient population. That's really the primary intent.

Nicholas Abbott: Great. And are you able to elaborate a little bit more on what these subgroups are or might be?

Elliot Norry: Well, I think that it would be typical subgroup analysis of looking at differences in age, differences in tumor size, et cetera. And just having a broader database helps to look at smaller numbers of patients that fall into specific subgroups. I'm not sure I can provide more specific details than that.

Adrian Rawcliffe: Yes. Can I get some...

Nicholas Abbott: I guess, no, I just want to confirm that this does not affect the overall timing for the registration component?

Elliot Norry: Hypothesis testing will be based on cohort 1, and it should not introduce a delay.

Adrian Rawcliffe: No. We said that we dosed the 45th patient just recently. And that group of 45 patients, that will provide the basis for registration and the hypoth testing and registration. And so that will be available for analysis later on this year. And I think the initial data is coming up at ASCO. And we're optimistic about the opportunity to present that initial data and to show what afami-cel can do in patients with synovial sarcoma, full on track.

Nicholas Abbott: Maybe just following up. So afami-cel has RMAT and PRIME. Can you remind us how these potentially assist in accelerating approval process and time line? And are there any other strategies that you're considering to further accelerate registration and approval of afami-cel?

Adrian Rawcliffe: Elliot?

Elliot Norry: Yes. So both of those designations are associated with accelerated review capabilities and provide us with increased access prior to submission with both agencies for planning purposes. So they also -- I just will mention are based on preliminary data that demonstrate a promising efficacy. Those designations -- neither of those designations are provided just based on sort of the rarity of the tumor. So they both provide us with advantage from that standpoint.

The other pathways that you're describing are generally already included in the RMAT and PRIME accessibility options and capabilities. So there's really no need to seek additional designations.

Nicholas Abbott: I look forward for the data update next week.

Elliot Norry: We're looking forward to providing it.

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

Kelsey Goodwin: This is Kelsey on for Michael. I guess, just kind of building actually on that question a bit, kind of preparing for the upcoming launch. I guess, maybe could you provide some color on what that entails? And maybe what -- remind us what needs to get done to get sites online to kind of eventually treat commercial patients for those that maybe weren't included in the initial trial?

Adrian Rawcliffe: Sorry, I'm not sure I fully got the last part of your question. Patients that weren't included in the initial trial?

Kelsey Goodwin: Sorry, for sites that weren't included, I guess, just kind of getting them online for potential launch and -- yes, exactly.

Adrian Rawcliffe: Yes. Yes. So maybe I'll comment generally, and then I'll ask John to pick up on one aspect that we feel is particularly important, which is the ability to actually service patients in a commercial setting. So we've obviously begun building our commercial team, and that includes a lot of mostly internally facing roles at the moment, market access, marketing, et cetera. Looking forward, we are planning on the more externally facing roles. And obviously, we're initiating the interactions externally as you'd expect on discussions about thinking about pricing, et cetera.

The -- I think the thing that we are also paying a lot of attention to as a fully integrated cell therapy company is the opportunity to enhance the patient experience by optimizing the whole process from identification of the patients all the way through to the infusion and subsequent follow-up. And that patient services activity, I think, is a key demarcation of successful autologous cell therapy companies.

And John, do you just want to touch on our activities in that space and our thinking in that space?

John Lunger: Sure. Thanks, Adrian. From a capacity and supply chain perspective, we will be commercializing out of the facility that we've been running our clinical trials out of, and we have the capacity to do so. So we feel very good about the fact that we're already in a position to serve the markets we'll be launching into for sarcoma next year. To Ad's point, we're well underway with digitizing the patient journey. As everybody knows, this autologous treatment is a challenging one, and we spent the last couple of years putting systems in place and getting ready to launch, one that will be a -- what I think is a really important part of execution of the patient journey.

And finally, to Ad's point, we're focused on this thing we're calling eye-to-eye. I think everyone in this space is familiar with V2V, which is that vein-to-vein part of the patient journey from apheresis to infusion. But the fact of the matter is the patient journey starts well before that. So we're putting in place people, processes and technology to start from the very beginning of the process, which is the identification of the cancer and the ability to screen into this particular therapy.

Operator: Our next question comes from the line of Tony Butler with ROTH Capital.

Tony Butler: Elliot, Ad, Karen, you've spent some time this morning having some discussion about the HiT program. Probably, I just wondered if you could just spend a minute on the relationship with Astellas. Importantly, given what you've been -- what I think you're seeing preclinically, it would stand to reason that you would want to move this program fairly rapidly into the clinic. Does Astellas make that decision?

Do you make that decision? Can you just give us some idea of next steps in that program? Importantly, next steps with Astellas. That's question one, if I may. And the question 2, Karen, I just wanted to ask, if one did not have a cleavable, soluble target for which a TCR or a construct needed to be directed toward, would a TRcC be useful then? Is the advantage here really this notion of having an antibody sticking out of the epsilon receptor and it being bound by antigen and therefore, no longer available as a therapeutic?

Adrian Rawcliffe: Thanks, Tony. I'm actually going to ask Helen to comment on the Astellas relationship and the next steps with Astellas on this. And then I'll -- and then Karen, you can talk to the advantages of TCR or CAR targeting. Helen?

Helen Tayton-Martin: Yes. Thanks, Ad. And thanks, Tony, for the question. You're absolutely right. This is a co-development program with Astellas on the mesothelin HiT, and we are working very closely with them in the optimal way to advance it as quickly as we possibly can to, first of all, derisk the target and then accelerate it within our allogeneic program of work. So we can't say any more about that at this point in time, but rest assured that we are actually working very closely with them to accelerate it based on the promising results that Karen has outlined today. Karen?

Karen Miller: Okay. And to answer your question about whether or not if a TRcC targeted a non-cleavable protein, would that be better? I think the best way I can answer that is to say that, that truly depends on the actual constructs that are being compared. What I can say is with our TCR products, including the HiTs, we go through a process of affinity optimization of those TCRs.

And we also optimized the expression of the TCRs on the cell surface in order to develop a product that is highly effective, which is very different, of course, to a TRuC, which is an antibody moiety bound to the epsilon chain of the CD3 portion of the receptor. And that being generally a high affinity, binding will not be so easily, I think, optimized in the same way that we can with the TCR products. But I think at the end of the day, what we need to do is to compare them in the clinic.

Operator: Our next question comes from the line of Jonathan Chang with SVB Leerink.

Jonathan Chang: First question, I just want to clarify something that I heard in the beginning and what I'm reading in the footnote of the press release. And that is, will the press release on the 19th describe the full ASCO data or the press release just describe the data from the abstract?

Adrian Rawcliffe: The press release on the 19th will describe the full ASCO data.

Jonathan Chang: Got it. And okay. So second question, I'm curious if you could just help set investor expectations ahead of the SURPASS next-gen MAGE-A4 update at ESMO?

Adrian Rawcliffe: I think the expectations that we have of that data set is that it will represent the patients that we have recruited across a range of tumor types, and we've been focused on lung, bladder, head and neck and gastroesophageal. Although I will point out that, that focus does not -- has not historically precluded other tumor types from being in that patient group. So it will be a broad set of tumor types. And the objective that we have for that data set is that we will be able to understand the breadth of activity that we're seeing. And start to think about what the development pathways might be going forward for that agent in those tumor types individually or generally.

However, I'm just going to point out, given that we have -- we're obviously recruiting those patients now. And over the course of the recruitment in Q1, which, as I say -- as I said, gone very well. That, that data set will not have the most durability data that you might expect given that it will be coming out in a few months' time.

Operator: (Operator Instructions) Our next question comes from the line of Mara Goldstein with Mizuho.

Mara Goldstein: Firstly, on the SURPASS-2 trial that will initiate this year. I'm wondering if you could give us kind of just a forward look of what the enrollment and the size and scope? And when we can begin to see some clinical data of that program? And then secondarily, I appreciate the color on the HiTs program. I'm curious about the TIL program given that, at least on the pipeline chart, it certainly looks a little bit more advanced. And where and when you think we'll get some more information on that program?

Adrian Rawcliffe: Thanks, Mara. So I'm going to ask Elliot to comment on the status of the SPEARHEAD-2 program. And then I'm going to ask Karen to comment on the status of the TIL program. Elliot?

Elliot Norry: So first of all, Mara, I just want to clarify, you said SURPASS-2, right?

Mara Goldstein: Correct. Correct.

Adrian Rawcliffe: SURPASS-2, sorry.

Elliot Norry: Yes. No, I just wanted to make sure -- I wanted to make sure I was answering the right question.

Mara Goldstein: But I'm happy to take any additional info on SPEARHEAD-2 as well, if you wanted.

Elliot Norry: Of course. Yes. Well, with respect -- I'll answer your question. So with respect to SURPASS-2. We really haven't guided as to the protocol specifics and size of the trial. It will take into account the recent changes in the treatment paradigm for those types of cancers that is esophagogastric junction cancer and esophageal cancer, that have

-- there have been some recent approvals for combination first-line therapy. And the patient population that we're trying to address will take that into account.

With respect to when you'll see data out of that trial, it will be designed as a potentially registrational trial, and we won't be providing regular updates with respect to the data as the trial unfolds. It will probably follow sort of similar pattern as to what we've done with SPEARHEAD-1 and the approach that we've taken with respect to data in the sarcoma population.

Karen Miller: And I'm happy to answer a question on TILs. Our collaboration with Inge Marie Svane and her team at CCIT is going extremely well. As you know, they're experts in TIL therapy, and we're working with them to develop a next-generation for patients with melanoma. Our first product that we've chosen to address is a TIL product with IL-7. This is progressing well, and we'll be giving you further updates later on in the year.

Operator: I'm not showing any further questions in the queue. I would now like to turn the call back over to Adrian Rawcliffe for closing remarks.

Adrian Rawcliffe: Thanks. And thank you, everyone, for your questions and for your continued interest in Adaptimmune and our progress. As is apparent from the discussion today, we are heading into a period of significant data updates, beginning with ASGCT, which will showcase the potential of an element of our preclinical pipeline. And then ASCO, which chose the first pivotal clinical trial data from our most advanced cell therapy. So you'll get an insight on both ends of the pipeline. Look forward to discussing those data and continuing to make progress to bring our cell therapies to people with cancer. Thanks again, and have a great day.

Operator: Ladies and gentlemen, this concludes today's conference call. Thank you for your participation. You may now disconnect.