Adaptimmune Therapeutics
Closing of Strategic Combination with TCR2
Announcement Transcript

Date: **Friday, June 2, 2023**

Time: **8:00 AM ET / 5:00 AM PT**

Presenters: **Juli Miller**
Vice President, Corporate Affairs and Investor Relations

Adrian Rawcliffe
Chief Executive Officer

Operator:
Hello, and welcome to Adaptimmune Announces Closing of Strategic Combination with TCR2.

I will now turn the call over to Juli Miller. Juli, please go ahead.

Juli Miller:
Good morning and welcome to our webcast to discuss completion of our strategic combination with TCR2.

I would ask you to review the full text of our forward-looking statements. 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, is here with me for the prepared portion of the call and will be available for Q&A. With that, I'll turn it over to Adrian. Ad?

Adrian Rawcliffe:
Thanks Juli, and thank you everyone for joining us. My comments today are going to be brief, and we can go directly into any questions you have.

I'll start off the call by welcoming all of our new colleagues to Adaptimmune and say how excited I am to be working with such a committed and talented team who share our mission and our vision. Now we have the opportunity as one company to advance our deep pipeline of products with the goal of making cell therapies mainstream for the treatment of solid tumors.

To date, approved T-cell therapies have been exclusively focused in the hematological malignancies or liquid tumor space, and these therapies have been very effective for patients and have led to CAR T therapy sales last year of a little less than $3 billion, and yet the hematological malignancies represent less than 10% of all cancers, which leaves the 90% of the space—namely solid tumors—untapped. This is where Adaptimmune as a preeminent T cell therapy company for solid tumors differentiates itself and is set to succeed.

We are on track to have the first engineered T-cell therapy product on the market for the treatment of a solid tumor, namely afami-cel for synovial sarcoma. We announced that we completed Part 2 of the BLA submission in Q1, and Part 3 is in progress, targeting completion in mid-2023.

Beyond afami-cel, we have a deep clinical late-stage pipeline targeting MAGE-A4, NY-ESO and mesothelin. Adaptimmune and TCR2 have spent our entire histories focused on the solid tumor space with experienced teams who have advanced this strong clinical pipeline. And we have value-creating catalysts that are significant during our funding runway, which extends now into 2026.

We are a purpose-built company with an industry-leading late-stage cell therapy pipeline and the capabilities to deliver these products for people with cancer.

Turning to our pipeline, we remain focused on developing our MAGE-A4 franchise with afami-cel and our next-gen CD8 therapy, and progressing more products to market. We now have NY-ESO back from GSK, which could make an additional treatment option for people with synovial sarcoma and MRCLS, and we now have gavo-cel targeting mesothelin as well as PRAME and CD70 programs preclinically. This is a significant opportunity to make cell therapies for solid tumors accessible and mainstream, and we will prioritize the development of this portfolio in a thoughtful, data-driven fashion.

The flow of catalysts and the cadence with which we expect to make decisions on our pipeline is outlined here. We have several near-term data readouts with lete-cel targeting NY-ESO and with gavo-cel targeting mesothelin. With our MAGE-A4 programs, we will submit our BLA for afami-cel in mid-2023 to become the first marketed engineered T cell therapy for a solid tumor, synovial sarcoma.

If you want to understand the incredible impact afami-cel is having for people with synovial sarcoma, I encourage you to attend the poster presentation showcasing the overall survival data from Cohort 1 of our pivotal SPEARHEAD-1 trial. These data will be presented by Dr. Brian Van Tine of Washington University School of Medicine at ASCO on Saturday and was the subject of a press release we issued last Thursday.

Behind that, we have our late-phase registration-directed SURPASS-3 trial in ovarian cancer with readouts expected late next year, and our additional cohorts in the Phase 1 SURPASS trial in earlier line combination setting for bladder and head and neck cancer will also read out next year.

At the end of Q1, you will recall we had $170 million of liquidity on our balance sheet and TCR2 reported $110 million of cash and cash equivalents. With the completion of this strategic combination and the recently reported commitment from GSK, we are funded into 2026. This will enable us to deliver the catalysts I just outlined and to make smart, data-driven development decisions to advance our cell therapies to serve as many patients as possible.

With that, I'll turn over for Q&A. Operator?

Operator:
Thank you. We will now begin the question-and-answer session. (Operator instructions).

Our first question comes from Marc Frahm of TD Cowen. Please go ahead.

Marc Frahm:
Thanks for taking my questions and congrats on closing the deal yesterday. Maybe, Adrian, can you just walk through—since the next kind of update is from gavo-cel, just kind of the standards by which you will be making that decision of what the next steps may or may not be for that program as that's now in-house.

Adrian Rawcliffe:
Thanks, Mark. Gavo-cel, as you probably know, is being developed in a Phase 2 trial in combination with checkpoint inhibitors. That trial initially was recruiting in a range of tumor types and is now restricted to ovarian cancer, although we have a range of patients who have mesothelioma also enrolled in that trial in combination. We anticipate that the patients enrolled roughly to date to the middle of this year will be the basis upon which we'll be able to understand the nature of the signal that we're receiving, and there's two objectives here; one, of course, is the response rate and the other is the duration of response.

I think we've been reasonably consistent for a long time in thinking that the sort of threshold hurdle rate for cell therapies is probably around about 30% generically in these late-stage settings, where there are few other alternatives, so where you're comparing to a standard of care that has a very low response rate. That's sort of the starting point for the benchmark for us.

Then I think, again, in these settings, we're looking to see duration of response that is at least around six months in order to be confident that there is benefit in the very, very late-stage patients that are typical of these trials. That's sort of generically the benchmarks that we've set before, and I think that's how we're viewing the gavo-cel data as we go through the remainder of this year. We want to see not only a reasonable cohort of patients and a response rate, but also get to durability of that response which is why we are positioning those data towards the end of this year, beginning of next.

Marc Frahm:
Okay. That’s very helpful. Then, I guess similar to that idea of patients enrolled kind of middle of the year are the ones that can be evaluated for gavo-cel, maybe the same could be said for SURPASS, where we're, I think, expecting a Phase 1 update later this year? Just can you maybe outline the patient numbers and types of things that we should be expecting in that update, given that those patients should be on trial about now?

Adrian Rawcliffe:
Yes. I think you're correct that there is a SURPASS-1 update later on this year. We've sort of said previously that is intended to be for the monotherapy in late-stage patients, somewhere between 50 and 60 patients, and, therefore, representing an incremental addition to the previous data set from last year of about 43 patients in monotherapy. For combination therapy, we're targeting getting over the 10-patient threshold.

I think the most important thing to understand with those data, I think they will be useful in supporting the signals that we've seen in ovarian, head and neck, and bladder cancer, but I don't anticipate that those are going to be hugely transformative to the overall data set. Going from 45 patients with a 37% response rate to 55 patients with a similar response rate I don't think is going to change—it doesn't change our perception that we have a product here in those indications that is genuine and that we are moving forward on.

Then in the checkpoints, I think with the checkpoint combination, again in this very late-stage patient population, we are looking for initial safety, of course. Then we're looking to understand in these patients whether there is anything that supports the combination with checkpoints, although I think that's going to be difficult on an indication basis to see given the low numbers of patients who are indication. I think there you're going to be looking at the SURPASS-3 trial in ovarian cancer, and the combination cohorts in head and neck cancer and bladder cancer which read out next year.

Marc Frahm:
Okay. That's very helpful. Thanks.

Adrian Rawcliffe:
Thanks Mark.

Operator:
Our next question comes from Tony Butler of EF Hutton. Please go ahead.

Tashdid Hasan:
Thank you. Good morning. Adrian, it's Tash Hasan on, by the way, for Tony.

Adrian Rawcliffe:
Hi.

Tashdid Hasan:
Adrian, I wonder what you can share with us today about, let's say differences and similarities between the afami-cel and CD8 as it pertains to baseline versus post infusion lymphocyte infiltration, differences in response rates. I understand that you have shared with us in the newest slide data with afami-cel, but if there's anything that you can share with us about your observations with the CD8 that would be helpful.

Furthermore, your experience and your thoughts on what is driving the responses among patients with lowest baseline infiltration would be helpful, too. Thank you.

Adrian Rawcliffe:

Thanks. I think the underlying rationale for the CD8 program that appears to have played out in the clinical data to date is that with a more potent T-cell from afami-cel—they share the same T-cell receptor, of course—with a more potent T-cell you will achieve in indications beyond synovial sarcoma what we achieved in synovial sarcoma. In synovial sarcoma with afami-cel we have a response rate of between 35% and 40%. It's been relatively consistent as the data's evolved; it's trending upwards very slightly towards 40%. We did not see that with afami-cel in other solid tumors, and we are seeing that in SURPASS, obviously, with a 35% to 40% response rate across a broad range of tumors in heavily pretreated patients. So, the starting point for this is that's exactly the efficacy that we were intending to achieve via the modifications that we made with CD8.

Then the question is, well, how is it doing that? I think the next sort of interesting piece that we are now understanding is that it is doing it by a much broader immune response than simply that is engineered by—engaged by our T-cells. The T-cells drive a broader infiltration of the immune system—and particularly of the T-cell population but also other immune cells—into the tumor, and we see that with both afami-cel and we see it in synovial sarcoma. We also see it with CD8.

I think one of principal differences we do see with CD8 is we see a clear—a clearer signal of broader engagement of compartments beyond the T-cell compartment. In particular we see increases in, for example IL-12, indicative of dendritic cell engagement because IL-12 obviously isn't produced by T-cells, and we see that with CD8 preferentially to afami-cel. Clearly, CD8 is doing more than afami-cel, but the infiltration into the tumor is, relatively speaking, consistent for all of our T-cell therapies.

The one thing that I do think we are now seeing is that the—and we have translational data in the corporate deck that is published and we'll be talking to people about this at ASCO—is we are seeing that the population of patients who are responders tend to be characterized by lower infiltration initially and significant infiltration after infusion. That is different to the stable disease population and to the progressive disease population where there is higher baseline tumor infiltration of T-cells. I think that drives both a good understanding of patients who might benefit from this more, but also the PD-L1 combination in checkpoint, I think it gives us further background support that the strategy for our T-cells may indeed prove to be effective from a translational evidence perspective

Tashdid Hasan:
Thank you.

Adrian Rawcliffe:
Thanks.

Male Speaker:
Thanks Tash.

Operator:
Our next question comes from Michael Schmidt of Guggenheim Securities. Please go ahead.

Paul Jeng:
Hi. This is Paul on for Michael. Thanks for taking our question.

Adrian Rawcliffe:
Hi Paul.

Paul Jeng:
First, I just wanted to clarify your cash runway projection and sort of what clinical studies are factored into that. Does this include just the advancement of the ongoing studies, or are there any sort of future initiations of potential Phase 2s also factored into that?

Then it looks like the SURPASS bladder and head and neck Phase 1 updates are coming in the second half of next year. Is it correct to assume that possible Phase 2s decision won't come until that time? Is that primarily a response rate strategy, or is there also potential to make a decision earlier based on biomarker or translational data? Thank you.

Adrian Rawcliffe:
Thanks. With respect to the cash runway question, this is quite obviously a complex portfolio, and there's a lot of permutations that could come. The cash runway covers a reasonable percentage of those including the ongoing development of the existing studies, but clearly there are outlying cases involving the need to develop everything in Phase 3 studies that are probably

not covered by the ‘26 runway, but it does cover reasonably running this portfolio for the next 2.5 years, which I think is a fairly decent position for a biotech company to be in at this point in time in our evolution. It also covers, importantly, the BLA filing and the approval of that product of afami-cel for synovial sarcoma, so the first commercial product. So by the end of this period, we are in a very, very different position to the one that we're currently in.

With respect to your second question on the head and neck and the bladder cohorts, I think, in particular, was the question on for CD8, the critical thing to realize about those is that our strategy with those cohorts is in earlier lines of therapy. We don't have any evidence in earlier lines of therapy. We have a spectacular response rate and a durability that's consistent with the stage of patients, so reasonable but not, obviously, very long in head and neck and bladder cancer in very late stage, very heavily pretreated patients. If you just look at the responses in the patients in, for example, head and neck cancer where every single patient we have dosed to date, which is only four, has had a significant reduction in their target lesions, that's the base point. Our objective is to move into earlier lines in combination with standard of care, i.e., in first line and first line sequence, and second line in head and neck cancer in combination with standard of care, and in second line and ongoing in bladder cancer.

The first thing we've got to do is we've got to get data in those settings, and so that's why we're developing these cohorts. These are hypothesis testing cohorts that in those settings—earlier stage, in combination—we will see not just what we've seen in the late stage but an improvement on that, and really, the opportunity, I think, to change the experience of the patients in those settings from one where 1 in 5 responds to something where responses are expected and then the opportunity to continue those responses in those patients with checkpoint inhibitors.

Once we have those data, I think it will become very clear how we can develop those. I am on record previously saying that at some point, we are going to have to, as an industry, get out of this focus on responses and start to actually get to endpoints that are meaningful for patients. and for payers on a broader scale. So whilst we will undoubtedly try to pursue the most accelerated approaches for that, I think you should also anticipate that as an industry and us leading that industry, we are going to need to deal with driving for overall survival benefits in some of these patient populations.

To that point, I will point you to the sarcoma data that is presented at ASCO and I think - it's a single-arm study and therefore one is obviously caveated about what one can say, but there is, I think, a compelling overall survival signal, particularly in those patients who respond to therapy. That's the first—as far as I'm aware, that's the first engineered T-cell therapy in a solid tumor setting that is showing with a mature data set on overall survival. I think as we move forward as an industry, we'll increasingly have to focus on that; particularly to be competitive in the space, but also to show the transformative benefit of cell therapy in earlier line settings.

Paul Jeng:
Great. Very helpful. Thank you.

Adrian Rawcliffe:
Thanks.

Operator:
Our next question comes from Jonathan Chang of SVB Securities. Please go ahead.

Faisal Khurshid:
Hi guys. This is Faisal on for Jonathan. Thanks for taking the question. I know you guys have talked about this 30% response, six-month duration as a general benchmark in late line settings, but I wanted to ask specifically how you're thinking about the bar for success in platinum-resistant ovarian cancer, given you have a couple of programs prioritizing this indication. Also, if your thinking about that bar has evolved at all with some of the recent data that we've seen in the space with drugs like ADCs?

Adrian Rawcliffe:
That's a really good question. I think that space obviously is evolving, although it has to be pointed out that a lot of people are still dying from platinum-resistant ovarian cancer and so I don't think there are many curative approaches in that space at this point in time. Therefore, the opportunity for additional therapies remains and is significant in that space. That's the first point.

I think the space, however, has got increasingly—over the timeframe that we've been looking to this—more complicated with the PARP inhibitors, with the (inaudible 23:14) and then with the NaPi, so that sequentially impacts the space. It will impact the patients that we see in our trials.

And I think therefore that's one of the reasons why I'm excited and confident in the response rates that we're seeing in I think very late-stage patients, much more heavily pretreated than just simply being platinum-resistant, in the SURPASS trial in ovarian cancer where we have a response rate that is 40-odd-plus percent, and that I think is highly likely to be a developable asset.

Now. it is also quite a focused asset because based on selection of HLA-A2 and of MAGE-A4, so it makes this quite a targeted population and I think within that population it is able, therefore, to compete. It will be able to compete effectively either against those, depending on what the data comes out at, or in sequence with those on the grounds that very few of them are actually curative at this point in time. That's the starting point.

Then we have obviously gavo-cel with ovarian cancer and we will need to see what the data says, the readout on that and how we can develop that. But the one thing that I will point to is there's obviously an interesting opportunity to develop that in parallel with a CD8 if indeed both of them show a sufficient signal and be able to select patients to put on to either of those studies as we move forward. We look forward to seeing the data later this year and making those decisions appropriately.

Faisal Khurshid:
Got it. That's very helpful. Thanks for the thorough response.

Operator:
Our next question comes from Mara Goldstein of Mizuho. Please go ahead.

Mara Goldstein:
Great. Thank you so much. Two things. Can you just confirm how much free cash will be coming from the TCR transaction? Then also, just on the BLA submission for afami-cel, you talk about mid-2023 and that's been consistent for that final CMC module submission, but is that sort of this side of the first half of this year or sort of the far side of the first half of this year?

Adrian Rawcliffe:

Good questions, both. Short answer on the first one is no. We're not confirming. We will update the financial guidance at the end of our Q2 and we'll then be able to put consolidated financials out there and be clear how much cash we have at the end of Q2.

What we have done is said at the end of Q1 we had $170 million, a little less than $170 million, $167 million, and they had $110 million of cash, cash equivalents and short-term investments. We're a couple of months on, but that's the baseline we're giving for that.

For the question on afami-cel, I think you're right; the midyear is there and the midyear is quite deliberate. I've been quite consistent about the timeline. The first module I said we were going to put in, in Q4. The second module I said we were going to put it in Q1 The third part of it, I said we were going to put in, in mid-2023. I deliberately didn’t say Q2. So, I think you can interpret that it is not therefore going to be Q2, but we are targeting midyear. You can imagine that the Company and the team is working incredibly hard to deliver that module.

Mara Goldstein:
Okay. If I could just sneak in one more question.

Adrian Rawcliffe:
Please.

Mara Goldstein:
Just on the gavo-cel, on the evaluation of the gavo-cel ovarian cancer data, how many patients will you have data for at the time you're looking at making those decisions?

Adrian Rawcliffe:
We haven't said specifically how many patients, but we're looking to have a cohort that we would think of as usefully signal finding, and historically for us that's been in the 10 to 15 patients range.

Mara Goldstein:
Okay. Thank you. I appreciate it.

Adrian Rawcliffe:

Thanks. Cheers Mara.

Operator:
Our next question comes from Peter Lawson of Barclays. Please go ahead.

Male Speaker:
Good morning. It’s Alex on for Peter. Congrats also on closing the deal.

Adrian Rawcliffe:
Thanks.

Male Speaker:
Just a few quick ones on SURPASS-3. Any interim analysis we should expect from the study before the top line later in '24?

Adrian Rawcliffe:
That's a great question, actually. We are working on the basis that SURPASS-3 has the potential to be a registrational study. We have RMAT designation for that with the agency as a result of the data from SURPASS-1, SURPASS in ovarian cancer, and SURPASS-3 is designed with the potential that it can be registrational with either arm compared to historic controls with overall response rate as a primary endpoint. As such, we will do what we did with the SPEARHEAD—very successfully with the SPEARHEAD trial, which is that we won't put out any data, efficacy data on that study until we have enrolled the entirety of that study. That's obviously in order to avoid any changes or bias creeping into the patient selection for that study from a premature disclosure.

The opportunity, first opportunity, which will be, we believe, towards the end of 2024, depending on enrollment of that trial, will be to see the interim analysis when we've enrolled the final patients. That’s the data point, the first data point that you'll see out of SURPASS-3, and we’re targeting having enrolled that study through the course of 2023 and 2024, such that by the end of 2024 we are comfortable putting out the interim analysis from the futility analyses which are at, I believe, 13 patients per arm and 23 patients per arm. That's how that will flow.

The only possible exception to that is if we actually made a decision on the basis of the futility analyses earlier on, then obviously that would become public in itself.

Male Speaker:
Great. Very helpful. Thank you.

Adrian Rawcliffe:
Thank you.

Operator:
This concludes the question-and-answer session. I would like to turn the conference back over to Adrian Rawcliffe for any closing remarks.

Adrian Rawcliffe:
Thanks everyone, and thank you all for your time today. Obviously we are delighted to share the news of the conclusion of the combination between Adaptimmune and TCR2, and we are also really pleased to welcome our new colleagues to Adaptimmune.

I'm looking forward to updating everybody as we go through the remainder of this year, and in the meantime, please do feel free to reach out with any questions. If you're at ASCO, we will be happy to meet up. Thanks again for your time today.

Operator:
This concludes today's conference call. You may disconnect your lines. Thank you for participating and have a pleasant day.