

The following is the transcript for a presentation given on March 6, 2023 in connection with the previously announced strategic combination of Adaptimmune Therapeutics plc and TCR² Therapeutics Inc.



**Adaptimmune Therapeutics
Q4 Financial and Business Update
Transcript**

Date: Monday, March 6, 2023

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

Presenters: **Juli Miller**
Vice President, Investor Relations, Adaptimmune

Adrian Rawcliffe
Chief Executive Officer, Adaptimmune

Dr. Garry Menzel
President and Chief Executive Officer, TCR² Therapeutics

Operator:

Welcome to Adaptimmune and TCR²'s joint webcast to discuss their strategic combination, announced earlier this morning.

I will turn the call over to Juli Miller, VP of Investor Relations and Corporate Affairs at Adaptimmune. Juli?

Juli Miller:

Thank you, Operator. Hello. This morning we issued a joint press release with TCR² Therapeutics, announcing entry into an agreement for the strategic combination of our two companies. In a second press release, we provided our Q4 and full year 2022 financial and business updates. I would ask you to review the full text of the forward-looking statements. We anticipate making projections during this webcast, and actual results could differ materially due to several factors, including those outlined in our latest filings with the SEC, as well as our 10-K filing for the year ended 2022, which will be filed later today.

Of note, we will share slides during this webcast, which are also available on the presentations tab of our investor Relations website.

Adrian Rawcliffe, our Chief Executive Officer, and Garry Menzel, TCR² Therapeutics President and Chief Executive Officer, are here with me for the prepared portion of the call, as well as Q&A.

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

Adrian Rawcliffe:

Thanks, Juli.

We're delighted to welcome you to this webcast to discuss the strategic combination of our two companies, which creates a preeminent cell therapy company to treat solid tumors.

The details of the transaction are set out on the next slide. This is a stock-for-stock transaction, by which Adaptimmune shareholders will own 75% and TCR² Therapeutics shareholders will own 25% of the combined company on closing.

This is anticipated to extend the runway for the combined company into 2026, following closing, and enabling a series of catalysts, which we'll come to later.

I will be the continuing CEO, and we will have a strong Board with members from both Adaptimmune and TCR², including Garry.

We anticipate the transaction to close in Q2 2023, subject of course to shareholder approval.

That's the what of what we are doing. However the purpose of today's call is to tell you why we are doing it, and why we are excited about this combination particularly at this time in the evolution of cell therapy.

Here are the five compelling reasons why this strategic combination is the right thing to do.

First, we're two companies that have spent their entire history focused on solid tumors, the largest unaddressed opportunity for cell therapy.

Second, we each have a strong clinical pipeline that has been highly focused on MAGE-A4 and mesothelin, and has significant value-creating near-term catalysts, including the filing and potential approval of the first engineered T cell therapy for a solid tumor indication. We also have medium-term preclinical pipeline focused on PRAME and CD70.



Third, together we have an innovative next generation toolbox designed to enhance the functionality of our products in the tumor microenvironment as we aim to develop cell therapies that are both curative and mainstream.

Fourth, we have end-to-end capabilities because both companies have been entirely dedicated to discovering, developing and delivering T cell therapies, and both have knowledgeable and experienced teams who have successfully advanced these therapies into late-stage trials.

Finally and critically, this combination enables us to continue the focused development of this strong pipeline, with an extended cash runway of approximately three years, into 2026, due to significant operational advantages.

We're now going to cover each of these five points in greater detail on the following slides.

Garry and I, along with our collective management teams, share the conviction that cell and gene therapy are about to have an impact on the therapeutics landscape comparable to that of monoclonal antibodies 25 years ago. We believe these therapies will transform the treatment of cancer. But to do that, they clearly have to move out from the narrow confines of CAR-T and hematological malignancies, which nonetheless have realized nearly \$3 billion in sales in 2022, because the significantly larger opportunity is in the solid tumor space.

Treating solid tumors has been the life's work of the exceptional employees at Adaptimmune and TCR². The programs we have in clinical development are amongst the leading cell therapies for solid tumors, where we have already seen robust response rates in multiple cancer indications.

These T cell therapies in the clinic and others coming behind will enable cell therapy to complete the transformation of this landscape, providing hope to people living with cancer.

At a macro level, treating solid tumors with cell therapies is the ultimate value creation thesis for this industry. This is why our companies exist. Accessing this opportunity with a breadth of pipeline and a depth of runway is why this combination makes sense.

Although hematological malignancies are only 10% of U.S. cancer deaths, the majority of cell therapies and all approved CAR-Ts are focused on these diseases. Ninety percent of cancer deaths are from solid tumors, and this space is largely untapped by cell therapies. We assert that, as living medicines able to respond to the tumor and its microenvironment, cell therapies have distinct advantages to treat solid tumors.

I believe that our combined company will have a strong leadership position in this rapidly growing and evolving field, due to its complementary technology platforms, which Garry is going to talk about now.

Garry Menzel, Ph.D.:

Thanks, Ad.

As Ad said, this is truly an exciting time for cell therapy focused on solid tumors, with many cancer patients already benefiting from treatments in clinical trials. Together, we have complementary platforms that will allow us to address a broad universe of both intracellular and extracellular protein targets with our SPEAR and TRuC-T cell therapies.

Adaptimmune's proprietary SPEAR T cell technology is based on the affinity enhancement and engineering of T cell receptors or TCRs to specifically target peptide:HLA complexes that are uniquely expressed on solid tumors. TCR²'s proprietary TRuC-T cell technology uses an antibody-based binding domain fused to TCR subunits to reprogram an intact TCR complex to recognize tumor surface antigens. Both technologies can be further leveraged in the combined Company's allogeneic platform. With SPEAR T cells and TRuC T cells, we have an opportunity to increase patient access to cell therapy.

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Ad?

Adrian Rawcliffe:

Thanks, Garry.

With these complementary platforms, we are prioritizing and focusing on key validated targets for cell therapy in the solid tumor space. (Inaudible 07:48) a wide range of tumors, targets that we know we can address with our T cell therapies, and targets that are expressed in cancers that between them kill more than 300,000 people a year. We have the opportunity to make cell therapy a mainstream option for people with cancer, through our focused pipeline against these targets.

And our technologies against these targets have enabled a deep pipeline across multiple cancer types. Our lead programs will target MAGE-A4 and mesothelin in the clinic, and our preclinical development will focus on PRAME and CD70. As Juli described, this pipeline is available for you on the website, so I won't go into it in great detail, because I want to focus on the clinical data and the catalysts that we believe are going to create near- and mid-term value.

We have compelling clinical efficacy from our two lead franchises. With afami-cel, we're on track to complete a BLA submission for the treatment of synovial sarcoma in mid-2023, which would mean a possible approval in 2024, the first engineered TCR T cell therapy for a solid tumor.

Our next generation cell therapy, targeting MAGE-A4, ADP-A2M4CD8, is delivering an overall response rate of 37% in our Phase 1 signal-finding SURPASS trial across a range of solid tumors. In ovarian, bladder, and head and neck cancer, we see a response rate of 52%, improving still further to 75% in patients with these tumor types who have received three or fewer prior lines of therapy.

Going forward, we are initiating new cohorts in first line head and neck and second line bladder cancer, in combination with pembrolizumab, and a Phase 2 trial, SURPASS-3, which we intend to become registrational, for patients with platinum-resistant ovarian cancer.

Gavo-cel and the next generation therapy TC510 target mesothelin, which is also expressed in a broad range of cancers. In the Phase 1 dose-finding trial, there was tumor regression in nearly every heavily pretreated patient, and an overall response rate of 22%. In patients with ovarian cancer, the response rate was almost 30%.

Going forward, we have the potential to screen patients with ovarian cancer for both MAGE-A4 and mesothelin, which would significantly improve the screening success rate. This type of joint development is one of the distinct operational advantages of this strategic combination.

The Phase 2 trial with gavo-cel is ongoing, and includes options for multiple doses and combination with checkpoint inhibitors to potentially enhance response rates and persistence.

The next generation product targeting mesothelin is TC510, which incorporates a PD1 CD28 switch designed to increase potency. The Phase 1 trial is currently in dose escalation across a range of tumors.

Touching on safety across our combined programs. Whilst more specifics are available in the materials, generally speaking, we see adverse events that are consistent with those associated with lymphodepletion and the administration of cell therapies, mainly CRS at various levels, which is typically manageable and reversible using existing approaches. Over all, the benefit-risk profile to date has been acceptable.

On closing this transaction, the combined Company will have anticipated funding into 2026. We expect to deliver multiple value-creating catalysts from these programs within that financed window.

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Here's a long list of what you can expect over the next 22 months. Of course we'll continue to optimize the combined portfolio, making data-driven resource allocation decisions, and focusing on those programs that will deliver greatest value. I'm going to touch on a number of these items. For afami-cel, it's all about BLA submission and the potential for approval. For the CD8 next generation program, we have trials ongoing or initiated with a potential for readouts this year and next: firstly for the combination in late line patients with a checkpoint inhibitor, and then readouts from cohorts in front line head and neck cancer and second line bladder cancer. For gavo-cel, later this year we anticipate the first readout from the Phase 2 portion of the trial in platinum-resistant or refractory ovarian cancer in combination nivolumab. We will also have a midyear readout in mesothelioma patients, who were enrolled before the focus was narrowed to ovarian, which will include key translational data speaking to the impact of checkpoint inhibitors.

In 2024 we can expect additional readouts in the gavo-cel trial. For the TC510, the next generation version of gavo-cel, the trial is dose-escalating and we anticipate initial safety and then potential efficacy along with dose-finding result in 2024.

For PRAME and TC520, which target CD70, we'll be moving these to be IND-ready in '23 and '24 as both Companies have previously outlined.

Now I'd like to turn over to Garry to explain some of our next gen enhancements, some of which are already in use in our clinical trials.

Garry Menzel, Ph.D.:

Thanks, Ad.

Not only do we have compelling clinical data and exciting preclinical programs, we also have a toolbox to further enhance our T cell therapies. When we think about how best to treat solid tumors with a T cell therapy, several factors come into play: trafficking of our T cells to the solid tumor, persistence in the hostile tumor microenvironment, and a killing effectiveness once they are there. Our CD8 and PD1 switch next generation technologies have already made it into the clinic as autologous therapies. We also have many others, such as IL15 and IL7 CCL19, that can be thrown into the fight. One of the most exciting aspects of our complementary technology platforms is the ability to target multiple antigens.

Importantly, all of these approaches can also be used in our allogeneic platforms as well.

Not only does it take a technology toolbox, it takes a unique set of capabilities to make cell therapies work.

With that, I turn it back over to Ad.

Adrian Rawcliffe:

Thanks, Garry.

One of the realizations that both Companies have had is that cell therapies are a truly unique class of medicines, and that to convert complex technologies into actual products that benefit patients requires a highly specialized set of capabilities that need to be tightly integrated in ways that are particular to cell therapy.

Our combined Companies have been wholly focused on cell therapy for solid tumors since the beginning. We have experienced teams who have a proven track record in this field. Between us we've taken seven programs into the clinic. Five of those are ongoing. The first BLA for an engineered TCR T cell therapy will be submitted this year by us.

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The capabilities we've outlined in our U.S. and U.K. facilities on the right hand side of this slide are not there by chance, they are not optional. These are the capabilities that we have deliberately built from the ground up by each of the Companies. As we bring together our complementary technologies, teams and infrastructure, there will be significant operational advantages, as we aim to transform the cell therapy landscape for solid tumors.

Now when this transaction closes, we will have cash into 2026. This will enable us to finance the catalysts on the slide I showed you earlier. As a combined company, we will continue to focus on investing our balance sheet in a data-driven manner to create maximum value from the portfolio.

I'd like to return to the key differentiators that make this strategic combination attractive. A shared focus on solid tumors, by far the largest opportunity for cell therapy. Compelling data and clinical progress in solid tumors with our existing clinical pipeline. A deep preclinical pipeline focused initially on PRAME and CD70, backed up by expert teams, specialized end-to-end capabilities, a decade in the making. All made possible by our extended cash runway. We have the opportunity to deliver against our catalysts, and against our ultimate goal of making transformative medicines for people with cancer.

With that, I'll open up for questions. Operator?

Operator:

Thank you.

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

Ernesto Rodríguez Dumont, M.D.:

Hi, good morning, this is Ernie Rodriguez for Marc. Thank you for taking our questions. Just two for us.

One is, if you can provide more color on the cash runway extension that you have once the transaction closes, like how much cash, what was the cash balance and would be, and what are the assumptions that you have, thinking about all the catalysts that you and other, what assumptions would that have for the cash extension?

The second question is about the afami-cel BLA, just wondering what are the gating factors right now, what needs to be done in order for you guys to be able to complete it by mid '23? Thank you.

Adrian Rawcliffe:

Okay. Thanks, Ernie.

On the cash runway, both companies' pattern is to give cash runway guidance but not obviously detailed cash flow guidance, and that's compounded in this case by two things: one, integration planning is obviously only just starting on the back of this; and two, we just put out our Q4 results, but TCR² have not done so. It's a bit early to be giving detailed forecasts on cash utilization, but you can anticipate more information in due course. I think the key thing is, we are confident that the cash runway can be extended in 2026 and can deliver on those catalysts.

It's obviously a range of things that you could look for in terms of the advantages that this come from, both the operational advantages that I've talked about during the scripted portion of the discussion, such as the ability to jointly screen with it for ovarian cancer, such as the obvious potential synergies over time associated with the manufacturing capabilities that Adaptimmune has created as we think about putting multiple products onto the market in due course; and obviously establishment costs. We have just simplistically two DNO policies, for example, which we won't have going forward. But I think we still need to go through the integration planning, between now and the close of the transaction.

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Secondly, on the afami-cel BLA, we've laid out the pathway that we have agreed with the agency to submit the elements of the rolling BLA, and just to remind you that was the preclinical module initially, which was submitted in December, the clinical module, which we anticipate going in shortly, and then the CMC module which will be the final piece, anticipated in the mid-2023. The work to complete those is the gating item between now and getting there. We're compiling all the information for the clinical pieces, as we speak, and we will be doing the same for the CMC piece and finalizing the work required to submit that with the information that we agreed with the agency.

Ernesto Rodríguez Dumont, M.D.:

Thank you, that's very helpful. Thanks again.

Operator:

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

Mara Goldstein:

Hey. Thanks so much for taking the question. I'm just hoping that you can maybe review for us a bit, or perhaps even confirm that, as the deal comes together, the TCR² pipeline and the expectations for that pipeline for this year, that those will be consistent with what TCR² has previously guided to; and then secondarily, I'm just curious about, once you put the two companies together and you have greater scale, what you think, from a time perspective, where is the advantage, let's say, with TCR²'s TC510 program, which is in a Phase 1 at this point, and where can you bring synergy to bear there?

Garry Menzel, Ph.D.:

I guess I'll take that one. This is Garry speaking. First of all, I think the guidance is similar to what we've provided before, in the case of ovarian cancer where we have a readout at the end of the year for that particular cohort. On 510, the same. The difference, I think, is, and the new guidance provided today, is that in the middle of the year we intend to showcase the mesothelioma patients that we treated in the Phase 2 trial before we narrowed the focus to ovarian cancer. If you recall, we did let people know that, if there was any excess manufacturing capacity, we would devote it to mesothelioma patients. We now intended to release some of that clinical data, including key translational data that speaks to the impact of checkpoint inhibitors, in the middle of the year. That's in terms of guidance.

In terms of where there are synergies going forward, I think there are a number, because we have several overlapping clinical sites between the two companies. We also have some unique clinical sites between the two. We have an ability, since both of us are focused on ovarian cancer, to co-screen for MAGE-A4 and mesothelin, which makes us a little more attractive to physicians, who know that they'll get a cell therapy treatment for their patients if they work with us. I see synergies there which may help us, as we go into next year, move things along a little faster.

510 is more constrained, because of the design, remember it's dose-escalating, you have to move in a steady fashion, cohort by cohort, as you move up each screening, so I don't think we can move that along much faster than we're doing already.

Mara Goldstein:

Okay, thanks so much.

Adrian Rawcliffe:

Thanks, Mara.

Operator:

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

Tony Butler:

Thanks very much. Adrian, two questions.

One is on the CD8 program in ovarian cancer. I just wanted to, while in the other cancers of head and neck and bladder, there were first- and second-line patients. Are these later-line patients in ovarian cancer that will be treated? That's question one.

Question two, there was some statements about expanding the clean room space in the Navy Yard, vis-à-vis manufacturing. I assume that is not necessarily a component of what is required to complete the CMC components et cetera, as it relates to afami-cel, and even though the expansion would allow for more afami-cel to be created, I just wondered if you could provide a few words on that rationale. Thank you.

Adrian Rawcliffe:

Thanks, Tony. You are correct, whilst the cohorts that we are initiating in the SURPASS trial in head and neck cancer and bladder cancer are designed to be in earlier lines, first and second line roughly, in conjunction with standard of care, pembrolizumab; the patients in SURPASS-3 and the population where we believe we can develop that towards a registration is in the platinum-resistant setting, and again I just want to touch on that that trial has two arms to it, both monotherapy with cells alone and combination with pembrolizumab, both independently designed against historic controls, giving us potentially sort of two shots on goal there. That's based on—this is important, because I think what we're doing now is we're transitioning out from, and we have been for some time in sarcoma, from the proof of principle of a technology into actually developing products in specific indications, taking account of the treatment paradigms in those indications. That's why this makes sense in that ovarian setting. That's the ovarian study, and the future for SURPASS.

With respect to the manufacturing, you're correct, we've built out our facility in the Navy Yard, expanded capacity to—and we did that over the course of the last year, hence the fairly heavy capital expenditures in the last year that won't be repeated necessarily going forward. That gives us the ability to manufacture many more products. It doesn't really affect the afami-cel development, since the suites that we currently have open for afami-cel, where incidentally we manufactured all of the Spearhead-1 patients and where we will be launching from, those suites are likely to be able to cope with the capacity needs of afami-cel as a commercial product and for the continued clinical trials associated with afami-cel. It's more that, as we get into larger patient populations in SURPASS, that that space becomes more useful with the manufacturing methods associated with SURPASS.

Tony Butler:

Thank you, Adrian.

Adrian Rawcliffe:

Thanks, Tony.

Operator:

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

Michael Schmidt, Ph.D.:

Hey guys, good morning, thanks for taking my questions.

Just a modeling question, perhaps, TCR² obviously did announce some cost reductions earlier this year; how should we think about the potential for additional cost synergies following the merger, later this year, and then I had a partner (phonetic 28:11) question as well.

Adrian Rawcliffe:

Why don't I start with that, just at a high level, and then Garry, if you want to comment specifically on the shape for TCR² to the extent, obviously, that we can.

I think one of the challenges that you guys are going to have modeling this is that both Companies have actually gone from a larger cash burn in 2022 to a much smaller cash burn in 2023. Talking from the Adaptimmune side, last year you'll see that our net cash burn was approaching \$200 million, \$170 million net. That's come down substantially on the basis of the decisions that we took, both to focus the pipeline onto the key assets where we've got a really strong signal and product opportunities, but also to reduce the size and shape of the Company, which we executed on over the course of the last few months. I know that the TCR² team have done similar, which makes it difficult to look at the 2022 numbers and project forward.

That's partially why we've done some of that work in the run-up to the combination that we announce today, in order to enable us to project forward the runway into 2026, and as we continue with the integration work between now and the close of this deal—integration planning between now and the close of this deal, obviously ultimately the integration work, we'll be able to say more about that in due course.

Garry, anything to add to that?

Garry Menzel, Ph.D.:

No, I think you got it right. The only thing I'd point you to, Michael, is that in an 8-K I think we filed an updated cash position, so there's a little bit of information in there. But the reality is, not all of the impact of the changes that we made at the beginning of the year are reflected in that, there are some other moving parts; and then of course you layer in this transaction. Sorry that we're not able to give you precise numbers, but, as we begin our integration planning, perhaps we'll be able to say more going forward.

Michael Schmidt, Ph.D.:

Okay, sounds good, thank you.

Then, just on the ADP-A2M4 program, what else have you learned from the ongoing Phase 1 study this year? I know that Phase 2 cohorts will read out next year, but anything else we'll learn on the Phase 1 in 2023? Thanks.

Adrian Rawcliffe:

Thanks, Michael. I think that the Phase 1 program for SURPASS for CD8s, the SURPASS trial itself, and the original cohort of that, which was recruiting across a basket of tumor types, all of whom are reasonable or high MAGE-A4 expression, in late-stage patients, having heavily pretreated multiple prior lines of therapy obviously.

That study has two parts—that piece has two parts to it. The monotherapy arm, where we reported 43 patients in monotherapy, and that 37% response rate last year. We anticipate completing that arm, and the guidance we've given is that will have ultimately 50 to 60 patients in it, and reading that out in 2023. We also anticipate—we're also recruiting in parallel a combination arm, again in that range of tumor types, and again in late-stage patients in combination with nivolumab, and that arm we intend to enroll between 10 to 20 patients to give us experience using checkpoints in combination with our cells, as a precursor for all the other work that we're doing further downstream, and that will also read out, we anticipate, this year, later on this year.

That's what you can expect from the original. I just want to make sure that everyone understand, though, the two cohorts, in first line head and neck and first line bladder, are also part of that SURPASS trial, albeit that they're separate cohorts in different patient populations.

Michael Schmidt, Ph.D.:

Great. Thank you.

Adrian Rawcliffe:

Thanks, Michael.

Operator:

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

Jonathan Chang:

Hi guys, good morning. Thanks for taking my questions.

First question, how are you thinking about strategic priorities following the combination? More specifically for gavo-cel: is the focus still ovarian cancer? What would you need to see in the data by year end, to continue further development of the program in ovarian cancer?

Then second question, just for emphasis, following up on the prior questions, can you give us more granular color on how we should be thinking about expenses of the combined company moving forward? We're just trying to make the model work. Thank you.

Adrian Rawcliffe:

Okay. Maybe I'll start on sort of the view of strategic focus, and then maybe I'll ask Garry to comment on the focus in ovarian cancer with gavo-cel, and perhaps what a good signal looks like there, and then I'll come back to the cost discussion.

In terms of strategic focus, one of the things you have is you have two Companies who have already gone through a very significant portfolio rationalization as part of their becoming fit for purpose for the world that we find ourselves in. For us, that was narrowing down our focus clinically to afami-cel for synovial sarcoma, and for CD8 to the three indications at different stages, as we just talked about, for MAGE-A4 and focusing on MAGE-A4. Then in preclinical, that was us focusing really heavily down on PRAME in the short term, and moving forward to IND with that.

For TCR², the focus is on mesothelin, focus on ovarian, specifically for gavo-cel, and then TC-510 in dose-escalating trials. Again, first- and second-generation programs in one target, essentially, in the clinic on each side. That's the narrowing of the focus, and then behind it for 510, obviously, TC-520 for—with the CD70 in preclinical. I think you've got a very nicely focused pipeline, two clinical targets, two preclinical targets, within the clinical targets focus down on indications.

Nonetheless, we as a Company will look to make rational data-driven decisions as we go forward about how to develop this combined focused portfolio. You can anticipate that, not just immediately but over the course of the entire financing window as well. We are going to focus the resources of the Company on those areas where we feel, as a combined Company, we have the most opportunity to create real value on products for patients. That's that.

Garry, do you want to talk a little bit about specifically gavo-cel focus and signals there?

Garry Menzel, Ph.D.:

It's a good question, Jonathan. Good to hear your voice.

Basically with gavo-cel, what we have been advised is that, if we can maintain the objective response rate that we showed in Phase I, which, if you recall, was around 30%, and demonstrate durability, that is a positive outcome.

What's durability? It's basically being able to get responses that last six months or more, and then feeds ultimately into overall survival, since that's what the patient cares about more than anything else. We're obviously employing checkpoint inhibitors, in order to help with that, from the Phase 1, and re-dosing strategies as well as moving to earlier lines of therapy. There'll be some translational data presented in the middle of the year. We haven't decided exactly at which conference, but we'll present that in the middle of the year. The goal, as I said, is to be able to showcase that the checkpoint inhibitors are indeed helping us with durability. But that's the readout that we're looking for at the end of the year.

Adrian Rawcliffe:

Thanks, Garry.

Then, on to your last question or request for increased granularity on the cash flow. The short answer is, we can't give increased granularity at this point in time, as I referred to previously. However, maybe I could say a couple of things that might be useful as you think about the modeling.

I think the first is that both companies have executed a fairly significant downsizing, so the 2023 spend looks nothing like the 2022 spend for both companies. That's the first point.

Second point: the profile of financing for Adaptimmune specifically, as we've talked about before, is historically, and we anticipate being in the future, quite lumpy. Specifically, we tend to spend the majority of the net cash burn in the first part of the year, and our burn is then offset by both tax credits and payments from partners that we typically receive in the second half of the year. The combination of that makes the cash flow through the year quite spiky.

When we put all of this together and make reasonable assumptions about the levels of efficiency going forward, we believe that we are financed into 2026 with this combined portfolio delivering the catalysts that we have outlined previously.

Jonathan Chang:

Got it. Thank you.

Operator:

Our next question comes from Asthika Goonewardene of Truist Securities. Please go ahead.

Asthika Goonewardene:

Hey guys. Thanks for taking my question. All right. I get it. I know what's going on here. Just a secret—this merger's a secret plot for (inaudible 39:45) to take over cell therapy, isn't it?

Garry Menzel, Ph.D.:

Absolutely.

Asthika Goonewardene:

Okay. On a serious note, Ad and Garry, okay. A question I'd like for both of you to answer independently is: from a scientific standpoint, what technologies are being brought together from both your companies that you're most interested in putting into a single cell?

Then, a question on using the manufacturing capacity, when do you get to use the—sorry, when the TCR², once absorbed, gets to use Adaptimmune's manufacturing capacity, and related to that, does the merger in closing in the second quarter allow you to build more capacity to treat lung cancer patients with gavo-cel, rather, approach it on opportunistically, how you outlined earlier à la—you'll treat a lung cancer patient if there's no ovarian cancer slots being used? Thanks.

Adrian Rawcliffe:

Okay. Why don't I take a stab at what I'm most excited about from a tech platform perspective? Garry, I think you could do the same. I'm actually going to focus on three things that I think are really, really interesting from a technical perspective. I'm going to go with the first.

First is, the combination of the fundamental platforms is actually really interesting. We will then have access to the entire target universe. I will point out that TCR² are, I believe, the only company who have a robust efficacy signal with a mesothelin-targeted cell therapy. I think that is indicative of the potential of the TRuC platform for cell surface antigens. Between the two of us, we then cover the entire target universe. Point one.

Secondly, I think the combination of the next-generation approaches has a lot of leverage associated with it. I'm particularly interested personally, given that it's in clinical development, in the PD-1 CD28 switch that operates differently to most—our existing next-generation approaches, and I think that would be really interesting to see the applicability of this.

Then lastly, I think the opportunity to—and this is obviously over the longer term; to take the broader pipeline and put it onto Adaptimmune's allogeneic platform as that matures, I think, is also a really key long-term benefit of this combination.

Garry?

Garry Menzel, Ph.D.:

Asthika, since Ad has basically managed to grab all of the innovations and tell you about them, I'm going to tell you ...

Adrian Rawcliffe:

Still got membrane-bound IL15, Garry.

Garry Menzel, Ph.D.:

That is very true. I guess I could throw that in there. But I'll tell you what I'm in some respects most excited about, it's perhaps a softer issue but a really important one, that almost gets to your first comment about is this the beginning of consolidation within the cell therapy space on the solid tumor side. That is that what I've observed is the leadership teams on the scientific side in these conversations have been excited about each other's technologies and begun riffing over what they might do together in the future, new ideas that will emerge from the combination of the two companies into one combined entity, I really do feel that there's going to be a lot of innovation that comes out of that, and this is a space where we do need continued innovation.

Beyond the items that were mentioned by Ad, which I fully endorse, I'm really excited about what the teams will create together going forward.

Adrian Rawcliffe:

Then your next question was on sort of manufacturing capability and manufacturing capacity and things like that, and access to that for the—and I think there's an interesting balance that will need to play out over time. One of the things that I am really excited about is, both of our companies are very pragmatic when it comes to developing cell therapies. I think developing cell therapies teaches you humility, and it teaches you pragmatism. We are going to need to make pragmatic choices about the development of these, on the basis of the existing platforms that we've got. Largely, TCR² is on a Miltenyi Prodigy platform, and largely we are on other platforms that we've developed internally, two different ones for afami-cel and CD8.

Having said that, over time, there is obviously the opportunity to either bring the Miltenyi Prodigy platform into our capacity, our capabilities, and/or, as the pipelines evolve, move to common manufacturing processes over time. That's an obvious synergy.

I just want to point out something that's really interesting about these companies. As you think about putting the two together, I would encourage you to think about the fit of these companies, because we are both solid tumor, both engineered TCR-cell therapies, we both use a number of the same platforms and approaches. Just pick one, a lentiviral vector transduction to insert the genetic material into the cells.

There. We're both on common platforms. We have, for some of this. Then we have other areas where we can, over time, combine and bring synergies. There's a great deal of intellectual synergy associated with the act of developing engineered T-cell therapies for solid tumors.

But at the same time, the engineering allows us to do different things, because TCR² is focused on extracellular proteins, and we've been focused almost entirely on intracellular proteins and the expression on a peptide MHC complex, and targeting that.

It's this very unique combination, where there's a lot of intellectual platform capability advantages, but at the same time it expands the universe of the things that we're able to address, and build a company that really has left in the solid tumor space.

Asthika Goonewardene:

Great, thanks for taking my question, guys.

Garry Menzel, Ph.D.:

Thanks, Asthika.

Operator:

Our next question comes from Kelly Shi of Jefferies. Please go ahead.

Kelly Shi, Ph.D.:

Thank you for taking my questions, and apologize if this has been asked. I'm curious to how do you allow (phonetic 47:17) manufacturing for the combined business unit to supply future clinical and commercial demand? Should we expect a cost savings on this front, with a synergy cost to companies? Thank you.

Adrian Rawcliffe:

Garry, do you want to have a go at that in addition to what I've just said?

Garry Menzel, Ph.D.:

I think from our side, Kelly, what excites me are many of the things that excite me about this deal. Manufacturing is one of them. We have adopted a policy, up to this point, of relying on external agencies in order to do our manufacturing. That's worked very well for us up to this point. Now we don't need to build internal capabilities, because those exist already at Adaptimmune. We'll be able to rely on that, it's great, that gives you greater control over your patient delivery supply chain, and I'm happy about that. For me, this is one of the major advantages of the combination.

Kelly Shi, Ph.D.:

Thank you.

Operator:

Our next question comes from Soumit Roy of Jones Research. Please go ahead.

Soumit Roy, Ph.D.:

Good morning, everyone, and congrats on all the progress.

One question on the MAGE-A4 on the ovarian side, and the gavo-cel R. Trying to understand if this is going to be competing products, or they are mutually going to be exclusively developed, or address the patient population, or is there any overlap in the expression of MAGE-A4 and mesothelin, or they are exclusively expressed in different patient populations, in ovarian or head and neck or any of the other indications?

Adrian Rawcliffe:

I think we have most insight into probably the ovarian space. Maybe I can just think about that and guide as to how to think about that.

We're actually really excited about the opportunity for developing these in parallel. I think it is in parallel because, although I'm sure there are some patients who express both MAGE-A4 and mesothelin, we don't think that they're unlikely to be completely separate populations. Nor is the overlap likely to be enormous, given that both of these are expressed in a subset of the ovarian population.

We think that there's a real opportunity to do a couple of things. One, and probably in sequence first, is to look at how we screen patients onto the trials. It's obvious that, if you could reduce the screen failure rate, increase the screen success rate by having both of the trials ongoing at a particular site, that would be a fantastic opportunity to capture a larger portion of the ovarian cancer patients.

Then the second sort of piece of that is obviously then in commercial you can offer a cell therapy to a broader commercial population as well.

Then the other piece is, I think, longer term, scientifically, it will enable us to explore, well what happens in those patients who have both—do have overlapping expression? Is there the opportunity to either give the products in sequence or together, to enable for that patient population an even deeper response? I will add to that that PRAME also has significant, if not in the majority of patients, but significant expression in the ovarian cancer population. Actually, long term, you can think about MAGE-A4, gavo-cel and PRAME, all expressed in a minority of ovarian cancer patients, but together, the opportunity to offer a cell therapy treatment to a larger population of ovarian cancer patients, and to look at the patients with multiple antigens and think about where there's the opportunity, through multi-antigen strategies, to be able to get to better outcomes for patients with multi-antigen strategies. Long term, of course, you think about all of that on the allo platform as well, and the opportunity there.

I just think there's a real opportunity, over the long term, to think about how to optimize this. In the short term, however, I think what we've got is MAGE-A4 CD8 in a Phase 2 trial that we hope to become registrational or SURPASS-3, that could become a product for us there, and gavo-cel in a trial in combination with checkpoint inhibitors with a readout this year, and that's very pragmatically where we need to be focused in the short term.

Soumit Roy, Ph.D.:

Got it.

On the commercialization side, we see Cintia Piccina is leaving, so is there a reshuffling going on on the commercial team? How are you going to combine the R&D team from these two different companies? Because they seem to be specialized in their own ways with their own products. Is that expense going to be completely additive with probably 25% reduction on the TCR² side? Also the clinical team: it seems like everything is adding up rather than having a synergy there?

Adrian Rawcliffe:

I think we're just starting integration planning, so it's not appropriate for us to talk specifically about particular areas. However, I think for Cintia leaving as Chief Commercial Officer, Cintia's built a great team, that decision was associated with the reductions that we announced as an organization last year. But Cintia's built a great team that will enable us to continue with the commercial planning and strategy for afami-cel in due course. In addition, Cintia will continue as a consultant for us, in particular on commercial strategy associated with that program. That relates to the previous discussions that we've had and the decisions we made last year.

With respect to synergies, we're just starting integration planning, and we'll have more to say on that in due course. Clearly, the balance of this is that there are unique skill sets on both sides that we will need to preserve and leverage in order to be able to realize our ambitions for this pipeline. At the same time, it's obvious that there are things like establishment costs, et cetera, that are duplicated between the two companies.

Soumit Roy, Ph.D.:

Thank you for taking all the questions, and good luck in 2023. It's going to be a busy year for you guys.

Adrian Rawcliffe:

It certainly is. Thanks ever so much.

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Operator:

Our next question comes from Yanan Zhu of Wells Fargo Securities. Please go ahead.

Yanan Zhu, Ph.D.:

Hi. Thanks for taking the question. I just have a quick one on timeline to durability of response data for the respective ovarian cancer product candidates from both companies. Maybe for MAGE-A4, if you could also comment on the IO combo, when might we see durability of response? When might we have a sense of the potential extension of durability of response? Thank you.

Adrian Rawcliffe:

Okay, I think that's right, so specifically on the MAGE-A4, because I think we've answered that on the gavo-cel side, because that's in progress at the moment. With respect to MAGE-A4, actually, the reason that we designed the SURPASS-3 trial in the way that we did, with an independent monotherapy and combination arm, is because we want to assess the potential for the CD8 program as monotherapy to actually be a registrational program. That's why we did that. It's pretty obvious we think, from that, that there's a reasonable chance that the durability is sufficient to enable end registration there; otherwise we wouldn't have designed the trial in that way. However, the add-on with PD-1 is to drive depth and durability, and potentially number of responders in that setting, and it's just worth pointing out that, in ovarian cancer, checkpoint inhibitors typically do not have a significant efficacy signal, and so it's a real opportunity for synergy associated with the cells.

In terms of timeline, from that trial, SURPASS-3, because that is a registration-oriented trial, we do not anticipate releasing data from that until we have fully enrolled that trial and that cohort. That won't happen until sort of tail end of 2024, when we've fully enrolled that registration-oriented trial. So I think the data from ovarian cancer, in combination, will be related to a small number of patients that we have been able to recruit, or will be able to recruit, in the Phase 1 study, so, slightly different patient population, in combination with nivolumab. That we would anticipate being probably tail end of this year or into early next year before we have durability data in that relatively modest number of patients.

Garry Menzel, Ph.D.:

Then I think just to reaffirm on gavo-cel again, in ovarian cancer, you'll see clinical durability data at the end of the year, that's what our intent is to present. In the middle of the year, you'll see some translational data, which hopefully will provide a pathway to that clinical data at the back end of the year.

Yanan Zhu, Ph.D.:

Great, thanks a lot. Also I have another, kind of a related question. I think Adaptimmune obviously is advancing the head and neck and urothelial cancer studies in earlier line setting. I was wondering if, on the mesothelin side for the combined company, would exploring earlier line also potentially be a potential strategy for that side of the combined company? Thanks.

Adrian Rawcliffe:

I'll talk maybe in principle, and then maybe Garry, you could touch on, and thinking on from your side, on mesothelin in earlier lines of therapy.

In principle, we think that there are substantial advantages to moving into earlier line for cell therapies. In addition to the normal oncology development advantages that you get, which is healthier patients, fewer levels of pre-treatment and a less advanced tumor, there's a really critical piece in cell therapy that everything that we know says that the earlier you can get cells from a patient, the more pristine those cells are, the less damaged by repeated assaults from chemotherapy or other therapeutic regimens: the earlier you can go, the better those cells are likely to perform. The ultimate starting point is that when we do work in cancer patients or healthy donors, the healthy donor cells typically grow better and produce fitter engineered T-cells.

Everything suggests that getting in earlier will be better for cell therapies. That's why we believe that there's this opportunity in head and neck and bladder cancer to go in in these earlier settings and potentially transform those spaces with the response rates that we're seeing in very late-stage patients, replicated, potentially improved in the early line settings.

Garry?

Garry Menzel, Ph.D.:

I would just endorse that. In our own data set, we just don't have enough patients to be able to parse out lines of therapy versus dose escalations or use of checkpoint inhibitors or re-dosing or other strategies, but the principle that's been shown, I think, in many other studies in oncology is that the earlier lines of therapy give you a better shot at treating patients. If you think of gavo-cel in Phase 1, we were treating a lot of patients who were either in or going to hospice, who had other comorbidities, just incredibly sick, five–six–seven–eight lines of therapy before them, and it just makes it very difficult. Having healthier patients who can tolerate therapies more, and whose cells are likely to be more robust, logically you would hope that that would lead to better clinical benefit. We just don't have the data to prove that out yet from our own studies.

Yanan Zhu, Ph.D.:

Got it. Very helpful. Thank you.

Adrian Rawcliffe:

Thanks.

Operator:

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

Peter Lawson:

Great. Thanks for taking the questions. Just going back to the cash guidance, just curious if that includes commercial products from both Adaptimmune and TCR?#

Adrian Rawcliffe:

The only product that would be launching within that timeframe would be afami-cel for the treatment of synovial sarcoma. It doesn't include revenue from those products, no. From that product, no is the simple answer to that. That would be additive to that. We've said that we will comment more on our commercial plans as we get through registration. It's inherently a conservative approach to what we might do with afami-cel.

Peter Lawson:

Perfect, thank you; and then a question for Garry, whether this was a competitive process, how long did this take, and is there any breakup fees for this?

Garry Menzel, Ph.D.:

Last question first, yes, there are breakup fees, fairly standard breakup fees. I would say, first of all, that there will be an S-4 coming out that will provide full details of the dialogue. What I can tell you now, because you'll have to wait til then for that, is, Ad and I have known each other for a couple of decades, so even before we were both specialized in cell therapy we had an ongoing dialogue, and of course we've both been in cell therapy for a number of years now. Not surprisingly, being at the forefront of our fields, we've had ongoing dialogue just in terms of our thoughts in the field. But in terms of this particular process, the fall of last year was when we began to have discussions in earnest, and you'll see more of that. In other words, this was a thoughtful process, and we're always talking to a lot of people in the field, so, that's all I think we can say at this point.

Peter Lawson:

Got you. Can you disclose the breakup fees, or do we have to wait for the filings?



Garry Menzel, Ph.D.:

You'll have to wait for the filings.

Peter Lawson:

Okay; and then just going back to the cash runway guidance. Does that include potentially further rationalization of the combined pipelines? Is that something you foresee doing? Is that something we have to wait until 2Q? Or is it a data-driven thing? Or should we just look at that pipeline as the go forwards?

Adrian Rawcliffe:

I think all of the above. Yes, it's a data-driven thing. The pipeline that we've put out there is the pro forma combined pipeline of the companies, and we will make data-driven and based on the catalysts that we've outlined to you, those will be the data points when we'll be able to make decisions about development pathways for those assets.

Peter Lawson:

Perfect. Thank you.

Adrian Rawcliffe:

Did that answer the question?

Peter Lawson:

Yes, no, I think about the (inaudible 65:11)

Adrian Rawcliffe:

Thank you very much.

Operator:

This concludes the question-and-answer session. I will now turn the call back over to Adrian Rawcliffe for any closing remarks.

Adrian Rawcliffe:

I'd just like to close by referring you back to the five rationales for why this is a compelling transaction at this point in time: the solid tumor focus, the catalysts achievable within the extended runway, the deep innovative pipeline, and the end-to-end capabilities that both Companies have shown that I think, between them in the combination, will make this a compelling cell therapy company for the future.

Thank you very much, and look forward to catch-up conversations with many of you in due course.

Operator:

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

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Forward-looking Statements

This communication relates to the proposed transaction pursuant to the terms of the Agreement and Plan of Merger (the “Merger Agreement”), dated March 5, 2023, by and among Adaptimmune Therapeutics plc (“Adaptimmune”), CM Merger Sub, Inc. (“Merger Sub”), and TCR² Therapeutics Inc. (“TCR²”). This communication includes express or implied forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), about the proposed transaction between TCR² and Adaptimmune and the operations of the combined company that involve risks and uncertainties relating to future events and the future performance of Adaptimmune and TCR². Actual events or results may differ materially from these forward-looking statements. Words such as “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “future,” “opportunity” “will likely result,” “target,” variations of such words, and similar expressions or negatives of these words are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. Examples of such forward-looking statements include, but are not limited to, express or implied statements regarding: the business combination and related matters, including, but not limited to, satisfaction of closing conditions to the proposed transaction, prospective performance and opportunities with respect to Adaptimmune or TCR², post-closing operations and the outlook for the companies’ businesses; Adaptimmune’s, TCR²’s or the combined company’s targets, plans, objectives or goals for future operations, including those related to Adaptimmune’s and TCR²’s product candidates, research and development, product candidate introductions and product candidate approvals as well as cooperation in relation thereto; projections of or targets for revenues, costs, income (or loss), earnings per share, capital expenditures, dividends, capital structure, net financials and other financial measures; future economic performance, future actions and outcome of contingencies such as legal proceedings; and the assumptions underlying or relating to such statements.

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A more complete description of these and other material risks can be found in Adaptimmune's and TCR²'s respective filings with the U.S. Securities and Exchange Commission (the "SEC"), including Adaptimmune's Annual Report on Form 10-K for the year ended December 31, 2022 and TCR²'s Annual Report on Form 10-K for the year ended December 31, 2021, subsequent Quarterly Reports on Form 10-Q and other documents that may be filed from time to time with the SEC, as well as, the Registration Statement on Form S-4 which includes the joint proxy statement of Adaptimmune and TCR² that also constitutes the prospectus of Adaptimmune, which joint proxy statement/prospectus will be mailed or otherwise disseminated to Adaptimmune's shareholders and TCR²'s stockholders when it becomes available. Adaptimmune and TCR² also plan to file other relevant documents with the SEC regarding the proposed transaction.



Any forward-looking statements speak only as of the date of this communication and are made based on the current beliefs and judgments of Adaptimmune's and TCR²'s management, and the reader is cautioned not to rely on any forward-looking statements made by Adaptimmune or TCR². Unless required by law, neither Adaptimmune nor TCR² is under no duty and undertakes no obligation to update or revise any forward-looking statement after the distribution of this document, including without limitation any financial projection or guidance, whether as a result of new information, future events or otherwise.

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Additional Information and Where to Find It

In connection with the proposed transaction, Adaptimmune and TCR² expect to file with the SEC a Registration Statement on Form S-4. The Registration Statement on Form S-4 will include a document that serves as a prospectus of Adaptimmune and a joint proxy statement of Adaptimmune and TCR², and each party may also file other documents regarding the proposed transaction with the SEC. INVESTORS AND SECURITY HOLDERS ARE URGED TO READ CAREFULLY THE REGISTRATION STATEMENT ON FORM S-4, JOINT PROXY STATEMENT/PROSPECTUS AND OTHER RELEVANT DOCUMENTS FILED OR WILL BE FILED WITH THE SEC, AS WELL AS ANY AMENDMENTS OR SUPPLEMENTS THERETO AND ANY DOCUMENTS INCORPORATED BY REFERENCE THEREIN, IN THEIR ENTIRETY IF AND WHEN THEY BECOME AVAILABLE BECAUSE THEY CONTAIN OR WILL CONTAIN IMPORTANT INFORMATION ABOUT THE PROPOSED TRANSACTION, RELATED MATTERS AND THE PARTIES TO THE PROPOSED TRANSACTION.

You may obtain a free copy of the Registration Statement on Form S-4, joint proxy statement/prospectus and other relevant documents (if and when they become available) that are or will be filed with the SEC for free at the SEC's website at www.sec.gov. Copies of the documents filed with the SEC by TCR² will be available free of charge on TCR²'s website at <https://investors.tcr2.com/> or by contacting TCR²'s Investor Relations Department at <https://investors.tcr2.com/contact-ir>. Copies of the documents filed with the SEC by Adaptimmune will be available free of charge on Adaptimmune's website at <https://www.adaptimmune.com/investors-and-media/sec-filings> or by contacting Adaptimmune's Investor Relations Department at IR@adaptimmune.com.

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Participants in the Solicitation

Adaptimmune, TCR² and certain of their respective directors and executive officers and other members of management and employees may be deemed to be participants in the solicitation of proxies in respect of the proposed transaction. Information about the directors and executive officers of Adaptimmune, including a description of their direct or indirect interests, by security holdings or otherwise, is set forth in Adaptimmune's proxy statement for its 2022 Annual General Meeting, which was filed with the SEC on April 21, 2022, the Annual Report on Form 10-K for the year ended December 31, 2022 filed with the SEC on March 6, 2023, subsequent Quarterly Reports on Form 10-Q and other documents that may be filed from time to time with the SEC. Information about the directors and executive officers of TCR², including a description of their direct or indirect interests, by security holdings or otherwise, is set forth in TCR²'s proxy statement for its 2022 Annual Meeting of Stockholders, which was filed with the SEC on September 1, 2022, the Annual Report on Form 10-K for the year ended December 31, 2021 filed with the SEC on March 22, 2022, subsequent Quarterly Reports on Form 10-Q and other documents that may be filed from time to time with the SEC. Other information regarding the participants in the proxy solicitations and a description of their direct and indirect interests, by security holdings or otherwise, will be contained in the joint proxy statement/prospectus included in the Registration Statement on Form S-4 and other relevant materials to be filed with the SEC regarding the proposed transaction when such materials become available. Security holders, potential investors and other readers should read the joint proxy statement/prospectus, included in the Registration Statement on Form S-4 carefully when it becomes available before making any voting or investment decision. You may obtain free copies of these documents from Adaptimmune or TCR² using the sources indicated above.

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