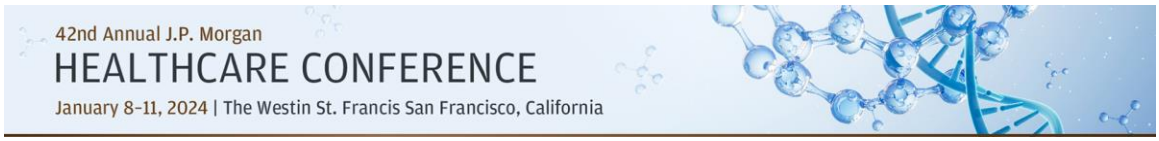

Adaptimmune

Adaptimmune presentation delivered at the 42nd Annual J.P. Morgan Healthcare Conference on Thursday, January 11, 2024 at 8:15 AM

Jem de los Santos: Thank you for coming. My name is Jem de los Santos. I work in the Investment Banking Practice at JPM based in London. Very pleased today to present Adrian Rawcliffe of Adaptimmune.

[applause]

Adrian Rawcliffe: Thanks, Jem. Thank you, everybody, for joining us. I'm Ad Rawcliffe. I'm the CEO of Adaptimmune. I'm absolutely delighted to be here at the beginning of 2024, because 2024 will be the year where Adaptimmune transforms from merely the pioneering force in bringing cell therapies to solid tumors into an integrated, commercial cell therapy company.

Through the approval and launch of afami-cel, the first engineered T-cell therapy for the treatments of solid tumors, and the start of a sarcoma franchise that we believe will be highly valuable and a beachhead for getting cell therapies into the solid tumor space and becoming mainstream in that space.

This is the disclaimer which will cover the forward-looking statements I plan on making during this presentation. I'm going to spend the majority of the time today on that sarcoma franchise. That sarcoma franchise consists of two products -- afami-cel coming to market in 2024, this year, and lete-cel - in two years' time.

Between them, we believe they are a highly valuable opportunity with peak year sales of up to 400 million for Adaptimmune. But that is just the start, a beachhead of the opportunity of cell therapies in solid tumors, an opportunity that will be realized from our wholly owned pipeline, which I will show you has multiple large commercial opportunities and where we have really encouraging clinical data.

All of that is built off the fact that Adaptimmune has been designed from the ground up as a cell therapy company and with the capabilities necessary to discover, develop, and deliver cell therapies.

That last piece is probably the most important and the investments that we made over the last decade in our integrated in-house cell manufacturing are what enable us to have confidence that we can deliver. This franchise and these products, not only with an attractive sales profile, but also with an attractive P&L.

Drilling down into that sarcoma franchise, as I said, it consists of two products - afami-cel and lete-cel. These are both engineered T-cell therapies for the treatment of soft tissue sarcomas, particular soft tissue sarcomas. They are both given as a single dose of cells from which they derive all of their benefit.

Afami-cel targets a protein called MAGE-A4, a cancer antigen called MAGE-A4, and it's been developed for the treatment of synovial sarcoma. Lete-cel targets a protein called NY-ESO, and it's being developed for the treatment of synovial sarcoma and another soft tissue sarcoma, myxoid round cell liposarcoma.

Synovial sarcoma and myxoid round cell liposarcoma between them make up 10 to 20% of the soft tissue sarcomas in the United States and there are 13,000 cases of soft tissue sarcoma in the United States each year.

Both synovial sarcoma and myxoid round cell liposarcoma are both young people's diseases. Average age of diagnosis of synovial sarcoma is 32. Prognosis is incredibly poor. Once you've failed first-line therapy, which is almost inevitable, there are no existing therapies that are effective in the second-line setting. There have been no new therapies in the space for over a decade.

When I show you the clinical data from afami-cel, I think you'll see that this one-time therapy has the opportunity to transform the patient experience and the treatment paradigm in synovial sarcoma, and has the opportunity to lead to significant sales opportunity. There are estimated over 1,000 addressable patients with our therapies.

To put that in context, that's about twice the size of the addressable US patient population of immunocore's KIMMTRAK for uveal melanoma. As a consequence of that, we estimate peak year sales of $400 million in the United States for the indications that we anticipate for afami-cel and lete-cel on approval.

Where is afami-cel? Well, we filed the submission of our BLA in December last year, and we anticipate acceptance or filing of that BLA by the FDA in February this year. Afami-cel has RMAT

designation. That means we're eligible for priority review, so we anticipate a six-month review cycle, which would lead to approval somewhere in Q3 in August.

We anticipate that we will be ready to launch afami-cel in the United States on approval. Afami-cel has the opportunity to redefine the synovial sarcoma space. This means redefining the experience of patients like the one shown here.

This patient has successfully completed first-line therapy and is in remission with synovial sarcoma. She subsequently had her first child. Her biggest fear is that the cancer returns. Well, that's the biggest fear of almost everybody who's had cancer. This fear that's enhanced by the fact that there are no effective second-line options for her, and she knows that.

Our ability with a differentiated clinical profile, with a one-time treatment, to redefine that patient experience is the basis upon which afami-cel will be successful.

It's an addressable patient population as well. The reason it's addressable is because there's only 100 sarcoma centres of excellence in the United States. Almost all of the metastatic cases are treated in those sarcoma centres of excellence.

These are physicians and centers that have a lot of experience with cell therapy. Many of them were involved in our clinical trials, particularly towards the top of that list of Sarcoma Centers of Excellence, and it's those physicians and those patients that we'll be targeting as we seek to launch afami-cel.

We'll be doing it on the basis of the clinical data from our SPEARHEAD-1 pivotal trial. This data is now well established and was the basis of the BLA. It has demonstrated a 40% response rate, and these responses are deep and they're durable. Median duration of response is 12 months, and that's translating to a median overall survival in this patient group approaching 18 months.

For context, therapies that are used in the second-line setting typically have a response rate in the single digits or the low teens. Responses are not durable, lasting a few months. Median overall survival in the second and third-line patient setting is well less than 12 months.

This therapy has the opportunity to completely redefine the patient experience, and we have the opportunity to commercialize this, and we've made a lot of progress already.

Early engagement of payers and patient groups, early engagement of the sites through our

clinical trials, and subsequently this has enabled us to be in a good position to build and to convert our operations from clinical operations to commercial operations. Whilst there are a lot of things that we're doing to make the patient experience as seamless and routine as possible.

The biggest challenge in this space is the supply chain and how to deliver autologous cell therapies to patients. I'll talk a little bit more about that on the next slide.

We anticipate a scaled and scalable launch. We will launch in treatment centers that have experience of afami-cel from the clinical trials and expand it to approximately 30 centers, the very top tier of the Sarcoma Centers of Excellence, over the first two years of launch.

That's what this footprint looks like. We are building the field force in Q1, both on the commercial side and the medical side, to enable us to do that, having already put in place commercial leadership in the last year.

I spoke about how the key thing to success in the autologous cell therapy business is the supply chain. This little schematic shows our supply chain, delivery time of four to six weeks, and it's on the basis of the investment that we've made over the last decade in our integrated cell therapy manufacturing in-house.

Why is this important? Well, if you've been paying attention to the CAR-T therapy launch, you'll know that the clinical data is absolutely stunning, as is the clinical data for afami-cel. All of the challenges with CAR-Ts have been in actually supplying patients. The critical success factor for autologous cell therapy is in the consistent, efficient, and effective delivery of cells to patients.

There's two principal reasons why this is so critical. First off, the effective delivery, which means delivery on time, reliably, defines the patient experience. Different to all other modalities of therapy. If you do not deliver consistently for physicians and for patients, they will not use your product.

The efficiency with which you do that defines whether you can make a profit on any of these products ever. Our investment in in-house cell therapy enables us to have confidence that we will achieve a 70% margin on our sarcoma franchise at peak year sales. That is a critical differentiation point for us as a cell therapy biotech.

Let's talk about lete-cel. Lete-cel is coming two years behind afami-cel’s launch - approval, and launch in 2026, but it has already met its primary endpoint from its pivotal trial conducted by our

partner GSK.

That pivotal trial was conducted in synovial sarcoma and myxoid round cell liposarcoma with equal numbers of patients, and at the interim analysis conducted last year, has already met its primary endpoint.

That analysis showed a 40% response rate and 11 months duration of response. These data look very similar to afami-cel. However, they look very similar to afami-cel, but they are in both synovial sarcoma and myxoid round-cell liposarcoma.

Therefore, they expand the addressable patient population by more than twofold to over 1,000 patients. But they don't require significant new commercial infrastructure. They will go through almost identical channels to those that we build for afami-cel.

These are the same treatment centres, these are the same prescribing physicians, this will be the same field force and the same supply chain at the front end at least. As such, there is both significant synergies associated with this from a financial perspective and an operational perspective.

There is also the opportunity to accelerate the uptake and adoption of lete-cel because we will already have invested in the infrastructure with afami-cel.

I previously talked about $400 million of peak year sales opportunities. I want to be very clear. That is in the indications that we anticipate on approval only, and it is in the United States only. There are obviously significant opportunities for expansion from there. There is the opportunity to move into earlier lines of therapy or to enable use in combination or in sequence of these therapies.

There is the opportunity for additional HLA types to expand the patient population with these targets. There is the opportunity for additional targets that are expressed in these cancers. Everything that I've talked about is United States only. There's obviously the opportunity to expand geographically, either ourselves or through partnerships.

This is how we see our sarcoma franchise building over the next few years. We have two products. First launches this year, the next launches in two years' time. We anticipate peak year sales of $400 million, addressable at a 70% margin. We anticipate being able to do this with a focused commercial footprint that we are already embarking on.

That's only the beginning of the cell therapy ambitions for the field and for Adaptimmune, the prime mover in the field. Cell therapy is not actually completely new in the cancer space. There are six existing CAR-Ts on the market in the hematological or liquid tumor space, blood tumors. These products between them sell almost $4 billion a year despite only targeting 10% of cancer cases worldwide.

The remaining 90% is where we're playing. The remaining 90% is where our technology gives us a competitive advantage. There are no existing engineered cell therapies on the market in the solid tumor space until Adaptimmune is the first company to launch with afami-cel later this year. Afami-cel and lete-cel are the front end of our pipeline. This pipeline is wholly owned.

I've talked about the first two lines on it, so I'm going to move straight to talking about CD8, that program in the middle there. CD8 is an engineered T cell, like afami-cel, but it is a next-generation version of afami-cel targeting MAGE-A4.

We are developing CD8 in ovarian cancer, in bladder cancer, and in head and neck cancer. I'll talk a little bit about the data for that on the next slide.

Behind CD8, we have two very large preclinical opportunities. Firstly, targeting PRAME, which is expressed in multiple tumor types, including breast and lung cancer, and they'll be first into the clinic.

Then secondly, targeting CD70. CD70 is a cell surface antigen, and it's particularly excitingly expressed on renal cell carcinoma at high levels, so kidney cancer, and on AML, hematological malignancy. All of those preclinical opportunities are significant commercially.

Moving back to CD8 for a second. We have been conducting a phase one trial with incredibly encouraging results. We've identified three tumor types where we have very high response rates. On the basis of those, we are moving forward in those three tumor types as follows.

In ovarian cancer, we have initiated SURPASS-3, which is a phase II potentially registrational trial in platinum-resistant ovarian cancer. We did that on the basis of a 40% response rate in the patients dosed in our phase I trial.

In head and neck cancer, we're taking a slightly different tactic. The response rates there are even higher than we've seen in ovarian cancer, but we have fewer patients. We are continuing

the development of that in our phase I, those two indications in our phase I trial, with the intent of moving out of very, very late-stage patients and adding early-aligned patients in combination with standard of care.

We'll be able to make a decision on the development pathways towards registration with those two indications, based on that data, towards the end of this year.

That pipeline has the opportunity to significantly increase the addressable patient population for cell therapies in the solid tumor space. The late-stage pipeline, which we count as the sarcoma franchise that I talked about, plus ovarian cancer in that registration-oriented trial SURPASS-3, has an addressable patient population of up to 6,000 patients, in the EU and the US.

Just to point out, the $400 million of sales that I referred to from the sarcoma franchise is from the little light blue bar on the left-hand side of that slide at the top of that range. That's the US patient population.

Then we go beyond that with the head and neck and bladder cancer indications from CD8 and with PRAME and with CD70. It's clear that this pipeline has the opportunity to address over 100,000 patients who are currently dying from their tumors.

We are well capitalized to execute on these ambitions. We have over $300 million of anticipated capital over the next two years, both cash on our balance sheet, liquidity on our balance sheet, and payments anticipated from partners as a result of historic business development deals.

We have a good track record of business development and active discussions ongoing at the moment. We feel we are well placed to be able to execute on our ambition to launch afami-cel and invest in our sarcoma franchise.

In summary: A sarcoma franchise that is highly valuable with peak year sales of $400 million, driven off two products in soft tissue sarcomas, launching in 2024 and 2026. Acting as a beachhead for an addressable patient population of over 100,000 people from our wholly owned cell therapy pipeline for solid tumors.

All based on the fact that we have, from the start, built Adaptimmune to be able to deliver, in the real world, cell therapies for patients at an attractive profit margin.

It would be obvious from that that we at Adaptimmune are pretty passionate about the opportunity

for cell therapies to change the lives of people with solid tumors. This year, we have a particular focus. We are going to launch the first engineered T-cell therapy, afami-cel, for the treatment of synovial sarcoma and initiate our sarcoma franchise.

This is the starting point of making cell therapies a reality for people with solid tumors and gives us the opportunity not only to create near-term commercial value but set ourselves up for long-term success as well. With that, I'll take questions.

[applause]

Jem: Thank you, Ad. We're now moving over to the Q&A portion of the presentation. Please note that if there are any questions in the room, there's a microphone available in the back, so please raise your hand and they'll deliver the microphone to you and you can ask your question. With that said, are there any questions in the room from anyone? In that case, I may ask if you Ad, if that's OK?

Adrian: Go for it.

Jem: You've recently completed your BLA submission for afami-cel, as you just noted during the presentation. While the data is continuing to mature, it's quite clear that there's a benefit to responders in terms of not only efficacy, but also durability and survival. Is there anything you can reveal at this stage on how this impacts your view on pricing for the product?

Adrian: I think you're correct. I mean, obviously, the trial was a single-arm trial, so one can't make comparative statements. When one looks at the response rate, the durability, and the survival of this cohort of patients, one can't help but be very, very encouraged.

I think the FDA sees that in the data that we've submitted, and we've managed to reach alignment with the FDA that the work that we've been doing in the second cohort of that trial will act as confirmatory evidence and enable full approval in due course. That cohort is fully enrolled and showing similar levels of efficacy. We're very confident in the efficacy profile.

I think we feel that pricing we will obviously be talking about when we launch the product. But we think that pricing commensurate with the outstanding efficacy that we've seen in a very rare patient population, I think, gives us the opportunity to create an attractive franchise for us.

We look at the reference points like the CAR-T pricing reference point, but we don't feel

completely tethered to that pricing point for this particular indication.

Jem: Great. I see one question in the back.

Audience Member: Thank you, Adrian. I wonder if you could double-click a bit on the manufacturing and supply chain topic that you raised before and how much of that strategy is what you'll do in-house versus through partners and just how will you get that advantage coming up in the next year?

Adrian: We have the advantage of having around the table on our board and our executive team includes people who have deep experience of the benefits of manufacturing and manufacturing control out of other modalities like biopharmaceuticals.

Since I joined the company nine years ago, we've been investing in manufacturing as a key differentiator, because it's been obvious to us that this is the critical component of this and we've done that in-house. Usually, we opened our Navy Yard Centre in Philadelphia in 2017, and every single patient that has been manufactured for the pivotal trial, was manufactured out of that Navy Yard facility.

All of the BLA work to file module three of the BLA, which is the CMC section, was done out of that facility. Every commercial patient for afami-cel will be manufactured out of that facility. That continuity and that experience, I think, is a key differentiator, and we will manufacture afami-cel in-house completely, and we have the capacity to be able to do that.

The exception on that is that the lentiviral vector for afami-cel is provided by a third party, and that's unusual because the other lentiviral vectors for our pipeline of products CD8 backwards are made with our own in-house lentiviral vector.

Lete-cel is a little different because we have inherited a manufacturing process from our partner GSK and that process is based on the Milteni Prodigy machine which is a different process to the one that we have and initially, I believe that will be manufactured through a CDMO for the launch because that will be the fastest way to launch, and over time, we'll consider how we think about that in-house versus third party.

Audience Member: As you look to build your pipeline by expanding into different HLA types or a given antigen, what do you expect with respect to the regulatory? approval pathway to expand HLA types in a given antigen target?

Adrian: Yes. Whilst I do think that there are likely to be some efficiencies in that space, the reality is that a TCR targeting a different HLA peptide complex is a different TCR with a different target. We anticipate that it will be viewed as a different product. That's not to say there won't be efficiencies in the development and the regulatory pathways.

One of the principal efficiencies that we see is actually that from a clinical operations perspective, if you could have a trial that had multiple HLA types in, you would dramatically change the dynamics of patient selection from a place with HLA-A02, which is the most prevalent, but it's still only in a little less than half of the patients. Half the patients just are not eligible on HLA.

If you had other HLAs in that space, you would significantly change the dynamics of patient selection from a clinical trial perspective, and obviously, ultimately, from a commercialization perspective as well.

I do think that there will be ongoing discussions about what can be more efficient and what can be common on the regulatory pathway, and particularly on the manufacturing side. At the same time, these are different products.

Now, they will be de-risked substantially because it will be essentially the same protein target, but the expression and presentation on HLA can be different. I think they are best viewed as separate products, albeit lower-risk products.

Jem: Great. Are there any more questions from the audience?

Audience Member: [inaudible] .

Adrian: The question was, what is the manufacturing time to make afami-cel? Vein-to-vein time, or from the time we get the cells to the time we release and return the cells, is four to six weeks for afami-cel.

Jem: Which HLA type of PRAME target that you work with?

Adrian: Which HLA types?

Jem: Yeah.

Adrian: Initially, we're targeting HLA-02, but it will be, it won't be that much of a secret that we have research endeavors into other HLA types as well. A24, for example, A01.

Jem: Any other questions?

Audience Member: I might have a couple more then. Ad, are you able to comment on the release data for lete-cel in MRCLS? I mean, while the full pivotal data set will only be released later this year, as you mentioned, is there anything at this stage that you can comment on maybe in regards to comparability with the data for afami-cel and read across how this might translate to a survival benefit?

Adrian: The afami-cel data for cohort one, which is the registrational cohort that I showed you, really is quite mature at this point. Although we still have a lot of patients on the study, we are starting to see the overall survival picture there.

Just to flag on that, median overall survival is 17 months at the moment. What's interesting is that the survival for the responders is that the survival for the nurses is 17 months at the moment, to afami-cel in that cohort.

The median overall survival has not been reached 70 percent of them are still expected to be alive at two years. There's clearly a significant benefit to those patients who respond from a survival perspective.

With lete-cel, what was interesting about lete-cel is that when we got that data cut, our first gut reaction was, ha, this looks exactly like afami-cel, at the same time point. We have immature duration of response because we only have 11 months and about half the patients are still in active follow-up.

That's immature, but that doesn't compare that unfavorably with the 12 months from afami-cel already. And the response rate across the indications is really consistent. We are optimistic that there is the opportunity for that to convert into the survival that we see in the afami-cel product.

Actually, that won't be available for some time, largely because the ongoing patients, if they remain ongoing, will be censored. It will still be an immature picture, probably when we reach the data point next year. But we are encouraged. From the afami-cel side, it took about another year for the overall survival maturity to play out.

Jem: Great. Then maybe one last one for me. It's regarding the commercialization plan. Just given that you mentioned that there was significant overlap between afami-cel and lete-cel, it's clear that obviously the centers of excellence, and there's some overlap there between synovial sarcoma and MRCLS.

Are there any incremental capabilities, do you think, that will need to be developed to support a lete-cel launch in 2026?

Adrian: Maybe just to double-click first on the nature of the overlap that we see. Afami-cel targets MAGE-A4. MAGE-A4 is expressed in something like two-thirds, 70 percent of synovial sarcoma patients. That will be first onto the market.

There's then a third of synovial sarcoma patients who have the right HLA but don't express MAGE-A4. And NY-ESO and MAGE-A4, from the data that we have, appear to be essentially independent variables. NY-ESO was expressed in something like 80 percent of synovial sarcoma patients.

We believe that of the remaining third of patients who will not be eligible for afami-cel, something like 80 percent of those would be eligible for lete-cel. I think we get to cover the vast majority of the synovial sarcoma population between these two, sequentially.

But of note, afami-cel will not have an indication at launch for MRCLS, whereas lete-cel will. Lete-cel (targeted antigen NY-ESO) is expressed in something north of 80 percent of MRCLS patients. That's a really significant expansion opportunity. But it does go through essentially the same commercial footprint.

There are important differences. I referred earlier to the fact that lete-cel has a different manufacturing route. Whereas bits of the front end of the supply chain may be common, the back end of the manufacturing is different. We will need to establish that in the same way that we have done with the afami-cel manufacturing.

Then the second piece is obviously we will need a diagnostic for NY-ESO. that mirrors the diagnostic that we've developed for MAGE-A4 for afami-cel, and so we're working on that too. We anticipate that that will be a companion diagnostic in the same way that afami-cel has a companion diagnostic.

From an actual commercialization perspective, whilst I think that there are likely to be sites that

see a few more MRCLS patients and sites that see a few more synovial sarcoma patients, the overlap of sites and treating physicians is really quite substantial and significant. That's why we believe that we have a very synergistic franchise opportunity with these two products.

Jem: Great. Maybe just going to ask one more time, are there any questions from the audience? In that case, I think, Ad, thank you so much for the presentation, and thank you, everybody, for your time.

Adrian: Thank you.

[applause]
