Adaptimmune Therapeutics
Third Quarter 2024 Conference Call Transcript

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Presenters:

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Investor Relations

Adrian Rawcliffe
Chief Executive Officer

Gavin Wood
Chief Financial Officer

Dennis Williams, Pharm.D.
Senior Vice President, Late Stage Development

Operator:
Hello, and welcome to the Adaptimmune Therapeutics Third Quarter 2024 Results Conference Call. As a reminder, all participants are in listen-only mode and the conference is being recorded. After the presentation, there will be an opportunity to ask questions. To join the question queue you may press star, then one on your telephone keypad. Should you need assist during the conference call, you may signal an Operator by pressing star, then zero.

I will now turn the call over to Dan Od-Cohen, Investor Relations for Adaptimmune. Dan, please go ahead.

Dan Od-Cohen:
Thank you Operator. Good afternoon everyone and welcome to Adaptimmune's conference call to discuss our third quarter 2024 financial results and business updates. I would ask you to review the full text of our forward-looking statements from this morning's press release. We anticipate making projections during this call, and actual results could differ materially, due to several factors, including those outlined in our latest filings with the SEC.

Adrian Rawcliffe, our Chief Executive Officer, is here with me for the prepared portion of the call, and other members of our leadership team will be available for Q&A.

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

Adrian Rawcliffe:
Thanks Dan, and thank you everyone for joining us today.

So, I'd like to start by addressing the announcement we made in today's press release regarding our new strategic business plan. This plan has three main objectives: one, to streamline operations to focus on our commercial sarcoma franchise; two, to prioritize the R&D programs that have the best return on capital and the best opportunities for transformational medicines for patients; and three, to set the Company on a course to operating breakeven during 2027.

The plan was a result of a thorough review of the entire Company and investments across the organization, and it follows the successes we've had in the initial stages of the Tecelra launch, which is progressing very well against our objectives, and which I'll discuss later.

It also follows the successful primary analysis data from the pivotal IGNYTE-ESO trial with lete-cel that we announced earlier today. The positive results from this pivotal trial, which has met its primary endpoint, demonstrated even better outcomes than the interim results we announced back in June. It will form the basis of the BLA submission for lete-cel starting next year.

Based on these data and our successful approval of Tecelra in August, we have increased confidence that lete-cel has a high probability of approval and will become an important medicine for people with both synovial sarcoma and MRCLS.

Now that we have a very clear path towards a successful sarcoma franchise with potentially two FDA-approved products, we have even greater conviction in our projection of $400 million in combined U.S. peak revenue for Tecelra and lete-cel. As such, we believe that maximizing the value of this sarcoma franchise is the highest priority for the future of the Company, for its shareholders, and for the patients we serve. We also felt that now was the right time to make these tough business decisions to achieve this objective.

So, to that end, we will reduce our cost structure to ensure we achieve operating cash flow breakeven during 2027. We will reduce our headcount by about 33% and, compared to our estimated '24 cost base, we will reduce our total operating expenses by approximately 25% next year, and over 30% in subsequent years. In total, this represents a savings of $50 million to $60 million in 2025, and in the range of $300 million in the period from 2025 to 2028, before one-time restructuring costs. These savings substantially reduce the financing needs of the Company between now and the transition to cash flow positivity. As a result of this restructure, we will reduce our U.K. footprint and research functions and suspend clinical trial activities with uza-cel for ovarian cancer, which will remove the associated CMC and development costs in the coming years.

The Galapagos collaboration on uza-cel for head and neck cancer, and other indications, is going well and will not be affected. We will be continuing with our lead preclinical assets PRAME and CD70, and will suspend investment in other earlier-stage pipeline programs. We

continue to seek strategic partners for PRAME and CD70, as well as our leading IPSC allogeneic platform.

Following the successful launch of Tecelra and the great lete-cel data we're presenting at CTOS, the Company is now fully focused on building a successful business with a cost-efficient commercial infrastructure, focused on what we anticipate will be two FDA-approved products in sarcoma, achieving our cash flow breakeven objective in 2027, and substantially reducing the need to bring in additional capital before becoming cash flow-positive.

This strategy, whilst involving difficult choices to reduce costs, is in the best interests of our stakeholders and of the patients who need our transformative cell therapies.

Now, moving on with an update on the Tecelra launch, which is tracking very well against our plan. Tecelra is the first FDA-approved engineered cell therapy for a solid tumour, and was approved in August for treating synovial sarcoma, so we're now about three months into the launch. With previously available treatment options providing low response rates and a five-year survival rate of only 20%, we're finding that Tecelra is being embraced by the sarcoma community as a transformational treatment option for this devastating disease.

We now have nine authorized treatment centres or ATCs accepting patients and referrals from health care providers, and that can initiate the Tecelra treatment journey across the U.S. This is at the upper end of the guidance we provided previously of 6 to 10 centres within the first 90 days. Furthermore, we have an additional four sites that have signed contracts, and a further 15 sites that are in active contract negotiations. Our ultimate goal has consistently been to have a network of approximately 30 ATCs offering Tecelra to patients within two years of launch, since those ATCs would cover an estimated 80% of the patients treated in sarcoma centres of excellence.

We are confident we can now activate our full network of ATCs by the end of 2025, two to three quarters ahead of our previous projections. This is a testament to the team's focus and to their execution, but also to the high level of engagement of each of our targeted sites.

On the payer side, Tecelra is approved for a rare and serious form of sarcoma, with demonstrated clinical benefit for patients. We've seen significant engagement by insurers, and

currently insurance plans representing over 67% of commercial lives formally cover Tecelra, and this continues to increase as planned.

For these types of therapy, the insurance approval process is almost always conducted individually for each patient by the treatment centre and the patient's insurer, and our Adaptimmune Assist team is involved in every step of the process to support the centres and the patients to navigate through financial and logistical needs and to make sure that they have a seamless treatment experience.

On the patient side, we're also very pleased to have apheresed our first patient and manufacturing is currently ongoing. There are now approximately 15 patients that have been confirmed as double positive following biomarker testing, meaning they tested positive for the right HLA and for MAGE-A4. Furthermore, there are at least an additional 25 patients in various stages of biomarker testing before this. Whilst not all of these patients will be eligible for or will opt for Tecelra treatment over a particular timeframe, we provide these metrics so you can see where our level of excitement and confidence is coming from. It is now very clear that we have a robust flow of patients that will progress to treatment with Tecelra in the remainder of '24 and '25. The patients are there, and the commercial model that we've built is working to make Tecelra available to appropriate patients.

Going forward, though, we're unlikely to continue to provide this level of detail regarding launch metrics, and all of this is in line with our previous guidance of expecting our first commercial revenues in Q4 of 2024. Just as a reminder, revenue is recognized when the treatment centre receives Tecelra, so we don't expect meaningful revenues in Q4 of this year, but as we progress into 2025, we'd anticipate modest revenue in the first two quarters, that will continue to accelerate throughout the year as patients flow through our expanding network of treatment centres.

With the commercial launch tracking to plan, along with extremely encouraging feedback from centres and from physicians, we're very excited about Tecelra's potential to improve and extend the lives of people with synovial sarcoma.

But this is only the first foundational medicine in the sarcoma franchise, and in a separate press release this morning we announced the results of the primary analysis of the full data set from

lete-cel's IGNYTE-ESO pivotal trial, which met the primary endpoint and are even more positive than the interim data we released back in June. The full analysis of IGNYTE-ESO reinforces the achievement of the primary endpoint for efficacy in the full data set of 64 patients treated, with a 42% response rate over all. This included six complete responses, which is a complete response rate of almost 10%. These responses are very durable and, although this data set is not fully mature, the median duration of response in the MRCLS population is currently just over a year, and in the synovial sarcoma population the median duration of response is just over 18 months. The full data set will be presented at the Connective Tissue Oncology Society or CTOS meeting on November 16, and will serve as the basis for the BLA filling planned in 2025.

We expect lete-cel to expand our reach beyond Tecelra, and in NY-ESO-expressing synovial sarcoma and MRCLS patients. This will more than double the number of treatable patients, and we estimate that lete-cel will eventually make up over 60% of the combined sarcoma franchise revenue. Since the commercial footprint and the ATCs for lete-cel are essentially identical to that for Tecelra, we will have significant operational, channel and cost synergies when we launch this second product.

Following CTOS, on November 18, we will hold a virtual investor event to further elaborate on these findings from the pivotal IGNYTE-ESO trial, and expand upon what it means for the treatment landscape in sarcoma. The event will feature Doctor Sandra D'Angelo, sarcoma medical oncologist from Memorial Sloan Kettering Cancer Center. She was an investigative clinician in both the Spearhead-1 clinical trial, the pivotal trial for Tecelra, and the IGNYTE-ESO trial, the pivotal trial for lete-cel. Details are available in today's press release and on our website, and we hope you join us.

Moving on to the financial results. At the end of Q3 we had approximately $186 million in total liquidity, after further drawdown of $25 million from our debt facility, following the FDA approval of Tecelra. In the third quarter of this year, our total operating expenditure was $55.6 million. For Q4 we expect our run-rate operating expenses to be broadly consistent with the first three quarters of '24, and the impact of the cost reduction initiatives I spoke about earlier will take effect starting in 2025.

In closing, Adaptimmune has successfully discovered, developed, and is commercially delivering the first ever engineered cell therapy for a solid tumour. We now have clear line of

sight to our second approval, and commercial launch of a wholly synergistic product in this franchise. We've achieved this with the expertise and commitment from our entire team. Now we've made difficult decisions that are necessary to set the Company on the path to cash flow positivity, as we bring the benefit of this cell therapy franchise to the sarcoma community. We will continue to make decisions to enable us to provide therapies with transformative benefits to patients, thus delivering long-term success and value to the Company and to its shareholders.

With that, the leadership team is happy to take questions. Operator?

Operator:
Thank you. To join the question queue, you may press star, then one on your telephone keypad. You'll hear a tone acknowledging your request. If you are using a speakerphone, please pick up your handset before pressing any keys. To withdraw your question, please press star, then two.

First question is from Mark Frahm with TD Cowen. Please go ahead.

Marc Frahm, Ph.D.:
Hi guys, thanks for taking my questions. Maybe just to start off with on the launch. Can you just remind us how long that process takes from a physician first expressing interest for a particular patient and getting to that 15 patients who have now cleared HLA and MAGE testing, and then how should we think about the timeline from getting that double positive result to actually working through the process of negotiating contracts and all that to then ultimately dose the patient?

Adrian Rawcliffe:
Thanks Mark. So yes, so we provided details in my prepared comments that I think is the first time we've provided those, which was that those 15 patients that have tested positive for both biomarkers and then additional at least 25 that are in various stages of biomarker testing. I think it's important to understand that whilst we're super happy to see that patients are having the opportunity to be identified and testing, we think that primarily confirms the unmet need there and the pent-up demand for Tecelra. It's important to note that testing can happen at any time during the treatment journey, so not all of those patients will necessarily flow through to become treated with Tecelra in any specific time period. But, we do expect the majority of double positive patients to continue their journey and be treated with Tecelra in the first two quarters of

next year. Obviously the patients that are coming through the other stages of testing will flow through in proportion to their testing positivity, and then over that sort of similar timeframe and subsequently.

We previously stated that we thought that the period from the very start of a physician first wants to test the patient through to being treated with Tecelra could take approximately three to four months. I think that's important but that also assumes that the patient is being tested and then going straight into treatment, not being tested really early on in their diagnosis process. So that three to four months, I think, is a reasonable estimate as we start at launch of Tecelra.

So, I think the long and short of that is that we don't expect meaningful revenues, we do expect first commercial revenues, but we don't expect those to be huge in Q4, but we do expect them to ramp into 2025 as those 15 patients come through in Q1 or the majority of those come through in Q1 and Q2, and then subsequently—I think the other thing to note is that we've currently got nine ATCs up and running, accepting referrals, and we expect that to continue to escalate as well, to get to the full network of approximately 30, plus or minus, by the end of next year. So, as that ramps as well, patients' access to Tecelra through the expanding treatment centres will be increased.

So, all of that together, I think, makes us really confident about the shape of the funnel of eligible and potentially eligible patients, and that that will continue to grow and come through as we look at the patient flow into 2025, and we therefore feel quite confident the patients are there, and quite confident in both the revenue coming through in 2025 and of course ultimately of the peak sales of the sarcoma franchise, which is driven off essentially the same funnel and process.

Marc Frahm, Ph.D.:
Okay. That was very helpful. Then maybe just on the decision around Surpass-3. Can you maybe speak to the data that's evolved in there, and just how much of the decision was driven by the data evolving in a way that was a bit different than what led you to start Surpass-3 in the first place, the prior data that led into it versus just the treatment landscape in ovarian just it being in flux?

Adrian Rawcliffe:

I think the way we thought about that decision was, we looked at the entire portfolio. We looked at it from a capital allocation perspective. What you've got if you look at that is you look at a sarcoma franchise that has capital requirements but is super close to being commercially real for us and producing sales, one product on the market, one product with these latest data with a clear route through, and this sort of hugely synergistic commercial front end on that. That seems a very high return on invested capital. At the other extreme of the pipeline, you've got a couple of opportunities in CD70 and PRAME that are absolutely enormous upside, so despite the fact that they're early and have some capital requirements, more limited capital requirements over the next few years, there's a massive potential opportunity in both of those.

Then we have uza-cel, and uza-cel, well obviously we did the partnership with Galapagos, which we feel really good about, and we have ovarian cancer remaining. So we looked at the requirements and the investment requirements over the next few years for uza-cel, where we've got to effectively qualify an entire manufacturing process, etc., and get a BLA filed for what will ultimately be a single indication, because all the other indications have the potential to go onto Galapagos's platform. That just didn't stack up relative to the other opportunities. So, it's really a purely capital allocation portfolio prioritization decision for us, as opposed to either—we still believe very strongly in the CD8 next generation construct, as evidenced by the push that we have with Galapagos to put it on their platform. We also, I think, still are confident that uza-cel is producing meaningful responses in patients. But from a total capital allocation and portfolio prioritization perspective, it just didn't make the cut.

Marc Frahm, Ph.D.:

Okay. Thank you.

Operator:

The next question is from Tony Butler with Rodman and Renshaw. Please go ahead.

Tony Butler:

Thanks very much. Adrian, a few questions, I'll ask them all if I could, because some are connected. The first is around lete-cel. It's a question around bridging studies that may need to occur. What's the risk to that and how does that apply to CMC? Importantly, would you anticipate the cost of goods of lete-cel to be higher or the same as that for afami-cel? Then

finally, back to uza-cel, I wondered if in fact you simply go to Galapagos and offer them whatever data you have for platinum-resistant ovarian cancer and that could be in lieu of some capital that comes back your way. Thanks very much.

Adrian Rawcliffe:
Thanks Tony. With respect to lete-cel, we have a commercial process for lete-cel that was established by GSK and the IGNYTE-ESO trial, the 64 patients that I referred to were all manufactured with that commercial process, that process was conducted by Miltenyi Biotec, and we plan on going to market with Miltenyi Biotec's process, manufactured at the same site that manufactured for a lot of the lete-cel patients in that pivotal trial. As such, whilst we will need to conduct normal validation work that was not conducted by GSK in the run-up to the BLA, we don't anticipate that we're changing manufacturing sites in order to go to market on that. So that's one element of derisking.

With respect to the cost of goods, I think we'd say two things. One, there isn't a massive difference between the cost of goods we anticipate for lete-cel and for Tecelra, and we would just point to the previous guidance of 70% cost margin at peak sales is sort of how we think about that for the sarcoma franchise. But it doesn't differ dramatically for lete-cel and afami-cel or Tecelra.

With respect to uza-cel, I wouldn't want to prejudge; it is worth pointing out, though, that the approach that we took with Galapagos was that the proof of concept trial that we're doing with uza-cel on the Galapagos distributed manufacturing platform is in head and neck. They then have the opportunity to option a range of other indications, up to and including all indications associated with uza-cel, on their platform. I wouldn't want to judge what other discussions might happen with respect to the uza-cel data.

Tony Butler:
Thank you.

Adrian Rawcliffe:
Thanks Tony.

Operator:
The next question is from Michael Schmidt with Guggenheim. Please go ahead.

Paul:
Hi, this is Paul on for Michael. Thanks for taking our questions and for all the details on the launch. I have a couple follow-ups on the aphoresis.

First, have there been patients who have been confirmed double positive so far but opted not to receive apheresis for whatever reason, left the patient journey?

Then, what's your baseline expectation for conversion rate of getting a patient who does test positive for both HLA and MAGE to that apheresis step?

Then secondly, you mentioned one patient has been apheresed in the third quarter; has there been any additional progress here, or patients near that stage in the fourth quarter, given that we're about halfway through the quarter? Thanks.

Adrian Rawcliffe:
With respect to the patient conversion rate and what we would anticipate and to the question about whether there are patients who have not opted to move forward with Tecelra, I think it's just way too early for us to be able to put metrics on that. The one thing that I think I would say, though, is, just to put it in context, there's some variation obviously in the timing of when patients get tested in their journey. We will be pushing in order to get patients tested as early as possible, in some cases way before they're actually eligible for Tecelra, which requires prior chemotherapy. But it would be very useful to know, for those patients, whether they would be eligible when, as invariably happens, the chemotherapy ceases to work. So we'll be pushing that to be early. So, I think the discussion on where the patients are moving forward into Tecelra is too early, and we haven't really got good data on the timings and the flow of those patients.

It is worth pointing out that Tecelra is just so much better than the standard of care that our assumption is that the majority of those patients who would be tested and double positive will, at some point, move forward into being treated with Tecelra. It just may take a little time. But we do anticipate the majority of those 15 patients to move forward in the first two quarters of next year, and be treated in the first two quarters of next year.

With respect to the apheresis, we have one apheresis to date. So we have lots of other patients at various stages of the pipeline, but that one apheresis was as of this point in time.

Paul:
Great. Thanks very much.

Adrian Rawcliffe:
Thank you.

Operator:
The next question is from Jonathan Chang with Leerink Partners. Please go ahead.

Yen-Der Li, M.D., Ph.D.:
Hi. This is Yen-Der Li for Jonathan Chang. Thanks for taking my questions.

So first question, I have a follow-up on the Surpass-3 study. Can you comment on the accrual rate for ovarian cancer patients in this study? Did this factor into your decision to discontinue enrolment? Additionally, when can we expect the data from the patients who already enrolled, would the timeline for 2026 data readout still be the same?

Thank you.

Adrian Rawcliffe:
In terms of accrual rates, actually that trial was accruing reasonably well in 2024. We'd previously planned on the interim analysis in 2025; that interim analysis would be on the basis of 13 patients, first interim analysis is based on 13 patients per arm of that study, so 26 patients in total, and I think we were on track to be able to do that. We will probably release the data that we have accumulated at some point over the course of the next 12 months, when it's reasonable and meaningful to do so. But we are terminating that, so we won't have the full data set that we were previously considering in 2026.

Yen-Der Li, M.D., Ph.D.:
Understood. Thank you. So, I have another follow-up question. You mentioned that the preclinical development for PRAME and CD70 is ongoing. How would these two early-stage

programs be impacted by the headcount reduction and the cost-saving plan you just announced? Thank you.

Adrian Rawcliffe:
We will be focusing the resources that we have in the early phase pipeline on those two programs, and moving them as quickly as we can into the clinic, and we anticipate IND for PRAME now next year, and CD70 following that. So, I think that will become the key focus for our teams in the early stage research and early development teams.

Yen-Der Li, M.D., Ph.D.:
Understood. Thanks for taking the question.

Adrian Rawcliffe:
Thank you.

Operator:
The next question is from Graig Suvannavejh with Mizuho Securities. Please go ahead.

Graig C. Suvannavejh, Ph.D.:
Good afternoon. Thanks for taking my questions and congrats on the great data for NY-ESO. I've got three questions, if I could. Just first, I think I heard you say this earlier in the call, but can you just remind us on when there is a time in the future where lete-cel is perhaps on the market, how you would think about the shape of the uptake or trajectory curve vis-à-vis what you are currently anticipating for Tecelra, so just comparing and contrasting kind of a view of revenue trajectories for each of those products. That's the first question.

Then second question, just on the cost savings, any colour around how to think about the split between SG&A and R&D in terms of those cost savings?

Then lastly, just on the PRAME opportunity, really interesting target, I think we've seen a little bit of mixed success thus far in terms of targeting PRAME? Could you just maybe remind me how you are viewing your level of confidence in either the target itself or perhaps the constructs that you're advancing to get optimal efficacy and safety. Thank you.

Adrian Rawcliffe:
Thanks Graig. I'll take questions one and three, and then I'll ask Gavin to comment on the split of the cost savings.

In terms of the shape of the uptake curve, I think there's one element that will be the same, that's driving that, and then there's one element that we think will be quite different. The element that will be the same is that the process of testing a patient, aphorizing a patient, manufacturing a patient, the negotiations with the insurance company, and then returning that, we think that will be roughly the same both for Tecelra for lete-cel when it comes to market. But the thing that will be quite different is that, by the time we have lete-cel approved, we will have stood up the full network of approximately 30 ATCs for afami-cel. So therefore we anticipate that we'll be able to engage and have many, many more of those sites active from day one for lete-cel than the current ramp for afami-cel, which we're very happy with at 9 so far and on our wait route to 30. But you can clearly see that, if we could go through the full 30 from day one, which we will be able to do, we believe, with lete-cel, that will be a significant advantage. That would translate into a faster uptake relative to Tecelra.

With respect to PRAME, we feel that PRAME is a fantastic target for us doing what we do, engineered TCR T-cells. There probably is not a more broadly expressed cancer-testes antigen out there. The data that we see where people targeting it seems to demonstrate that PRAME is a good target. I think the cell therapy data that we've seen, I think, gives clear indications that it's possible to see substantial and prolonged responses in the melanoma space, in particular, and we think that that bodes very well for cell therapy treatments that target PRAME, and we think this sort of demonstrates as well why cell therapy has the potential to be the gold standard of efficacy for targeting these types of targets, versus bi-specifics or other types of targeting.

With respect to why we are so confident about our program, we think we're very good at designing T-cell receptors. This has been our life's mission, and we have taken everything we know about designing T-cell receptors to be able to engage T-cells to target cancer, and we've put that into our PRAME program into ADP-600. We've previously shown a very highly sensitive TCR, and we believe that this will drive, based on all of our knowledge about how these things work and all the experience with MAGE-A4, we believe this will drive a clinical benefit in patients, and will potentially also drive the ability to target PRAME at concentrations that are exhibited across a much broader range of tumour types than current therapies are showing

efficacy. So, that's why we believe that there's an opportunity for a best-in-class program, particularly when you then combine that with next-generation approaches and other engineering to further enhance the program.

Then the last thing I'll say is, there are really two, maybe there's a couple of others in preclinical development as well, but a very small number of PRAME cell therapies that are credible programs moving forward into development. For such a huge potential target, a massive unmet medical need, we feel the space is wide open relative to almost any other target out there. So, we're quite excited about the opportunity to put ADP-600 into the clinic next year.

Gavin.

Gavin Wood:
Hi Graig. In terms of the $50 million to $60 million worth of savings we expect next year in 2025, the split of those savings is roughly 60:40, R&D to SG&A. As we look out a little bit further, as we think about the $300 million worth of savings we anticipate over the next four years, actually the split is probably slightly more heavily biased in the out years to R&D, and that's because we've continued to invest behind the commercial team and the success of bringing Tecelra and lete-cel to market.

Graig C. Suvannavejh, Ph.D.:
Thank you.

Adrian Rawcliffe:
Thanks Graig.

Operator:
The next question is from Arthur He with H.C. Wainwright. Please go ahead.

Arthur He:
Hey, good afternoon, Ad and team. I had two quick questions. One is, during the screening for the MAGE-A4 and HLA type for afami-cel, how is the rate you guys see the real-world screening, versus the previous guide of 70 and 40?

Adrian Rawcliffe:

I'm going to start by saying, impossible to tell at the moment, and then I'll explain a little bit why. The HLA test that we developed is—there's nothing particularly special about it, and there are many, many ways of testing for HLA. Indeed we anticipate that sites will use a wide range of HLA tests. The uptake on our HLA test indicates that they are indeed using a wide range of HLA tests. So we don't get to see the vast majority of the HLA testing that gets done. But given that the HLA prevalence has been sort of relatively well characterized, including in our clinical trials, which were after all conducted at almost exactly the centres that we're going into, we feel reasonably confident about the 40% to 45% range that we've put out there before, and don't really see any reason why it would be different.

On the MAGE-A4 testing, we have had significant uptake of our test. However, I don't think that the rate there is—the rate there is quite high at the moment, and we anticipate that that's actually because maybe some of the patients coming into that MAGE-A4 testing have previously been tested with MAGE-A4 and found to be positive, but they want it confirmed with our IHC diagnostic. So I don't think we're really in a position at the moment where we have sufficient data and sufficient time to be able to confirm or deviate from the previous estimates, which—I will point out those previous estimates were conducted on pretty decently sized populations during the clinical trial, so I'm not sure we would anticipate much deviation from that anyway.

Arthur He:

Got you. Thanks for the colour, very helpful.

My second question is regarding the lete-cel data. I noticed that, for the synovial sarcoma for lete-cel, the duration of response is about more than 18 months, significantly higher than the afami-cel. Is there a reason or we can figure out in terms of patient baseline, or something else you guys can tell us more colour on that?

Adrian Rawcliffe:

I'm going to answer that very briefly, and then I'm going to ask Dennis Williams to comment on that. My brief answer would be that I think those data are somewhat immature. The duration of response is great. It's worth noting that in the *Lancet* article for afami-cel, Tecelra, the duration of response was about 12 months based on that data cut. The median duration of response

numbers are quite volatile when you're dealing with relatively small numbers of patients. But we're very pleased that we have 18 months at this data cut, and we look forward to presenting that data for the BLA.

Dennis, do you have additional colour you could provide on that?

Dennis Williams, Pharm.D.:
I want to say that they're sort of, in some ways, comparing apples to oranges. I mean, it's difficult to compare median duration of responses, particularly a subpopulation in IGNYTE-ESO, to another trial. I would say in both cases the median duration of response is very impressive. It's very different-looking than you would typically see for available second-line therapies. But I expect when CTOS, when the data gets presented this weekend, there'll be some discussion around that, and I would love to hear what the scientific community thinks about it.

Arthur He:
All right. Thank you for taking my question.

Adrian Rawcliffe:
Thanks.

Operator:
The next question is from Yanan Zhu with Wells Fargo. Please go ahead.

Kwan:
Hi, thanks for taking our questions. This is Kwan on for Yanan. Our question is around lete-cel. What are the remaining items need to be done before you can file the rolling BLA—start the rolling BLA? Thank you.

Adrian Rawcliffe:
Three things that we need to get the BLA. One, positive clinical data from the pivotal trial, which we now have the full primary analysis of, and so we'll be rolling forward to file that as the first part of the rolling BLA. Secondly, the CMC parts of the file, which we will be working to analyze that, validate that process etc., and be able to file the module three of the BLA in due course. Then lastly, I think you got to remember that we are going to be having a parallel file with the

NY-ESO diagnostic, so we're working already with a partner to be able to develop and then have that diagnostic registered. Those are the principal components that will go into the approval package for lete-cel.

Kwan:
Got it. Thank you for that. Assuming a patient is eligible for both Tecelra and lete-cel, how do you think a patient would choose between these therapies? Is there a possibility of sequential dosing of these two therapies? Thank you.

Adrian Rawcliffe:
Really, really good question.

The MAGE-A4 and NY-ESO are both significantly expressed in synovial sarcoma patients; both have fairly high levels of expression. It's worth pointing out that the MRCLS population, NY-ESO is very, very highly expressed in that population, and obviously we don't have an indication for that for Tecelra at this point. So, that would be entirely additive sales.

For synovial sarcoma, I've just mentioned that the sales projections that we've put forward assume that only the NY-ESO-positive MAGE-A4-negative patients would be treated with lete-cel, and so it's entirely based on incremental patients. Therefore, as you pointed out, may be a little conservative because there's a bunch of patients who are dual positive, a significant proportion, and there is the opportunity, maybe in due course, for sequential treatment as people build familiarity with that and as data comes out on patients that have received both of these therapies, or sequential treatment with NY-ESO- and MAGE-A4-targeting cell therapies.

In terms of how patients will choose, I think that sort of remains to be determined, how patients and physicians will choose. Obviously we anticipate that potentially target expression will play a part, but also and physician familiarity with the treatments. Ultimately, I think what is clear is that we are launching two therapies into this patient population who currently have no options, and therefore, for eligible patients, treatment with one or both of these is going to be transformative for them, compared to the existing second-line treatment options. So that, I think, means that this just means that there's an opportunity here to provide cell therapies to more patients with synovial sarcoma and now MRCLS.

Kwan:
Got it. Thank you for all the colours.

Adrian Rawcliffe:
Thank you.

Operator:
The next question is from George Farmer with Scotiabank. Please go ahead.

George Farmer:
Hi, thanks for taking my questions. Couple from me. I actually just get on the topic of double positive synovial sarcoma. According to the afami-cel label, it looks like the duration of response is 6 months, and you're seeing 18 months with lete-cel. Shouldn't the choice be obvious about which cell therapy one may want to select?

Adrian Rawcliffe:
I think you've got to Dennis' point, that Dennis mentioned. I think the duration of response of 6 months for Tecelra in the label is slightly different to the data set that was published in the *Lancet*, which had 12 months. That was down to the fact that there were a couple of patients included in the FDA's data analysis, a couple of responders that had shorter duration of responses that were incremental to the data that was in the *Lancet*. I think that shows you the variability of the median duration of response data. What is clear is that, for lete-cel for afami-cel, about 40-plus percent of patients had durations of responses that were more than a year. So, there's some very fine lines that are being dealt with here. I think that would be a factor to consider, but I'm not sure that that will be the only factor to consider as patients make that choice. If they do choose that they would like Tecelra, then that's great, and does not change our overall sales projections for our sarcoma franchise, because whether they get Tecelra or lete-cel, we still benefit from the sale and that patient still benefits from an Adaptimmune cell therapy for this rare disease.

Does that make sense?

George Farmer:
Okay. Yes, it does. Thank you.

Also at the ASCO presentation earlier this year, there was a single grade 5 adverse event. Have you seen any since then in this expanded safety analysis?

Adrian Rawcliffe:
Dennis, do you want to comment on that?

Dennis Williams, Pharm.D.:
No, that's correct, there was one Grade 5 T cell-related event, and that will be discussed at the presentation this weekend.

George Farmer:
So, there were additional Grade 5 adverse events, over and above what was presented at ASCO?

Dennis Williams, Pharm.D.:
There have not been new Grade 5 events since ASCO.

George Farmer:
Okay. That's great to hear.

Then finally, in this restructuring process, is there any impact on current executives?

Adrian Rawcliffe:
We are still working through the impact on the organization, and we'll communicate that when those decisions are taken.

George Farmer:
Okay. Great, thanks very much.

Operator:
The next question is from Michael Kim with Zacks Small Cap Research. Please go ahead.

Michael Kim:
Hey everyone, good afternoon and thanks for taking my questions.

First, Ad, in terms of the increased confidence in reaching $400 million in peak year sales for the sarcoma franchise, I know you talked about the early success you're seeing with Tecelra as well as the strong results coming out of the lete-cel pivotal trial; but anything beyond that, that is maybe driving higher conviction in that number?

Then, related to that, any shift in the timeline for hitting peak sales as part of that step-up in confidence?

Adrian Rawcliffe:
We started the year guiding the $400 million peak year sales number. I think all that's happened since then has just increased that confidence. So walking through. We got Tecelra approved, the first engineered cell therapy for a solid tumour, by no means a given in the marketplace. The launch of that is going really well. The discussion about, well, how many patients are there, are the patients there, I think, have been thoroughly—our view has been thoroughly vindicated by our experience in the screening and testing process in the first period of time. So, the fact that we have now sitting here 15 double positive patients and a further 25 at some stages of testing at least, given that we don't see all of the testing that's ongoing, that's just what we can see, I think gives us really good confidence in the sales uptake for Tecelra, and also, I think, helps validate our underlying assumptions about the incidence prevalence rate. Not exactly, we can't be super precise on it, but I think it helps give us confidence that the patients are there and that they are flowing through the system and they are addressable by us.

Then the data at CTOS, I think, just confirms the efficacy profile that you can anticipate in these rare sarcomas from cell therapy. The fact that this data has continued to improve as we go through the clinical trial, from the first interim readout, the second interim readout, and now the primary analysis data set, I think, just says that this is a building confidence in the efficacy profile.

The relationship to the $400 million, I think, is also the fact that the efficacy profile in MRCLS is very similar to the efficacy profile in synovial sarcoma, with a more than 40% response rate and really strong durability. Obviously that's key, because the MRCLS population is an important addition in order to get to the $400 million sales.

So, all of that together, I think, adds up to that increasing confidence.

Michael Kim:
Got it. That's very helpful, appreciate that.

Then, maybe just to follow up on the capital front, I know you mentioned drawing down on the $25 million tranche as it relates to the loan with Hercules, but can you just update us on where things stand as it relates to the other tranches that are, I think, built into that agreement?

Adrian Rawcliffe:
Happy to. Gavin, do you want to touch on that?

Gavin Wood:
There's a further three tranches which are drawable: $5 million which is drawable on a certain criteria associated with afami-cel and lete-cel, $30 million on approval of lete-cel, and then $40 million on terms to be decided between both parties.

Michael Kim:
Got it. Okay. Appreciate that. Thanks for taking my questions.

Gavin Wood:
Thank you.

Adrian Rawcliffe:
You're welcome.

Operator:
The next question is from Peter Lawson with Barclays. Please go ahead.

Peter Lawson:
Great. Thanks so much. I guess a couple of quick questions. When do you expect the next patient to be apheresed? Then, with current cash in the loan, what's your projection for the cash runway?

Adrian Rawcliffe:
I think the answer to is soon—that first question is really soon. We anticipate that those patients that are currently double positive to start flowing through 2024 through the ordering process and into 2025. I think that's really underlying our confidence in the ramp of sales as we go through 2025.

In terms of cash runway guidance, I think, we closed the quarter with $186 million in liquidity. We have announced the restructuring and the impact on the expenditure next year relative to our guidance in 2024. I think it's important to remember that, as of the last Q call, we stopped providing forward cash runway guidance, and the principal reason for that was because smart people like yourself, Peter, could easily calculate from our expenses base and runway guidance what our forward sales projections were, and we are not interested in giving forward sales projections until we have significantly more experience under our belt, so that will be sometime probably next year, late next year sometime.

So, because of that, we're not providing cash runway guidance, but we have $186 million liquidity, and a restructuring program that is designed to shape our P&L and get us to cash flow breakeven on an operating level in 2027.

Peter Lawson:
Thank you. Do you think you'll provide revenue guidance next year?

Adrian Rawcliffe:
I think once we've got a few quarters of sales under our belt, I think that's when we'll be able to be more useful to you in providing forward-looking guidance.

Peter Lawson:
Got you. Okay. Thanks so much.

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

Adrian Rawcliffe:

Thank you ever so much for joining us to hear about the launch of Tecelra and the great progress there, and the data from the lete-cel IGNYTE-ESO pivotal trial, and the restructuring that will enable us to deliver a profitable sarcoma franchise and cash flow breakeven in 2027. Look forward to updating you in due course as we execute on these things. Thanks for your time.

Operator:

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