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ESMO-GI Data Call

July 5, 2019

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PRESENTATION

Operator:

Ladies and gentlemen, thank you for standing by and welcome to the Celyad call to discuss the SHRINK and alloSHRINK trial data presented earlier today at the ESMO World GI Congress. At this time, all participants are in a listen-only mode. I must advise you all that the conference today is being recorded.

With that, I would like to turn the call over Dr. Anne Moore, Celyad's Vice President of Corporate Strategy. Please go ahead, ma'am..

Anne Moore:

Thank you Operator and thank you everyone for joining us for call today to discuss our SHRINK and alloSHRINK data presentation at ESMO World GI Congress. Joining me today is Filippo Petti, our Chief Executive Officer and interim Chief Financial Officer; Dr. David Gilham, Vice President of Research and Development, and Dr. Frédéric Lehmann, Vice President of Global Clinical Development.

We will start the call with an update on our solid tumor program and then open up the line for your questions.

Before I turn the call over Management for their prepared remarks, I would like to take this opportunity to remind you that this call may contain forward-looking statements including statements regarding the safety and efficacy of our drug product candidates and the manufacturing methods used to manufacture these drug product candidates, as well as statements concerning the ongoing and planned clinical development of our drug product candidates including the timing of trials, enrollment, data readout and presentation, and refer you to our regulatory filings for additional information of the Company.

With that, I'd like to turn over the call to Filippo Petti. Please go ahead, Filippo.

Filippo Petti:

Thank you Anne and thank you everyone for joining us for today's conference call. Earlier today at the ESMO World Congress on gastrointestinal cancer which is being held in Barcelona, Spain, Professor Dr. Eric Van Cutsem from the University Hospital of Leuven in Belgium provided oral and poster presentations regarding new preliminary data from the SHRINK and alloSHRINK studies for our NKG2D based autologous and allogeneic CAR-T candidates CYAD-01 and CYAD-101. We are excited to announce this preliminary data for the SHRINK and alloSHRINK trials for a number of reasons. In addition to offering an update to our solid tumor program, we also believe that allogeneic or 'off the shelf' CAR-T cell therapies offer a tremendous opportunity in the advanced of cancer immunotherapy, in particular for the potential treatment of solid tumors.

In addition, the similarities of the CYAD-01 and CYAD-101 product candidates along with these comparable trial designs should provide us with a unique comparison of the autologous and allogeneic engineered cell therapy approaches.

I will now turn the call over to Dr. David Gilham to provide additional color on the NKG2D-based CAR-T clinical candidates and on our non-gene edited allogeneic technology TIM or T cell receptor inhibitory molecule. Then, Dr. Frédéric Lehmann will provide a background on the SHRINK and alloSHRINK trial designs and highlight the results reported earlier today at the ESMO World GI Congress.

David, the floor is yours.

David Gilham:

Thank you Filippo. This is an exciting day for our solid tumor program as we get to announce the preliminary data from the SHRINK and alloSHRINK studies. However, before we get into the data announced earlier at ESMO-GI, let me take a minute to provide a brief overview of these two therapies.

To start with CYAD-01 and CYAD-101 are both NKG2D-based CAR-T cell therapies. As a reminder, NKG2D is a receptor expressed by natural killer cells that binds to eight stress-induced ligands expressed on tumor. CYAD-101 is a non-gene edited allogeneic version of CYAD-01. It uses a healthy donor derived cell. In order to avoid the donor cells from being rejected by the patient, CYAD-01 co-expresses a null inhibitory peptide TIM or T cell receptor inhibiting which we believe could reduce or eliminate Graft-versus-Host-Disease in patients along with the NKG2D receptor.

The TIM itself is a truncated form of the CD3 zeta chain which when expressed as part of a CAR vector competes with the endogenous CD3 zeta within the T cell receptor complex. The T cell receptor is the driver of Graft-versus-Host response which is the major limiting factor in allogeneic T cell therapy. Through

competing out the endogenous CD3 zeta protein, the ability of the T cell receptor to initiate the signal is much reduced since the CD3 zeta protein provides the majority of the signaling element required to initiate the Graft-versus-Host response. In this manner, the T cell receptor remains on the T cell surface but with a much reduced signaling capacity when combined with our NKG2D CAR, the T cell self-induced Graft-versus-Host-Disease in our preclinical models. However, the activity of the NKG2D CAR is maintained as the TIM does not interfere with the CAR itself.

Allogeneic therapies are an exciting opportunity in the industry as the use of donor cells avoids many of the complexities in terms of manufacturing and logistics that are required for use for autologous CAR-T therapies. I think it is also worth mentioning that to our knowledge CYAD-101 is the industry's first off-the-shelf investigational non-gene-edited CAR-T candidate for the treatment of solid tumors, therefore, we are especially excited to see this data and continue the alloSHRINK study.

With that (inaudible) I'll hand over to Dr. Frédéric Lehmann, our Vice President of Clinical Development to provide with the clinical update.

Frédéric Lehmann:

Thank you, David. As Filippo mentioned, I will first review the study design of the SHRINK and alloSHRINK trials, then I will review the data that was presented earlier today by Professor Van Cutsem at indeed the ESMO World GI Congress.

The SHRINK and alloSHRINK trials are similar Phase 1 dose escalation studies that are evaluating the safety, the clinical activity and the CAR-T cell kinetics of CYAD-01 and CYAD-101 in the treatment of metastatic colorectal cancer patients. The SHRINK study is an open label Phase 1 dose escalation trial evaluating multiple doses of the autologous CAR-T CYAD-01 administering concurrently with the standard FOLFOX chemotherapy. Patient eligibility include neoadjuvant first line metastatic treatment for colorectal cancer patients with resectable liver metastases population, and another patient population which is the unresectable refractory metastatic colorectal cancer patient population who has already received multiple lines of chemotherapy including FOLFOX. All patients received six cycles of FOLFOX chemotherapy every two weeks according to standard schedule, and three administrations of the CYAD-01 every two weeks 48 hours after the chemotherapy at Cycle 3, 4 and 5 of the FOLFOX. (Inaudible) trials include 3 dose levels - 100 million, 300 million and the third dose level at 1 billion of cells per injection.

The sister study, the alloSHRINK study is also an open label Phase 1 dose escalation trial assessing the safety as primary endpoint of, again, multiple doses of the allogeneic CAR-T CYAD-101 administered, again, concurrently with the FOLFOX chemotherapy only in patients with unresectable refractory metastatic colorectal cancer patients who, again, have received already multiple metastatic chemotherapy lines including, therefore, FOLFOX chemotherapy. Here, patients are receiving six cycles of FOLFOX chemotherapy, again, every two weeks, and three administration of the CYAD-101 every two weeks 48 hours after the chemotherapy but this time at Cycle 1, 2 and 3. Again, the three dose levels being evaluated are 100 million, 300 million of cells and 1 billion of cells per injection, respectively.

Let's turn now to the preliminary results. As of May 2nd of this year, nine patients were treated in the SHRINK trial including three for each of the dose levels. At April 16, '19 the alloSHRINK trial includes six patients with three patients each in the two first dose levels, 100 million and 300 million respectively.

Looking at the primary endpoint of the studies, of those two studies, we have observed a very well tolerated safety profile. Specifically, there were no reports of Grade 2 or higher cytokine release syndrome, CRS; no related serious adverse events; no dose-limiting toxicity; and strictly no on-target off-tumor toxicity.

Importantly, no clinical evidence of Graft-versus-Host-Disease have been reported across the six patients treated in the alloSHRINK trial.

This initial data supports the ability of the Company's novel inhibitory peptide TIM to reduce signaling of the TCR complex as mentioned by David earlier. In addition, Host-versus-Graft reaction threat (inaudible) against the allogeneic CYAD-101 CAR-Ts appears to be well controlled in the study design as evidenced by similar levels of CYAD-101 cell engraftment following the second and the third infusions of these allogeneic cell therapies.

Looking at the clinical activity endpoint, we have observed encouraging antitumor activity. This includes one person response and six stable disease out of the nine patients enrolled in the SHRINK study. Important to note out of the five unresectable refractory metastatic colorectal cancer patients who have already received multiple lines of metastatic chemotherapies including FOLFOX, four patients are presenting as stable disease for more than three months with two of them still ongoing as of today.

For the allogeneic program, interestingly, in the two first dose levels of the alloSHRINK study one patient is presenting a partial response and three patients stable disease out of the six patients with, again, on heavily pretreated relapsed or refractory disease, all of them having received priorly FOLFOX chemotherapy.

For both trials preliminary data show a dose-dependent effect on the kinetics of the CAR-T cells with a higher level of engraftment at the higher dose for both CYAD-01, the autologous, or the allogeneic CYAD-101 therapy. Interestingly, at the same dose the allogeneic CYAD-101 appears to provide the better engraftment compared to the CYAD-01. As already mentioned, the Host-versus-Graft response, again, the allogeneic CYAD-101 cells, appear to be well controlled as evidenced by those similar levels of dose cells engraftment following further infusions.

I will now turn the call back to Filippo for some conclusions. Filippo?

Filippo Petti:

Thank you, Frédéric, for that recap of those two programs and for the presentation of the new data.

I want to say again just how pleased we are with the initial results from the alloSHRINK study. Upon reviewing this data and comparing it with the SHRINK study data, we have decided to enroll and additional three patients for a total of six at the 1 billion dose level per injection in the alloSHRINK trial. We are currently planning to announce the full data for the dose escalation alloSHRINK Phase 1 trial by year-end 2019.

To our knowledge, the alloSHRINK trial is the first study with an allogeneic CAR-T cell therapy for the treatment of a solid cancer indication and the preliminary data from the alloSHRINK trial show no evidence of GvHD despite increased engraftment, which is certainly encouraging as we move forward with the program and future development of our allogeneic technology platforms.

As we conclude this portion of the call, I want to notify you that we have placed the poster presentation from the ESMO-GI Congress on our corporate website www.celyad.com in the Library section of the website.

Before I open up the call for questions, I want to say how delighted we are with all the progress we are making with our clinical programs, and we look forward to the various upcoming clinical milestones for year-end 2019 and into early 2020. As a quick recap for these milestones, we expect to have: one, full data from the dose escalation alloSHRINK Phase 1 trial by end of this year; two, new data from the THINK and DEPLETHINK trials for the treatment of relapsed refractory acute myeloid leukemia and myelodysplastic syndromes including initial data from the new OptimAb manufacturing process in patients treated in Cohort

4 of the DEPLETHINK trial by the end of 2019; and lastly, we are preparing to initiate our Phase 1 CYAD-02 trial in early 2020 with initial data from the program expected by mid 2020.

With that, I will now turn the call over for your questions. Operator?

Operator:

Thank you. We will now be conducting a question and answer session. If you would like to ask a question, please press star, one on your telephone keypad, and a confirmation tone will indicate your line is in the question queue. You may press star, two if you would like to remove your question from the queue. For participants using speaker equipment, it may be necessary to pick up your handset before pressing the star keys. One moment, please, while we poll for questions.

Thank you. Our first question is from Peter Lawson with SunTrust Robinson Humphrey. Please proceed with your question.

Peter Lawson

Hi. Thanks for taking my questions. I guess congratulations (inaudible). Just thinking about 01 initially, from the last update it seems that in the THINK CyFlu you had a pathological CR. What happened to that patient?

Filippo Petti:

Thank you, Peter, for that question. Just to follow-up on the THINK CyFlu cohort, and for all those that are listening, the THINK CyFlu cohort was a specific cohort of three patients that we enrolled in the THINK study, one single injection following preconditioning cyclophosphamide and fludarabine. For that one patient, as you may recall, we initially reported data at SITC of last year for that first cohort. We had a complete response, a pathological complete response as well as two partial pathological responses. Earlier this year, to be conservative, we migrated to a RECIST criteria, a 1.1 criteria to make the analysis a little bit cleaner for us with respect to the programs and how we look at the overall solid tumor program in particular around metastatic colorectal cancer, so that one patient that was originally classified as a complete pathological response was reassigned to a partial response based on RECIST criteria.

To provide additional thoughts, maybe I will hand it over to Frédéric to give you some additional details on that one patient.

Frédéric Lehmann:

Yes. Thank you, Filippo. Really nothing to add. Indeed, this patient—the three first patients of the SHRINK study, indeed for the first dose level, those patients have been enrolled in the neoadjuvant setting of patient populations, and the first patient you are referring to still goes to as plan, which is already somewhere—success of the study go to the surgery, so remember neoadjuvant setting. Neoadjuvant setting is to give the chemotherapy before the surgery and in that context so this patient goes to the surgery, a complete resection has been done and therefore now as of today makes more than six months post surgery the patient is still in complete response, if you want, post the surgery. The patient is still under follow-up.

Peter Lawson:

Perfect, thank you. (Inaudible) autologous versus the allogeneic program for the cells?

Filippo Petti:

On the persistence, David or Frédéric, I'll defer to you in terms of what we're seeing with regards to the allogeneic versus the autologous. David?

David Gilman:

Frédéric, would you like to discuss those clinical results?

Frédéric Lehmann:

The cell engraftment. In terms of cell engraftment, indeed, when we are comparing the autologous and the allogeneic program, and as mentioned by Filippo, you will see all those data on the poster that has been posted on our website, clearly two elements. The first one you see an increase of the engraftment according to dose. Within the autologous or allogeneic program, remember, we are not yet disclosing the data of the dose level three, so 1 billion of the allogeneic program, this specific dose level is ongoing. Again, when we are looking, when we are comparing dose level by dose level for the two first dose levels, the autologous and the allogeneic program, the allogeneic CAR-T in the same context, so post FOLFOX chemotherapy, clearly, with the few patients enrolled in each of those levels, three patients, it looks like there is an encouraging difference in terms of engraftment in favor of the allogeneic product. As you will see in the details of the cell kinetics on the poster, as we mentioned also the fact that after the second and the third injections of the allogeneic CAR-T we still see systematically a peak of engraftment showed typically in such kind of study design most probably therefore and on purpose the need for depletion induced by the FOLFOX chemotherapy can control adequately the Host-versus-Graft reactions and therefore you see such kind of engraftment.

Having said that, yet, remember and in comparison with the THINK trial, for example, that have been discussed several times in the previous occasions, those cells, the autologous and the allogeneic, so CYAD-01 and CYAD-101 have an engraftment and a persistence around two weeks, so they come back more or less at the baseline before the next further injections which is at two weeks apart.

David, do you want to add some other information?

David Gilman:

No, I think those are the salient points, Frédéric. I think just to emphasize that the therapy here is based on FOLFOX which generates a transient lymphodepletion. There's no (inaudible) by any means as would be expected with that of CyFlu, and so the kinetics we see are similar to that insofar as that the patient engraftment sees a peak and then starts to drop really within that period of time of the transient lymphodepletion. Yet, we see repeated peaks after each infusion and effectively there's an increase in the SHRINK and in the first two cohorts of alloSHRINK we've seen a dose-dependent increase in terms of the magnitude of those peaks after infusion.

Peter Lawson:

Perfect. Then just maybe a further question around (inaudible) the focus of the spend and the selection of the program versus (inaudible) and then autologous versus allogeneic?

Filippo Petti:

Good question, Peter. I think, look, based on the results that we're seeing, we'll continue to move forward with regards to the solid tumor program. We've talked about the strategy here; relapse/refractory is still kind

of the today (phon) part of the strategy. We are looking to continue to develop both our allogeneic approaches, the TIM peptide as well as our shRNA approach and how that eventually falls into the solid tumor program still is kind of an assessment we're going through. We are committed to pushing for the therapies, in particular around the alloSHRINK study as we talked about, adding some additional patients to that high-dose level.

As we think about it from an autologous perspective, I think we're working on additional biology there to try to improve our prospects. How that folds into maybe next generation candidates specifically that are autologous or allogeneic towards solid tumors, we'll make that assessment as we gather additional facts here.

For us, we're excited about the alloSHRINK trial data. It's preliminary. We'll look to add to that and provide an update later this year, and then think about how a potential allo-treatment for solid tumors could be taken forward and progressed into the future.

In terms of spend, I think it's, again, the majority is shifted towards AML in the near term, but allo and solid are certainly top of mind for us.

Peter Lawson:

Perfect. Thanks so much.

Filippo Petti:

Thank you, Peter.

Operator:

Thank you. Our next question is from the line of Raju Prasad with William Blair. Please proceed with your question.

Raju Prasad:

Thanks for the question. Maybe just a little bit of follow-up on that last question, but given the data you're seeing so far, how should we think about using TIM versus shRNA moving forward? Will the TIM molecule primarily be towards 101, and shRNA will be used moving forward, or just the fact that you're seeing no GvHD in this data you may use TIM kind of in some of your allo products even on the haem side?

Filippo Petti:

Thank you for the question, Raj. Look, I think from our perspective we want to continue to push towards a larger data set from the TIM program, in particular around 101 and alloSHRINK. I think following that data set we'll make an assessment as to how we continue to evaluate that and thinking about maybe additional indications, but I believe where we are now and the fact that we haven't seen any GvHD is certainly encouraging. We've always talked about TIM being really connected with NKG2D. It is in the clinic. There is obviously an opportunity for us perhaps to evaluate some additional indications following a data set that continues to point to promising both activity and as well as to more importantly safety.

As we think about shRNA and building a larger platform that technology, as you know, we are trying to push into the clinic for 2020, primarily around our first candidates 211 and 221 focused on BCMA and CD19, respectively, and there, those two trials again are going to try to prove out the platform and the technology

with well-established targets. I think as we continue to build a broader allogeneic platform, we'll look to put resources behind the ones that will continue to provide promising opportunities for us, and we are not, I don't think, running a head-to-head and it becomes a TIM versus shRNA for us; I think we are looking at a holistic approach and kind of really have taken a broad view in terms of allo being a big part of the Celyad portfolio going forward, and it could be TIM NKG2D, it could be shRNA with some additional opportunities outside of BCMA and CD19. We have talked about this 231 program where we believe we can marry shRNA with NKG2D down the line as well. So, I think we're just taking a broad perspective of allo and we're very fortunate to have two non-gene-edited platforms here to be moving the ball down the field.

Raju Prasad:

Great. I'm just kind of taking a look at the poster. Do you have any color on the amount or the percentage of TCR inhibition in the three allo products?

Filippo Petti:

I would have to defer to David if he can provide some thoughts there.

David Gilham:

Yes, of course. Hi Raj. The TIM on its own generally speaking results in a retrodepression of around 50% response in terms mitogenic activity, and this seems to correlate to an ability to control GvHD in the setting, particularly with the NKG2D receptor.

Looking at the CYAD-101 product itself, and the lots that are generated, basically we have a threshold cutoff for interferon gamma. This is one of our release criteria and of course these products we would use is below that level, which sets a—it's actually a very minimal level of response to myogenic activation. The CYAD-101 product as it is really has a very low mitogenic potential in terms of responding in vitro to T cell receptor stimulus.

Raju Prasad:

Great, thanks. Then just one quick last one. Just thinking about moving the program forward, how would you think about enrollment of neoadjuvant patients kind of as you're looking to kind of later stage trials?

Filippo Petti:

Good question. I think in general I think we'll continue to focus on the refractory patient population within the alloSHRINK trial in terms of recruitment and enrollment. Following that data set, we'll look to see how additional neoadjuvant patients could perhaps be included on future programs. I think right now we're just trying to—and then the refractory patient population allows us to really parse out the signal in terms of what perhaps 101 to be adding to a FOLFOX chemotherapy regimen.

I think we'll continue to focus on that patient population to better assess the potential of the therapy and that product candidate, and decide there as to how we think about a broader metastatic CRC program.

Raju Prasad:

Thanks, Fil.

Filippo Petti:

Thank you, Raj.

Operator:

Thank you. Our next question comes from the line of Ed White with H.C. Wainwright. Please proceed with your questions.

Ed White:

Hi. Thanks for taking my questions. Actually, most of them have been answered already, so I just want to ask maybe about timing. You gave us some timing on alloSHRINK with more data by the end of this year. Just thinking about what medical conferences you're thinking of presenting data at over the next year.

Filippo Petti:

Thanks, Ed. Appreciate the question. I think from our perspective I think there's a few conferences in the fall and at year-end that we can potentially aim for. We're in the process of reviewing when we would have a meaningful data set for us to provide the update. You can imagine it could be perhaps at the ESMO conference, but I would say for us to maybe target at SITC conference similar to what we did last year for the initial SHRINK data release, those are probably two top of mind that we're thinking of.

Ed White:

Okay. Thanks, Filippo. Then just I did miss what you had said was the third one you would talk about a data timeline for early 2020 to mid 2020. If you could just please repeat that? Sorry, I missed it.

Filippo Petti:

Sure. I think as we talked about earlier this week with regards to the relapse/refractory program, we'll have data from our schedule optimization Cohort 11 from the THINK trial by year-end. We'll have data from Cohort 3 of the DEPLETHINK trial by year-end as well, and we'll have some initial data from the Cohort 4 OptimAb process for CYAD-01 in relapse/refractory AML. Again, that will be initial data for year-end. The full data set we hope to have in the first quarter of 2020. As we get into 2020, obviously kicking off the CYAD-02 Phase 1 for us is certainly a high priority as we think about perhaps providing initial clinical data to folks by mid-year 2020.

Ed White:

Okay, great. Thanks. I appreciate it.

Filippo Petti:

Thank you, Ed.

Operator:

Thank you. Our next question comes from the line of Gary Waanders with Bryan, Garnier & Company. Please go ahead with your question.

Gary Waanders:

Hi there. Thanks for taking the questions. Just in terms of deciding the future strategy for auto versus allo and sort of 01 versus 02 and the various sort of next gen products, do you have enough data in terms of the dose-ranging studies you've talked about here and earlier this week to reach a decision on which of the options you'd take forward? Sort of related to that, is there a possibility that you can get ahold of tumor samples, either from biopsies directly or post surgery, in the case of SHRINK, to help you reach those decisions and look for in situ responses?

Filippo Petti:

Thanks, Gary. Maybe I'll turn it over to Frédéric to answer your second question first in terms of tumor samples and what we've been able to obtain so far from the SHRINK trial, and then I'll come back to your first question with regards to kind of the data sets that we'll look for in terms of progressing the programs. Frédéric?

Frédéric Lehmann:

Yes. Thank you, Filippo. Indeed, that was the primary intent in the context of the neoadjuvant setting that we set in the SHRINK study, so in the autologous program to go to the surgery at the end of the neoadjuvant treatment and therefore to have access to the tumor to have an evaluation of the tumor.

Having said that, we have enrolled four patients in that setting, three at the Dose Level 1 and one at the Dose Level 3 but we are in the context of a neoadjuvant standard therapeutic approach with FOLFOX so we have to remind us that it's really standard of care, it's by the way one of the very first times certainly in in solid cancer indications that the CAR-T has been proposed to patients in the first line metastatic treatment which is already quite shaking (phon) for some ethics committees but we have succeeded for that. Now in that context because of standard, because it's standard and we want to combine with FOLFOX 3, 4 and 5, all those patients on the standard schedule receiving a sixth cycle of FOLFOX before going to surgery, and on the thought based on the fact post cycle of chemotherapy usually you have one month of delay that all those patients 'recuperate' from those cycles of therapy before going to surgery, we have around one month and a half, two months between the last CYAD-01 infusion and the surgery and another FOLFOX chemotherapy, the sixth one, in between. So, in that context, plus the context of the type of quality of samples that we have analyzed, we have not seen any CAR-T cells into he tumor sampling that we have received, having said that with all the caveats as background that I provide to you.

In terms of global strategy, yes Filippo, you can hand over here.

David Gilman:

Frédéric, can I just add to that, please?

Frédéric Lehmann:

Sure.

David Gilman:

Yes, Gary. From the sample, as we say, the CAR-Ts are not so evident and this isn't surprising because, as Frédéric says, the dose of FOLFOX given after our last CAR-T cells will really be lymphodepletive. We are looking at those samples, of course, for NKG2D ligand expression as well and we will be discussing

the results of that much more as we get these data out in the coming months. Just wanted to add that. Thank you.

Gary Waanders:

Thank you. Thanks.

Filippo Petti:

Gary, with regard to kind of the data sets and what we have to date in terms of let's maybe tackling first on the solid tumor side, what we can say is we will continue to push forward on 101 for solid tumors, in particular metastatic CRC within the alloSHRINK trial. I think we've committed to adding some additional patients on the 1 billion dose level. We really want to see a larger data set to provide the analysis that we can get to in terms of moving that program forward. I think right now it's going to be a pause in terms of the autologous approach onto solid tumors until we get a better assessment of what 101 could provide.

Now, that doesn't preclude us from not having an autologous approach, but we have talked in the past about being able to have an allo approach and candidate for the treatment of solid tumors just because of David's remarks earlier around the logistics and the complexity, in particular around solid tumor indications and the high incidence rates associated with that.

We'll continue to evaluate 101; the opportunity to maybe—leveraging one of the questions earlier—to embed some additional thoughts around an allo program that could be anchored by TIM I think is, again, something that we are thinking about going forward. Let us pull together the next cohort of data and then make I think the right strategic decision in terms of how we move that forward, in particular around TIM.

For the relapse/refractory AML program, obviously the update earlier this week around OptimAb has us very excited, some of the initial data that we've generated on the in vivo side there. When we came out of the R&D Day in March, obviously for us there was this idea how do we get 01 closer to 02, and I think the OptimAb process, manufacturing process offers us a bridge towards that next generation approach. That being said, we will move forward with the 02 program as well. We'll have initial data that we'll be able to really make an assessment and I think it's a broader look at OptimAb, kind of a backbone approach to the 01 or 02 autologous programs. For us, too, I think in early 2020, based on the Cohort 4 data set, perhaps by mid 2020 based on the initial data from the 02 programs that we could decide which one of those programs we would think about moving forward into a potential expansion trial to really make an assessment on the program and the approach using autologous CAR-Ts in AML. But, you know, I think the initial data around 01 and Cohort 4 are going to really be kind of the first signpost for us to make a decision in terms of how do we perhaps add some additional optimization around and evaluating—and we talked about this the other day—evaluating perhaps some additional preconditioning in AML as well.

We'll continue to build that and built a larger data set that is OptimAb focused for relapse/refractory AML and I think it's a kind of hybrid between Q1 and Q2 that we kind of decide where we should go next with that program.

Gary Waanders:

Right. Can I just follow-up with a couple of short questions? Is it possible in alloSHRINK to give a second cycle of three injections of the product? That's the first one, simply. Then, is each patient in the alloSHRINK trial getting the same material from the same donor or are they all receiving different donor allo product? Thanks.

Filippo Petti:

Thanks for that follow-up. I think one of the questions we have had in terms of at least in the alloSHRINK program since we're starting it following the first cycle of FOLFOX, could we extend that out to six injections to layer on with all FOLFOX cycles I think is certainly something that's come up with the team and how we could potentially modify that, thinking about maybe that going into maybe next steps for the program.

With regards to the product itself, I'll maybe perhaps turn it over to David to provide some thoughts around the product and what was being provided to the full alloSHRINK patient population.

David Gilman:

Yes. Hi there, Gary. The cells are all generated from a single run. There's a single bank that's supplying all of the cells for this aspect of the clinical trial, so we estimated how many cells we'd need for this phase of the clinical trial and we generated a bank according to that, and so we're still continuing to work through those cells. The bank will last us through all of the clinical work that Frédéric discussed earlier. All from the same donor for this stage of the trial and it is of course really testing the allogeneic approach for us where we look to try and use a single bank to supply as much material as we possibly can for the clinical trial.

Gary Waanders:

How would future donors selected or chosen for future trials?

David Gilman:

There's no set criteria. What we did in-house for our 101 is we actually did test some different donors and all of them, actually, acted in a very similar manner and so we went ahead with one of those donors, and I'm sure that depending on next bank we would carry out an initial screen to ensure that cells from donor would be transfused and produce an initial product that looks like it had the very similar characteristics to the original bank of 101 and then we would culture those cells accordingly. But, of course, each individual bank generated from individual donors will all have slight differences, but we tend to find that the differences are much more minor when working with healthy human donors as compared to patients who are generally elderly and have a much more variable immune system. This is, of course, one of the underlying premises of using allogeneic cell therapy.

Gary Waanders:

Sure. Thank you very much.

Frédéric Lehmann:

Frédéric speaking. Maybe specific elements here on the clinical point of view. For this very specific patient population of the alloSHRINK, so patients who have received already FOLFOX, some of them also FOLFIRI or FOLFIRINOX, so four to five lines of metastatic chemotherapy, they have usually a lot of side effects, persistent chronic toxicity due to their previous chemotherapy lines, and mainly for oxaliplatin and 5-FU they have huge paresthesia, and therefore, in this rechallenge patient populations where, by the way, when we do rechallenge those patients by FOLFOX you have a lower objective response rate that that we are describing here with those very few patients today, it's not easy because by rechallenging them by FOLFOX you reactive, I would say, all those toxicities. In other terms, in the alloSHRINK where we are depending to combine with lymphodepleting FOLFOX as we selected, we are sometimes stopped by the fact that those patients due to the toxicity of the FOLFOX are not able to receive further administrations, which is obviously

one of the critical elements of our future development according to data generated in all those early clinical trials in 'Phase 1' patient populations, we can (inaudible) in the early stage where FOLFOX therefore has never been given to the patients and therefore you can go from six to even more cycles of chemotherapy and then we can imagine to indeed sustain the potential synergic effect of the two therapeutic approach to the patient by more than three cycles of administration of the CYAD-101.

Gary Waanders:

Lovely. Thank you very much.

Filippo Petti:

Thank you, Gary.

Operator:

Thank you. Our next question is from the line of Jim Birchenough with Wells Fargo. Please proceed with your question.

Male Speaker:

Good morning. It's Nick on for Jim this morning. As you know, we spent a lot of time earlier in the week talking about the OptimAb process, so is there any opportunity to introduce the OptimAb process for the 101? I mean I'm assuming that healthy donor T cells also express NKG2D ligands on activation. Then I have a follow-up.

Filippo Petti:

Sure. Thank you, Nick. It's a good question and I'll maybe hand it over to David to provide some initial thoughts there.

David Gilman:

Hello Nick and good morning to you.

Male Speaker:

(Inaudible).

David Gilman:

Yes. The OptimAb process that we really focused on is really looking in the autologous setting, first and foremost, and this really relates to the issues that deal with growing T cells from generally elderly patients who have advanced cancer and their lymphocytes are generally skewed. All of us have a long lived response against herpes viruses, for instance, and there's a skewing and exhaustion of the immune response as part of our every day life of getting older. So, the OptimAb process really is about trying to take cells from patients who have advanced cancer and try to encourage those cells to have a phenotype that looks more attractive for adoptive cell therapy and can potentially generate a more robust response in vivo.

The question around the healthy donor, of course, and one of the main rationales of using the allogeneic approach is that the cells are generally taken from younger and I hesitate to say they're fitter people, and their immune is similarly in much the same way.

So, we're not sure. We're sure there could be a benefit of increased—of introducing the OptimAb process into the allogeneic setting, but we're not quite sure what the magnitude will be simply because of the comparison of the dose of cells. This is certainly something that we'll look at but certainly one of perhaps the first indications that there is this real difference between healthy cells, healthy donor cells and those of patients actually is in this study where at the same dose we seem to see a higher relative increase in the number of cells you can select (phon) in the peripheral blood in the alloSHRINK trial as compared to the same dose in SHRINK, suggesting that perhaps these healthy donor cells are able to actually engraft and have higher activity, which of course the OptimAb is trying to bring into the autologous situation.

That's a long answer to say I'm not sure it is needed but we'll certainly look to investigate whether the OptimAb brings something to the allogeneic setting that gives a significant improvement, but at the moment, of course, it is too early for us to be able to say. We're really focusing on the autologous situation at the moment.

Male Speaker:

Thanks. I think if we're looking at the poster I think I know the answer, the type of patients then who have had a partial response in 101 trial, that patient remained unresectable throughout the duration of that partial response?

Filippo Petti:

Frédéric, would you like to provide some additional thoughts around that partial response in the 101 alloSHRINK trial?

Frédéric Lehmann:

Yes, correct. Very good questions. Yes, unfortunately this patient has multiple metastases in the lung, in the liver and et cetera. This patient was not in a setting where you could potentially go to a resectable mode.

Male Speaker:

Okay. Thank you. (Inaudible) earlier about GvHD but did you look at—is there a cytokine profile that might give you insight into subclinical GvHD with 101?

David Gilman:

Thank you. I'll pass over to Frédéric, actually, because we were discussing just this earlier from the biochemistry of the patient. Frédéric, would you like to discuss those results?

Frédéric Lehmann:

Thank you again for the question. There is two levels of the question. The first question is, is there any biological/biochemistry impact of the biology that we can see in terms of impact of the Graft-versus-Host-Disease? For example, liver dysfunctions, renal dysfunctions, etc. Obviously, strictly no impact on organs, on the different organs,

Now in terms of indeed cytokines induced either by the context of the cytokine release syndrome, by the engraftment of the cells, by the inductions of the FOLFOX chemotherapy and by potentially subliminal Graft-versus-Host-Disease I have to say that the first data are very preliminary and still under analysis, we do not see any major point of attention. And again, as mentioned by the Filippo, with the embedded—because we do believe that it's more important with the highest dose where potentially we could have such a kind of effect for the Dose Level 3 with 1 billion of cells where we will have six patients. At the end of this year either ESMO, SITC or other peer-review congress, we will have generated all those data to have a compiling and global vision of the situation.

Male Speaker:

Thank you. Then the last one for me, I'm just looking at the swimmer plot from the poster and so starting with the 01, there's the one patient who is now out at seven months; it looks like they received an additional dose of FOLFOX (inaudible) he just got a single treatment, not a new course. Why was that?

Frédéric Lehmann:

It's Frédéric speaking. This is a very good question. We always have to pay attention as soon as we are discussing about case report (phon), but indeed this is a very interesting case report, so we are referring to the first patient of Dose Level 1 of the alloSHRINK trial, the patients in which there was an induction of the partial response. Interestingly, the patient received six cycles of FOLFOX initially with the three first ones with the CYAD-101 and the patients we induced a partial response. Then the study design the patient was not receiving any more CYAD-101 in combination of the three next, so Cycles 4, 5, 6, cycles of FOLFOX, and you can see according the arrow that indeed patients remained in partial response but actually one or two months after the patients, so approximately at Month 7, the patient was considered as in progressive disease. But, because we are in the context of the patients where there is no standard therapy anymore, so typically these patients receive a cycle of chemotherapy for FOLFOX, FOLFIRINOX, and FOLFIRI (inaudible) so he received Lonsurf and rego, the patient had no standard treatment anymore, and because of progression—actually, I'm entering here in details—out of each number of metastases of the patients, the very large majority of those lesions are stable and actually this progressive disease, according to RECIST international criteria 1.1 was driven by one main lesion that was increasing, making that the sum makes SPD, and therefore in that context the principal investigator decides in this global context with the patient in front of him to continue to receive another FOLFOX chemotherapy, and that's the reason that you see in the context of this progressive disease still the site have took the options to continue the FOLFOX chemotherapy.

Male Speaker:

(Inaudible) the first patient for the third dose level also had a novel dose of FOLFOX. That was the PL (phon) patient that you described, but in the 01 there's a stable disease patient had their six cycles and then there was a break and they had this other cycle; they're now still in stable disease at Month 7, so that again was …

Frédéric Lehmann:

Correct.

Male Speaker:

That again was FOLFOX therapy?

Frédéric Lehmann:

Again, we are in the very good point of detailed questions here. Indeed, we always have to pay attentions case report, but indeed, if we are referring to the first patient of Dose Level 3 of the SHRINK study, so the autologous CAR-T, indeed, this patient received six administrations of the CYAD-01 in combination with the different initial FOLFOX, the patients was considered as stable disease. It's actually even now on Month 7 still ongoing so the patient is in stable disease, which is already pay attention to case report but in the context of this kind of patient population it's quite interesting, and again, in the absence of any other 'options' and especially that the patient is in stable disease, the site preferred to provide to the patients from time to time some FOLFOX chemotherapy, but after, indeed as you highlighted, after a gap of two months between the end of the study treatment protocol and the first and single FOLFOX administrations in order to potentially consolidate the stable disease.

Again, in the context—and I'm referring to previous discussion—importantly, in that context the toxicity induced by the FOLFOX chemotherapy, and again mainly important visibility in terms of paresthesia of the hands of the patient was not able any more even to make daily activities, they had to stop the even FOLFOX consolidation chemotherapy.

Male Speaker:

Great. Thank you very much. Maybe just one quick one for Fil. Fil, I mean in terms of a small molecule and (inaudible) your old Wells Fargo hat on, I mean these (inaudible) are really quite encouraging in very advanced patients. I think the question was asked before about strategy. I mean what do you need to see in colorectal cancer before you decide, 'Okay, we really have something here. We should really increase our investment in this particular indication?'

Filippo Petti:

A very good question, Nick, and look, I think from our perspective we're encouraged by the data set we've seen so far and to your point in a very heavily pretreated patient population. In particular around the 101 candidate, I think we want to get to the additional dose level of 1 billion cells injected three times from Cohort 3, and that's why to a certain extent we're extending that out to at least six patients now, to not only evaluate the potential clinical activity there but also the safety side of it. I think as we dose escalate up we want to make sure that we continue to control the GvHD part of the equation and based on that I think, to your point, we really—we need to consider how we move that program forward into a broader approach for the treatment of metastatic colorectal cancer.

I think to your question earlier also around some of the translational work, I think we want to have a very broad picture of the program and the alloSHRINK trial before making a decision on how we progress that.

Male Speaker:

Thank you very much.

Filippo Petti:

It's certainly encouraging. Thank you very much, Nick.

Operator:

Our next question is from the line of Ingrid Gafanhão with Kempen. Please proceed with your question.

Ingrid Gafanhão:

Hi there. Thank you for taking the question and congrats on the presentation. I think my question was more or less already answered, but anyway. I think it might be too early for me to be asking this, but do you believe that at this point we are able to single out how complementary the activity of CYAD-01 and 101 to FOLFOX? Just basically, in short, what kind of benchmark would we be looking at from the clinical relevance perspective that would influence your moving forward decision?

Filippo Petti:

Ingrid, thank you very much for the question and the comments. Look, I think for us in terms of the refractory patient population in metastatic colorectal cancer I think that we talked about earlier in one of the other questions with respect to kind of focusing on this patient population at the moment given it provides us a better opportunity to decipher what the signal to noise is and being able to have a treatment such as 101 on top of a standard of care such as FOLFOX, primarily not only around safety as Frédéric has certainly detailed, but also in terms of objective response rate and what we know and obviously having one patient out of the six show a partial response I think is very encouraging for us, but we'll need to continue to build upon that data set.

If we look historically, and our understanding of the treatment of patients with refractory colorectal cancer and rechallenging them with FOLFOX, the data that we have provides response rates in the mid single digits perhaps to the low teens, so I think we just wanted to make sure that we take a conservative perspective in terms of what the benchmark should be for us to better assess the program there, but I think we're certainly encouraged by the initial partial response. We want to continue to see if we dose escalate up that we continue to build upon the clinical activity seen to date without having to sacrifice the tolerability of the agent, but we're certainly encouraged by the preliminary results seen from the first two cohorts of the alloSHRINK study.

Ingrid Gafanhão:

Thank you.

Operator:

Thank you.

Filippo Petti:

Thank you.

Operator:

The next question is from the line of Thomas Landemaine with Kepler Cheuvreux. Please proceed with your question.

Thomas Landemaine:

Good afternoon and congratulations for these results. Could you please repeat what are your plans for CYAD-01 in solid tumors?

Filippo Petti:

Sure. Thomas, thanks for the question. I think at this point based on this SHRINK data, we've completed the dose escalation for 01 within that clinical trial. We'll continue to provide some additional analyses there, but I think at this point we will focus our attention to the 101 candidate with regards to the treatment of metastatic colorectal cancer.

I think, you know, in one of the other questions that has come up in I think part of the discussion earlier this week is would there be a potential to maybe evaluate an OptimAb process or OptimAb-01 focused product perhaps in the solid tumor context of metastatic colorectal cancer, I think we'll look to unveil some of the initial data from the Cohort 4, perhaps from 02, to make a decision on how we circle back with using an autologous program at this stage in the context of solid tumor. Right now, I think we will be judicious in trying to tease out the remaining alloSHRINK Cohort 3, build a data set for us to make an analysis around 101 and then ponder as to how we think about 01 in the context of the treatment of solid tumors, and I think that's a little longer in terms of the assessment there.

Thomas Landemaine:

Thank you.

Filippo Petti:

Thank you, Thomas.

Operator:

Thank you. At this time there are no additional questions. I'd like to turn the floor back to Management for any further remarks.

Filippo Petti:

Great. Thank you, Operator. If there are no more questions, I wanted to just quickly recap that we are very excited about the progress made in our clinical development programs across a number of different trials, in particular our solid tumor program for the treatment of metastatic colorectal cancer, as well as the update we had earlier this week with respect to our relapse/refractory AML and MDS program. We believe our platform of technologies have provided us a number of opportunities to drive near-term and long-term value to our stakeholders.

We thank everyone for joining the call and we look forward to speaking with you again soon.

Operator:

Thank you. Today's conference has concluded. You may now disconnect your lines at this time and thank you for your participation.