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EDITED TRANSCRIPT

REGN.OQ - Regeneron Pharmaceuticals Inc at TD Cowen Oncology Innovation Summit (Virtual)

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CORPORATE PARTICIPANTS

Israel Lowy Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences - Oncology

L. Andres Sirulnik Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences, Hematology

Ryan Crowe Regeneron Pharmaceuticals, Inc. - VP of IR

CONFERENCE CALL PARTICIPANTS

Tyler Martin Van Buren TD Cowen, Research Division - MD & Senior Equity Research Analyst

PRESENTATION

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

All right. We'll give it a couple of seconds for everyone to join. Okay. So with that, welcome, everyone, again, to the TD Cowen's Fourth Annual Oncology Innovation Summit: Highlights for ASCO and EHA. My name is Tyler Van Buren, senior biotech analyst here at TD Cowen. For our next session, we're very pleased to have a fireside chat with Regeneron. And it's my sincere pleasure to introduce Izzy Lowy, Senior Vice President of Solid Organ Oncology Development; and Andreas Sirulnik, Senior Vice President of Heme-Onc Development. Izzy and Andreas, it's a privilege to have you both here. Thank you very much for joining me.

L. Andres Sirulnik - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences, Hematology

Thank you for having us, Tyler.

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

Ryan, Head of IR -- Ryan Crowe, Head of IR, thank you very much for being here as well. I know you have some forward-looking statements to go through, so I'll hand it over to you for that.

Ryan Crowe - Regeneron Pharmaceuticals, Inc. - VP of IR

Most important part of every presentation, Tyler. I would like to remind you that remarks made today may include forward-looking statements about Regeneron. Each forward-looking statement is subject to risks and uncertainties that could cause actual results and events to differ materially from those projected in such statements.

A description of material risks and uncertainties can be found in Regeneron's SEC filings. Regeneron does not undertake any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

That was awesome. Very exciting. And I'll hand it back to you for a brief overview, but before I do, for those of you tuning in, feel free to e-mail me at first.last or tyler.vanburen@cowen.com if you have any questions for the team during the fireside. You can also submit them via the Ask a Question box in the panel.

So with that, Ryan, to start, maybe you could provide a brief overview of the data sets that we can expect to see across Regeneron's pipeline at ASCO this weekend, and then we'll pass it over to Andreas and/or Izzy, if they'd like to add anything as well.

Ryan Crowe - Regeneron Pharmaceuticals, Inc. - VP of IR

Yes. Thanks, Tyler. I think this is another important oncology conference that shows the incremental progress that Regeneron continues to make in expanding its presence in oncology, and it's really centered around 2 foundational and synergistic approaches, PD-1 inhibition with Libtayo and our investigational bispecifics. In the 2 presentations that are oral at ASCO, we're going to be sharing longer-term results for the BCMA targeting bispecific linvoseltamab, which Andres will speak to.

This is in a relapsed/refractory multiple myeloma setting. Most of these patients have had at least 3 prior lines of treatment. And then we also have an exciting update for the fianlimab program with results in advanced melanoma patients that were previously treated with anti-PD-1 therapy in the adjuvant setting. So important updates for both of these programs.

We actually issued 2 press releases last week previewing these data sets. So you may have seen some of the highlights there. And our comments are going to generally remain within the balance of that until the presentations.

Linvoseltamab data will be presented on Saturday afternoon in the heme malignancies session, while the fianlimab-Libtayo data will be presented on Monday morning -- I'm sorry, Monday afternoon during the melanoma and skin cancers oral presentation session.

With that, I'll hand it to Andres for some brief remarks about linvoseltamab and then Izzy can speak to fianlimab, and then we'll get to your specific questions, Tyler.

L. Andres Sirulnik - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences, Hematology

Yes. Thank you, Ryan. So an oral presentation at upcoming ASCO, we will be presenting longer-term follow-up of our ongoing Phase I/II potentially pivotal study with our linvoseltamab, BCMAxCD3 bispecific. In a press release last week, as Ryan mentioned, we highlighted some of the key outcomes of what we'll be presenting. We continue to be very encouraged with data that is emerging with longer follow-up in terms of the level of efficacy, durability and safety profiles that are emerging.

Just to give you a quick bottom line is that our response rates continue to increase in our higher dose of 200 milligrams that has been chosen to move forward. The safety profile remains very manageable and promising. And I think that in terms of dosing is a place where we will be differentiating and we'll talk a little bit more about it later. But I think that when you put it all together, we have a highly active competitive BCMAxCD3 bispecific with an overall response rate of 71%, which is very encouraging and competitive.

And as I mentioned, the safety profile with us to highlight low levels of CRS in the level of 45%, but mostly grades 1 that reassure us that we are on the right track there.

So saying that, maybe Izzy, you want to highlight a little bit what we will be sharing.

Israel Lowy - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences - Oncology

Sure. Thank you. So the other oral abstract we have at ASCO is on our updated data on our fianlimab program, anti-LAG-3. It includes additional follow-up from -- 2 cohorts that we previously discussed that gave us test and retest confirmation of very high response rates in patients with first- or second-line melanoma who are naive to anti-PD-1 therapy with response rates north of 60%.

And in this abstract, we're also providing information on patients who receive systemic therapy in the neo-adjuvant or adjuvant setting, including over a dozen patients who received anti-PD-1 as their adjuvant therapy, but unfortunately, after completing that therapy, subsequently relapsed, and they too had a -- in that group of 13 patients, we had a 62% response rate in these patients. So what we are very excited about is that we're looking at responses -- response rates that are double -- nearly double that of what you would get with anti-PD-1 alone and highly competitive with the currently approved anti-LAG-3 therapy out there -- and give us a lot of confidence and hope there are ongoing Phase III studies in melanoma,

both in advanced melanoma and in adjuvant melanoma will be successful. We have quite a few other studies also underway, and I'm happy to answer any additional questions as they come up.

QUESTIONS AND ANSWERS

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

Great. Andres and Izzy, those were perfect introductions. Thanks for all the background.

I'll plan to start with linvo and a couple of questions on Odro and maybe a CD28 before we get into fianlimab. But so -- with the linvoseltamab data, very pleased to see the updated data in the abstract, right, 3 months of follow-up at ASH, very limited follow-up.

So I'm not surprised to see the response rates continue to deepen. But I guess -- so we have 6 months as of the ASCO abstract. When we get the ASCO presentation, we should have hopefully, even more time right with an additional cut?

And I guess my question is, would you expect that -- is there a potential for that 30% CR rate to continue to deepen as we look to compare it to program -- other programs like Tecvayli's 39% CR rates.

L. Andres Sirulnik - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences, Hematology

Maybe I'll start with the last part of your question, I want to highlight that based on what we have learned and as we are following the data and what we know about the linvo. We do expect those CR rates to increase over time. Again, you highlighted that what we will be presenting at ASCO is a longer follow-up on, I would say, 2 large cohorts of patients. A patient that was -- a cohort of patients treated at 50 milligrams and cohort of patients treated at 200 milligrams. Those were the 2 doses that we expanded.

And at ASCO, there will be approximately 60 additional patients in the 200-milligram cohort compared with what we show at ASH and for both, we have longer-term follow-up, particularly for the patients at 50 milligrams because we initiated that expansion earlier.

And what I can say is that we continue to see high rates of responses. I mentioned to you the overall response rates of around 71%. And we are seeing a consistent safety when it comes at what we've seen at ASH and we will be presenting now. So both remain consistent with high response rates, the manageable safety profile that we will be showing. So the safety is based on the pool of patients, over 200 patients and then we'll talk about efficacy, primarily at the 200-milligram dose, which is the one that we have chosen to move forward.

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

Okay. That's clear. And in terms of linvo safety profile, I think it'd be helpful to just understand the evolution of safety in these trials and the changes that you made over time to get to where you are today.

L. Andres Sirulnik - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences, Hematology

Yes. So I think that when it comes to safety, most people focus on cytokine release syndrome for the class, all right? And I am very pleased to say that -- even when you look at the 50-milligram cohort, the 200-milligram cohort, we see consistent rates of CRS and that is to the point that CRS occurs almost invariable in the first 1, 2 doses of linvoseltamab with very rare cases beyond that.

And we observed 45% of CRS in the 200-milligram cohort. And as I mentioned to you earlier, there were no cases of grade 4, no cases of grade 5. I think all you know, there was 1 case of grade 3 and the rest were, primarily out of 45%, the vast majority were grade 1. Just to remind you, that's just fever.

So we touched about, in terms of the cytokine release syndrome, of course, the overall safety remains very consistent with what we presented at ASH and in line with CRS, the most common adverse effects reported. I think that I alluded to this, but what is important to note is that we have a very predictable and early onset of CRS. As I mentioned, it occurs in -- mostly in the first 2 doses within 15 hours of initiation and results within 1 day. And this has led to how this program evolved in terms of hospitalizations.

And I think that that's where we have, what I believe, a competitive edge. Unlike other CD3-BCMA bispecifics, we only have 2 in total hospitalizations as per protocol. We hospitalized for 24 hours on the first dose, and we hospitalized for 24 hours on the second dose on day 8. And that's it. In fact, we are -- per protocol allows investigators potentially to do away with the second hospitalization if they have not experienced any CRS and they are tolerating well the treatment.

And in addition to that, we allow investigators in the trial to reduce the infusion time. So we initially start with 4 hours. And if patients are tolerating this well, we reduce it to 30 minutes. An infusion of 30 minutes is the time that you spend on a chair for subcutaneous dose, all in all. So we think that this is the -- a very competitive edge to linvoseltamab.

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

Yes. Yes, that's clear. So the rates are a lot lower. It's earlier, more predictable, clearly differentiated on the safety side, particularly with respect to CRS. Why do you think you guys may be seeing that. Is there a clear mechanistic reason or a way that linvoseltamab was designed that explains it?

L. Andres Sirulnik - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences, Hematology

I think that it's very difficult to tease out what is due to the antibody vis-a-vis the treatment paradigm in terms of how we premedicate and so forth. But all in all, I would say that not all bispecific antibodies are the same. And we are starting to see this not only here, but we're starting to see that with other bispecifics. So I think that, that is important. And talking about differentiation, I'm going to focus for a minute on efficacy.

I mentioned we have 71% overall response rate. These are incrementally better than what we showed at ASH, but very competitive and very impressive in my view. I think that -- what is important here is that when you look at the patient population that was included in this trial vis-a-vis the patient population that have been reported for teclistamab, for example, and others, and I mentioned teclistamab because we have a label to look at. Our patients seem to have higher disease burden. And when we see our responses, what we see is that there are consistent both in patients that have low disease burden and patients that have high or very high tumor burden.

And what we look at is, for example, the number of plasma cells, tumor cells in the bone marrow. When we look at patients that have high-risk cytogenetics, when we have patients that have high soluble BCMA, which is another market of a tumor burden, our patient population have, I would say, more than double on what the patients that have been included in other studies and we would see consistent, very good responses in all these subpopulations that we study. So that, again, is very encouraging on how this antibody is differentiating.

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

Okay. That's very helpful additional context as we think about comparing the efficacy data. So you guys remain on track to submit the BLA for linvo in third line plus multiple myeloma in the second half. Before we leave linvo and ask odronextamab question, can you briefly discuss your future plans for linvo in terms of earlier lines of therapy and what the broad strategy looks like there?

L. Andres Sirulnik - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences, Hematology

Absolutely. So for linvoseltamab, yes, we will remain on track for filing in the second half of this year. And we are expanding the program. We're moving to early lines of therapy. We are initiating a pivotal trial in second plus lines of therapy where we are going to be comparing linvo monotherapy versus standard of care.

I mentioned the overall efficacy that we are seeing is such that we believe that monotherapy is an option for patients and could potentially spare the toxicities associated with multidrug regimens. And with that in mind, we are exploring as well combination with other therapies in early lines of therapy as well as late in lines of therapy, we are moving into first line and potentially even into premalignant conditions. That's one aspect that I think may differentiate us here. So that's it.

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

Okay. That's great. In the essence of time, I'm going to get to fianlimab, but because there's so much to discuss there as well. Obviously, the odronextamab follicular lymphoma data at ASH looked great. DLBCL is strong, and that data will probably continue to improve and you guys plan to file by the end of the year, and you'll have CD28 updates as well, more and more to discuss in oncology for you guys as time goes on.

But now turning over to Izzy and LAG-3 and fianlimab, very helpful overview of the data that we've seen a nice continuance in the naive data that we saw at ESMO. But in checkpoint experienced patients, I saw that 62% response rate and was pretty surprised, frankly, albeit a small sample size, but surprising, nonetheless. Can you explain why you guys might be seeing that in this patient population and how you view the opportunity moving forward?

Israel Lowy - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences - Oncology

Sure. Thank you. So let me make sure people really understand the patient population because I don't want people to get the impression that we're taking patients who are progressing on PD-L1 or PD-1 and adding LAG-3 and getting a high response rate.

We're talking about people who, at the time of their resection of their melanoma, a curative intent resection, but with certain high-risk features, receive a course of adjuvant anti-PD-1, finished, and then were followed, and 6 months or more after that relapse. So I think the question that we all had was that pre-existing relatively remote exposure to anti-PD-1 going to impede the ability of a PD-1 containing therapy to cause a profound response rate.

And the answer so far in this small set of patients is very encouraging and seems to be no that after 6 months or more after therapy if patients have relapsed, they basically have reset and they can receive a combination of PD-1 and LAG-3.

We do -- we have reported in the past that if you add LAG-3 to patients who are rapidly or in the process of progressing on anti-PD-1, we don't see the same kind of response rate. It's much more in the order of like 10% to 15%. They're real, but it's much lower. And that's consistent with what everyone else has seen in the field. But I think given the increasing prevalence of patients who will receive an anti-PD-1 in the adjuvant setting or the neoadjuvant setting, it is good to know that should they recur in the future, a PD-1 containing regimen including LAG-3 has the potential to be just as potent as if they were completely -- PD-1 completely naive.

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

Okay. Very interesting. I guess obviously, Merck and Moderna have presented and will present more data at ASCO with PCV combination in the adjuvant setting, but that is kind of more the true adjuvant setting and not after they're relapsing, right? So you guys would be looking to kind of come in even after then, right, with the LAG-3 combination.

Israel Lowy - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences - Oncology

No. We're -- well, we're doing a study in patients who are -- we have 2 studies underway that are registrational. One is in the advanced melanoma setting, patients who have unresectable or metastatic disease, whether or not they received adjuvant PD-1 at this point for the testing of the combination of fianlimab and cemiplimab against standard of care pembrolizumab.

We also have an adjuvant study underway for patients who are having a resection of the high-risk -- resection of melanoma with high-risk features at risk for recurrence. And there, we're also testing the ability of anti -- of cemiplimab and fianlimab to offer a better relapse-free survival than the use of anti-PD-1 alone.

Now whether or not the combination of an anti-PD-1 and an individualized patient vaccine also offers a benefit remains to be seen. That was -- it was an initial promising data, although it was a relatively small study. But we're very optimistic based on the high response rate that we've seen.

The fact that we have not seen the duration of response has not reached the median yet. And a progression-free survival in the advanced setting of 15 months based on current estimates compared to the 10 months that was presented in the Opdualag study, we think we have a very promising option for these patients.

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

Okay. That's very clear. And then could you just give a brief overview of the potential timeline to top line data for both of those Phase III studies?

Israel Lowy - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences - Oncology

Sure. So we've given general guidance that we hope to have data in 2025 from both the advanced melanoma setting and potentially an interim look in our adjuvant study as well.

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

Okay. And then for the advanced melanoma Phase III readout, what do you think you guys need to show to be successful and compete effectively against Opdualag.

Israel Lowy - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences - Oncology

Well, I think if the data that we've seen in the 3 different cohorts that we've tested now holds out, and we continue to show a higher response rate, a longer duration of response and an even better progression-free survival, we'll be in a very competitive space.

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

Yes. And in the metastatic setting for IO-LAG-3 combination, how do you view the ultimate long-term opportunity? Where do you think this combination will truly exist? And what sort of share do you think it might be able to take?

Israel Lowy - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences - Oncology

Beyond melanoma, you mean?

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

Sorry, within melanoma. Obviously, even Opdualag is still relatively early in its launch.

Israel Lowy - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences - Oncology

Well, I think we're relatively -- we're not very far behind. So if we have a better agent, usually the better agent wins. So as I said, we have really compelling efficacy. The first cohort we did where we saw a 62% response rate. We were stunned, so we repeated it. We saw another one. And now the third time around, we're seeing it again even in patients who had adjuvant PD-1. So we believe it.

It's obviously a total experience of only 100 patients or 98 patients. So we need to have a full-fledged Phase III to nail it, but this is not subtle. And it rivals the type of efficacy that has been observed with combinations of anti-CTLA-4 and anti-PD-1 with a much superior tolerability and safety profile. So we have to see that it -- so we have very high expectations for it. And we believe it has potential in multiple other indications.

So we are running a Phase II/III lung cancer pair of trials, one with chemotherapy and one without chemotherapy to nail down and see whether or not our initial signal in a much smaller cohort really holds up as well.

And if it does, we'll flip that to Phase III programs and we're exploring a number of other indications as well. We don't know for sure, but we're hoping that LAG-3 -- fianlimab in combination with cemiplimab can emerge to be a next sort of incremental step-up from PD-1 monotherapy that is versatile, well-tolerated and applicable on a large number of tumor types.

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

That sounds good to me. We're -- we're over time now, but maybe we'll just wrap up with a final question. Both Andres and Izzy, what would you consider the most underappreciated aspect of Regeneron's oncology pipeline by investors?

Israel Lowy - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences - Oncology

The most underappreciated is our people.

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

I like that. Andres?

L. Andres Sirulnik - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences, Hematology

I think that people -- I think that we have a tremendous opportunity to make a difference. And when I look at linvoseltamab, for example, I think that we have the potential to be best-in-class when we look at our CD20xCD3 bispecific, odronextamab, I think that we have an opportunity, particularly in follicular lymphoma to differentiate. And I think that when you look at the potential of continuing to solidify our presence in oncology, we will bring a tremendous value proposition to the table.

And to highlight, I think this is the same in the solid tumors as in the heme space, we are coming with the next generation of co-stimulatory molecules. We are already in the clinic in prostate cancer. We are combining already.

We dosed our first patient with odronextamab with a CD28xCD22 bispecific and eventually, we'll enter the clinic with a CD28 by another antigen in myeloma, giving us an opportunity to really differentiate from others.

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

Absolutely. You guys have a lot going on. Andres, Izzy, Ryan, thank you very much for your time.

L. Andres Sirulnik - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences, Hematology

Thank you, Tyler.

Israel Lowy - Regeneron Pharmaceuticals, Inc. - SVP of Translational & Clinical Sciences - Oncology

Thank you.

Ryan Crowe - Regeneron Pharmaceuticals, Inc. - VP of IR

Thanks, Tyler.

Tyler Martin Van Buren - TD Cowen, Research Division - MD & Senior Equity Research Analyst

Take care.