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Q1 2021 Agenus Inc Earnings Call

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PRESENTATION

Operator

Good morning, ladies and gentlemen. Thank you for standing by and welcome to Agenus First Quarter 2021 Conference Call and Webcast. (Operator Instructions) Please note that this event is being recorded and may be used in future Agenus promotional material.

I would now like to turn the conference over to Jan Medina, Director of Investor Relations. Jan, please go ahead.

Jan Medina *Agenus Inc. - Director of IR*

Thank you, Rebecca, and thank you all for joining us today. Today's call is being webcast and will be available on our website for replay. I would like to remind you that this call will include forward-looking statements, including statements regarding our clinical development, regulatory and commercial plans and timelines, as well as timelines for data release and partnership opportunities. These statements are subject to risks and uncertainties and we refer you to our SEC filings for more details on these risks. As a reminder, this call is being recorded for audio broadcast.

Joining me today are Dr. Garo Armen, Chairman and Chief Executive Officer; Dr. Jennifer Buell, President and Chief Operating Officer; Dr. Steven O'Day, our Chief Medical Officer; and Christine Klaskin, Vice President of Finance. Now I will turn the call over to Garo to highlight our progress during 2021 so far.

Garo H. Armen *Agenus Inc. - Founder, Executive Chairman & CEO*

Good morning, everybody and thank you, Jan. Thank you all for your participation and interest in Agenus. In the past 7.5 weeks since our last call, we have continued to make progress on our key programs and milestones. These include additional clinical trial data advancing our iNKT programs in COVID and cancer, earning 2 presentation slides at ASCO, filing our first BLA, defining our strategy for 1181 and being on track for cash-accretive corporate transactions for this year with a start in the current quarter.

Firstly, we announced that we submitted our balstilimab BLA to the FDA for the treatment of recurrent or metastatic cervical cancer under the accelerated approval pathway. Second, regarding our next generation CTLA-4 inhibitor AGEN1181, at the AACR Annual Meeting in April we disclosed new clinical responses for this antibody. There has been steady and impressive results continuing the trend we had previously disclosed. Additional data and clinical responses will be presented at upcoming conferences. Third, regarding our iNKT program, we had indicated in our last call in March, we extended our iNKT clinical development program into cancer. While we continue to advance iNKT cells in patients with acute respiratory distress syndrome secondary to COVID-19, we have recently announced the initiation and dosing of our first patient with cancer and will soon initiate our cell therapy combinations with checkpoint antibodies in solid tumor cancers.

Turning to TIGIT, we have advanced our efforts and expect to file an IND for our lead anti-TIGIT program AGEN1777 bispecific during this current quarter.

Next regarding corporate transactions, we continue to expect cash-accretive corporate transactions this year starting in the current quarter.

While there has been tremendous upheaval around the world over the last 12 months, Agenus' core mission is unchanged and we are on track with the delivery of our objectives. Speed and quality of our innovations is and will continue to be the core to our strategy. We will continue to marshal the best people and the resources that are paramount to achieve success for us.

I would like to now turn the call to our President and Chief Operating Officer, Dr. Jennifer Buell. Dr. Buell?

Jennifer Buell ***Agenus Inc. - President & COO***

Thank you, Garo. As Garo described, we made great progress during the opening months of 2021 advancing each major program efficiently towards our major objective. He also mentioned that speed of innovation remains our imperative. The industry standard for timelines and drug developments from ideation to the clinic is 4 years. But in that same time, we've actually delivered 15 new discoveries. This is in part attributable to our technology integration. This is realized in our VISION platform, short for virtual systems for immuno-oncology.

What is VISION's purpose? The purpose of VISION is to generate superior I-O assets in less time by quickly defining why and how immunotherapies work to control tumors. VISION enables quicker validation of drug targets. It empowers faster-optimized molecule design, faster drug candidate selection. It defines biomarker signatures that predict which patients will respond to therapy and VISION offers ways to customize those treatments to expand patient benefit.

What is VISION? VISION is a virtual drug discovery system. It mimics or recapitulates a patient's tumor microenvironment and their immune system. It uses artificial intelligence and predictive algorithms to explore a much broader range of drug biology interactions than any human capability. We can generate data and provide feedback in real-time to enable better drug discovery decision-making.

More importantly, VISION has helped give rise to our pipeline of differentiated molecules. This includes balstilimab, our PD-1 inhibitor, which we believe is showing differentiated activity preclinically and clinically. This also includes AGEN2373, that's our CD137 antibody. Both antibodies will be featured in an upcoming virtual ASCO Annual Meeting in early June. And of course, this also includes AGEN1181, our anti-CTLA-4 antibody, we believe is showing the potential to have best-in-class activity in the clinic.

And with that said, I'll turn the call over to Dr. Steven O'Day, our Chief Medical Officer, to provide his insights on 1181 including the differentiated activity we disclosed at this year's AACR Annual Meeting. Steven?

Steven J. O'Day ***Agenus Inc. - Chief Medical Officer***

Thank you, Jen. As Jen and Garo discussed, we've made additional progress with AGEN1181. The evolving clinical data strongly supports the preclinical slot bindings and continues to show the strength of the engineering behind this antibody. We anticipate additional AGEN1181 clinical data disclosure at upcoming clinical conferences. As the data matures, we continue to see responses in cold tumors, traditionally a very difficult set of tumors to treat with IO therapy. These cold tumors are typically low in tumor mutational burden, they are microsatellite stable, and they have lower negative PD-L1 expression. This is in contrast to warm or hot tumors that typically have higher tumor mutational burdens, they can be high microsatellite tumors, and they have higher levels of PD-L1 expression. These warm or hot tumors are typically related cancers to environmental exposures like tobacco, alcohol or viral pre-tumors. In addition, we have noted responses in patients with the low-affinity CD16 allele, which data suggest would be expected to have an inferior response to first-generation CTLA-4 antibodies.

The clinical trial to date has been dominated by traditional cold IO tumors due to referral patterns to Phase I IO trials. Recently we have treated our first patient with melanoma, a hot IO tumor, with single-agent 1181 with a rapid objective response. This patient was PD-1 refractory and importantly had CD16 low-affinity allele. Regarding adverse events, no immune-mediated hypophysitis, pneumonitis or hepatitis have been reported to date, which is encouraging and favorable compared to patients treated with Yervoy based IO regimens. As of our latest disclosure at AACR's annual meeting in April, we've observed a total of 7 objective responses, including 2 responses in endometrial cancer, 2 responses in colorectal cancer, 2 responses in ovarian cancer and 1 response in melanoma.

We believe we have tremendous flexibility with the clinical development of AGEN1181 and the potential regulatory path. Studies are

continuing as monotherapy with 1181 and in combination with our PD-1 inhibitor balstilimab. We plan to develop AGEN1181 in indications that represent large market opportunities. This strategy is exemplified in our ongoing Phase II expansion cohort of MS-stable colorectal patient in our current trial, which is actively accruing patients. Our initial registration plan targets indications for rapid launch by seeking approval through the accelerated approval pathway as monotherapy 1181 or on top of our PD-1 balstilimab or any approved PD-1 including patients with unmet need.

I'd like to now turn the call over to Christine Klaskin to discuss our financials.

Christine M. Klaskin ***Agenus Inc. - VP of Finance, Principal Financial Officer & Principal Accounting Officer***

Thank you, Steven. We ended our first quarter 2021 with a cash balance of $119 million as compared to $100 million at December 31, 2020. Cash used in operations for the 3 months ended March 31, 2021 was $43 million compared to $35 million for the quarter ended March 31, 2020. Net loss for the quarter ended March 31, 2021 was $54 million or $0.27 per share which includes non-cash expenses of $12 million compared to a net loss for the same period in 2020 of $45 million or $0.31 per share, which includes non-cash expenses of $3 million.

We recognized revenue of $12 million and $15 million for the quarters ended March 31, 2021, and March 31, 2020, respectively, which includes revenue related to non-cash royalties earned and revenue recognized under our collaboration agreements. I now turn the call back to Garo.

Garo H. Armen ***Agenus Inc. - Founder, Executive Chairman & CEO***

Thank you very much, Christine, and thank you all again for your interest in Agenus and for joining us this morning. The progress Agenus is making so far this year is positioning us for a strong 2021. Looking into the current quarter and beyond, we expect to achieve value-driving events with our clinical and preclinical pipeline and this includes an extensive list of important items starting with: This year we expect to further detail our BLA strategy for the combination of balstilimab and zalifrelimab. Two, having filed our first BLA, continuing to work with the FDA for our first productive tool. Three, beginning for commercial launch for second-line cervical cancer. Four, continuing with our Phase II development for AGEN1181 plus balstilimab with a strategy to transition these studies to registrational trials. Five, additional data presentations for our own pipeline of agents and partnered programs. Six, advancing our AGEN1777 TIGIT program into and through the clinic. Seven, completing enrollment of the Phase I iNKT study in intubated COVID patients. Eight, expanding and generating clinical data from our recently initiated iNKT cancer trials. Nine, progressing with our commercial manufacturing facility for antibodies. Ten, progressing with our sustainable supply of QS-21. And, eleven, progressing and delivering on our cash-accretive corporate transactions.

Thank you again for your attention. Now we will open the call to questions. Rebecca?

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) And our first question is from Mayank from B Riley Securities.

Mayank Mamtani ***B. Riley Securities, Inc., Research Division - Research Analyst***

Congrats on the progress. So if I may ask quickly on the 1181 to Jen or Dr. O'Day. In terms of patients that you're continuing to treat, could you provide more color on -- you said melanoma, but what sort of patients do you anticipate having update this year, and specifically to Garo's comment on what could allow you to transition to a registration trial?

And then just a follow-up to that, there was an ODAC committee meeting on checkpoint inhibitors very extensively over 3 days. So I was just curious broadly, as you are one of the pioneers developing different approaches of checkpoint, like what did you think were the implications for your portfolio?

Jennifer Buell ***Agenus Inc. - President & COO***

So maybe, Mayank, what I will do -- what we have publicly disclosed based on the data from AGEN1181 is we have seen responses, as Dr. O'Day mentioned, in tumors that are otherwise unresponsive to immune therapies, those being microsatellite stable endometrial, microsatellite stable colorectal, ovarian and now also in tumors considered hot or warm, those being melanoma. Now that has been the extent of what we publicly disclosed and so if the data have been driving our decision on areas to pursuing which were eligible for fast-to-market opportunities like accelerated approval as well as very large market opportunities such as Dr. O'Day mentioned and that being colorectal cancer, MSS colorectal cancer. So I'll just ask Dr. O'Day if he has any other feedback.

Steven J. O'Day ***Agenus Inc. - Chief Medical Officer***

Yes. I mean thank you for the question. I mean what's exciting to us is that we have a designed next-generation CTLA-4 that's showing activity in the clinic, as I've said, particularly in tumor types that traditionally don't. I -- we're obviously expanding colorectal as we publicly disclosed and that's going well. We will continue to expand the other areas where we're seeing signals and the science will follow us here. As we expand these cohorts, depending on the strength of the signal, our goal is fast-to-market and we're not shying away from large markets because cold tumors are traditionally large markets and we will pursue the science.

Jennifer Buell ***Agenus Inc. - President & COO***

And Mayank, related to the ODAC meeting, this was, as you've seen, predominantly focused on different product opportunities and I think consistent with what our expectations were from the meeting. We don't perceive any negative impact to our portfolio of course. Products that show tremendous efficacy will continue to be fast-tracked and made available to patients, and so those are the products that we're pursuing obviously. So I think the outcome was not impactful to us in any negative way.

Mayank Mamtani ***B. Riley Securities, Inc., Research Division - Research Analyst***

And maybe just a couple more. Any incremental color on the CD137 data coming up at ASCO, sort of how many patients, combination versus monotherapy, hard versus cold tumor, any color on that? And then maybe also if you have any update on the sustainable supply of QS-21 and sort of where you are with the synthetic manufacturing process?

Steven J. O'Day ***Agenus Inc. - Chief Medical Officer***

Thanks for the question. Obviously, we have embargo data from ASCO. So obviously I can't give any details around that except to say that as you would expect, all Phase I IO trials are with -- the tumor types that come into these trials are typically cold tumors and we're very pleased with how this trial is progressing in monotherapy and we anticipate -- we have not seen any major toxicity signals. And we're looking forward to do combinational approaches very soon. So more to come from ASCO where the detail of the trial to date will be summarized.

Jennifer Buell ***Agenus Inc. - President & COO***

Maybe a few words on the molecule or the differentiation design. Mayank, maybe I'll just say though, as a reminder for those new to this, this product AGEN2373 was designed -- it's an anti-CD137 agonist. We know that these molecules and mechanisms are really critical for bringing durable, long-term immune response for patients with cancer. The problem with preceding molecules is that they have been toxic. Predominantly, a lot of liver toxicity has been observed. We designed our molecules to actually be -- to not induce any liver toxicity. So essentially the molecule binds only in the presence of the ligand. So effectively, we call that conditionally active. There's a condition to its activity that we believe will support a more safer profile or better tolerable profile. So I think more data will come out on the mechanism as well as what we're seeing in the clinic to support that mechanism.

Steven J. O'Day ***Agenus Inc. - Chief Medical Officer***

It's fair to say the color is green.

Mayank Mamtani ***B. Riley Securities, Inc., Research Division - Research Analyst***

And QS-21?

Steven J. O'Day ***Agenus Inc. - Chief Medical Officer***

QS-21, as -- Mayank as you know. So there is no ambiguity about the fact that QS-21 is a highly active, perhaps one of the most, if not the most active adjuvant. Now what does that mean? That simply means that vaccines that have QS-21 as an adjuvant drive both PH1 and PH2 components of the immune response. That's a very, very important element. Now the problem, as you know, has been that in the past, because we haven't had the kind of pandemic that we're experiencing right now, the typical requirement for a vaccine has been, such as for example shingles vaccine, in the tens of millions of doses per year. It hasn't been in billions of doses per year and now that we are confronted with this reality, because we don't know if the current pandemic is going to go away, if it's going to continue, we don't know if we're going to be confronted with new pandemics that we are not even contemplating right now.

However, what we know is that the world's state of mind has dramatically changed from one of a state of compliance -- or complacency rather to a state of heightened urgency to be ready for pandemics. That requires that we need to be ready with a very highly effective adjuvant like QS-21 to be able to produce enough of it to accommodate very large quantities of vaccine doses. And in order to do that, the only way to do it, in our opinion, is to try to replicate the raw material from a natural source to a man-made source and here we are talking about making it with plant cell lines, which we have started the process. So right now, as I've said earlier, it's a question of engineering, not a question of can this be scientifically accomplished, because we've done the science part. We've shown it in small-scale quantities that we can make it. And scaling up of course is a different kind of an effort and that's what we're in the process of doing and I'd say we're probably a third of the way into it right now in that scale-up process. Does that answer your question, Mayank?

Mayank Mamtani ***B. Riley Securities, Inc., Research Division - Research Analyst***

Yes, it does.

Operator

And our next question is from Kelly from Jefferies.

Jason Thomas Bouvier ***Jefferies LLC, Research Division - Equity Associate***

This is Jason Bouvier on for Kelly Shi. We were wondering if you can discuss a little more how you're thinking about the development of the second-gen CTLA-4 anabolic, for example, how do you prioritize? You prioritize the combination therapy with PD-1 or the monotherapy such as in the PD-1 refractory setting?

Garo H. Armen ***Agenus Inc. - Founder, Executive Chairman & CEO***

So let me make a general statement and then I'm going to let Steven and Jen address it. So our strategy from a big-picture perspective is very simple. And our strategy is based on data that we have disclosed as well as data that we have in our possession that factors into our planning, very important point, because we make decisions based on science. Now at one end of the spectrum, as Steven said, we're seeing very, very pronounced activity in tumors that are cold and represent very large markets because no immunotherapy in those tumors has shown real profound activity so far. So on one hand, our strategy is to pursue that very, very expeditiously. On the other hand, there are other cancers, there are specialty cancer so to speak, where there may be a path for approval that is very rapid. So we're looking at both of those strategies. And Steven, why don't you elaborate on this?

Steven J. O'Day ***Agenus Inc. - Chief Medical Officer***

Yes. I understand people really want some detail around the development plan. I think what we've said is that there is going to be a lot of flexibility and options here and we simply need to see the strength of the signals as we expand some cohorts to know the path that's most rapid to approval and it may be single-arm studies, if the strength of the signal is high enough, it may involve some comparative trials in each of the diseases whether it's a cold or warm and hot tumor. Obviously, it's a very competitive landscape. What I can tell you is we're thinking through this very carefully and we're in parallel thinking about where we want to go as the data evolves, and we will be ready as soon as we have more data. What we have been able to do is to reach doses that we're comfortable with both in single-agent and combination with a favorable toxicity profile and so we're ready now to expand these cohorts and see where the data takes us.

Operator

(Operator Instructions) And our next question is from Matt Phipps from William Blair.

Hunter Rogers ***William Blair & Company L.L.C., Research Division - Research Analyst***

This is Hunter on for Matt, just on the -- I know you guys are having ongoing conversations with the FDA. I was wondering if you could provide any color on sort of the focus of those conversations. And then the alignment that needs to occur between you and the agency there, then I believe you mentioned that you plan on presenting additional responses from the 1181 trial and at upcoming conferences. I was just wondering if I heard that correctly. And if so, if you could provide any color on -- if those are in similar cancers to what you've seen responses before those in new indications.

Steven J. O'Day ***Agenus Inc. - Chief Medical Officer***

Yes, I think our previous statements hold there. We are actively expanding these cohorts. And we expect to present updated clinical and safety data at meetings this year. And regarding the additional color on FDA conversations. I think those are confidential, then it will be inappropriate for us to talk about or speculate.

Jennifer Buell ***Agenus Inc. - President & COO***

I think the one addition, I would say on is we've disclosed previously, the trial has been enrolled, the large trial over 150 patients. We've concluded follow-up period, the median follow-up period that was necessary and the data continue to look very strong. So this combination, we believe is a real potential opportunity for patients with cervical cancer. We'll look forward to continuing to keep you updated.

Hunter Rogers ***William Blair & Company L.L.C., Research Division - Research Analyst***

Okay, great. And maybe one more real quick. On the COVID trial, I think last quarter you had mentioned that you expected the dose escalation to wrap up here in the first half of the year and now I think it's sort of shifted to just general finishing in 2021. So I was wondering if you could provide any color on how the enrollment is going in that trial, especially given that the vaccination efforts that are ongoing in the U.S.

Jennifer Buell ***Agenus Inc. - President & COO***

So, I'll say just a couple of points on this, but we have -- we are still on track to complete dose escalation in the first half of this year and then of course expand to Phase II and where we see a real opportunity here in patients who have sequelae, so it's acute respiratory distress syndrome secondary to COVID. I mean we have a real opportunity to expand to bring potential benefit to those patients as well as beyond those suffering from ARDS, independent of COVID. So, we see a number of opportunities for development of these cells in pulmonary disorders that are quite prevalent and that will be untouched or be able to proceed independent of the continued high prevalence of COVID. Although I will say, despite the vaccine efforts, we are still seeing that the pandemic is ravaging certain communities and this still remains a real problem.

Operator

And we have another question from Mayank.

Mayank Mamtani ***B. Riley Securities, Inc., Research Division - Research Analyst***

I would like to ask the COVID question, Jen. And also just the implication of that in cancer as obviously these cell types, the source has to be also very scalable. Like how are you sort of making choices what goes towards COVID versus your cancer study. And also in terms of the communities that are ravaging, to your point, then are you considering doing trials in those territories where the pain is greater?

Jennifer Buell ***Agenus Inc. - President & COO***

So I'll say Mayank, with respect to scalability, the real differentiation of AgenTus, and it's based on our manufacturing prowess, is that we actually have been able to address. This is not a biology problem, it's an engineering problem, the scalability of iNKT cells. And we have publicly presented data where we're seeing exponential scalability with these cells. I'm now producing nearly 10,000 doses for patients at our current capability and then we're prepared to go far beyond that. So for AgenTus, manufacturing has been addressed and now scalability is very straightforward for us. It's just a matter of the numbers and we don't need to scale far beyond what we have right now. It will address our current needs in the clinic and cancer as well as in COVID. As far as the expansion of this trial, we will provide more detail on the AgenTus' plans for the iNKT and COVID and beyond.

Garo H. Armen ***Agenus Inc. - Founder, Executive Chairman & CEO***

And by the way, just to address this point very clearly, God forbid, should the viral variants and mutations keep ahead of our ability to develop vaccines that are going to be able to confront the future challenges, should that happen and should, for example, iNKTs be a viable therapeutic approach, so lot of shoulds here, but if that were to happen, we do not foresee that manufacturing or cost of treatment will be an issue on a large scale.

Mayank Mamtani ***B. Riley Securities, Inc., Research Division - Research Analyst***

And maybe a follow-up to this is how -- any update you could provide on what things you might be looking at going by yourselves versus that there could be a lot of support from external stakeholders, public, private towards some of these activities. So any color you could provide from a time line standpoint when we could expect some of the strategic discussions you might be having.

Garo H. Armen ***Agenus Inc. - Founder, Executive Chairman & CEO***

All of these prospects are being actively pursued, Mayank.

Operator

And we have no other questions at this time.

Garo H. Armen ***Agenus Inc. - Founder, Executive Chairman & CEO***

Great, thank you everyone for joining us. I will talk to you soon.

Operator

Thank you, ladies and gentlemen, this concludes today's conference. Thank you for participating. You may now disconnect.