agenus

Agenus (NASDAQ: AGEN) Q1 2019 Earnings Conference Call

May 09, 2019 8:30 AM ET

Introduction and Forward-Looking Statements in APPENDIX

Jennifer Buell

I will begin by stating that 2019 is off to a strong start.

- **Enrollment in our two trials which are designed to support a BLA filing has been faster than our earlier projections. Hence clinical data from these trials may come before the end of this year or early next. Which means we may be able to file our first BLA earlier than anticipated in 2020.** As you know, we have 2 registration trials underway; either trial or both could potentially support BLA filings. The first of these is our PD-1 monotherapy trial in 2L cervical cancer and the second is a combination trial of PD-1 and CTLA-4, also in 2L CC. I would like to state that our combination trial strategy can provide us with an important competitive advantage in this cancer type and in others.
- **Secondly, enrollment in our second generation CTLA-4 trial is also proceeding**. We believe our second generation CTLA-4 could be a best in class molecule. And it has the potential to expand the commercial potential of our PD-1 beyond what our first Gen CTLA-4 combination offers. We anticipate early clinical readouts of our second Gen CTLA-4 also by the end of this year. W**e plan to commence combination trials of our second generation CTLA-4 with our own PD-1 in the next several months. Clinical data from our second gen CTLA-4 could represent a very important value inflection point for us for defining our own US commercial opportunity as well as for our ability to monetize on the ex-US right for this molecule.**
- Our product discovery and product development focus are on achieving *high and durable responses. This means shorter trials, lower trial costs and more rapid product registration or combination product registrations; Our opportunities for combinations also include combinations with our checkpoint antibodies and bispecifics, our cell therapies, and our vaccines. Our access to these combination agents is a major advantage which helps our ability to rapidly deliver on our high impact strategy.*
- We define **high impact products as products with durable high responses and/or strategies that address cancers for which viable treatment options do not exist**. Generally, these attributes translate to shorter, less costly trials designed for accelerated FDA approval.
- Our integrated capabilities, from antibody discovery to cell line development to GMP manufacturing are also **key to our ability to build a pipeline of products quickly and at lower costs**. These advantages also allow us to manage a larger

portfolio of discoveries and development programs at much lower costs and with higher quality than would be possible without these internal capabilities.

- **Our innovation and our speed in drug discovery have enabled us to deliver the largest preclinical collaboration in oncology in 2018, the Gilead transaction with $120M upfront cash, $30M equity investment and potentially $1.7B in additional payments plus royalties.**
- Today we will highlight two of our most exciting novel antibodies: one has entered the clinic already and the other is expected to be in clinical development in coming months. Our second generation CTLA-4, AGEN1181 and our novel anti-CD137 molecule, AGEN2373 which is an option program as part of our Gilead collaboration and we believe has unique advantages over other antibodies targeting the same receptor. A key contributor to these potential best in class antibodies, Dr. Dhan Chand, is going to tell you more about these molecules and their unique attributes shortly
- We are also advancing our second generation, *currently undisclosed*, bi-specific antibodies towards IND.
- **AgenTus, our cell therapy subsidiary**, has made significant progress. Last year at this time, the company was building a team, and advancing a single lead candidate. Today, AgenTus has 39 employees, a robust pipeline of (5) TCR and (2) CAR-T candidates and are on track to file INDs for a **proprietary allogeneic cell format and an autologous** TCR for patients with cancer. Bruno, the CEO of AgenTus, is with us for this call and will provide an update on the progress of AgenTus.
- **Lastly, our earlier innovations have been important catalysts for at least one blockbuster product for our partners.**
    - Sales of GSK's SHINGRIX vaccine powered with our QS-21 has achieved over $1B in revenues in its first year of launch and is expected to reach $1.3Bn in revenues this year.
    - Also, this year, GSK announced the launch of a large trial with the QS-21 containing vaccine, Mosquirix, the first ever malaria vaccine. The global burden of malaria is immense, and more than 400,000 people dies each year. We are excited to contribute to the potential eradication of this deadly disease.
    - Lastly, the Bill and Melinda Gates foundation provided us with a grant of ~$1M to enable development of an alternative manufacturing process of QS-21 to ensure continuous future supply of this important adjuvant.

I will now turn the call over to Garo

Garo Armen

Thank you, Jen.

As Jen mentioned, **our highly productive discovery capabilities have resulted in our broad pipeline of I-O agents which we intend to use for establishing our own commercial presence in NA**. These productive discovery capabilities have also resulted

in the largest upfront payment for a preclinical collaboration last year. This collaboration with Gilead was an important defining point for us which among other things served as an important external validation of our innovations of the past 5 years. As you know with the 4AB acquisition we transformed Agenus into a broad based I-O engine covering Abs, Cell therapy, vaccines and adjuvants. We consider individual elements of our portfolio and the ability to generate smart combinations to be key to developing second generation I-O therapies for patients who need effective and durable treatments.

We are a company with the capacity to create. We invent and advance novel products. At Agenus, we have the foundation – the tree, not just the fruit. We nourish our creativity, we cultivate our innovation, we harvest our productivity. We make important advancements for the benefit of all of our stakeholders, including patients, the healthcare system, our shareholders and our team.

- We have delivered and continue to deliver with a high sense of urgency, because we know that lives are at stake.
- In the past 3 years we have delivered 11 INDs with additional INDs planned for the first half of this year; setting records in our industry.
    - We filed 6 INDs in 2018 and among these include our proprietary second generation CTLA-4. This is a **very exciting molecule which we plan to generate meaningful data this year, and engage a partner to commercialize in ROW, while we retain the US commercial rights.**
    - In addition to our second gen CTLA-4, we are also on track to file an IND for our CD137 agonist and an off-the shelf phosphorylated neoantigen vaccine.
- In a few minutes you will hear Dr. Chand speak about our second generation CTLA-4 and anti-CD137 molecule – and specifically what makes them so powerful. These are just 2 in our pipeline of novel molecules that we will specifically showcase during this call.
- **Our operational successes have put us in a powerful position this year**. ***We have enrolled our PD-1 and CTLA-4 trials faster than our original projections*** and ***we could potentially file our BLAs earlier than anticipated in 2020.***
    - **We plan to develop, register, and launch our PD-1 and CTLA-4 in the US with a first indication in 2L cervical cancer.** We will explore rest of world partnerships to expand our footprint and allow access to patients outside of the United states.
    - Cervical cancer is a formidable disease and the best available medicine delivers up to 15% responses with a PD-1. We believe we have an opportunity to improve these response rates with our combination strategy.
- *We also plan on pursuing opportunities beyond cervical cancer. Our second generation CTLA-4 can potentially provide us with the opportunity to significantly expand the utility of our PD-1 in other cancers.*

The genius of Agenus lies in the intelligent design of our molecules and intelligent design of our clinical trials. Our objective is to develop high impact therapies designed to achieve

high response rates and long durability of responses. Having our own discovery, manufacturing and combination development agents is key to achieving this objective.

This is core to our advantage.

Last year, one of the Nobel Prizes for medicine was awarded for work done to block CTLA-4 to stimulate the immune system to attack cancer. First generation agents, including our own CTLA-4 blocking agent, AGEN1884, have shown curative benefit in a small portion of otherwise incurable cancer patients. We believe we can expand the benefit to more patients by improving on first generation CTLA-4 blockers. We believe we have achieved this with our second generation CTLA-4, AGEN1181. I will invite one of our lead innovators, Dr. Dhan Chand, to discuss why CTLA-4 is so important and why we believe our second gen CTLA-4, AGEN1181, has best in class features and will be so important for treating patients. Dr Chand will also discuss our novel CD137 blocker expected to be in clinical development this year.

Dhan Chand

Thank you, Garo.

I am delighted to discuss two key assets in our novel second generation pipeline – why they are important, and how we believe they will change the treatment paradigm.

First, I will discuss CTLA-4 and emphasize why it is so important. CTLA-4 blocks the ability of the immune system to kill cancer. It prevents the initial T cell response to cancer and furthermore, it augments the immune suppressive function of regulatory T cells. Together, CTLA-4 inhibits the ability of the immune system to effectively fight cancer. Blocking CTLA-4 with antibodies like AGEN1884 or AGEN1181 unleashes the ability of the immune system to kill cancer. Importantly, blocking CTLA-4 also improves the durability of the anti-cancer response.

These are critically important pathways in our efforts to conquer cancer. Durability of response is one of the hallmarks of anti-CTLA-4 therapy. When we block CTLA-4, like in metastatic melanoma, we see durable anti-tumor immunity. In fact, it was the work by Nobel laureate Jim Allison on CTLA-4 and anti-CTLA-4 therapy that allowed us to start putting the words cure and cancer in the same sentence.

In multiple cancer types, where PD-1 brings clinical benefit, adding a CTLA-4 blocking molecule, increases the response rates and durability of responses. We have observed this in metastatic melanoma, MSI-H colorectal cancer, and Renal cell cancer, to name a few. Today, the combination of CTLA-4 and PD-1 are the only clinically validated immune-oncology combinations.

As remarkable as anti-CTLA-4 therapy is at promoting durable anti-tumor responses, only a small subset of patients today benefits from anti-CTLA-4 therapy, highlighting the need for better anti-CTLA-4 agents and/or combination therapy.

Early data on CTLA-4, in patients treated with a higher dose, revealed some immune-related toxicities and therefore CTLA-4 was perceived as "Toxic". Moreover, early clinical data involving anti-PD-1 therapy demonstrated similar response rates as anti-CTLA-4 therapy and with a more favorable toxicity profile. As such, we saw a shift away from the use of CTLA-4 in favor of PD-1 antibodies. As a matter of fact, there are a scarcity of first generation CTLA-4 molecules and even fewer next generation molecules. Today we believe that we have the most advanced clinical stage antibodies in both categories.

I will now briefly discuss why AGEN1181 expands the criticality of the benefit of this target.

AGEN1181, our second generation anti-CTLA-4 antibody, leverages a breakthrough discovery made by Agenus scientists which was published in the journal Cancer Cell in June 2018. It represents a significant advancement in anti-CTLA-4 therapy with the potential for deeper clinical responses and better combination potential.

We discovered that one of the key factors that influence the therapeutic activity of anti-CTLA-4 antibodies is their ability to interact with cancer-fighting T cells and a subset of immune cells known as antigen presenting cells. This interaction is accomplished, in part, by the "Fc region", an important section of the antibody that binds to Fcy (Fc gamma) receptors on antigen-presenting cells. Optimizing this interaction through "engineering" of the Fc-region of the antibody to better engage a specific Fc-receptor, FcyRIIIA, on antigen presenting cells, significantly enhanced the therapeutic potential of anti-CTLA-4 therapy.

AGEN1181 was designed to block CTLA-4 and harness this novel Fcy-related mechanism that is not captured by the first generation anti-CTLA-4 therapies.

Compared to the current generation, AGEN1181 has an enhanced ability to promote superior T cell priming and T cell activation. T cell priming is a crucial step in launching potent immune responses against cancer.

Moreover, AGEN1181 is better designed to promote the depletion of intratumoral regulatory T cells as compared to the current generation of anti-CTLA-4 antibodies. Intratumoral regulatory T cells represent a significant barrier to successful anti-cancer immune responses.

In addition to improved single agent activity, AGEN1181 has shown superior combination potential in preclinical tumor models with other cancer therapies such as immune modulatory antibodies, including anti-PD-1 therapy, and vaccine therapies.

We are advancing our second generation CTLA-4 molecule, AGEN1181, as a monotherapy and in combination with our anti-PD-1 molecule and anticipate data readouts as early as the second-half of this year.

Now, very briefly on AGEN2373, our anti-CD137 molecule. AGEN2373 is a fully human monoclonal antibody that boosts the immune response to cancer cells by enhancing CD137 co-stimulatory signaling in activated immune cells – both adaptive (T cells) and innate (NK cells). The potential to dually target innate and adaptive immunity makes CD137 a highly attractive target for cancer immunotherapy. Additionally, the unique binding properties of AGEN2373 are expected to limit its activity outside of the tumor site and mitigate toxicities that may be associated with systemic activation of CD137 in humans.

Garo Armen

Thank you Dhan.

I will now switch to a very exciting new paradigm, represented by our second generation bispecific checkpoint antibodies.

Our emphasis is **new discoveries that can have high impact in the treatment of patients with cancer; what we mean by this is that products can move to market faster, and hence benefit all our stakeholders.** Therefore, our objective is to emphasize high impact therapies which lead to small, shorter trials, in our efforts to achieve patient benefit and regulatory approval and commercial launch rapidly.

Our first-generation bispecific molecules targeting important tumor escape mechanisms were the subject of our recent collaboration with Gilead. Our second-generation bi-specific molecules are rapidly progressing towards IND filings; and these second-generation bispecific antibodies address additional important mechanisms such as co-inhibitory pathways in NK and T cell biology, targeting tumor associated macrophages, tumor/stromal-targeted neutralization, and multi-specific cytokine targeting agents. I realize that all of this sounds like a mouthful, but the biology and our understanding of cancer immunology has advanced for us to have validated the importance of these mechanisms.

- **Our capabilities and pipeline have been key to our ability to enter into important partnerships with Gilead, Incyte, Merck, and GSK.** We expect additional partnership transactions to be an important part of our strategy going forward including this year. Given the productivity of our discovery engine, we also expect our pipeline of innovation to be driving our own commercial strategy.

- ***Our strategy is to balance between monetizing a portion of our discoveries every year, while keeping rights to north America. We expect to generate meaningful clinical data this year in our efforts to monetize on ex-US rights with significant value consideration. This strategy will be tested with our second generation CTLA-4 antibody currently in clinical development with prospects of generating clinical data by year end both as monotherapy and in combinations.***

- ***We possess key components of IO approaches – checkpoint modulating antibodies, neoantigen vaccines, adjuvants, and adoptive cell therapy approaches, both TCR and CAR-T therapies – in-house. Cancer is a complex disease and we believe that combinations will be necessary to deliver optimal benefit to patients.***

Our cell therapy business, AgenTus, has made important progress on the advancement of the pipeline to IND filings this year, as well as progress towards our first round of private financing ahead of a potential IPO.

I am delighted to invite the CEO of AgenTus, Bruno Lucidi, next, to provide you with the progress we have made at AgenTus. Bruno….

Bruno Lucidi

Thank you, Garo and thank you for the opportunity to provide an update on our exciting cell therapy company AgenTus. Agenus had the foresight to separate its Cell therapy efforts from the parent company 18 months ago. Recently our collaborator Gilead decided to do the same with its pioneering cell therapy company Kite. Separation of cell therapy from rest of I-O is a prudent strategy based on business model considerations.

Let me start by stating that as Jen eluded to earlier, AgenTus has made very important progress in building a team, expanding our cell therapy construct capabilities, substantially expanding our pipeline of TCRs and CAR-T candidates, and very importantly, advancing our novel and proprietary allogeneic cell format. As you all know allogeneic format is critical to broadening the applications of cell therapy from the limited market served by cell therapy today.

On this note, despite the remarkable success and clinical benefit demonstrated by, what we call, first generation cell therapies to date, current approaches have limitations. These include, the very limited cancers indications today's cell therapy serves, long lead times for manufacturing, complicated logistics and very high costs. Our technologies, assets and capabilities are designed to address every one of these issues. In addition, because of our ability to piggy back on our discovery capabilities at Agenus, AgenTus has a significant advantage in delivering high impact cell therapy products and consistent with our overall strategy do it rapidly. A number of our lead cell therapy candidates which are in the category of what we call second and third generation cell therapy products, are targeting solid tumors which account for more than 90% of today's cancers.

In the past year alone, at AgenTus, we have built a proprietary TCR discovery platform which is based on our clinical validated and highly productive antibody discovery platform. Our core capabilities in bioinformatics, structural and computational biology, molecular and cell biology, and importantly, our access to Agenus' pipeline of rational I-O antibodies which constitute intelligent cell therapy combinations provides AgenTus with a unique advantage not common in the cell therapy universe.

I will now provide you with some highlights of our capabilities and accomplishments

1. **In the past year we have built and perfected a high throughput discovery engine that is unique to us. This engine can generate** high quality TCRs and CAR-T therapies. TCRs are critical for targeting solid tumors and our TCR discovery capabilities provides us with very unique advantages over most others.
2. **Another important critical success factor is our proprietary allogeneic platform** – we are on track for our first IND filing of our allogeneic cell format by year end.
3. Our ability to have access to Agenus antibodies for **optimal combinations** is yet another major advantage for AgenTus – immediate priorities for combination agents for our portfolio of cell therapies include our PD-1, CTLA-4 (first and second generation) and CD137.
4. **Our novel and proprietary phosphorylated antigen targeting platform** provides us yet with another unique technology advantage. Agenus has developed a library of over 2000 phosphopeptide targets and AgenTus is the only cell therapy company with access to TCRs to some of these phosphopeptide targets.

As you can see the progress we have made in such a short period of time is a tribute to our stepped up I-O efforts at Agenus over the past 5 years as well as the advances made by our team at AgenTus. In the past months we have also secured a substantial grant-based funding from the Belgian Wallonia Government to advance our cell therapy manufacturing capabilities. Currently, we are in advanced stage discussions for a private round of financing which we are aggressively targeting to close over the next few months.

Now I will turn the call back to Garo.

Garo Armen

Thank you, Bruno for articulating the exciting developments at AgenTus. Before turning the call over to Christine for recapping our quarterly financial report, I wanted to summarize a few key points:

- We have developed and have been successfully practicing a complete set of capabilities and I-O agents in our efforts to rapidly deliver high impact products.
- We have an outstanding pipeline of novel and second generation I-O agents that we expect will deliver substantial benefit to patients with cancer.
- Our operational excellence has put us on a path to a BLA filing that remains on track and could even be ahead of schedule.
- We are emphasizing smaller, focused trials to achieve high response rates specifically targeting patients who are not being effectively served by today's first generation I-O agents.

To appreciate the full value of our portfolio and protect the interests of our shareholders, we recently launched an innovative first of its kind financial mechanism which we call **BEST**. BEST is designed to preserve maximal value for our existing shareholders while providing funding for the expanded development of our PD-1 antibody beyond cervical cancer. BEST is a digital security which provides the opportunity for investors to invest in a single, late-stage asset. **And to be clear BEST is not a cryptocurrency**. BEST is a financial instrument designed to have minimal dilution to our shareholders. Given our decision to limit the money raise through this innovative financing mechanism, BEST will only impact a small portion of the initial PD-1 income. As you know, the quicker and broader we expand the opportunities for our PD1 antibody, the greater the leverage and value for our current shareholder as well as BEST holders!

I know that a lot of you are wondering about the status of our BEST offering. We are taking our time, besides the fact that we are not in a rush to do this, we would like to make sure that it is done properly. It is after all a first of its kind biotech financing instrument… its structure must be perfected, and the potential audience is properly selected and qualified. For those of you who may think BEST is a gimmick, we would like to encourage you to read more about it and approach us with your questions that surely deserve clarification. In addition to BEST being an innovative biotech, we believe it has the potential to streamline health care commerce down the road.

There are some lingering questions out there, will investors sell Agenus stock and buy the digital security. Based on everyone we have spoken to, **this is not** the case and we don't expect this concern to be an issue as is the case when companies issue convertible securities.

So, for clarity we will take our time to test BEST and expect to complete the offering before the end of the year.

Now I will turn it over to Christine Klaskin to provide financial highlights.

Christine Klaskin

First Quarter 2019 Financial Results

We ended the first quarter of 2019 with a cash balance of $158 million as compared to $53 million at December 31, 2018.

For the first quarter ended March 31, 2019, we reported net income of $17 million or $0.14 per share compared to a net loss for same period in 2018 of $54 million, or $0.53 per share. In the first quarter we recognized revenue of $80 million which includes revenue from our transaction with Gilead and non-cash royalties earned.

Garo Armen

Thank you, Christine.

In closing,

We expect the following key catalysts for 2019:

- Completing accrual of PD-1 and CTLA-4 trials by year end; both are designed to lead to product approval in the US based on the data outcomes.
- Upon a successful outcome of these trials, we expect to file our first BLA in 2020.
- Initiate first in class combinations with our second generation CTLA-4 with our proprietary PD-1 molecule.
- Advance additional breakthrough discoveries and file at least 3 additional INDs in 2019.
- Advance our next generation, best-in-class molecules into the clinic, including our selective Treg depleting bispecific, AGEN1223.
- Advance our cell therapy programs and have AgenTus funded independently in anticipation of a potential public offering.
- Complete our BEST offering.
- And very importantly we expect to complete one or more BD transactions in 2019.

We are committed to our mission of delivering for our patients and for all our stakeholders. Our efforts and staying power over the last 25 years speaks to this commitment. We thank you for your staying the course and joining us on this journey. Now we would be happy to entertain your questions.

Appendix

Introduction and forward-looking statements: Jennifer Buell

Today's call is being webcast and will be available on our website for replay.

Before we start, we would like to remind you that this call will include forward looking statements, including statements regarding our clinical development plans and timelines, partnership opportunities and timelines, and our financial position. 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.

I am Jennifer Buell, Chief Operating Officer of Agenus. We are delighted to provide an update on our business.

Joining me today are Dr. Garo Armen, Chairman and Chief Executive Officer, Mr. Bruno Lucidi, the CEO of our AgenTus Cell Therapy Business Entity, Dr. Dhan Chand, a key member of our innovation team, and Christine Klaskin, our Vice President of Finance.