agenus

**Agenus (NASDAQ: AGEN) Q2 2018 Earnings Conference Call**

August 9, 2018 8:30 AM ET

**Introduction and Forward Looking Statements in APPENDIX I**

**Garo Armen**

Good morning and thank you for joining us for our quarterly update.

In 2014 we started the transformation of Agenus with an intent to make it an I-O engine. In the past 4 years we have built a company that is delivering innovation with speed. Today, I will describe our progress and achievements in three areas which are of great interest to you and to us:

1st - We have made substantial progress in delivering our discoveries into the clinic and advancing our PD-1 and CTLA-4 programs which are in the clinic and on a path for a potential BLA filing. The evidence for our progress is easy to track. We filed five INDs in the 18 months prior to the start of 2018. Our programs are on track for additional six IND filings this year – three of which have already been filed. Furthermore, we are working to file two more INDs in the first half of 2019. All of these represent discoveries from our own research pipeline and are either best-in-class and/or first-in-class compounds. They also represent products designed to address tumor resistance pathways with the potential to be the next major breakthroughs in I-O. In addition, as I alluded to, our proprietary CTLA-4 and PD-1 antibodies are progressing towards a planned BLA filing in 2020;

2nd - I will discuss our cash position and **balance sheet**. Please know that we are aware of the concerns related to these issues and I will address them.
As I mentioned we are progressing our programs and filing INDs at record pace. At the same time, as you will hear shortly, we are prudently satisfying our near-term cash needs.

3rd - I will provide an update on our recent progress in establishing **new strategic partnerships**. We expect these to result in potentially significant cash infusions into Agenus this year.

I will start with what I believe is in your minds and something which is very important to us - our balance sheet:

Our cash balance at the end of 2017 was $60M; at the end of Q1 it was $51M and we closed the 2nd quarter with $43M in cash. We've been managing our cash position prudently with an intent to minimize dilution to shareholders.

At the same time, we have been advancing our compelling and exciting pipeline of programs. We expect these 14+ innovative I-O candidates to be major near-term value drivers; hence advancing them rapidly is critically important! Until we secure additional cash, which I will speak more about when I discuss our partnership prospects, we will continue to prudently manage our finances. What this means is that our cash position at the end of our current quarter is expected to be near or above current levels.

**Next item, which is pressing in everyone's mind is the status of our partnering activities:**

I will now provide an update on this with transparency, while respecting the sensitivity of these discussions.

I have outlined our partnering strategy and our plans in prior calls, however, we have not yet made an announcement. In spite of the additional time that it has taken to close on a transaction, we are working to maximize value to Agenus and to our shareholders with the right fit. Let me first speak to what has changed in the I-O landscape and how this has influenced the prospective partner profiles and transaction types that we are pursuing.

The first major change is unanticipated successes and failures in the clinic in the past year alone. The complexity of I-O is better appreciated today than it was even 6 months ago. Most biopharma companies are looking to in-license assets that belong to one of the following categories: (A) first-in-class and multi-functional assets, to exploit complementary biological pathways, or (B) later stage compounds with clinical safety and efficacy data with an intent to mitigate development risks.

Over the past year with the advancement of our pipeline, we have strengthened our position in both of these categories.

To be specific, late last year, we made a deliberate decision to accelerate our two first-in-class bispecific programs; this resulted in advancing timelines by 6 months. Since then, these programs have attracted substantial new interest from partners. Why? Because they modulate multiple immunosuppressive pathways that address the limitations of currently approved as well as clinical-stage I-O agents.

We also advanced our PD-1 and CTLA-4 programs. We confirmed that our antibodies are equivalent, if not superior, to competitor agents. This has generated interest from new prospective partners seeking foundational therapies to establish a footprint in I-O and explore combinations of their own novel I-O agents.

The second major change has been that new and sophisticated players are entering the I-O filed. These companies have invested significant time and resources in understanding the broad and deep I-O portfolio that Agenus has built. Agenus' pipeline of antibodies, bispecifics, vaccines, and cell therapies is unparalleled in the field. A broad partnership can offer significant financial resources to advance our pipeline, while also retaining commercial rights to part of our portfolio.

So what does all of this mean to us? Multiple discussions for broad strategic transactions have matured over the last quarter, and we are currently working 24/7 to bring one or more of them to closure with a target announcement date possibly as early as the next 8 weeks.

**Next I will say a few words about the progress we have made with our existing partnerships: to date, we have delivered on all our obligations in our partnerships with INCYTE Merck and GSK. We have met or exceeded all research, IND filing and commercialization milestones. In the current quarter, we expect to receive two additional payments for milestones that have already been achieved and a third is expected by end of year. Our QS-21 adjuvant is a component of GSK's Shingrix vaccine. As you may be aware from media coverage, sales for Shingrix**

**are substantially ahead of earlier forecasts, making additional milestones from our recent royalty transaction more likely.**

***And lastly before I turn the call to Dr. Sunil Gupta, I will provide a summary of our operational activities in the 1H of the year:***

This year three of our discoveries resulted in three IND filings – these include filings for LAG-3 and TIM-3 antibodies under our partnership agreement with Incyte. We also filed a third IND which covers our next generation neoantigen vaccine, ASV. We expect our ASV neoantigen vaccine to be developed in combination with our CTLA-4 and PD-1 antibodies.

***The next IND filing*** will be for our next generation CTLA-4, designed to deplete T-regs while improving T cell priming. *Our discoveries covering this and other antibodies were published earlier this year in a peer-reviewed publication in the high-impact journal Cancer Cell.* Our NexGen CTLA-4 has both potential efficacy and safety advantages relative to approved and clinical-stage molecules, and is designed to address the limitations of current I-O products.

In addition to our next gen CTLA-4 IND filing, *we are on track to file INDs for two of our first in class bispecific antibodies. T*he first of these improves the tumor microenvironment through multiple mechanisms to enable a better anti-tumor immune response when combined with standard of care and other immunotherapies. The second depletes T-regs specifically in the tumor microenvironment but not in the periphery.

These two tumor microenvironment conditioning agents offer critical solutions to also overcoming the limitations of current I-O treatments. You will hear more specifics on these compounds as they enter the clinic early next year.

Speed and innovation for meaningful clinical advances are our dogma. *Our discovery platforms* have enabled our pipeline of 4 therapeutic classes: checkpoint modulating mono and multi-specific antibodies, cellular therapies, neoantigen

vaccines, and adjuvants. ***Our cell line development and manufacturing platforms*** enable fast path to INDs which give us an advantage in advancing products to BLA filings. We've demonstrated this speed in advancing our CTLA-4 and PD-1 combinations towards potential BLA filing in as early as 2020. This is just 4 years after our FIM monotherapy trial commenced.

**Additionally, earlier this year we set another record for production of GMP-grade product for our lead bispecific programs**. Our completed development and at scale manufacturing of our AGEN1223 compound in under 2 months from research to cell bank *is – to our knowledge – the fastest ever, surpassing even conventional antibody development timelines in the industry.* I want to highlight these accomplishments, because without them it would be impossible for us to be filing so many INDs in less than 4 years.

***I will now turn to our progress in the clinic.***

- **To date, we have treated a total of approximately 115 patients with our CTLA-4 and PD-1 antibodies separately and in combinations**. This year we presented compelling data on the pharmacodynamic activity of our anti-CTLA-4 and anti-PD-1 antibodies at AACR and ASCO.
- We reported at ASCO that our PD-1 monotherapy, AGEN2034, generated clinical benefit in more than 40% of treated patients; *we look forward to presenting updated data later this year. We anticipate clinical benefit to be even more robust and importantly, more durable.*
- We have reported exciting results from our CTLA-4 monotherapy trial at ASCO, with 31% of treated patients with refractory cancers showing clinical benefit. An angiosarcoma patient, who was refractory to multiple prior therapies, had a complete and durable response to the lowest dose of AGEN1884. The patient remains disease free today, over one year later.
- Our CTLA-4 and PD-1 programs are advancing in 3 active clinical trials designed to take advantage of accelerated pathways, with a BLA filing as early as 2020. My colleague and head of regulatory and

pharmacovigilance, Dr. Sunil Gupta, will describe our plans in more detail.

- *In summary, our active clinical trials include*
  - *PD-1 monotherapy in patients with refractory cervical cancer;*
  - *CTLA-4 plus PD-1 combinations that we anticipate will further expand response rates and durability of response in the same cervical cancer setting, and*
  - *CTLA-4 monotherapy in patients refractory to PD-1 – a significant unmet clinical need.*
- *All of these trials require relatively small numbers of patients required for approval and short-term endpoints for approval.*
- In our trials so far, we have observed particularly exciting clinical benefit in gynecologic cancers. These findings impressed KOL experts and catalyzed our recent engagement with the Gynecologic Oncology Group (GOG). This is a group that has had a terrific track record for patient enrollment and trial successes, including the approval of topotecan and later, Avastin for patients with cervical cancer.

- Our initiatives to advance programs in 2L cervical cancer exemplify our commitment to provide access to effective agents where current treatment options have limitations. At the same time, these efforts represent important commercial opportunities. This year alone, aggregate commercial revenue for antibodies targeting PD-1 and CTLA-4 is expected to reach $15B. We have defined several development paths, including in 2L cervical cancer, which we expect will enable us to capture a meaningful portion of this large market. There are 13,000 new cases of cervical cancer annually and 4,000 deaths in the US alone.

As we aggressively engage regulators and secure our BLA filings, our regulatory team is under the guidance of an industry veteran, Dr. Sunil Gupta. Dr. Gupta is a trained oncologist with nearly 30 years in senior leadership positions. He joins us from Sanofi where he had a distinguished 22-year career which included leading

the filings of Cemiplimab (anti-PD-1) and Iniparib (PARP inhibition), and approval of Oxaliplatin and cabazitaxel.

**Sunil Gupta**
Thank you, Garo. I am very excited to be a part of a very talented team at Agenus and furthermore, I am awed by the prolific pipeline and aspire to rapidly take these programs into the market in the next few years.

- CTLA-4 and PD-1 is the only validated IO + IO combination. *In fact, this is the only Immuno-Oncology – I-O – combination with approvals in three distinct indications, two of which were secured this year.*
- Today, the regulatory landscape is changing rapidly and is focused on science, and adaptive and seamless clinical trial methodology, including acceptance of surrogate or early markers of activity.
- Recently, the FDA commissioner has outlined a plan for modernizing drug development, to keep pace with rapidly advancing science, and to ensure that innovation remains affordable for patients. We intend to leverage these initiative to take Phase 1/2 trials to product registration.
- The FDA Oncology division has been very progressive and has taken actions to promptly approve products that provide greater clinical benefit to patients in relatively small trials; in some cases, in single arm trials using surrogate endpoints in a few dozen patients and in a few years of first in human (FIH) studies.
- From a regulatory perspective, we are positioned to take advantage of this more progressive landscape and accelerated pathways for approval. We intend to have early and frequent interactions with the FDA in this endeavor
- CTLA-4 and PD-1 antibodies have been such programs, with accelerated approvals granted for these products in in less than 4 years after FIH studies.
- In cervical cancer, our AGEN1884 and AGEN2034 regimen represent the most clinically advanced combination with registrational potential in 2L cervical cancer. This an indication for which there is still a large unmet need for a durable treatment option.
- In June of this year, pembrolizumab was approved in patients with cervical cancer via accelerated approval pathway in a small trial, with fewer than 100 patients. The reported response rates were around 12-14%. We have an opportunity to pursue a similar path of securing fast accelerated approval

with our PD-1, AGEN2034, with comparable data as a monotherapy in this indication.

- Early signals from our trials provide support that this is a viable approach and we are moving quickly to take advantage of this path.
- Where PD-1 is active, specifically in tumors with some baseline immune recognition, like cervical cancer, we expect the addition of CTLA-4 will improve both response rates and durability of responses compared to PD-1 monotherapy. We have most recently seen this combination's approval in MSI-H CRC, where PD-1 was approved initially. The label for the CTLA-4 + PD-1 regimen has a higher response rate with greater durability than PD-1 monotherapy.
- We have upcoming discussions with the regulators scheduled for later this year and look forward to providing further updates at the relevant time.
- Going beyond CTLA-4 and PD-1, I would like to share a glimpse as to how we will advance the other programs in our pipeline, for which we have or will be filing INDs in 2018:
    - As Garo mentioned, our next generation neoantigen vaccine is advancing in the clinic. Clinically, we had demonstrated that vaccines are important to expose tumors for immune attack and we have outlined our findings in recent presentations and our latest newsletter. We are positioned to combine our vaccine with our proprietary CPMs and/or bispecific antibodies and further take advantage of other accelerated pathways such as the RMAT, or Regenerative Medicines and Advanced Therapy designation. RMAT is equal to breakthrough designations in CBER and allows sponsors to have more frequent interactions with the FDA
    - Our next generation CTLA-4 and tumor microenvironment conditioning bispecific agents, AGEN1223 and AGEN1423 have unique mechanisms that are definable. Our translational scientists will validate these mechanisms and in clinical trials, will allow us to selectively accrue patients most likely to benefit from these treatments.
    - We will bring meaningful and effective therapies to patients quickly and will leverage innovation at the bench, in the clinic, and in partnership with regulators to do so.

**Garo Armen**

Thank you, Sunil.

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

**Christine Klaskin**

Thank you Garo and I am happy to review our Second Quarter 2018 Financial Results

Let me update you first on our cash position. At the end of 2017 our cash balance was $60M. We closed the first quarter with $51 million and closed the most recent quarter with $43 million.

As you can see from these numbers, we have managed our cash prudently from quarter to quarterly. As Garo said earlier, based on our current plans, we expect our cash balance to be similar or higher at the end of the current quarter.

For the second quarter ended June 30, 2018, we reported a net loss of $25 million or $0.24 per share compared to a net loss for same period in 2017 of $32 million, or $0.32 per share. In the second quarter, we recognized net revenues of $16 million which includes milestone achievements and non-cash royalties earned.

For the six months ended June 30, 2018, we reported a net loss of $80 million or $0.76 per share compared to a net loss for the same period in 2017 of $49 million or $0.51 per share. The increased net loss reflects reduced revenue due to an accelerated milestone received during 2017 from Incyte and the loss on early extinguishment of debt.

**Thank you, Christine,**

**In closing,**

Our key milestones over the next 12 months are,

1. Complete accrual of our CTLA-4 and PD-1 trials; results are expected to support our path to BLA and our endeavors to develop, register, and launch our CTLA-4 and PD-1 antibodies.
2. Advance 6 new discoveries to patients, namely our 2 first-in-class bispecific antibodies, our next-generation CTLA-4, TIGIT and CD137 antibodies, as well as our personalized neoantigen vaccine.
3. Initiate combination of neoantigen vaccines with our CTLA-4 and PD-1 antibodies.
4. Close at least one of our ongoing partnership discussions
5. With AgenTus, we expect to complete a private placement followed by a potential IPO in an ex-US territory. We are progressing our lead AgenTus cell therapy program into the clinic and expect to file an IND within the next 12 months.

**APPENDIX I**

**Introduction and forward-looking statements: Jennifer Buell**

Thank you. Welcome to the Agenus' second quarter financial results conference call. Before we provide an update, I 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.

Joining me today are Dr. Garo Armen, Chairman and Chief Executive Officer, Dr. Sunil Gupta, Head of Regulatory and Pharmacovigilance and Christine Klaskin, our Vice President of Finance.

During this call, Garo will provide a corporate update, Sunil will summarize our clinical progress and path to BLA and Christine will provide a financial review. We will then open the call for questions.