

PDS Biotech rapidly gaining recognition with Transformational Cancer Immunotherapies and Vaccines



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CEOCFO: *Dr. Bedu-Addo, would you give us a little background on PDS Biotechnology Corporation?*

Dr. Bedu-Addo: PDS Biotech is a New Jersey-based clinical-stage biopharma company. The company develops novel therapies for cancer as well as novel infectious disease vaccines. PDS Biotech has a deep pipeline of products in development which are based on our proprietary Versamune® technology platform, which overcomes some of the key limitations of cancer immunotherapy and vaccine development. Our lead program is in Phase II clinical development to treat various advanced HPV-associated cancers. Our lead infectious disease program is focused on the development of a second generation COVID-19 vaccine.

CEOCFO: *Can you tell us what the science is behind the Versamune® platform?*

Dr. Bedu-Addo: The Versamune® platform has a number of promising attributes. With a cancer immunotherapy, one of the things that we have to do is to train a component of our immune system called our T-cells. These T-cells are really the attacking component or the attacking arm of our immune system. The killer T-cells, which are the most powerful type of attacking T-cells, have to be trained to effectively recognize the tumor as the tumors have developed mechanisms to evade our immune surveillance. We take a protein that is unique to the cancer that can be recognized by our immune system and combine it with our Versamune® technology which is able to effectively deliver that protein into a pathway called the MHC (major histocompatibility complex) Class 1 pathway. This pathway is critical to training the killer T-cells to recognize that protein as a foreign agent. These proteins, since they are expressed or contained in the specific cancer, allows our killer T-cells to recognize the

cancer as a foreign agent. This has been one of the major obstacles facing immunotherapy today, which is training these killer T-cell populations to effectively recognize the cancer.

Now, once we have trained the killer T-cells, the second thing that must be done is to arm the killer T-cells with the ammunition they need to go out and effectively kill the tumor cells. To do that, the Versamune® technology activates an important pathway known as the Type I interferon pathway. This pathway is now known to be quite important in our ability to mount an anti-tumor or anti-viral immune response. Therefore, by being able to both train the killer T-cells and arm them adequately, they can go out and effectively kill the cancer cells. With this ability, Versamune® overcomes two of the important obstacles that have historically faced immunotherapy. Our preclinical data and early human clinical data suggest that these mechanisms are being effectively activated in humans. The early data is very promising.

CEOCFO: *How do you train a cell?*

Dr. Bedu-Addo: Our immune system is quite complex. There are a number of mechanisms that have been built in our bodies to really facilitate this. One way this happens is that there is a population of our cells known as dendritic cells. These cells are part of our body's defense system and their job is to identify foreign agents and present them to the immune system as an invader. So, when we inject a Versamune®-based immunotherapy or vaccine right beneath the skin, the dendritic cells take that protein and become activated. When the dendritic cells are activated, they move into our lymph nodes and send signals out to the T-cells, essentially saying, "Hey, we have an invader that we need to defend against." What we see for about a week after being injected is a heavy infiltration of T-cells coming into the lymph nodes, which indicates Versamune®-based immunotherapies and vaccines are working to activate the immune system.

It is that physical process of actually handing over that processed protein to the T-cells in the lymph nodes that tells the T-cells, "Hey, this is a foreign agent, you need to recognize this as "not supposed to be here," go out seek and kill any cell that contains or expresses this foreign agent." Therefore, that process of activating the dendritic cells, processing that protein, moving in to the lymph nodes, sending out signals and having the T-cells come in to retrieve the processed protein is actually a key process by which our immune system trains these T-cells to recognize those foreign agents and foreign proteins.

CEOCFO: *Your lead candidate, PDS0101, targets HPV associated cancers. What is the status of your Phase II trials for the PDS0101?*

Dr. Bedu-Addo: We have three planned Phase II trials for this product. The first is a trial that is being led by the National Cancer Institute. This trial addresses HPV-associated cancers, so this is an all-comers trial. As long as you have an advanced HPV-associated cancer, you will be eligible for this trial. Therefore, it could be head and neck cancer, cervical, anal, vaginal, or vulvar cancer. This trial was initiated in June of this year and it is based on the administration of a novel and promising triple combination. This triple combination consists of our drug,

PDS0101, EMD Serono's bi-functional check point inhibitor called M7824 and NHS-IL12, which is also an EMD Serono-owned immunotherapy. This trial was initiated based upon results of preclinical studies of this triple combination that were performed by the National Cancer Institute. The preclinical data was extremely promising and were published just last month in the Journal of Immunotherapy for Cancer. That is the first Phase II trial that is recruiting and is underway.

The second Phase II trial is being led by Dr. Ann H. Klopp of the MD Anderson Cancer Center. This trial addresses advanced localized cervical cancer. In this trial, PDS0101 is combined with the standard of care, which is chemo radiotherapy or CRT. This trial is expected to start in the next few weeks at MD Anderson Cancer Center and we believe that this combination has strong potential to provide enhanced clinical benefit to cervical cancer patients over just chemo radiotherapy alone.

The third trial is also a Phase II trial in which PDS0101 is combined with a checkpoint inhibitor KEYTRUDA®, owned by Merck. This trial targets recurrent or metastatic HPV-positive head and neck cancer. Many people do not realize that the incidences of head and neck cancer are drastically increasing due to HPV infection and this cancer has been described as a silent epidemic. What is unique about this trial in the combination immuno-oncology space is that it addresses first line treatment of the recurrent or metastatic cancer. That means that these patients will be able to get the combination before they even have to take chemotherapy, so this is an option that they would have versus going onto chemotherapy. We announced in April that we would be putting initiation of this trial on hold due to the COVID-19 pandemic and we anticipate initiating this trial before the end of the calendar year.

CEOCFO: *Speaking of COVID-19, would you tell us about expanding into infectious disease or how the Versamune platform works in that way? What have you learned about the SARS-CoV-2 virus?*

Dr. Bedu-Addo: In terms of applying the Versamune® technology to infectious diseases, let's use the SARS-CoV-2 example that you just provided. As the COVID-19 pandemic has progressed, we have learned much more about how the body responds to the infection. Today, the current focus has really been the development of vaccines that induce neutralizing antibodies. However, recently emerging data has really highlighted the important role of T-cells in COVID-19 immunity and the importance of developing COVID-19 vaccines that are actually capable of generating high levels of the active, virus-specific killer T-cells in addition to the neutralizing antibodies in order to provide a potentially more durable protection against infection. Then we took a step back and said, "Look, if we are going to get into development of COVID-19 vaccine we want to make sure that our technology is adequate to actually provide the kind of an immune response that will be required to provide broad, durable and long term protection against the virus."

We understand the importance of T-cells and also recognize that killer T-cell induction is one of the significant limitations of the current vaccine technologies. We have a technology that has demonstrated very clearly, both in preclinical models and in humans, that it induces both these

strong killer T-cell responses and neutralizing antibody responses. That is why we decided to initiate work in COVID-19 and focus on developing a second generation COVID-19 vaccine. Now, the reason we call it a second-generation vaccine is because many of the vaccines that are already in rapid development have really focused on neutralizing antibodies. We said, "Let us just develop a vaccine that generates a broader range of protective immune responses, that could also potentially provide protection against future mutations of the virus," so that is what we are doing. Our initial preclinical studies looked at a couple of things. First, could our Versamune®-based vaccine generate a rapid T-cell response as well as a rapid antibody response? The answer to that question was yes. We show that within fourteen days of vaccination, we could induce about a thirty to forty-fold increase in both virus-specific helper and killer T-cells against SARS-CoV-2, the COVID-19 virus.

What we also did was look at the neutralizing antibodies, we found out that by day fourteen we could induce about a twenty to twenty-five-fold increase versus the vaccine without Versamune® included. That level of neutralizing antibodies at day fourteen was very similar to what we see in some of the sickest COVID patients. However, what surprised the investigators was that even after day fourteen we continue to see a dramatic increase in the levels of neutralizing antibodies beyond thirty days. What we demonstrated here was that Versamune® was able to present the COVID-19 protein into the right immunological pathways and activate the right mechanisms to create strong antibody responses as well as powerful T-cell responses against the virus.

The other thing we know is that there is an important kind of T-cell response known as the memory T-cell response. As the name suggests, these are T-cells that will lie almost dormant for a long period of time. But, when the virus shows up they are well-trained to immediately recognize it as a foreign agent and kill the infected cells. We also demonstrated that Versamune® was able to prime the immune system to generate these long-lasting memory T-cells against COVID.

We have just presented our initial strategy to the FDA and have received their feedback. So, we are just finalizing our preclinical work and should hopefully move it into the next stage, which would be human clinical trials.

CEO/COO: *How far will your recent fund raising get you?*

Dr. Bedu-Addo: The funds we just raised will support us for approximately two years. Our current goal is really to focus those funds on progressing our oncology pipeline. With the infectious disease programs, we are looking to focus more on partnering with either governmental or non-governmental organizations. We just got an award for our universal flu vaccine from the NIAID. For our COVID-19 program, we are also still in discussions with a number of governmental and non-governmental agencies. We also have the partnership with the Brazilian company Farmacore Biotechnology. Therefore, our goal would be to preferably bring in some non-dilutive financing to move the infectious disease programs forward, while we focus the funds we just raised on progressing our oncology pipeline.

CEOCFO: *What have you learned from your past experience on the business side, on the organization side? What do you understand that gives PDS Biotechnology a leg up?*

Dr. Bedu-Addo: I think from my experience and the experience of the management team, what we have learned is that it is very important to be focused and really have a very well laid out strategy. Also, with a company like ours, one thing you may notice is that we have quite a deep pipeline for a company our size and at this stage. One of the reasons we have been able to accomplish that is the strategy of partnering. For example, with PDS0101, each of those clinical trials is partnered with a leader in the field. With the advanced HPV cancer trial, we have the partnership with the National Cancer Institute. We also have the partnership with the MD Anderson Cancer Center. However, not only are those programs progressing, but it is also important to have a clear goal and define what we really want to achieve with these trials and establish the most efficient way to get there. One of the things we do not really want to do is to get into a situation where we are completing clinical trial after clinical trial without achieving any goals or progressing the program.

What you will notice with our PDS0101 trials, for example, is that two out of the three are combined with this standard of care. An important question we are asking with these trials is whether we can improve the clinical benefit to the patients over the standard of care without compounding toxicity. If we can answer that question and the answer to that question is yes, there is a very clear line of sight as to how we commercialize PDS0101 and exactly what we have to do. That means there is a very clear path forward for two of the clinical trials. The third, as I mentioned, is a novel triple combination and what we have done here is combined PDS0101 with two of the more promising clinical-stage immunotherapies out there. If we are able to demonstrate that our preclinical efficacy data translates well to humans, then this is a candidate that we can very easily and rapidly apply to multiple solid tumors. Therefore, we have a very well laid out strategy as to how we move the product forward with these partnerships.

Our goal is for PDS0101 to hopefully get to the interim data points with these trials in the next one to one- and one-half years. We have taken a very similar approach with the infectious diseases programs, as I have mentioned, really partnering with the experts like NIAID, partnering with the company Farmacore Biotechnology and in that way we mitigate the risk, but also bring in non-diluted financing to help us progress in some of those programs moving forward. Really, that is our key strategy, to be really focused on exactly what we need to achieve and also to be very financially efficient in how we go about building out a broad pipeline of successful products.



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