

Q&A with Dr. Paul Lammers, President and CEO of Triumvira Immunologics developing their T-Cell Antigen Coupler Technology to activate T-Cells in the treatment of Advanced Hematological Cancers and Solid Tumors



Dr. Paul Lammers
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Interview conducted by:
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CEOCFO: *Dr. Lammers, you have been president and CEO for a little over a year now. What attracted you to Triumvira Immunologics, Inc?*

Dr. Lammers: When I started to look at my next opportunity, I came across a number of companies and was really intrigued by the Triumvira technology. Given the fact that CAR-T therapy is about the hottest area in immune-oncology, and the TAC technology is very well differentiated from CAR-T cells and invented by a very reputable professor at McMaster University in Hamilton, Ontario. I thought, "Man, would it not be great to build a company around this technology and bring this technology into the clinic for patients."

CEOCFO: *What has happened over the last year at Triumvira? How are you leading the charge?*

Dr. Lammers: When I joined on January 1st of 2018 there were two full-time Triumvira scientists up in Hamilton at Dr. Bramson's lab. Right now, we have fourteen. The typical conundrum in biotech is that 'you need a team to raise the money and you need money to raise the team'. Therefore, I told the board of directors, "If you want me build the team, then get ready, because I will build the team." I then started to build the team and hired the best people in T-Cell therapy that I could find, no matter where they lived. We have an R&D group in Hamilton, Ontario that we moved out of the academic labs into a separate lab facility there. Then we opened a corporate headquarters here in Austin, Texas, where we have six people. Then we have a number of experienced professionals around the country, from Miami, to Seattle, to Houston. So far it is working very well, and a great deal of progress has been made! We had a great pre-IND meeting with FDA last December. We are moving our pipeline forward and aim to have our first IND submitted in March, which means that we could have our first patients treated with our technology in the middle of the year. Then we will move our second program forward into the IND-stage later this year. We also expanded our Board of Directors. We brought in two very strong independent

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directors with a lot of experience in oncology and cell therapy. Therefore, it has been a fantastic ride so far!

CEOCFO: *What, if any, are the challenges of collaboration in science when you are working remotely? What have you learned over this year about how to do that successfully?*

Dr. Lammers: I think the two critical components for any business are information and communication. I think that when you have a semi-virtual business model, it requires you to be more informative and communicate more often. Therefore, we have our weekly management team calls, and every other week we have a teleconference with the whole team. I want to make sure that the R&D group in Hamilton knows that there is a management team to support them, and so members of the management team try to spend two to three days a month up in Hamilton to make sure that we have presence and visibility. That is important, because for me, leadership is visibility to a large extent as well. I want to make sure that they realize that we come to work every day and we work hard to make things happen. So far it has been going really well.

CEOCFO: *Let us talk about the technology. What have you figured out?*

Dr. Lammers: Basically, CAR-T therapies have done really well, and they have become a game changer in how we treat patients with advanced hematological cancers, such as lymphoma and leukemia. The basic principal appeals to everybody, because the idea is that you teach a patient's own immune system to identify, track and kill their own cancer cells. That is truly personalized medicine. You take blood from a patient. You isolate their T lymphocytes. Then in the lab you genetically engineer them to start expressing a protein on the surface of those cells. Then you expend them in the lab and you give them back to the patient. Now the patient receives their own cells back, but now armed to recognize and kill the cancer cells. It is a beautiful principal. The challenge with CAR-T cells is though, that it is a system that activates T cells by itself and is either 'on' or 'very on'. There is no off switch to a CAR. The CAR-T cell is always activated, which means it is always releasing cytokines which often leads to two things. One, it leads to the fact that these cells get exhausted, because they are tiring out. Secondly, it leads to toxicity, which we know is the big challenge in CAR-T therapy. The toxicities are substantial in terms of cytokine release syndrome and neurotoxicity. Triumvira's technology, the TAC, also known as T-Cell Antigen Coupler technology, was designed to overcome these issues by activating T cells utilizing the endogenous T-Cell receptor complex that is normally present on every T-Cell. Therefore, we are co-opting the natural function of the T-Cell with our technology, so it is a more natural way to basically achieve the same goal. However, we expect to do it in a safer fashion. On top of that, we have shown in preclinical studies so far that our TAC technology is very effective also in solid tumors, where CAR-Ts just have had a very difficult time so far to show robust effects.

CEOCFO: *Why does it work?*

Dr. Lammers: Basically, the TAC is a chimeric receptor that connects a T cell with a cancer cell. It recognizes an antigen on the surface of the cancer cell, like a CAR-T does as well, but then through another single chain antibody it pulls in the whole T-Cell receptor and moves that towards the cancer cell and says, "Now we need to go to work." This interaction and T-cell activation is then further enhanced by the presence of the third component of the TA, the CD4 co-receptor. This three-domain protein structure is known as the TAC.

CEOFO: *How is your method more effective?*

Dr. Lammers: Jonathan Bramson has been working with CAR-Ts for ten, twelve years now in his lab. He said, “CARs are very effective, but we have killed a lot of mice with CAR-Ts. They are extremely toxic.” They looked at different ways and they said, “Nature has designed its own way of activating T-Cells, known as the T-Cell receptor. Therefore, would it not be neat if we could co-opt that system and have nature do its own work?” That was the concept behind it. They developed different structures and ultimately decided on the T-Cell Antigen Coupler structure, which has three separate domains. One binds to the cancer cell, another one binds to the T-Cell receptor, and the third one is the CD4-co-receptor, that brings additional important aspects for T cell activation. Therefore, it truly is a natural system that we are using.

CEOFO: *What is next on the agenda? You mentioned there are a couple of things in the works.*

Dr. Lammers: Right now, we have an interesting and broad pipeline. Our first program is directed against CD19, a well-known target in the CAR-T world that is expressed on the surface of Non-Hodgkin’s Lymphoma tumor cells. The CD19-TAC program will go into the clinic in the middle of this year. The second TAC is directed against HER2, which is a well-known target for, for example, breast cancer, brain cancer, sarcomas, and gastric cancer. The third TAC program is an allogeneic TAC directed against BCMA (B-cell maturation antigen), a well-known target for Multiple Myeloma, which is another deadly disease. Then we have a number of other TAC targets in the pipeline as well. Therefore, we have a very ambitious program as we intend to bring four of our pipeline TAC products into the clinic in the next two to three years.

CEOFO: *How do you decide what to work on?*

Dr. Lammers: It is basically driven by a combination of what is happening in the market, including working on a de-risked target like CD19, and finding the shortest route for us to show a clinical proof of concept for the TAC technology. As a small company working in a very competitive field, it is really crux for us to show that the technology works in the clinic, because that would open up many doors, as you can imagine.

CEOFO: *What is your funding situation at Triumvira?*

Dr. Lammers: We have basically about \$13 million of funding. About \$5 million was through research grants to Dr. Bramson’s lab. The rest was raised with the help of Bloom Burton & Co. Bloom Burton & Co is an investment advisory firm out of Toronto. They are advising a network of high net worth individuals and family offices on unique investment opportunities, and they have in fact been co-founders of the company. We are currently in the process of raising a large thirty to forty million dollar Series A round of financing that we hope to complete in the first quarter of this year.

CEOFO: *Does the medical community and the investment community understand the concept?*

Dr. Lammers: Yes. When I started last year, I told the board, “We have a new technology that is trying to compete with a well-entrenched technology, CAR-T.” You can only do that if you can create a buzz around the company and its technology. We have hired a PR firm to help us with that, and also built a new website. Then, a key paper on our technology was published last year in *Nature Communications*, a highly

respected, peer-reviewed scientific journal. Also, we are now being invited to give talks at various CAR-T and TCR medical and scientific conferences. Therefore, it is all about creating a buzz around who we are, what the technology stands for, how well it is differentiated from CAR-T and what the technology promises for patients.

CEOCFO: *How does Triumvira Immunologics stand out at a conference when there are so many ideas and so many companies competing for attention?*

Dr. Lammers: That is a good question. If you think about it, in the US there are about forty CAR-T companies now. In China there are about seventy CAR-T companies now. However, the point is that we are not a CAR-T company. We consider the TAC technology to be a next step forward in T-Cell therapy. Ultimately, our clinical data will be compared to CAR-T products. We see ourselves as the next step forward, because there are significant limitations to the use of CAR-Ts. Many patients are ineligible to receive CAR-Ts because of the toxicity. Patients that are either too old or too frail are not eligible because of the toxicity. Therefore, if we can come up with an effective but safer T-cell therapy approach for liquid tumors like, leukemia and lymphoma, then that would represent a big step forward. On top of that, if we can show that TAC T-cells actually work in solid tumors, where CAR-T cells have not been very effective to date, well, that could be a game changer.

CEOCFO: *What have you learned over the past year, as you have been testing, that surprised you?*

Dr. Lammers: As they always say, persistence pays off. As a late comer, as a company in this crowded space, you need to make sure that you catch the wave of enthusiasm. So far about eight billion dollars of venture funding went into the CAR-T space. Many of the big VCs have already placed their bets in various CAR-T companies. What you need to make sure of is that you tell the story often. Sometimes it takes more convincing. It might not take a first meeting, or a second, but only the third and fourth meetings before people appreciate how we are different. Therefore, we have to just keep going at it. You have to be out there and go to Boston, New York and San Francisco, beat the pavement and put yourself in front of VCs and tell the story over and over again. However, I am glad to do that because it is a very exciting story, with a very exciting technology.

CEOCFO: *What should we expect in the upcoming year from Triumvira Immunologics?*

Dr. Lammers: We hope to finish this year by having data on the first five or six patients treated with our first TAC product, which will be extremely exciting. Then will also have submitted our second IND to the FDA, which means that early next year we can hopefully start our second clinical program. Therefore, this is the year we have to make it happen. This is where the rubber meets the road. It is all about getting into the clinic. The FDA was very supportive when we had that pre-IND meeting in December. We are looking forward to getting our first IND submitted. We have manufacturing set up, we have the clinical sites for the study identified and they are very excited to take part. It is about putting all of your ducks in a row and then execute on the program.