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Developing the first Drug Candidates based on Phospholipid that Activates Natural Killer Cells, Machavert Pharmaceuticals is leading the way in this new approach of Harnessing the Power of the Human Body to Fight Against Cancer

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"Our phospholipid nanoparticles can activate NK cells and also directly cause antitumor effects at the same time, through the CDK8 signaling pathway inhibition. This is something new and unique, especially if you take into account that we see no adverse effects."- Dr. Jakub Staszak-Jirkovsky

CEOCFO: ***Dr. Staszak-Jirkovsky, what is the idea behind Machavert Pharmaceuticals?***
Dr. Staszak-Jirkovsky: Machavert is a preclinical stage development company. We currently develop two drug candidates. One, MP1115, is a bioactive nanoparticle for immuno-oncology. MP1115 activates Natural Killer cells to attack cancer. The second, MP2019 is a small molecule RAL GTPase inhibitor against liquid and solid tumors with KRAS mutation that is primarily being developed for non-small lung carcinoma treatment. MP2019 is also being combined with MP1115 for enhanced anti-cancer action.

CEOCFO: ***What is it about your approach that is different than some of the other methods that are being looked at today?***
Dr. Staszak-Jirkovsky: What is most unique about us is the first and most developed drug candidate, the bioactive nanoparticle MP1115. It is based on phospholipids, and it has been built upon, to our knowledge, the first-time discovery of a phospholipid that directly activates natural killer cells to kill cancer. MP1115 also shows anti-proliferative activity against cancer at the same time. Because it is a phospholipid, you can create liposomes out of it. The liposomes are nanoparticles that can be further loaded with other therapeutics; other drugs that can be delivered as payloads into the tumors by the nanoparticles.

CEOCFO: ***What have you discovered?***
Dr. Staszak-Jirkovsky: The most exciting recent development in cancer treatment has no doubt been immuno-oncology. This approach activates or enables the immune system inside the body to attack cancer and can give patients much better outcomes than some treatments that have been available in the past. This immunotherapy is what we are building on. For instance, the biggest success of immunotherapy to date are anti-PD1 checkpoint inhibitors, including KEYTRUDA® or OPDIVO®. They are blockbuster drugs already, and it has quite recently been discovered that agents that activate Natural Killer cells can synergize with these inhibitors. In other words, a drug that would activate Natural Killer cells would make these anti-PD1 immunotherapies even more effective.

CEOCFO: ***What is your approach?***
Dr. Staszak-Jirkovsky: This is what we are building on. We have discovered the phospholipid active pharmaceutical ingredients that can activate Natural Killer cells, and trigger an immune attack against cancer. On top of that, if you combine it with some already approved immunotherapies, it would synergize with these and can provide better outcomes for cancer patients.

CEOCFO: ***Do we know why it works?***
Dr. Staszak-Jirkovsky: Yes. We inhibit or disrupt the CDK8 signaling pathway. CDK8 is a very promising target for cancer treatment. There are few drug candidates in development now that go after this target; so it is quite new. There are some of these CDK8 inhibitors that are currently in the clinic, but only in the early stage. However, some significant issues with toxicity were reported with these competitive CDK8 inhibitors. We do not see this toxicity with our bioactive lipid nanoparticle, so this differentiated us further from our competitors. We believe that MP1115 can deliver advantageous results that include both efficacy and very good safety.

CEOCFO: ***Where are you in the development process?***
Dr. Staszak-Jirkovsky: We have recently brought the phospholipid nanoparticle MP1115 to the point where we are confident to take it to FDA-IND enabling studies required for approval to enter human clinical testing. We see good efficacy *in vivo* in human cancer models, and we see that we successfully activate NK cells *in vivo*. We will have to scale up manufacturing, and we have to complete animal safety studies. We anticipate filing the IND and initiating clinical trials in the first half of 2020.

CEOCFO: ***Are you funded for further research and development?***
Dr. Staszak-Jirkovsky: We are currently in the process of raising money. We are looking for money to fund the next development stage, which is the IND development. We have raised $5.5 million from private investors so far. We also received a grant from the State of Colorado, which was the largest that you could get there, $250K. We will need an additional $6 million on top of that to complete the IND for initiating human trials.

CEOCFO: ***Do investors, as well as the medical community, understand the difference in what you have come up with?***
Dr. Staszak-Jirkovsky: I hope so! Yes, I think what we have is something special! Natural Killer cells and CDK8 are targets that are well established. Some big pharma companies are investing in this direction because there is a lot of promise with this strategy. The main advantages to our therapeutic includes the synergy between already approved immunotherapies and Natural Killer cell activation, and an additional direct anti-cancer proliferation effect. We also have an excellent safety profile and the ability to deliver therapeutic payloads. I hope we will be able to get this message across and spark some interest in the investment community.

CEOCFO: ***How does Machavert standout at a conference? How do you garner attention among many other ideas?***
Dr. Staszak-Jirkovsky: We are attending and presenting at global scientific and investment conferences on a regular basis and talk to people as much as we can. For instance, we started this effort last year at the Bio International conference in June in Boston, and we had some first meetings. We continued our efforts at BIO Europe in Copenhagen last Autumn and we presented our scientific results at the EORTC-AACR-NCI scientific conference in Dublin, Ireland. We most recently presented this January at BioTech Showcase in San Francisco, which was a satellite meeting during the largest annual investment event in Biotech, the JP Morgan Healthcare conference. We have been recently accepted to present at the aclimed international AACR meeting this Spring in Atlanta. At these conferences, we progressively keep meeting update interested investors and generate new interest with follow-on investors. I hope they see that we are making a lot of progress continually that sparks their serious interest. We are excited with our progress and successful meetings to date.

CEOCFO: ***When did you know you were on the right track?***
Dr. Staszak-Jirkovsky: That is a good question. This discovery that we actually activate natural killer cells was a big satisfaction for me, because for a long time I was convinced that what we were working with, basically a phospholipid library, was doing something with the immune system. However, for a long time, we did not have any direct proof of this. Once we finally managed to make our *in vitro* assays working that made efficient *in vitro* screening possible, we discovered that we trigger NK cell activation, not only in a dish, but also *in vivo*, in animals. Well that was a big deal. I was very happy at that point! Then of course, the *in vivo* activity or efficacy in cancer models is a big deal for me, too.

CEOCFO: ***Your site shows, "We believe that the key to our success is close collaboration and a creative team." How does that play out in day to day activity, day to day interaction?***
Dr. Staszak-Jirkovsky: That is a good question, too. It is tough. Scientists always like to have different opinions, and I think it is a good thing. That is because if you are creative you want to be the one to discover something new and it does not always work great in a team if there is always a lot of tension or internal rivalry. However, we all see that we are

working on something great that has a huge potential to help many people, and we always manage somehow to get together and work as a team toward the ultimate goal, to create a game-changing product for cancer treatment.

CEOCFO: ***How do you deal with the frustration of having something that is so potentially meaningful, but a slow and arduous process to get it to a point where it is available?***
Dr. Staszak-Jirkovsky: Yes, that is tough. I think that, for me, the most important thing is to know we work on something meaningful. That it is worth my time, it is worth the effort, and I would just do anything that it takes to make it happen. It brings a great satisfaction, but of course, it is going to take a while. However, if it were easy, then everybody would be doing it which makes me feel we do something special. Also, we want to make sure that our shot at delivering advantageous therapeutics for cancer would count and we do not want to make any errors.

CEOCFO: ***Are there particular types of cancers you are looking at initially?***
Dr. Staszak-Jirkovsky: The first thing to say is that, because we synergize with PD1 inhibitors, we will go into the areas where these therapeutics are effective and approved. However, generally speaking, we go primarily in the direction of solid tumors, where we focus on lung, colon and melanoma cancers. We also have promising results in hematology cancers including non-Hodgkin's lymphoma, AML and multiple myeloma. Those are the main areas that we are targeting.

CEOCFO: ***That is a wide range!***
Dr. Staszak-Jirkovsky: Obviously, we will have to narrow our focus, in clinical trials. Our drug candidates do show a wide range of applicability though, so there is a huge potential for the future. This is also because our drugs activate natural killer cells directly to stimulate their action against cancer.

CEOCFO: ***What and how you are going to combine with already approved drugs?***
Dr. Staszak-Jirkovsky: Our NK cell activating nanoparticle drug will synergize with other immono-oncology treatments such as anti-PD-1 inhibitors such as KEYTRUDA® or OPDIVO®. While loading of the nanoparticles with other drug payloads is not our primary goal, we have successfully loaded our nanoparticle drug with other novel therapeutics. For instance, the second asset that we have is a small molecule against RAL GTPase. This is a new target against KRAS mutation cancers, against which there is currently no effective treatment. However, KRAS mutant cancers represent about thirty percent of all cancers! What we are trying to do is always something novel, something new that no one else is doing. That is our approach.

CEOCFO: ***Why take note of Machavert Pharmaceuticals now?***
Dr. Staszak-Jirkovsky: I think we have something really unique! Our phospholipid nanoparticles can activate NK cells and also directly cause antitumor effects at the same time, through the CDK8 signaling pathway inhibition. This is something new and unique, especially if you take into account that we see no adverse effects. On top of that, you can combine this nanoparticle with other therapeutics that can deliver payloads into tumors as well. That is something really really special. We also have a good team. We have Dr. Neal C Goodwin, Ph.D. who is our Chief Scientific Officer; Dr. Goodwin has been previously working at Champions Oncology (NASDAQ: CSBR) and The Jackson Laboratory. He has led the development of humanized immune system mice, which is something very important in the field of immuno-oncology that provides an important tool to model the human immune system in animals. This is very important to us, too. He also has founded an oncology drug development company, that made it to an IPO. Therefore, he has already done in the past what we are trying to achieve right now. On top of that, we have an experienced, seasoned scientific advisory board. We have been working with Dr. Dan Theodorescu, M.D., Ph.D. for several years now already. He is the cancer center director at Cedars-Sinai in Los Angeles. We are in the process of establishing a collaboration with Cedars-Sinai, as well. Dan was previously the director of the cancer center here at the University of Colorado Medical School. This is how we started to work with him, and we have formal collaborations with the University of Colorado, too. Our science advisory board also includes Norman M. Greenberg, Ph.D., who is the CSO of Atreca, a successful immuno-oncology therapeutic firm that we regard as our role model company. Norm previously served as the global head of oncology at AstraZeneca/MedImmune and as a senior director of oncology at Pfizer. There are several more other prominent people on our science advisory board and our team, but in brief, I think we have a really good team that can make it happen.

CEOCFO: ***Is there anything that people might miss or misunderstand when they first look at Machavert?***
Dr. Staszak-Jirkovsky: That is a tough question. It could be the novelty, that we have something really unique. That can, to some extent, turn some people off, because tit might be hard to understand what it is that we are doing and why it is so different and orthogonal to what everyone else is doing. That is the tough part. I think that this can be actually turned into a a big advantage, but it is also our job to try to explain this to people and convince them that this is actually something extraordinary that can impact cancer treatment by doing things differently.