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Q&A with Mark Leuchtenberger, MBA, President and CEO of IRX Therapeutics, Inc. developing a New Immunotherapy Candidate containing Numerous Active Cytokine Components that Turn Cold Tumors Hot and is currently in Clinical Trials for Head and Neck and Breast Cancer

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"The activation of T cells, NK cells, dendritic cells and macrophages observed in the TME following the administration of IRX-2 may explain the compelling multiyear survival data in our Phase II A study in head and neck cancer."- Mark Leuchtenberger, MBA

CEOCFO: ***Mr. Leuchtenberger, according to the IRX Therapeutics Inc site, you are unlocking the power of immunotherapy. How so?***
Mr. Leuchtenberger: We have a product that is a collection of cytokines that are critical for overcoming tumor-induced immune suppression and activating the immune system to launch an attack on tumors. We think that we are alone with this particular type of product, having an effect on activating the entire tumor microenvironment (TME), having biomarker data, and with proven clinical data including progression free survival and multiyear survival benefits. While many companies aspire to "turn cold tumors hot", we believe our data prove that we are accomplishing just that by boosting the entire TME.

CEOCFO: ***What is special about your cytokines or is the combination that makes it happen?***
Mr. Leuchtenberger: It is the mixture of cytokines. The seven main cytokines that comprise IRX-2 are critical for activating various stages of the immune attack. While other related therapies may activate one component or limited aspects of the TME, such as IDO, we bring multiple cytokines that are critical for activating all the essential classes of immune cells that are responsible for the attack; the T cells, dendritic cells, the Natural Killer (NK) cells and macrophages. Our biomarker data that we have obtained in the last year, from multiple clinical trials in head and neck cancer and breast cancer demonstrates that these specific immune cells are upregulated in the TME. Prior to administering our therapy, we were able to collect biopsies from patients where you can observe the resting levels of these immune cells. Following our treatment at the time of surgical resection of the tumor, we are able to see boosting of all the immune cells that I just mentioned in the TME. This helps prove that we are launching an immune attack prior to surgery that helps the body to fight the tumor and increase the prospects for survival.

CEOCFO: ***What is the science? What is happening in the body with your compound?***
Mr. Leuchtenberger: Dr. John Hadden, the inventor of this regimen observed breakthrough results using a single cytokine, Il-2, in head and

neck cancer in the 1990s. His research focused on whether or not the collection of all the relevant cytokines would have a greater effect in the treatment of head and neck cancer. He designed a biological process to reliably reproduce a heterologous group of cytokines that we still use today involving the extraction of white blood cell donor lymphocytes known as leukopaks. We use a proprietary process to amplify the cytokines from a pack of twenty-four or more patient leukopaks. Once the cytokines are extracted and filled into 1 mL vials, they can be injected subcutaneously near the lymph nodes of cancer patients. These cytokines are drawn into the lymph nodes, activating the immune cells which travel through the system to find and fight the tumor. The activation of T cells, NK cells, dendritic cells and macrophages observed in the TME following the administration of IRX-2 may explain the compelling multiyear survival data in our Phase II A study in head and neck cancer.

CEOCFO: ***Why are they drawn in? What is it about them that would cause the tumor to like them?***
Mr. Leuchtenberger: IRX-2 inspires the body's own authentic immune attack by providing physiologic doses of cytokines. This means that rather than a massive dose of cytokines that could cause a "cytokine storm" resulting in uncomfortable and difficult-to-manage side effects, we provide doses that are naturally available in the patient's body. IRX Therapeutics' data show that this level of dosing activates the immune system, turning 'cold' tumors 'hot' to mount the immune attack, and is well tolerated, avoiding the negative side effect profiles of massive doses of cytokines. Therefore, we believe we have developed the optimal solution by encouraging the body's own immune attack with physiologic doses that do not have compromising side effects.

CEOCFO: ***Would you tell us about your proprietary enhancement process?***
Mr. Leuchtenberger: That is the production process. There is a stimulant called PHA – PHA stimulates the leukocytes to express the cytokines. We then collect them, screen out all the extraneous material and turn these cytokines into a frozen liquid, then vial it to be shipped to the hospital where the patient is treated. The nurses and physicians with whom we have spoken say that this process could not be easier, either for the physician in the hospital or the patient. The injection is administered using a 25G needle (similar to an insulin needle). Typically, the injections take place over ten days and do not leave a scar. The therapy is well tolerated with some mild side effects, but nothing like the compromising side effects often seen with high doses of cytokines.

CEOCFO: ***You became President and CEO this past year. Why did you choose to work with IRX?***
Mr. Leuchtenberger: I was very fortunate to start my career in a very auspicious place, at Biogen in 1990. I worked there for twelve years where I led the development of what became their first drug, AVONEX® for multiple sclerosis. We launched AVONEX® in North America, built a sales force team and an international commercial operation with sales in sixty-five countries. Thereafter, I sought out opportunities to have a transformational impact on severely affected patient populations. I have worked in antibiotics, cancer, and cardiovascular; I think the common thread has been companies that are at an inflection point where commercial, funding or later stage trial guidance is needed, with an end goal of creating a potential game-changing therapy. When I look at an

opportunity; I ask, “What is the power and potential of the therapy being developed?” AVONEX® now has $40 billion of cumulative revenue and I believe that IRX-2 may have the potential to equal that in terms of impact. We believe that our trials will show that IRX-2 has the ability to perfectly complement all the checkpoint inhibitors such as KEYTRUDA®, OPDIVO® and TECENTRIQ®. When I saw this opportunity at IRX Therapeutics I did my diligence and reviewed the science, market research, IP, manufacturing, etc. All the boxes were checked and one year later, I am even more excited than when I first joined in March 2017.

CEOCFO: ***What is going on today at IRX?***
Mr. Leuchtenberger: When we began last year – our Chief Operating Officer Monil Shah and I joined at the same time – we faced some immediate operational challenges. We had a Phase 2B trial – INSPIRE – up and running, but only a few sites were open and enrollment needed to be boosted. I am proud to say that the team has done a terrific job. The trial is now fully enrolled with over 100 patients and with interim event-free survival data expected in mid-2019. We were able to quickly open sites, globally, and boost enrollment very rapidly. I think it is a testimony to the excitement about the therapy, about the investigative field, that is building the enthusiasm of the patients to have access to this type of immunotherapy. However, I will also say, the potential of this drug is much larger as it could be the foundational therapy in numerous other indications. This has led us to establish ISTs – Investigator Sponsored Trials – at a number of prestigious institutions. Providence Cancer Center, Memorial Sloan Kettering, the Moffitt Cancer Center, USC, Emory, University of Michigan, University of Pennsylvania are just some of the institutions that are now running what we call investigative studies. Providence Cancer Center in Portland, Oregon has fifteen women enrolled in a breast cancer study and we are excited to have been able to present data from that study at SITC in November 2017, showing the activation of the entire TME in the majority of twelve women whose samples were analyzed. It is very exciting data that we believe supports the hypothesis that this therapy is working across multiple indications. That is one of ten investigative studies we have planned or are underway currently.

CEOCFO: ***What have you learned in the studies that was unexpected?***
Mr. Leuchtenberger: We are at the sharp edge of the cutting edge, if you will, of the science of checkpoint inhibition. The checkpoint revolution is well underway but it is hard to remember that it is only four or five years since the Phase 3 results of Opdivo were presented back in 2014. Every week there seems to be a new exciting confirmation, but also a disappointment. Where we see ourselves and what we wanted to do in the last nine months is push the science forward to understand whether or not we were having a beneficial and complementary effect with these checkpoint inhibitors. We now know that is the case because we are seeing that checkpoints including PD-L1, OX40, CTLA4, and others are upregulated by IRX-2. In order for the checkpoint inhibitors to continue working and having activity, we need these checkpoints in the TME. The depletion of these checkpoints from the TME could potentially be the reason for some of the survival failures with CIs seen recently. IRX-2 is actually providing the critical first step to mounting and continuing the attack of the cancer. We have biomarker data based on new technologies from NanoString Technologies Inc. and PerkinElmer Inc, quantifying and qualifying the lymphocytes infiltrating the TME post

treatment of IRX-2. This has garnered enormous excitement from potential partners. We now have investigator studies collaborations planned or ongoing with Bristol Myers Squibb, AstraZeneca, and other companies developing CIs. Therefore, I would say there is excitement across the board. That is important because we are in the middle of fundraising activity, the goal of which is to raise the funds to complete the Phase 2B study and complete these investigator studies.

CEOCFO: ***Are long term side effects of less concern when you are facing life and death situations, so that you can move faster?***
Mr. Leuchtenberger: It is important when they are considering these cancer therapies, that multiple therapies now have such added side effects that the long term is not even the issue. It is the short-term tolerability and even survivability of multiple checkpoint therapies. We look at our therapy and see that we hope to be adding to the potential efficacy of these checkpoints, yet not adding to the side effect burden. I am thinking about the current choice that the physician and patients face, which is, "We want to have the luxury of not worrying about tomorrow if I survive long enough." We now have over one hundred patients treated with the therapy and there are no long-term side effect profiles that have been identified. It is reassuring to both the patients and the physicians that we have these data. That is another differentiating feature of IRX-2 from therapies that are brand new or only tested in mice and just entering the clinic for the very first time.

CEOCFO: ***Why was breast cancer the second target?***
Mr. Leuchtenberger: Our therapy was originally chosen with head and neck because of the ease of accessing the local tumor for biopsy and resection, as well as access to the lymph nodes in the neck for easy subcutaneous administration. Therefore, you are proximally very close to the tumor. The next therapeutic target, breast cancer, was chosen because the axillary nodes are also very proximal to the breast. We are gratified that in the majority of the twelve patients that have been treated and for whom we have biomarker data, we are seeing a similar type of activation of the entire TME as seen in head and neck cancer. The next step is to move into metastatic disease in various tumor types. Those investigator studies are close to starting to enroll patients.

CEOCFO: ***Do you find that the investment community recognizes the potential of IRX Therapeutics?***
Mr. Leuchtenberger: The company has been around for a while. As you know, there is always a premium placed on things that are shiny and brand new. The advantage we have is that we have brand new data that essentially re-launches and recreates this story in a much more powerful way. Therefore, as Monil and I go into these investor meetings we are able to share this compelling new data. However, it is a process; I think that the immuno-oncology world, as I am sure you know, is so crowded with so many different voices speaking at the same time, that differentiating is a challenge. We like to point to the fact that we have several ways to differentiate that are unique. First of all, we have multi-year survival data from the Phase 2A. We have biomarker data from multiple indications; breast cancer and head and neck right now, and we believe we will have more along with clinical data from numerous indications as IRX-2 monotherapy and in combination with other agents. Then the manufacturing process is incredibly well characterized for a company in Phase II. We completed twenty GMP lots at this point in our history and over seventy lots overall. The FDA, EMA, and even the Paul-

Ehrlich-Institute (the German Federal Institute for Vaccines and Biomedicines) have all signed off and approved our drug for progression to later stage trials. We think our characterization of this as a unique opportunity in immuno-oncology and the ideal complement to these checkpoints is the compelling argument we can make. And we are making our case successfully, building by building, block by block.

CEOCFO: ***Why should people pay attention to IRX Therapeutics Inc today?***

Mr. Leuchtenberger: When we are on the road we jokingly call ourselves the best kept secret in immuno-oncology and we are trying to dispel that secret a bit. The company has been working for quite a while and unlike many of the companies that are two or three or four years old, we have the benefit of multiyear survival data. We have the benefit of confirmed anti-tumor activity and we have the benefit of a well-characterized and favorable long-term side-effect profile. That is the reason to pay attention. We are like one of those overnight successes; the garage band that has played for ten years and now has hopes of playing arenas. We have been doing this for quite a while and we are proud and excited about what we have. Our mission now is to make sure that we are communicating that story and that it is broadly understood just how much potential this therapy has to help patients.