ceocfointerviews.com

Issue: February 4, 2019

CEOCFO Magazine

Mary T. Szela, CEO and President of TriSalus Life Sciences, Discusses a Novel Technology That Improves Patient Outcomes in the Treatment of Pancreatic Cancer

Mary T. Szela
Chief Executive Officer and President

TriSalus Life Sciences
www.TriSalusLifeSci.com

Contact:
Mary Szela
1-224-515-0576
mary.szela@trisaluslifesci.com

Interview conducted by:
Lynn Fosse, Senior Editor
CEOCFO Magazine

"Our technology is a simple, elegant approach utilizing principles of physics to more efficiently and effectively deliver therapeutic agents into the solid tumor, leading to improved outcomes for patients."- Mary T. Szela

CEOCFO: ***Ms. Szela, according to your TriSalus Life Sciences site, your team is "on a mission to improve outcomes in cancer treatment." How are you doing that?***

Ms. Szela:

One of the reasons treating cancer patients with solid tumors is so difficult is that a vast majority of the drugs administered systemically don't get access into the tumor. When tumors grow in body cavities, stroma is created, which includes connective tissue, blood vessels, and very often inflammatory cells, all of which are interposed between the malignant cells and normal host tissues. This stroma is very dense and can envelop the tumor, compressing the lymphatic and blood flow. This high-pressure environment limits therapy uptake of therapeutics into the tumor.

TriSalus has developed Pressure-Enabled Drug Delivery™ (PEDD™) technology that addresses some of these drug delivery barriers, and it allows for improved penetration and distribution of the therapeutics into the solid tumors. Which, in turn, can improve outcomes and reduce toxicities.

CEOCFO: ***Would you give us some background?***

Ms. Szela:

My background is in large pharma, where I spent 25 years in a variety of marketing and senior management roles. Following pharma, I was CEO of an emerging antibiotic pharma company, and then CEO of a rare disease company.

Throughout my years in the pharmaceutical industry, an area of significant interest to me was always oncology. There has been so much progress in treating cancer, but really the last area we have not had great success in is treating high-mortality cancers with solid tumors. The big question is: why?

In solid tumors, we know the microenvironment of a solid tumor is very different than normal tissue. In many of the high-mortality cancers, like pancreatic cancer, we know that the stroma tissue I spoke about above is particularly dense and creates a high-pressure environment that is often much higher than normal blood pressure. So, essentially it is a physics problem. When the pressure within a tumor is 150 mmHg, and your mean arterial pressure is between 70 to 90 mmHg, very little drug ends up flowing into the tumor. Imagine that our circulatory system is a river, and the tumor you are trying to get to is on the banks of the river. You can add as much therapy as you want into the river, and none will get to the banks of the river. The only way for you to have the therapy reach the tumor on the banks is by raising the level of the river to overflow the banks. That, in a nutshell, is what we are doing with our technology. Our PEDD technology can: temporarily increase the pressure and forward flow during infusion; overcome the pressure within tumor; open up collapsed blood vessels; and deliver therapy deeper into the tumor. Importantly, since we can exquisitely target the therapy delivery in specific organs, we can significantly increase the therapeutic index, giving higher levels of the drug to the cancerous tissue while avoiding healthy tissue. This can improve patient outcomes while decreasing the side effects.

Over the years, many pharma companies have focused drug development on how to overcome the tumor microenvironment using a pharmacological approach, with limited success. When I was first introduced to the company, I felt that this novel drug delivery approach could be beneficial for use in combination with current standard-of-care agents, as well as some of the emerging new immunotherapies that require direct contact with tumor cells to be effective.

CEOCFO: ***Would you explain where the pressure comes in with a tumor?***

Ms. Szela:

This wound-like tissue called stroma is the body's response to malignant cells. It is believed that stromal tissue contains factors that aid in tumor survival and growth. The stroma and proliferation of other extracellular matrix components in the tumor creates solid stress that compresses blood vessels in the tumor. Think of it as a dense material that keeps growing and growing to the extent that it shuts off circulation into the tumor. How can one effectively deliver therapy into the tumor if the vessels into the tumor are blocked?

Additionally, the vasculature within the tumor is often quite leaky, and fluid leaks out into the interstitial space. Since blood flow and lymphatic flow is dysfunctional in tumors, fluid pressure begins to build to the point where the pressure outside of the vasculature is higher than the pressure inside the vasculature. So, even if therapy gets into the vasculature of

the tumors, there is no pressure gradient that pushes the therapy out into the interstitial space. It can't get into the cancer cells.

What's compelling about our technology is that we provide a simple, elegant solution to the issue. Our technology consists of a design to increase pressure within the vasculature to overcome the high-pressure environment in the tumor. By exerting the pressure within the vessel, you can open the collapsed vessels and deliver therapy deep into the solid tumor.

CEOCFO: ***Would it be the same for every tumor you are treating and for every patient?***

Ms. Szela:

Pressures vary across different tumor types and different organs, so we envision our technology to be specific to the therapeutic agent and the type of cancer we're targeting. Today, an interventional radiologist is aware that a tumor is high-pressure when a physician feels back pressure while infusing the therapeutic. Through imaging, fluid can actually be seen during infusion backing up and not penetrating the tumor. However, one of the challenges today is that we don't know which tumor is high-pressure.

CEOCFO: ***Where are you today in development?***

Ms. Szela:

Originally, the company was founded on addressing solid tumors in hepatocellular carcinoma (HCC). The technology is FDA- and CE mark-approved and has been used successfully and safely in over 11,000 procedures in the US, Europe, Brazil, and Canada.

Over the past year, we have outlined a pipeline of new technologies that addresses many of the unmet medical needs in treating a variety of solid tumors and improving treatment outcomes for patients. We have a series of new technologies launching, adding a new one each year, up to 2022. We have improved the ease of use of our current technology, and we've added new capabilities and tools for the physician to deliver positive outcomes, as well as make it more accessible for patients.

We also believe it is critical to have evidence to support the value of our technology. To that end, we have embarked on a number of clinical trials in pancreatic cancer, and liver metastasis, to demonstrate and validate the value of the technology in improving outcomes for patients. Recently, in collaboration with a pharma biotech, our technology was utilized to deliver anti-CEA CAR-T therapy to patients with stage IV pancreatic cancer with liver metastases. Two of the 4 patients had a complete response on PET scans, one of which was durable for over 12 months. None of these patients experienced serious adverse events, and they tolerated the treatment well.

This exploratory study is the first study in which CAR-T therapy was administered regionally, experienced minimal side effects, and showed improved outcomes. The study is continuing enrollment in the second phase to further accumulate additional data.

CEOCFO: ***Why pancreatic first?***

Ms. Szela:

Today, we believe our technology has the greatest value in delivering therapeutics to what we call “high-pressure” solid tumors. That is why we have intentionally shifted our focus to demonstrate the clinical application in pancreatic cancer, which has one of the most challenging tumor microenvironments. Not to mention, the mortality rate in pancreatic cancer has not significantly improved in the last decades. Something needs to be done to address this devastating disease. Based on preclinical data, we are optimistic that our novel delivery technology can significantly increase the therapeutic index.

CEOCFO: ***Is the medical community beginning to understand what you do? What has been the reception?***

Ms. Szela:

There is a great deal of increased attention and interest from the medical community because of the increased awareness about tumor microenvironments, and the challenge of immunotherapy in solid tumors. I think with some of the transformative results that immuno-oncology (I-O) has seen with hematological cancers, and their interest in delivering these therapeutics to solid tumors, the field is finally recognizing that delivery is a challenge. With the new novel immuno-oncology agents, one requirement is for these agents to have direct interface with tumor cells, so there is a willingness from biotech and pharma to explore alternative drug delivery options.

We have engaged with key pancreatic oncologists and key patient associations to help create awareness and understanding of our novel approach. Thus far, we have had a very enthusiastic response from everyone.

Despite being a small company, we are generating clinical evidence that this technology can make a difference in administering therapeutics into solid tumors and creating the clinical data that would give oncologists, interventional radiologists, and surgical oncologists confidence. However, there is now increased research that the combination of some novel immuno-oncology agents with regional delivery could be quite synergistic with current treatment regimens.

CEOCFO: ***Is the administration a series of treatments or a one-time treatment?***

Ms. Szela:

We are beginning several clinical trials using standard-of-care regimens with the goal of determining the optimal time to use a regional infusion. What we do know about the current regimen patients receive for pancreatic cancer is that the drugs work, but they are highly toxic. The majority of patients experiences side effects, and a subset of them must stop treatment because the toxicity is just too unmanageable.

I think ultimately the regimen of the therapy will be dependent on the type of cancer, the stage of the cancer, the drug that you use, etc. One thing we're optimistic about is that we know we can expand the therapeutic index (deliver higher doses directly into the tumor) and not expose the systemic tissue to all these toxic agents. So, repeat treatments might not mean increased toxicity for the patients.

There is really no single answer for it, so that is why we are investing in clinical trials that study a range of regimens, to give oncologists and patients several options that can improve outcomes.

CEOCFO: ***Why are you called TriSalus Life Sciences today? Why do you have a new name?***

Ms. Szela:

Our new name reflects a year-long review of our strategy, which strengthened our commitment to become a leading oncology drug delivery company. It reflects our aspiration to improve outcomes for patients being treated for cancer.

We have come to believe that the field needs to consider other aspects of therapy beyond just the drug in order to beat cancer. So, Tri represents the three strategic pillars of integrated cancer treatment: the administration of the right therapeutic, the stimulation of the immune system to fight the disease, and a targeted delivery system to augment the therapeutic effect.

The word Salus derives from the Roman goddess Salus, who represents health, prosperity, safety, and welfare. We are confident that our new name creates a stronger connection to our mission. In choosing TriSalus, we were inspired by the attributes of health and prosperity on behalf of patients. We hope others are too.

CEOCFO: ***Put it together for our readers in the healthcare and investment communities. How does TriSalus Life Sciences stand out?***

Ms. Szela:

The drug delivery field in oncology has seen little, if any, innovation in recent decades, and it is overdue for a technology that improves therapeutic uptake and truly makes meaningful differences in clinical outcomes. Additionally, the explosion of new immunotherapies, many of which require the drug to have direct contact with tumor cells, creates a significant opportunity.

Cancer is formidable, and we need to think about what problems we are trying to solve. In my pharma days, I would tell you that I never thought about drug delivery. I only thought about how the therapeutics would solve certain situations. It never occurred to me to utilize a technology to overcome these physical barriers. Now, after seeing how our technology works and seeing the clinical results it brings, I think this technology is a very simple, elegant approach of using physics to more effectively deliver the drugs into the solid tumor. This can enhance the therapeutic effectiveness and improve outcomes for patients.

I am a cancer survivor, and I watched my sister battle triple-negative breast cancer (TNBC). As her treatment progressed, her willingness to endure these treatments became less and less because they are so toxic.

Everyone at TriSalus is inspired by personal stories like mine. We see a world in which this regional targeted therapy is incorporated into every regimen, because we believe reducing tumor burden is a significant component of long-duration stable disease.

I do not ever want to say that we, as a technology, could ever cure someone. But we do think ours is a treatment modality that could be quite powerful when added to other therapies.