Personalized cell therapies offer hope for some of the toughest cancers

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June 17, 2021 -- Complete with a long-term vision of developing a pipeline of oncology therapies that modulate the functional immune system, Sotio of the Czech Republic is breaking into the world of autologous immuno-oncology therapies. The company's goal is to eventually become a prominent European pharmaceutical firm, according to Radek Špíšek, PhD, CEO and founding scientist of Sotio, who spoke with *ScienceBoard.net* in a recent interview.

Sotio is a unique biotechnology company in several ways. First, it is headquartered in Prague, a region that is not known for being a biotechnology hub and has a limited history of housing biotech and drug development companies.

The company was founded by PPF Group, a privately held international financial and investment group led by recently deceased Czech billionaire Petr Kellner. Together, Kellner, Špíšek, and one other scientific founder started the company in 2010. With a very specific vision for PPF, Kellner decided that he wanted to diversify into biotech, and Sotio was the result of that decision.

Sotio early on began building a large good manufacturing practice (GMP) facility in Prague, which it still utilizes today. The site was used to manufacture cells for Sotio's initial platform technology, dendritic cell vaccines. Since then, the company has become active in three modalities including cell therapies, antibody-drug conjugates, and interleukin 15 (IL-15) superagonist immunotherapies.

Leveraging the body's most potent antigen-presenting cells

The company's foundational technology is an autologous (individualized) dendritic cell therapy platform called DCVAC. The idea behind DCVAC is the modification of dendritic cells, which are some of the body's most potent antigen-presenting cells, so that they produce an immune response against a desired tumor protein.

To do this, the team starts by collecting a large quality of monocytes (precursors for the generation and manufacturing of dendritic cells) via a blood transfusion procedure called leukapheresis. Essentially, white blood cells are collected as blood is circulated through a transfusion machine.

Sotio has over 100 accredited leukapheresis sites throughout Europe and the U.S. Once the cells are collected from a patient, the team has 30 hours to get the fresh cells to the Prague manufacturing facility, Špíšek explained.

At the manufacturing center, Sotio scientists perform an eight-day process to differentiate the monocytes into dendritic cells. Importantly, the dendritic cells next need to be modified to express specific tumor antigens.

"We have a very elegant way and very sophisticated way to induce a complex, broad immune response that targets multiple targets on the tumor cell," Špíšek said.

During this process, the generated dendritic cells are combined with killed cancer cells, coming from very specific cancer cell lines (in this case either prostate, ovarian, or lung). The dendritic cells take up the dead tumor cells, cleave them, and process individual tumor antigens. Consequently, the tumor antigens are expressed on the surface of the dendritic cells. The final product can be frozen in liquid nitrogen and can be stored indefinitely.

To complete the process, a small amount of the final dendritic cell product is shipped back to the patient and is injected subcutaneously. Repeated injection should help the patient fight tumor cells and hopefully improve their prognosis, Špíšek noted.

Sotio is developing DCVAC products targeting prostate, ovarian, and nonsmall cell lung carcinoma. The company is expecting to announce the results of a phase III clinical trial for the dendritic cell therapy targeting prostate cancer soon and is preparing for a phase III clinical trial for ovarian cancer in combination with standard-of-care chemotherapy. The therapy provides a "statistically significant survival benefit" in all the programs, according to Špíšek.

Unique opportunities for CAR T programs

While Sotio was focused on its other programs, a unique opportunity in the chimeric antigen receptor T-cell therapy space became available. The company's leadership had expressed interest in pursuing programs in this field but decided that there were already larger pharmaceutical players at work and did not feel that the firm could compete in the "classical CAR T-cell therapy" arena.

But when Unum Therapeutics approached Sotio looking for a reverse merger partner, the Sotio team discovered that Unum had an early-stage, next-generation CAR T platform called BOXR that had the potential for targeting solid tumors. This is an area that has remained challenging for many classical CAR T technologies.

The BOXR platform provides an advantage by including a second transgene that increases the fitness of the T cell, in addition to a classical CAR T transgene targeting a specific tumor cell. This approach makes the product more resistant to the hostile tumor microenvironment in solid tumors, and the Unum team had the preclinical data to prove it. Based on this information, Sotio decided to acquire Unum's BOXR technology in 2020 and established a team in Cambridge, MA, near Unum's headquarters at the time. Unum subsequently changed its name to Cogent Biosciences.

Moreover, when Sotio researchers were looking for CAR T programs, the BOXR technology was attractive because of the synergy between each company's manufacturing requirements and capabilities. In the production of clinical trial materials, Sotio can use its pre-exisiting supply chain and manufacturing facilities in Prague, Špíšek explained.

The company is now in the early stages of developing a BOXR CAR T program targeting glypican-3 (GPC3) as a tumor antigen. Sotio is on track to file an investigational new drug application (IND) for this program before the end of the year and hopes to begin clinical testing early in 2022.

Individualized versus off-the-shelf therapies

When asked about whether autologous or allogeneic approaches to cell therapy are more effective, Špíšek prefaced his answer by noting that he is aware of the logistical challenges associated with the production of autologous cell therapy products. For instance, having to fly cells around the world, twice, for every patient.

While he noted that allogeneic therapies may be the gold standard that the industry is working toward, the field is just not quite there yet. The primary issue with allogeneic cell therapies is that in order for classical cell therapies to function, they must persist in the body for a prolonged period of time.

Allogeneic cell therapies are lacking in this aspect because within minutes or hours of administration, allogeneic cells are recognized by the functional immune system as a foreign entity and are destroyed.

"At the moment, autologous cells are a must to ensure that the cells given to a patient have enough time to perform their action," Špíšek concluded.