

Medical Device Solutions for Unmet Medical Needs



Ronald J. Solar, Ph.D.
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About ThermoPeutiX, Inc.

THERMOPEUTIX, INC. is a San Diego-based privately held company that offers imaginative, innovative and economical solutions to unmet medical needs. The medical specialties that are currently targeted include interventional cardiology and radiology, neuroradiology, neurosurgery, and oncology. The Company's current product line — a proprietary family of patented and patent-pending CoolTools™— addresses the next frontiers in interventional medicine, advancing the treatment of vascular-related disorders and using the body's vascular system to provide therapy. These products include "contrast-sparing" support/microcatheters, local drug delivery systems, and a novel catheter system and technique for the treatment of ischemic brain injury (e.g., stroke, cardiac arrest, trauma). In addition, the Company's current R&D product pipeline includes a patented endovascular coil/embolic-agent delivery system to treat brain aneurysms, next-generation angioplasty catheters, a thrombus management catheter, and a novel endovascular myocardial protection system with applications in acute myocardial infarction and cardiac surgery.

Interview conducted by: Lynn Fosse, Senior Editor, CEOCFO Magazine

CEOCFO: Dr. Solar, what is ThermoPeutiX?

Dr. Solar: We are a medical device design, develop and manufacturing company. Our objective really is to discover and find solutions to very important unmet medical needs. We do that through research and development. We then take the product through a phase where it may be ready for clinical studies. At that point we make a decision to spin it off, license it, or manufacture and sell it.

CEOCFO: There are hundreds, thousands of unmet medical needs. What is your criteria?

Dr. Solar: Most of our work and ideas really come from the clinicians. Our experience and our expertise have been in the area of catheter-based medicine. These are less invasive techniques to treat many disorders. Most of our focus is in treating diseases of the vascular system. Also, because we are using catheters that are placed into the blood vessels, we use the blood vessels as more or less a transportation system to provide therapy. The primary fields that we work in are cardiovascular medicine and that also includes areas such as stroke. The physicians that we work with are specialists in those fields. By working with them, watching procedures, and talking with them about what works and what doesn't, we decide what projects to undertake. These physicians come to us and say, "Here is a problem we really need to fix." Some of the problems that we are asked to solve are seem relatively simple. Then, there are the major ones; our "Holy Grails." For example, we are taking on acute stroke. We think that is probably one of the most important unmet medical needs today.

CEOCFO: Would you tell us about some of the products that you have available now? Who is using them, how do they get them and why do they want them?

Dr. Solar: We currently have three product lines that we have developed through to the point where we have received clearance from regulatory agencies, such as the Food and Drug Administration (the FDA) in the United States and notified bodies in Europe, that allows us to market the products. Two are designed primarily to treat disorders of the vascular system; in other words, opening blockages in arteries and veins, removing clots in those vessels, and delivering drugs locally to provide therapy. The other area is a catheter technique where, through a small puncture in the groin, we insert a catheter, advance it up towards the brain, and position it in a major artery leading to the brain. Once in position, the catheter system is designed to selectively cool the brain very deeply. That cooling stops the processes that cause brain cells to die when you have a scenario, such as stroke, where there is no blood getting to the brain.

CEOCFO: Are these better or newer versions of what might be available? Would you give us some of the distinctions?

Dr. Solar: As far as the product areas, one is, I would say, a better version of what is available today. A second area, local drug delivery, is a different version of the products that are available in Europe, but not yet in the United States. In

the US, our system not only fills a need where there is no alternative, it is a more versatile product. It can deliver many different kinds of drugs, as opposed to just the one drug delivered by the local drug delivery products available in Europe. And, unlike these European products, our device allows the physician to remove the drug after the procedure. Now, regarding our selective hypothermia product for cooling the brain to treat stroke, there is no competition. Each year, we have all these people that are suffering strokes, and there is really very little that we can do for these stroke patients — until now!

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CEOCFO: *Would you please explain to us how cooling the brain works with stroke?*

Dr. Solar: For decades, researchers all over the world have been trying to address stroke. When a patient has a stroke, what do we do, how do we treat them? There have been hundreds of drugs that have been tried and developed and tested, and probably on the order of billions of dollars have been invested over the last four or five decades. We really have no solution yet. There is one drug that was approved about fifteen years ago. It is a drug that we call a thrombolytic drug. That means that it dissolves a clot. This is the only drug that really has been shown to have some benefit. The problem is that because of safety issues and concerns it can only be used in about two percent of the stroke patients, and it only works about half the time. There are many patient characteristics that go along with whether or not they would be eligible for this type of therapy. After all of this work, this is all we have. The reason for the lack of success in finding an effective treatment for stroke has to do with what happens when you stop the blood flow to the brain. There are a number of biological and physiological reactions that occur that cause the brain cells to die. There are many different pathways. One drug may work on blocking one pathway and providing protection there, but there could be ten or twenty other pathways that cause the brain cells to die. Most of these mechanisms that cause the brain cells to die have some relation to metabolism. In other words, it goes back to basic chemistry. You may remember your high school chemistry class where you put some powder into a beaker of liquid and nothing happens. Then you heat it up, the heat speeds up the reaction, and you see some result. It is kind of the same thing with metabolism. When metabolism is high, it heats things up and causes reactions to proceed and move faster. On the contrary, if you cool things down you actually slow down the reaction or even stop the reaction. This is exactly what we are doing with cooling the brain. As it turns out, almost all of the pathways that lead to cell death are metabolically related, so that simply cooling the brain can slow down and even block them. About eighty-seven percent of the time stroke is caused by a clot or blockage in one of the major arteries leading to the brain. Therefore, the first thought is to attempt to remove or open that blockage. That is a great idea. The problem with that however, is that when the brain is deprived of oxygen and you immediately open it up, that sudden rush of new oxygenated blood can also lead to processes that cause additional cell death. Collectively, these processes are what we call reperfusion injury. Cooling the brain, hypothermia, actually stops, and protects against reperfusion injury as well. Therefore, we believe that this is probably the best way to protect the brain in an acute stroke.

CEOCFO: *Are the segments of the medical community that should know about what you do aware? Are they using the products? Where are you in the process?*

Dr. Solar: For selective hypothermia, we are still in, you might say, the infancy and the pioneering stage. We have a great deal of animal data, and a very inspiring initial clinical case. We actually have FDA clearance to market the product, but it is not specifically indicated for stroke or any other ailment. So, we cannot go out and claim that this should be used for stroke. We have to do clinical studies first, and that is where we are with this product; to begin some of those studies. In the initial clinical case, our product; was used during neurosurgery in a procedure where they had to stop the blood flow for a long period of time to do the repair a very large aneurysm in the brain. Normally, they would actually do a bypass, which takes hours to do, then repair the aneurysm, and then they would reverse the bypass. With our system however, they simply cooled the brain locally, clipped off the artery stop the blood flow while they did the repair, and then surgically repaired the aneurysm. With the brain cold, there was no neurological damage, because the brain is protected. This is the application that has been used so far clinically. Regarding stroke, the scientific and medical industry recognizes that hypothermia has the potential to be a blockbuster. However, up until now no one has figured out a way to administer the hypothermia. Therefore, all of the previous attempts to study this in stroke used techniques that cool the whole body. These techniques used specialized pads that you put on the surface of the body and it cools the body down. There are also devices that you place inside a portion of the heart, and this device has a cold tip, so that the blood running over this cold tip is cooled and then the heart pumps that blood to the brain, which then cools the brain. All of these techniques cool the whole body in order to cool the blood that is going to the brain. The problem with that is that there are many complications when you cool the whole body. First of all, the body does not like to be cold, so what is the first thing you do when you are cold? You shiver. What shivering does is increase metabolism and heats things up. Therefore, the body naturally fights your attempt to cool it. That is one problem. The other problem is that at lower temperatures you are susceptible to infections, in particular pneumonias in the lungs. Probably the most important detrimental affect of cooling

the whole body is that the heart may not function properly, and even stop. When you get to temperatures down to around thirty-two degrees or below, you start seeing electrical disturbances of the heart, including the heart actually stopping. Therefore, you are limited to the temperature and which you can cool the whole body. Extensive research has shown that to be effective in stroke you have to cool much lower than the level that is attempted in total body cooling.

CEOCFO: How do you get from the point where you are to the point where people are aware of and ultimately will be looking for your products? What is the strategy for the next year or two?

Dr. Solar: The strategy is actually pretty straightforward, at least in theory. We have to really demonstrate clinically that our products are safe and effective. We are in the era now of what is called evidence-based medicine. In the past someone would have an idea and you would try it. Someone writes a little anecdotal report, and people start using your devices and drugs and so on. It is more difficult now. Even if you can get clearance from the regulatory bodies such as the FDA, to really get widespread application, you have to do significant studies that really clearly show that the technique is safe and that it works. This is what we have to do now. Our challenge, of course, is now we are back to a mode of raising money, getting investment so that we can do these trials.

CEOCFO: Areas of health fall in and out of favor with the investment community. Where does stroke stand today? Are you working in an area that investors are recognizing?

Dr. Solar: It is a two-part answer. Number one, in stroke there is absolutely tremendous interest. The problem though is that our approach is using hypothermia. This has been tried this before by using whole body cooling techniques, and, as I noted before, this does not work in stroke because you cannot cool the brain deep enough with these techniques. Many investors lost a ton of money. They invested in companies that attempted to do stroke studies without really doing their homework. They did not realize that you had to have the brain at temperatures lower than you can safely achieve by cooling the whole body. Therefore, after doing a number of studies and investing quite a bit of money, these companies essentially went away. Therefore, the investors have been kind of leery about hypothermia. Therefore, our challenge is to convince them that the science is there. It is just the way it was applied that was wrong before, and that we have a much better solution.

CEOCFO: How are you so sure? What gives you the confidence TheropeutiX is on the right track?

Dr. Solar: That is a wonderful question, and I am glad you asked that. Part of it is my training, my background and my faith in science. There has been so much research that has been done, and in understanding the basic mechanisms you can clearly see why cooling works. That part is so clear. The naysayers say, "We tried this before, and it does not work", but they are not looking at the whole picture. They are not paying attention to what they have done. We believe that by totally isolating the brain that we can succeed. We do know from, again back to science, that the brain can be cooled to very, very low temperatures, and it just goes to sleep; you do not kill it. On the other hand, if you cool the heart to low temperatures, it will actually stop. We have known this for decades. For example, we have been doing coronary bypass surgery for about fifty plus years. When we do a coronary bypass on a patient we basically stop the heart, and use the heart / lung machine to provide blood flow to the brain and the body. However, that blood flow is also cold blood. Therefore, those patients are chilled down to maybe eighteen degrees centigrade. We have doing that, as I said, for fifty years, and we know it works. It protects the brain. The science is there. We have done a considerable amount of animal work studying our selective cooling technique, and it really works amazingly well. Just this last year we completed a study with a group of neurosurgeons up in Canada where they actually created a stroke in pigs. We studied, in a randomized fashion, whether or not cooling with our technique could reduce the volume of the stroke. It was concluded that it did indeed reduce the stroke volume. The results were analyzed blindly, so there was no investigator bias in the analysis. We believed that was the result we were going to achieve and we achieved it. Consequently, we are very excited. Now we have to embark on human studies. Stroke is not such a straightforward malady. There are many things that go on, and many reasons why there is a stroke. Therefore, we do not expect that we are going to have a one hundred percent cure rate. No, that is not going to happen. However, we do think we will have a significant improvement. We can also look at what has been going on in cardiac arrest in the last decade or so. In cardiac arrest the heart stops, and there is no blood flowing to the brain. You can defibrillate the heart. We have these wonderful defibrillators now, and we are training more and more people in CPR, so these patients are getting treated much faster with CPR. However, the big problem is that because there was no blood flowing to the brain, the brain cells are dying. By the time they get the heart going, if enough of the brain cells have died, the patient is brain dead. Brain death is the most significant cause of death in cardiac arrest. In 2002 there were two landmark studies that showed if you do mild hypothermia, between somewhere around thirty-three, thirty-four degrees centigrade, you could protect the brain and improve the outcome in these patients. Today, mild hypothermia in cardiac arrest is becoming more of a standard of care. Stroke is different however, because the amount of time from when the stroke occurs till when the patient actually realizes there is something wrong and gets seen is on the order of hours, whereas with cardiac arrest the patient falls down and you know immediately there is something wrong. You know they are having a heart attack. Therefore, they are treated within minutes. Because of the early treatment, mild hypothermia seems to have a benefit. However, in stroke, with a significantly longer time before treatment begins, mild hypothermia has not worked. There have been a number of studies that has shown that temperature is probably the most important parameter, and with our selective cooling technique, we believe we can safely reach the required temperatures.

BIO: Dr. Ronald Solar received his Ph.D. in Biomaterials and Materials Science from the University of Pennsylvania in 1977, and has been designing and developing medical devices for over 35 years. He currently holds over 50 patents. Ron was a co-founder of a number of successful medical device companies, and also played key roles in the successful launch of others, such as Advanced Cardiovascular Systems (now Abbott), SciMed (now Boston Scientific) and Medtronic Vascular. In 1989, Dr. Solar was recognized by President George H. Bush as one of the Ten Outstanding Young Americans, and Junior Chamber International selected him as one of the Ten Outstanding Young People of the World for his contributions in medical innovation. His current research interests include vascular injury related to intervention, and selective hypothermia as a means to treat stroke and other cerebral ischemic injury.



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