

Novel Antifibrotic Drugs Show Promise for the Treatment of Triple Negative Breast Cancer and Heart Failure



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CEOCFO: *Dr. Swindlehurst, would you tell us the idea behind NovoMedix?*

Dr. Swindlehurst: NovoMedix is a small molecule drug discovery and development company. We are focused on the treatment of fibrosis with initial emphasis on cancer and heart failure.

CEOCFO: *Is there a relation between cancer and fibrosis?*

Dr. Swindlehurst: Yes. The tumor stroma or the tumor microenvironment is considered a fibrotic tissue. The tumor cells secrete factors that recruit and change the surrounding fibroblasts to become what we call activated fibroblasts or cancer associated fibroblasts. Those activated fibroblasts in turn provide the structural support and secreted factors that promote tumor survival and metastasis. By preventing the activation of fibroblasts in the tumor microenvironment, we can remove the critical support needed for tumors to survive. Although our lead cancer drug candidate has the potential to work as a monotherapy, we believe that it can also significantly enhance patient outcome as a combination therapy with drugs that directly target cancer cells to more effectively eradicate tumors.

CEOCFO: *What are you working on specifically now?*

Dr. Swindlehurst: We have a novel patented series of lead compounds with demonstrated efficacy in cancer and in heart failure animal models. The lead compound for triple negative breast cancer is in the late pre-clinical stage and has both antifibrotic and anticancer properties so it hits the tumor from multiple angles and represents a novel approach for the treatment of triple negative breast cancer.

CEOCFO: *Were you looking for something related to breast cancer? Why is that what you are working on first?*

Dr. Swindlehurst: We started with developing translation initiation inhibitors to treat cancer. Our compounds work in the eIF4E pathway, which is a critical regulator of translation initiation. Triple negative breast cancer has high levels of eIF4E. Abnormally elevated eIF4E correlates with recurrence and death and provides a biomarker for precision medicine to better treat patients by maximizing efficacy while minimizing toxicity. In addition, our lead compounds also play a key role in neutralizing the tumor stroma. Triple negative breast tumors are highly dependent on the tumor stroma so the properties of our lead candidate are ideally suited to treat triple negative breast cancer. Most importantly, triple negative breast cancer is a devastating form of breast cancer for which there is no effective treatment.

CEOCFO: *What phase of the research are you in at the moment?*

Dr. Swindlehurst: We are ready to start our IND enabling studies for triple negative breast cancer.

CEOCFO: Are you funded or seeking investment or partnership?

Dr. Swindlehurst: We have been funded to date by non-dilutive means, mostly in the form of SBIR grants for both cancer and fibrosis. We have received Phase I and II SBIR grants for triple negative breast cancer and have recently applied for a Phase IIB Bridge award. The Phase IIB award is for \$1M a year for up to 3 years, so \$3M total. It requires matching funds, so we are looking to raise \$3-5M, giving us a total of \$6-8M which will allow us to complete our IND enabling studies as well as a Phase 2a clinical trial for triple negative breast cancer.

CEOCFO: Is there much research in the area you are looking at or have you come upon something that has not had too much attention as yet?

Dr. Swindlehurst: There is strong interest in drugs that can treat the tumor stroma, heart failure, and fibrosis in general. We believe this is a very exciting area of drug discovery and development. More importantly, our small molecules are novel and orally available, which are very desirable properties for drugs.

CEOCFO: Is the medical community aware and is the approach at least interesting if not totally accepted at this point?

Dr. Swindlehurst: Triple negative breast cancer is particularly aggressive, with higher rates of recurrence, resistance, metastasis, and death than other forms of breast cancer. There are currently no effective therapies for this devastating disease. Clinicians will welcome anything that can help improve survival rates for patients. Our lead drug candidates have the added advantage that they are orally available, which means that patients will be able to take a pill in their own home instead of receiving intravenous infusions in the doctor's office. This will make our drugs available to more patients and decrease the cost of administration.

CEOCFO: Where does heart failure come into play?

Dr. Swindlehurst: One of the causes of heart failure is cardiac fibrosis, so that is where fibrosis comes into play. Based on how our compounds work, we had a hypothesis that in addition to being effective in many cancers, they would be effective in treating fibrotic diseases. The reason we decided to test our hypothesis initially in heart failure is because we have a colleague, Dr. David J. Lefer working in this field. In collaboration with Dr. Lefer, a leading heart failure researcher at LSU, we found that our lead drug candidate significantly improved cardiac function in a mouse transverse aortic constriction model of heart failure. This model is a hypertensive model of heart failure with significant cardiac fibrosis. We waited six weeks after the surgical aortic constriction, which mimics what happens in a clinical setting, and found that our lead drug candidate prevented heart failure (maintained left ventricular ejection fraction in the normal range). There was also a significant decrease in collagen and fibrosis and improvement in many other relevant markers for heart structure and function. Based on those data, we applied for and received an SBIR grant to continue work in that area. These data will be submitted for publication shortly. These preliminary results suggest that these drug candidates should benefit patients with other fibrotic diseases such as lung, liver, and kidney fibrosis. We are looking for other collaborators to help us test these compounds in these devastating fibrotic diseases.

CEOCFO: You have twenty-five years of experience in the industry. What have you learned that has been helpful in getting NovoMedix off the ground?

Dr. Swindlehurst: I think for us, it was not bringing in outside money too early. We have been doing this for quite a while on SBIR funding and are just now going out to look for a significant round of funding as well as corporate partners. That has allowed us to be flexible and to get to a point where we have something of value. I had an experience in another company where we took in outside money too soon and it wound up not being a good thing. I think taking the technology as far as you can with SBIR and other forms of grant funding really makes a big difference. Things take time and you have to be flexible. You have to be willing to go where the science takes you. Our first grant was for diabetes and for a variety of reasons, that did not work out but we had some other ideas which lead us to where we are today. I think that being flexible is really important for a small company.

CEOCFO: You recently presented at the Life Sciences Summit. What was the reception?

Dr. Swindlehurst: The reception was good. The presentation itself was very well received. Unfortunately for us, because it was in New York, many of the investors that were there had geographical constraints, and are more interesting in funding east coast companies and we are on the west coast, in San Diego. It was a good experience and we got a couple of promising leads. It has only been a few weeks, so it is too early to tell where that will all lead, but it was a good experience. We have been fortunate. The NCI, which awarded us the phase I and II SBIR grants for triple negative breast cancer, considers us one of the stars in their portfolio, so they have paid for us to present at three different conferences. Prior to the Life Sciences Summit, we presented at BIO, which is a much bigger venue and that was very interesting as well. We are in several discussions, mostly with potential corporate partners, as a result.

CEOCFO: *Why pay attention to NovoMedix?*

Dr. Swindlehurst: NovoMedix has developed a series of unique small molecule drug candidates that have the potential to make a significant impact in the treatment of a number of fibrotic diseases such as cancer, heart failure, lung, liver, and kidney fibrosis, and more. So far, these drug candidates seem to have very good safety profiles. I believe once we get these drugs into the clinic, we will see some impressive results. I think our drugs have a very high probability of significantly improving patient outcomes.

