ceocfointerviews.com

Issue: September 19, 2016

CEOCFO Magazine

With Rigosertib in a global Phase III Trials as a Standalone Drug for MDS, And in Phase II as a combination therapy, along with a Drug Candidate Ex-RAD having completed Phase I trials for protection against Harmful Radiation, Onconova Therapeutics is positioned for a Breakthrough

Dr. Ramesh Kumar, PhD
CEO

Onconova Therapeutics
(Nasdaq: ONTX)
www.onconova.com

Contact:
Ramesh Kumar
267-759-3680
rkumar@onconova.us

Interview conducted by:
Bud Wayne, Editorial Executive
CEOCFO Magazine

"Onconova was founded to solve three interrelated problems faced by cancer patients: therapy was too toxic, certain types of cancers could not be addressed by available therapies, and available treatments worked only for a short period of time before the patients developed resistance and could not benefit any more. A new holistic approach taken by our scientists is allowing us to overcome these barriers."- Dr. Ramesh Kumar, PhD

CEOCFO: ***Dr. Kumar, how long have you been with Onconova Therapeutics and what attracted you to the company?***
Dr. Kumar: I have been with Onconova since it was founded in December of 1998. A few months before that, I met two amazing scientists, one, Dr. E.P. Reddy, from Philadelphia and one, Dr. J. Jenkins from the UK. These scientists told me in confidence that they had a solution that could transform cancer therapeutics. More importantly, it could have a huge impact on how cancer patients tolerated chemotherapy. That was the origin of our story. We started with science and with the need of the patients as the founding principal.

CEOCFO: ***Would you explain your chemistry platform and how it deals with the problem of targeting cancer cells while not harming normal cells?***
Dr. Kumar: The scientists who came up with the platform and I felt that there were three fundamental flaws in cancer therapy in 1998. The first one was that the therapy was too toxic, so it was hurting normal cells with equal vigor as it was cancer cells. There was no way for the patient's normal cells to escape the onslaught of chemotherapy. That was problem number one. Problem number two was that there were certain types cancers that could not be addressed by anything available. The third problem, which was even more of a hurdle was that where a therapy was available, it worked only for a short period of time and then either the patients could not take it anymore of the cancer cells developed resistance and could not be effected by the drug any more. Therefore, there was the problem with safety and toxicity, the problem that some cancers remain intractable to available therapies and the third problem was that the drug worked briefly before the patient became

resistant. These problems seemed to be different, but in our thinking they were interrelated. The first problem was that of specificity, the second with lack of specificity, not knowing what to target, and the third problem was that was what we were targeting was changeable so that resistance could develop. Once we figured out that A, there were three key problems, B, they were interrelated and C that the scientist had a potential way around these problems, we figured there were two ways to go about solving the problem. One was that we could publish a nice article and let other scientists take advantage of these insights and develop drugs, or we could develop a new venture around these drugs, that could take the drugs from the labs to the clinic and from the clinic to the pharmaceutical market. And that is what we did. We decided to name the company Onconova, because Nova is a new star and Onco denotes cancer, and this was a new approach to address cancer. The name Onconova was based on where one of our scientists lived (Villanova) and both or our scientist were editing a journal called Oncogene, which is one of the premier cancer journals. We took Oncogene and Villanova and came up with Onconova.

CEOCFO: ***How is it that your technology is able to target specifically the cancer cell?***
Dr. Kumar: This was not serendipitous, but by design, because the way the scientists were looking for these new drugs was by purposely taking a plate full of normal cells and a plate full of cancer cells, and they used the same drug on the normal cells at the same time they used it on the cancer cells. Then they looked at what we call differential screening, so the screening was cell based, not enzyme or test tube based, but based on living cells, and it was based on real-time differential analysis. If a drug hits and kills cancer cells, but at the same time the same drug did not harm normal cells, that would be our ideal drug candidate. Instead of saying target A or target X was what we wanted to go after, we decided to go after a ”phenotype”, which is the effect of the drug on the cell, rather than the effect of the drug on the target enzyme. We took a holistic approach, going after the outcome of therapy, which would be selective destruction of cancer cells and protection of normal cells.

CEOCFO: ***You have three different small molecule programs that you are running: Rigosertib, Briciclib and Recilisib. Where are you in development and with clinical trials?***
Dr. Kumar: The three names, Rigosertib, Briciclib and Recilisib, came through an international consortium called ICANN, and the names are very informative. For example, Rigosertib, ends with “ib”, which means that this is an inhibitor or certain types of enzymes. Briciclib ends with “clib”, which means that it is an inhibitor of cycling enzymes. Similarly, Recilisib means that it inhibits an enzyme, so all of these three drugs are specifying that they are inhibiting, blocking or knocking out something. Then the other words tell you what they knock out. Rigosertib is our most advanced cancer drug, which is now in the middle of a Phase III, or the final stage of testing for a cancer called MDS, for Myelodysplastic Syndrome, which is a cancer affecting the bone marrow, and affects mostly elderly people. Briciclib is a drug that inhibits a key mechanism that controls how proteins are made. Remember that we are made up of proteins, carbohydrates and nucleic acids, and proteins are the regulatory and structural components of a cell. Each protein is made under the control of numerous enzymes. Our drug inhibits an enzyme called eIF4E, which is an enzyme that people thought would be very difficult or impossible to inhibit, but Briciclib has done just that. Briciclib

has not yet completed Phase I trials, which is the first stage of clinical development. The third drug Recilisib is very interesting because it is really not a cancer drug. It is a drug that can protect you from harmful radiation. For example, if there is a dirty bomb attack or a nuclear power plant leakage, in those circumstances either willingly or unwillingly, you are exposed to harmful radiation, which can disfigure you, make you sick or kill you. Our Recilisib, which has completed multiple Phase I studies is designed to protect you if you are unfortunately exposed to harmful radiation. Unlike the first two drugs, which are cancer drugs, which we are developing ourselves, the third drug Recilisib is being developed by the US Department of Defense in collaboration with us. Our focus is to make this available after testing, so that we can have it in Emergency Rooms, or Civil Defense Units, eventually in the average person's medicine cabinet, so that you can take this drug as an antidote to harmful radiation.

CEOCFO: ***Is Rigosertib an adjuvant or a standalone cancer drug?***
Dr. Kumar: That is an excellent question. Rigosertib is a standalone drug because when you take this drug and expose it to cancer cells, it can kill cancer cells by itself. However, Rigosertib can also help with the problem of drug resistance; we found that our drug, in combination with older drugs, can work together synergistically, and make those older drugs much better. Therefore, Rigosertib can be used as a standalone drug, is in a Phase III trial for MDS patients as a standalone drug, or secondly you can use it in combination with a well-known older drug that is subject to drug resistance. Therefore, we are doing a Phase II trial in patients where we are combining our drug Rigosertib with another drug Azacitidine that has been around for more than 40 years and is still useful. This combination approach is one of the ways that you can combat resistance, and help a number of patients with the older drug.

CEOCFO: ***Would you explain what you are looking for in the Phase III trial, and if you were to cross that hurdle, what would come next?***
Dr. Kumar: Drug development is a very long and iterative process, because of the regulations by the FDA in the US and EMA in Europe. You have to go by stepwise trials. In Phase I you establish the safety, Phase II you establish the right dose and Phase III you either do a head-to-head comparison of two drugs, or you do your drug testing in patients who have failed everything, so there is no other hope. In that case, if your drug works you can get drug approval. In our Phase III trial, the participants are MDS patients, and this is a second type of trial where we are taking patients who have failed known therapies, so they have nothing else available, and unfortunately in our situation, these patients have only a few months to live. Therefore, what we are asking in our Phase III trial is if survival can be extended significantly. We are comparing two groups of patients. One group gets our drug and the other group that we are comparing our drug against, does not get our drug. If you can significantly enhance survival, then the FDA will allow us to market the drug.

CEOCFO: ***Drug development takes a long time and is very expensive. Where are you with funding? Are you looking for investors or partners at this time?***
Dr. Kumar: Funding is the lifeblood of biotechnology and oncology companies, so we need funding as it takes a long time. I mentioned earlier that we founded Onconova in the last Century, at the end of 1998, so we have been in existence for 17 years, and in the last 3 years we

have been a public company. Therefore, we have raised our money through the sale of public equities, and before that we sold stock to private investors. However, we have all along done two other things on top of raising money through sale of equities. One, we have relied a great deal on non-dilutive financing, meaning where you can get money without having to sell stock. This comes from two sources, for example our radiation defense pill that we are developing with the Department of Defense, so the government pays for a good chunk of that development cost. The other is that we were able to develop alliances with patient advocacy groups, such as the Leukemia and Lymphoma Society, which gave us our initial support for doing the MDS trial. These non-dilutive supports are very important, because A, you do not have to sell stock to get the money, and B, this is the stamp of approval from patient advocacy groups telling you that what you are doing is of great importance to patients. Therefore, they are willing to support the cost of clinical trial. Third way to raise money is to make partnerships. Remember that we have a drug that is patent protected through the entire globe, and we as a small company cannot expect to be selling the drug outside of the United States, so we have the option to find partnerships. For example, 5 years ago in 2011, we partnered with a Japanese company called SymBio Pharmaceuticals, to give them rights to develop our drug in Japan and Korea. Rigosertib is now in a Phase III trial, and our partner is a part of that trial. They are doing the trial in Japan, whereas we are doing the trial in twenty other countries. This kind of collaborative approach, where you work with patient advocacy groups, the government, companies, and then collaborate with your investors, allows you to raise all of the money you need for as long as the development takes.

CEOCFO: ***In closing, address potential investors and people who may look at your company as the future of cancer therapy?***
Dr. Kumar: Inspite of great progress in the last two decades, there continue to be difficult to treat cancers and as of now impossible to treat cancers. The only way we can go after these cancers and address the needs of those patients is to look at new approaches. These are approaches which are able to overcome drug resistance, extreme toxicity, and have activity against the formerly intractable cancers. Therefore, new approaches are needed, and every new approach opens the door for multiple new combinations, because the existing therapies, when appropriately combined with new therapies can have a transformational effect on these cancers.

ONCONOVA

TARGETING CANCER | PROTECTING HEALTHY CELLS