

With their drug Rigosertib now in Phase III Trials for the Bone Marrow Disorder Myelodysplastic Syndrome used in over 500 Patients, Onconova Therapeutics brings hope to many Elderly Suffering from this Devastating Disease



Dr. Ramesh Kumar, PhD
Chief Executive Officer

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

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- Dr. Ramesh Kumar, PhD

CEOCFO: *Dr. Kumar, when we spoke last September, Onconova Therapeutics had 1 drug in Phase III clinical trials addressing MDS or Myelodysplastic Syndrome. Would you tell us about MDS and how common it is?*

Dr. Kumar: Myelodysplastic Syndrome is a bone marrow disorder. Myelo is Greek for bone marrow, and dysplastic means the disease. It affects quite a few people. We call it an Orphan Disease, but just in the United States there are 59,000 patients that are diagnosed with MDS or Myelodysplastic Syndrome. In MDS patients the bone marrow does not function normally. Normal bone marrow function is to make red blood cells, which are important for breathing, our white blood cells, which are important for fighting infections, and platelets, which are critical for stopping bleeding. Therefore, for a patient whose bone marrow does not make enough red blood cells, white blood cells or platelets, he or she would be in very bad shape. In addition, there is no cure for MDS patients. The only thing that approximates a cure is bone marrow transplantation, which is still quite dangerous and not commonly available. MDS is a bone marrow disease that affects mostly older people, the median age is the high 60s to low 70s years of age. As I mentioned, there is no cure and only two or three treatments approved by the FDA, all of which were approved more than a decade ago. Hence, in the last ten years, for this important disease that affects primarily the older population, there have been no new treatments developed. We are very optimistic that our drug Rigosertib, which is currently in a Phase III trial, could provide the first new option for these patients in over a decade.

CEOCFO: *Given the recent healthcare debates, does the government care as much about curing diseases that affect the elderly as they do the young, and do they see the financial benefit of addressing diseases of the ageing population?*

Dr. Kumar: There are two ends of the spectrum. You have the youngest of the young, the new born, pediatric patients, and then there are the older patients. These two groups consume most of the healthcare dollars. Therefore, most of the research being done is aimed at these patients to ensure the young kids live long, full and healthy lives and older folks can live to their full potential and do not have symptoms that require very expensive care or hospitalization. It is in the Nation's best interest to address the diseases of older people in order to help to control the healthcare costs. Generally, we have a great deal more freedom to study diseases in older population because patients are available, like to get involved in clinical trials, have very good patient advocacy support, such as AARP and various disease foundations and there is a great deal of interest and awareness in this area. Unfortunately, as you grow older your diseases, like MDS, become more complex. For instance, MDS is not caused by a single gene or single protein going wrong. It is caused by the culmination of a series of mutations that a patient has accumulated throughout your life, which leads to a point where the patient has many things wrong with their cells and bone marrow, resulting in MDS.

CEOCFO: *Would you explain to our readers the accomplishment of getting a drug to Phase III, some of the hurdles you had to make to get in this position and what allowed you to get this far with your Rigosertib?*

Dr. Kumar: That is an excellent question, because when we say Phase III, many people know that there is Phase I, Phase II and then Phase III, so they believe there are only three steps involved. However, there are actually six steps to get to Phase III. First, you discover a new molecule or new drug and show that it has potential in the laboratory. Then you test it to make sure it is safe, which is the toxicology testing that is done in animals. After that you have to go through a process with the FDA in the United States, called the IND, or the Investigational New Drug application. Then Phase I starts, followed by Phase II, all before you get to Phase III. An organization called fdareview.org, has estimated that 9% of every drug that is invented, or 1 in 11, gets into Phase III. That means that 89% would have failed before they get to Phase III. Knowing this, I consider it a great achievement that we are in Phase III. Moreover, we are approaching the last stages of Phase III. We started our Phase III trials in December of 2015, and we expect to complete this trial in 2018; less than a year from now. That is remarkable! The fact that we were able to go from the invention of the molecule through the toxicology, through the IND, Phase I, Phase II, and now to Phase III. Once the trial is complete we will share the data with the FDA, European and Japanese authorities, and upon approval of the drug, it would be commercialized worldwide.

CEOCFO: *Would you tell us where you are today with Rigosertib and some of the results of your trials?*

Dr. Kumar: We are very fortunate that Rigosertib in MDS, the disease that we are studying, has gotten a great deal of positive reception by key opinion leaders including doctors, scientists, medical experts, patient advocacy organizations and the patients themselves. One such example would be the commitment we received from the Leukemia and Lymphoma Society. In 2009, we were approached by the Leukemia and Lymphoma Society and in 2010; they gave us \$10 million grant to conduct our first Phase III trials. Then in 2011, SymBio, a Japanese pharmaceutical company, partnered with us so that they could buy the rights to sell our product in Japan and pay us future royalties. SymBio continues to be our partner and is working with us in the ongoing Phase III trials by enrolling patients in Japan, while we enroll patients in North America, Europe, and Australia and in Israel. It is a true global trial. We are also conducting trials in Russia, the United Kingdom, and as I mentioned, Israel and Australia. Why? Because MDS does not know any boundaries. It is a global disease, it affects people from all countries and of all ethnic origins. While we are now conducting Phase III trials, we have already treated more than 500 patients in our Phase I and II trials leading into our current Phase III trial. Each of the steps leading to this point has helped identify appropriate drug dosage for patients in the trials as well as the best way to monitor results.

CEOCFO: *Is partnering a core strategy for Onconova? Are you looking more for the financial support or how it may enhance the progress of your drug?*

Dr. Kumar: The same report I referred to earlier, by fdareview.org, gives you a tally of the minimum amount of dollars that goes into getting a molecule from discovery to Phase III, and that number is several hundred million dollars. Then it takes many more million dollars to get through approvals because you have to get ready to sell the drug via a commercial company and a pharmaceutical company. A company cannot do this by itself. Since MDS is a global disease, and we have tested the drug globally, we would like to develop partnerships that allow other companies who are experts in China, Latin America, and Europe to become partners and eventually be responsible for sales on our behalf. Partnerships start to be formed prior to when the drug is approved. This way the partners can fund further development of the program, and then eventually they can commercialize it in their territory. Our strategy is for Onconova to focus on commercialization in the United States, while allowing our partners to commercialize worldwide. Partnerships can bring in significant dollars to the Company without dilution. We also received money from patient advocacy organizations that raise money to help companies develop new drugs for orphan indications (diseases for which drugs are not available). Finally, we also raise money through equity financing via the public markets.

CEOCFO: *Onconova announced a collaborative research and clinical programs evaluating Rigosertib in pediatric "RASopathies". Would you tell us about this, who the collaborative partner is and why Rigosertib could be used in this indication?*

Dr. Kumar: I mentioned that MDS is a disease of older patients. The question is why we are going to younger patients now. You may remember Shakespeare said something like, "In old age we recapitulate our infancy" and become like children again. It looks like there are some genetic factors that create in young children a disease that looks like MDS. The RASopathies are a group of rare genetic conditions caused by mutations in genes of the Ras-MAPK pathway. For a long period of time these rare diseases were baffling and it was not clear what could be done about them. What we know the diseases all have in common is that they have some problem with the RAS pathway. New research, including research done by our scientists, has shown that there is a potential that new drugs could help treat these diseases. One such drug that has shown promise is Onconova's Rigosertib. We recently announced our collaborative, multi-institutional research and clinical program with the National Cancer Institute (NCI) to evaluate Rigosertib in pediatric RASopathies. We

will also work with a group on the West Coast at UCSF (University of California San Francisco) to study Rigosertib as a treatment for the disease. Although the diseases are very rare, with probably 2,000 cases per year worldwide, these are diseases that affect the lives of children and their families. This would be less commercial, but more on a medical need rationale that takes us into this area. And since we have the drug, so why not use it.

CEO CFO: *Would you tell us where you are with Briciclib and Recilisib today?*

Dr. Kumar: Briciclib is a cancer drug we developed, but we decided last year to put it on hold while we get Rigosertib through the finish line. For small companies, the most important thing is focus, focus, focus, much like in real estate where it is location, location, and location. We have to put all of our resources into Rigosertib to get it through the finish line. Briciclib was in Phase I, but we decided to stop it right there and come back to it at a later date. Briciclib is a very interesting and one day we will be able to develop it for other diseases besides MDS, such as lymphoma. What we are currently trying to do right now with Briciclib is that we are looking for partnerships. We are looking for other companies to pick up this drug and develop it. The other drug Recilisib is very different in that it is not a cancer drug. We are working with it because it is useful to protect animals and potentially humans from radiation damage. We all know that radiation is a danger, but most people are not aware that it is a danger for cancer patients who get radiation therapy, because radiation kills cancer cells, but it also causes side effects by killing non-cancer cells as well. With Recilisib we did Phase I studies, supported by the Department of Defense, and are hoping to receive future grants to resume the program.

CEO CFO: *Where do the names of drugs come from? Are they chosen by Onconova?*

Dr. Kumar: These names are not chosen by us. They are selected by an international organization called ICAANN, and they pick names so that there is no confusion with other drugs and the names are descriptive to the science.

CEO CFO: *You participated at two Investor Conferences in September and at the BIO International Convention. How has the reception been and what are some of the questions you were asked to answer?*

Dr. Kumar: We want to be very visible in order to update our investors, doctors and patients on our progress. One way we connect with them is by attending and presenting at key scientific and investor conferences. For instance, one major scientific conference we're getting ready to attend in December is ASH (American Society of Hematology). Hematology is the science of blood and we work with bone marrow, which affects blood, so this is a very important conference for us. We also attend several conferences throughout the year hosted by BIO, the largest trade association representing biotechnology companies. Some of these include BIO CEO, the BIO Annual Convention and the BIO Investor Conference. By regularly attending and presenting at these conferences, we're able to update the public on our progress in the clinic while also connecting with the people who are most important to us – the doctors, patients and investors who are the reason why we are here today.

CEO CFO: *How have your fund raising efforts been going? Are you looking to raise more funds to continue your clinical trials and other efforts?*

Dr. Kumar: The last time we raised money was in July of this year (2017). Obviously, like most companies in our position, it takes an extraordinary amount of capital in order to progress through clinical development. Ideally, money is raised as milestones are achieved. We are currently waiting on a very important milestone for the Rigosertib Phase III trial called the Interim Analysis, which means that we would be half way through the Phase III trial. This is where you make sure that everything is going well and get a "green flag" to complete the trial. Although we are not actively looking to fund, that would be a time where we might consider some form of capital infusion. And of course, we will always be opportunistic depending on market conditions.

CEO CFO: *In closing, what sets what you are doing at Onconova Therapeutics apart from other efforts to find a positive therapeutic response to cancer?*

Dr. Kumar: That is a very good question. In our business, if you do not have differentiation it is very difficult to survive. The best way to differentiate is to be the only solution to the problem, which is not always possible, but in our case it appears to be so. We are currently in a Phase III trial for MDS patients, for whom there is no therapy available, and when we look on the horizon we see nothing else close behind us. If our drug is approved, Rigosertib will be the only treatment available to 2nd line MDS patients for a number of years. That puts us in a very advantageous position, because we may be the only drug in this class for the foreseeable future and more importantly, since our drug works by a completely new mode of action, we think we can use our drug in combination with drugs already in the market. The synergistic use of our drug and an existing drug is the next frontier, because combination therapy is the way to go. That is how drugs tamed HIV AIDS, and Hepatitis. One or two drugs could not do it. In the case of Hepatitis it took a three drug cocktail to cure patients. Therefore, we would be going from one drug where we are well situated, differentiated and ahead of the competition, to the next stage, which is combining it with a known drug to impact more patients. That is where we are headed.



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