ceocfointerviews.com

Issue: October 17, 2016

CEOCFO Magazine

Oncolytic Virotherapy Platform is offering hope in using Engineered Viruses to Destroy Cancer Cells

Stephen J. Russell MD PhD
Founder, Director, CEO & President

Vyriad
www.vyriad.com

Contact:
Stephen J. Russell, M.D., Ph.D.
(507) 284-8384
sjrussell@vyriad.com

Interview conducted by:
Lynn Fosse, Senior Editor
CEOCFO Magazine

"We are clinical stage and we do have data with our viruses showing systemic efficacy. We have a very strong team. We have an excellent and broad portfolio. All in all, we think we really are a very strong company in that space, and the other thing about us in relation to our fundraising efforts right now, is that we are ready to move extremely aggressively with two FDA-approved clinical trials ready to launch immediately."
- Stephen J. Russell MD PhD

CEOCFO: ***Dr. Russell, what is the idea behind Vyriad?***
Dr. Russell: We are an oncolytic virotherapy company based in Rochester, Minnesota, and we are essentially using viruses as a novel cancer therapy.

CEOCFO: ***Why should viruses work?***
Dr. Russell: Viruses naturally infect and damage or destroy tissues in the body and everybody understands that. Hepatitis damages the liver, HIV damages the immune system, flu virus damages the lungs, etcetera. The idea here is have viruses that specifically attack a cancer and kill cancer cells, and in so doing not only shrink the tumor but also provoke an inflammatory immune response so that the immune system is much better equipped to mop up those tumor cells that did not get infected. It combines those two methods of killing the cancer: direct viral infection and spread in the cancer, killing the cancer cells, followed by immune mop-up of residual cancer cells.

CEOCFO: ***Is it generally accepted that this could work? Where is it in the continuum of the oncology community?***
Dr. Russell: It's mid-stage I would say in terms of its development. There are several oncolytic viruses currently being developed by different groups. The one furthest down the road in terms of FDA approval process is a virus that Amgen currently owns called T-Vec, or IMLYGIC, and that's a herpes simplex virus that's been engineered to make it cancer specific, and also so that it can more efficiently boost the immune system. That's been approved for the treatment of malignant melanoma. It was approved at the end of last year both in the USA and in Europe, and it's given repeatedly by intratumoral injection into a skin lesion, which results in the regression of other skin lesions and sometimes deeper tumors, so called visceral tumors. That's one virus, but there are quite a few studies using other viruses (including the viruses we are developing at Vyriad) that have generated early clinical data indicating that even a single dose of a virus given intravenously or intratumorally can mediate wholesale destruction of cancer anywhere in the body.

CEOCFO: ***Where have you started? What viruses, why, how, what are you aiming for?***
Dr. Russell: We have been founded based on work that was done at Mayo Clinic. Mayo Clinic has, since 1998, had a major academic translational research effort in oncolytic virotherapy. Multiple different viruses have been developed and tested pre-clinically there, and the two leading viral platforms that have been taken to clinical trials are measles and vesicular stomatitis virus. Those are the two platforms that Vyriad has licensed and is taking forward. In fact, at Mayo already there were three completed Phase I clinical trials using measles and one ongoing Phase I trial using the VSV when Vyriad was founded. It was a pretty strong academic platform from which we can launch into the commercial arena.

CEOCFO: ***Would you tell us about the recently announced agreement with Imanis Life Sciences?***
Dr. Russell: Well, Imanis Life Sciences is a Rochester based service provider which Vyriad has been working closely with to have new viruses made and tested in various different ways. Imanis Life Sciences had intellectual property that covered the use of viruses as diagnostics. Because we want to, as we move forward, be able to more accurately identify those subsets of patients who are going to have good responses to virotherapy, we think a predictive test makes great sense for increasing the probability of product approval in Phase III clinical trials when we get to those. So we've joined forces with Imanis Life Sciences and are working to develop diagnostic tests that use these viruses engineered in different ways, applied to tumor cells in order to determine whether the patient is going to be likely or not to respond.

CEOCFO: ***Where do you start - how do you know which virus and what dosage might be a good baseline? What goes into that initial decision?***
Dr. Russell: It is the standard Phase I dose escalation process that one goes through with a lot of FDA input to determine the dose levels that ought to be used. Interestingly for oncolytic viruses this is very different from small molecules, in that the dose ranges are enormous. So our starting dose with measles was 1,000 infectious units given to patients with ovarian cancer, and the top dose we ever gave was 10 million times higher than the starting dose. What dose is ultimately used will depend on clinical outcomes, both in terms of toxicity and anti-tumor activity, as well as ease of manufacturing at high versus lower dose levels. As you would expect, there are many factors taken into consideration in determining what an appropriate dose is. Fundamentally, it's down to the therapeutic index; the efficacy, toxicity sweet spot, or efficacy with no toxicity.

CEOCFO: ***Are you funded? Are you seeking additional partnerships or investment?***
Dr. Russell: We have money in the bank. We have had some angel investment right at the get go, and we also licensed one of our products to AstraZeneca and that deal provided additional capital to get the company moving. Right now, we are moving towards a private offering in order to raise money through that mechanism. In addition, we are exploring the possibility of working with a major venture capital firm - we are talking to more than one of those.

CEOCFO: ***You recently appointed Dr. Alice Bexon as your chief medical officer; what will her role be and why now?***
Dr. Russell: She's a really phenomenal addition to the team. Alice has a great deal of experience developing drugs in a large pharma environment and subsequently a small biotech before she launched her own company, which essentially provides services to small companies getting in to the area of developing their own drugs. What we already had in our company before the arrival of Alice was a team that was very familiar with translating oncolytic virus therapy from lab to clinic in an academic setting, but not in a pharmaceutical setting where the rules of engagement are quite different. So having Alice Bexon join us has really greatly empowered us to aggressively move forward with our company sponsored clinical trials. We already have our first two INDs approved. One for the use of measles virus in patients with lung cancer, and the other for the use of VSV coding for interferon beta and NIS (the thyroid sodium-iodide symporter) in a Phase I intratumoral all comers dose escalation trial.

CEOCFO: ***Is it easy to get people to participate in trials in this particular arena?***
Dr. Russell: It's increasingly attracting the attention of patients who are looking for experimental therapy. I think in that domain of cancer care where conventional therapy has failed there's definitely a great deal of interest in exploring oncolytic viruses. With the approval of Amgen's product, there's gradually an increasing acceptance, not just by the patients but also by the treatment centers that are being asked to use oncolytic viruses. There are some additional considerations when using viruses as therapy versus using conventional small molecules because you have to think about the possibility of the virus infecting someone other than the patient. So there are containment issues. Those are relatively straight forward, but they're nevertheless something that I think people need to be familiar with before they're comfortable using the oncolytic viruses.

CEOCFO: ***What surprised you throughout the process so far as you have been working in this area and with these drugs?***
Dr. Russell: That is a difficult question. I'm not sure that I've found things surprising so much as interesting and fun engaging with the process of drug development in a commercial setting. I do think it's wonderful that there's such an enthusiastic reception for a completely new modality to be used in the cancer armamentarium. Possibly, the most surprising development in recent years has been the demonstration that we really can harness the immune system to attack cancer. There were so many years of animal experiments that did not translate to human success, and then with the advent of the Checkpoint Inhibitor Antibodies, it became clear why the immune system was not really helping cancer

patients and how it could actually be engaged. I think with that major advance in the field oncology, the use of oncolytic viruses as a cancer therapy really has come into its own because a great way to wake the immune system up and to help it to recognize the cancer and use in conjunction with these Checkpoints Inhibitor Antibodies, you can then allow the immune system to have at the cancer.

CEOCFO: ***There are many companies in healthcare and many new ideas? Why pay attention to Vyriad today?***
Dr. Russell: Well, in the oncolytic virotherapy space, I think we really have some significant advantages. We are clinical stage and we do have data with our viruses showing systemic efficacy. This is a major goal of oncolytic virotherapy, to show that they can be active when given into a vein as opposed to when injected directly into a tumor, so that's important. We have a very strong team; we have a team of people who are very familiar with manufacture, pre-clinical toxicity testing and translation to the clinic of oncolytic viruses. We've also now have Alice Bexon on-board as our CMO with her company in tow to assist us with that process, so that's a real strength. We have an excellent and broad portfolio. We have more than one oncolytic virus in our company, in fact we have two that are clinical stage and then we have a pipeline of additional viruses and technologies because we envision viruses as a whole new domain of therapeutics that will be used in combination and sequentially. One of the interesting things about viruses, versus the conventional small molecules, is that the immune system is configured in such a way that when it sees a virus a second or third or fourth time, it much more efficiently eliminates the virus. So sequential use of different viruses we think will be very important. All in all, we think we really are a very strong company in that space, and the other thing about us in relation to our fundraising efforts right now, is that we are ready to move extremely aggressively with two FDA-approved clinical trials ready to launch immediately. Those are the key strengths of our company.