Inovio Pharmaceuticals 2015 BIO CEO Investor Conference presentation

Dr. Joseph Kim, President, CEO, and director of Inovio Pharmaceuticals {NASDAQ: INO} recently made a strong presentation to the 2015 BIO CEO Investor Conference held in the Waldorf Astoria, Park Avenue, New York City.

Dr. Kim outlined the planned developments for this year and confirmed a solid cash position of $100 million.

Transcript of Dr. Joseph Kim's presentation to the 2015 BIO CEO & Investor Conference

February 9, 2015

For some time, scientists have believed that T cells play a vital role in controlling and clearing diseases. So the important question is, how do you control that? How do you help the immune system recognize the fast-growing tumours or even the slow, evasive tumours? Or the rapidly-mutating infectious disease-causing agents?

Also, the big challenge is, how do you address that using the newly-important immunotherapies and approaches? Another question to ask is, is there an ideal immunotherapy for generating those important T cells which are functional, durable and effective in the clinical setting? As a scientist who's spent most of my adult life devoted to this field, the answer is yes, and I'm going to talk to you about how Inovio is doing this. But overall, obviously you want the immunotherapy to be effective, efficient and safe. You want to do the work, you want to do it as cost-effective as possible,

and you want to do no harm. But how do you do this in a way that can engender the most effective outcome?

What Inovio believes is you want to do this in the body. If you can do it directly in the patient's own body, why mess with the bothers of doing manipulations outside the body—the cost and the potential toxicity, and efficiency and quality of doing so? The second is, Inovio believes we can do this directly by generating powerful T cells in a patient's own body which can attack the infected or cancerous cells. So I want to cover the important attributes of Inovio's immunotherapies. I'm going to show you the data from our phase II clinical study, which solidifies what I'm going to say, and the best attributes of the T cell generating platform and the products, as you want to do this very specifically, on an antigen basis. You want to have functional efficacy by generating these important and powerful T cell immune responses with things like granzyme and perforin, which are the weapons that these T cells use. You want the high magnitude and durability. Obviously you don't want unwanted side effects or inflammatory responses, but you also have to bring about clinical efficacy.

I'm going to spend the next few minutes showing how Inovio is addressing this very important advancement in new medicine called immunotherapy.

So how do we do this?

We use the known sequences of DNA sequences of every marker of tumour cells or infectious agents called the antigen and we use the DNA sequences so that we engineer them to be our product sequences. We put it in a carrier DNA, and then we deliver it using brief electrical energy directly into the muscle cells of our body— direct as intramuscular injection. The DNA goes into our cells, and using the already existing cellular mechanism for protein production, we can generate very high levels of specific antigens targeted to a disease,

and those antigens then get produced, processed and presented to the immune system in a very efficient and effective manner where we can generate very high levels of killer T cell immune responses as well as other immune responses. And they go out and traffic to the site of interest and kill those tumour cells at the tissue level. So that's how Inovio is doing it. We have a platform that is protected by over 600 patents, both issued and pending globally, and our platform covers different target products, mostly antigen targeting immunotherapies and vaccines which are in phase I and phase II clinical testing.

We also have immune activators, including DNA forms of IL-12, IL-33 and IL-28, other immune activators that can amplify and direct these important immune responses in the patient.

And lastly, we just received at the end of last year a $12 million contract from DARPA, and they're funding our work in applying our DNA-based platform to generate a new class of monoclonal antibody products using just the DNA-based delivery system. So I'm not going to dwell too much on this in today's presentation, but in 2015 you will hear a lot more about this.

Currently the monoclonal antibody product class accounts for over $50 billion in product sales in 2014, and we expect to have a large chunk of that using our technology to deliver some of the blockbuster and new monoclonal antibodies.

So, what are the products that are in our pipeline today? It's broadly divided intothree areas. The top, are our products to treat post-HPV infection diseases. These are cervical dysplasia, which is a pre-cancer, cervical cancer, head and neck cancer, and other types of ailments caused by HPV, and I'm going to show you some of our phase II efficacy and immunogenicity data which demonstrates the power of this platform and products going after this very lucrative target area.

We've expanded into other cancers caused within the solid

tumor areas, and we're using other novel antigens to go after these cancer targets. And lastly, mostly funded by other people's money, including over $60 million in grants and contracts from the DoD, NIH and others in the past, we have very exciting antiviral/anti-infection programs which I'll highlight. This includes a product that we have licensed out to Roche for treating hepatitis B chronic infection – INO-1800 – for which we'll be launching our first clinical study later this half. So I'm very excited to tell you about some of these programs.

Let's talk about human papillomavirus. It's a very promiscuous virus. A vast majority of our population have been exposed to this virus. It causes multiple ailments, including the pre-cancers and cancers of the cervix, head and neck cancer, and anogenital cancers as well. The data from US and EU5 incidences are shown here. This is every year of new cases, and we have targeted to take VGX-3100, which is our lead product, to go after high-grade pre-cancer, which is the last [disease stage] prior to full-blown cancer, and then expand out with our successful results into other parts. So our goal, I want to say here, is to be the main therapeutic provider for all diseases caused by HPV infection. So that is one of the major goals of Inovio Pharmaceuticals.

Let me just quickly go into the disease progression. On the left-hand column is the Pap smear, immunohistochemical staining, and the colposcopy of normal cervical tissue. In the middle, as you can see, the cells are starting to transform.

This is a high-grade late-stage cervical dysplasia. That's CIN3, so your cells are transforming – and obviously you don't have to be an OB/GYN to see that that cervical tissue and colposcopy is not healthy – and the right-most column is an invasive cervical cancer. Our goal is to intervene and treat the women in a nonsurgical, non-invasive way at the CIN3 level using our immunotherapy by Generating powerful T cell responses against two of the most important oncogenes causing

these transformations to occur – the E6/E7 oncogenes of HPV.

Currently the only treatment option available for women with CIN2 or 3 diagnosis today is surgery. As shown here, you have a lot of side effects and potential issues associated with surgery, and I think it's inherent [to have a] dislike or distaste for having any parts of your body taken out by a surgical procedure. And there are other issues such as pre-term birth, and obviously the surgery in which a surgeon takes out the bad dysplasia areas with ablation doesn't necessarily get rid of the virus that caused the disease in the first place. So our goal is to generate and produce a product that can non-surgically, using an immunotherapeutic approach, clear the lesions, as well as the cause of the lesions in the first place, which is the HPV infection.

Our VGX-3100 data was published from our phase I studies, where we were able to generate very high levels of T cells in patients. It was published in Science Translational Medicine a couple of years ago. And then we embarked on a phase II double-blind, placebo-controlled efficacy trial in 148 patients. It was 3:1 randomized. All women were confirmed to be at a CIN2 or 3 state, and all women were confirmed to have HPV infection from a cervical swab, either HPV-16 type or HPV-18 type. And all women received three injections into the arm at months zero, 1 and 3, and at month 9, both primary and the secondary endpoints were determined in blind session, and we just reported last year the top-line data from the efficacy, and let me get to them.

So our primary efficacy was, just by three monthly injections into the arm of a patient, can we clear the lesion that was at the CIN2 or 3 stage, and the answer is clearly yes. On the left-hand panel you see the reduction of a cervical lesion of CIN2/3 with the treatment of VGX-3100—about 50 percent of the women who were treated with the product were able to regress using her own T cells to do so

[which Inovio helped activate]. And the placebo effect, which is about 30 percent here, when using the primary regression parameter of regression down to CIN1, which is a low-grade to normal. But if you treat them more constrictively in a post-hoc analysis, if you look at the [complete] regression down to normal, you can see most of the drug effect of VGX-3100. We were able to regress the women's lesions down to a fully normal status – full, complete response in over 40 percent of the patients – and the placebo effect went down [to 16%]. So this shows that there is some balance between CIN2 and CIN1 in a placebo effect, but if you use a stricter guidance of regression to normal, you see a tremendous impact delta in a treated versus non[treated]. And both analyses had a significant p-value with a very low p-value.

The secondary endpoint was actual regression of the lesion, but we also wanted to ask, can these women also clear the virus that caused the disease in the first place from their cervical swab? And that answer also was clearly yes. The drug-treated patients were able to clear—40 percent of the women were able to clear the HPV-16 or 18 [virus], compared to about 14 percent of the women in the placebo group. So this is a very important finding, and I'll come back to how we tie this into our newly-presented immune response data that you're going to see.

I said these efficacy results were due to the generation of powerful CD8 killer T cell immune responses in the patient's own body using a very non-invasive, three injections into the arm, and this is a longitudinal T cell immune response analysis in over 140 patients from our phase II study. These are the type of data that you see from animal studies, not in people. You will not see this type of immune response data from phase II large controlled studies laid out like this from the rest of our field. As you can see, you don't need to be a scientist to see the significant difference. At three injections, after each injection you see a strong induction of

T cells in these patients' blood. This is peripheral blood immune response measured from blood that was extracted from the patients at each time point. As you can see, the peak T cell responses are after three injections at week 14, and then there are persistent T cell responses in the 3100-treated women at the primary and secondary endpoint time period of week 36. So we know we can generate T cell responses in the whole periphery of the patients, but it's important to see, can these T cells that are circulating in your body that are looking for these HPV targets, E6/E7 targets, can they traffic to the tissue and also clear the disease and the virus? And as you've seen in the efficacy data, clearly the answer is yes, and we can track that.

So we looked at the tissue level of the cervical tissues, and I'm going to go through this very clearly. On the first row is the week zero of a placebo-treated patient, and the same slides were looked at week 36

. The first column is staining [brown spots] for the presence of HPV. The second column is staining for the presence of CD8 T cells from this cervical tissue. So the bottom line here is the HPV persists from week zero to week 36 in the patient. And you see some T cells, but not in the epithelium where the infection occurs of the CD8 T cells.
So picture this – and I'm going to the drug-treated women who were able to clear from a slide using the VGX-3100 treatment. So similarly here, from week zero to week 36, this patient, who was treated with VGX-3100, was able to clear the virus, the HPV stain here with the brown spots on the first column. The virus is gone. And then on the right-hand side, even though the virus is gone and the lesion has regressed from week zero to week 36, you see pervasive CD8 T cells – these are the brown spots shown on the right-hand column at week 36 –surveilling and patrolling the cervical tissues in the stromal epithelium, and back and forth.

So the significance of this is, we have been able to tie this

from a peripheral generation of important CD8 T cell responses that are high and robust and durable. We can also observe these T cells trafficking into the tissues of interest and doing their function in the right way.

I'm not going to show additional data we have, but which we have put into a publication that we expect to come out by mid-year this year in a top medical journal where we are actually numerically correlating between the magnitude and the characteristics of our CD8 T cells to the successful clearance of the clinical outcome – clearance of the lesions and the clearance of the virus.

So I think Inovio has the most amount of immune analysis data in the field of all immunotherapies out there, and we look forward to presenting more data as we come into the rest of 2015.

So let me just quickly tie the impact of this. What we have generated is a DNA based therapy with three monthly injections into the arm of a patient. We've seen that we can generate high levels of killer CD8 T cells in the blood which were observed to go into the tissues. We see the T cells infiltrating at the disease site, and they can clear the disease – both the lesions as well as the virus. And there's a huge implication for our development for all of our immuno-oncology products targeting other targets caused by the HPV infection, as well as other cancer therapies I'm going to touch on, including lung, breast, pancreas and prostate, using INO-1400 and INO-5150, as well as our ability to clear chronic infection has huge implication for our HIV as well as HBV [hepatitis B] and HCV [hepatitis C] products.

So what we're doing now is we're preparing for a phase III registrational trial [for VGX-3100]. At the same time, we are working on getting the paper published in 2015 which outlines all of these analyses. I must tell you here that there were no safety concerns from our phase II study, and we expect to have

the full data out there. The other highly important preparation for our first phase III study is the scaling up of our manufacturing of the plasmid products [to a commercial scale], and making commercial-scale devices ready. We've done qualitative and quantitative market research, as well as the payor research that's ongoing now, so all of this pre-commercial production is getting done.

We also hired Mark Gelder, a Gynoncologist, to head up and quarterback this phase III study, as well as Ms. Jennifer Laux from big pharma, who has experience in the commercialization and the launch of these products. So we're getting all of these things ready.

As I said to you earlier, we want to own the whole post-HPV infection therapeutic space, so we've launched into different cancer studies already, one for treating cervical cancer, more invasive cervical cancer patients – this study is ongoing –and the second study for treating head and neck cancer. As you know, head and neck cancer caused by HPV is the fastest-growing cancer in men today. So we have two pilot-scale studies ongoing. We expect to have from these INO-3112 studies later this year T cell immune responses from these cancer patient studies.

We hope to translate our ability to generate high levels of T cell immune responses in cervical dysplasia patients using the same approach and demonstrate our ability to generate these high-quality and quantity levels of T cells in these more invasive cancer patient settings.

Moving on, I want to touch in the next couple slides on our very exciting programs. We started at the end of last year our study of INO-1400. This product targets human telomerase reverse transcriptase as the target antigen. An hTERT defect is prevalent and is over-expressed in over 85 percent of all cancer types – over 95 percent of pancreatic cancer, breast and lung cancers -and obviously we chose these three cancer

types to go after in our initial clinical study which we launched. We have also added the IL-12 immune activator which can amplify and accelerate the induction of CD8 T cells. This is a 54-patient study in breast, lung and pancreatic cancer patients. We are hoping to see from this open-label study some immune response data in the last part of this year, but this was just launched a couple of months ago.

We're very excited about this potentially universal cancer therapy because of the pervasiveness and importance of this hTERT antigen.

The last trial description I'm going to cover is INO-1800. In 2013 we licensed out this product to Roche. This product is a multi-antigen core, and surface antigen based product that's designed to clear HBV-infected cells using the same product strategy that we were able to show in clearing human papillomavirus from CIN women in our phase II study. Roche has asked us to quarterback this study, although they're funding all of the trial. And this collaboration has been going extremely well. We expect to start the clinical study in the first half of this year, which will obviously trigger the first of the milestone payments from Roche. So we're very excited to apply what we saw in clinical efficacy from our phase II HPV study into our chronic HBV therapeutic in INO-1800.

So let me quickly go into management. We have very capable management who can execute the strategies of our company. We have a very extensive and experienced board to help guide us.

Financially, we ended the last quarter with a little over $100 million in cash. Our burn is around $25 million per year, currently, and we have no debt. So we have a very strong financial position.

So what are the value drivers for the rest of the year?

We’re going to get phase III ready for VGX-3100. We’re going to publish the [phase II] data. We’ll have the end of phase II meeting with the FDA where we’ll get the clinical and protocol and endpoint concurrence for the phase III. We look forward to launching phase III about the time you’ll see me [here] next year, if not earlier. We also have data from 3112 cancer studies. We want to show our T cell immune response data from this study.

We’ll also launch a 5150 study in prostate cancer, as well as our trial for INO-1800 for treating hep B, and we’ll have some early data readout from our hep C trial that’s ongoing with our affiliate in South Korea from the therapeutic hepatitis C product, INO-8000.

Last but not least, our Ebola vaccine [INO-4200]. We’re on track to start our clinical studies in the next few weeks, and we look forward to getting additional capital from government sources to help accelerate and expand this program.

So these are some of the very few catalysts that we expect to drive the interest and the value of Inovio going forward.

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Please Note: This text contains minor edits for clarification and ease of reading.