Biomarck Pharmaceuticals

Viviana Limon: Good morning, everyone. Thank you for joining us today. My name is Viviana Limon. I'm with the J.P. Morgan healthcare investment banking group. I'd like to introduce the next speaker today, Brian Dickson from Biomarck Pharmaceuticals. He'll be presenting today.

Brian Dickson: Thank you, Viviana. Good morning. I applaud you [laughs] , who stay right to the end of a conference. I know what that's like. I am Brian Dickson. I'm the CEO of Biomarck Pharmaceuticals.

We are a company that are taking our peptides through clinical for two significant disease states, non-small cell lung cancer and acute respiratory distress syndrome. We are in phase 2 clinical in both of those.

The purpose of this talk is to highlight how far we've got, what our achievements are, and then what are the opportunities of going further. In summary of where we are, I'm going to highlight some of these. We are first in class in both disease states.

Our method of action is clearly defined. Both the government and other companies want to see method of action. We have selective inhibition. That is really important because the protein we're acting against -- I'll describe that later, it's called a MARCKS protein -- is ubiquitous. It's in all cells.

We don't want to damage normal cells. We have evidence that we are not doing that. It's only the diseased cells we're affecting. That is important because it contributes to our safety profile in the clinic. Dose response, has been demonstrated, also important.

We have run a clinical study, which I'm going to describe, in non-small cell lung cancer. It's a small study, but we achieved statistical significance at p of 0.02, which is very significant. We were surprised in such a small study but delightfully surprised in getting that response in overall response rate.

We've also run a COPD study and achieved statistical significance in that in FEV1. We've achieved in the clinic evidence of efficacy in more than one disease state. The two indications we're studying, non-small cell lung cancer and ARDS, are both blockbuster potential.

Then lastly, we have an IP portfolio that I want to emphasize is issued. It's not applied for or pending. It's issued worldwide through 2035.

We have a small team. We operate, in a practical sense, through CROs. The team we have is very experienced, both in management and our board and our scientific advisory board. Everybody on that group has been involved in the successful sale or development of other companies.

Our lead compound, the one we've put through the clinic, is BIO-11006. This is a peptide, as I mentioned. It's a 10-amino acid peptide, quite a short one. Our portfolio covers peptides between 6 amino acids and 20 amino acids. It's a very broad portfolio. We developed this one first as we considered it the best for these disease states, looking at the half-life and the solubility.

It is active against a protein. The protein is a 332-amino acid chain protein called the MARCKS protein, which I'm going to describe to you in a few minutes. The peptide, the short amino acid chain, is the N-terminus, in other words the end of the naturally occurring MARCKS protein.

In a way, the peptide is controlling the big protein. It's like the tail wagging the dog, but we can control the dog with the tail. The MARCKS protein is well-known. It's been in literature for 20 to 30 years, but it's been mainly looked at in respiratory disease.

Obviously, ARDS is a respiratory disease. I'll come back to that. I'm going to go through lung cancer first.

As I said, it is a big protein, 332 amino acids. It sits on the inside lining of the cell membrane. It's very important in terms of inflammation control, secretion control.

Remember we were looking at COPD in the beginning? Also, it's been increasingly recognized as being important in terms of cell motility and cell division. In terms of recognition in oncology, this is an NIH listing of number of studies being published regarding cell motility, cell division, and how important this controlling protein is. There's been an upswing certainly in the last 10 years.

There's a lot of noise about the control or attempted control of cancer by using this protein. BIO-11006 peptide is well-tolerated. Remember I was talking about how selective it was? I'll show you more data in the clinic for that. It is, as I said, the same N-terminus -- that's also an end, E-N-D, terminus -- of the MARCKS protein.

Underneath, there's a representation. You can see those amino acid sequences that are exactly the same as the MARCKS protein itself with a peptide. The only change is the MA for the MARCKS protein is myristoylated. The AC, the acetyl, on the peptide is a chain. The reason for that change was to increase solubility of the peptide.

The peptide is controlling the release of the MARCKS protein from the inside of the cell membrane. It's released by phosphorylation. The peptide reduces significantly that phosphorylation and therefore stops MARCKS protein being released into the cell.

Here is a schematic of a cell. You can see the green areas are the MARCKS protein and then the phosphorylation areas. What is the big deal? This is a protein that's in pretty

much all cells. You need it. When you get a bronchitis or an inflammation, some of the MARCKS protein should be released. It has a function.

The issue becomes in cancer or ARDS, it's over phosphorylated. You get a flood of the MARCKS protein into the cytoplasm. That causes cytokine release. The cytokine release, the inflammatory factors, go on to cause rapid cell division, and cell movement.

An example of this, on the left-hand side, you can see these are human lung cancer cells. They are generally circular. They've been stained with actin just to show, with green, where the actin is. It's on the periphery of the cell, just lining the cell.

The cells are dividing. They're moving. That's why they're lung cancer cells. These are the same cells on the right. If we expose them to our peptide, in this case for four hours, you can see a dramatic change. There's a dramatic change in cell morphology, in other words the shape of the cell.

They've flattened. That's why they look brighter. This is the same magnification on both sides. They look brighter because they're only two-dimensional as opposed to the three-dimensional normal cancer cell.

They've also put out what's called focal adhesion points. It's hard, probably, to see with that magnification from where you are. These are the strips that are coming outside of the cell from the cell lining. They are like anchors. They stop the cell moving.

The cells on the right that are treated are neither moving nor dividing. Remember, they are human lung cancer cells.

A lot of people want to know, "What's the clinical experience?" Preclinical I haven't gone through it yet, but we do have good preclinical data. Sounds really exciting, but what happens if you go into the clinic?

We've done phase 1 studies, both single and multiple dose. What I'd point out there is we've gone as high as a thousand milligrams. It's way above our human dose that we're using therapeutically, but it's expected in phase 1 studies. We found the only adverse events that occurred were headache and cough, nothing significant.

We did the COPD study that I mentioned. It was in 172 patients. It was placebo controlled. It looked at different dosing, dose ranging, different dose intervals, once a day, twice a day. It did achieve significance in FEV1, as I mentioned, at the 0.029 level. We had no significant side effects, but we suspended that program and you may wonder why.

It was because we had very good data coming out on the cancer program, such as the one I just showed you before, and in ARDS. These two disease states are much more significant than COPD, both to the patient and to the commercial aspects.

In terms of ARDS or cancer, if it worked there, that is a much higher return on investment, so strategically, we changed the direction of the company. We then went on

to do ARDS. I am going to discuss that at the second half of this presentation and non-small cell lung cancer where we have completed enrollment, and I'm going to show you the initial results.

The overall comment though is the safety profile in over 300 patients has been very good. Where the only things that occur and that's less than five percent is headache and cough. If in fact that profile stands up in future studies as we go along compared to cancer drugs, that is trivial.

As I said, I'm going to look through the non-small cell cancer program first. I'm sure people in this audience know how big this market is, but it is the most common lung cancer. Even with all the research being done and the products being approved, immuno-oncology, for example, has made great strides here, especially if you have a PDL-1 ratio of more than 50 percent.

They work very well, but they have significant side effects in about a third of the patients. There is a large opportunity remaining in non-small-cell lung cancer, because the five-year survival rate is around 20 percent. That's better than it used to be, but there is still got a long way to go.

Just to give you a comparison, the five-year survival rate for breast cancer is around 80 percent. Non-small cell lung cancer even with all the immuno-oncology that's come through is still not very well treated...

We have preclinical efficacy. There are two validated predictive animal models, orthotopic lung injection and tail vein injection. Here you are injecting human cancer cells straight into the animal either into the lung or into the tail vein, and these are SCID mice. That means they're immuno-compromised mice. They will get the lung cancer. It's not a maybe. They will get it.

Then you test your drug. In both of those models, BIO-11006 reduce the primary tumor size and prevented metastasis further. The important thing that's on this slide though is that it was distally active. We give this by a nebulizer, twice a day, so it's inhaled into the lung.

Where does it go? Does it act beyond the lung in other words? We do full body animal scans to see if there are tumors developing, where are they developing. If you're having an effect, are you having an effect just in one part or all? The answer is we have an effect in all. It's acting distally in the mediastinum, for example, or the diaphragm or heart.

We've tested against a lot of solid tumors, not just the lung -- but breast, sarcoma, glioma, for example, and it's worked in all of them. We have, in passing, tested it in non-solid tumors too, such as leukemia. It did not work. It's a product for solid tumors.

Interestingly, there was a synergistic effect with carboplatin. We tested carboplatin first and then carboplatin plus BIO-11006. Carboplatin was effective, but it was much more effective, if you add BIO-11006.

Why? Because 11-006 holds the cancer cell when it's dividing in what's called the G2-M phase, which is a division phase which is where carboplatin works. It's allowing carboplatin more time to be effective.

Now, as I said, we've finished enrollment in our clinical study and the green on this slide is our drug plus standard of care. The blue is standard of care. Standard of care in this case is carboplatin-pemetrexed. That's an FDA-approved combination as being safe and effective. It's commonly used in the United States.

In fact, it's the same combination that Keytruda was compared against for its pivotal studies through the FDA. We compared it against the same dublet.

If you look at the first set of columns, that is looking at partial responses, at six weeks, and the second set of columns is partial response at three months. Partial responses, I'm sure you know, is defined as more than 30 percent reduction in the primary tumor and no further metastases.

Clearly, we've added the benefit. The blue is an approved therapy and the green is adding our product to it. We increase the response. The opposite way of looking at is what about disease progression? Who gets worse? You can see on the third column, a lot fewer patients in green, in other words, without our product it gets worse.

In market potential for non-small cell lung cancer, clearly, any product that would be approved for an indication such as that would be over a billion a year. You may think, "Well, it's very well satisfied by immunotherapy." It is if you have a PDL-1 over 50 percent, which is about 50 percent of the market.

Those who have PDL-1 less than that it's not as responsive. Take Keytruda, for example, it is approved. It is being used empirically, but clinicians are frustrated because they're not getting the efficacy they want, and they are getting the side effects.

The markers and gene expressions such as EGFR or STK11, are other gene expressions. They tend to be tyrosine kinases. The KS on the MARCKS protein stands for kinase substrate. BIO-11006 is in fact a kinase inhibitor and that's where we should be marketing.

Having said that, the aim in cancer treatment as you know, is maybe two years extra life and of course the quality of life is very important, I understand that and that's where we are going. I've said, we've got a very good safety profile and we're showing efficacy. That's excellent.

If you then switch to ARDS, acute respiratory distress syndrome, this is totally different, because now if you can get these people to survive just 30 days, they go on to have almost a normal life. Now we're saving a life, not just prolonging a life.

I'm not going to go through this slide in detail, but ARDS, acute respiratory distress syndrome, occurs in 200,000 patients per year in the US. 40 percent of people die within 30 days. That's huge. That's on a ventilator in an ICU and they still die. That's about

80,000 people in the US and over a million worldwide are dying each year.

If you can get them past the 30 days, as I said, they go on to live almost normal life. They may have some residual lung disease but fundamentally they survive. We have done preclinical work in ARDS. We've got positive results out of the three predictive animal models. We can prevent ARDS developing in animals.

One thing that has never been shown before that we've published with BIO-11006, we can reverse it if we give the stimulus, such as bacterial pneumonia that causes ARDS in these animals. We know they've got ARDS. They're moribund. If we then give them the drug, BIO-11006, we know we can actually get these animals to get up and roam around the cage again as normal.

We're doing a phase 2 study, as I said. It's a placebo-controlled study. All patients are on a mechanical ventilator. They're in ICU. They get placebo on a randomized basis or our drug. I can't give you the results of this study. We've almost finished it. We've got 36 at 40 enrolled.

If 40 percent of patients, historically, are dying in these clinics, and in fact, the five clinics we're using its 47 percent, but that's because they are referral sites and they get the sickest patients, we would have expected out of 36 patients about 15 deaths.

I know how many deaths we've got. It's eight. The reason I know that is I have to report them to the FDA, obviously. If you would have expected 15 deaths and we've only got eight, and we've almost finished the study, something is clearly going on. I don't know which drug they're on, but I will very soon, because we should finish this study by the end of this quarter.

If this is the case, obviously we'll get FDA advice, but depending on the data will likely get fast track. This is classified as an orphan drug disease.

Clearly, the market potential is over a billion dollars a year in the US alone. It's unopposed, there's no other drugs. I will want to recognize that we've had support from NC State University. We were given the best pipeline of promise in BIO2018, and we've had a repeated support from the NIH.

Groups like J.P. Morgan look to see if you can hit all their important points. We believe we do. We do have compelling clinical data. We do have first-in-class. We do have a strong safety profile. We have blockbuster potential, and we've got long-lasting IP. We believe we've got two opportunities here to make a significant difference in people's lives. Thank you very much.

[applause]