ZIOPHARM Oncology, Inc.

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It's good to be here everyone. I appreciate the opportunity to be at Stifel, and to tell you the story perhaps with a different lens through the lens of an investor. Because I think as a company, we really are at the inflection point of some – particularly awesome cool and interesting science academic pursuits. It's now time to focus on the next phase for us, which is becoming the business. The paradigm shifting business, we think we can become in cancer immunotherapy.

Obviously I have to start with the forward-looking statements slide. We obviously make the disclaimer that the results that we discuss today may differ materially from those projected and we undertake no obligation to publicly update any forward-looking statements.

For those of you that have the deck in front of you, this looks familiar. This is the same deck essentially we presented on the Q call last week. But I want to tell you the story in a different way. The first thing I'd like to do is give you my background. I'm an M.D. by education, in the mid to late 1990's by luck serendipity, nepotism ended up in Palo Alto where I was exposed to the life science industry. And I was fortunate enough to be involved with a couple of startups both of which ultimately went public and were later acquired for attractive returns. And through that process, I was exposed to the investment community largely the venture capital community.

Through that and this kind of reminds me where ZIOPHARM sits today. In 1999 the idea of starting a healthcare only venture fund was somewhat of a stiff headwind because the dot-com boom was happening. And what we saw instead was an opportunity to create a fund that could buy late-stage assets for early stage prices, late-stage assets for early stage prices. Fast forward to today, I think ZIOPHARM actually falls a little bit into that same bucket. We've clearly been decoupled from the upward surge that we've seen particularly in 2017 in the space of cancer and immunotherapy. And we can ask ourselves, why but I would submit to you that the scientific foundation that has been in place for several years and especially since Dr. Cooper joined in 2015, is not only valid, it's stronger than ever.

And so I want to stress that we recognize where we are in the market. But we also believe that we represent an opportunity to be a true paradigm shifting company and ultimately plan on being recoupled with the surgeon immunotherapy as we see it today. So the question is how do we do that? Where are we? And if we look at Slide 3, it's just a reminder of what we have and what

we're going to focus on. We have two key platforms with essentially three main projects that are really going to be the value driving assets for our company both in the near and the long-term.

The first and you've heard this before is what we call gene therapy. And gene therapy in our case is essentially taking your existing immune system and cranking it up in the localized responsible, inducible, tunable fashion, so that we can help eradicate cancer. In the case for ZIOPHARM, our gene therapy program is centered around a key cytokine called IL-12, interleukin-12. And as you've heard before interleukin-12 is a very powerful and is the master regulator of our immune response. The trouble with it is it's very, very difficult to control, it has a very tight zero therapeutic window, which means that if you induce it, you can create a response that can actually harm the patient. Two years ago, it was actually considered undoable, but I submit to you that as we sit here today, we've actually shown definitively that we can induce control and regulate IL-12 and we'll talk about that in the brain cancer programs in particular.

The other platform we have is what we call cell therapy. In the case of cell therapy, we have two major shots on goal both of which are centered around the same concept, which is we don't believe that the practice of immunotherapy in the next two, three, five years will be centered around viral-based systems. And the reason we believe this is because viral-based systems, which should be congratulated for where they are today, as a first mover cannot technically address the broad market of all blood cancers and all solid tumors. We need a cheaper, more cost effective, less complex system and it needs to be non-viral, it needs to be new, it needs to be a shift in paradigms.

And so with ZIOPHARM our cell therapy platform is centered around something called Sleeping Beauty. And Sleeping Beauty is the first clinically validated non-viral system for delivering genetic information into cells. We enjoy a tremendous group of partners with the names on the list at the bottom between Intrexon and Merck Industry. We've got one of the world's leading cancer centers and MD Anderson is our partner. And earlier this year, we announced when Dr. Rosenberg called us that we had signed a credo with Intrexon and the NCI to investigate solid tumor therapies.

Moving along to Slide 5, the pipeline slide. Really what you want to see is you want to focus on the three main buckets. The first bucket is our gene therapy program, which is the ad-RTS-hIL-12, and where we are there is we have a Phase 1 to Phase 3 approval meaning that we've demonstrated in our Phase 1 patient's data that allow the FDA to give us the go ahead and bypass Phase 2. So we recently announced that we are going for a randomized trial and we will update the design of the trial which we expect to initiate by the end of this year at a later date.

The second bucket you see is named CAR. I think it's actually a misnomer because we're really not in the race of CAR specifically. Again, let me remind you, we are trying to shift the paradigm from viral systems to non-viral systems. So when I look at our competitors or our peers, who use viral systems in CAR's for CD19 for example their differentiation really is at the margin. They may have slightly different ways to manufacture their product, they might use a different virus but they're using technologies that have been around for years and they're required to propagate their cells offsite at a GMP facility because the viral-based systems require the cell membrane to be deconstructed.

In our case, we have a CAR but we are interested in providing the platform to change the way these cells are manufactured and delivered. And so when you look at the middle bucket, what have we done. Well, we have the first-generation set of patients for CD19, which actually aren't on the slide, they were treated about four years ago and so we can say definitively that we have patients that are answering the telephone when we call them today mean they're alive, who's cells are still proliferating that were delivered – that we can measure that were delivered to them with our Sleeping Beauty construct between four and six weeks of delivery time, as a proof-of-concept.

So we can check the box, we prove – we have proven that we can use a non-viral system to deliver genetic information to cells and it just so happens that four years later we also believe we have a survival advantage relative to just bone marrow transplant, which we will update – continue to update at ASH in December.

The second thing we've done which is on this slide, is we've taken that proof-of-concept for the one-two punch to do a second-generation cohort of patients which will also be updated at ASH. And in this case the main difference is we shorten the manufacturing time from four to five weeks down to two weeks, it's an evolution, it's a step wise function to prove that we could still deliver the genetic information with a non-viral system. Those patients will be updated at ASH, which then gets us to what I believe is the key value inflection point for this program – for this particular CD19 program, which is the third-generation cohort.

Laurence recently guided us that we will be in the clinic with this cohort in 2018 and it's worth noting what we will be doing for these patients. We will be delivering cells that had the genetic information programmed into them by the same Sleeping Beauty platform and we will be delivering those cells in less than two days, less than two days. Those cells will be put into the body and the key difference here is the body will become the bioreactor, not a GMP facility that you have to send product to and wait for the cells to propagate and then freeze them and then send them back to the patient and infuse them in the patient. We're going to essentially have less than two days, i.e., real-time infusion of cells with Sleeping Beauty modified CD19 targeted CAR's.

Now, one thing to add is these cells will also have a co-constituent something called membrane-bound IL-15, which is actually tethered to our CAR, there's significant IP around this. And the goal is to give the cells since we're putting in fewer in the body, the body needs to grow the cells, we need to give them a growth advantage. IL-15 is a growth factor and it refers memory, so that our cells should have a survival advantage. All of this will be under the control of a switch. So we're very excited, we think that in 2018 when this first – when we get the first patients dosed, we will have significantly taken the steps towards the business shifting paradigm of non-viral real-time point-of-care cells.

The third bucket, I want you to focus on is TCR. And TCR is again using the Sleeping Beauty platform a non-viral platform to deliver a different cassette if you will, a cassette that has something called a T-cell receptor. A T-cell receptor aimed at the cancers own specific signature that's called a neoantigen signature. And it's important to note that neoantigens are not shared.

What that means is your cancer and my cancer and the next person's cancer each has its own unique signature. The antigens are not shared with normal cells, they're not shared within an individual's, it is an algorithm of your cancer signature, truly personalized medicine.

Now, this is a huge, huge shot on goal, this is the big prize. And what's interesting about it is that we don't believe that viral-based systems can do this. The technical hurdles, the cost hurdles you would have to have a facility of several million square-feet to accommodate a local neighborhood of patients because the viral systems require so much more complexity to generate the cells outside of the body. In our case, Dr. Rosenberg had some interesting data around tumor-infiltrating lymphocytes where he could clone – he could find the clone of lymphocytes that had the closest resembling signature to the neoantigens and propagate them outside of the body and then redeliver them. The goal of this project is to actually design the cells based on the signature we get right away rather than trying to find the clone cloning it outside the body propagating et cetera. This is groundbreaking efforts.

Are we early? Probably not as early as people think, I think that there is an assumption that the credo was signed in January and we should be treating patients within let's say, three weeks, five weeks, six weeks, six months. I think the difficulty that the company has faced is silence must mean bad news, not the case. In fact, Laurence announced last week that we've blocked and tackled our way towards significant progress where ultimately you have to get to a final validation, a dry run if you will before you infuse the full system in the patient. We're in the final throes of that process validation and we expect as you can see on the slide to be in the clinic in 2018.

So if you add all that up, and I'd submit to you that we have a Phase 3 study, ready to initiate third-generation and real-time point-of-care CAR cells induced by Sleeping Beauty, non-viral system and the potential for TCR neoantigen work all to enroll or to initiate in 2018. To me that's a powerful story.

So one way to think about ZIOPHARM then is we're running our own race, we are not a fast follower, we're dreaming big, we're thinking big and when we can say now that we have the ability to control IL-12 we're giving neuro-oncology to patients a much needed therapy when others have failed. When we say we can change the foundation for how the business of immuno-oncology is practiced that's a big story.

So let me just give you – touch on briefly actually our clinical updates. If you go to Slide 8, which I've just turned to in the presentation, where are we and we're going to update this at SNO. We have seen sort of three or four effects here. We have safely called IL-12 into the brain, we've taken a cold-tumor and made it hot and I'll show you a picture of that in a second. We're having an anti-tumor effect that is significantly better than historical controls, and we'll update that at SNO this weekend. We've clearly activated the immune system and then we've seen evidence where steroids matter. It makes sense that if you're calling the immune system to attack cancer then giving a drug like a steroid, which diminishes that immune response likely has a negative effect and we've seen that.

In fact, the lowest dose thyroid patients of which there are four are all still alive. In addition, we have a second potential biomarker concept where we're seeing a baseline suppressor to cytotoxic T-cell ratio. The more cytotoxic T-cells you have versus suppressor the better the response will be. And then finally, we actually have biopsy data to prove it, and I'll talk to you about that on the next slide. I should add that in the 20 milligram veledimex patients the therapy was well tolerated and we did not have significant adverse events like cytokine release syndrome.

On Slide 9, I'll just touch on it briefly. This is a picture of a patient whose MRI signal lit up and the question was whether or not this was the cancer or the inflammatory response. And a series of three consecutive patients like this the biopsy was done and actually the signal was caused by T-cells not tumor cells. So what we can say here is that we have a sustained effect of T-cell inflammatory response, which is exactly the mechanism we were seeking. In this case 22 weeks after the last dose of veledimex was taken. The last time that IL-12 was called. This is pretty powerful stuff, this is a mechanism of action which we believe is unprecedented.

And as I said before in Slide 10, we're going to have some significant updates at SNO this weekend. The two to focus on you'll see Dr. Chiocca who's the Head of Neurosurgery at the Brigham and Women's and Dana-Farber Cancer Center will be giving his update of these patients and then we will also have Dr. Stew Goldman, from Lurie, who just dosed our first pediatric patients discussing our progress to date.

And I won't touch on this briefly in Slide 11, but clearly we're at the doorstep of the pivotal trial. And one important note if you're making a cold tumor hot with T-cells it goes without saying that deductive logic says that a checkpoint inhibitor would be an interesting trial. The reason being, if you don't have T-cells to have the checkpoints disinhibited then the effect of a PD1 blocker anti-PD1 would not be sustained. So we believe we have a real mechanism of action opportunity to see if we can turbo-charge the effect of the monotherapy.

So, on the cell therapy side I've already touched on it. But if you look at Slide 13, as you build the slide ZIOPHARM has always had this mission to challenge the viral-based therapies, T-cell therapies. And the challenge needs to be around cost and scale. As I've said before a number of times the idea of taking cells out of the body, putting them in a bag, shipping them to a GMP facility, taking the best cells and cloning them, putting the genetic information in with a virus, refreezing it, sending it back to the hospital, infusing it in the patient has a lower limit in terms of time, cost and complexity. We believe we offer a significant advantage for that and we intend to prove it as we evolve into the next year.

On Slide 14, we have three components, I'll cover this briefly. We have the non-viral gene transfer, which is Sleeping Beauty. We've demonstrated in humans it's clinically validated, it's the only non-viral system that has been clinically validated. We expect to have the third-generation product in the clinic in 2018 that will have the IL-15 engrafted to the T-cells. And finally as I've told you, we will have it under the control of a switch to control the response. This scalable process will reduce cost by removing the need to grow the T-cells outside the body that's a key point, removing the need to grow the T-cells outside of the body.

Slide 15 is really nothing but more than a graphic of what I just mentioned. The key point being, we believe that with electroporation and a fairly simplified technology that could be applied in a variety of hospitals blood banks et cetera, to a expanded patient-base we can do this in less than two days.

So on Slide 16, the progressing to point-of-care, I've already mentioned, we've already done our first-generation patients, we've demonstrated safety, feasibility and efficacy of Sleeping Beauty. We've proven that we can use this system to genetically modify T-cells. We've gone to the second-generation cohort where we've shorten the manufacturing time of the same Sleeping Beauty modified CAR T-cells and we are now at the doorstep in 2018 of a rapid under today's manufacturing of our CAR T-cells. And again we are the first-in-class.

I won't belabor the point but ASH is in December and we have Dr. Kebriaei, I always miss pounce the name, Partow let's call that, is presenting the data on our first and second-generation updates and Dr. Tim Chan will update – will do a paper on the third-generation CD19 studies.

So finally, touching on the big one is TCR. So this is early, but Dr. Rosenberg called us and he called us because he believes or we believe together that the solution to solid tumors is personalized. It has to be personalized and we need to fight the cancers own specific antigens. We have the credo in place, we have the pre-clinical data the animal data to prove it. We have clinical protocols in place and we are going through as I mentioned a series of steps to do the final validation that will allow us to file the IND and go into the clinic in 2018.

At the end of the day, if you think about ZIOPHARM, I want you to think about it as a game changer. And remember, we are decoupled from the market I think in large part because we're misunderstood or poorly understood. And our jobs are to make that more clear, we are at a inflection point where in the next year checking the box of starting a Phase 3 trial for GBM, checking the box for delivering cells with a non-viral construct that were created in under two days and checking the box for using that same non-viral platform to deliver cells in the goal of treating solid tumors those are monumental milestones.

And I would submit to you that we are asymmetrically undervalued relative to where we stand in that progress. At the end of the day, our scientific foundation is not only intact but significantly strong. We will build our story, we will optimize our time and resources towards the key value driving assets, we will shift, I believe the entire paradigm of immunotherapy for cancer and for that we believe we have a company that you should own for the long term. Thank you.