

Inhaled Insulin Products for Diabetes Treatment



Dr. John Patton PhD.
CEO & Chairman

CEOCFO: *Dr. Patton, your site indicates Dance BioPharm, is transforming the treatment of diabetes. How so?*

Dr. Patton: The gold standard for the treatment of diabetes for years is insulin. Insulin has always been invasively delivered, either by injections and now there are a variety of pump technologies being used. The main type of diabetes in the world is Type 2. It is very different from Type 1 where you lose your insulin making ability in weeks or a few months and you either inject insulin or die. However, with Type 2 it is much more insidious. For years people often do not know that they have Type 2. They are tired and just think they are getting old, but what is really happening is that their blood sugar is too high and they are gradually killing the beta cells in the pancreas that make their insulin. They are recommended to go on a diet and exercise and a series of oral medications. Traditionally, it had been that insulin was recommended as a last resort in Type 2 patients. A doctor would tell patients, "If you do not exercise and eat better you are going to have to go on insulin." Usually, the gradual loss of insulin production could take anywhere from five to ten to fifteen years for people to get to the very bad situation where they became completely dependent on insulin, just like Type 1's. However, now the American Diabetes Association and the other learned diabetes societies in the world realize that in Type 2 diabetes that insulin should be introduced much earlier and that if you present with signs of diabetes complications upon diagnosis insulin should be considered right away. Therefore, there has been a sea change in the appreciation of how valuable insulin is in Type 2 and it has been moved from a therapy of last resort to one to be considered much earlier in the disease process. But people don't like injections. Inhaled insulin is preferred by most patients and we believe this is how the treatment of diabetes will be transformed.

CEOCFO: *Is that because the various medications do not work for Type 2?*

Dr. Patton: Historically, the oral medications did not work over the long term. They were used sequentially or in combination in what turned out to be a treat to failure mode in most cases. However, there are some new medications and combinations out there and we will have to see how they do. Regardless, people now believe that insulin should be taken earlier. Therefore, what is the problem? The problem is that people avoid injections and they refuse or postpone them, especially in a subtle disease like diabetes that kills slowly. Everybody gets that. When we were developing inhaled insulin (Exubera®, the first approved inhaled insulin) with Pfizer we were told that Type 1s were used to the needle and they did not mind it after a while and that is just not true! They inject in certain patches and those patches become sore and bruised over time and they get tired and weary and some people get depressed with having to inject all the time. It is not pleasant. Even though the needles have gotten really small, if you miss a nerve you can have an injection that you do not feel, people still get very tired of them and many refuse and delay taking insulin. If you read the responses of people who have been on inhaled insulin - many loved it! "It's my cure!" "It is like taking a pill without a glass of water". Our feeling is that in the future, many diabetes patients will switch from injected to inhaled insulin.

CEOCFO: *It seems as though it would be a no-brainer that people would rather inhale insulin than inject it. Is there any reluctance?*

Dr. Patton: I know. Dr. Marcia Testa at Harvard has been doing patient preference studies for thirty years. She said that in thirty years of working with big pharma on what patients prefer and comparing and contrasting different dosage forms, she had never seen such a strong signal between one route of delivery versus the other; inhaled versus injected (when she was studying Exubera). Therefore, you are right. It is a complete no brainer, so how come it is not out there? As Dr. Neville Jackson, Pfizer's head of clinical development of Exubera said, "When something is really really fantastic and a game changer, it takes time to break through established practices". When you are talking about inhaling a new medicine, it takes time to establish safety and for people to feel comfortable about it. Today inhaled insulin is now available once

again. The Mannkind product, Afrezza® is FDA approved and is in Walgreens since February 2nd. We are very excited about their product and think they are going to do very well.

CEOFO: *What is the Dance BioPharm version?*

Dr. Patton: The Dance BioPharm version is a liquid and we still have a few years to go before we complete the development and FDA approval process. It has a different absorption profile from the Mannkind product. The Mannkind product is a powder, but we think they are complimentary. The Mannkind product is super fast acting. Many people are really going to appreciate that, because the one side affect of insulin is hypoglycemia. It can be a serious side affect, where your blood sugar gets too low because you have too much insulin. Therefore, the Mannkind product is quick in and quick out. For some patients they can really cut down the risk of hypoglycemia. Our product is a soft mist. It is made by a little electronic device. It has pretty fast action; not quite as fast as Afrezza®, but it lasts longer. If you look at normal people when they process a typical meal, it usually takes them three to four hours or longer to digest a typical meal. Our profile mimics that natural insulin secretion profile in response to a meal. Therefore, it is a different profile from Mannkind's profile, but we think both of them are going to be embraced by diabetes patients.

CEOFO: *Where are you in the process?*

Dr. Patton: We are putting together our commercial system. We do not want to enter our final trials, our pivotal Phase III trials with prototypes. Therefore, we are putting the finishing touches on our device and drug product. We have a lot of testing, verification and validation of that to do. We have also put together our supply chain. We have several suppliers of our insulin. Then we have our dropper which we use to load the device. We are completing stability studies on that. We are in the final stages of working out with the EMA and the FDA exactly what they will want for registration of the drug. Therefore, we are in discussions, both in Europe and the US.

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CEOFO: *What have you learned from your prior experience that is helping smooth the process?*

Dr. Patton: We worked with Pfizer for twelve years on Exubera. Before that we worked four years on our own and then we partnered with them. We partnered early in the development process, so we were the technology supplier and they were running the show. They did a great job until the end. One of the problems in big pharma, at least in this particular experience with Pfizer, was that the personnel kept changing; not so much in the deep science, but more in the marketing and senior management and clinical. The faces kept changing. Then ultimately the CEO and the senior management changed right when the product was approved. The guy who came in was not about science or medicine. He had a lawyer and accountant background, so they did not really know that much about insulin. Insulin is a serious drug and it takes a couple of years for a new insulin form to take off. Then they usually become multibillion dollar products. Those guys pulled the plug on the product that we had been giving our lives to for almost two decades. They just decided that it was not selling fast enough they never really gave the drug a chance (it was pulled after only about 9 months on the market). One of the things you learn is that when you are building a biotechnology company investors want you to partner with big pharma because they have lots of money and supposedly know what they are doing. Often they do not know what they are doing. It is better for you to hang on to your product and carry it as far as you can, even though investors are driving you to partner or sell out. It is not necessarily the best thing for the product. In this case, here was something that we knew that the patients really wanted and with Pfizer's mighty help, we had gotten it approved in Europe and the US as effective and safe and then here comes a naive executive team that would rather take a tax write off on the program, had no faith in it and killed a product that would have benefited millions. Therefore, the big lesson there is, "Do not get yourself in that situation again, John!"

CEOFO: *Do you find reluctance from people with Type 2 because they may not want to acknowledge the disease and the need to go to that next step for insulin?*

Dr. Patton: I think there is an element of truth in that, especially if you are going from a pill to an injection. I have heard this comment before, "Oh gosh, that is the next step and I am not really that sick." There is going to be that reluctance, I am sure. However, I think that reluctance is going to be much less if you have a silent, convenient inhaler that gives you your insulin and is not an injection. There are four published small studies that do not have many patients, but these studies are tantalizing. What they show in a number of patients is that if you take insulin just for two or three weeks intensively and stop, you give your pancreatic beta cells (the ones that make your insulin) a rest and they come back and

then they produce the insulin the patient needs for up to 2 years. These studies suggest that you can actually reverse Type 2 diabetes with insulin if you get subjects early. Therefore, it is not like a sentence of injections for the rest of your life because it has to be that way. Ultimately, we are going to make Type 2 diabetes go away in the world. However, unfortunately there are tens of millions of patients on the planet right now for whom it is too late. Their bodies can no longer recover and make enough insulin on their own.

CEOFCO: *There are many companies with a vested interest in injectable insulin. Is that a concern and if so, how do you advance your product?*

Dr. Patton: That is really going to be true. Vested interests are always like that. Look at the power companies with solar and the oil companies with electric cars. They are going to dig in their heels and they are going to fight like crazy to keep their franchises. I do not know what is going to happen, but that is one of the criticisms of big pharma; that they are not very interested in curing or preventing disease. They just want to keep their cash cows going. However, we do not really feel that way at all. We want to provide options for patients and ultimately we would like to help to contribute to make Type 2 diabetes go away completely.

CEOFCO: *Why is Dance BioPharm exceptional?*

Dr. Patton: It is vogue now to go after orphan diseases, which is wonderful for people who have these rare diseases and you can charge two or three hundred thousand dollars a year for treatment and insurance will cover you. There is a tremendous amount of investor enthusiasm for these indications because the cost to develop is small. However, we are going after probably one of the biggest diseases on the planet and we know we have a great idea. Inhaled insulin products have already been approved twice by the FDA. We think we have the power to make a global impact in every country in the world; a massive global impact on a disease that some people think is responsible for one third of all health care costs. If you look at the complications of diabetes, they are just enormous! Just one of the many devastating side effect of diabetes, kidney failure, costs \$38B in the US in dialysis costs. I think we are exceptional because we are addressing a monster problem, a global problem. We are exceptional because we have been doing it for thirty years and we know what we are doing. We have a great team. We think we have the best. There are many reasons for naming the company Dance, but we think the best reason is that diabetes patients are going to dance when they get our product!

Interview conducted by: Lynn Fosse, Senior Editor, CEOFCO Magazine



Dance BioPharm Inc.

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