

Transcript Details

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Moving Toward Synthetic Alternatives to Heparin

With questions being raised about the manufacturing of the blood thinner heparin in China and whether one day there could even be a shortage of this popular blood thinner, some are wondering whether there is a need for new heparin alternatives. Welcome to the clinician's roundtable on ReachMD XM 157, the channel for medical professionals. I am Bruce Japsen, the healthcare reporter with the Chicago Tribune, and with me today is Dr. Ted Love. Dr. Love is the Chief Executive Officer of the San Francisco Biotech Company Nuvelo. He was appointed to this position in 2001 after previously holding several senior management positions in medical affairs and product development at the well-known biotech company Genentech where he oversaw many drugs and development including the breast cancer treatment Herceptin. Dr. Love earned his bachelor's degree in molecular biology from Haverford College and his medical degree at Yale Medical School. He completed his residency and fellowship training in internal medicine and cardiology at Massachusetts General Hospital and Harvard Medical School and he joins us today from his company's office in beautiful San Francisco, California.

BRUCE JAPSEN:

Dr. Ted Love, welcome to ReachMD.

DR. TED LOVE:

Thank you very much. It is a pleasure to be here.

BRUCE JAPSEN:

Well, I am either fortunate or unfortunate to have written this last year so much about the whole heparin situation because Baxter is based here in the Chicago suburbs and this has been a huge problem. One of the things is now we only have (01:30) 1 version of this generic blood thinner heparin and some people do wonder I get e-mails from people all the time; they wonder, my goodness what if something were to happen to the other heparin, we do not know that there will be, but there really aren't a lot of alternatives and you are going to tell us about what your company is doing and what we could do to possibly remedy this situation down the road?

DR. TED LOVE:

Well, the reason heparin contamination issue is obviously an issue that has brought a lot of attention to heparin, but in reality, heparin is

a drug that has been around for many, many, many years, many decades, that has a number of limitations well beyond the contamination issue. Our company actually started to work on replacement for heparin long before the contamination issue because we recognize it is important to have a drug that does not create a lot of the problems that are associated with heparin such as the allergic reactions, the heparin-induced thrombocytopenia, the classic thrombocytopenia the people get after prolonged exposure to heparin, the bleeding that is associated with heparin, the long half-life which necessitates using a reversal agent called protamine, so we have actually been working on a drug that is a synthetic product so none of the contamination concerns are there. It is a very specific product that directly binds the thrombin in our body and inhibits thrombin and creates an anticoagulant affect. The beauty of the drug also is that (03:00) it is very rapidly self-inactivated. So, when you turn off the infusion, the blood goes back to normal almost immediately without the requirement of a reversal agent.

BRUCE JAPSEN:

The interesting thing about this is that because the product is synthetic, you are not using livestock intestines where the risk of contamination is high, and could you talk a little bit about that, I mean lot of our listeners are physicians and they do understand some of the science, but when this whole heparin thing emerged with contamination issues, you know you had people saying "you gotta be kidding me." This is made with pig intestines and then they remember that back in the day, it was derived from cattle intestines, which also had problems. So, this is really not a new thing and we are seeing these issues and if you could talk a little bit about that.

DR. TED LOVE:

Well, it certainly is not a new issue. The DFE scare, particularly in Europe, let us in biotech to think about trying to make all of our products, in fact, without introducing any kind of animal derived element into the product heparin. It is actually a product where it is essentially made by starting with pig intestine as you know and they have written about. So, it is actually antithetical to the principles and the approaches that we have been using in biotech to try to make sure that products are made from fully synthetic materials without the introduction of livestock-based elements, which run the risk of bringing in contaminant. So, it is somewhat amazing (04:30) that heparin has been the dominant agent that has been and I think over time, we will find that heparin will be replaced by fully synthetic products.

BRUCE JAPSEN:

And if I could put you on the spot a little bit, how far away are we from perhaps synthetic heparin, if you could talk a little bit about that and also what you have seen in your trial and where we could be headed with that?

DR. TED LOVE:

One of the things about heparin from a drug development perspective is that it is a drug, which actually does not cure a problem typically. It is typically given to create what we call a pharmacodynamic state. Essentially, it makes the blood resistant to clotting. So, we have a variety of tests that we can measure the effect of our agent and also heparin in terms of how effective it is at preventing blood from clotting. One we use is the so-called activated clotting time or ACT, so we have actually completed already two phase-I trials where we have shown that our molecule, which is a DNA product that binds the thrombin creates the anticoagulant affect very potent. It is also very predictable unlike heparin you give a specific amount of our drug, you are able to get a very predictable affect in the anticoagulant measurements based on these tests. So, we have actually now begun to design our phase-II trials and look forward to getting through those trials fairly quickly. In those trials, we are actually going (06:00) to focus on getting patient through coronary artery bypass surgery, which is a surgical procedure where a machine essentially replaces the heart and the lungs, and while the blood is in that mechanical device, it would normally clot without any anticoagulant on board. Heparin is the predominant agent that you use today and we expect in the future that a drug like NU172 would become the dominant agent because it would not introduce the risk and the

side effects associated with heparin and protamine in the case of bypass surgery.

BRUCE JAPSEN:

Well if you are just joining us or even if you are new to our channel you are listening to the clinician's roundtable on ReachMD XM 157, the channel for medical professionals. I am Bruce Japsen, the healthcare reporter with the Chicago Tribune and with me today is Dr. Ted Love. He is the CEO of Nuvelo which is a biotech company in San Francisco and it is developing a synthetic alternative to Heparin. There are a lot of physicians out there who probably ran into issue of their hospitals with heparin shortages and with heparin facing some challenges in manufacturing over in China and Dr. Love was just telling us about how close we are perhaps to a synthetic.

Dr. Love, I think one of the things about the heparin that why it hasn't been a synthetic for a long time is the fact that it is cheaply made using livestock and if you can tell us a little bit about that whole pricing (07:30) issue if you will because synthetic heparin would be more expansive, but people would probably pay for it if there was a situation that arose such as the situation we had with Baxter's Heparin in China.

DR. TED LOVE:

I think that is absolutely right. In fact, in medicine, the cheapest thing to do is to get an excellent outcome for the patient very efficiently. While the acquisition cost of a drug like heparin are very modest, in fact, when you spend time in resources managing complications and side effects, even death rarely, you know that is a very big price to pay, so I think synthetic products that don't introduce these issues of contamination and side effects will ultimately be not only the best agents for patient, but also the cheapest agent to long term.

BRUCE JAPSEN:

And, we have already seen this. I know that you are an industrial executive, but you also are a former practicing cardiologist, but we have already actually seen this effort with other products where they are trying to free the drugs of animal proteins and so this would seem to make sense.

DR. TED LOVE:

It makes perfect sense. In fact, when I was at Genentech, we spent a lot of time in our manufacturing facilities trying to remove even any trace element of animal-derived products. So, heparin is almost the extreme of that where it is a product that literally is made by starting with (09:00) purification from pig intestine.

BRUCE JAPSEN:

And, how many companies are out there. I do not want you to throw out the names of your competitors unless you want to, but is this a large universe where companies are developing different products, different blood products that could be a response to synthetic heparin or anything else or is this is something that is lagging or what is the state of the industry?

DR. TED LOVE:

Well, there are at least a couple of companies that I know of that are focused on one aspect or another of replacing heparin. There is actually a very successful product called Angiomax, which is widely used today in the cath lab for percutaneous coronary procedures, which has replaced heparin in many, many settings. It is more expensive and so some people feel want to try to get by with the cheaper acquisition cost, but as I said earlier, managing the side effects of heparin can be quite expensive. So, paying a higher price initially for a superior product ultimately is the cheapest investment for society and certainly for the patient. We focused on developing a novel product, which is a DNA-based product that specifically binds to thrombin and creates a very predictable anticoagulant effect. In addition, this molecule is rapidly self-reversed and that means that there is no requirement to reverse it. Heparin is a fairly long-lived molecule, so at the end of the procedure where there is a bleeding risk that you need to correct, we introduced (10:30) protamine, which is another by the way animal-derived product, which has significant side effect. So, we actually are focused on replacing not one but 2 animal-derived products and the associated side effects of those products.

BRUCE JAPSEN:

And, how close do you think we are, I mean I don't think anybody is really looking forward to heparin shortage in this country, so you have given us a little good news in knowing that there is actually a synthetic heparin out there. How close would we be to, you know, something that could replace the existing product?

DR. TED LOVE:

Oh, one of the wonderful things about small companies is that we move fairly quickly. We just started a phase-I program this year. We actually completed already two phase-I trials and we followed essentially beautiful results with our DNA-based product. It has very predictable, very potent anticoagulant effects that we measure by a series of test that is literally measuring how long it takes the blood to clot when the product is introduced. We have now completed, as I said, two phase-I trials, and later this year or early next year, we expect to start additional trials, phase-II trials where we will literally be taking patients through coronary artery bypass surgery, which critical that the blood be anticoagulated and at the end of the procedure, it is critical that you are able to reverse that. In the case of heparin, you get protamine. In the case of <____>, you simply turn it off.

BRUCE JAPSEN:

Well, with that, I would like to thank Dr. Ted Love who has been our guest. He is the president and CEO of Nuvelo. He has joined us from their offices in San Francisco and we have been talking about very excited product they are developing, just one of many products that they are developing, a synthetic alternative to heparin.

If you are wanting to know what that is so important, all you had to do was visit your hospital and find out that there were issues this year with one of the major suppliers of the blood thinner heparin having some manufacturing issues in China and that product is still not on the market today. My name is Bruce Japsen. I have been your host. We would like to once again thank Dr. Ted Love, who has been our guest today on ReachMD XM 157, the channel for medical professionals.

If you have comments or suggestions about today's show, please call us at 888-MDXM-157, and I would like to thank you today for listening.

Hello, my name is Dr. William Franklin Peacock. You are listening to the first radio station created for medical professionals, ReachMD XM 157.