

New Biomaterials Platform providing opportunities for Targeted Drug Delivery and offering hope in a Non-Opiate Morphine Strength Pain Treatment



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“Opiate and Opioid Addiction have been a plague on society and on the healthcare system for decades. At PixarBio I led the invention of a morphine replacement that is a non-opiate and non-addictive post-surgical pain treatment. Because carbamazepine is FDA approved for pain in pill form, and PLGA has been FDA approved since the 1960’s we have a speedy 505(b) 2 pathway through the FDA with expected FDA approval in 2018.” - Frank Reynolds

CEOCFO: *Mr. Reynolds, PixarBio Corporation™, has developed NeuroRelease a morphine replacement, non-opiate, non-addictive pain treatment. What is the science behind what you have developed?*

Mr. Reynolds: It is based on a speedy FDA pathway called the 505b2, where we pick FDA approved components that are either delivery systems or drugs, cells, or they could be biologics and we use them in a new way. They are already FDA approved and we use them in a new way. Therefore, we use PLGA microparticles for the drug delivery system. PLGA has been FDA since the late 1960’s so there are decades of safety data on PLGA. For an FDA approved drug we use carbamazepine in pill form, which is an antiepileptic drug that is also FDA approved for pain associated with trigeminal neuralgia (TN), which is a severe facial pain that typically results from a stroke. We use carbamazepine in a new way, by locally injecting it and eliminating or reducing side effects by using a therapeutic dosages that are extremely low. However, with a local Depo injection delivery we can deliver the drug up to six months. Our first NeuroRelease product will treat post-surgical pain for fourteen days and is expected to receive FDA approval in 2018, and we have a seven day post-surgical pain treatment that’s expected to receive FDA approval in 2019.

CEOCFO: *How is the drug delivered?*

Mr. Reynolds: It is delivered through local depo injection. We can also sprinkle it on to wounds and incisions. Therefore, it is quite revolutionary. We do have a member of the Pentagons pain management research team on our advisory board, Dr Steve Cohen. He is also head of pain management at Walter Reed. We have been developing some technologies for soldiers in the battle field in having a sprinkle on pain powder that is morphine replacement and non-addictive. It gives the soldier a lot better advantage over morphine injection where they immediately become immobilized and have to be carried off by other soldiers. NeuroRelease does not affect locomotion so soldiers stay mobile and they are able to provide pain treatment to any injury, so it is very exciting! It can be injected, for surgeries in the hospital. There are over 90million surgeries in the United States every year and over one billion surgeries worldwide. It can be sprinkled on in a powder and take effect quickly, just like other drugs like Vancomycin. Surgeons during surgery will sprinkle Vancomycin into an incision to reduce infection; we would sprinkle on our NeuroRelease for pain treatment.

CEOCFO: *How did you know what to try?*

Mr. Reynolds: Basically, I spent twenty years in college. It is very important, if you are in the sciences, to get a formal education. My favorite science school, you could say, is Chestnut Hill College. I am on the Board of Directors at Chestnut Hill College. It is where I received my key graduate neuroscience degree. Then I followed that with drug discovery and drug delivery degrees, R&D Management from the Wharton School, Entrepreneurship and Innovation at MIT Sloan, with some Healthcare Venture Capital and Science Commercialization from Harvard Business School. Therefore, you could say that I combined all of the right formal education to become an expert in my field and I have had a lot of success doing it. I know many people say that failure is a big part of science. I say it does not have to be.

CEOFO: *Where are you today?*

Mr. Reynolds: We are actually in a very exciting position! We just opened our Fort Lee, New Jersey office, expanding us down to the New York, New Jersey market to recruit some of the commercialization talent that we are bringing on board. We are a little over two years from market now. We are starting human studies. For a 14-day pain product, our human studies are only thirty days long, so they do not take long. From patient enrollment to FDA submission is only ninety days. Therefore, we will be completing those studies and awaiting FDA approval by the end of 2018. However again, the materials and the drug are already FDA approved and we have fifty years of safety data on both of them. Therefore, because of that the 505b2 pathway through the FDA gives is a very speedy process, by combining Phases I and II into one study. That is because, again, we know that these are non-toxic. The Phase I studies are focused on safety. Since we know that the FDA has monitored these materials for now fifty years each that they are non-toxic and essentially we will be able to Phases I and II saving millions of dollars. Again, the study is only thirty days long. Then we simply follow on with a thirty day Phase III study and we're finished. Again, all the studies should be done in 2018, and we expect FDA approval in 2018. That is where we are we are preparing for the clinical studies and we just added seven-day pain product to our clinical study plans in 2018. We are very, very proud of this! Some large Pharma's have maybe three of what are called the Knee Society members as advisors. We just signed seven of the top twenty Knee Society members as clinical advisors to our studies. The entire anesthesia industry and you can say the entire surgical industry; the trauma experts are more than excited about having something that is morphine strength, non-addictive, where the FDA has just declared all opiates black label. Of course the CDC put out a guidelines statement saying that people in chronic pain over seven days should not take opiates. Many people say that is why opiates exist; for people in pain over seven days. What we have at the FDA today are basically four companies with competitive products of the future where the other three are all based on bupivacaine, which is a neurotoxic drug when in the body over four or five days. Therefore, bupivacaine is a drug that will never become a chronic treatment and today has a lot of problems removing opiates from the clinic and from being adopted by surgeons. Therefore, we decided to bring a non-toxic pain treatment to market.

CEOFO: *What are the target applications? Is it particular types of pain or particular locations? What is the FDA's range of approval?*

Mr. Reynolds: We are very excited about our meetings with the FDA, because we only have two studies to receive approval to treat pain around the entire body. If you can think about the nervous system it comprises of a lot of cables that run to the brain or from the brain. All signals away from the brain are locomotion or movement signals and all signals coming back are sensory signals or pain signals. Therefore, pain signals are the ones that come back towards the brain. What we will do is we will inject along that cable, between the injury and the brain at key points of the nervous system and we will stop the pain signal from coming back to the brain for as long as our drug is there. We have no effect on locomotion, so you can walk and body parts function. Therefore, in theory people will wake up from hip replacement surgery and they can walk off the operating room table, pain free and have no pain and no locomotion effect. That is what we see in our preclinical data. That is exactly what the drug is designed and FDA approved to do already in pill form, to treat pain. Unfortunately in pill form humans develop a resistance and have cognitive side effects at doses as high as 1200 mg/day. With a local injection of just 50 mg, then released over 14 days, you average 3 mg/day so side effects are significantly reduced. Therefore, in pill form patients only see therapeutic affect for six months to a year, where of course we will not have side effects or a resistance problem. Therefore, we are excited for local delivery. With long term release we can go up to six months. Again, I mentioned that our first product is fourteen days followed by seven and three days, but we have our ninety day pain product under R&D. I mentioned that there are other competitors and that are all bupivacaine based drug delivery systems. They all chose bupivacaine. That is a drug on its own that lasts only about eight hours. When it goes into the body it does not last long at all. We know that with our competitor Exparel®; seventy two percent of Exparel patients are taking opiates within twenty five hours of surgery. That is according to Pacira's Pharmaceuticals own published research on Exparel. Imagine it is the only non-opiate approved right now by the FDA for post op pain for the seventy million surgeries a year and it lasts no more than a day for seventy two percent of patients before they need addictive drugs. The average time to opiate rescue for Pacira's Exparel is fifteen hours after surgery. You can barely call that a treatment and yet it is FDA approved for three days. That is a problem! When your drug is approved for three days and it lasts one you have got a big problem. If it lasted three and a half days maybe people would not be so upset! Our drug will last right up to the timeline and within hours degrade, so our fourteen day will probably last fourteen days and a few hours. Our seven day treatment will be timed to treat pain for 7 days and a few hours. With NeuroRelease we can have controllable, predictable results. And that is because we chose the PLGA micro particle delivery system. It is a delivery system that has been developed for cancer to fight tumors and to treat schizophrenia. It has been an amazing delivery system developed primarily by my business partner, Dr. Robert S. Langer. Bob Langer is at MIT, he is the number one medical researcher in history. I have been inventing with Bob now for over a decade and it has been an outstanding relationship. Bob has used PLGA microparticles around the body in other areas with great success. I have been in chronic pain; since I was paralyzed in December of 1992. I had spent seven years in a body brace from my

knee to my neck, pretty much most of the time staring at the ceiling. Therefore, I developed treatments for spinal cord injury and for pain. I am in chronic pain. I suffer from Arachnoiditis, which I would not wish on anybody, as they say. Therefore, I have been trying to develop an Arachnoiditis treatment and I have succeeded. I am very excited! It is only two years to market now or less. In addition, we will be applying to the FDA for expedited review later this year. However, without expedited review we will still be approved in 2018. Therefore, we are excited. No one else at the FDA has a material that can be re-injected. All of the bupivacaine drugs that are out there cannot be re-injected, because the delivery systems are not biodegradable. NeuroRelease is biodegradable so we can reinject to extend treatment timelines.

CEOCFO: Do doctors know where to do the injection? Is there any question on where or how or is that just a no brainer?

Mr. Reynolds: What is beautiful is the injection can be anywhere along the nerve, anywhere along the cable. Therefore, for anything in the right leg we would inject the femoral nerve near the hip. That allows you to do a foot surgery or knee surgery or if someone came into the emergency room with compound fractures of the thighs that you see with motorcycle accidents, you would do a quick femoral nerve block and treat that pain in a non-addictive way. Many times in the emergency room you do not know who your patient is, because the patient comes to you in a desperate state. You are giving them morphine and they might be drug addicts that do not want it or just a person that avoids addictive products. Addicts might want opiates, but we do not; society does not. Therefore, NeuroRelease buys time for care givers to have time to see if the patients are prone to addiction. We give them a pain treatment and they are not screaming anymore and it is non-addictive. It takes effect pretty quickly. The doctors know exactly how to use it. They have used the technique as nerve blocks. I guess you could say the standard injection would be called the nerve block. Therefore, anyone that has done nerve blocks and finally some of the anesthesiologists that I speak with perform over one million nerve blocks in their careers. I know I have had almost one hundred injections in my spine for pain treatments over the last twenty three years. People do these injections all day long. There is no new technology. We use a standard syringe. We ship as a powder. We actually also ship in 20cc vials and reconstitute with Saline. Our competitors ship cold in what they call cold shipment, which costs more than it does to make my product. However, we ship in a 20cc vial powder and you just reconstitute it with saline. We interviewed about one hundred surgeons and asked them what they want in a pain product about three years ago and we built it for them. They said they did not want addiction, they did not want it frozen and they wanted something that could be shipped as a powder and re-injected to extend pain treatment. All of the competitors, especially Exparel release this from the minute it is manufactured. While it is sitting waiting to leave the warehouse it is already being released and it is not going into a patient and on the trains and automobiles and trucks; still releasing in their hospital waiting room. Ours will not release until the minute it hits the body. That is when our releases when NeuroRelease contacts water in the body. Really, it is a targeted, controlled delivery system developed by Dr Criscione over a decade. He is one of our superstars! Of course, you put together the team I have; I hired Bob Langer back in 2006. I started my first pharma company in 2005 and no one was really interested in partnering to cure paralysis at the time, so I did it alone and then brought on Bob Langer and many others and got the job done on paralysis. Now we are getting the job done on pain.

CEOCFO: Would you tell us a little more about the powder?

Mr. Reynolds: Again, the marketplace told us they wanted a powder, not something that had to be shipped cold. They told us they wanted something morphine strength and we could do that. There are different types of manufacturing processes where you could take a drug and have it end as a pill and have a delivery system based on pill form, which is important in some environments. Maybe you might not have the ability to inject, but you could also take that drug and have it come out in powder form. You could have it come out in a pre-loaded injectable syringe. There are all types of different things that you could do with drugs to get them to where you want them to be effective. One of them is, of course, a powder form. Vancomycin is the drug that saved my life, big time. In January-April 1993 I almost died from a staph infection contracted in a hospital. Vancomycin is one of the drugs that everyone does use and sprinkles right into incisions when they do surgeries. They sprinkle it right in. It is an antibiotic. It kills infection. I remember when they put it in me, it was an IV direct into my heart through a Hickman catheter. It went in through the vena cava vein in my heart through a Hickman catheter back then. I do not know that they use today. That was about twenty three years ago. However, Vancomycin is a sprinkle on. It saves people every day now in surgery. They sprinkle it into the incision and close them up and it kills infection. We will sprinkle it on just like that. Again, it is a powder. If you looked at it a vial, I do not know if you were out in the middle of somewhere and you needed a desperate powder pain treatment because you could not inject it, you could get it out of that vial and sprinkle it on, so it would work right out of the vial.

CEOCFO: PixarBio was named to the 2016 Best Places to Work from the Boston Business Journal. Would you tell us about that recognition?

Mr. Reynolds: It goes back to all my academic training, great professors and MIT Sloan, Wharton, St Joseph's University, Temple University, Rider University, Chestnut Hill College; it had great academics and taught me how to build a culture

and that it was important to build a culture where people want to come to work. Some of my peers that I graduated with at MIT Sloan are the founders of HubSpot. HubSpot is a \$1B+ inbound marketing leader, receiving a lot of attention with thousands of employees at HubSpot and HubSpot leadership is talking about their culture. I love it, because we sat in the same courses and learned the same types of, you could say, pathways forward for companies. Those guys at HubSpot are in IT and I am in pharma. You have a different kind of people that you have to lead for yourself and to create an innovative environment for others. First of all, we are all employees and as founder I own company. I own over 60% of a public Pharma. It is 70% my money at risk. Therefore, I make sure that when I invest in my people they are here to stay. There is the old joke about, "If you do not train teams, then they are going to be working for somebody else," and that is very true. With the people that I have recruit; I am very picky. I just rejected someone yesterday and I think they are dumbfounded today. However, you have to get the right culture. You have to get the right fit. That is what it is about. I have a master's degree in counseling psychology. I have treated patients for years. I kind of know that makes people tick, so I know how to put a team together. I know how to put that chemistry together. I have had multiple Nobel Prize nominees in the same room with me. You have to manage egos. I have had some of the biggest jackass egos, you could say, probably in the industry and I have had some of the most pleasant of global award winning scientist egos to work with in pharma. However, you have to work with the good and the bad. A lot of that goes on. My degree in psychology helped me build the team and the innovative culture, it is a lot about the chemistry, but then again, you have to have accountability through structure. We just opened Fort Lee, New Jersey, in August and we had a great turn out at the ribbon cutting. We are actually working on a lot of stuff today around Wall Street, so I have a different objective today than ribbon cuttings, but that is what we do. Our place in Fort Lee looks just like New Hampshire, and Medford, Massachusetts. We have the same furniture, the same vendors and we work with the same people. We have the same sign guy. We keep that culture direct. When people join our company they watch movies on their first day. They watch "Lorenzo's Oil" and the new movie, "Concussion". They watch those because those are movies about, you could say, warriors in medicine who were told that they were wrong, BUT THEY KNEW THEY WERE RIGHT, because they had common sense and logic. Therefore, much of what we do at PixarBio is based on, what I call, the Reynolds School of Business (RHB). By the way, we are working on creating a real Reynolds School of Business at Chestnut Hill College, which is one of the reasons I am on the board there now. However, we have a defined culture based on innovation. Therefore, the first day people watch movies. They come in and they get shirts, hats and they get a popcorn ball. They sit down and they watch two movies and they write me a letter that night about what those movies meant around innovation. I fought those wars. I fought the stem cell industry around spinal cord injury for ten years. I had to sit on panels with the Christopher Reeves Foundation and the Miami Project and be told, even though I am the only one to get every rat, every monkey and now 7 of 8 humans, so I proved them all wrong. Therefore, it is a very important culture. It is a culture that uses common sense and logic around science to weed out the scientific fudging in data. It is funny, as a CEO with pharma, when I ask scientists "What percentage of literature do you think is fudged or fake or not legit or Replicable," some people will say, "It is well over fifty percent fudged." Therefore, you sit back and you think, "Everybody you are interviewing thinks a lot of literature is fudged and the FDA is using it to approve products," then maybe part of your job as CEO in this industry is really to make sure you weed out fraud. Sometimes you get it and you have to fire them quickly. Anyway, so that is the culture. People know that we innovate and we do not put up with fraud in science. We do not believe that it is ninety nine failures for one success. We believe that we have a success rate well, well, well over seventy percent once we leave the bench. It is the culture. It is built by design. It is based on many great professors. I remember Dean Arnoldo Hax at MIT, Professor Tom Malone at MIT taught us a lot about innovative cultures. I had Anjali Sastry at MIT also, who taught about the systems and the people on it and what moving the coffee pot does to the whole innovative ecosystem. We are building a culture that is integrative and innovative.

CEOCFO: Are you funded for your next steps? What is your status?

Mr. Reynolds: Yes. We just completed a public offering under stock symbol PXR, and the stock has been well received so we believe we have enough runway through 2017 but we'll be looking for strategic partners to help us get over the finish line for shareholders. I've never done a down-round in my career and the shareholders respect my stewardship. We are popular on Wall Street. There are events like in 2015 one of our competitors Exparel was rejected by the FDA as a nerve block. They are the only non-opiate post-surgical pain treatment that is FDA approved. When Exparel was rejected by the FDA, of course that made our value go up, so we cancelled that 2015 public offering and went public in 2016 at a higher valuation. We'll be able to defeat our competitors in the marketplace so we have a pretty strong situation occurring. We have a lot of great value creating events in the last six months. We're trading on the OTC under stock symbol PXR, with plans to up-list in the Q4 2016 to the NASDAQ. We have all the momentum we think we will ever need to raise the cash we need, and we're looking to outperforming the biotech/pharma space. .