**VO:** The Bioworld Insider podcast.

**Lynn Yoffee:** This is the BioWorld Insider Podcast. I'm Lyn Yoffee, BioWorld's publisher.

Opioid overdoses are the number one killer of Americans under 50. There are 10 million high-risk opioid users in the US with more than 80,000 deaths every year. 70% to 80% of overdose deaths occur when no one else is around. So there's nobody to administer naloxone, which could be a lifesaver. Today, Bioworld staff writer Lee Landenberger is talking with Brad Holden. He's the CEO of Resilient Life Science, which is developing a solution to this very modern problem. The company is working on a wearable, the company is working on a wearable metal, the company is working on a wearable medical device designed to automatically detect and then reverse an opioid overdose. Brad has medical device experience at GE Health Care, Edwards Life Sciences, and Spry Health. Before that, he was a Marine Corps officer. Welcome, Brad.

**Brad Holden:** Thanks for having me on the show.

**Lynn Yoffee:** Over to you, Lee.

**Lee Landenberger:** Thank you, Lynn, and thank you, Brad. This is a fascinating device and I was really curious. I had a lot of questions about it because it's something that could dramatically save lives that don't need to be lost. So could you give me an idea of how exactly this works?

**Brad Holden:** Yeah, absolutely. So I'll start by talking about the physiology of an opioid overdose. What happens when someone receives a potentially deadly amount of opioid is that it depresses their respiratory drive. So essentially that person is gonna dramatically slow and reduce or even stop their breathing. And then running out of oxygen is what leads to death of that patient. So while that is obviously a terrible thing and something that we want to prevent, it's also the way that we can detect whether or not an overdose is occurring. So what we're developing is a, like you said already, a wearable medical device that can detect and reverse an opioid overdose. So in terms of form factor, this is a patch-based device that's worn on the abdomen. similar to how you might see a insulin pump on the market today. There are sensors on the device. First, reflective photoplethysmography sensors or PPG sensors, similar to what you'd have on an Apple watch, as well as accelerometers. And with those sensors, we can tell a lot about the patient. So what is their oxygen saturation? How is their heart rate? What is their breathing rate? And even the... size of each breath or the tidal volume. With that we can tell if that patient is experiencing impairment of their respiratory drive and eventual hypoxia. So we can detect whether or not an overdose is occurring and that's when our device will determine that the automatic dose of naloxone is needed.

**Lee Landenberger:** So you have people who have drug problems who would have this. But I'm curious about how you get, there are some people who would say, yeah, I'll wear that. But how do you get a drug abuser who may not be paying that much attention to, how do you get their attention to try something like this?

**Brad Holden:** Yeah, that's a great question. And I'll talk a little bit about how we've determined the right audience for our technology. As we've mentioned, there's roughly 10 million Americans that are using opioids in a high risk manner in the US. And that opioid use is now leading to 80,000 deaths plus per year. We've done research with over 300 opioid users and their family members in all stages of addiction, from long-term recovery to active use in the depths of addiction on the streets in Kensington, Philadelphia. And through this research, we've found that the folks who are most likely to embrace the adoption of a device like ours are people who fall into one of two categories. First, they're actively using opioids and they know that they are likely to use again in the future. And then either they are receiving treatment for opioid use disorder, potentially medication-assisted treatment like buprenorphine treatment or methadone or just outpatient counselling, or they're living with their family members. So you have people that are using while going through treatment and then people that are using while living with family. So in general, both people that fit into this category have a support system around them that can encourage use of a device. They've shown interest, and by they I mean the individuals that are using the drugs and might use the device, have shown interest in recovery and getting better and have people that they want to get better for in their lives. So that group of people, which we estimate at 1.7 million, folks in the US is really who we're focusing on getting this up to first. In our research that we completed in February of this year, we found that 87% of people that fall into this description would be interested in wearing this device. And we have research staged for later this year to collect data on adoption adherence with an investigational version of our device. So that's how we plan on entering the market, is focusing on those folks. And again, that's 1.7 million out of the 10 million people in the US. And from there, you've probably seen that the government and state programs are putting a lot of effort into Naloxone awareness programs and Naloxone distribution programs. So we'll of course be investing a lot of our own efforts in spreading the news about the life-saving potential of a device like ours. But we also plan on working closely with governments that are working to promote products currently on the market like Narcan, for example, and getting that out to communities. We plan to be part of that arsenal that states and local governments are using to fight the opioid epidemic.

**Lee Landenberger:** Tell me about the creation of the device. I'm curious, how did the idea come about? Was it yours or someone else's? And I guess that also sort of ties in with the creation of the company too.

**Brad Holden:** Yeah, so it's a long story potentially. I'll be as concise as possible, but in my time between serving in the Marine Corps and going to Harvard Business School, I worked at a company called Spry Health and we were developing a wearable medical device for remote patient monitoring, using a lot of the similar technology that are device uses now, so that reflective PPG sensing as well as accelerometery. And I was amazed by how much we can tell about a patient just from these sensors. And now you see it in consumer products like the Apple Watch, for example, just more and more capability in those devices each year. And then in 2021, I was working for a conversational AI company in San Francisco and was working remotely actually living in Pittsburgh, Pennsylvania at that time. And the news came out that the overdose death rate crossed 100,000 per year, 75,000 of which were from opioids and now that number is over 80,000. And I thought to myself, hey, wait a minute, the technology that I was working on years ago... could be used to detect an opioid overdose. And we're all familiar with auto-injector products and on-body drug delivery systems, like your insulin pumps or even like an EpiPen auto-injector. So why can't we take these two proven technologies and combine them into something that can both detect an overdose and then automatically administer this lifesaving naloxone? So at first it was a thought of, Why isn't anybody else doing this? And as I looked more and more into it, that evolved into a, wow, we really need to do this. And that was the inspiration for launching the company, which we launched in April of 2022.

**Lee Landenberger:** suppose that question, why isn't somebody else doing this, must have been, it was it tough to answer? I would, because I would think you would think, well there's, this is a great idea, somebody must be doing something like this.

**Brad Holden:** Yeah, and we did our research in the beginning and found that there's certainly been research in the university setting on devices like this. So University of Washington published a paper on this in Nature about the development that they did on a prototype of a similar technology to what we're building here. And there's been other attempts on similar technology along the way. ends up being challenging with this and things that we're now really focused on getting right in our development or finding the right target market to get this to. I talked about the folks that we believe are going to be the right adopters. There's a lot of different ways that you could focus on the 10 million Americans and getting that sector right is important. And then also navigating the FDA process. This is a closed loop, life-saving medical device. And making sure that we can demonstrate what the FDA is going to need to see in order to get approval as we bring this to market is going to be critical too. So it's certainly a large undertaking, but absolutely one that is worthy of pursuing.

**Lee Landenberger:** So where do you stand now in your development?

**Brad Holden:** Yeah, so right now we are focused on developing the sensing technology to the point where we can get that in front of the FDA. So in our early development in 2022, we built a proof of concept device, right? That was able to sense respiratory depression and trigger a subcutaneous injection of saline, which we just used to test. And now as we think about bringing a product to market and through the FDA process, the first thing we want to do is say, hey, we have a device that can detect an opioid overdose. And there's actually recently been a FDA de novo clearance for a Massimo product called the Opioid Halo that is approved for detection of opioid overdose or opioid impairment of oxygenation. So, we can use that as a predicate device to say, hey, now our patch-based wearable device is a similar technology that can detect overdose. From there, then we'd look to pair this with the auto-injector technology that we're developing into that single close-loop system. But focusing first on the sensing technology allows us to demonstrate the effectiveness of that before we're then saying that that's being relied upon to accurately deliver the lifesaving dose of naloxone. So our first prototype devices are going to be ready in this July, so coming up quite quickly. And we plan on executing a feasibility study to gather data on our device compared to reference devices and then validate the accuracy of our device against reference devices using healthy subjects. in August into September of this year. So we're at the still early stages of development. We have prototypes that are going to be ready soon and we're planning our first large feasibility study for later this year. We'll take that into the next stages of our development where we will subject our device to the clinical testing that would be needed for FDA approval as a pulse oximeter. Once we can show at the level of proof that the FDA would require for our device to be an effective pulse oximeter, we'll then take this and put it in a scenario with real cases of opioid-induced respiratory depression and show that our device is accurate at detecting opioid-induced respiratory depression, which is that sign of an overdose. Did that answer your question?

**Lee Landenberger:** Yeah, it does. What's a realistic forecast for assuming you get FDA clearance? What's a forecast for hitting the market?

**Brad Holden:** Yeah, so we do plan to launch a version of our device that simply detects an overdose and alerts a loved one or emergency responder first. And our goal for getting that in front of the FDA as an opioid overdose detection system is submitting for FDA clearance in 2025 and having on the market. towards the end of 2025. For the closed loop system that includes the drug delivery, we are targeting 2027 for that.

**Lee Landenberger:** I'm curious about how Resilient got its start. Pittsburgh's an unusual place seemingly for a med tech company. Tell me about your experience there and how the company was born.

**Brad Holden:** Yeah, so I moved to Pittsburgh in 2021 before having the idea for this company. Our son was born that July, and my wife and I knew that Pittsburgh is where we wanted to raise our family. And since launching the company, it's been amazing to see the ecosystem in Pittsburgh for health tech startups. So there's actually 160 life sciences companies in the area, and 90 of them are in the medical device space. And then if you think about Pittsburgh, and the resources here, it's actually pretty incredible. The top tier universities, we have Carnegie Mellon and University of Pittsburgh, and then University of Pittsburgh Medical Center, a leading research institution, as well as Allegheny Health Network. So it was actually top institutions and alongside that incredible talent in the area for everything that you can imagine around the world of medical devices. So we've been really fortunate to be just within that ecosystem. There's also a lot of resources specifically for startups like us, right? So early stage medical device startups, we went through Lifex Labs and the end of 2022. So MedTech focused startup accelerator in Pittsburgh. I'm a Carnegie Mellon alum. So we've actually now been connected with Carnegie Mellon and we're working with their Project Olympus, which is a CMU program aimed at supporting companies in commercializing technology. So. been incredible so far to see the amount that Pittsburgh's investing in this area. And finally, I should point out that there's a, another incredible thing in the city, which is the presence of foundations and specifically for us, the Richard King Mellon Foundation. So the RK Mellon Foundation has an annual social impact venture competition, which we took part in 2022 and actually won first place. And that came with a $500,000 investment in our venture, as well as a ton of support from the organization. So it's been really critical to our development. Um, so overall building a company in Pittsburgh has really been an incredible experience and moving from San Francisco, I like to tell people that Pittsburgh is the best ratio of talent to cost of living you're going to find in the U S because we can do a lot with the. or because we can do a lot with a lot less money in Pittsburgh than you might be able to do in higher cost living areas.

**Lee Landenberger:** I'm curious when you talk to investors, what are the top questions, maybe one or two questions that they ask you when you're describing the device?

**Brad Holden:** Yeah, that's a great question. So there are two really common questions that I think we get. And the first one is what I like to call the moral hazard question. So that is this question of, okay, if we're producing the moral hazard question, what is the moral hazard question? And then the question is, what is the moral hazard question? So there are two questions that we really frequently get from investors as we discuss what we're building here. The first one is what I refer to as the moral hazard question. So that is a question of, okay, if you have this device that can detect and reverse an opioid overdose, are we then creating an incentive for people who are using opioids to use in a riskier fashion because they know that they have the safety net? And our answer to that question is no, and that's really based on two things. First is the psychology of what causes somebody to use opioids, especially for our group that's in recovery. Opioid addiction is an incredibly overwhelming drive or produces this incredibly overwhelming drive to use, whether it's incredible feelings of sickness. of opioid withdrawal. It's been described as the worst flu you've ever had times 100 that just creates this need for someone to use opioids to numb that pain or this craving and feeling of emptiness of not having the opioid in the system. So what we see in as evidenced by the amount of overdose deaths in the US is people are driven to use opioids regardless of whether or not there's safety. in doing so. That's what causes these deaths right now. People are using, they're using in isolation whether or not it's safe for them. So we don't believe that making it safer is going to inspire more use just because that use is already being inspired by such a powerful psychological and physiological drive. Second, and the other point I'd like to make is that if you put a seatbelt on, does that mean that you're more likely to drive recklessly and get in a car accident? And I think the answer is generally going to be no. And obviously, that's slightly facetious in how I say it. But the idea is that it's going to suck to overdose, regardless of whether or not you're wearing a device. It's a terrifying experience. Naloxone can actually knock enough opioid molecules off of the opioid receptors in the body that it forces some level of precipitative withdrawal, which is an unpleasant experience. in general, it's something that people really don't want to experience, whether or not there's naloxone around. So even though, yes, our device can save a life, it's not going to be a situation where they walk away as if nothing happened. It still is going to be something that they certainly want to avoid. So that's the first question is, is our device going to inspire riskier use of overdose and actually increase the number of overdose incidences? And we believe the answer to that is no. The second question is one that you already asked, which is how are we confident that people are going to use this? And we've really just dedicated our time to making sure we really understand the people that we're building this for, in-depth conversations with people who are in recovery, in active opioid use, and all stages in between, understanding what's going to be important to them. For example, part of the reason that we're building this as a device worn on the abdomen is that it's very concealable there and it's discreet. So if somebody's employed while going through opioid, excuse me, so if somebody is employed while going through treatment for opioid use disorder, they don't have their employer showing or seeing something on their arm or wrist and saying, hey, what's that for? Right, this is something that they can have in a discreet fashion. So those are the two largest questions that we. get frequently from investors.

**Lee Landenberger:** You've got your hands full developing this device, but you must, I wonder if you think about other device development and when you look at the landscape for devices that have not exactly this kind of mechanism or indication, but perhaps other kinds of devices that would, I'm not saying this very well. Let me ask this question again. So you've got your hands full. with this device and developing it. What about other devices that you may think of in the future that you may want to develop or that there's a need and you have some ideas that might solve that problem?

**Brad Holden:** Yeah, great question. And we think about this in terms of what can the hardware and software that we're developing right now be scaled horizontally to work with other indications, right? So what we have at the end of the day is a wearable medical device that uses non-invasive sensors to detect an emergency medical condition, and then administer a subcutaneous injection of drug. And there are a couple of indications right on the top of our minds that we believe this could be used for. We haven't done a ton of research into this yet, just because we're really focused on solving the opioid overdose problem first. But a couple that come to mind are epileptic seizures, heart attacks, and potentially hypoglycaemia. We have a team that's going to be spending time diving further into these other indications that this platform technology can be used for this summer. But really, again, just anything where it would be beneficial to have this wearable sensor plus drug delivery together. Before moving into other form factors for products, that's really what we're excited for is what else can we scale this platform?

**Lee Landenberger:** Well, terrific. We want to wish you the best of luck in your development. We look forward to hearing more about this. And thanks very much for your time, Brad. It was a fascinating discussion.

**Brad Holden:** Lee, thanks for the great questions. And thanks Lee and Lynn for having me on. It was a great experience.

**Lee Landenberger:** Our pleasure. Lynn?

**Lynn Yoffee:** Thank you both. This is really exciting and I'm very hopeful because certainly it's a huge problem, the addiction issue in the US and around the world, and we need as many tools as possible in the armamentarium to care for these patients. Thank you everyone. As always, Bioworld will continue to keep you informed of all the most important scientific, clinical, and business updates. That's our show for today. If you need to track the development of drugs, turn to bioworld.com, follow us on Twitter, and you can email us at newsdesk at bioworld.com. If you're enjoying the podcast, don't forget to subscribe. Thanks for joining us.

**VO:** Bioworld, published by Clarivate, is a subscription based news service that delivers actionable intelligence on the most innovative therapeutics and medical technologies in development.