Q1 Update and Up-LIFT Pivotal Trial Results Panel Webcast

Thu, May 23, 2024

[Aditi Roy]
Welcome to today's webcast, hosted by ONWARD® Medical. I'm Aditi Roy, VP of Communications at ONWARD. Today's call will be hosted by Dave Marver, CEO. During the first part of this webcast, Dave will provide a brief presentation detailing ONWARD's first quarter 2024 financial and operating highlights. During the second part of this webcast, Dave will host a presentation and panel discussion that covers results from our Up-LIFT pivotal trial, which were published this week in *Nature Medicine*. A reminder that today's event will contain forward-looking statements which often differ from actual results. Any forward-looking statements communicated today will reflect the company's current views and are subject to risks and uncertainties. I will now hand the call over to Dave Marver, CEO of ONWARD Medical. Dave.

[Dave Marver]
Well, thank you, Aditi, and thanks to all of you for joining, as well as for the panelists for generously giving us your time today to share more of the results from the *Nature Medicine* publication this week. Some of you are new to the company, so I'd like to start with just a brief company overview. So, this is ONWARD at a glance. We were founded in 2015. We have about 100 people now. We're headquartered in the Netherlands, but we have a science and engineering center in Switzerland, also a growing US presence. We did an IPO in late 2021 on Euronext, and we're currently followed by five equity research analysts, as shown. ONWARD has three technology platforms, and they're all purpose-built to stimulate the spinal cord to restore movement and other functions after spinal cord injury. ARC$^{EX®}$ delivers ARC Therapy^{TM} via an external platform, so through the skin. ARC$^{IM®}$ delivers ARC Therapy via a fully implanted system. And we also have ARC$^{BCI™}$, which pairs ARC^{IM} with an implanted brain-computer interface to restore thought-driven movement via a wireless DigitalBridge^{TM}.

We're a very innovative company, we have 10 FDA Breakthrough Device Designation awards, and now 265 issued patents worldwide. And we've also demonstrated clinical success. You're going to hear today about how we've demonstrated the safety and effectiveness of ARC^{EX} Therapy for upper limb function. Again, those results were published in *Nature Medicine* just this Monday. We've also released positive interim results for our ARC^{IM} Therapy, our implanted therapy, to address blood pressure dysregulation, and we expect a major publication on that front in the second half of this year. We're launching into what we believe is a large market opportunity, and we expect first revenue late this year - fourth quarter starting in the US. Our vision is that empowered by movement, people with spinal cord injury will enjoy life in the ways that matter to them. Some want to stand and walk again, others want to use their hands and arms more effectively. Others want to go to the bathroom without frequent catheterization, and fortunately, our therapies have the potential to help in every one of those areas. These are the three technology platforms that we've developed: ARC^{EX}, you see at left, the external platform; ARC^{IM}, which is our fully implanted platform here in the middle; and at right is our ARC^{BCI} platform, which combines ARC^{IM} with an implanted brain-computer interface. Our focus is to launch ARC^{EX} here in the short term, get that into the clinic, into homes where they can help people with spinal

cord injury and their loved ones. Then, start a study for ARC^{IM} this year - or potentially early next year - and get this on the market by late 2026. Then after these two platforms are out there and available, we want to expand into other platforms and even other populations. Going forward this year, we have a lot of additional milestones.

No, sorry, forgive me. This is our Q1 update. So, this is what we've already achieved this year. We expanded our clinical feasibility trial for blood pressure with ARC^{IM} to the Netherlands. We had two additional banks initiate coverage of the company with buy ratings. Two developments with the brain-computer interface system. We were awarded our 10th Breakthrough Device Designation award, and we were admitted into the FDA's new TAP program to streamline commercialization. We raised 20 million euros in additional capital. That's $22 million. We submitted our application to FDA for our ARC^{EX} system. And, of course, we published the results from our ARC^{EX} pivotal study called Up-LIFT.

I'd now like to introduce Amori Fraser. She's our Finance Director. The last couple of updates you've heard from Khaled Bahi, who was our interim CFO. He has since taken another job, so Amori is going to step up and fill the role for the time being. I would expect us to hire a permanent CFO probably sometime in the second half of this year. In the meantime, Amori's going to do a fantastic job filling that void. Amori, do you want to give a financial update, please?

[Amori Fraser]
We are pleased to announce that we have sustained the cash burn rate from the second half of 2023 into the first quarter of 2024. With a cash burn of 6.8 million euros. We completed our first quarter of 2024 with a net cash balance of 42 million, and this includes the proceeds from the successful capital raise we had in March. As a result, we reaffirm our expectation that our existing cash will be adequate to fund the operations through the mid of 2025. Back to you, Dave.

[Dave Marver]
Thank you, Amori. So, this is what we can expect going forward this year. Still many, many milestones. I won't spend time on each of those, just the two that are completed. One is submitting the *de novo* application to FDA. This is why we believe we have the potential to release this important therapy to the market in the US late this year, and then Europe sometime in 2025. And then, of course, the publication of this very important Up-LIFT manuscript in *Nature Medicine*. And that's a really nice transition to our panel.

So, we put together a really esteemed panel to describe these results in more detail for you today. This is the panel. We're joined by three of the principal investigators - Dr. Chet Moritz, who was one of the Co-lead PIs [principal investigators]; Dr. Candace Tefertiller, who is the PI out of Craig Hospital in Denver; and neurosurgeon Jim Guest, who is a PI out of University of Miami. We also are very privileged to have two trial participants here - Jessie Owen and Sherown Campbell - who are going to generously share their experience and how the exposure to the therapy impacted them. And then I have my colleague, Erika Ross Ellison, who's our VP of Clinical, Regulatory, and Quality as well. So, thank you all for joining.

So let me just start off with a system overview here. So, this is the ARC^{EX} System in its entirety. We have the stimulator – I'm using my cursor, but also if you can see my picture, this is what it looks like. So not terribly big, easily it can sit on a tabletop next to the person using it. The neurostimulator here at the ARC^{EX} connects to leads that are placed on the skin near the area of the spinal cord responsible for a given movement or function. In this case, we've used ARC^{EX} Therapy to address upper limb function, which is controlled in the cervical spinal cord. That's why we have the leads here in the neck area. And then clinicians use this tablet programmer here to define the programming or stimulation parameters. And you'll hear more about that from Dr. Moritz later. All right, Erika, take it away.

[Erika Ross Ellison]
Thank you, Dave. So, before we go into details of the study, I want to start with our punch line. The outcome - our primary safety and efficacy endpoints - were all met in this study, as well as our secondary endpoints. The outcome - ARC^{EX} Therapy responder rates - were conservatively defined as meeting both a strength and a functional outcome. We saw 72% of people in the study responded to this conservative effectiveness outcome measure. We also observed no serious device-related adverse events in the study.

Move to the next slide here. This Up-LIFT pivotal study was run by 14 leading clinical sites in US, Canada, and in the European Union. We are fortunate to have three of our study PIs here today from University of Washington, Craig Hospital, and looking forward to Jim Guest speaking next from University of Miami, where he was also a study PI. Jim, I'll hand it off to you.

[James Guest]
Thank you very much, Erika. So, the slide that you're looking at now has the title *Demographics*. And so we wanted the study to be representative of the population of people who are living with spinal cord injury. And so, you can see two pie charts there. One is the cause of injury, the other is the injury severity. So, amongst the causes of injury, we have causes that are quite common. They include sports injuries, falls, [recreational injuries], vehicular crashes, and then other. In terms of the injury severity, it's also very representative of the population of people who are living with spinal cord injury. You will see ASIA B, C, and D. These are classifications of people who have incomplete injury, meaning they have some preservation of either sensory or motor function. The study did not enroll people who have ASIA A injury, which is complete motor and sensory injury.

The injury site was in the cervical spine, and the injury levels were representative of the commonest injuries around C5. Typically - something that was very important - is that this study enrolled people who had spinal cord injury for a few years or for many years. And the purpose was to determine if [those] people who had long-standing spinal cord injury could respond to the therapy. And it was very exciting to see a few people with long-term spinal cord injury, even as long as 30 years [ago], who were able to demonstrate a response to ARC^{EX} therapy.

Most of the people enrolled in the study were able to complete the study. There were just a handful of people who left the study. And that typically was for personal reasons. And it was not related to the ARC^{EX} Therapy itself.

So here, if you look across the top, you see sort of the timeline of the study. This was very important, this was carefully designed. The idea was to take people from whatever state they were in, living with their chronic spinal cord injuries, and then to do a baseline assessment with a set of standardized tests that are used in spinal cord injury. And then the subjects who met the criteria entered the study. They then underwent two months of functional task practice. And what this means is that working with the therapists who participated in the study, those exercises that they could do with their arms and hands that were most suitable for them, and that had the best chance to help them achieve recovery, were conducted three times a week, one hour a session, the first two months. After the first two months, there was another assessment. And then the same subjects entered the period of time where they did functional task practice plus the ARC^{EX} Therapy. And so the purpose was then to determine, after they had sort of baselined with their functional task practice, whether they would show an accelerated recovery when they experienced the neuromodulation.

So the recovery trends that were observed were very strong, which Chet will talk about in a few minutes. And what was very interesting - Chet will also show this - is that even at the end of four months, most of the subjects were still strongly improving. So that opens up the possibility that with longer durations of therapy, people might have even more recovery.

Something that's also important to realize is that Erika mentioned that 72% of people met the responder definition, but 90% of people in the study improved in either strength or function. So the incidence of recovery in the study was very high. Something else that many participants reported - including the ones that I was involved with - is that they really felt better, or they experienced an improvement in their overall quality of life. People reported they had an increased sense of wellness, energy, and alertness. And even patients who've been injured for a long time reported that they felt much better. So, the pre-specified endpoints of the study were met.

There were other benefits that the subjects have reported as well, including better sense of touch, and even sensory scores, reductions in spasticity in their arms and other parts of their body, and improved sleep. So with that, I will now hand over to Chet. Thank you.

[Chet Moritz]
Wonderful, thank you so much, Jim. So I want to tell you about how versatile the platform is, and how the researchers and clinicians could easily adjust the stimulation location and parameters to really optimize performance for each individual in the study. So on the left, in part a, we see that the researchers typically chose to place the electrodes over the spine between the third and fourth vertebral process and the sixth and seventh. But there was flexibility. Some people could choose to move those electrodes to different parts of the spine if they wanted to specifically target different functions of the hand and arm. The middle panel, in part b, actually shows that most of the researchers chose to use a biphasic pattern, which is shown on top in part b. There, the current rapidly oscillates between positive and negative charge to stimulate the spinal cord. But there was that opportunity in about 20% of the cases [where] the researchers chose to use a monophasic pattern when there's a primarily negative pulse - shown in the bottom of part b - [and] which then returns very slowly in a charge balance pulse to make sure that these pulses have an equal charge. Either stimulation pulse contained a very high frequency waveform that was overlaid on each pulse - a 10 kilohertz waveform.

What that means is that during a one millisecond pulse like you might see from other stimulators, that waveform oscillates 10 times in that millisecond. And what we found is that that 10 kilohertz waveform will effectively numb or anesthetize the skin immediately under the electrodes. And that allows us to pass about five times more current through the skin to activate the spinal cord for the same level of sensation experienced on the skin. That gentle buzzing or tingling, as you'll hear some of our participants describe later in the call.

We can also adjust the amplitude of that stimulation, that's what's shown in part d on the right. Typical scenario would use between 30 and 40 milliamps, which is higher than most commercial stimulators can deliver. But because we use this high frequency waveform, I actually have some sessions where we're stimulating up to 180 milliamps to activate the spinal cord through the skin.

Now what we see when we apply this optimized stimulation is shown on the next slide. And that's improvements in strength, in sensation, and in function. So just to remind you, as Dr. Guest nicely described, the study began with a two-month period of just therapy alone. It was very good therapy functional task practice. And those are shown by the gray data points on all of these figures. After those two months, the ARC^{EX} Therapy was added to that same functional task practice, and that's shown by the red lines and red data points. So if we look across the top row of graphs, we'll see that functional, or excuse me, that clinical measures such as the upper extremity motor score, measures of grip force or grasp force in the middle, or pinch force, either didn't improve during just that functional task practice, or if they did improve, they plateaued after that first month. And so the second month of therapy resulted in very little increased improvement. When we added the stimulation - the ARC^{EX} Therapy shown in red - that's when we see these dramatic improvements in upper extremity strength, grasp function, and pinch force. Same exact pattern is seen in the middle row for the sensory scores. Here essentially no improvement - which is therapy alone - which is what we would expect. But very large improvements in three different measures of sensation, including that sensory measure from the ISNCSCI, focused on the upper extremity as well as the entire body. We've seen changes throughout the trunk, which is quite remarkable well below the injury - all these injuries were in the cervical spine. And also detailed measures of sensation in the hand and fingers done with Von Frey filaments to actually test the tactile sensation of the hands both on the front and the back of the fingers.

The bottom row shows mostly research measures of function. And here, it's actually interesting to note that function continues to improve throughout the FTP - the functional task practice - which tells us that people need more therapy in general. But it does begin to plateau, and we see a continued improvement in all these functional measures when we add the stimulation to that therapy. And this strongly suggests that additional stimulation, be it in the home environment or with continued therapy in the clinic, will lead to continued improvements in these functional outcomes. So I'll pass it to Candy now to summarize these results and begin to tell us about the experiences of some of our participants.

[Candace Tefertiller]
Yes, thanks, Chet. Good morning, everyone. You know, as we've reported already, we had a very conservative, effectiveness endpoint in which individuals needed to meet both this minimally important difference in improvement in strength as well as in function. And so, when you look at that, the fact that 72% of our participants met that very conservative endpoint is really exciting. But it’s also really

important to know that 90% of participants had improvements in either strength or function. So even though they didn’t meet that [conservative pre-defined trial] endpoint, we still made improvements and helped them improve in really important domains of strength and function for these chronic injuries, in which we wouldn't necessarily expect any improvement. We also saw 87% of individuals report improvement in overall quality of life. And if you look at the literature on spinal cord injury, that's really important. And people generally have reported that if you help them improve their hand function, it will result in an improvement in quality of life. So that's a really nice tie to see that we also saw that relationship in this study.

And then finally, when you talk to individuals with spinal cord injury, they'll often tell you that one of the most limiting factors associated with their condition is spasms - or the fact that sometimes their body will just contract, and they don't have voluntary control of that. Or, when they go to complete a movement, they can't necessarily grade the movement - all of their muscles are going to fire and they don't have the ability to isolate specific muscle groups. And so the fact that we saw a reduction in spasm frequency I think is also a really important finding in this study. We all know how sleep is important in our lives. And the fact that people report it improves sleep I think also has a relationship with quality of life. And then one of the factors that I don't think we bring enough attention to in spinal cord injury is the importance of sensation and being able to feel and touch. We did see a nice improvement in sensation in this study as well, which not only is exciting but also leads us to believe that that's probably helping us drive this motor recovery and helping us better understand how these interventions can help - not only in this study, but help us improve recovery in other studies, and more importantly, in clinical care.

In terms of where we are next, we're all really excited that the US market launch is expected in the second half of this year. I know that there's been a lot of buzz around these devices, and clinicians are very excited to get them in their hands and to start using them with individuals with spinal cord injury to improve outcomes. We also know that the European application is on track to be submitted in the first half of 2025. So as both a clinician and a scientist, I think it's really encouraging that we will have something on the market in the next year that will definitely make some improvements in the care that we can provide to individuals with spinal cord injury. And then I'm really excited about the fact that we also have demonstrated that these devices can be safely used in the home. And for many of our patients, they have very limited outpatient benefits, so their ability to recover is often limited by how much therapy they can receive. So, the idea that we can send a device home with them that they can use safely and demonstrate improvements, I think is going to really change lives for people with spinal cord injury, especially after they leave both inpatient and outpatient rehabilitation. So lots of really good things coming from this pivotal trial.

And then I'm really looking forward to having both Sherown and Jessie share some of their experiences with us today. I've been fortunate enough to work with Sherown in quite a few studies. Actually, I treated him from a clinical perspective when he was an inpatient at Craig Hospital. And Sherown is one of the most hardworking people I've ever known in my life. He's also incredibly intelligent and articulate, and so I'm excited that we'll be able to share some conversation with Sherown today about his experiences in the ARC^{EX} trial. And then we also have Jessie, who was a participant at the University of Washington. And so after Sherown and I talk a little bit about his experience, I'm going to turn it over to

Chet and Jessie to talk about what her experience was during the trial at University of Washington as well.

So, good morning, Sherown. I'd love to start with just a couple of questions. One, I'd love for you to introduce yourself, tell people a little bit about your injury. And then tell us what your experience was in this trial.

[Sherown Campbell]
Yes, I'm Sherown Campbell, I have a C4C5 spinal cord injury. I was injured in 2014, wrestling with a friend. Broke my neck and ended up paralyzed from the shoulders down. So it's been about 10 years of trying to regain and recover anything that I can. And then also having great experience of learning through some of the best doctors and researchers going through studies, a lot of PT and a lot of OT, and that has led me to here.

Craig Hospital reached out to me about the ONWARD and Up-LIFT study. And of course, I wanted to participate; they have tons of my trust. And then of course, anything that can help me improve, I want to participate in, at least find out if it works for my body or not. Fortunately, I received quite a bit of recovery from that - improved sensation, grip strength, pinch strength, some unexpected measures. One thing that they've mentioned before was some of the sensations. So I started sweating towards the end of the trial, which was really good for me because it helps with temperature control.

The unfortunate side of it was the study was only 12 weeks. So like some of the other people have mentioned, I was progressing towards the end of the study so I didn't get to see the full effects of what could possibly come from it. I am a huge workout junkie, so I do believe over time progressing and building these blocks helps with recovery. So 10 to 12 weeks is right around where I usually see some types of results from working out. But it's the continuous effort, the continuous building of this that hopefully would get more recovery and that I was hopeful to see. And hopefully when this gets to market, then I get more from that.

[Candace Tefertiller]
Yeah. So Sherown, can you tell us what the stimulation felt like?

[Sherown Campbell]
It's a pretty unique sensation on the lower frequency side. I couldn't feel too much [but] as it starts ramping up, I could feel twitching. The only way that I can explain it is similar to early on in my recovery, you see muscle twitches in the fingers. They're very subtle, not really functional, but there was twitching without me interacting with it. And I do believe when I was grasping or pinching, then I'm allowed to actually contract those muscles. And then that's where I was seeing like an increase in function or grip strength while the device was on. I did notice after a couple of weeks, when the device was off, I was getting that twitching without the device on. I was getting increases at home without the device on. So that was really cool to see.

Yeah, that was that was most of it. But I could feel it throughout my body, which is really cool. Unlike regular electrical stimulation where you're only seeing muscle contractions where the pads are placed, I

was seeing this in areas that are very hard to stimulate. So those small finger movements - thumb, hand, index finger - just areas that I wasn't ever able to stem with regular electric stimulation.

[Candace Tefertiller]
Yeah, that's great. Thank you. I'd forgotten about you getting sweating back. And so many of our patients with spinal cord injury have disrupted sympathetic system, meaning that they can't regulate their temperature well, and they have difficulty regulating heart rate and blood pressure. And so I also think that's a really exciting potential indication for this device as well. So thanks for sharing that. All right, so question for you. When this is out on the market again, would you plan or would you like to use our ARC^{EX} Therapy again? And for what reasons would you hope to use it, if you would plan to use it again?

[Sherown Campbell]
Yeah, if I had the ability to use it, I'd keep utilizing it.

The hard part about this study is that there's so many protocols, and we're kind of limited to what we can do. So I'm able to walk with crutches at home - the study was primarily focused on upper extremities. So I would have loved to have been able to use this while I was on a stationary bike or while I'm standing or getting to walk, doing functions and tasks at home. There's a lot of other applications where I just like adapting and modifying things that I could find uses for on my own, and I'm sure Candy and the other researchers and physical therapists at Craig Hospital, their minds would run wild finding different things for me to do and work myself to the bone. So hopefully I get that chance. And hopefully we can find more applications for it.

[Candace Tefertiller]
Yeah, that's great. And just so you know, Sherown, you will work yourself to the bone, and we just try to keep up with you most of the time. So last question for you, what would you want others to know about ARC^{EX} Therapy? If you could tell both people with spinal cord injury and those people without spinal cord injury, what would you want them to know about this therapy?

[Sherown Campbell]
One thing that was cool about the therapy is so when I've used electric stimulation in the past, some people can kind of zone out. The muscle contraction is going to happen, whether you're working with it or not. With this, there is almost a direct relationship to when I would try to work with the device on and seeing results. And so it encourages movement a lot more. You don't zone out as much. You do actually get to see the effect of like trying to send that signal from the brain to the body was really good. The other thing is always, you know, patience and persistence. Usually results don't come in the first week or second week. It does take time, just like anything else with our health, and those changes build over time. So it's not just, you know, that first week of therapy, but you have to actually like, stick with it, work with it, and you'll see results as they come.

[Candace Tefertiller]
Thanks, Sherown. You've brought up another key differentiator with this technology in my mind, in that [with] the current devices that we have in the clinic, we put stimulation on - we stimulate a peripheral

nerve - and it's going to fire whether we drive it with intent or not. And I think one of the most exciting and innovative pieces of this specific technology is that we're just trying to put your nervous system in a place that is able to activate your intentional movement. We're trying to raise that excitability so that you can send a signal down and drive that movement versus forcing that movement with electrical stimulation. And so I appreciate you bringing that up as well because I think that is a very important differentiator to what this technology does in terms of what we have clinically available now. Thank you, as always, so much for your time. Always a pleasure to work with you. And I will turn it over to Chet and Jessie to share your experience as well.

[Chet Moritz]
Wonderful. Thank you, Candy. And thank you, Sherown, for taking the time to share your experiences. It's very exciting. It's my great pleasure to introduce Jessie Owen, who is a study participant at our site at the University of Washington. And so I'll let Jessie tell her story, maybe starting with how you ended up in this adventure that we call spinal cord injury.

[Jessie Owen]
Yeah, hi, my name is Jessie Owen. I have C4C5 spinal cord injury. Actually broke my neck at C3/C4 in 2012 in a vehicle accident where a tree fell on my car. And so at the time of the study, I'd been over five years injured. You don't have to be an expert in science or pop culture to know that if you receive a diagnosis of spinal cord injury, it is scary and devastating because we know that there's not a lot out there to fix it. And so a lot of us never, ever, give up hope because the difference in a little bit more function and a little less function is huge in our daily lives. So I found Dr. Moritz through University of Washington. We have a spinal cord injury community here, and they were offering a study. I asked if I would be a good participant.

He said yes, and so this was a huge commitment. As you can see, it's four months, and for lots of folks [things] like transportation can be really challenging. So it's an investment. And personally, in the study, I found the first two months very frustrating - the time without the stimulation - because we are doing small Montessori toddler tasks, right? We are stringing beads, we are stacking blocks, things that folks around us can do all the time. And it's challenging for us. So when month[s] three and four hit in the study, and I found myself having a good time - I was competitive, I was making improvements, I was enjoying myself – I noticed a marked difference. And then I also made huge differences in my personal life. Between the time of the study and the time after the study, I was first living with a friend. After the study, I felt confident that I had enough function to go out and live on my own. After the study, I met a husband, and I now have twin boys. So it is a huge quality of life difference for me. The difference in being able to prepare a bottle for my children, the difference in opening the peanut butter jar, to opening the door to my house is life-changing. And so this has been a very big passion project of mine, and something I feel very strongly that folks with spinal cord injuries need in their household because it would bring so much hope and restored function. And it is so vitally important to all of us.

[Chet Moritz]
Wonderful, thank you so much, Jessie. I think rather than me asking more questions, I'll turn it over to Dave, and maybe we can open it up to the audience.

[Dave Marver]
Well, yes, please. So if you have questions, please populate the Q&A box in the Zoom or Teams or whatever platform we're using. While you're doing that, I do want to follow up on what Jessie was just talking about - this desire to have this technology available in the home setting. Sherown said the same thing. Candy, you led a home study for this transcutaneous technology. How do you envision this being used in the home? You know, as part of the way that you manage clinical practice there at Craig?

[Candace Tefertiller]
Yeah, I'm excited about the home transition. I think, you know, as a therapist, prior to being a researcher, I sent many, many, written home exercise programs home with patients, and I know that many of them never even opened them. And what we saw with this study is that people use the device in their home, and so that tells me that they must have found benefit from using it and that it must be feasible to use in the home. So they figured out how to do it, and they saw benefit from it. So I really see this as a partnership with clinicians and families and participants, and really understanding what are the things they want to be able to do better in their home. And then how do we integrate the technology so that they are bringing on those specific tasks that will improve their activities of daily living - improve their ability to open their doors, and to prepare their bottles the way that Jessie shared with us this morning, and whatever those tasks are that are going to improve their life - [i.e.] help them figure out how to train with the device to be able to do that so that they can improve their performance.

[Dave Marver]
Well, thank you. And Sherown talked about potentially using this technology to assist with lower limb movement and function. Chet, as a researcher - and this is another question that came in in the Q&A - what recovery targets are you excited to explore using this technology? Again, I'm not trying to encourage off-label use or anything else. But I'm just curious as a researcher, what your perspective is on this.

[Chet Moritz]
Absolutely. So we've observed so many improvements in function that go beyond the hands and arms that I think, really the sky's the limit with this technology. And I'll just mention a few. Most of these are anecdotal observations in the preliminary study, but some of them do show up in the survey results of the pivotal trial that was just published. So improvements in bladder function and bowel function for some individuals - certainly an exciting target. Improvements in blood pressure is a possibility. There are implantable ways to target that as well, but some of our participants have improved heart rate or blood pressure. Improvements in autonomic function as Sherown mentioned - several participants have started sweating below their injuries, being able to control their temperature for many months after the stimulation was applied. So that's just a few. And lower extremity function, I see, was one of the questions as well. There are several published studies showing that transcutaneous stimulation can help with walking function. We're currently investigating that as well in the lab. So I think there are many, many targets beyond hand function, but I will reiterate that hand function is the highest treatment priority for people with tetraplegia. And so that's why we're on target to begin with that as the on-label use.

[Dave Marver]

And just to continue with you on the mic here, Chet. There's a question that just came in from the UK, which is, I think, an important question to fundamentally understand what we're talking about here. Do you observe the gains when stimulation is off? That's the question.

[Chet Moritz]
Yeah, absolutely. As Candy mentioned, that's what we think is one of the most exciting things about this technology - that it's not what we call a prosthesis, not something that has to be used all the time. So functional electrical stimulation. Yes, it can shock a muscle - it can make a muscle contract - but those muscles fatigue rapidly. And as soon as the stimulator is turned off, all that function goes away. With this stimulator, we see function gradually improved while the stimulator is being used. But for some period of time after the stimulation, most of that function persists. Now that's not to say that we don't want to apply more stimulation in the next therapy session or the next home use session, because when we do, we see function continue to improve. But the evidence that the function remains after stimulation gives us encouragement that we're actually helping to heal or rewire the nervous system around that spinal cord injury.

[Dave Marver]
And indeed, Dr. Guest, in the data that you reviewed, all those assessments occurred without stimulation, correct?

[James Guest]
Yes, that's true. And so we do believe that there is neuroplasticity or reorganization in the system. Some of the time you can see it right away when the stimulation is being applied. But even after the first few sessions, we noticed that there were some persisting benefits. And these seemed to accumulate as patients went deeper into the second month of stimulation.

[Dave Marver]
And back to you, Chet, and just one of the questions that came in how do we think about how persistent the gains are? As Jessie said, I mean, it was just a two-month study. Sherown said the same thing. You know, what do you expect for folks that have ongoing access to the therapy, even in the home setting?

[Chet Moritz]
Yeah, I expect the function to continue to improve with ongoing access to the therapy. And I also expect the function to be maintained outside the time when the stimulator is running. In this pivotal study, we did not have any follow-up measures. The primary endpoints were right at the end as Jim mentioned - after stimulation had been turned off, but right at the end of one month, and then two months of stimulation. Some of our preliminary studies have followed people for three months after the stimulation, and [we're] seeing that most of those gains are maintained, even [for] six months. We have a new study we're just preparing for publication following out to a year showing that most of those gains can be maintained. Now they're flat - it's a plateau after the stimulation turns off in almost all cases. So that's where we're excited to see access to the stimulator continue to improve during that time.

[Dave Marver]

And so one of our research analysts, Thomas [Vranken], asks at what point do you expect to see a plateau. You know, you talked about going out one year? Do you have any sense for when the gains may cease.

[Chet Moritz]
We do not. We don't, Dave, because we've never been able to stimulate for more than two months at a time. Although I guess there are a few anecdotal cases where some of our participants in the preliminary study will return for another study. Not this particular Up-LIFT trial - it only recruited [spinal cord stimulation] naive participants. But we've had several people return for second studies, usually for other functions, but they do continue to improve when they re-enroll, even several years later. So again, I think the sky's the limit. And we really have no sense of what that maximum capacity for recovery could be.

[Dave Marver]
And here's a question from one of our research analysts for Jessie and Sherown. What one thing do you think was most impactful to you? Which improvement, as you think about and perhaps try to rank them. Maybe start with you, Jessie.

[Jessie Owen]
It's hard to tell because it [therapy and improvements] started slowly and ramped up. I hadn't been able to do things for five years, so I'm not sure I really tried them at home. But all of a sudden, I found [I was] able to stick the key in my front door, tie my shoes, drive a car, open the peanut butter jar, like, I could click the leash on my dog's collar. Maybe I would say my favorite thing is that all the participants here had some incomplete functions. So we all had some function, but everything takes so long. And something that used to take 15 minutes, maybe takes two, maybe takes five now, but it is so much quicker and so much faster, which is basically nice, but also a little easier on the on the mental game.

[Dave Marver]
Sherown?

[Sherown Campbell]
For me, it's a lot of the things that happen at home. It's not always exciting talking about hand function and some of these OT tasks. But being at home, being able to open jars - I used to really rely on my teeth in my mouth a whole lot, which drives my family members and probably a future dentist crazy. So being able to open a jar, use tools to actually do things at home and in the kitchen was really huge. Like Jessie said, it's just these small things - like the way I was gripping a steering wheel. Being able to drive I noticed being able to use my left hand a lot more and being able to turn easier. There were a couple of times I got out of my vehicle and [my] balance was slightly improved. So I would move, and instead of immediately needing to rely on a crutch, I almost forgot - like, hey, I need to actually grab my crutches out of the car. I need to do this more just because function was smoother and easier. And that level of uncertainty was just like a little bit less. So it's little things like that. And I did notice - hopefully it's not too much information - but I usually keep like a urinal in my vehicle at home. Even the effort of getting into Craig … usually I'll use the bathroom before walking into the hospital because it's a longer walk and I don't know if I can make it. I did find myself being able to get to the hospital and being able

to walk into the therapy session without having to make these extra pitstops, without having to do these extra things, or being able to leave a session and get back out to my vehicle instead of having to worry about where the next bathroom is, where my next stop is, what I needed to do next. So those little things really add up and make a big difference.

[Dave Marver]
Ah, thank you. Jim, there's a question here about any insights from subgroup analysis, in particular, time-since-injury? I think one would assume that the fresher the injury, the more the effect, but did the data demonstrate that or was it not quite large enough?

[James Guest]
Yeah, I'm not sure that we were able to get a definitive answer for that. But the fact that people with very chronic injuries were able to respond to the therapy - that's extremely encouraging. So I think it will probably take some more time before we really understand whether it's true that people who are soon after injury will show more benefit. And of course, this brings up the question as to whether the therapy could be implemented, you know, within the first year after spinal cord injury to help people have even more recovery during their rehabilitation.

[Dave Marver]
Do you plan to explore that at University of Miami? Apply the therapy shortly after injury when people come into your clinic to initiate the rehab?

[James Guest]
Yes, so we're planning several investigator-initiated studies. Right now we're looking at spasticity and motor control in people who have significant upper extremity spasticity. I think there is enthusiasm to begin to evaluate its use during inpatient and outpatient rehabilitation, that'll, you know, that'll come incrementally. But I think that will be exciting.

[Dave Marver]
And Candy, I think this is a good one for you. We have a few questions here on complete ASIA A. What do you believe is the potential applicability of this therapy for folks with ASIA A?

[Candace Tefertiller]
Yeah, I think it's a really great question. And honestly, I think we're really early to understand that at this point. I do have evidence in pilot trials that individuals with motor-complete ASIA A - motor and sensory complete injuries - have been able to demonstrate voluntary movement below their level of injury, even though they were chronic, and even though they had had a lot of therapy prior to participating in ARC^{EX} Therapy. So I'm cautiously optimistic that even individuals with very severe injuries can benefit from this type of therapy. I think we need to do a lot more from a scientific community in understanding how to optimize the stimulation parameters, to really excite that nervous system to the threshold that it can recover and provide that voluntary movement. But I am optimistic, and I have seen it in our early pilot studies.

[Dave Marver]

And just while you have the floor here, a question just came in that I think is well suited for you. When you're thinking about prescribing this for home use, do you think about time since injury at all? Is that a consideration for you?

[Candace Tefertiller]
Yeah, so that's a great question. You know, as Jim said, I don't know that we have the data right now to identify or to define when somebody will benefit most from this type of therapy. But in general, I think the literature suggests that earlier after injury is better. And so I think I am going to be really excited about getting it into the hands of our participants and our patients as soon as we can after injury and transitioning that into the home environment. One of the things that you hear from people with spinal cord injury often is that, you know, they oftentimes love therapy, and they have such a limited benefit that they feel like sometimes they're falling off a cliff once they transition fully into the home environment because they don't have as much opportunity to practice and to try to promote recovery. And so I do believe that this intervention will provide hopefully a bridge across that cliff, that people will be able to continue working on recovery even after formal rehabilitation has ended.

[Dave Marver]
And the electrode placement - is it required that it be terribly specific? Or could some of the participants put the electrodes on themselves at home? That's another question that came in. Or will they need to depend on a caregiver?

[Candace Tefertiller]
I think it's going to be participant specific. You know, I think many individuals will need to rely on a caregiver to apply the electrodes, because you know you are on the very back of your neck. But I also think that there are some individuals that will have enough upper extremity function that they can apply the electrodes themselves. So I think, again, in the home study we found that caregivers were able to apply these electrodes and able to help participants use their devices in the home environment. And I do think some people were using it on their own as well. So I think it'll be important to understand how we best educate both the participants and their caregivers to really increase the success of that transition in a home environment.

[Dave Marver]
Thank you. We have a few questions about when the device will be available. Erika, I think this is for you. First, we have a Brit who was a bit offended because we talked about the EU - of course, the UK is not part of the EU any longer. But when would it be available in the UK do you expect? And another question came out of Australia, which I think respects CE mark but could you comment on expected availability timelines in the UK and Australia, please?

[Erika Ross Ellison]
Yes, absolutely. As Dave said, we're planning on launching ARC^{EX} in the US later this year, and in the EU in 2025. After that, we have a series of additional countries, including the UK, later in 2025. And Australia, beyond that. We want to get this as broadly available as possible. We're a global company and very much intend to make our therapies available globally - just in a cadence that makes sense to the resources that we have in our start-up company.

[Dave Marver]
Scale up.

[Erika Ross Ellison]
That’s right.

[Dave Marver]
And Chet, this one's for you, because you talked about the frequencies and how the high frequency makes the delivery of the low frequency more tolerable. Question that came in: how many times per week could a person - let's say like Sherown, who's super motivated and works out a lot and wants to make gains - how frequently could they use this therapy, and for what duration?

[Chet Moritz]
Great question. So in our very earliest pilot studies, we actually delivered the stimulation five days a week, Monday through Friday - a typical work schedule here in the States - and then took the weekends off. And although that participant did improve function dramatically, we actually found that he was better on Monday after two days of rest - further improved, right, as he came back in on Monday morning. So that has led to this recommendation of stimulation maybe every other day, which is very similar to an exercise routine or a strength training program, especially if the stimulator is applied in a way with intense training, where those muscles are really being turned on sometimes for the first time since injury. It can be helpful to rest those muscles, rest that nervous system a little bit in between. Now that said, if someone was a routine user, and was using it maybe for fine dexterity tasks in their home, we don't know whether it would be better to apply that stimulation every day. It's certainly possible. But at the moment, we're recommending three to four days a week with, ideally, a rest day in between each application.

[Dave Marver]
Thanks. And a question about waveforms - why ARC^{EX} has two different types of waveforms here.

[Chet Moritz]
Yeah, that's a really important distinction. With a typical stimulator - like a functional, electrical stimulator that Sherown mentioned, that Candy mentioned - those stimulators are limited with about 30 milliamps of current because above that, it can become quite uncomfortable on the surface of the skin. This Up-LIFT stimulator - this ARC^{EX} stimulator - will go up to several hundred milliamps. And the reason it can do that is that [it has a] 10 kilohertz carrier frequency. It's believed to provide a nerve block or numb the pain fibers - the C-fibers - in the surface of the skin. And we've tested this in 20 people with normal sensations, and not people with spinal cord injury [but] people with intact sensation. And we just asked them to turn the knob on the stimulator until they could reach the limit of their tolerance. And when that 10 kilohertz waveform was used, they turned that knob five times further before they reached their limit for sensation on the scan. So, that tells us that with the 10 kilohertz waveform, we can deliver about five times more current to activate the spinal cord that's underneath the skin, underneath some thin muscles there. And so that's I think the game changer here to be able to activate the spinal cord from outside the body.

[Dave Marver]
Thank you. And Jim, a question came in - did we learn anything from the non-responders, let's say the 10% that didn't improve strength, or function, or the 28% that didn't improve strength and function? Anything that we learned that could be applied that maybe would improve this responder rate in clinical practice?

[James Guest]
Yes, so one of the sub-studies was to work out what were sort of the minimum scores on strength and function tests, when people started therapy, that would predict that they would be responder. You know, a big part …[audio cuts out briefly] that really needs to evolve together with this neuromodulation. So what I'm thinking is that there will be an optimal physical therapy protocol to help people to be more responsive to the treatment. I think we still have quite a bit to learn as we extend the use of the stimulation. I'm very excited because I think we're opening a new chapter in our ability to help people recover. And so we've got this far, but we still have a lot to learn.

[Dave Marver]
That's great. Okay, just wrapping up any final comments? Candy? Chet? Sherown? Jessie? Erika?

That's a difficult prompt, isn't it? Anyway, thank you, everybody, for joining. We really appreciate it. Especially Sherown and Jessie, thank you for sort of opening up and sharing your story and experience with us. We really appreciate it. It's going to serve the entire community.

We've recorded this. We're going to make it available on our website, and we'll post it where appropriate, but again, thank you, panelists, for joining. And thank you, all attendees, for listening in and engaging with all the wonderful questions. Alright, so thanks, and I can assure you from ONWARD's perspective, we cannot work any harder to get this approved and available so you can use it in the clinic and the home.

Thanks again.

*All ONWARD® Medical devices and therapies, including but not limited to ARC-IM®, ARC-EX®, ARC-BCI™, and ARC Therapy™, alone or in combination with a brain-computer interface (BCI), are investigational and not available for commercial use