Company Name: Frequency Therapeutics, Inc. (FREQ)
Event: Oppenheimer 32nd Annual Healthcare Conference
Date: March 16, 2022

<<Jay Olson, Analyst, Oppenheimer & Co. Inc.>>

Hello everyone, and welcome to Oppenheimer's 32nd Annual Healthcare Conference. I'm Jay Olson, one of the Biotech Analyst at Oppenheimer. And I want to thank you all for joining us here today. It's my pleasure to welcome Frequency Therapeutics to our conference. And it's an honor to introduce David Lucchino the CEO of Frequency. Thank you so much for joining us here today, David. It's really a pleasure to catch up with you.

I'm going to turn it over to you and then if there's time at the end, we'll do a little Q&A after your presentation. So thank you again, David. And with that over to you.

<<David Lucchino, Co-Founder, President and Chief Executive Officer>>

Thank you, Jay. This is one of the conferences we really look forward to. And so again my name is David Lucchino and I'm the CEO of Frequency Therapeutics. And we really appreciate the Oppenheimer team for inviting us here today. And I just want to thank all of you out there for joining us.

Today, we're going to discuss several really exciting recent advances our company has made and how those advances have set the stage for important clinical milestones over the next 12 months. Having built the broadest clinical data set ever created in the hearing restoration space, we are now running a large Phase 2 trial that we believe is optimally designed to maximize hearing signal.

As we shared late last year, our emerging pipeline of regenerative therapies has yielded two new promising programs, one in hearing restoration and the other addressing the largest unmet need in multiple sclerosis and I'm excited to detail these for everybody today. Today, we'll be making forward-looking statements and I of course refer you recent SEC filings for additional information.

For those who may be new to our story, Frequency is focused on developing a new category of regenerative medicine using small molecules to activate a person's innate regenerative potential. We call our approach progenitor cell activation or PCA, where we identify the signals and pathways necessary to awaken or regenerate cells already in place within the body. We believe this is an approach that can have a significant impact on a range of degenerative conditions.

In our view, PCA has three key advantages compared to other regenerative modalities such as cell and gene therapy or gene editing. First, no genetic changes are made as PCA reactivates the body's natural genetic programs. Second, we harness the native architecture of tissue activating the right cells in the right location all within the body. And finally, our approach uses well understood small molecule manufacturing and drug delivery. This small molecule approach is

particularly important in our most advanced programs as we target the cochlea and the brain areas that are very challenging to access with biologics.

Today, Frequency continues to lead the field of hearing restoration as we work to develop the first potential therapeutic for acquired sensorineural hearing loss. As I mentioned, we are now enrolling a Phase 2b study for FX-322, our lead candidate for the treatment of sensorineural hearing loss having shown positive safety and efficacy measures and several earlier studies.

Moreover, we believe we have addressed study design issues based on our learnings from our prior development efforts. As I will show you shortly, it is the data from all of our earlier studies that has enabled us to refine the disease types and the severities where we have seen the greatest response. Our research engine has also been highly productive with two new recently announced programs based on our PCA approach.

These include a new preclinical hearing program, FX-345 that may give us a greater ability to treat more hearing loss types. We also have compelling data from our preclinical program for remyelination in multiple sclerosis, where we have discovered a novel target and demonstrated a powerful remyelinating effect.

As you can see from this slide, the next 9 months to 12 months will be rich with significant readouts and milestones. Giving us multiple shots on goal, as we advance our hearing and MS programs. We anticipate a readout for our Phase 2 study of FX-322 in either Q4 of this year or Q1 of 2023. We're planning to have our 345 study ready for the clinic in the second half of this year, with a readout in 2023.

And we also plan to nominate our MS candidate in 2022 and advance our remyelinating program into the clinic next year. Needless to say, it's a very exciting and an important year ahead. What many don't fully appreciate is that hearing loss represents one of the largest causes of disability across the globe. The overall need for treatments is massive. The World Health Organization estimates nearly 1.5 billion people suffer from some form of hearing loss, and there are more than 41 million individuals with sensorineural hearing loss in the United States alone.

Today, there are no restorative treatments, and only 20% of the people that could be using hearing aids actually do so. Still, the U.S. hearing aid industry brings in more than $10 billion annually, not including those sold over the counter. Hearing loss is also linked to other conditions including depression and dementia, and we believe that a safe and effective treatment would drive an enormous market for new therapeutics.

Yet, saying you are a leader is one thing. Demonstrating is another. In the hearing space, our leadership starts with having shown hearing improvements in individuals with permanent acquired sensorineural hearing loss, something that has never been done before with a drug. We were the first to deliver data showing statistically significant and clinically meaningful improvements in hearing function.

These improvements in speech reception were sustained in some subjects for almost two years, suggesting a potential disease-modifying benefit. Importantly, we've also shaped a regulatory

path for our approach and we are aligned with the FDA on speech reception as the primary endpoint for future studies. We believe alignment around endpoints at this stage of development greatly reduces risk to the program and increases the probability of both technical and regulatory success.

We have had more than 200 individuals go through our hearing loss studies, and FX-322 has shown a favorable safety profile with no treatment-related serious adverse events. Our clinical work has been essential as we've determined how those with different hearing loss severities and etiologies may respond to drug, and how to best design clinical studies to maximize signal.

A central underlying biological cause of sensorineural hearing loss is the damage to hair cells in the cochlea. This can occur due to age, noise, medications, viral infections, or the result of sudden trauma in the ear. Our focus is on sensory hair cells development, where we decode the signals that drive these cells and then modulate those signals with the combinations of small molecules, a unique approach in the hearing loss space.

FX-322 is made up of two small molecules designed to activate progenitor cells and regenerate lost hair cells. Hair cells are critical for hearing as they translate sound into signals that the brain can interpret. Many species like birds or reptiles can regenerate the sensory cells and restore hearing. While humans are not programmed to activate these cells once they are gone, the machinery to restart the process is in place. It just needs to be turned on.

FX-322 is injected into the ear locally, a standard procedure that can be done in most ENT offices. On the right, you can see that FX-322, shaded in orange, concentrates mostly in the base of the cochlea following injection. It is at the base of the cochlea where high-frequency signals are processed, which is important as humans typically start losing hearing in this exact range.

Our clinical work demonstrating delivery of FX-322 to the cochlea and the associated hearing signals were published last year in Otology & Neurotology, the premier journal in our field. Clinicians generally agree that real-world baseline impact on hearing is at least a 10% absolute improvement, or specifically, an improvement of at least 5 words out of 50 on a word recognition test.

A minimum five-word improvement can be very meaningful, because it can lead to changes in a physician's treatment recommendations and to a patients' quality of life. For example, at 20 words out of 50, the individual shown here is on the board of a cochlea implant candidacy. A five-word improvement could delay that surgery and significantly improve an individual's ability to communicate. However, a five-word decrease could leave them functionally deaf.

Let me now show you data from two clinical studies where we have demonstrated these clinically meaningful improvements using a single dose of FX-322. FX-322-201 and FX-322-111 were both controlled studies, the first placebo-controlled, and the other using the contralateral untreated ear as a control. Study participants had established hearing loss for a minimum of six months. These are individuals that do not spontaneously recover.

As you can see on the chart, in each study, more than 30% of subjects had a greater than 10% absolute improvement in the word recognition scores. Moreover, when we invited patients back to retest one to two years later, several had maintained these improvements. It was remarkable to see sustained improvements following a single injection, clearly suggesting a disease-modifying effect.

The scale of our FX-322 clinical program has enabled us to post single-dose trials to look for patterns in the data while giving us important insights into the characteristics of responders. On this slide, you can see two ways that we have evaluated pool data to inform our broader program. Moreover, you can see the breakout of subjects who show at least a 10% absolute change in speech perception from baseline.

When we pool the data from these from three of our single-dose trials, you can see changes in FX322-treated patients that clearly exceed the threshold for meaningful improvements, including some subjects that had a 40% absolute word increase. Only a small fraction of placebo-treated patients or untreated ears land above the threshold.

Looking at the pooled data, we can also see the percentage of individuals who exceeded the 95% confidence interval for this test and how placebo-treated patients and untreated ears are consistent with historical literature standards. This approach also helps and comparing our single-injection studies to our multiple-injection FX-322-202 study.

In our post hoc analysis of what the study of the study, we found that design flaws that led to inconsistent baselines and bias issues. Further, in the study, we saw changes in both untreated and placebo ears that were completely out of sync with historical standards. These insights led us to fully rethink study design to help ensure consistent baseline measures in the future.

Using these pooled data, we were then able to refine our patient populations for our new Phase 2b study, FX-322-208. You can see in this diagram, our prior studies helped to find a clear sweet spot around moderate to moderately severe subjects with noise-induced and sudden sensory hearing loss.

Here, we saw a 30% to 40% response rate of FX-322. The orange circle is indicates our focus for the FX-322-208 trial, a hearing loss population that represents 7 million to 10 million people in the U.S. alone. It is important, as you look at the totality of data to remember that these are subjects that had permanent hearing loss, and where now – where data now shows clinically meaningful improvements in speech perception, something that has never been seen before.

Our 208 study is now recruiting and aims to include 124 subjects in total. It is equally balanced with 62 patients per cohort and has a primary endpoint of speech perception. As I mentioned, we have implemented several key measures to mitigate bias and work with the leading experts to design the optimal study for this kind of subjective testing.

These design updates includes a leading phase with multiple visits to establish clear baseline values. The ability to disqualify those with poor consistency across visits, the massing of both

patients and sites to further mitigate potential bias, and ongoing surveillance so we can provide feedback to the sites, allowing us to enhance compliance and consistency across the study.

We are very confident these design components bring a crucial level of clinical quality control and rigor, and we strongly believe that by focusing on individuals that are the best candidates for our therapy, that we will be able to show the greatest separation from placebo as we continue to advance a hearing therapeutic towards commercialization.

Finally, late last year, we reported our third study to show a hearing signal, this time with severe hearing loss. Our FX-322-113 study enrolled individuals likely to be cochlear implant candidates. Because of the subjects' hearing deficits, we added an additional measure called the sentence and noise test, which is commonly used with this patient population.

In the study, we saw a clear hearing signal in the sentence and noise test, with several subjects exceeding the signal-to-noise ratio that is considered clinically meaningful. While early, we believe these are important data as we look at how FX-322 may work as a monotherapy or in combination with hearing devices for these more severe populations.

And our efforts to restore hearing have not stopped there. Throughout our journey, we've asked ourselves whether we could create a new candidate for hearing restoration that could directly reach a larger portion of the cochlea. We recently announced that we have done just that.

FX-345 is a hearing restorative clinical candidate that achieves broad exposure through a large portion of the cochlea. We believe this will enable us to access – excuse me, we believe that will be enable us to assess whether our approach can have an even greater patient impact or help a broader population.

Given the significant heterogeneity across hearing loss types, deeper delivery into the cochlea using FX-345 may extend the reach of our treatment. We are now aiming to bring this asset into the clinic in the second half of 2022.

Another key question we have worked to answer is, how can we apply PCA to create therapies for additional degenerative diseases? To address this opportunity, we recently unveiled preclinical data for our novel potential therapy for remyelination in multiple sclerosis.

MS is a devastating neurological disease that affects nearly one million people in the U.S. alone. The disease causes the patient's immune system to attack myelin, the protective coating on the neural cells in the brain.

While existing MS therapies work to slow this attack, not rebuild the myelin, repairing neurological damage remains the critical unmet need for MS patients. Our approach is to activate natural progenitors that create myelin to restore structure and function.

To that end, we have identified a novel target that is highly effective at driving remyelination. We've also developed multiple NCEs that outperform previously reported remyelination candidates in rigorous in vivo models. The target we are most excited about, we call Target 14,

which we have yet to disclose. We confirmed Target 14 by using specific antibodies in cell culture, and we believe our discovery gives us a key competitive advantage as, to our knowledge, it is not a target that others are pursuing.

As MS is a demyelinating disease, we assess remyelination by running our compounds against other advanced and well known remyelination candidates. We also challenged our compound with a very stringent test, remyelination of mice with an agent called cuprizone for 17 months.

In this image, the green staining shows myelin. The image on the far left is the vehicle. The other panels show modest changes from three well known comparators, T3, the anti-ligand antibody, and chlomastin, all of which were dosed at or above levels used in the literature.

Now, let's look at the Frequency compound. We administered just a single dose of our compound called FREQ-162 at 5 mg/kg. And as you can see, there is a dramatic increase in myelin-based protein in both white and gray matter throughout the brain.

We don't know of any other remyelinating agent with this magnitude effect. And we believe the fact that we saw this robust effect after a single dose is quite promising. Overall, results from our study show remarkably consistent response in every animal treated with FREQ-162.

Our plan now is to advance our remyelination candidate into the clinic in 2023. And we will keep you informed as the program advances through IND-enabling studies. 2021 was a highly productive year, which now sets up multiple events in 2022 and early 2023.

With FX-322, our collective clinical data indicates that we have a promising drug candidate for hearing restoration. From our expansive clinical work, our team clearly understands what groups have shown the most pronounced response to FX-322. Our previous trials have also informed what we believe is the most robust and well controlled hearing study ever conducted, and one that benefits from having FDA-aligned clinical endpoints.

We now have an exciting second hearing program that will allow us to explore if we can expand the hearing loss populations we can help. And our PCA research engine has generated a novel remyelination program in multiple sclerosis, with a target we believe no one else has explored and preclinical results that thus far exceed the gold standard in the space.

We are well capitalized with the resources to achieve the next set of milestones for these programs and we believe we will deliver real innovation and value for patients and shareholders.

I'm very proud of the Frequency team and their continued focus on the potential of our science, and I want to thank all the people who have participated in our clinical studies, as well as the investigators leading them. We deeply appreciate their ongoing commitment to innovation and to advancing new medicines for hearing loss and MS.

Thank you for your time today. I will now be joined by our CFO, Peter Pfreundschuh; our CSO, Dr. Chris Loose; our Chief Development Officer, Dr. Carl LeBehl; Dr. Kevin Franck, our SVP

of New Product Planning; and Dr. Sanjay Magavi, who heads our remyelination research. We look forward to your questions. Thank you very much.

Q&A

<Q – Jay Olson>: Thank you, David. And to your whole team for joining us here today, it's really great to catch up with you and learn more about the impressive work you're doing at Frequency and really appreciate that comprehensive overview, perfect setup for a few questions. And one of the questions that we've gotten from investors is around the refined patient population that you're pursuing in your 208 study for FX-322. Can you maybe just help us scope out the size of those populations that you're targeting in that study. And how large the commercial opportunity is there and then also maybe any sort of competitive dynamics in that space.

<A – David Lucchino>: Yeah. Thank you, Jay. Again, it's a real pleasure to be here. I'll ask Kevin Franck to sort of kick things off, it's a great question. Maybe stepped out for a dish of ice cream, it's getting warm up here in Massachusetts. Pete, do you want to take that question?

<A – Peter Pfreundschuh>: Yeah. Jay, in terms of the patient population, I think there's a slide in our corporate deck that we talked about the focus around the patients from the five continuous trials that we ran over the last couple of years and where we really saw a response from an etiology and severity perspective. When you really look at that in terms of the size and shape of that marketplace, that's somewhere between 7 million and 10 million people that we believe FX-322 can really address from a commercial perspective in a very helpful manner, obviously, reaching a little bit broader from that. As we think about FX-345, we think that that could be broadened obviously from a size and scope perspective into other patient populations from an etiology and severity perspective. And potentially, you could even build that out towards 15 million plus people. So hopefully that helps provide a little bit of the commercial context and some of the answers to your question there.

<Q – Jay Olson>: Yeah, absolutely. That's super helpful. And any comments on the competitive landscape in those target patient populations?

<A – Peter Pfreundschuh>: Yeah. I don't know. Carl, do you want to provide a little context there? Do you want me to jump in?

<A – Carl LeBehl>: We're aware that there have been other groups that have been studying really the acute phase of sudden sensorineural loss? And that's a very different Jay than what we're looking at. We have a requirement where individuals that qualify for our study, they have to have permanent loss and we put a six-month requirement in there. And so when people present with sudden loss, they're getting treated hopefully immediately. But oftentimes, they don't recover. And so six months later, they can then gain access to our trials. So that's the difference between the populations.

<Q – Jay Olson>: Okay, great. That's perfect. Thank you for that. And then just to follow-up on some of your comments about FX-345. I think you said you would be in the clinic in the second

half of this year. Can you just maybe comment on the ongoing IND work there? Any gaining factors in the work that remains to be done to get your IND filed for FX-345.

<A – David Lucchino>: Carl?

<A – Carl LeBehl>: Yeah. So we're doing the IND-enabling tox studies. Those are on track. We expect that at some point third quarter or so we're filing, and then we'll certainly be starting that study as soon as we can with the planned readout for the first half of next year.

<Q – Jay Olson>: Okay, great. And then Peter, I know you mentioned that FX-345 could potentially broaden the target patient populations. Could you just help us to understand the strategies for differentiating the role of FX-345 versus FX-322? And how are you going to fit these two complimentary hearing restoration programs together?

<A – Peter Pfreundschuh>: Yeah. I think first off in terms of FX-345 and its ability to get the deeper and more broadly into the actual cochlea. I think that from a restoration perspective, potentially could expand that patient population. I think the way we think about it from a commercialization and launch perspective, obviously, FX-322 is way out ahead of FX-345 in terms of clinical development, the data that we've collect to date and where we're at in that program. Obviously, we've seen a very strong signal in some of these trials that we've run. We believe in the 208 trial design, where we're going with regards to that.

We believe that it makes a lot of sense to continue to push that forward. I kind of equate a little bit the FX-322, FX-345 story to you remember the early days of statins and even Merck, you think about that with MEVACOR, ZOCOR, obviously of course the agents were kind of playing in the same space and domain, but they really differentiate themselves from each other. I think as we get further clinical data with regards to FX-345, that'll help us really shape that narrative and understand kind of where we can play with FX-345 relative to the patient populations versus FX-322. And we can kind of see those two playing together and from a commercialization perspective as we get into the market and try to broaden out that market over the course of time. So that's kind of how we think about it.

<Q – Jay Olson>: Okay, great. Thank you. That's very helpful. And then maybe just to talk about your MS program, I know this is an area of high interest amongst investors, very excited about it. Can you just talk about, I guess, in terms of your candidate selection – you showed some preclinical data for FREQ-162. Is that the candidate that you're nominating to move forward? And I guess, what maybe the – if you could just walk us through the next steps and timeline to IND for your remyelination program.

<A – David Lucchino>: Sanjay?

<A – Sanjay Magavi>: Yeah. FREQ-162 is one of our candidates. We are currently assessing a number of different compounds in terms of preclinical toxicology, pharmacokinetics, manufacturability. We're sort of blessed with a number of options. We think we'll be able to select one of them by year end. Then we'll drive this through the standard IND-enabling toxicology studies and hopefully have an IND in 2023.

<Q – Jay Olson>: Okay. Understood. And appreciate the fact that you're keeping your remyelination target on under wraps for the moment. You did show how your molecule compares to a number of other remyelination agents in a preclinical model. Can you just maybe talk about how your target compares to other targets of remyelination. And maybe including some other experimental competitive agents that are being studied.

<A – Sanjay Magavi>: Yes. As you point out, we amongst others are trying to activate oligodendrocyte progenitor cells to differentiate restore myelin in MS patients. And this is obviously sort of a holy grail for the field. We can't say too much about this target. It is as far as we know a novel target that others are not pursuing. And we can say that the target is expressed in humans. We are optimizing our drugs against the human version of this target. And when you examine where the target is expressed, it's in the right place at the right time to be useful for MS patients.

<A – David Lucchino>: I think that's right. Well, Sanjay, that's really nice.

<A – Sanjay Magavi>: Thanks.

<<Jay Olson, Analyst, Oppenheimer & Co. Inc.>>

Excellent. Well, thank you so much. I think we're just about out of time, any additional comments that you'd like investors to know about Frequency before we wrap things up.

<<David Lucchino, Co-Founder, President and Chief Executive Officer>>

Yeah. We continue to have a strong cash position and getting through 2023 and really, if you like this is the IPO and we had a successful IPO. Investors should really be enthusiastic about what we're doing now with the clarity we have on hearing and the additional potential for shareholder value around MS. And we look forward to answering additional questions if investors have them at any point. So thank you so much, Jay, for your time today.

<<Jay Olson, Analyst, Oppenheimer & Co. Inc.>>

Excellent. Well, thank you, David, and team. It's really been a pleasure catching up with you here today. It's always great to learn about all the amazing work that you're doing for patients and we'll stay tuned for future updates. So thank you very much.

<<David Lucchino, Co-Founder, President and Chief Executive Officer>>

Thank you. Have a great.

<<Jay Olson, Analyst, Oppenheimer & Co. Inc.>>

You too.