(Tim Frank, IRSF Chief Marketing & Development Officer):
Hi, thanks for joining us. My name is Tim Frank. I'm the Chief Marketing & Development Officer here at the International Rett Syndrome Foundation. Our community is celebrating some exciting news we received earlier this month. Trofinetide received FDA approval, which makes it the first-ever treatment for Rett syndrome. As we eagerly await more information from Acadia Pharmaceuticals, who will market the drug as DAYBUE in the United States, we know our community has a lot of questions about the treatment and what comes next.

So we put together a three-part Q & A series to start to answer those questions, share what you need to know, and discuss the impact this treatment could have for you, your loved one, and your family. Today, in part two, we talked to Melissa Kennedy, IRSF's Chief Executive Officer, about our advocacy efforts to ensure that DAYBUE is accessible and affordable to everyone with Rett syndrome. We'll also discuss what you can do right now to ensure our loved ones have access to treatments like DAYBUE in the future.

As a reminder, the thoughts and opinions discussed in this video are not meant to be medical advice. We encourage you to please speak with your doctor for individual advice on DAYBUE and your child's treatment plan. Melissa, thanks so much for being here today.

(Melissa Kennedy, IRSF Chief Executive Officer):
Thanks for having me.

(TF)
Yeah. So we got this great exciting news very late on March 10th. Tell me how did you feel when you heard the news that the FDA approval that had come in?

(MK)
Thanks for asking that, Tim. It was 6:12 and I got a text saying it's been approved, and I think all of us knew that there might be an announcement on that Friday, but we all believed we were outside of the window. So I had actually just gotten up from my desk and was getting ready to take a walk just to kind of walk all the excitement and tension off, and the text came through. I have to say the word that comes to mind is just overwhelmed. I was immediately overwhelmed. I immediately felt intense relief for the entire Rett syndrome community because there was a path. There was a path to FDA approval, and it meant that there was currently a treatment, and it also meant that there would be future treatments, which was incredibly exciting. I felt a lot of gratitude to the families who have had participated in this trial. You know more than 90% of rare diseases don't even have a treatment, and so we were catapulted into that very lucky 10%, and I knew that we were in a new world for the community.

(TF)
So you mentioned the path to get here. Let's talk about that a little bit, that it's been a long road. How has IRSF been a partner and advocate for families through this journey? What's been our involvement?

(MK)
I mean, that's a great question, and I think the answer is, we were different things at different points in time. So the thing that's fascinating about the molecule trofinetide is that it was actually created at the University of Auckland as a potential treatment or therapy for traumatic brain injury. Our prior Chief Science Officer, Steve Kaminsky, was at the Department of Defense, and that molecule came to his

attention, and because he knew about Rett syndrome, he thought, "Huh. I think this actually would be really effective for Rett." And he reached out to the IRSF Board of Directors and brought the molecule to their attention. And the IRSF Board of Directors did two things. They hired Dr. Kaminsky as the Chief Science Officer at that point, and he spent quite a bit of time with us and did wonderful things for the Foundation.

They also invested in the Phase Two Clinical Trial. So the compound at that point was owned, still is, by a company called Neuren, and IRSF invested over a million dollars in the Phase Two Clinical Trial. Once that trial was completed, and the results were promising, the decision was made that there should be a Phase Three Clinical Trial. Neither ISRF nor Neuren were able to finance that. So Neuren found a partner in Acadia Pharmaceuticals who has the license to commercialize - commercialize trofinetide for the treatment of Rett syndrome in North America, and Acadia financed the Phase Three Trial.

During that Phase Three Trial, I would say we were more like a traditional advocacy organization. We helped the company and the employees at Acadia get to know the community, get to know Rett syndrome, and share insights. They were a wonderful partner to us during that process.

(TF)
That's great. As you mentioned in our message to the community on approval day, so we sent out a message right away - that FDA approval is just the beginning for us as a community. What are the next steps in the process for us as a community?

(MK)
Well, the next steps specifically around trofinetide, which is now known as DAYBUE, and will be commercialized in the United States as DAYBUE, the next step for us as a Foundation is to make sure that anyone who wants to have access to DAYBUE is able to access it, and that it is affordable. That work is going to be a little different depending upon who a family's health insurance is.

So I'm going to start talking a little bit about Medicaid because we know that over half of the IRSF families who have a loved one with Rett, their loved one is covered with Medicaid. And so the work is pretty straightforward. Families need to set up meetings with their elected officials at the state because it's going to be the State Department of Medicaid that's going to make the decision about whether or not trofinetide or DAYBUE, will be on the formulary.

What I know about Rett syndrome families is that they are fierce advocates for their children in every aspect of life. So this is going to feel like very familiar territory for many families. It's also similar to what a lot of families do with state proclamations, just raising awareness at the state level.

For the families who have a private payer, the process is kind of the same. I would suggest that they reach out, and ask for meetings with the medical directors of their health insurance plan and just make sure that they get to know what Rett syndrome is and raise awareness.

I'm going to say, as I say a lot, it's really important that the community is aware that IRSF wants to work to make sure families have access to any treatment that becomes available. While we're doing this advocacy work around DAYBUE right now, we will do this advocacy work as every single treatment and therapy becomes available. And whatever treatment a family chooses to take advantage of, is really a decision between them, and their provider.

(TF)
Thanks for that, Melissa. There's been a lot of talk and a lot of numbers floating around about the price of this new drug, this new treatment for Rett syndrome. What can you tell us about the cost?

(MK)
So, I listened to the investor call as did many other people a week or so ago now, and on that investor call, and the link is publicly available, they said that the list price will be a little over $300,000 a year if I recall correctly. I think what's really important to understand is that, like everything else in healthcare, what a family pays for healthcare, drugs, if you go to the hospital... it really is not necessarily what is charged. Most often drug companies, healthcare systems, and hospitals, negotiate rates with health insurance companies. So there is going to be a negotiated rate that payers will agree to pay.

And then beyond that, families pay a portion of negotiated rates. The portion that a family pays differs dramatically depending upon their insurance. So I would simply say that we can't really say what any individual family's cost is going to be because there are too many factors at play, but I would encourage families to reach out through Acadia Connect, and the resources that they've provided. I do know that Acadia has expressed a very strong desire to help any family access the compound regardless of their ability to pay. So I would really encourage families to reach out through Acadia Connect to find out what resources are available to them.

(TF)
Thank you. So right now, DAYBUE is only approved in the United States. What can you tell us, Melissa, about the process for trofinetide access to expand to other countries?

(MK)
Thanks for asking that question, Tim. I really think that's the question we are receiving more than anything else. Since March 10th, I think we've probably had we've had hundreds of outreaches with exactly that question. Understandably, families outside of the US have a level of desperation to have access to this compound. Like those families, we are waiting rather impatiently for the next steps.

Here's what I can say right now. Acadia is working to have access to DAYBUE in the US by the end of April, and they are the ones responsible for overseeing a possible expansion of access into Canada and Mexico. There are different regulatory agencies, and different processes that need to be adhered to, and that process is just going to take a little bit of time.

Outside of North America, Neuren maintains the license to commercialize trofinetide for the treatment of Rett Syndrome. They intend to pursue registration, and commercialization of trofinetide for Rett through partnerships. More information will be forthcoming from Neuren directly and when permissible, but there's just not a lot that can be said about that process right now. So we will wait patiently.

(TF)
Thank you. What can families in the US do right now, Melissa?

(MK)
Yeah, we talked a little bit about that. I think, you know, talk to your physician. Educate yourself about DAYBUE, and advocate. I think what we want to do right now in terms of kind of a call to action is, to make sure that DAYBUE is available and accessible to you. If you and your physician decide that it's the

best thing for your loved one. so much as I said a little bit earlier, go to our website, go to the advocacy portion of our website because there are some very specific things that you can do to advocate for access.

Share your story. It's very powerful. I know it can be intimidating for many to go up and talk to elected officials about your personal story, but it's the most powerful thing that any of us has, and elected officials want to hear them. They want to meet with you, and they want to hear your story. So please, please go share your story.

(TF)
That's great. Anything else, Melissa, that you think parents should know?

(MK)
As we said, DAYBUE's not going to be for everyone, which is why we are continuing as a Foundation to invest in research that will continue to bring therapies and treatments through the pipeline. We as a Foundation still need folks to fundraise so that we can continue to invest in research. So I'm going to put in a shameless plug for that.

I will say, from an advocacy perspective as well, you're going to hear from us a little bit more because you know, family foundations, private foundations, and private donors can only fund so much research. We need federal dollars, and so we are going to continue to advocate that federal dollars are available to fund research in Rett syndrome, which is why we continue to advocate that Rett syndrome be listed as a topic eligible for funding through a DOD program called the Congressionally Directed Medical Research Program. So in FY22, Rett syndrome was listed as a condition of interest and Rett researchers actually received $663,000 in federal funding to support research. Our goal is to keep that happening every single year. So that's going to be the next little bit of advocacy as well. Our team is honored and humbled to serve this community, and we're just very grateful for the community's support and trust in us.

(TF)
Absolutely. Thanks, Melissa. Thanks for joining us today. Thank you for everybody who's watching.

Make sure to visit DAYBUE.com. For more information, that's Acadia's website specifically for this drug. You can register for their upcoming webinar, which is on March 28th for caregivers, and you can learn specifically about their Acadia Connect program, the patient and family support program that they're bringing alongside DAYBUE.

As we said at the beginning. we encourage you to contact your doctor about this and there's information on DAYBUE.com that you can give your healthcare provider.

And then as we've said before, we want you to share what this approval means to you. We've created a contact form on our website under our trofinetide news page where you can share a bit of your story, whether you were in the clinical trial at any phase or just have been expecting a treatment for a long time, and are excited or a little fearful even about what this means for you. We'd love to hear from you. So please let us know. You can also email us at treatment@rettsyndrome.org.

We'll be back with our Family Empowerment Team later this week. Paige Nues and Samantha Brant from our Foundation will be joining us, and they will do our third, and final video coming out on Friday,

talking parent-to-parent about this first-time treatment, and what that means for our community, and sharing some of the experiences that we've been hearing as well. So we hope that you'll join us then. Again, thanks so much for being a part of it today.