(Tim Frank, IRSF Chief Marketing & Development Officer):
Hello everyone. Thanks for joining us. My name is Tim Frank. I'm the Chief Marketing & Development Officer here at the International Rett Syndrome Foundation. It's been two weeks since our community came together to celebrate a milestone for Rett syndrome. Trofinetide became the first-ever FDA-approved treatment for Rett syndrome. And as we eagerly await more information from Acadia Pharmaceuticals who will market the drug as DAYBUE in the United States, we at IRSF want to make sure you and your family are empowered with all the information and resources you need. So, we put together a three-part series to start to answer your questions, share what you need to know now and discuss the impact this treatment could have on your family and your loved one.

For our final video, I'm joined by some very familiar faces within our community. Family empowerment director, Paige Nues, and family and community engagement manager, Samantha Brant. As parents to a child or young adult with Rett syndrome, each of us experienced so many emotions when we heard that trofinetide was approved. Today we want to share our personal experiences and what we're hearing from families in the community as we prepare for this treatment.

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. Paige, Samantha, thank you so much for joining us.

(Paige Nues, IRSF Family Empowerment Director):
Thank you.

(Samantha Brant, IRSF Family & Community Engagement Manager):
Thanks. Great to be with you.

(TF):
So, tell me, I know where I was. I was in the park with my wife. We'd gone out for the evening when we got the news. Where were you when you guys got the news that DAYBUE had been approved?

(PN):

Oh my gosh. It's a moment I'll remember forever. It was Friday, early evening here on the west coast and my family had just arrived into town, had gotten here from the airport, and I had hoped that we were going to hear the news on Friday, March 10th, 2023, but it had already reached 5 o'clock here on the west coast and I thought, oh, the east coast is all closed up for the day. I guess we're not gonna hear anything now. Darn it. Getting ready to, you know, sit down and have dinner with my family who had just come into town, looked at my phone, the press release had dropped and I was able to share with my parents, my spouse, my teenage kids, and most importantly my daughter, Katie, the very core circle of people who have been around us and around me from day one of her diagnosis, that the first drug ever to have been approved for Rett syndrome, it had been approved by the FDA. And it's a day that I will remember just like I do her diagnosis day, her birthday... It'll be a day I remember forever. And we were able to sit down at the table with a wonderful meal and we popped a bottle of bubbly and celebrated. It was wonderful. And that's exactly when my phone started exploding and social media messages started coming in, particularly from the people on the west coast who were still awake. It was amazing. It was amazing. So, thanks for letting me share that beautiful moment.

(TF):
That's awesome, Paige. Sam, how about you?

(SB):
Yeah, mine was a little different. I, too, thought it was going to come out earlier in the day and I remember being on pins and needles just continuing to refresh and look for this press release to happen. I had many families reaching out asking, "Do you know yet? Have you heard yet?" And letting me know that they too were refreshing for this press release. By central time - by five o'clock, I thought, gosh, we're not going to hear. And so, I went ahead and went out for the night with some of my family and extended family. I can remember getting the news that this press release had come and this history had been made for our Rett syndrome community. And it took my breath away - literally took my breath away. I remember standing there and just feeling it and feeling what a change had just happened in history for our community. I got to share with some extended family. We didn't sit around and have a beautiful meal at that point - We were out and about and just couldn't believe it! Social media just started filling up and I just sat back and took it in awe, watching the closeness, and emotion, and love our community shared with each other. So, a little bit different. I sat back and took it in, and I'm still sitting back and taking it in thinking, do I pinch myself? Is this real? We've waited for this for so long.

(TF):
That's so good. Thank you guys, both.

I know you had mentioned both of your phones blowing up. I'm going to ask, I'm going to share a story that one of the families submitted, a family in Michigan. We had sent out the email shortly after the announcement went out to everybody knowing that some on the east coast were going to get it really late. The west coast is going to get it at a decent time. But one parent wrote that she got the email that it was approved and wanted to scream to the world, but also didn't want to wake and scare her daughter. So, turned to the Facebook community until 4:00 AM, just going crazy there. Woke her daughter the next morning, asked if she remembered all of the flights, the late night hotel check-ins, rental cars and everything that was involved in the trial. She was involved in the early stage of the trial. Her daughter listened intently and gave a little smile when her mom told her that she was going to take the drug again, and this time never go off it. She smiled even bigger and closed her eyes and for her that was her, "yes."

So, it was just exciting to see too and to hear from families about their experience telling their children. It's emotional just to think about it, you know, that our children are involved, many children have been involved in these studies, many children have been waiting for something. And you know, as families, we've all had to tell our child that there isn't anything yet. You know, and so just hearing the emotion of getting to tell our kids that there finally is something that may be an option for them is just huge. Paige, you've been a leader in our community, you've been part of this community for so long, and you've seen a lot of progress of trofinetide from the beginning. What does this journey look like for families who have been waiting for this news for more than a decade?

(PN):
Oh my gosh. I think it's still sinking in. Kind of as Sam said, it's like, pinch me, pinch me and wake me up because I'm not sure, is it really real? Is it real? Families have been so committed to this journey, but it's been a lot of ups and downs.

I remember in 2012 when Larry Glass from Neuren joined us on the stage at our conference and said, "I'm in. I'm all in. We are committed to your children." And the room erupted with joy. But as we say in Rett syndrome, you know, the days are long and the years are short. And yet these years have been long years, from that moment of really trusting and believing that this company believed in our kids, that our clinicians believed in the drug as well. Creating that community of trust with our families to entrust their children to try an experimental drug.

For me, as a parent whose child was too young to enroll in the early phase and then was too old to enroll in the next phase to be asked again and again, "Would you put your child into this trial?" And for me to be able to say with honesty, "Yes, I would." I trust our doctors. I trust this drug, I trust the process. I trust the regulatory systems that are putting all these protocols in place to keep our kids safe. Is there risk? Yes. Do you know what that risk is? No, because we haven't been through clinical trials.

We spent years holding meetings, webinars, conferences, and educating families about what it meant to enroll your child in a clinical trial. We held hands with parents as they had to make decisions because our kids, for the most part, are nonverbal. They're some of the most severely affected, neurologically involved kids with a genetic disorder to exist. So, to take all of that in and as a parent make the decision to trust your child to a trial when they can't tell you necessarily themselves how they're feeling, whether they want to do this or not. You have to do some deep thinking and some deep reflection.

And so, I would say that these decades, this entire decade has been about unifying our community to make the best decisions that we could together. Because it's when you can hold someone's hand, you get through the hard times. We've had other trials fail, and we've had travel be difficult. It's difficult to travel with a child with Rett syndrome. So, most families never take a vacation. But to commit to another doctor appointment when your life is already filled with so many doctor appointments, and already filled with so many therapy appointments, and you already take off so much time from work when your child is sick and can't go to school or the bus doesn't show up. There are just so many reasons to not participate in research.

But being part of the Foundation, I was there to say to families, the day is going to come. I know it's going to come, be research ready, contribute to the Natural History Study, and participate in trials. If you want to see this happen, whether it's going to happen for your child or not. If you want to really make your dreams and hopes a reality, commit to the process. And they did! And the joy and disbelief are just incredible. It's incredible.

And it gives so much hope to our other related disorders. I'm hearing from communities outside of Rett syndrome who are so happy and they are inspired and they're renewed and they're reinvigorated. Again, it's a process and you need these moments in time to come. It's just, it's incredible. I'll share one more story. One of the families who was able to get on the stage after completing the first phase that was open for adults with Rett syndrome, got on stage at one of our family conferences and said, you know what? I know I've been told I cannot say whether I thought my daughter was on drug or on placebo, but you know what, I don't care because I know her fingerprints are on this trial. And that is a powerful statement and such a commitment to our community. And I'm so grateful to every parent.

(TF):
Paige, are there any, just again with the history of this, you know, with those early trials back in, what was it, 2012, 2013, that the phase two trials came out? You know, we didn't have a big sponsor with lots

of money to be able to fly people in or to be able to help. Who are some of the unsung heroes that helped make that possible for our community?

(PN):
Oh, thanks. I'd really like to give this moment to Colleen English and the families who started an organization called Rettland. What's amazing to me is that 10 years ago in the rare disease space, clinical trials, there was this feeling that families should not be compensated for participating in trials because that might be conceived or perceived as coercive. And we had to do a lot of advocacy to drug companies, to the FDA, to the regulatory agencies to say, you know, compensating is different than reimbursing somebody for travel. We're a rare disease. Our centers are not proliferated in places all over the country. It's not easy to get to. It's expensive. And our families are already doing the most difficult thing that they can, which is offering their child to participate. It shouldn't be much to reimburse them for the expense of participating. And in that time when we needed to bridge that gap for that logic to be understood, Colleen English took the initiative to form an organization called Rettland. And she enabled the funding of travel for families who had the emotional wherewithal and the ability to do the travel, but not the financial means to do the travel. And so, she made that happen. And that's another unsung hero and a critical piece to why this was able to be accomplished in the exact decade that we said it would take to happen. So, we'll forever be grateful for Rettland, which was started by parents, for parents to be able to make research progress a reality.

(TF):
That's awesome. So, one quote that I remember reading and have here to share is similar to what you shared Paige about just the fingerprint. But one parent in South Carolina, a mom said that by participating in this trial, her daughter has given her time, her blood, and much more to help thousands of other people. She has made her mark on history. Somewhat like what you shared, the approval of trofinetide brought her to tears, tears of joy and hope. No more children will be diagnosed with Rett syndrome and their families told your child has Rett syndrome and there is nothing to treat it. Now families will be told your child has Rett syndrome, but there is a medication that may help him or her. It brings so much hope is what that mom said. Sam, you work mostly with our newly diagnosed families. What does this change for them? How does this change for those families?

(SB):
Oh gosh, hope! The mom in South Carolina hits the nail on the head with hope. Our community is always and continually full of hope. But this brings something new, right? Not only hope but fruition. As I speak to new families, I know my voice cracks when they ask, "Is there treatment?" And I have to say no, but we're working, we're all in, we're all trying. Now I get to say yes. Talk to your clinic. Go speak to your physician. There is a treatment that the FDA approved. That just takes a thousand bricks off of a parent's shoulders, mine included. And I just think that the conversations with newly diagnosed families and beyond, this is a change that occurs for both females and males.

(TF):
Absolutely. I know there's a lot of excitement out in the community. Our phones are blowing up, our emails are blowing up. What are some of the common themes that you guys are hearing from our community?

(PN):
I'd particularly like to take this moment to acknowledge the families who have children that are no longer with us because they're experiencing such mixed emotions at this time. A lot of bittersweet emotions that their children didn't live long enough to see this day. And I want to remind them that we all stand on the shoulders of giants who came before us. Today would not have been able to happen without their children participating in the early studies, without their children being known by the doctors and by saying so much more inside of them than they can express. And that it is their very commitment and their participation in this whole process that has enabled us to get where we are today. And they're so excited, right? This means that their children's lives had meaning if they donated organs to brain repositories, if they participated in trials, if they did blood draws and spinal taps and natural history studies, all of that - it got us here. And their children are watching from above and they are so happy that their brothers and sisters who are alive today will get to have an opportunity to live a better life.

And this just opens the door for more treatments and for more trials. So, I want to really acknowledge and thank those families that have come before us. Because it's wonderful. And especially I have to say to Claire English, Colleen English's daughter, the family who started Rettland. Claire's not here today to benefit from that work, but Rettland still is. So, we are a forever family. And we will see this day just to start a new journey and a new chapter for all children. So Sam, I don't know if you have anything else that you'd like to share?

(SB):
Yeah, it's always one of the most exciting things that I get to share with families, new families that, number one, that they're not alone. And then sharing how alone they are not. And it's those families before that blaze these trails for our young children to be able to benefit from this. Without those Colleen English's and Rettland and all those families that put their blood, sweat, tears, miles on their car, miles on their flights, blood pricks, spinal taps, like you said. And the emotional investment of going through these phases to bring this to fruition. Without them, we wouldn't be here. So, I know on behalf of our Foundation and behalf of all the families that I get to work with now and in the future, we're grateful, thank you. Thank you for blazing those trails. And I assure you we're going to continue to keep that going as we continue moving forward with more and more treatments.

(PN):
And to the siblings. Right? To the brothers and sisters out there who have missed out on so many things in life for them to get to see here, sit here and see that all of the promises that we as parents have made to them, that there will be better days ahead for their sister, which means better days ahead for the entire family. But it's here for them too. And I know how excited my kids are for their sister and how much we have to thank them for loving their sisters and trusting in their brothers and promising a better day for them. But knowing that now they can also rest a little easier, knowing that the future that we've promised would get better. Really is. It's a new day. It's just a beautiful moment.

(TF):
Yeah. It's the first of many to come. You know, we know that this treatment may not work for everybody, but it certainly is the beginning and it brings a significant amount of hope. What is our community saying about just the excitement around the label and the fact of who it's approved for?

(SB):
I've heard a lot from both male and female families and you know, 10 years ago, I'm not sure that this would've been possible, but to know it's possible for our males and females just makes the excitement even more. It's for both. It's for someone with Rett syndrome, both males and females. What an amazing journey that has been for those families and all the male families that have battled uphill battles for males to be included. What a win for our entire community.

(TF):
Yeah, I was just thinking about that. As a Foundation we've fought so hard because we've heard the voice of the families with males and how they wanted to be a part of trials, they wanted to be included, and we have brought, behind the scenes, we have brought males to the table every time, I said, what about males? What about males? And so it is such a huge win and bittersweet, like you said, Paige, knowing that we've lost so many who didn't get to see this day, but their fight was not in vain, you know, that we heard them and that now industry has heard them, the FDA has heard them, and we have this label that we can celebrate.

(PN):
Yeah. And then it's relevant for adults, right? For everyone who felt unrecognized or if a trial, the inclusion criteria did not include them. If they had a male, if they had an adult or their child was too young, they took it personally and felt like they were being personally excluded from the opportunity of this drug. So, to have it approved for every age, every stage, every gender is just extraordinary. It goes to show that nobody was excluded. Everybody was thought of. This truly is a compound for people with Rett syndrome. End of story. It may not help everybody, but it's eligible for everybody. And that was just something that people had to trust the process. And here we are.

(TF):
Yeah. What other stories or feedback are you guys hearing from the community?

(SB):
Like I said, after hearing the news, I really got to enjoy the social media celebration that went off like fireworks. And one by one I read different family stories of things that had happened on this trial with their children. And it brought me to tears. It chokes me up to think that these parents watched their children lose skills and were able to gain these things back. You know, I've also heard for some it didn't work and that hurt just as much as hearing the diagnosis. But I just really felt a part of each person that shared these stories, lives and the joy it's given and it's given our Foundation to be able to hear and see is like no other.

(PN):
And I think not just the families, but I'm hearing from the therapists, the physical therapists, the occupational therapists, the music therapists, the special educators, the pediatricians who have believed in our kids and have committed to work with them daily, weekly, for months, for years, knowing that the enriched environment is so important in a disorder that's not degenerative, but it is progressive. And so, that enriched environment and that continuous therapy matters, but we don't always see progress. But to now know that there is a therapeutic, that when paired with this enriched environment, when paired with those hours in clinic and therapies, they'll get to see the change and the improvement. They're part of history too, and it's so invigorating for them as professionals and motivating that they are happy, they're as happy for their families because we've become family after working with them for so long,

right? So, this is really a moment to celebrate across so, so many circles of people in our communities and so many professions. I'm so glad that Acadia is going to be doing some webinars specifically for families on March 28th, and they're gonna be doing some additional webinars just for professionals. So, I hope that everybody visits their website and looks for the webinar that's just right for them, for whether they're professional or a family, to get the answers. They do have the ability to write in questions that are on their minds that we may not have the answers to, but hopefully Acadia can share on these upcoming webinars. And it's just a further testament to the fact that they're a true partner in this process with us.

(TF):
Absolutely. Anything else you guys think the parents should know, that our community should know right now?

(SB):
Yeah, I'll piggyback on Paige, what she's sharing about Acadia on March 28th. I think families should plan to join that. You know, any family who needs any further information, Paige and myself, we're here to navigate and direct you guys to the resources you need, to the toolkits - Acadia has a wonderful website and toolkit to help. I know I've heard a lot of families wanting to call their clinics and they're ready to get in! Let's be patient with our physicians and our clinics. Can you imagine how many of us want to just get in tomorrow? But they're still caring for our children and making sure that they're at the tip top of their health and shape as well. So, let's just have some patience as a community. It's coming. And you know, for those folks who have seen the RettAway, if you have not, please visit our website and look under "events" for the RettAway. It's going to be extra special and an extra special celebration, in person! Vacationing with each other this June at Morgan's Wonderland and Inspiration Island - and what an inspiration this is for that.

(TF):
Absolutely. Paige, anything you want to share?

(PN):
Oh gosh, I just, I hope everyone can make it to San Antonio in June. It's going to be such a celebration. And, you know, this isn't the miracle cure. We still have to learn from each other. We still have to bond together as a community. We have to learn how to travel with our children who have seizures, who have sleep disorders, or who need special equipment. And the purpose of the RettAway is for us to learn how to do all of that in a safe space with each other. But now it's going to have a little bit of a different feel, I think. It's going to be a major celebration! And I won't have to jump through the screen or through the phone to give everybody a hug. We can do it in person. So, like Sam said, I can't wait to see everybody in person in June and look forward to that. And I want to thank every single family who has not given up hope. We know you love your children and you know that you would do anything that you can for them. And I know that you'll continue to do that. And just don't give up hope. If this treatment doesn't work for your child, another one will. The door is open and more people are going to be inspired. Their work is gonna be more meaningful to them, knowing that this approval could come. Can't even tell you how many seizure medications we've tried for Katie and have failed, but we never gave up hope that someday something would work. And so, don't give up hope. Keep believing, knowing we're not going anywhere and it's just congratulations everybody and thank you.

(TF):
Awesome. Paige, Samantha, thank you guys so much, and everybody watching this, this episode and the previous episodes that we did, thank you guys so much for tuning in it.

As Paige shared, we are incredibly grateful as a Foundation to be able to support your families and our goal is not only just to support your families, but to accelerate research. And so, it's exciting to be able to have done both, to have journeyed with the research all this time and made significant contributions that have gotten us to this point, but also to be working with the families, carrying with you, carrying the burden and shouldering the burden with you on a daily basis, but also empowering you to help others and to give back to our community and to be research ready and to be participants in clinical trials and to make those amazing sacrifices that you guys have made. Thank you so much for entrusting your families to IRSF and to the belief in the work that we're doing.

As Paige and Sam communicated, we do encourage you guys to visit daybue.com to register for Acadia's upcoming webinar on March 28th. It's at 7:00 PM Eastern. You can do that. They also have information for your healthcare provider under a healthcare provider portion of their website. So, if your doctor's curious, they have information there - really strongly encourage you to do that.

And we also encourage you to talk to your doctor about this because as we said, this may not be right for everyone, but it's important for you to talk to your doctor or to visit our clinics to find out what they say.

As we're continuing to gather content, as we're continuing to share these stories, we want to hear what approval means to you. Were you a part of one of the clinical trials? How does this news give you hope? Please tell us. We have an email set up at treatment@rettsyndrome.org or you can use the contact form on our website. Thank you guys so much for being a part of this and we hope you're all healthy and well.

(SB):
Thanks everyone. Be well.

(PN):

Thank you.