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>> SANDRA SOO-JIN LEE: I would like to extend a very warm welcome.

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My name is Sandra Soo-Jin Lee and co-director Mildred Cho with Center for ELSI Resources and Analysis or CERA.

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>> SANDRA SOO-JIN LEE: I would like to extend a very warm welcome.

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My name is Sandra Soo-Jin Lee and co-director Mildred Cho with Center for ELSI Resources and Analysis or CERA.

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For those of you that support research on the ethical and legal and social implications of genetics and genomics or ELSI.

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Served to help scholars and journalist and members of the public and others to engage ELSI issues.

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The CERA is funded by the National Human Genome Research Institute at NIH and is managed by teams at Stanford and Columbia University with the Hastings center and Columbia University.

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I am delighted that you joined us for the fourth year of ELSI Friday Forum.

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It is held the second Friday every month for one hour starting noon Eastern Time.

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We have a Zoom room for informal discussion after the panel for 30 minutes.

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ELSI Friday Forum is organized by a multiand plan topics and work with speakers and collect and curate literature and resources.

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We are extremely grateful for ELSI Friday Forum committee members.

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I would like to recognize Maya Sabatello, Aaron Goldenberg, Lauren Brown, Sheethal Jose, Josie Johnston, Mildred Cho, Dounya Alami Nassif, Tiana Sepahpour and Rachel Yarmolinsky.

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Today's ELSI Friday Forum focuses on Fair Access and Equity of Individualized Interventions for Ultrarare Genetic Conditions.

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I would like to encourage you to check out our related ELSI Hub collection titled paying for cures, the ethics in economics of gene therapies for rare diseases.

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This is curated by our moderator today Meghan Halley.

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The link is in the chat.

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To that collection.

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This resource is one of many that you will find on ELSIhub.org.

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I encourage you to join the ELSI Scholar Directory and examine up for the newsletter and updates and news on LinkedIn and Twitter.

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You will find the recording and transcript of this forum and related references that will appear on the chat.

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Now for quick logistical infection for this Webinar.

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If you wish to use closed captioning please turn on the CC button at the bottom of your screen.

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The panelist presentations will be very brief in order to ensure that we devote significant time for discussion.

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So we encourage you to submit your questions using the Q&A button which you will find at the bottom of your screen.

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In that box you can register your enthusiasm for the UPVOTE button.

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In the chat we will post links to resources referenced in today's discussion.

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The resource list will be available on ELSI Hub following the forum.

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If at any point you need assistance e-mail us the info@elsihub.org at any time.

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So now it is my distinct pleasure to introduce our moderator for today's discussion.

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Dr. Meghan Halley is a Senior Research Scholar at the Center for Biomedical Ethics for Stanford University.

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She is a medical anthropologist and ELSI scholar.

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Her research focuses on ethical challenges in research and clinical care for patients with rare and undiagnosed genetic conditions.

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I will hand off to you Meghan.

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>> MEGHAN HALLEY: Thank you, Sandra.

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I'm delighted to moderate today for ultrarare genetic conditions.

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>> MEGHAN HALLEY: Thank you, Sandra.

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I'm delighted to moderate today for ultrarare genetic conditions.

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It is a bit of background.

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In the United States a rare disease is defined as one affected less than 200,000 individuals.

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Collect Ingrid Holmly the more than 10,000 known rare diseases affect between 25 and 30 million Americans and hundreds of millions more worldwide.

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Estimated 80% of rare diseases have a known or genetic it is rapidly advancing thanks to technological innovations.

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Rare diseases affect both children and adults.

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Three manifest in childhood.

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They are morbidity and mortality and estimates suggest that rare diseases are responsible for a full third of deaths in children before the age of 1.

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Despite the high contributions to mortality over 90% of diseases lack FDA approved therapy.

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The landscape is exceedingly challenging one.

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Given the high cost of drug development and analyst reach $2 billion and the numbers affected developers face an unlikery return on investment or the possibility of drug prices that put the therapies out of reach.

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These challenges are further amplified in the patient population that we will focus on today that are ultra rare diseases.

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Nano rare and ultra ultra rare and N of 1.

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There is no codified definition of any of these terms.

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In practice the concept of ultra rare is typically used to refer to diseases affecting 1 to 20 patients per million people.

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A key feature of these diseases until very recently these patients lacked any potential pathway due to low prevalence.

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Then a team from Boston Children's Hospital led by an 8-year old girl with Batten Disease.

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The drug was a nucleotide or ASO.

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They are made up of synthetic DNA or RNA.

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Increased gene expression by modulating gene splicing or shut down genes by targeting RNA for destruction.

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The nature of ASO means they can be customized using the same chemical process by changing the sequence of nucleotides.

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This makes ASO simple to manufacturer and deliver.

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Leveraging the platform nature of this technology they were able to complete the process of drug development in just one year.

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While the break through advances demonstrated are justifiably exciting the path forward remains unclear as we talk about today.

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Though less than industry estimates for new drug developmented cost of developmenting was still substantial and estimated $3 million.

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A charitable organization.

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Further though she did not experience for the small number of patients for any of these individualized therapies inherent the option for safety and can and has had deadly KWENGSs.

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consequences.

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Though she did appear to she was far from a cure and did pass away in 2021.

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Today our panelist will share with you more details and many developments in more recent years.

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They will did you see the ELSI related questions raised by individualized therapeutics with safety and equity.

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Let me introduce my esteemed panelist.

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Dr. Ingrid Holm faculty in genetics and genomics in Boston as a pediatrics genetics and researcher her primary area is the integration of genomic sequences and early childcare and could lead with children are rare diseases and potential of early treatment.

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Dr. She specialized with ethical issues pertains with therapeutic.

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With that I want to turn the floor over to my colleague Ingrid Holm.

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>> INGRID HOLM: Thank you, Meghan.

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I want to share my screen and hopefully everybody can see this.

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>> INGRID HOLM: Thank you, Meghan.

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I want to share my screen and hopefully everybody can see this.

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So as Meghan discussed this is, I'm going to start just with six year old girl with and had a skin biopsy.

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She had Batten Disease.

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This is a neuro logic and a number of different forms and pathogenic variant.

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Both her copies of gene called CLN 7.

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One of them disrupted splicing of this gene.

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It made it so the gene and kind of came out of that was the potential that maybe we could develop a couple medicine to silence it and rescue the gene function.

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I should say that these slides are from Tim Yu and showed with his permission.

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This gets back to another ASO that was developed for spinal muscular at trophy called and ASO was a supplied modulator for this disease that was now in clinical use.

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So the question was, it could be made for this type of patient.

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Led by Tim Yu Boston children to the referral to receive the first medication.

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It is important to be clear what are some of the candidates for ASO therapies?

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Most ASO therapies are in disorders that were treating can lessen or prevent symptoms.

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Most are neuro logic and delay and rest development and lead to death.

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Symptoms manifest in in fancy.

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Mila was for all accounts totally typical at birth and had a progressive disorder that led to death.

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The order candidates are the variants.

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ASO are targeted to specific genetic variants.

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The variants that an individual has has to be a minimum of ASO therapies.

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They are not applicable to a lot of pathogenics variants.

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They are variant specific.

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You make an ASO is made specifically for one person for the variant they had and that is what kind of leads to this real concept and these can be truly end of one therapies and not gene or disorder specific or actually variant specific.

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And since I think as you all know since Mila and batten disease and other advise ASO trials in progress and we'll be going forward.

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So the ASO's have led to this as we developed this first ASO it is significantly abbreviated proof of concept that rely on the appropriates of ASO as a class.

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As Meghan said, these are somewhat kind of programmable medications.

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So in other words, you can take a particular variant and make that segment of RNA and you can use that for your treatment and that can be, you can then use whatever your patient's variant is and put that variant in and it is very specific but it is a class medication that you program the specific variant.

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And this leaves to questions in terms of things like what is a nature and extent of the evidence needed to implement these treatments and, for example, for Mila it was a short timeline.

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There wasn't a lot of evidence to look at her specific variant.

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What are standards for evaluating the efficacy of these treatments?

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What is the minimum assurance and safety that is needed?

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How pervasive or mechanicshould data be?

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There are clinical trials and clinical care.

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In other words if this is just one patient, is this a trial or just clinical care of one patient?

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Our ethical obligation is to promote the patient but also to gain generalized knowledge.

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Which somewhat leaves the question if there needs to be a band width or research.

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Providing the best possible care to an individual patient could in inherently be greated into gaining knowledge.

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The integration of clinical research is also done by collecting and analyzing data alongside of clinical care.

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Maybe there is not much of a band rate.

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There is a roll of regulatory oversight given this issue of patient clinical trials and clinical care and the need for registerries and standardized outcomes and assetment of treatment.

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You can still look at the outcomes in a more standardized fashion.

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Then there is issues from the patients or the participants perspective.

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So there is this, as a show in the last slide there is a continuum of therapeutic optimism and misconception.

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That is an aspect from the patient perspective.

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The other is informed consent.

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How can one best communicate and manage risk with congratulationses and uncertainties and draw expectations.

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Then there is the question of deciding to treat.

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Should the urgency of the patient's situation be a deciding point for treatment?

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Is the number of people who ultimately be treated factor into those decisions?

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Who might benefit most from these treatments?

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Is and when in the progression of the disease this most effective to intervene.

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The disease tend to be progressive and individuals start off being typical.

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When in that progression is it more progressive to intervene.

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Then there is societal issues.

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Allocation for these strategies, which Meghan said are extremely expensive.

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Equity and inclusion of criteria.

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Who should pay the high cost of developing and administering and studying the therapeutics?

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What about the access to underserved population and rational and socioeconomic communities?

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In a sense if we are not addressing this are we exacerbating health disparities?

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What is the role in governance and oversight of these therapies?

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Finally children are usually certainly so far and I think will continue to be the focus of N of 1 therapies.

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How do we weigh the harms especially when there are high risk and uncertainties with these therapies?

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How does the in ability of children to undergo these abilities because of their neurocognitive abilities?

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And children that can't assent what is the integration process?

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Is there a role or concern, a role I should say for the child's future atonomy in the future safety.

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Tim Yu and I have a grant to provide ethical, in the title to provide ethical guidance of the development of some of these therapies.

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Tim Yu and I have a grant to provide ethical, in the title to provide ethical guidance of the development of some of these therapies.

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We're trying to course and implementation of N of 1 therapies and transparent.

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We're trying to do so by delivering empirically informed stakeholder guidance.

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This is a stakeholder approach that we're taking.

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Our aims are to catalog and examines realigning and individualized rare therapies from the perspective of diverse stakeholders and then to conduct a process and brown tables to develop stakeholder based ELSI guidance that will inform the evolving provision of medicine for orphan diseases.

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Just there with our study team.

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Thanks for your attention.

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I will turn it over to Alison.

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>> ALISON BATEMAN-HOUSE: Thank you, Ingrid.

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Hopefully people can see me and my slides.

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I need to go back real quick.

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Can everyone see me I hope.

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So I am Alison Bateman House.

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I thank Ingrid for that great introduction and appreciate the opportunity to speak with you all today.

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Both Ingrid and Meghan touched the challenge to fair access and equities when it comes to these interventions when it comes to the cost of them.

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I want to touch on two other aspects.

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And before I do that I want to give you my disclosures just to sort of situate who I am and stand in this conversation.

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So, how do I get rid of this?

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Meeting, controls, yes.

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There we go.

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Excellent.

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The vast majority of my funding comes from my patient advocacy group called Parent Project muscular distrophy.

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She was talking about a rare disease and ultra rare disease.

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Muscular Dystrophy is a rare disease, but because it is an established advocacy group people that have no patient advocacy group are N of 1 or N of 4 come to it to seek guidance because they have no advocacy group of their own.

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They have become very involved in this particular topic.

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You can see here I'm involved in other institutions that are involved in the N of 1 plus, N ofU.

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There are top titles of this going around.

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I want to flag one in particular.

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I am a volunteer ethisist.

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It is a charitable foundation and nonprofit approach to developing ASO therapies that Ingrid was talking about.

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In this case instead of having to raise 3 plus million dollars as Mila's miracle foundation did.

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This is a situation that if an individual and child's disease is deemed a development, this foundation will take them on and try to develop the ASO and then provide it for life for that individual for free.

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We will talk about that later as I go along.

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That's who I am and I am solely responsible for the content of this talk.

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That's who I am and I am solely responsible for the content of this talk.

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So the two things that I really want to talk about in particular is, you know, in order to even be eligible to be one of the lucky few for whom an in a few intervention can be developed or, you know, tried on is there is this whole runway that you have to get through.

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That entails being diagnosed as having this very ultra - ultra rare condition.

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That entails having access to genetic testing.

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To have access to genetic counselors.

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There is a huge lack of genetic counseling in our country at the moment.

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People having to wait very long time to give access to even read outs of the genetic testings that they were able to get access to.

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They need specialist.

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We have this funnel situation where even if someone was able to tell a newborn child obviously had some you know situation and suspected maybe a genetic variant was at the root of it, it still may take quite a long time.

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Even potentially years for a diagnoses.

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That diagnoses is fundamental in order for that person, that family, that child to be routed towards research and then move forward to, you know, be able to try to move forward to getting into the pipeline for one of these in a few interventions.

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I want to point out in the Mila case that we talked about.

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When Mila's mom that talked to Dr. Tim-Yu that customized therapeutic.

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She was reaching out to have a diagnoses of a genetic test result.

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She had another child and was trying to figure out if her second child was likely to have the same situation as Mila.

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I want people to understand that we tend to focus on the cost and the inaccessibility in a few interventions but there are many steps ahead of that in which there is inequity and lack of access.

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The other thing that I wanted to talk about is this question of on what grounds do we justify differentiating our treatments of these novel therapeutics in a few indications from all novel therapeutics.

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That may sound confusing.

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What exactly am I talking about?

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This is drug development in general.

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I'm not going to go through the whole thing.

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I will note that this is from the pharmaceutical research manufacturers of America and vested interest in pointing out how difficult it is to develop a drug.

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But when you are normally talking about drug development you are talking about a multi-year process involving numerous trial participants and normally the trials fail.

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They fail either because they the product proves to be ineffectI ve or too toxic to receive the FDA approval to allow the drug to be marketed.

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That is the key issue.

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We're looking normally in drug development for a product that can can be marketed.

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When we're talking about in a few, we're talking about a drug that is never going to be marketed.

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There is not a population there.

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We're talking about something that even if it is an N of 1 or maybe an N of 4 or N of 15, there is not enough of a market there to make it worth the cost of doing this whole process.

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So you know we are talking about a situation where what is normally done for drug development doesn't work.

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There is no financial incentive for companies to undergo this process to bring the drug to market.

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The FDA FDA acknowledges this.

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Individualized ASO drug products are not expected to follow the traditional investigational phases and as described in the codes of federal regulations.

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That makes sense in the common sense level.

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Then it raises these questions about where do you draw the line between a rare disease that does go through that normal process to bring a drug to market and ultra rare disease or an ultra ultra rare disease in which we forego that process?

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When the Mila case was written up and published, at that very same time two officials at the FDA wrote it editorial in XH they started asking these questions.

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I'm going to read this directly because they phrased it he will low gently.

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In these situations what type of evidence is needed to exposing a human in a new drug precipitating severe complications or death is not acceptable.

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What is minimum assurance of safety is needed?

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How per how should the dose be selected?

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How much characterization of the product be taken?

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How should the urgency or the number of people who is could be treated affect the decision making process?

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In addition how should efficacy be evaluated?

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Even if it is one person that is in a desire situation we're not going to say just try anything.

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You're in a horrible situation.

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We're still going to have standards.

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What are the standards and how are we going to determine what they are?

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When I showed you this, phase 1 in a normal situation is when you figure out what is the maximum tolerable dose that someone can receive without horrible side effects?

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Well, if you don't have a phase one, if the only people receiving this drug is the actual individual, how do you know what the dose is and other such questions as that.

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My question is, where do we draw the line between what we say, I'm sorry.

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I understand that you're in a terrible situation and you really want to try an investigational product right now and you think that is the only thing that you might think is the possible treatment but you need to go through the typical, you know, characterization of a drug development.

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You know maybe not phase, 1, 2, 3.

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Maybe the drug will prove itself after phase 2 when we can bring it on to the market early but we're still going to adhere to the typical process as opposed to saying we're going to let you go this N of 1 route.

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Where do we draw that line and why?

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I just wanted to note that FDA has released several documents over the years addressing this individualized drug product for severely debilitating and life threatening disease.

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This is typically for one or two.

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This goes back to the quote where they said we are not expecting these to go through the normal clinical trial process.

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Now in Lorem they use the term nano rare.

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Their cut off is N of 30.

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We have a discrepancy that it is one or two to go through this different channel.

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Lorem saying you can go up to 30.

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I want to point out that once you start looking for a disease, prevalence is going to go up.

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If you don't look for it you won't find it.

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This goes back to the point of lack of access to testing.

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Lack of access to, you know, specialist and screening and genetic counseling and all the rest of it.

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Also at this point, you know, there is a global discrepancy of who can get this testing.

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We have people in the tourism trying to get into the United States or western Europe or other places in the world where they will be able to get this testing because it is not available in their home country.

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Just to touch into these post Milasen efforts so far no other patient in Milasen efforts was identified.

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They is one of one so far.

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KCNT 1 epilepsy is another product that they have developed a quote/unquote individualized therapeutic has been used in two patients.

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The initial recipient decide and the second one destined this treatment.

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This is publicly recorded knowledge.

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I'm not breaching confidentiality here

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In this case the patients is 10 globally.

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That does fit within in Lorem's description of nano rare if maybe not FDA's description.

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Maybe FDA's description depending on how many of those patients are in the United States.

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Then we have something called it is a rapidly genetic ALS.

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This is the second most common gene abnormality infamy LEEal ALS.

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You are starting to talk about larger numbers.

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They did allow small numbers treated with Jacifusen.

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Other use must be done in clinical trial.

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They did allow treating for individualized ASOs.

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There has been one public case with an N of 1 gene therapy.

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Gene therapies open up a whole other can of worms of ASOs and we can talk about this with Q&A.

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We know these cases are continuing to happen.

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We still see this question of what is the cut off number between when they should be allowed to happen through this, you know, as Ingrid said.

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Is this clinical care that we should be allowing to happen or is this something that needs to happen in a clinical trial and be considered research?

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Where is the avoiding line to consider ultra ultra rare and still a criminal trial and N of U or coming up with the sake of coming up with a number.

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How do we justify to the patient groups and say you must go through the traditional process.

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Especially if they say, look our prognosis is equally dire or potentially our prognosis is even more dire.

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I recall during COVID we allowed people to try products that were not vetted, that were not FDA approved but people were desperate to try anything that they think would help.

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Actually if you look the a COVID the mortality rates were not as high as other diseases that we said you need to go through a clinical trial whether it was ALS or breast cancer or et cetera.

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How do we justify the groups and what side of the line we're putting them?

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I just want to say, you know, there is this question of, what makes sense on a rational bases?

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You're saying obviously we can't do a clinical trial if there is a patient base of five patients that would be insane.

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Impossible.

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What is the point of doing a trial if we're not trying to bring a product to market anyway.

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There is also the question of fairness.

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When you are talking about an incredibly small patient group, is it fair to say that we think we can make money off a product to your group we need to go this way versus we don't think we're going to be able to make money through your group so we will allow you to go the other way.

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That is intentional provocative.

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We can talk about that during the Q&A.

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Maybe, it is not money that is the thing dividing things as I just put it.

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And then the last point I wanted to make is unless we do come up with a good rational of why we're treating different things, differently without, you know, really being able to explain why we're doing that, I do fear that we will be in a situation where people start saying well, I don't think we need to do a clinical trial for this particular agent.

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We should be able to do it through this N of 1 procedure.

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As we've seen, we've already started inflating the number of individuals, the prevalence through which we people have argued should be allowed to go through this pathway that has much less safety and much less, you know, sort of regulatory oversight.

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With that I'm going to stop and turn it back over to Meghan.

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I thank you for your attention and look forward to your questions.

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00:38:14.000 --> 00:38:18.000

>> MEGHAN HALLEY: Wonderful.

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Thank you so much Alison and Ingrid for those really thought provoking talks.

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There are already a lot of great questions in the chat but I am going to take moderator privilege and ask a couple of questions to get us start the.

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ed.

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My first question is for Ingrid.

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It is thought provoking to hear the work that you have currently ongoing on the how it engages stakeholders involving ethical questions.

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The question I have for you, how are you defining stakeholder in this context?

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How do you even decide who should be at the table in those sorts of discussions?

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>> INGRID HOLM: Yeah.

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That is a good question.

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What we've done is kind of define groups of stakeholders involved in different aspects of N of 1 therapies.

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For example, there are different academic institutions and sight teams that are doing ASO treatments.

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These include neurologist and researchers.

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We have stakeholders, parents of children who have not just rare diseases or ultra rare diseases or we're looking at parents as general as a stakeholder groups.

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We have individuals that have societal experts.

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For example, in ethics.

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People who are oversight expertise.

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For example, institutional review boards or IRB's.

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Stakeholders from foundations and advocacy groups.

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We're thinking you cover all the bases or groups of people that would be impacted in this.

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Then within those groups we pick, like I said neurologist and researchers in those groups.

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That's how we've done this.

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Landbush has thought a lot about this and developing kind of what stakeholders would be the most valuable for us to have as part of this grant.

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>> MEGHAN HALLEY: Yeah

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That's really wonderful.

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I think the question of which stakeholders is a research question in and of itself

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>> INGRID HOLM: We have like 96 interviews.

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We're doing interviews with stakeholders.

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There is a lot of interviews.

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Each one is kind of broken up.

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Within parents and parents with ultra rare eyeses and ASOs and common rare diseases and parents that don't have a rare disease.

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00:40:58.000 --> 00:40:59.000

>> MEGHAN HALLEY: Yeah.

00:40:59.000 --> 00:41:00.000

Yeah.

00:41:00.000 --> 00:41:01.000

>> MEGHAN HALLEY: Yeah.

00:41:01.000 --> 00:41:02.000

Yeah.

00:41:02.000 --> 00:41:03.000

Thank you for that.

00:41:03.000 --> 00:41:05.000

Alison I'm going to turn to you.

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You mentioned Lorem and they have this nonprofit model.

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You know this possible financial model to address equity issues and not put it entirely on families to raise the funds.

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I think that they indicated that is not a long-term sustainable solution.

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Even the resources that they have.

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Are there other financial models out there or approaches that people are thinking about or talking about to increase accessibility beyond Lorem.

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The answer is no, but I thought you would be the one to know if there was something.

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>> ALISON BATEMAN-HOUSE: There is one thing that I neglected to say something about Lorem.

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You mentioned the founders.

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>> ALISON BATEMAN-HOUSE: There is one thing that I neglected to say something about Lorem.

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You mentioned the founders.

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It is important to note that he is the founder I believe CEO or something like that of a company called Ionis.

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Develops ASOs.

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The way that Lorem works if they start thinking that an ASO is going to have a prevalence of more than 30 they sort of hand the product, they hand that idea off to IONIS for commercial development.

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So it is sort of like this mutually beneficial relationship in terms of Ionis provides lab support, you know, et cetera et cetera for the philanthropic foundation.

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But if a case comes in that they say this is too prevalent to us why don't we hand it to Ionis and have a trial and commercialized this product.

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I know in talking to parents of children in this situation that is actually one thing that has been a source of confusion.

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They say that, you know, wait is my child's data being commercialized?

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Is there a chance that I should get royalties of this?

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They're building whatever it is off of my child's data?

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I obviously think one thing that needs to happen in this situation is transparency and who is getting data and that is not the answer to your question.

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The answer to your question is, the one other idea that I've heard floated around and everyone is just sort of said this should happen, but with no real follow up is that oh, commercial payers should see that, you know, this is a value at in the long run because we're treating children that have these dire diseases early on and we're going to be saving them money.

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Where it cost $3 million or so now it will be saving money in the long run.

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It is the same argument being made for gene therapies.

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You have a gene therapy that is $2.3 million or $3.4 million or whatever.

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That is the argument being made.

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Of course the problem is that we're grappling for these expensive gene therapies.

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We're going to figure that out before we figure out the individualized therapy situation because payers are going to want to know that the intervention is effective and that is the problem therapeutic how do you approve someone up front that is going to be an effective intervention

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>> MEGHAN HALLEY: Right.

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Thanks for that.

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I'm going to ask one more question and then go to Q&A.

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If we don't get to your question there is a follow up session after this.

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I know both of you work closely with patient communities.

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One thing that I have been hearing from the patient community, well from various patient communities around this topic particularly when we talk about equity.

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Some frustration, we don't even have the science yet.

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How can we talk about equity and access when we don't even know if these are working?

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Sometimes I see in raising those concerns.

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I'm curious if you've seen that and to what extent do you think we could try to address that concern that patients communities are raising?

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And Ingrid if you can give your thoughts first and then Alison

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>> INGRID HOLM: Yeah.

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Basically the argument is we haven't developed the therapies and worry about equity later.

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That is not the way that we should operate.

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It is just not about trying it in the people who have access first and then trying it to other people.

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We want to give everybody an opportunity to be involved in those developing these treatments.

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You know I think the issue is Alison said it is just lack of access among a lot of communities.

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That doesn't mean that they don't shouldn't have as much of an opportunity as somebody else that has more access.

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It is not about trying it on the rich people first.

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That is not, we're all people.

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I don't know.

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To me that argument doesn't, it doesn't make sense.

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It seems, you know, to me somewhat kind of an unethical position to say try to serve people first and then go to the regular people.

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I think all people have the same want or need to have therapies for a condition that their child has that hasn't been treated so far.

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00:46:58.000 --> 00:46:59.000

>> MEGHAN HALLEY: Thanks Ingrid.

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Alison what are your thoughts?

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>> ALISON BATEMAN-HOUSE: I want to agree with Ingrid and say all lives matter and want people to have equal access.

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The fact of the matter is people don't have equal access to anything.

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They don't have equal access to shelter.

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They don't have equal to education.

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They don't have equal access to food.

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I don't think we should halt process to this field to get some kind of nirvana that we're going to be okay.

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I think I'm okay to get this few as the field develops as long as there is both ongoing discussion as we're having right now about, hey we are only addressing like a very small tip of the iceberg and we need to figure out how to reach the rest of the iceberg as soon as possible.

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And ongoing efforts to identify that rest of the iceberg and reach out to them.

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Right now n Lorem doesn't operate outside of the United States.

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What is happening outside of the United States.

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Maybe it is not n Lorem, but governments or other people do to try to reach those populations?

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We know, as I said earlier lack of access to testing is a huge burden.

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That's a problem in and of itself regardless whether it leads to individualized therapeutics.

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What can we be doing to work on that?

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I think that unfortunately we just have to accept the fact that we live in an unjust society.

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At the same time we should work or butts off to try to address that

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>> MEGHAN HALLEY: Wonderful

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>> ALISON BATEMAN-HOUSE: Ingrid I'm sorry I disagree with you.

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It is not because I want to

00:48:59.000 --> 00:49:01.000

>> INGRID HOLM: Alison what you say makes a lot of sense.

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The people who kind of show up.

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Like Mila's mom kind of showed up.

00:49:07.000 --> 00:49:12.000

You're not going to say that is a problem.

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I do understand what you're saying and in a sense agree with you.

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Some people are going to show up and get started in a group of people.

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The idea is as soon as that happens and maybe one person we really try to expand this beyond just waiting for more people show up.

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I think we're on the same page and understand what you're saying

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>> ALISON BATEMAN-HOUSE: I think those people that show up make the idea available to other people.

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>> INGRID HOLM: Yeah.

00:49:39.000 --> 00:49:40.000

>> INGRID HOLM: Yeah.

00:49:40.000 --> 00:49:43.000

Exactly.

00:49:43.000 --> 00:49:45.000

>> ALISON BATEMAN-HOUSE: When I first read about Mila's case.

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I had no idea that is even possible.

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>> ALISON BATEMAN-HOUSE: When I first read about Mila's case.

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I had no idea that is even possible.

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When you realize there is a possibility out there whether it is through formal educational channels and then you say do I have the resources to go get it?

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>> INGRID HOLM: I agree with you.

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Someone has to start that process.

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I think we're in agreement.

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>> MEGHAN HALLEY: Thank you.

00:50:07.000 --> 00:50:12.000

Thank you both for that great back and forth.

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>> MEGHAN HALLEY: Thank you.

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Thank you both for that great back and forth.

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I'm going to turn to the most popular question in the chat.

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Alison I think you know this is coming to you.

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Ingrid you are welcome to chime in.

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Jennifer asked how do all these concepts regulatory ethical issues related to this.

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With focus on children's potential such right to try in this regard.

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How is it similar to an adults option to try.

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Alison is an expert in this.

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Which I was really aware of.

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I is am curious to hear your thoughts and you Ingrid.

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>> ALISON BATEMAN-HOUSE: Thanks for the vote of confidence.

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I would like to differentiate between to things.

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>> ALISON BATEMAN-HOUSE: Thanks for the vote of confidence.

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I would like to differentiate between to things.

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One is the law and the ideology.

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So the idea that people have a right to try.

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Sure.

00:51:02.000 --> 00:51:07.000

That's what we're saying.

00:51:07.000 --> 00:51:12.000

Once you get the idea that this is a possibility go forth and try it.

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As we've been saying there are numerous obstacles in your way.

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I think we have a moral obligation to smooth that path.

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But to the extend that you can go down that path and there is something available for you.

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There is not going to be something available for everyone.

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There are diseases for which ASOs are not going to be appropriate.

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There are people who their disease, nobody is working on or nobody is interested on working on.

00:51:48.000 --> 00:51:53.000

Patients who will have comorbid disorders and render them not available for interventions et cetera.

00:51:53.000 --> 00:52:01.000

In the extend that you want to try, then go forth and good luck.

00:52:01.000 --> 00:52:14.000

When it comes to the law, I don't think that the right to try law is going to be appropriate in this situation.

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The right to try law basically says, if you have a willing doctor and a willing company they can give you an up approved drug outside of the clinical trial.

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We're already talking about something that is outside of the clinical trial.

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We're not talking about a situation where there is a company involved.

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This whole dialogue is a situation where companies are not involved because there is no profit motive.

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In this situation, the company, which we call the sponsor.

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Is actually the doctor.

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The doctor is wearing the hat of being the sponsor and the doctor.

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In that case the conflict of interest is too much to say I, the doctor and the sponsor think this is a good idea.

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We don't need sign off from any person.

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We don't need FDA or IRB or anything else.

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If I was a hospital administrator, which I'm not.

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I would say that looks sketchy to me.

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I'm not so okay with that.

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I would say we're going to go through the expanded access pathway.

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Which all of these to date have gone through, which entails going through the FDA following the FDA guidance that I talked about.

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Having IRB sign off et cetera.

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So the law, the right to try law, I don't think is appropriate in this situation for, you know, reasons of conflict and lack of oversight et cetera.

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I think the ideology is very much at the heart of this, which is you know there is nothing out there for me, there is nothing out there for my child.

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Let's try it.

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The worst that can happen is A, nobody is willing to help me, which is already the situation I'm in.

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Or B, I have a negative outcome.

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That's basically the situation any time you're faced with the decision of do I want to try a novel therapeutic whether it is in the trial or not in the trial et cetera.

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The major difference is you are working with a higher degree of uncertainty.

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>> MEGHAN HALLEY: Thank you Alison.

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Ingrid I have another question to you if you have anything to add

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>> MEGHAN HALLEY: Thank you Alison.

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Ingrid I have another question to you if you have anything to add

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>> INGRID HOLM: I don't have anything to add.

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>> MEGHAN HALLEY: I have a question if you would elaborate on the number of patients to be treated with an intervention should be treated with the first patient

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>> MEGHAN HALLEY: I have a question if you would elaborate on the number of patients to be treated with an intervention should be treated with the first patient

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>> INGRID HOLM: Oh, my goodness.

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The way that I see it, if the issue is a lot of these are treating a specific patient that has a specific variant.

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It is not the disease.

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The disease is rare but the variance that are really rare, and so I, you know, right now there is you know like with Mila I don't think there is anybody else that has the same variant.

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Most people with Batten Disease most are not going to be a minimal to this treatment.

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I think the way, to me the way to think about it and trying to think about this is as we talked about in the beginning is a class programmable therapy.

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You have this ASO and you can like put different sequences into it to kind of make it work.

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That's what the idea is is that we're so used to thinking of the drug as this is the drug and this thing.

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It acts on the protein.

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It doesn't act on the R NA.

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It acts on the protein.

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It doesn't matter what messes up the protein.

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If it is not there you can add it back.

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Proximal to that I don't think there necessarily needs to be more than one.

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I think a lot of the times there won't be.

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There are obviously a lot of times there are more than one person that has the same variant.

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The idea is that it would be in a class.

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There is a lot of people who can benefit from these therapies even though the actual sequence is different.

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So it is probably not more than one at this point.

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I don't know.

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Alison if you have any other kind of thoughts about that.

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That is the way that I think about it.

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>> ALISON BATEMAN-HOUSE: No.

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The only paint that I want to add is the point that I made earlier about our knowledge right now about prevalence is based on a skewed sample of the global population.

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I think it is reasonable to anticipate that the global prevalence is not going to be what the prevalence is going to be of the disease right now

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>> INGRID HOLM: Yeah.

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I think that is a very good point

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>> MEGHAN HALLEY: Thank you for that.

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We just have a couple of more minutes before I have to turn it back to Sandra to rap us up.

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I wanted to raise this question that actually came in from the orphan drug act.

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They note that it is celebrating its 40th year.

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They're wondering if you think it is time to introduce new legislation given the growth for therapies and rare diseases and if so what would that look like?

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>> ALISON BATEMAN-HOUSE: I think you are probably the expert that can answer that Meghan

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>> MEGHAN HALLEY: I don't know about that.

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Give me your thoughts first if you have some.

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>> ALISON BATEMAN-HOUSE: I have no thoughts.

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>> MEGHAN HALLEY: Yeah.

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You know what it is a really good question.

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>> MEGHAN HALLEY: Yeah.

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You know what it is a really good question.

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There is ongoing discussion about that.

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I think it is not just necessarily the question of these ultra rare therapeutics but the common disease side around negotiating drug prices and coming out of the place in reduction act.

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For those that are not aware of that issue actually is includes any rare therapy that has more than one indication even if the other indication is rare.

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It actually would allow negotiation for the price of those drugs which would significantly impact the Orphan Drug Act.

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I don't think it is necessarily just these therapies but the many different policies and technological changes that are on the way and going to require thought in terms of how well the act will stand the test of time.

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All right.

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Over to you Sandra.

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>> SANDRA SOO-JIN LEE: Oh, thank you, Meghan.

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What an incredible discussion.

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>> SANDRA SOO-JIN LEE: Oh, thank you, Meghan.

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What an incredible discussion.

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Thank you Meghan, Ingrid and Alison for today's forum and the audience for your veryproductive questions.

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We're going to continue the forum in a Zoom room and questions that were not answered.

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The link is in the chat.

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Before we end I want to make sure that you all know that ELSI Friday Forum will be back in November rather than October.

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As our usual second Friday of the month in October will be occurring during the ASBH in bioethics humanity annual meeting in Baltimore.

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We're looking forward to seeing many of you in there.

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We will reson vein on the next ELSI Friday Forum in November.

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In genomics PSTD risk and scientific ethical perspectives and moderated by Josie Johnson.

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It will take the day before veteran's day and take the question about the research and participation of those in the military.

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The registration link is in the chat.

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Please visit ELSIhub.org and subscribe to our newsletter for more details about this event and others.

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Trainees please mark your calendars for upcoming CERA events for you.

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Our second CERA event will be hosted October 3rd, at 3:30 people Eastern on finding and making sense of NIH funding opportunities.

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Again, you can find the registration link in the chat.

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We're going to build off that session with another Trainee Hub event mock review session hosted on October 25th.

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That will go 2:00 to 4:00 eastern.

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Chief it should be an incredibly rich and informative discussion.

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Find the registration link in that chat.

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Finally, you will receive a post event survey.

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I really want to encourage you all to complete this as our organizing committee takes your comments and suggestions very seriously.

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It has informed us how to improve the forums and topics and speakers to you.

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Please do fill that out.

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We will be very grateful.

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With that I hope to see many of you in our Zoom room.

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Have a wonderful weekend.

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Thanks.