Clinical Studies & ADPKD Patient Registry - How You Can Impact Research

Hello everyone. Thanks for joining us. My name is Stu Kaplan.

I am a financial services executive. I have had PKD for 20 years, at least that I’ve known of it. As of the last year, I've been a made member of the Board of Trustees of the PKD Foundation. And that's why I'm here to introduce this panel. As many of, you know the PKD Foundation is committed to creating a world free of PKD, and that is our ultimate goal.

Since our founding, the Foundation has funded over 1,300 research projects and more than $50 million for PKD research. We're committed to fulfilling our vision of ending PKD.

As the largest private funder of the early stage PKD science, we set researchers up for future funder and discoveries in PKD research. No one understands the PKD Foundation’s commitment to research better than Chief Research Officer, Dr. Chris Rusconi, and Director of Research, Elise Hoover.

They're joining us today to discuss the ADPKD Registry, the first Nationwide database of patients with ADPKD and PKD Clinical studies. Both the registry and the clinical studies are key in finding new treatments and a cure for PKD.

Also here today is Dr. Michal Mrug. He’s a professor of medicine in the division of nephrology at the University of Alabama at Birmingham, UAB, where he trains the next generation of physicians and scientists, and co-directs their clinic. He's an expert when it comes to the world of clinical trials for PKD. Since 2009 he’s overseen UAB’s clinical PKD research activities, including the CRISP study and the REPRISE trial. Outcomes of this trial played a critical role in the FDA approval of Tolvaptan.

Panel, I’ll turn it over to you.

Thanks, Stu, and hi everybody. Thank you for being here today. I’m Chris Rusconi, the Chief Research Officer of the Foundation and in this session what the three of us will do is as follows. I'll provide some information related to participation in clinical trials and background on clinical trials. Then I'll pass it over to Dr. Mrug who provide an overview of clinical trials in the PKD space and then Elise will provide a detailed update on our ADPKD registry.

So in the next 10-ish minutes or so, I'll touch on three topics. The background on what clinical trials are, what participation in clinical trials looks like, and then throughout I’ll talk about why participation in clinical trials is so important. So if we go to the next slide, Elise,

This is a slide of the industry-sponsored Pipeline, and Michael will provide a dive into these studies during his discussion.

The points I want to make on this slide and the next is that the PKD pipeline continues to grow, for which were quite grateful. And that's due to the ongoing collaboration between patients like you, between our industry and academic sponsors of these clinical studies and clinical trialists.

And if we go to the next slide, in addition to the industry sponsored studies, there are a number of other academic sponsored studies evaluating both drug repurposing and other non-drug interventions for PKD, some of which the Foundation is sponsoring, particularly in the area of diet and nutrition.

So now we'll start talking, yes, thanks Elise, there's two broad types of clinical studies that are outlined here. There's observational studies and these are studies where researchers analyze Health Data, to find links between, you know, diagnosis, disease progression, symptoms or quality of life. A great example of an observational study is the ADPKD registry.

And then there's Interventional studies and these are studies in which the sponsors are testing new ways to prevent, detect, or treat diseases and then intervention can take many forms. Most often we think of them as drug interventions, but they can be diet and lifestyle interventions, they can be device interventions. So if we go to the next slide, clinical trials, you know real basic level, are human studies and new treatments or therapies. It's how it's How We Understand, whether an intervention we

tested to ensure that it's both safe and effective. And we think about the role of patients in clinical trials. It's super important because one of the largest challenges in facing particularly drug development for PKD is under enrollment in studies. That under enrollment takes two forms. It’s 1) failure to recruit enough volunteers to complete the study, but then, similar but different, another form it takes is really failure to recruit patients quickly enough to make the study completion feasible. And so, as I’ll say throughout this, the role of you the patients play in drug development is extremely important and we're always grateful when you participate.

If we could go, thank you, for the next slide. So we began using the registry to help connect patients enrolled in clinical studies and as part of that we've asked about what your motivation is for participating, and here's what we've learned. I think, I think the vast majority of patients, and the most important takeaway is that folks participate in studies to

Contribute to the advancement of science and treatments, so very altruistic reasons. But there's also other really important reasons patients participate, and that includes access to Specialists and the opportunity to try Innovative treatments as major reasons.

And so while you're not always necessary going to benefit from participating in clinical trials, there are definitely some benefits from participating in clinical studies. So, Elise, if we should go to the next slide, many of you have likely heard somebody say, like, this is a fill-in-the-blank phase clinical study. And so what we want to do on this slide is give a quick overview of what the purposes of these different phases of clinical studies.

So I’ll start on the left with phase one studies. These are generally small studies. If it's a drug treatment, this would be the first time the drugs been tested in humans and the primary role of these studies gain an understanding of safety. Again, if it's a drug study to get an idea of what the appropriate dose might be, and to get that first understanding of how the drug behaves in humans, and if nothing untoward happens in a phase 1 study, treatments will often then Advanced into phase 2 studies. And phase 2 studies are not always, but often the first time, a drug is studied in the patient population for which its intended to be used.

These studies, we consider the moderate in size, and really designed primarily the in an understanding of the drug safety in the intended patient population. But they're also generally designed to gain early signs of efficacy, to help the sponsor determine if a drug should be studied further and taken into phase 3 studies.

Now, phase three studies of the ones we hear most about. These are typically large studies, they're designed to demonstrate that a drug is effective in treating a disease and to further understand the safety of the drug, again, in the Target patient population. And its results of these phase three studies that are submitted to the FDA for review and to determine if a drug should be approved to treat disease based upon the balance of its Effectiveness in treating the disease versus the safety again in the Target patient population.

And not always, but in some instances studies called phase 4 studies will be conducted after a drug is approved. And these are generally conducted to further demonstrate the efficacy of the drug.

So now let's transition into what participation in a clinical trial looks like. So now the first step in participation is informed consent. This is where you, the patient, will learn from the study personnel, exactly what being in a trial will look like so that you can decide from a position to truly be informed if you want to participate in the study or not.

Now, consent forms should include all of the following things listed here. And importantly, they must include the procedures you'll undergo, and the risk for participation along with other important details.

If we go to the next slide, Elise, thank you.

Now, another key consideration for study participation is whether you're eligible for the study based upon what we call eligibility criteria. And these are basically the characteristics that must be shared by all, by all participants.

Some examples are shown here like age, diagnosis, medical history, current kidney function, current medications. And sometimes these will get very detailed in terms of the medical information being asked and that's because treatment studies often require that the patients have a particular risk of progression or stage of PKD in order to participate.

And, you know, I suspect that from the patient perspective, often times these eligibility criteria can be frustrating if they prevent you from participating in a trial.

But they are really important because these criteria are how researchers en sure that the results from the studies will be due to what is under the control of the study and that helps researchers achieve accurate and meaningful results.

So now let's talk about what expectations look like, if you choose to participate. And I think that the main takeaway from this slide is the biggest commitment is your time.

Studies require your time for a variety of reasons.

They can be checkups, they can be visits to the clinic for urine test and throughout the study there's going to be procedures to monitor if the treatment is working and if it's safe. And so really being able to commit your time is critical because the best way to get good results from a study is for all participants to fully complete the study visits and tests so that the so that the trial results in a complete data set.

Now that being said, it's always important to remember as a patient that participation is voluntary. If at any time you no longer want to be in a study you have the right to remove yourself from the study. You can just reach out to your study team and they'll help you leave the study safely.

Speaking of safety, let's talk about risk. So every clinical trial is different. And remember that basically, as we talked about with informed consent, the researchers are required to tell you all the possible known risk before you agree to participate. Now, typical risks include these things like the known possible risks like side effects of the medication for the treatment being studied.

They also include unwanted events during the trial that may or may not be related to the study drug. And then the one universal risk that every study has, is the fail of the treatment to work. Now, that being said, keep in mind that the research team will continuously monitor your health and safety throughout the trial.

Whether you are receiving the study drug or treatment, or whether you've been assigned to receive a placebo or sugar pill.

If we flip to the next slide.

Thanks Elise.

So this is really important.

So study sponsors understand that when you participate in the study you place great trust in them and in sharing your data as part of participating. So they protect your identity and your data rigorously.

So we look up in the top left corner, first when you consent, you're assigned a unique study ID and all of your personal identification at that point is separated from separated, from your study ID. And that's your that personal identification information is placed in a secure location. Then when it comes time to actually start participating in the study, all the data that's collected from you is only identified by your unique study ID.

This is what we call de-identified data.

This data is all stored in a secure location. And again, the secure location where your data is stored is separate from the secure location where your personal information is stored. And then, finally, when data from studies are analyzed, only the de- identified data is analyzed. The people doing the analysis can't relate that data to you directly as a person.

And now there are members of the study team who are able to connect your identification with the study data, but they only rarely do that and it's only in usually fairly unusual circumstances. And that's usually for safety reasons.

So generally, your information, your personal information, and data are never going to be connected to each other.

So now, if we just go to the last slide, ao I wrap up this portion, I want to share this slide to highlight that the development of treatments is really a collaboration between researchers, basic scientists, between patients, between collaborative groups like PKDOC, between clinical scientists that to try list, and the clinical study sponsors. And so in the case of Tolvaptan, many years ago, researchers including our founder, Dr. Jared Grantham, develop data and animals that indicated that suppressing vasopressin may be a potential treatment for ADPKD.

And that was really the critical start to this journey. After that. greater than a decade of clinical studies. some of which are highlighted on this slide, were conducted that highlighted that I think, to me, and to all of us, that highlight the incredible commitment of patients. In terms of both the absolutely numbers of you who volunteered to participate in these studies, as well as the time required for your participation and that commitment really fueled and facilitated the development of this treatment. And so the message I want to leave you with is you are all essential to the development of treatments for PKD.

And so with that, I want to hand this session over to Dr. Michal Mrug, who, among other hats, chairs the Scientific Advisory Committee of the Foundation.

Thank you, Dr. Rusconi for this excellent introduction to this topic.

I'll just follow up with providing specific examples of which drugs and therapeutic interventions are currently tested in ADPKD and ARPKD.

Next Slide. Thank you.

So, this is the slide that you have seen in Dr. Rusconi’s presentation.

It basically shows that Tolvaptan is the drug that has been approved by FDA and they are several additional drugs that are in the pipeline.

What I'll do is I'll cover first those that are most advanced and will tell you about those that are still recruiting patients and those that completed recruitment.

And I'll move from those that are in more advanced phases of clinical testing to those that are in less Advanced testing, phases of testing.

Next slide.

The first drug I would like to mention is actually not on that list and it's Venglustat. That was studied under the staged PKD clinical trial and this study was discontinued earlier this month due to futility.

There was no dangerous side affect. The safety profile remained the same as the beginning of the trial. It was disconnected in you do to futility because the preliminary analysis of available data strongly suggested that this investigation will not impact favorably the disease progression.

So the study was closed and I would like to take this opportunity to thank everybody who participated in this study, so thank you.

So the track that is currently tested is a particle on metal. It targets the NRF to pop a, it's a phase, three, study of safety and efficacy of this drug. The study is recruiting total 550 participants are looking for patients with adpkd that are 18 to 70 years old and have egfr, or renal function, 30 to 90 millimeters per minute.

Also, for the study, the patients cannot participate if they use to tolvaptan or had kidney transplant and as concurrent use of other therapeutics. It's usually an exclusion criteria for most of these studies that are discussed today. So I will not mention that during my presentation, next.

The next drug that is being investigated in adpkd is Lixivapatan.

This drug is similar with its structure to tolvaptan. That is the FDA approved therapeutic for adpkd.

However, it's believed that it may have less liver toxicity.

So the study is now looking to recruit 50 participants that have adpkd and previously had adverse effects to taking tolvaptan in terms of liver toxicity. These participants should be 18 to 65 years old and have egfr more than 20.

Next is a phase 2 study. There are no more phase 3 studies. The phase 2 study was only with Tesevatinib in ADPKD and ARPKD. Both studies are fully enrolled and hopefully the results should be coming soon.

Next is the compound with the RGLS4326. This compound targets micro RNA. There are 17 that controls gene expression of several cystogenic genes, including pkd 1 and pkd 2. It's a phase 1 study. The that is recruiting 27. Participants that are 18 to 70 years old. The diagnosis of ADPKD and egfr 30 to 90. Earlier this month, I believe that there was a press release by the sponsor of this study on nine study participants, and it appeared that they were some favorable outcomes.

The next study is looking at the effects of curcumin, which is a dietary supplement or one of the compounds in turmeric that is used for flavorings. And this study is looking at the effects of curcumin on the function of blood vessels.

This study is fully enrolled, so we are waiting for the outcomes.

The study that is also fully enrolled is the study of metformin. And the metformin is a compound that has been approved by FDA for use for control of type 2 diabetes. And it has been studied in adpkd actually and in two different clinical trials. One in an multi-institutional obtained pkd trial and independently in a clinical study at University of Colorado.

So I mentioned, these both studies were fully enrolled. We are waiting for outcomes.

So the next study is looking at the effects of Pravastin which is an FDA approved therapy would take for hypercholesterolemia. The study is still recruiting. A total of 200 participants are needed at age, 25 to 60 years with adpkd and an egfr greater than 45 milliliters per minute.

Next, the effects of caloric restriction, or time restricted feeding, or intermittent fasting, as how it's called as well at University of Colorado in Denver is looking at fasting. The study is listed here is looking at 30 participants but there will be a new study starting there that is looking for over to 120 participants, basically looking at similar criteria, 18 to 65 years old with adpkd and egfr more than 30. But there is an additional restriction. These patients that want to participate in the study should have body mass index that is more than 27.

Okay, another study that is looking at the effects of caloric restriction is going on in Germany. And looking, basically, the intervention that lead to ketosis. A total of 63 participants are needed for this study. They are looking for patients, 18 to 65 years, old with adpkd an egfr more than 13.

For autosomal, recessive polycystic, kidney disease there are several studies of that are open to participation. And they include several databases or registries that are for arpkd and arpkd-related diseases. Novel imaging in arpkd at the Children Hospital of Philadelphia; novel MRI techniques to evaluate arpkd kidney, and liver disease progression at Cleveland children's; and Tolvaptan in arpkd.

And also, I would like to mention for patients that reached end stage kidney disease and that had a kidney transplant. There is this opportunity to participate in Freedom-1, transplant study. It is not pkd specific but pkd patients may participate. They are looking for 240 participants that are more than 18 years old and they had their first kidney transplant.

They are multiple addition studies and that include the registries or looking at specific parties, or specific manifestations of polycystic kidney disease has and just, you know, I'm not going to go, but I'll tell you that you can find a lot more information and in details on the clinical study tool that was generated by the pkd foundation. You can find it on the pkd foundation's website.

That's all what I had to say.

Elise Hoover will continue, please.

Hi everyone. So now that we've heard from dr. mrug about some of the clinical trials in the pipeline. I like to share with you some details of the foundation's own project.

So what I'll do is go through and talk to you about the patient registry.

Tell you about how we try to return value to participants. And then also talk some more about some of the tools we've created to help connect you to research.

So first of all, what is the registry is a collection of individuals with a given disease so in this case autosomal dominant pkd. And there are some similarities and differences between the clinical trials you’ve heard about. So the clinical trial you saw that you’re limited by those inclusion/exclusion criteria. They ultimately closed. And stop enrolling patients and they also have very clearly predefined research questions that they're trying to answer the study.

However, a registry. We put very little limits on who can participate. So, anyone who has adpkd can join regardless of age or kidney function. We also don't intend to close enrollment. So we hope that the number of people who participate will continue to grow. And we also have the flexibility that we can add new research questions as we go, as we think of new outcomes that we like to study.

But one very important thing that is similar is the participant data is separate from identifiable information, like patient name, address, email, content information. We take that very seriously, similar to a clinical trial.

Now, you may already be enrolled in a registry. Additionally, this is a clinic-based registry at an academic medical center. And what you would do is fill out a consent form to authorize the study doctors to look at your electronic health record and they can look at research questions based on your labs, your test results and other things.

What we've done is we've created you're calling a patient powered registry. So we're getting data directly from patients and because we are getting data that way.

We rely on participants to continue to engage with us.

So to keep coming back filling out our modules and telling us about their disease experience, so that we can see how that changes over time.

And that also means that we get to collect really unique data like quality of life that you can't get from a medical record.

So, the foundation, in 2019, launched our 80 pkd registry and we asked anyone in the US with adpkd to join. It's hosted on an online platform.

And there are two goals, you know, the first, of course, is to create a tool to better understand the disease in the lives of patients. But the second goal is to help connect patients to clinical trials which they may be eligible which we can tell by looking at surveys. So I'll tell you more about that in a minute.

I do want to say that in the foundation's history, we've traditionally funded research and this is the first time that we have created a program to do our own research.

So we're really excited about this program and especially with the covid environment from the last year and a half, it's been really valuable to have something that people can participate in remotely and ultimately the mission of this program is to advance research, help find therapies and a cure for pkdf but using the patient voice to do that.

So you saw this slide before Dr. Rusconi presented this for a clinical trial and we follow the same procedures. So, once someone signs up for the registry, we separate their personal information from their data in the portal and we use IQvia and their whole job is to do these kinds of things and store this data safely and confidentially.

So we assign everyone a unique ID and all the answers to our questions are recorded by that ID and similar to a clinical trial only very specific instances will someone be connected to their personal information. For example, if someone's locked out of their account then I will be able to connect them. But we make sure we do that only in very specific circumstances.

Okay, so this is some baseline characteristics of people who signed up.

We have over 2,000 who have agreed to participate which is really fantastic and they are from a wide range of disease stages. From early disease through post-transplant and one of our goals in this next year, is to work to invite participants to join to create a racially and gender diversity that matches pkdf patients in the community itself.

We can make sure when we were answering these questions we have a good representative sample of people, to make sure we know what that disease looks like.

So I mentioned that the second goal of the registry is to connect patients to trials. So the way we do that, as soon as you sign up the first module, we ask you to fill out is a core questionnaire and that tells us things like latest kidney, function, age, symptoms things that are common eligibility criteria like you saw in those studies that Dr. Mrug highlighted. And so when we have a study that would like to share, we can look at everyone in the registry and see who might match those eligibility criteria and then send them information about the study. One really important thing here is that we want to leave the power in that individual’s hands to participate. So we don't share their names, their kind of information with a study sponsor. We just give the patient details about the study and then it's up to them if they want to reach out and participate. Oh, and in the first year and a half, we've connected patients with five different studies which is really exciting.

So I mentioned to you that we wanted to be intentional in returning value to participants who are enrolling in this program with us. So one of the things we've done, everyone who joins has a individual portal where they will log in and answer our questions. And we have a dashboard tab. And on this dashboard we show some of the data we're learning and we also try to highlight that individuals answer compared to everyone else in the registry so they can see how their answers compare. And we change this up a couple times a year to keep it fresh.

We also do quarterly newsletters. So this is a little more detail about what we're learning. And most importantly, why it matters.

We also talked about what's coming up next.

next. Talk about what we're excited about with the program, and just share a little more with everyone who's participating in the world learning.

And then we also plan to publish an annual report every year. This was our first report. We put it out in March of this year and we went into a lot more detail about the research questions that were thinking about on the data, we're learning. But one thing that was really exciting for me, are the participant testimonials so that not only highlights some of the patient voice but also shares the everyone why we're so excited about this work and why it's so impactful and important to understand the patient journey.

So, if anyone is interested in signing up, this is our homepage for the registry on the foundation's website. You would go to sign in. There is a first time to the registry. Click there and we have four windows.

We ask you to fill out to complete your signup. So we ask for your name and your email and a unique password. We ask for your date of birth, your diagnosis. We asked about your contact information, so we know where the U.S. you are located.

And then we have our consent form. So this details what it looks like to participate in the registry. It is pretty small, no matter the size of your monitor. So I recommend downloading or printing a copy. So you can really read what this program looks like and understand what you're getting yourself into and then you would register there is

There is one last step you would need to confirm your email. So we know it's you and then you are officially enrolled in the registry. The Foundation also has an act alert program. So this is an email list where we ask for where you live and then once we know the new study has popped up in your area. We’ll send you information about that study, you can email. It looks like this we tell you what's important about that study and what eligibility looks like and then how to reach out to the study team.

As Dr. Mrug pointed out, we also have our clinical studies tool. So what we do if you click on find a study on that a page it'll take you to a list of questions and you can fill this out or not. But what it does is it helps filter the studies that are available for ones that might be more appropriate are interesting to you. So you can tell us about your transplant status your age, your current kidney function. And then the website will pull up studies that you may qualify for. And when you click on each study, you can find out more about what is involved with the eligibility are and how to sign up.

So speaking from the Foundation and for all the researchers doing this work, they could not do it without the people who sign up to participate. So thank you so much. Thank you for attending. This is the contact information for research team here at the foundation, as well as my private email address and hopefully we can answer some questions for you now.

Someone included me here but it looks like we have a bunch of questions that I leave to the panel to discuss.

Excellent. Let's actually start out. I have a few. So Dr. Mrug. Can you share with us why it takes so long for a.. to get results from a clinical trial?

Well, so first, the patient needs to be.. all the data he can be completed. And then when it's necessary to clean the data.

So, to look, you know, to make sure if there are any DNA technical errors within the data. Let's say the degree time trade and make sure, you know, that all the data is clean, and these errors have been identified. So after this has been completed, then it’s necessary to go basically through rigorous statistical analysis and try to look at different aspects of that analysis.

So there are some, there are some primary objectives of the study and secondary objectives of the study. So all these need to be evaluated at needs, to be looked at the context of some potential modifiers as well to be able to interpret the data well. And then the once the results are available, it's necessary to review them with appropriate committees

Before the data is actually releases and published. So this is why, you know, it's a lot of work to do after the completion of the study before, actually, the data is analyzed and they're ready to be shared with everybody.

Excellent. Also for doing listening the Foundation tries to keep up on these results as they come out. We have a webpage called, Our Treatment Pipeline. Check it out. Now, Dr. Rusconi, could you talk about what it means for the eligibility criteria, for example, for kidney function, once a therapy is approved? Does that mean that only the people who fit those eligibility criteria can now take that drug?

The not simple answer is not necessarily, getting a lot of echo.. So basically think of the practice of medicine, if the drug is approved, a physician has the right to prescribed that drug to whomever they see the drug fit. However, you know, in the coverage for insurance and in thinking about the use of that medicine, particularly if say, the lower limits of kidney function are going to generally define, whether a drug is safe. And whether there's sufficient safety data, in a person who has low egfr for a drug to be prescribed, because that can often kidney function depending on how the drug is removed from your body may lead to the drug accumulating your body. So it's really important that the drug have been studied in a patient who has a kidney function in the range in which it's being prescribed. Does that answer in a circular way? That is I think the answer to your question.

Excellent. Yeah, excellent. I'm a Dr. Mrug, could you talk about why tolvapan is an exclusion criteria?

Well, the question is, why you shouldn’t tolvapan for studies that are looking at therapeutic intervention. So, that’s a very good question. And of course, it might be interesting to answer, you know whether taking tolvapan and doing that other intervention adds, you know, additional benefit. But first you know it's important to determine if the candidate therapeutic compound has therapeutic benefits alone and for that it is necessary to exclude additional potential modifiers of the outcome and tolvapan as an FDA-approved drug out, there is one of them. So they may expect that once we have more therapeutic compounds that are approved for adpkd, one may start to look, you know, what happens if you have if you take both of them, do you get additive benefit? Yes or no.

But until then the tolvapan will remain the exclusion criteria for enrollment to therapeutic studies and like often, you know, that once patients took tolvapan and it doesn't mean they cannot participate ever. Often, there is a limitation, let's say, for patients, who took a tolvapan, they need to stay off my before three months, but it may differ from study to study.

Excellent, Dr. Rosconi, can you talk about why it's important that these clinical trials and roll a diverse cohort of people? And what some of those challenges are?

Yeah, sure. I mean, I think the most important reason is that

when clinical trials are being run, basically the goal is to collect data to understand whether the drug is safe or effective in use in a given person. And so the really the only way to understand whether it's they're safe and effective for a given person is to have a trial that's as represented as possible as the patient population. So that we know that there aren't differences in the drug efficacy, how the drug is metabolized as a function of someone’s race or ethnicity basically. And so that's why it's really critically important because there are some drugs that have different effects in people who say are identified, as white versus people, who identify as black, or African-American. The real challenge is there are challenges we face oftentimes the delivery of medicine which is creating trust in communities of color and trust in groups that are underrepresented so that they're willing to participate in clinical and clinical trials.

Great Point. Here's a question here that I can take. So we're wondering if clinical trial recruitment changes in the US based on if there is a local pkdf chapter or support group nearby and it's hard to track that because again, the information is de-identified. So we don't want to make sure we're pointing out where patients live who are enrolled in these studies.

But one thing was exciting about the registry is that as we recruit more people to participate and we understand where the adpkd patients live in the country, we can help inform those drug studies to put a clinical study study sites in those areas. So we can make sure that we're putting these studies where the patients are. Okay, all right. We’ve a question about what the pre-phase one pipeline looks like. Do we know how many people are currently doing pre-clinical studies?

You know, I don't, I can start Michael, that's an interesting question.

So I think that it's, it's almost impossible to know the work that's going on inside of a either a private or public biotech company until they disclose a drug candidate. That being said, you know, and at least an interesting data point is we had a polycystic kidney disease outcomes consortium regulatory summit last month that had about 40 percent of the participants were from industry. And I think they came from 22 different companies. And so I think it's I think it's a fair assumption to say that if people spent two days at a meeting, they are probably working in the pkdf space. So I say use that as maybe the benchmark minimally, there's in the low 20s. And I don't know Michael if you have any any additional thoughts there?

Well, I absolutely agree. It's difficult to say because you see only basically the tip of the iceberg, right?

So, but I think that I would encourage you to look for example at the pkdf foundation website and look at the investigators that were funded by the pkdf foundation. And this is like for most of those grants, you know. Still they are sort of in this preclinical phase of studies and you can get an idea and flavor of what type of grants, you know, are judged by review committees as most meritorious and funded by the foundation.

Could you also talk about why we often see pregnant or breastfeeding women excluded from studies?

Yeah. So major concern is that it is new compounds that are being tested in humans without a lot of experience. It's remains unknown what effects there might be on the developing baby and a lot of times if the drug is safe for and out, it may not be safe in the early development. And one of those drugs that are commonly used as, for example, is in a better group of drugs, like glycemic or phosinophile forcing approval that he tried to stop when somebody tries to conceive. So if we do a clinical trial you know typically the we are not aware of potential toxicities and the toxicity is in the mouse or lack of toxicities and mouse or rat doesn't necessarily mean like of toxicity in humans. And this is why there is a stronger time to basically exclude at least in the initial phases of clinical testing, the patients that are pregnant or could become pregnant and the same, you know,and the same, you know, as for breastfeeding.

Alright. Alright another question I'm going to take so we have some interest in mental health impact of pkdf an individual. So the registry one of the quality of life modules we have it's called the adpkd impact scale. It was developed by really fantastic group of researchers who wanted to understand, fatigue, social and emotional impacts of the disease on an individual. So, we have incorporated that into the registry and we ask all participants to fill that out four times a year. So quarterly. And the idea is to follow someone over time and as their disease progresses and see how those answers change. So that's one way that we're starting to really look at that and understand what the impact would like be.

I think we're almost up on time. Dr. Rusconi, anything else you'd like to add?

I think the main thing is just that is just again to say thank you for all who are participating and just to let you know that really, you're probably the most important or one of the two most important parts of developing the pipeline. There's the science, and then there's the people participating. And so just, please, consider participating in clinical trials, if the opportunity presents itself.

Dr. Mrug, any last comments?

Yeah, I absolutely with Dr. Rusconi and what you said about the importance of patients participating. But I would say that it's basically to finally, you know, adpkd patients are empowered to actually to change their future by participation in these studies or their cloak, you know, close ones. And I think a lot of times when you try to participate in clinical study, you are restricted by the inclusion and exclusion criteria. The think that the registry offers is basically for everyone with pkdf can participate and it empowers everyone to change the future. So I would encourage you at least to look at the registry and see what it can offer to you.

Thank you, Michael. Yes, really excited about that program. I do want to add as well that you know, I know that this presentation was pretty adpkd heavy, you know, the the treatment pipeline for AR is a little behind and we do have a few studies that we've listed that we would love for you to look at and consider and we all do our part to support that research. And if you have any questions about what participating looks like or any of our foundation research programs or tools, please reach out to us and things everyone so much for attending.

Thank you, Elise and Michael, and Chris for that wonderful presentation.