All right, welcome everyone. I see that everyone's piling in, so we'll get started shortly. But thank you for joining the Neuromod Prize webinar today. As you get settled in, feel free to say hello in the chat. Let us know where you're joining from. We'd love to hear more about your occupation. For example, if you're a neuroscientist, biomedical engineer, a clinician, or you work in some other field, and then if you do have any questions, please feel free to drop them in the Q&A box. We'll just give it a little more time just for everyone to join and we'll get started right after. All right, so let's go ahead and get started. My name is Alex Leader. I work for Luminary Labs, and we are the primary contracting agency for SPARC NIH. And we are going to be supporting them on the Neuromod Prize competition. So if you have any questions, as I mentioned before, please feel free to drop in the Q&A box. We just ask that you stay muted throughout this presentation. And also, if you do have questions that you would like us to answer in the latter half of this session, please don't use them in the chat. The chat can be for introducing yourself, stating your occupation, stating your interests and fields of study, but we won't be able to access them. We'll prefer for you to post your questions to the Q&A box so that we can best access them. As a reminder, there will be a video recording of this session, as well as a summary of questions and answers that will be shared following the event and it'll be made available on the Neuromod Prize website. So with that, let's go ahead and get started. I'll hand it over to the NIH SPARC team, and Tyler Best who can provide a little more detail on himself and his colleagues.

Thanks, Alex. Tyler Best, I'm a program officer in the Office of Strategic Coordination, which manages Common Fund programs of which SPARC is one of many. I am the SPARC team lead for the SPARC Neuromod challenge. On our team, we have Felicia Qashu, who is the SPARC Program Leader. Felicia, do you want to say anything?

Oh, hi everyone. Thanks for joining.

All right, thanks. We also have Kristi Faulk and who's on our team. She helps manage all sorts of logistics and other things, makes us keep on track and make sure that we know what we're doing and don't go to jail. Andrew Weitz from NIBIB, who's also on the SPARC team. Andrew, do you want to say anything?

No, just thanks everybody.

All right, and then last but not least, Taylor Gilliland, our NIH Challenge Policy Advisor. Taylor, Kristi. I forgot to ask Kristi if you wanted to say anything. Taylor?

Right, I see it's a great turnout. Thanks everybody for your joining.

All right, fair enough. Alex, back to you.

All right. So today, I'm also joined by a few folks from my company, Luminary Labs, Ben Adler, our President Janet Gilbert, and our Senior Director John Roberts. Together, we are going to be the primary contracting partner for NIH SPARC throughout this phase of the Neuromod Prize. So as far as today goes, we'll start with a presentation for the first half and then move it to a live question and answer in the second half. Throughout the whole session, you'll be able to submit questions through the Q&A function, and please use this function so that our team can collect and address your questions. First, Tyler is going to take us through

an overview of NIH SPARC and the background for the Neuromod Prize. And then we will share more details about specific elements of this prize competition, such as technical considerations for solutions and requirements for submissions. Finally, we'll spend roughly 30 minutes throughout the second half on the questions and answers. So with that, I believe Tyler, we will hand it over to you to walk us through the NIH Common Fund.

Great. Thanks, Alex. The NIH Common Fund was rooted in the NIH roadmap from 2004. The Common Fund was formally established by Congress in 2006 to enable goal-driven, trans-NIH research with dedicated funding. The Common Fund program budgets are separate from budgets typical from the NIH institutes and centers. To be supported by the Common Fund, programs must have the potential to dramatically affect a biomedical and/or behavioral research, a catalytic by having to find impact within 5-10 years and be synergistic with individual missions of the institutes and centers of the NIH, as well as cutting across missions and multiple institutes and centers and be something that no other entity is able to do on their own. And SPARC is one of these many Common Fund programs. Next slide please, Alex. The NIH SPARC program is an eight-year Common Fund program whose aim is to accelerate the development of tools and technologies that would drive therapies to precisely modulate nerve activity in order to improve function. The SPARC program has just finished up, is just finishing up its first five years and is transitioning to a second phase, which will span the last three years of funding of which I'll describe shortly. If you have more interests or want more information about the SPARC program, you can go to the sparc.science web portal where have data and tools and models. Simulations have been developed by SPARC teams over the last five years. Next slide please, Alex. The SPARC program in phase two, in its second phase during these last three years is divided into primarily three focus areas or spaces: SPARC-V, SPARC O and X. So called giving a voice or a vox, V-O-X, to SPARC and biomedical neuromodulation technologies and techniques. SPARC-V is primarily focused on mapping the human vagus nerve, both anatomically and functionally. SPARC O, O stands for open source where we're trying to fund the development of open source technologies needed to safely and effectively impact and modulate the nervous system. And finally, the SPARC X. This is our prize competition of which this webinar is focused on. Altogether, these are hoping to build on knowledge and collaboration that we're fostered through the initial phases as well as collaborate in the future to drive towards therapeutic capabilities. Next slide, please. Why a Neuromod Prize? Our Neuromod focus or, sorry, our Neuromod Prize aims to bridge the gap between early stage research and clinical application for these targeted neuromodulation therapies. And researchers have developed many devices to target only a few known neuromodulation pathways, but many of these devices are never directly compared, but could be tested across multiple pathways to assess whether or not they are paired with the best pathway to optimize therapeutic benefit. There's promising early stage research demonstrating that selective targeting and regulation of multiple autonomic functions of the peripheral nervous system. However, these novel methods have not necessarily left the lab, so to speak, in some cases. Treatments and therapies that can regulate multiple functions would be an innovative addition to the field that significantly would move the needle on what's possible for patients. Next slide please, Alex.

Sorry about that, so I'll take over from here. I'm going to walk through some of the primary elements of this competition in more detail. So the Neuromod Prize, as Tyler mentioned before, is part of a goal to bridge the gap between early stage research and clinical use. Really making sure that innovative neuromodulation therapies are made accessible to patients. This competition is planned to span three phases over the course of three years. Specifically, it seeks solutions that are capable of independently regulating two or more desired autonomic functions of the peripheral nervous system without unintended effects. The first phase of the competition is calling on all eligible participants. This includes scientists, engineers, clinicians to submit novel concepts and then plans for development. Participants to the competition are going to be asked to submit a concept paper for phase one. This paper should be a maximum of about 15 pages and should describe therapeutic approaches, like plans for conducting proof of concept studies, rationales for therapeutic use, and expectations for any clinical impacts. The planned second phase of competition is going to exclusively invite up to eight winning teams from phase one to build on their submissions by conducting proof of concept studies. That phase is anticipated to begin in summer of this year, and then conclude in summer of 2023. The planned third phase of the competition will again, exclusively invite winners from the previous phase. And it'll ask them to build on their submissions and their proof of concept studies by conducting IDE enabling studies. Phase three is anticipated to begin in summer 2023 and then conclude in summer 2025. So phase one is eligible to, or sorry, is open to all eligible participants with the winners exclusively being invited to compete in future phases. Future phases of this Neuromod Prize, we'll be possibly awarding non-monetary awards and supports for competitors and participants, but any sort of monetary award is subject to the discretion of the NIH and the availability of appropriated funds. So throughout phases two and three, the competition may provide technical assistance. For example, mentorship, government feedback, networking opportunities to help teams accelerate and develop their solutions. So phase one of the competition launched on January 18th of this year, all submissions have to be complete for phase one and submitted by 4:59 PM Eastern time on Thursday, April 28th of this year. We will have another virtual session on Monday, March 7th, to discuss some of the more specific technical considerations that you might be encountering. And phase two launch will be planned for late summer of this year. So the primary component of the phase one submission will be a concept paper. And like I said, 15 pages is the suggested maximum. This concept paper should summarize your solution and any proposed experiments that will be relevant to it. We recommend visiting the submission form, which is available on the competition website to see more details on the suggested format, the guidelines, the overall requirements. And we also suggest registering your team in advance, well before you have to submit your concept paper. The proposed solution that you are submitting should be describing a targeted neuromodulation therapy that is tunable, accurate, and precise. It should demonstrate an ability to quantitatively assess and control multiple on-target and related off-target functions. This submission should describe what the proposed solution is, what is already known about the solution's approach, why it's impactful and innovative, and how the corresponding experiments that you might have will be conducted. While they do not need to adhere to a specific structure or order, we do recommend that concept papers respond to the stated prompts that are available on the submission form. These prompts cover four considerations, which I have on the slide right here. It's therapeutic approach, the performance, basically describing how your solution is

capable of achieving its targets, the proposed or estimated impact of your solution, describing any sort of potential therapeutic applications, such as the specific conditions that it's going to treat. And then finally, the fourth category, plans for development. Describe the current state of clinical maturity and the development of your solution. So after phase one is concluded or the open submissions period is concluded, we will begin a judging process. The submissions will be evaluated by a judging panel composed of federal employees from across NIH and potentially other government agencies. This judging panel will select up to eight phase one winners based on the official judging criteria, which is publicly available on the website. This is also going to be subject to a final decision by NIH. When evaluating the submissions, the judging panel will assign a submission score of one to five, five being the highest, one being the lowest for each of the five criteria that are listed on the site. Together, that'll be a maximum of 25 points. Depending on the volume of entries, submissions may initially be evaluated by a multidisciplinary group of technical reviewers, including experts in biomedical engineering, in neuroscience, and systems biology and other disciplines. So I'm going to hand it over to Tyler now to talk us through the judging criteria in more detail.

Thanks, Alex. Our judging criteria is based on five primary categories. The first of which is targeting performance or the extent to which the concept could achieve or exceed the necessary requirements for selectively targeting two or more autonomic target indications with a high degree of tunability, accuracy, and precision. I'll go over the tunability, accuracy, and precision in the following slide. Second judging criteria is off-target mitigation. We're interested in the extent to which your concept will address potential adverse effects of the proposed approach, and also identify clinically relevant risks and ways to monitor those off-target outcomes related to the target function. A third judging criteria is the technical readiness or the extent to which the concept indicates readiness for proof of concept study design, as well as how well you identify the barriers to clinical translation and articulate the next steps to bridge those gaps. Fourth criterion is the scientific contribution, the potential that your concept has for advancing our understanding of the field of neuromodulation. How well your concept will help underscore and uncover underlying mechanisms that are going to yield additional insights into targeting specificity. And our fifth criteria is the clinical impact or the extent to which your solution addresses pressing therapeutic needs, how well it's translatable or how well it enhances or replaces existing treatments, as well as how that treatment could benefit the patients or our practicing clinicians. Next slide, please. Our performance considerations, as I mentioned, I'd address the tunability, accuracy, and precision. These are, in hopes that your target and your protocol for targeting a function can be tuneable, such that if you can adjust the parameters, pulse with amount of current, if you're using electrical stimulation, current steering, et cetera, to adjust or titrate the outcome of your function, such that you can ramp that function up or down in such ways that you can precisely generate a function within a range that's desired therapeutically. The accuracy is how, if you imagine those targets, you're shooting a bow and arrow. Accuracy is how well you're actually hitting your target and how well you're hitting that center bullseye. Precision, you know you got to hit that all the time. You can have a cluster of arrows up in one quadrant of a target, but you may not be accurate. You have to also then get within your bullseye. And so the accuracy and precision is both how well you can specifically target your function, desired function, and how often and how replicable you can do that on a day to day

basis. Next slide, please, Alex. The target performance considerations, we are using these as part of the measurement of the outcomes as well. We want a quantitative assessment for both on-target and off target events. And you may, in some cases, an off-target effect of one strategy may be an on-target effect in other contexts, but often remains incompletely characterized. We want you to measure the biomarkers in such a way that all of the biomarkers that are targeted and measured are directly as a result of the nerve you're targeting. So for example, if you're measuring gastric function, gastric motility, you wouldn't be necessarily measuring or stimulating the pelvic nerve, which doesn't necessarily innervate the stomach or vice versa. If you're going to be measuring bladder function as one of your biomarkers, then you should be targeting the pelvic nerve and vice versa, et cetera, et cetera, through all the different potential autonomic nerves in their target organs and functions. We define the biomarker as a characteristic that is measured as an indicator of normal biological processes. And you should be aware that those are relatively easy. Well, not easy to measure, but relatively standard and therapeutic care. If a solution stimulates, oh, I already mentioned this part. Sorry, nevermind. That's it for this slide, please. Alex, next. So our solution needs, as I mentioned before, we want tunable, accurate, and precise targets that are capable of completing investigational device exemption by the end of the three phases of the program. These targets and these solutions need to address pressing therapeutic needs and be translatable for immediate or near-term in-human use. And finally, as a reminder that they need to be enhancing or replacing potential or existing treatment, and that would benefit patients and practicing clinicians. Thanks, Alex.

All right, so I'm going to cover in the last section of our presentation time just how to enter, including some eligibility and IP and general federal requirements. So as far as eligibility goes, the Neuromod Prize is open to individuals, teams, entities, and we want to note that only one prize payment will be issued to each winning individual team or point of contact for an entity. Any subsequent distribution of prize funds to other team members or entities is at the prize recipient's discretion and is not the responsibility of the NIH. So another requirement to note though is that every team must be led by a U.S. citizen or a US-based organization. Non-US citizens are still welcome to participate as long as they join a qualified US-based team that is led by a U.S. citizen. A participant who registers on behalf of a private entity is eligible to win a prize, provided that the entity is incorporated, and it maintains a primary place of business in the United States. Also, assuming that all of their eligibility requirements are met. Moving on from that, as far as intellectual property goes, each participant will retain all other intellectual property rights in their submissions as applicable. To participate in the competition, we ask that each participant warrants that there are no legal obstacles to providing a non-exclusive license to the federal government. Participants will not be required to transfer their intellectual property rights to the NIH, but participants must grant to the federal government the non-exclusive licenses that are explained further within the rules, terms and conditions of the website. What the NIH requests is that participants in the competition grant NIH license to reproduce, publish, post, link, share, and display publicly the submission title, the headline, and the executive summary of the solution. As far as federal grantees go, federal grantees and recipients of cooperative agreements and other kinds of awards are eligible to participate in this competition, but they may not use federal funds from a grant award, cooperative agreement or OT award to develop their submission without, unless the use of such funds is consistent

with the purpose, terms, conditions of their grant. For the purposes of the original grant cooperative agreement, you can refer to the rules, terms and conditions that discuss the uniform administration requirements, cost principles, and audit requirements for federal awards. More information can be found on the RTC, the rules, terms, and condition page. So within mind collaboration for those who want to speak with or possibly join another team, we recognize that this is a great strategy for success. And in fact, success in all phases of the Neuromod Prize will require a breadth of experience and expertise. And participants are encouraged to consider how they can share that expertise and collaborate with one another and maybe expand their existing teams. So if you're interested in joining the Neuromod Prize Solver Community, please fill out a form on the Solver Community page. By filling out this form, you agree to share the information with other members of that community and you'll receive their information in return. We're going to send this list to everyone who signed up, the list to potentially sign up for the Solver Community. And so if you want to be first on that list, we recommend signing up shortly after this session. Please note that the Solver Community is not the same as registering for the prize competition itself. For example, you have to register for the prize competition in order to compete. You do not have to register for the Solver Community to be an eligible participant. This is a separate optional resource for participants if they choose to use it. I should also note that this is also different from signing up for the newsletter or any other sort of updates like this webinar. So in addition to the Solver Community, we also have a whole bunch of other resources that are available on the Challenge website. This contains helpful links that can assist you during the development and refining of your submissions. In a nutshell, the resources page covers details about the NIH SPARC program, informational resources on general advancements and barriers in the field of neuromodulation. It covers websites and platforms to support development, regulatory resources for neuromodulation therapies, and then also the technical performance considerations that Tyler had mentioned previously. So if you're interested in participating, we have outlined here four steps that we recommend following. We first suggest that you register your team on Luminary LightBox, which is the form and platform that the competition is going to rely on to collect and evaluate submissions. You can reach that registration area by clicking the Submit link in the top right of the website, or when you see this menu at the bottom of most pages, it will also have a link to register. We also recommend, second, reading the full details about the prize, including and especially the rules, terms and conditions. A lot of the items that I've discussed today are covered on respective pages throughout the website. Then you may consider exploring the resources on the resource hub that I had shared on the previous slide. And finally, when you're ready and you think you have a full grasp of what the submission requirements are, we invite you to enter your submission by April 28th. And again, that is by 4:59 PM Eastern on Thursday, April 28th. And you can also do that through the Submit link at the upper right hand corner of the website. So Tyler, I'll just hand this over to you if you want to touch on any other initiatives.

Yeah, we wanted to also make you all aware that we have other, the SPARC program has other funding initiatives currently open. The first is part of the SPARC-V or the human vagus nerve mapping and physiology initiative, SPARC-V. We have the REVA or reconstructing human vagal anatomy. Notice it's a solicitation for contracts to reconstruct the vagals in high resolution. We also have the VESPA or VNS Endpoints from standardized parameters.

U54 cooperative agreement that is asking for a large multi-clinical study to study a common vagal nerve stimulation protocol and its effects on multiple organ systems. Our SPARC O or open source neuromodulation technology, RFA recently closed a couple weeks ago, but that should be of interest to many that are in the device community. And then of course the SPARC X, our Neuromod Prize, which this webinar is the primary focus. And again, the web link there is neuromodprize.com. And as Alex mentioned, the submissions are due April 28th of this year.

Great, thanks, Tyler. So we are right on time to transition over to some Q&A. So I will conclude our presentation half of today's session. And I will start off by, we had several questions that we had received in advance of the webinar and also in the Q&A function today related to the scope of targeted neuromodulation in the context of this competition. So that could be, does targeted neuromodulation have to apply to internal organs only, or could it be applied to the peripheral nervous system? For example, treating chronic pain or plantar fasciitis. So Tyler, I'll hand it over to you to answer that question.

Yeah, those are some good questions. We've received a number on that kind of thread is what is the scope of what we're actually looking for? Is my device or therapeutic target of choice within the scope? And we refer you back to the actual text of the announcement wherein we mentioned that we are in particular seeking solutions that "describe methodology for targeting and modulating autonomic functions in the peripheral nervous system." So if you can sufficiently justify and provide rationale that your target of choice, that your organ function or whatever, meets that two or more autonomic functions in the peripheral nervous system, then that would be within scope of the competition. The SPARC program, the S-P-A-R-C stands for Stimulating Peripheral Activity to Relieve Conditions. So we don't want to step on any toes of the BRAIN initiative here at the NIH. So the BRAIN primarily encompasses the central nervous system. Our focus is on the peripheral nervous system. So any centrally targeting devices are likely going to be out of scope for this competition.

Great, thanks. And I forgot to mention that we cannot answer inquiries about specific solutions, but we can talk about the general technical considerations of submissions in general. So another question we received was, would deep brain stimulation or spinal cord stimulation fall under the criteria for this competition, or would they be considered localized to the central nervous system instead of the peripheral nervous system?

The DBS would be outside of the scope of our competition, because we are SPARC. Spinal cord potentially has that option within the SPARC program. We have been stimulating or funding efforts that do target the spinal cord. However, remember that we are looking for targeting two specific autonomic functions. And so being able to do that in the spinal cord, you need to be able to justify scientifically and technically why your approach would meet those goals and objectives.

Great. And another question we received was, is the eligibility of this program exclusive to surgical implant devices, or is there openness to approaches that are based in transcutaneous or microsystem stimulation?

Again, I refer you to our tunability, our precision and accuracy technical, what's the actual category for those three things? I forgot, but anyway, it doesn't have to be a surgically implanted device. It can be transcutaneous of different biophysics modalities, but remember that the more precise, the more accurate and the more tuneable your method is, the more likely it is to be successful in the judging criteria.

Thanks, Tyler. And another one is, would you consider up and down regulation of the same function? Would that be considered as two independent functions? For example, like the ability to increase gastric transit time?

Again, I refer to the tunability aspect of that. Up and down function within the same function is still the same function. It's just that you have the ability to tune that. And so being able to tune gastric motility or gastric transit time higher or lower, that's the same function. And we are looking for solutions that do that in addition to a second autonomic function.

Great. Now, is it possible to use an existing device which has its safety already demonstrated in human studies, in human subjects?

Absolutely. We encourage that.

Okay. And we also received a couple questions about the fidelity that we're looking for. First, are you initially looking for animal model proof of concept first, or are clinical studies investigating neuromodulation eligible for this mechanism?

At this stage, anything that can show that you can specifically and independently tune two or more peripheral autonomic functions regardless of the species involved, that would be within scope. We anticipate that doing that with such a high degree of tunability and precision and accuracy may be less available in human studies at this time, but we don't claim to know everything that's going on in the field. And if you can demonstrate to us that your approach meets those criteria, then that would be within scope of the competition.

Great. Now, is this competition only open to those who are already participants or funding recipients of the NIH SPARC program?

No, absolutely not. We encourage those from all walks of, from everywhere, outside, inside of SPARC. As Alex, you kind of went through the funding mechanisms as well. If you have federal funding for this, for similar studies, you need to read the rules of the challenge to apply, but there is no restriction on a prior SPARC award.

Great. Now, in that same vein, as far as eligibility and the types of participants go, do you have an ideal composition of a particular team, or is there an ideal academic industry mix, or is it up to the participants themselves?

Entirely up to the participants. We make no claims on what your team composition should be. Just know the requirements of the competition and meet those with the best of your ability.

Great. We also received a number of questions about non-US individuals and entities. To reiterate, our prize authority requires that each team is led by a point of contact or team lead or just an individual who is a U.S. citizen. But I think I can just address this real quick, but we want to make it very clear that to be eligible to win the prize, an individual submitting on their own behalf or named as a team lead must be a citizen or permanent resident of the United States. If an entity is named as the team lead, it must be incorporated in and maintain a primary place of business in the United States. Non-US citizens and non-permanent residents can participate as a member of a team that otherwise satisfies all the other eligibility criteria. So non-US citizens and non-permanent residents are not eligible to win a monetary prize in whole or in part. Their participation as part of a winning team, if applicable, may be recognized when the results are announced. And that brings me just to another point to add is that as I had mentioned previously, it really is up to whoever is designated as the team lead or team captain that they can decide how to allocate the prize money at their own discretion. Excuse me. So moving on just to another question on submission technology, can a submission use technology that is already developed on a federal contract, as long as the studies that are directly supported, sorry, as long as the studies that directly support the competition submissions are not charged to a federal contract? And maybe Taylor-

Yeah, I was going to say Taylor maybe ought to answer that one.

Sure, yeah. The short answer is yes. Presumably, if you are working on an existing federal contract, this competition would likely not be included in your statement of work. However, of course, if you are not directly using active contract funds to develop the submission to this challenge, then certainly, that is permissible.

Great.

So we had one question, I think on techniques of neuromodulation that you could answer, Tyler. Could the targeted autonomous neuromodulation, basically the therapeutic approach, include some irreversible techniques, such as denervation using RF ablation to relieve chronic conditions?

So one of the judging criteria and considerations we're looking for is how readily available this or readily translatable and how easily this could be moved to a pre-IDE or IDE study. There has to be justification for that approach and getting approval from regulatory bodies. So any sort of ablation or permanent effect on the nervous system or other organ systems needs to meet that readily translatable and near to in-human use kind of criteria. If you can sufficiently justify that approach and why you think regulatory bodies would be willing to let that be approved, then describe that and the risk mitigation as asked for in the announcement.

Great. We also have a question about preclinical animal studies for proof of concepts. Well, I think first off, in the proof of concept stage, can preclinical animal studies be used?

Yes, certainly.

Yeah. Yeah, there's just to elaborate. There really is no specific type of data that we are requiring here, but in phase one, we ask that you just describe how your solution is capable of achieving the target's outline and the target performance considerations. And you can use any applicable evidence that you're able to provide to accomplish that. So another question I'm getting from this is, sorry, I'm just seeing, we have a lot of questions about non-invasives and wearable approaches, and I know that we just touched on this a little while back, but yeah, as long as you can achieve that tunability, accuracy, precision, and the technical performance considerations, I want to reiterate that we're not here to prescribe or prohibit transcutaneous by any means. It's really about the meeting of those considerations and criteria. So we received a question that the FDA requires one to develop something for a specific therapeutic purpose. Would there be a concern that developing a device to influence two specific autonomic functions would be problematic and less modulating, both impact the same therapeutic indication?

So could you repeat?

Yeah, I can.

Or let me find where it is in the Q&A and read it. Okay, specific therapeutic approach. There's concern that developing a device to influence two specific autonomic functions would be problematic unless modulating both impacts the same therapeutic indication. Yeah, that's right what the FDA does require. Two autonomic functions could be within the same therapeutic area, or they could be outside in separate therapeutic areas. We're not going to dictate that, but also recognize that the FDA also has its regulatory rules and regulations and moving to in-human use in the near term would require you to consider the regulatory regulations.

Great. So we received, and I know we touched on this, but I just want to make this absolutely clear. We received a number of questions about the scope of the modalities for neuromodulation, such as ultrasound and light therapy. Just want to make sure that we're all clear on this, that there is no prescription around the kinds of modalities that could be used here as long as they are viable for FDA regulation.

Exactly, Alex, as well as the ability to have that precision accuracy and tunability.

So there's another question about the prize disbursement. And I want to, I think, maybe either Tyler or Taylor could jump in here. It was asking if each winner is granted a hundred thousand. We expect winners will have a share of the up to $800,000 prize purse for phase one. But some of the specifics about that will just be at the discretion of the NIH.

That's right.

And in a similar vein to a previous question, we had one about the amount of prelim, sorry, preliminary data that is required to produce in a particular submission. There is no threshold or minimum for data. We really want to leave it up to you to determine just how much data is

needed to demonstrate meeting of the technical performance considerations, meeting of those judging criteria. And just the general guidelines of tunability, accuracy, precision.

Exactly, Alex. There's no requirement for level of preliminary data, as long as you justify scientifically and technically your proposed solutions.

So we have another question on just the general motivation of the challenge scope and the overarching goal of modulating two functions independently. So I'll ask, is there a particular motivation, or just a general background that you can share on what brought us to this point of regulating functions independently?

Yeah, it's primarily driven by the fact that for the most part, what we have seen through our funding of awards and through the community in general is that oftentimes, groups will target one function and record and monitor their desired outcome from that function. And sometimes, not being able to or ignoring many other functions. And so we wanted to push the boundaries to be able to monitor not only the target function, but off-target effects. In addition to making this more of a challenge or more of a prize competition, pushing the boundaries of the limits for what a targeting a neuromodulation approach can do, we added that second function. Many of you are fully aware that you can target and affect one function, but doing that independent of another function is where we thought the challenge in this and was worthy of this prize competition.

Great. Well, we do have a question on small molecule drug-based solutions, basically a non-device solution. Is that something that is within scope or are there any requirements around that that you would like to note, Tyler?

So a small molecule pharmaceutical, pharmacological approach potentially could be. However, we're primarily focused on the neuromodulation side. So that's actually interacting and interfacing with the nerve. If your approach can, scientifically and technically justify that your small molecule or pharmaceutical approach does that, then that could potentially be within scope. Also, remembering that the tunability, part of that tunability is based on time. There has to be a temporal accuracy as well as precision involved in neuromodulation that may or may not be delivered through traditional or non-traditional or traditional pharmaceutical small molecule approaches.

Great, thanks. Now, we do have a question about the commitment for phase one winners and what they're expected to do if they move on, if they choose to move on to phase two. So in a nutshell, are phase one winners committed or required? Well, I should say, are they committed to submit proof of concept experiments in phase two?

No, not necessarily. If you are one of the winners from phase one, by no means are you obligated to develop proof of concept in animal studies in phase two. You can take your prize money from phase one and walk away. We don't necessarily, we hope you keep on going because we are limiting the phase two competition to phase one winners. If that's the case, we have no way of mandating you, you keep on participating.

And I'll just add another note on that. I know I talked about the prize pool in a prior slide, but similar to the phase one prize pool, the phase two and phase three prize pools are allotted to

or designated for winners. And they will receive up to a share, sorry, they'll receive a share of up to the total amount of that prize pool. And the nature and the details of that prize pool are subject to the availability of appropriated funds. But just to reiterate, the phase two prize pool is planned to be four million. And the phase three prize pool is planned to be five million.

Yeah, and Alex, I'd like to reiterate there that these are planned stages. The actual scope and boundaries and limits and rules of those competitions for those prize pools is still being planned and formulated. So those may change as we move through and into those phases.

Mm-hmm. I'm seeing a question here about tunability. So when we were describing tunability, they just wanted to clarify what we mean by that. Does this concern anatomic location such as affecting the sympathetic system in one site, or maybe the parasympathetic system in another? If you could just provide a little more clarity on what tunability means in this context.

Sure. We envision tunability more on the adjustment of the parameters and protocols for delivering the neuromodulation. If it's in two different sites, like on a sympathetic or parasympathetic nerve or target, you'd have to be able to independently control those. You'd have to consider how that's going to be translatable and more applicable for near in-human use. If I may use the example of an implanted device, if you're implanting two devices, the technological and regulatory hurdles for getting two implants versus one is different and may impact the relevance for a proposed solution in that way. And that's for implanted devices. For transcutaneous devices and so on and so forth, again, looking at how you're able to tune, be precise and accurate is going to be the judgment criteria there.

Okay, thanks, Tyler. We do have a question about eligibility. Now, is one individual or just one team, are they allowed to submit multiple concepts over the course of phase one? And I'll defer to Taylor.

Yeah, so participants, whether you're an individual, a team or an entity, you are not limited in the number of entries that you can submit. However, each entry submitted by each participant in this challenge must be substantially different from any other entries coming from that participant. So yes, you can submit multiple entries, but they have to be substantially different in order to be considered.

Great. So there's just a question about the on-target or what it means to be an on-target function. And then furthermore, multiple on-target functions. So to clarify, we received a question asking, is the expectation to affect two or more on-target functions with one stimulus, or can there be two separate stimuli? And does the modulation of those two independent functions, organs, what have you, does that have to occur at the same nexus point of the autonomic nervous system, or can it be at two separate points?

Again, two separate points could be a potential solution. Just remember, the regulatory, potential regulatory hurdles that would be involved in that approval down the road. Again, we're not anticipating or expecting you to do clinical trials in this phase, phase one, phase

two, or phase three of this prize, of the Neuromod Prize, but moving towards an IDE. So keeping those regulatory requirements in mind when you're using multiple sites, multiple locations is necessary.

Great. There is another question about just what this means for investigational device exemptions come phase three, because as we mentioned before, the FDA typically grants IDEs for a specific function indication. Would it be possible? The question we have is like, would it be possible that multiple IDEs would be a result of the device that successfully can independently regulate multiple functions?

Let's see, so state that again, Alex?

Yes. So given that the FDA might grant an IDE for one particular treatment for one particular function, the solution or device that can target multiple functions, is it possible that that might result in two separate IDEs?

Yeah, I think I would have to leave that up to the FDA on how to interpret that and decide whether or not it needs two IDEs or not.

Okay. We also have a question about defining the amount of team members that will conduct phase three, phase two clinical experiments. When the time comes, we do not ask, well, first off, we do ask that you name all team members for this phase and share their expertise when you submit and you register on our platform. But we also expect that winners will likely add to their teams as the development process continues, especially because it's an exclusive invitation to participate in phase two or three. We know that promising ideas that might be out there might want to collaborate with other teams, so we leave that open for you to adjust your team size as if you move through the competition stages.

It's primarily up to you on how you distribute the prize winnings. We are not, NIH does not dictate that. We give you the award, and it's up to your team and whoever's leading the team to distribute the prize according to how you've internally agreed.

Yeah. So I'm looking at the time. It looks like we have about two minutes left. So I'm only going to answer a couple more questions. So first, I'm seeing one about the general scope of using devices that are out in the market already. So are we looking for improvements on existing devices or only new devices? And how much, we'll start with that part of the question first.

Any device at any stage is open game, whether it's prior developed in your lab for use on your animal of choice, or if it's already clinically used by the community. That's also open game.

And I'll add that the operative word in the scope of this challenge is approaches. If we're really, these proof of concept papers are outlining an approach to a neuromodulation treatment. And then just there's a criterion that can speak to this, the potential for this concept that you're proposing to advance the field of neuromodulation by deepening our understanding of the underlying mechanisms and yielding additional insight into targeting specificity. So if the approach can borrow on an existing device but really makes that

significant scientific contribution that really deepens that understanding of what's possible, that is part of the criteria that we're looking for.

Great, well, I want to note that there's probably a lot more questions out there, and we appreciate your interest in the Neuromod Prize and all your thoughtful questions. I'm sorry that we were not able to get to all of them today, but I do want to acknowledge that we will be providing a recording of this webinar and making it available on the competition website, as well as we will be updating the website with frequently asked questions, such as the ones that we saw here today to add any more clarity that might be helpful to you and the rest of those who are trying to participate. So with that, I want to thank the NIH team for joining us. And thank you, Tyler, for not only presenting, but also these very, very thoughtful and helpful answers to these questions.