The Upcoming Externally-Led Patient-Focused Drug Development Meeting on Cerebral Creatine Deficiency Syndromes (CCDS)

Welcome

The Externally-Led Patient Focused Drug Development (EL-PFDD) meeting is an exciting opportunity to inform the U.S. Food and Drug Administration (FDA) and other stakeholders about the patient perspective of living with CCDS

Make Your Voice Heard!

This is your one-time opportunity to share your story of living with CCDS with these important decision-makers

It doesn't matter where you live, where you are in your journey, what matters is your story

The primary goal: to hear directly from patients and caregivers about their perspectives on living with CCDS and their experiences with treatments

Outcome: improve the development of new drugs in the research pipeline and inform the context in which regulatory decisions will be made for new drugs for CCDS

Sponsors

ultragenyx

Ceres Brain Therapeutics

Webinar Housekeeping

- Today's webinar is scheduled to last approximately one hour
- All participants will be muted to allow the speakers to present without interruptions
- The webinar will be recorded and available for later viewing on https://www.creatineinfo.org/el-pfdd
- To ask questions during the webinar, please use the Q&A box at the bottom of your screen and we will answer them at the end of the webinar.

What is the Purpose of Meeting?

To educate the Food & Drug Administration (FDA) and other stakeholders on:

- ✔ What it is like to live with CCDS
- ✔ How has CCDS impacted your life
- ✔ How you are currently managing CCDS
- ✔ What a meaningful treatment would look like to you

Why Should I Participate?

- Opportunity to have Your Voices heard
- The FDA approves all treatments for CCDS and needs to know what is important to you
- This knowledge will impact their decision-making, and lead to better treatments and potentially faster approvals for CCDS treatments

Why Now?

- The **Patient's Voice** has historically been absent from the drug development process
  - ✔ Until a drug was approved by the FDA (sometimes to treat symptoms not important to patients), or
  - ✔ A clinical trial was failing and the drug company or FDA wanted input from actual patients to understand the problem
- Want your Voices heard at the beginning of the process and throughout
- Stakeholder engagement = FDA Priority
  - ✔ Initiated a *Patient Focused Drug Development Program* to learn about disease impact on patient's lives <u>both</u> from patients and their caregivers

The EL-PFDD Meeting on CCDS & Your Role in Drug Development

What Is It? and How Can You Participate?

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Hyman, Phelps & McNamara PC

Overview

- Background on FDA & Drug Development
- Introduction to Patient-Focused Drug Development & Role of Patient Voice
- Overview of the EL-PFDD Meeting
- Guide to Participating in the Meeting
  - Logistics, Format, & Tips

Background on FDA and Drug Development

Drug Discovery

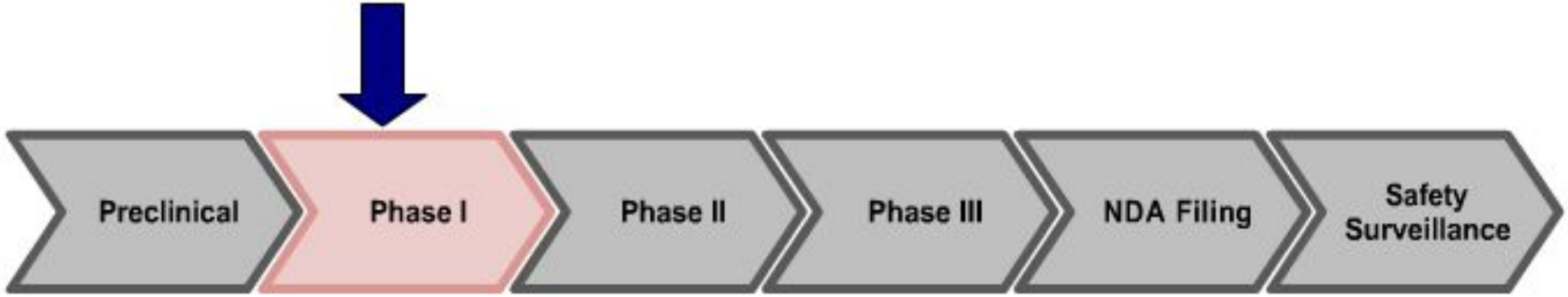
- Typically, researchers discover new drugs through:
  - New insights into a disease process that allow researchers to design a product to stop or reverse the effects of the disease
  - Many tests of molecular compounds to find possible beneficial effects against any of a large number of diseases
  - Existing treatments that have unanticipated effects
  - New technologies, such as those that provide new ways to target medical products to specific sites within the body or to manipulate genetic material
- Once researchers identify a promising compound, the development of drugs follows a well-established path to make sure that they are safe and effective when they reach the public

Preclinical Development

- Preclinical work occurs before a new drug or biologic is tested in humans
- Primary goals are to determine whether the product is
  - Reasonably safe for initial use in humans
  - Sufficiently effective against a disease target in chemical assay tests or animal models
- The end results of the preclinical stage of development is an Investigational New Drug Application (IND)

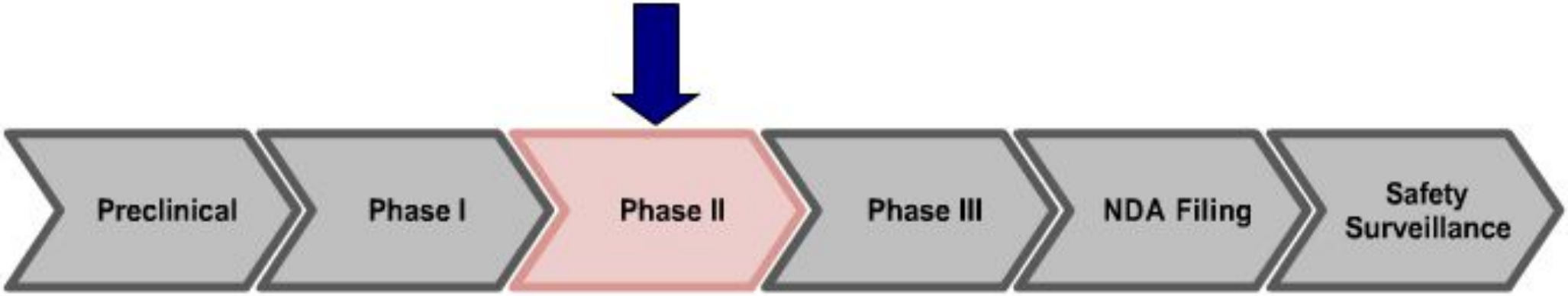
Clinical Development – Phase 1

- IND submission
  - Pharmacology/Toxicology Studies
  - Manufacturing Information
  - Clinical Protocols and Investigator Information
- Phase 1 primary goals
  - Place emphasis on a drug's safety
  - Determine the most common side effects of a drug



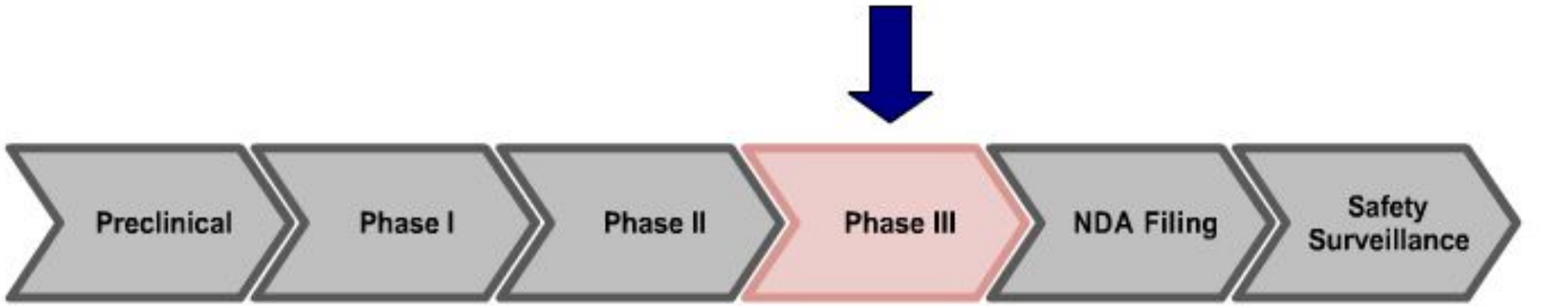
Clinical Development – Phase 2

- Primary goals
  - Place emphasis on a drug's effectiveness
  - Determine if the drug works in people who have a certain disease
  - Compare the drug against placebo
  - Continue to monitor short-term side effects and other safety



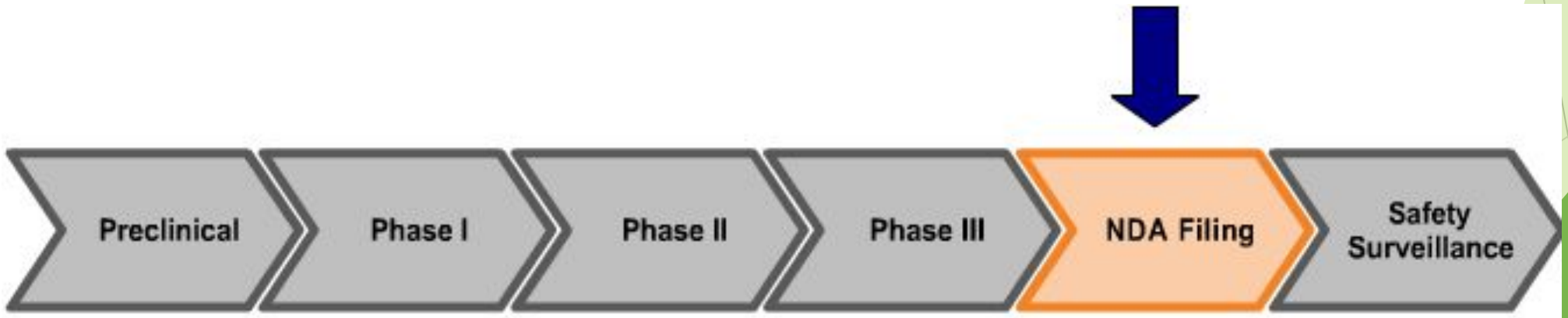
Clinical Development – Phase 3

- Primary goals
  - Traditionally large-scale, randomized, placebo-controlled trials
  - Continued assessment of effectiveness, duration of effect, effect in different populations, varying dosages
  - Safety evaluation continues, including potential drug-drug interactions



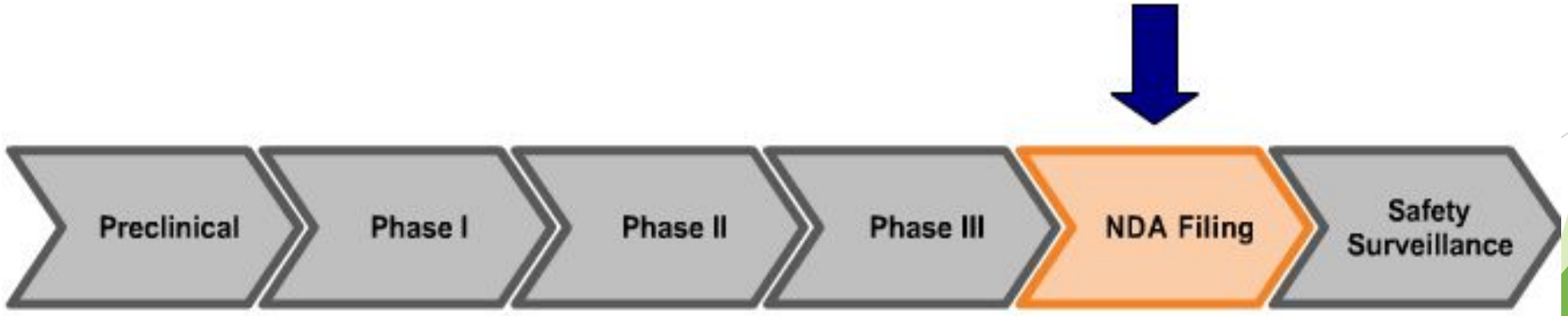
NDA/BLA Submission

- FDA holds Pre-NDA meeting
  - Identify pivotal studies
  - Discuss methods of statistical analysis
  - Uncover major unresolved issues
- NDA includes all animal and human data from the development program



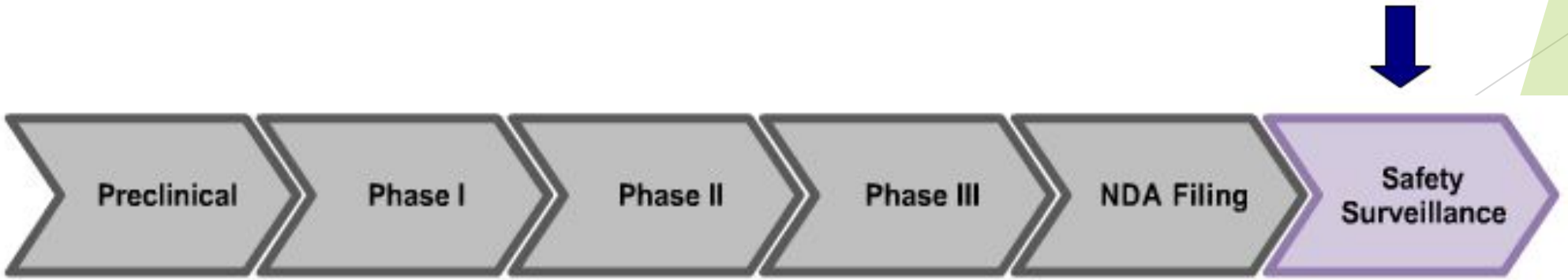
FDA Review

- FDA determines the application's completeness and assigns a review team to evaluate the application
- FDA assesses
  - Whether effectiveness has been demonstrated for the drug's proposed use
  - Whether the safety assessment is adequate to conclude that the drug is safe (i.e., the benefits of the drug outweigh the risks)
  - Whether the manufacturing methods and the controls used to maintain the product quality are adequate



Post-Market Safety Surveillance

- Knowledge about a product will always be limited at the time of approval
  - Clinical studies are brief in duration and involve a limited patient population
  - New safety information often emerges after a product is used in a wider patient population
- FDA maintains an active program in post-market safety surveillance to monitor adverse events



So what exactly is FDA's role?

Drug Development & Clinical Trials

- FDA *does not develop drugs*
  - Researchers, pharmaceutical companies, and nonprofit groups conduct disease research and drug development
- FDA *does not test drugs* in clinical trials
  - FDA does not run clinical trials
  - FDA staff are not onsite for clinical trials
  - Researchers conducting trials must seek FDA approval before beginning

Practice of Medicine & Drug Costs

- FDA does not have authority to regulate the practice of medicine
  - **FDA regulates the development and marketing of medical products**
  - Doctors are free to prescribe FDA-approved drug for other conditions (known as “off-label” use)
- *FDA does not regulate the price of medicine*
  - Consideration of drug prices is not part of FDA’s mandate
  - FDA cannot base an approval decision based on drug price
  - FDA does not even receive pricing information during a review

FDA's Role in Facilitating Drug Development

- FDA's mission includes "Promoting Public Health"
- FDA reviewers have expert knowledge on drug development and clinical trials
  - FDA provides technical help to researchers and drug developers
  - FDA helps companies design clinical trials and studies
  - FDA has numerous meeting with companies throughout the drug development process

For more information,
on FDA regulation of medical products, as well as other ways to get involved, visit:

http://www.fda.gov/ForPatients/

Introduction to Patient-Focused Drug Development

Image used with permission of the FDA

Purpose of the Meetings?

- FDA wanted a more systematic way to gather the patient perspective about the condition and available treatment options
- Helps inform their understanding of the context for benefit/risk assessment and decision making for new drugs
- Patient input helps the FDA during drug development and their review of an application for marketing a new drug

Benefit-Risk Assessment

- Analysis of Condition
- Current Treatment Options

→ Provides regulators with the clinical context for weighing benefits and risks

- Benefit
- Risk
- Risk Management

→ Incorporates expert judgments based on evaluation of the efficacy and safety data and the expected impact of efforts to reduce and further characterize risks

CCDS EL-PFDD Meeting

- Framework for discussion questions came from FDA's benefit-risk framework; represents important considerations in their decision making

- We reviewed this & other disease area questions and tailored our agenda/panel questions to communicate the most important information related to CCDS

- FDA emphasizes that:

ACTIVE PATIENT INVOLVEMENT & PARTICIPATION IS THE KEY TO THE SUCCESS OF THESE MEETINGS!

“Voice of the Patient” Report

- We will prepare a written “Voice of the Patient” report after the meeting
- Summary of caregiver & audience testimony, polling data & submitted written comments
- Key communication to FDA review staff & drug developers about what is most important in a treatment to patients and caregivers
- FDA wants this information; informs them about ways meaningful treatments for CCDS can be developed

Participating in the Meeting

Meeting Logistics

- Who?
  - ✔ CCDS patients and caregivers, FDA staff, and pharma and biotech companies, and anyone interested in learning
- When?
  - ✔ January 24, 2023 from **10:00 am - 3:00 pm EDT**
- Where?
  - ✔ Virtual - Anywhere
- How?
  - ✔ Interactive Live Stream at https://www.creatineinfo.org/el-pfdd

Overview of the Agenda

- Welcome and introductory comments from ACD & FDA
- Clinical background on CCDS by CCDS expert
- Interactive discussion broken into two topics:
  1. How CCDS symptoms affect your life
  2. How you manage symptoms and current & future approaches to treatment
- Topics will include pre-recorded patient panels and will include polling questions and a moderated discussion with the audience (YOU!)
- Summary & closing comments

Discussion Questions

Topic 1: *Living with CCDS: Disease Symptoms and Daily Impacts*

- Of all the symptoms of CCDS which 1-3 symptoms have the most significant impact on your or your loved ones life?
- How does CCDS affect you on best and on worst days? Describe your best days and your worst days.
- Are there specific activities that are important to you that you or your loved one cannot do at all or as fully as you would like because of CCDS?

Discussion Questions (cont.)

Topic 1: *Living with CCDS: Disease Symptoms and Daily Impacts*

- How have your symptoms changed over time?
  - How has your ability to cope with the symptoms changed over time?
- What do you fear the most as you or your loved one gets older?
  - What worries you most about your condition?
  - What frustrates you most about your condition?

Discussion Questions (cont.)

Topic 2: *Current Challenges to Treating CCDS*

- What are you currently doing to manage CCDS symptoms?
- How well do these treatments treat the most significant symptoms of your CCDS?
- What are the most significant downsides to your current treatments and how do they affect your daily life?
- Short of a complete cure, what specific things would you look for in an ideal treatment for CCDS?

Discussion Format

- There will be a panel of patients for each topic
  - The purpose is to set the foundation for the broader audience discussion
  - Panelists are selected to reflect a range of experiences with the condition
- Patients in the audience and online will have a chance to answer “polling” questions
  - Their purpose is as a starting off point for the discussion
  - Will use a browser on cell phone, tablet, or computer to respond
- Then move to a discussion with patients in the audience
  - The purpose is to build on the experiences shared by the panel
  - A moderator will ask questions and invite you to submit responses

Tips for Effective Participation

- Remember FDA's role & the purpose of the meeting
- Review each Discussion Questions in advance
- If you have something important to share, relate it to the most appropriate topic/panel question and **call in**
- It is okay to reiterate a feeling/experience already voiced by someone that is similar to your own, but give it a personal or unique perspective
- **Keep your comments concise & focused**; there are many voices to be heard about this emotional topic
- You can always send in additional comments after the meeting

Participating in the Discussion

- Participate in the meeting:
  - By webcast (remotely; polling questions, call in comments & written submissions)
- Register for meeting:
  - Pre-Register (NOW) at https://www.creatineinfo.org/el-pfdd
  - Comments with answers to the questions may be submitted prior to the meeting (NOW) and for up to 30 days after the meeting
  - Comments will be included in the “Voice of the Patient” report to be submitted to FDA

Summary

- This is YOUR OPPORTUNITY to be part of the process
- You can have a meaningful impact on clinical trial design & drug development
- Your (collective) voices must be heard at the *beginning* of the process to help:
  - ✔ Companies design trials that meet your needs
  - ✔ FDA assess risks & benefits with a full understanding of the impact of CCDS & the patient perspective
- HELP MAKE A DIFFERENCE!!

Questions & Answers

We look forward to your participation on January 24th!!

Thank You!