Endpoint Considerations to Facilitate Drug Development for Niemann-Pick Type C (NPC)

Virtual Public Workshop
January 24-25, 2022

Draft Agenda

Virtual Day 1: Introduction and Overview of Endpoints for Niemann-Pick Type C (NPC) Clinical Trials

January 24, 2022
12:00 pm – 3:40 pm ET

Background and Meeting Objectives
Niemann-Pick Type C (NPC) is a rare genetic disease that results in progressive neurological symptoms and organ dysfunction. NPC is caused by mutations in either the *NPC1* or *NPC2* genes, resulting in impaired intracellular transport of cholesterol and other lipids. Individuals with NPC have significant unmet treatment needs. Currently, there are no approved therapies in the United States for treatment of NPC. In order to advance NPC drug development, it is important that stakeholders work together and identify strategies to support ongoing and future NPC clinical trials. In this workshop, participants will discuss clinical endpoints relevant to NPC clinical trials and innovative strategies to support therapeutic development for patients with NPC.

In this workshop, participants will:

- Review endpoint considerations in NPC and consider challenges and opportunities to support product development;
- Consider functional assessments that could serve as clinical endpoints in NPC clinical trials; and
- Discuss innovative strategies to support product development, such as digital technology and biomarkers.

12:00 pm **Welcome and Overview**
Mark McClellan, Duke-Margolis Center for Health Policy

12:05 pm **Opening Remarks from FDA**
Patrizia Cavazzoni, U.S. Food and Drug Administration

12:15 pm **Clinical Overview of NPC**
Forbes D. Porter, National Institutes of Health

12:25 pm **Session 1: Challenges and Opportunities with the NPC Clinical Severity Scale (NPCCSS)**
Moderator: Mark McClellan, Duke-Margolis Center for Health Policy

Objective: Given the heterogenous nature of NPC, there are significant challenges in endpoint design and selection for NPC clinical trials. The five-domain NPC Clinical

Severity Scale (NPCCSS) has commonly been used in clinical studies and natural history studies in NPC. In this session, participants will review the NPCCSS and consider its strengths and limitations. In addition, participants will identify and propose strategies to address limitations of the NPCCSS, such as potential modifications, and consider strategies to leverage existing datasets to evaluate its validity.

Presentation: Naomi Knoble, U.S. Food and Drug Administration

Panel:

- Elizabeth Berry-Kravis, Rush University Medical Center
- Ebony Dashiell-Aje, BioMarin
- Lise Kjems, Cyclo Therapeutics
- Naomi Knoble, U.S. Food and Drug Administration
- Forbes D. Porter, National Institutes of Health
- Phil Marella, Patient Representative

1:25 pm **Session 2: Functional Measures for Swallowing**
Moderator: Robyn Bent, U.S. Food and Drug Administration

Objective: Given the impact of NPC on swallowing, it is important to assess swallowing in clinical trials of potential therapeutics for NPC. In this session, participants will review potential swallowing assessment tools and consider their strengths and limitations as clinical trial endpoints.

Presentation: Beth Solomon, National Institutes of Health

Panel:

- Kiera Berggren, Virginia Commonwealth University
- Diana Bohm, Northwestern Medicine
- Barbara Lazarus, Patient Representative
- Beth Solomon, National Institutes of Health
- Dina Zand, U.S. Food and Drug Administration

2:25 pm **Break**

2:40 pm **Session 3: Functional Measures for Ambulation, Speech, and Fine Motor**
Moderator: Mark McClellan, Duke-Margolis Center for Health Policy

Objective: NPC can impact ambulation, speech, and fine motor abilities. In this session, participants will review potential ambulation, speech, and fine motor assessment tools and consider their strengths and limitations as clinical trial endpoints.

Presentation: Dawn Phillips, REGENXBIO

Panel:

- Emily Freilich, U.S. Food and Drug Administration
- Eric Marsh, Children's Hospital of Philadelphia

- Sara McGlocklin, Patient Representative
- Marc Patterson, Mayo Clinic
- Dawn Phillips, REGENXBIO
- Kevin Weinfurt, Duke University

3:35 pm **Closing Remarks**
Mark McClellan, Duke-Margolis Center for Health Policy

3:40 pm **Adjournment**

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Virtual Day 2: Potential Innovative Endpoints and Strategies to Support NPC Product Development

January 25, 2022
12:00 pm – 3:30 pm ET

12:00 pm **Welcome and Overview of Day Two**
Mark McClellan, Duke-Margolis Center for Health Policy

12:05 pm **Opening Remarks from FDA**
Peter Stein, U.S. Food and Drug Administration

12:15 pm **Session 4: Exploring Digital Health Technology to Measure Functional Endpoints**
Moderator: Christina Silcox, Duke-Margolis Center for Health Policy

Objective: Digital health technologies offer potential opportunities for drug development as they allow physiological or patient-reported data to be efficiently collected from patients directly, and potentially more frequently, while lowering the burden of in-person clinical study visits. More frequent, or even continuous, data collection may better reflect disease course than less frequent snapshots in time. However, digital health technologies are also associated with potential challenges, such as the ability to make reliable measurements and validating novel measurements as clinically relevant endpoints. In this session, participants will discuss examples of digital health technologies and consider opportunities and challenges with their use to measure clinical endpoints.

Presentation: Ray Dorsey, University of Rochester Medical Center

Panel:

- Michelle Campbell, U.S. Food and Drug Administration
- Ray Dorsey, University of Rochester Medical Center
- Alec Koujaian, Patient Representative
- Harry Koujaian, Patient Representative
- Greg Licholai, Yale University
- David Lynch, Children's Hospital of Philadelphia
- Anindita Saha, U.S. Food and Drug Administration

1:15 pm **Session 5: Future Biomarker Considerations in NPC**
Moderator: Jeff Siegel, U.S. Food and Drug Administration

Objective: Due to the widely variable clinical presentation of NPC, there may be value in the use of biomarkers that can serve as measures of disease severity. In this session, panelists will discuss how novel and emerging biomarkers for NPC may be useful for tracking disease progression and supporting therapeutic development.

Presentations: Jeff Siegel, U.S. Food and Drug Administration; Daniel Ory, Casma Therapeutics

Panel:

- Patti Dickson, Washington University School of Medicine in St. Louis
- Carole Ho, Denali Therapeutics
- Daniel Ory, Casma Therapeutics
- Ed Schuchman, Icahn School of Medicine at Mount Sinai
- Jack Wang, U.S. Food and Drug Administration

2:15 pm **Break**

2:30 pm **Session 6: Closing Panel and Forward Looking**
Moderator: Mark McClellan, Duke-Margolis Center for Health Policy

Objective: Collaboration is critical for facilitating NPC treatment development. In this session, participants will discuss next steps for continued collaboration as well as broader considerations for NPC clinical trials moving forward, including clinical trial design and patient participation in trials, with the overall goal being the development of safe and effective treatments for NPC.

Panel:

- Debbie Kaflowitz, Patient Representative
- Janet Maynard, U.S. Food and Drug Administration
- Jennifer Pippins, U.S. Food and Drug Administration
- Forbes D. Porter, National Institutes of Health
- Sean Recke, Patient Representative
- Steve Romano, Mallinckrodt
- Segundo Mariz, European Medicines Agency

3:25 pm **Closing Remarks**
Mark McClellan, Duke-Margolis Center for Health Policy

3:30 pm **Adjournment**