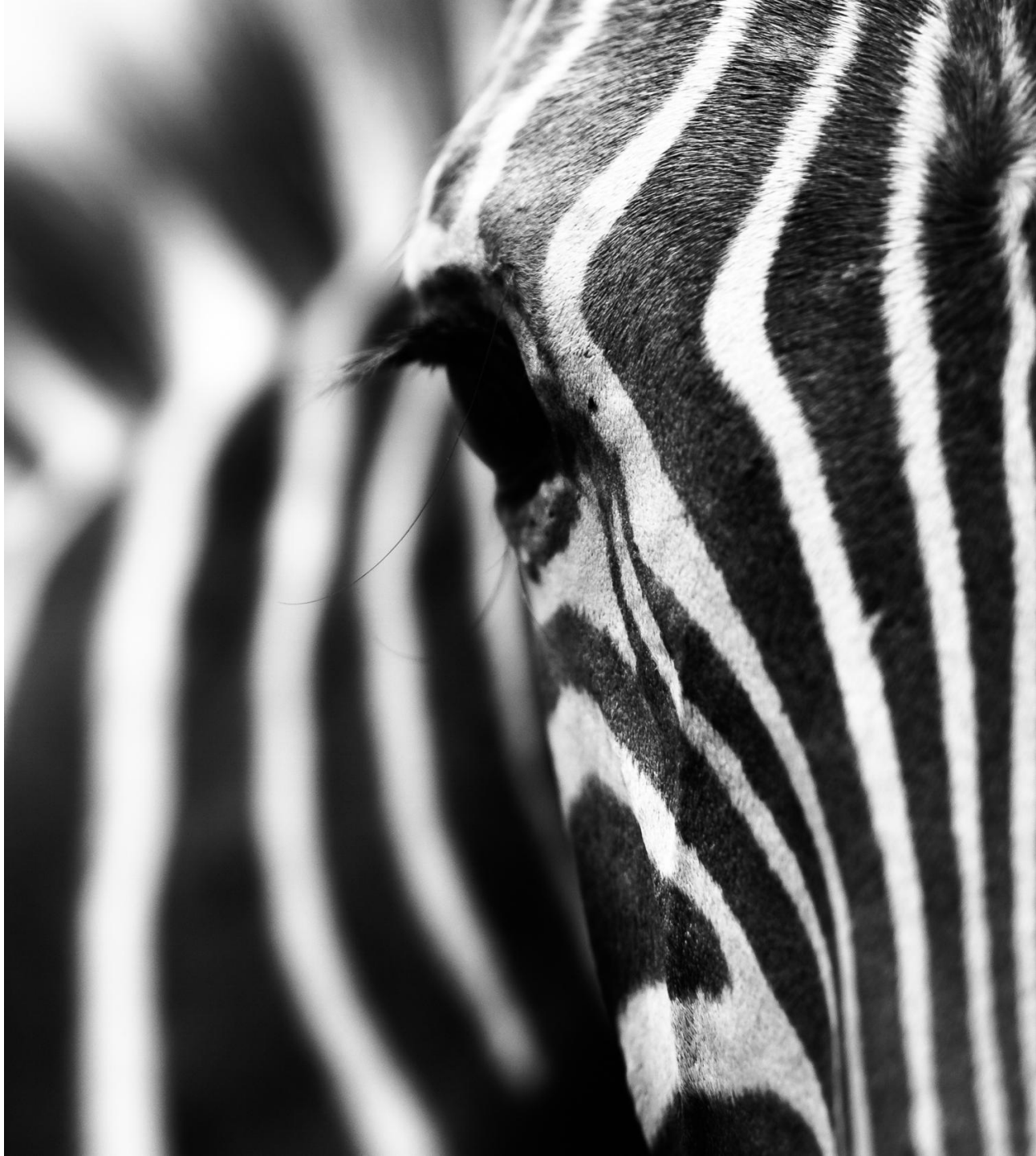
# Advances in Niemann-Pick Disease Type C Treatment: The Role of Arimoclomol

**Barbara K. Burton, MD**
Professor of Pediatrics
Northwestern University Feinberg School of Medicine
Attending Physician
Division of Genetics, Genomics and Metabolism
Ann & Robert H. Lurie Children's Hospital of Chicago

ZEVRA THERAPEUTICS



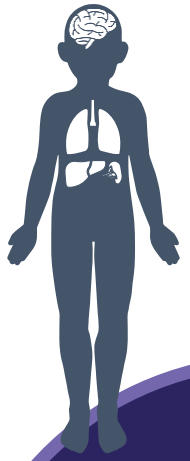
MRC-2500052 07/25

# Disclaimer

- Dr. Burton is a paid consultant for Zevra Therapeutics
- This program is sponsored by Zevra Therapeutics and is not certified for continuing education credit
- The information in this program is consistent with FDA-approved prescribing information
- Intended for US audiences only

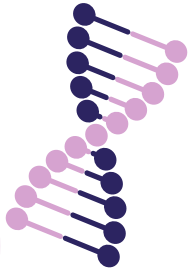
# Niemann-Pick Disease Type C Is a Progressive Neurodegenerative Disease

ZEVRA THERAPEUTICS



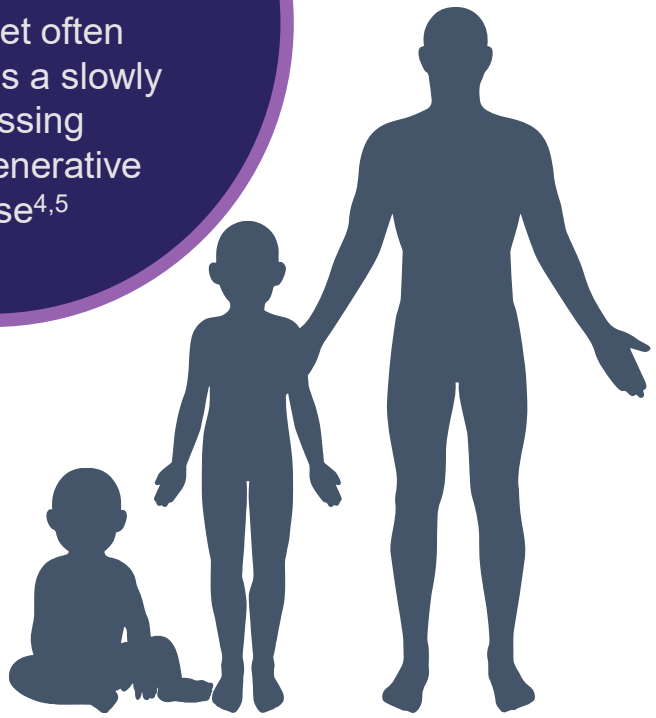
NPC is an ultra-rare, neurovisceral, neurodegenerative disease[1-3]

NPC is a genetic, life-limiting disorder[1]



Disease onset can occur throughout the lifespan[1]

Clinical course ranges from a more rapid, fatal neonatal or infantile disorder while adult onset often manifests as a slowly progressing neurodegenerative disease[4,5]

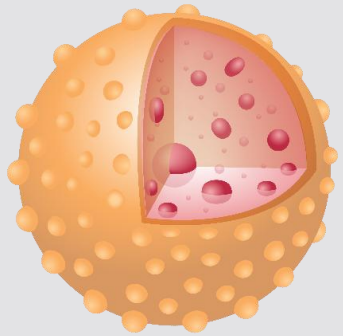


NPC, Niemann-Pick disease type C.

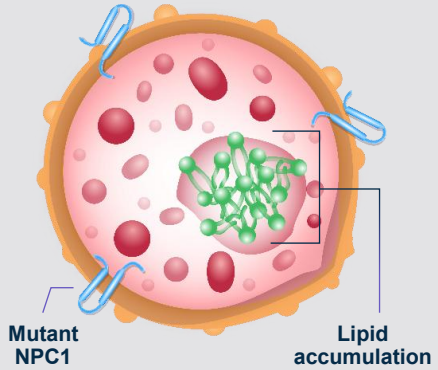
**1**. Geberhiwot T et al. *Orphanet J Rare Dis*. 2018;13:50; **2**. Shammas H et al. *Sci Rep*. 2019;9:5292; **3**. Yanjanin NM et al. *Am J Med Genet B Neuropsychiatr Genet*. 2010;153B:132-140; **4**. Vanier MT. *Orphanet J Rare Dis*. 2010;5:16; **5**. Wraith JE et al. *J Inherit Metab Dis*. 2014;37:93-101.

# Pathogenic Gene Variants Lead to Abnormal Lysosomal Function[1]

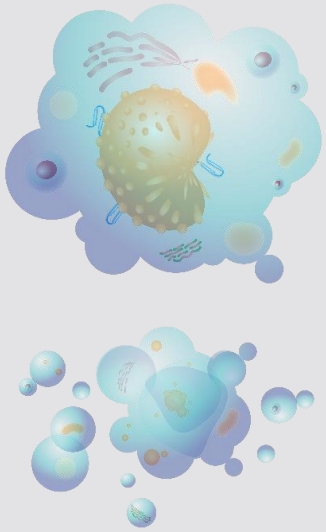
NPC is a **lysosomal storage disease with impaired lysosomal functioning**[1]



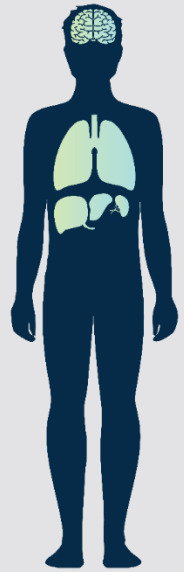
NPC pathogenic gene variants are associated with **accumulation of lipids** in the lysosomes[2,3]




This **accumulation of cholesterol** in lysosomes leads to **cell dysfunction and death**[2,4]



Over time, this leads to **neurodegeneration** as well as **peripheral organ dysfunction** [5,6]



**No curative therapies are currently available.**[7]

**1.** Shammas H, et al. *Mol Genet Metab*. 2025;145(1):109103. **2.** Platt FM et al. *Nat Rev Dis Primers*. 2018;4(1):27. **3.** Millat G et al. *Am J Hum Genet*. 2001;68(6):1373-1385. **4.** Hammond N et al. *Biochim Biophys Acta Mol Cell Biol Lipids*. 2019;1864(8):1109-1123. **5.** Yañez MJ et al. *Biochim Biophys Acta Mol Basis Dis*. 2020;1866(10):165875. **6.** Xu Y et al. *J Lipid Res*. 2010;51(7):1643-1675. **7.** Geberhiwot T et al. *Orphanet J Rare Dis*. 2018;13(1):50.

ZEVRA THERAPEUTICS

# MIPLYFFA®
# arimoclomol capsules

# Pronunciation Guide

**MIPLYFFA**

Pronounced

(mye-plye’-fah)

**Arimoclomol**

Pronounced

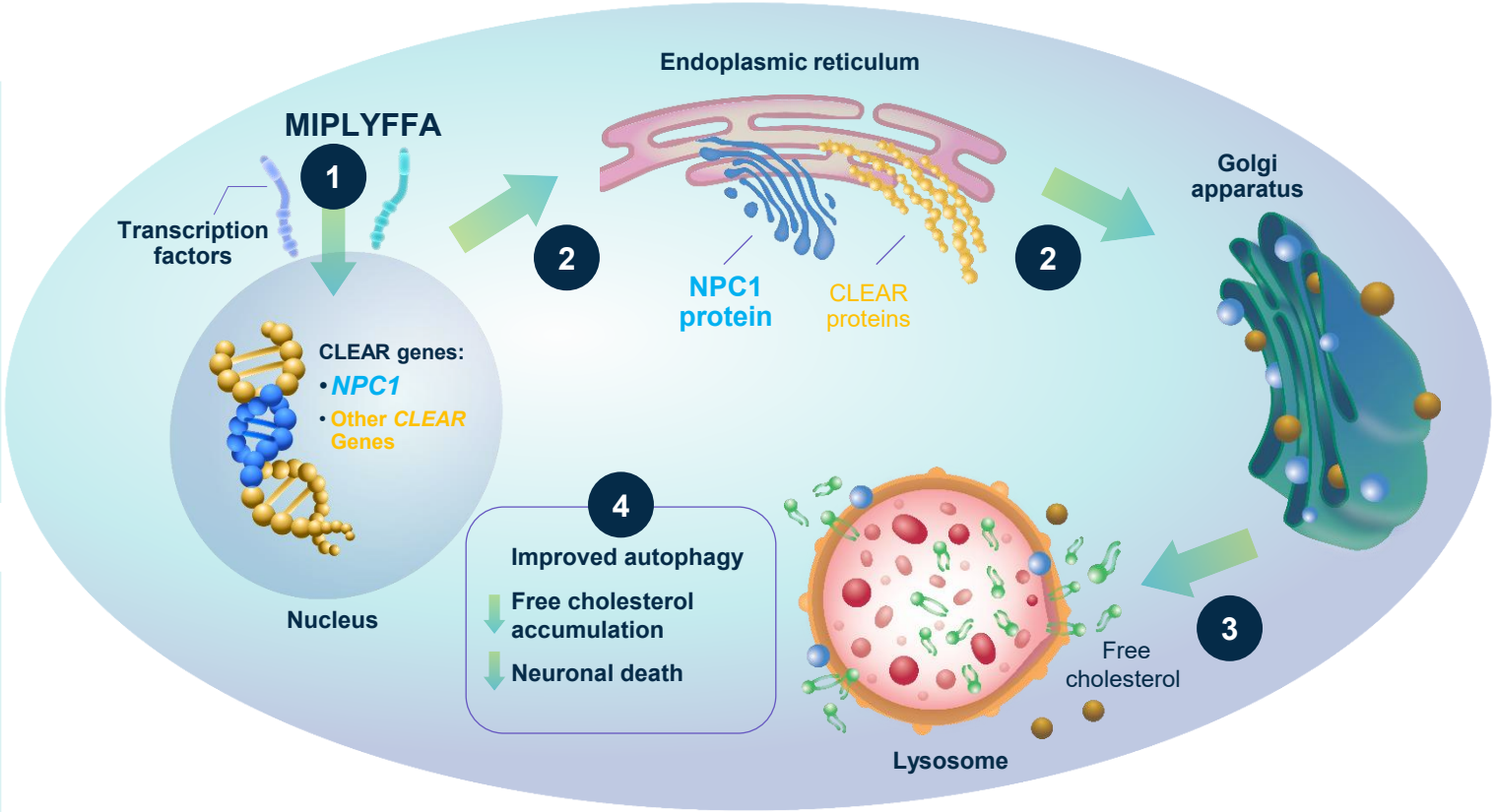
(air-im-OCK-lo-mall)

# Arimoclomol Improves Lysosomal Function in NPC[1]

ZEVRA THERAPEUTICS

**1**

**Arimoclomol activates transcription factors,** leading to **upregulation of CLEAR network genes** (including *NPC1* gene)[1,2]




**2**

These genes then express more of the NPC1 protein as well as other proteins belonging to the CLEAR network[1,2]

**3**

In the lysosome, **NPC1 protein helps with transporting cholesterol**[1,2]

**4**

This **reduces free cholesterol accumulation and prevents cell death**[1,2]

**MIPLYFFA, the first FDA-approved treatment for NPC, is designed to treat the underlying pathology of NPC.**[1-4]

CLEAR, coordinated lysosomal expression and regulation; ER, endoplasmic reticulum.

**1.** Data on file. Zevra Therapeutics, Inc. **2.** Shammas H, et al. *Mol Genet Metab*. 2025;145(1):109103. **3.** Mengel E et al. *J Inherit Metab Dis*. 2021;44(6):1463-1480. **4.** MIPLYFFA Full Prescribing Information. Celebration, FL, US, Zevra Therapeutics Inc.; 09/2024.

# Measuring the Efficacy of Arimoclomol

## Using a validated scale for the measurement of NPC disease progression

- The NPC clinical severity scales (NPCCSS) specifically measure NPC disease progression[1]
- The scales were designed with NPC physician, caregiver, and patient input[2]
- Rates of disease progression have been established using the NPCCSS for certain NPC populations[1,3]

### 5-Domain NPCCSS


**Ambulation**


**Swallowing**


**Fine motor skills**


**Speech**


**Cognition**

Individual domain score: 0-5 Maximum score: 25

### Rescored 4-Domain NPCCSS


**Ambulation**


**Swallowing**


**Fine motor skills**

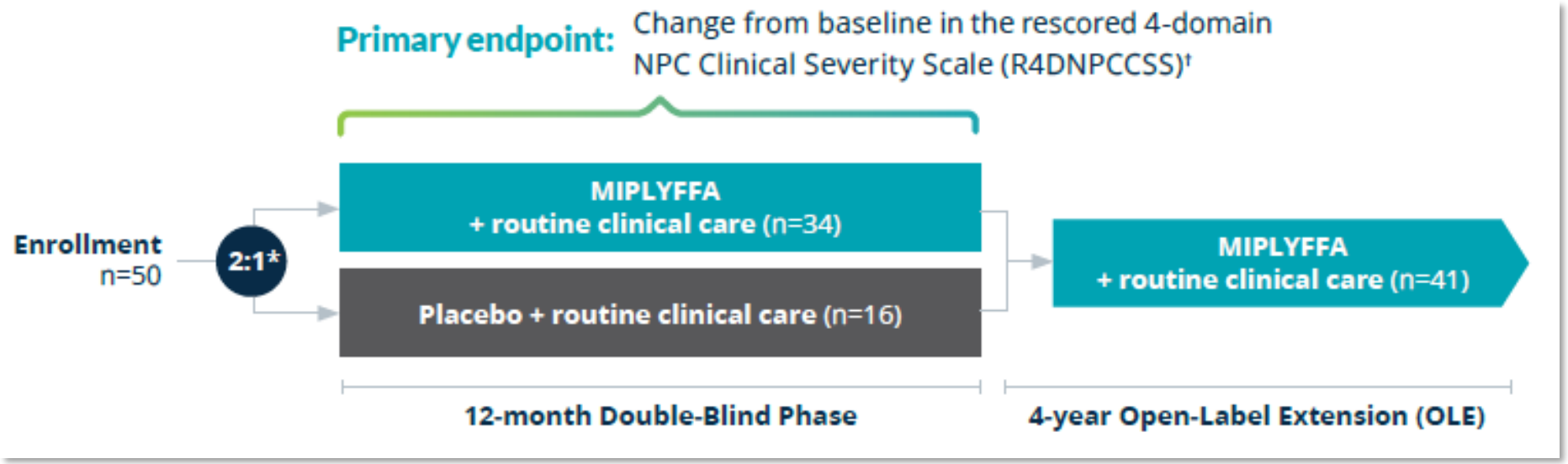

**Speech**

Individual domain score: 0-5 Maximum score: 20

**1.** Yanjanin NM et al. *Am J Med Genet B Neuropsychiatr Genet*. 2010;153B:132-140; **2.** Cortina-Borja M. *Orphanet J Rare Dis*. 2018;13:143; **3.** Mengel et al. *Orphanet J Rare Dis*. 2020;15:328.

# Studied in a Well-Controlled Clinical Trial

**Safety and effectiveness of arimoclomol was studied in a 12-month multicenter, randomized, double-blind, placebo-controlled trial in participants with NPC, aged 2–19 years[1]**




*Stratified for miglustat use.
†Observed values.

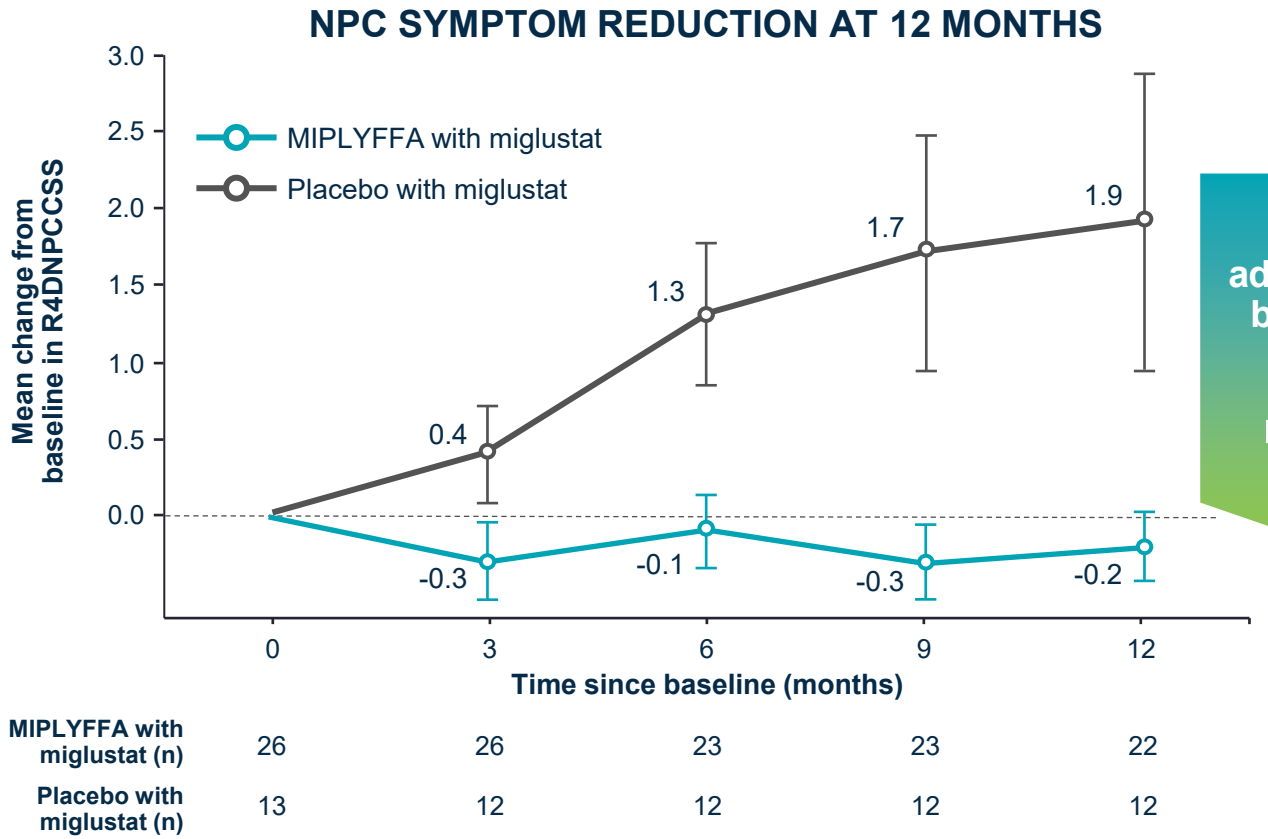
Trial 1, 76% of patients in the MIPLYFFA group and 81% of placebo group received miglustat as part of their routine clinical care.

Patients who completed Trial 1 were offered to continue into the open-label extension (OLE) phase.[1,2]

**1.** MIPLYFFA Full Prescribing Information. Celebration, FL, US, Zevra Therapeutics Inc.; 09/2024. **2.** Mengel E, et al. Poster presented at 21st Annual World*Symposium*; February 3-7, 2025; San Diego, CA.

# Proven Effectiveness in Halting Disease Progression in Patients who also Received Miglustat[1]

Arimoclomol, in combination with miglustat, halted disease progression through 12 months of treatment, as demonstrated by a decrease of 0.2 points from baseline on the R4DNPCCSS compared to 1.9 points of progression for patients with miglustat alone.[1]




**The estimated placebo adjusted mean change from baseline at month 12 was**

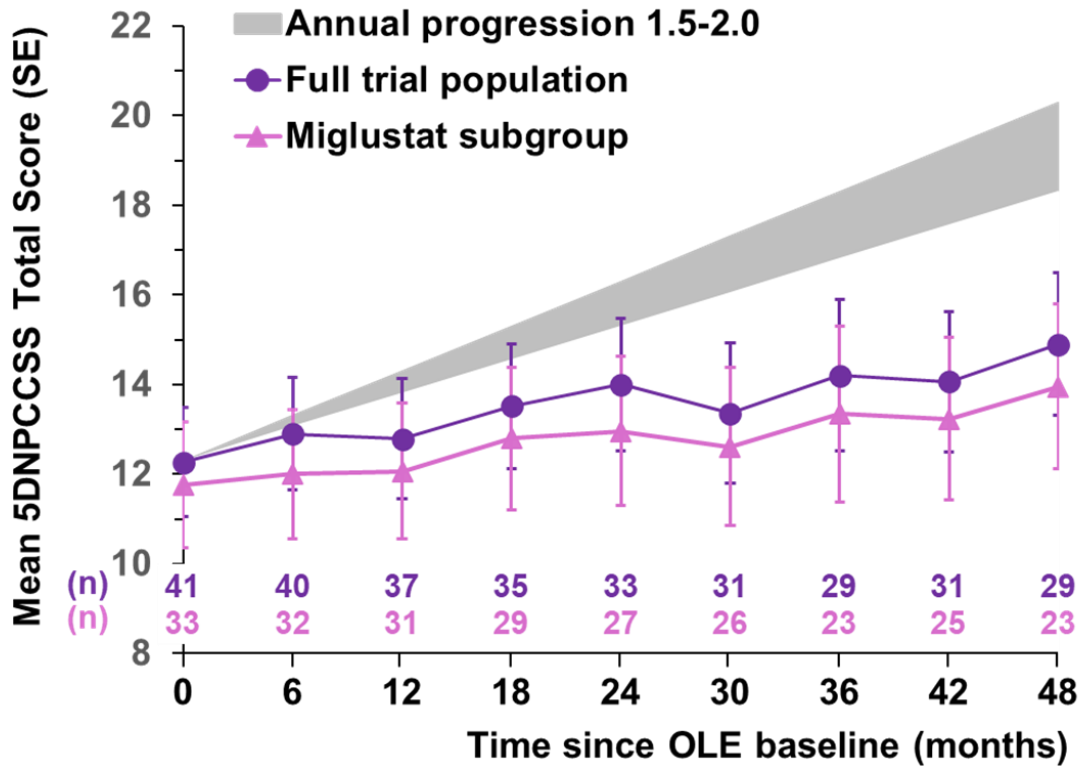
**-2.2pts**

**1.** MIPLYFFA Full Prescribing Information. Celebration, FL, US, Zevra Therapeutics Inc.; 09/2024.

# Arimoclomol is the First FDA-approved NPC Treatment that has Demonstrated Long-Term Effectiveness of up to 5 years[1,2]

## Continued effectiveness in open-label extension (OLE)

- Observed disease severity progressed slowly over the 48 months, with a stepwise progression pattern[2]
- Expected annual progression based on natural history and double-blind phase = 1.5-2.0 pts[1,3-4]




**1.** MIPLYFFA Full Prescribing Information. Celebration, FL, US, Zevra Therapeutics Inc.; 09/2024. **2.** Mengel E, et al. Poster presented at 21st Annual World*Symposium*; February 3-7, 2025; San Diego, CA. **3.** Mengel et al. *Orphanet J Rare Dis*. 2020;15:328. **4.** Mengel E, et al. *Mol Genet Metab Rep*. 2025;43:101233.

# In the 12-month Trial Adverse Events Were Generally Mild to Moderate in Severity, and Few Led to a Withdrawal of Treatment

| Adverse Reaction | MIPLYFFA with miglustat n=26 n (%) | Placebo with miglustat n=13 n (%) |
|---|---|---|
| Upper respiratory tract infection* | **8** (31) | **2** (15) |
| Diarrhea | **6** (23) | **3** (23) |
| Decreased weight | **4** (15) | **0** |
| Decreased appetite | **3** (12) | **0** |
| Tremor | **3** (12) | **0** |
| Urticaria** | **3** (12) | **0** |
| Headache | **3** (12) | **1** (8) |
| Lower respiratory tract infection | **3** (12) | **1** (8) |
| Seizure | **3** (12) | **1** (8) |

**Common adverse reactions occurring in ≥8% of patients treated with MIPLYFFA and more frequently than in patients receiving placebo†**

*Upper respiratory tract infection: combined incidence of upper respiratory tract infection and rhinitis.
**Urticaria: Includes one patient in which urticaria occurred alone (3%) and two patients who had urticaria with angioedema (6%).
†Placebo subgroup also received miglustat.

MIPLYFFA Full Prescribing Information. Celebration, FL, US, Zevra Therapeutics Inc.; 09/2024.

# Arimoclomol was Well-Tolerated with No New Safety Signals Observed over 4 Years[1]

The overall pattern of frequently reported AEs was stable over the 48 months and consistent with observations from the double-blind phase of the trial.

- 38 (93%) of any AE
- 15 (37%) severe or serious AEs
- 4 (10%) AEs leading to treatment discontinuation*
- 2 (5%) AEs with fatal outcome due to disease progression

| **The 3 most common AEs were:** | **MIPLYFFA with miglustat N=41 n (%)** |
|---|---|
| Diarrhea | **10** (24.4%) |
| Upper respiratory tract infection | **10** (24.4%) |
| Nasopharyngitis (common cold) | **8** (19.5%) |

N=number of patients in the extension analysis set; n=number of patients with event; %=percentage of patients with event.
*2 patients discontinued due to safety and 2 discontinued due to physician decision.
AE=adverse event

**1.** Mengel E, et al. Poster presented at 21st Annual World*Symposium*; February 3-7, 2025; San Diego, CA.

# Important Safety Information

**WHAT is MIPLYFFA [mye-plye'-fah]?**

MIPLYFFA is prescription medicine used in combination with a drug called miglustat to treat neurological symptoms of Niemann-Pick disease type C (NPC) in patients 2 years of age and older.

**IMPORTANT SAFETY INFORMATION**

**Before starting MIPLYFFA**, tell your healthcare provider about all your medical conditions, including if you are pregnant or plan to become pregnant, breastfeeding or plan to breastfeed.
**Tell your healthcare provider** about all the medicines you take, including any prescription and over-the-counter medicines, vitamins, or herbal supplements. MIPLYFFA may affect how other medicines work.

**What are the possible side effects of MIPLYFFA?**

**MIPLYFFA may cause serious side effects including:**

- **Hypersensitivity reactions.** Call your healthcare provider immediately if you get any of the following symptoms:
  - urticaria (hives),
  - shortness of breath,
  - persistent cough, or
  - facial swelling
- **Harm to your unborn baby.** If you are of childbearing age, take precautions to prevent pregnancy. Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with MIPLYFFA.

- **Infertility**. MIPLYFFA may affect your ability to have children.

# Important Safety Information (continued)

**The most common side effects of MIPLYFFA in patients also taking miglustat** include upper respiratory tract infection, diarrhea and decreased weight.

These are not all the possible side effects of MIPLYFFA. Call your HCP for medical advice about side effects. **You are encouraged to report side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.**

**Drug Interactions:** MIPLYFFA can cause side effects if used together with certain drugs called OCT2 substrates. Talk to your healthcare provider about any drugs that you may be taking for other conditions.

MIPLYFFA capsules for oral use are available in the following strengths in a 90-count bottle: 47 mg, 62 mg, 93 mg, and 124 mg.

# Clinical Trial Summary

- Arimoclomol specifically addresses the underlying pathophysiology of NPC[3]
- MIPLYFFA, in combination with miglustat, is the only approved treatment for NPC with a 12-month placebo-controlled trial using a validated scale for NPC showing a clinically meaningful improvement in disease progression[1,4]
- MIPLYFFA, in combination with miglustat, was well tolerated, with established effectiveness and durability through 5 years of treatment[1,2,4]

**1.** MIPLYFFA Full Prescribing Information. Celebration, FL, US, Zevra Therapeutics Inc.; 09/2024. **2.** Mengel E, et al. Poster presented at 21st Annual World*Symposium*; February 3-7, 2025; San Diego, CA. **3.** Shammas H, et al. *Mol Genet Metab*. 2025;145(1):109103. 4. Mengel E, et al. *Mol Genet Metab Rep*. 2025;43:101233.

# Symptom Management for NPC

## Specific Therapies Can Improve NPC-associated Symptoms

| Spasticity | Cataplexy and Seizures | Ataxia | Dystonia and Tremor | Psychiatric Illness |
|---|---|---|---|---|
| • Muscle relaxants[1]<br>• Anti-spasmodics[1]<br>• Tranquilizers[1]<br>• Botulinum toxin[1] | • Tricyclic anti-depressants[1,2]<br>• Antiepileptic drugs[1] | • Leucine supplementation[3] | • Anticholinergics[2]<br>• Benzodiazepines[2]<br>• Botulinum toxin[2] | • Antipsychotic medications[2]<br>• Atypical anti-psychotics[2]<br>• ECT (for catatonia)[2]<br>• Mood stabilizers[2]<br>• SSRIs[2] |

ECT, electroconvulsive therapy; MRI, magnetic resonance imaging; NPC, Niemann-Pick disease type C; SSRIs, selective serotonin reuptake inhibitors.

**1.** Geberhiwot T et al. *Orphanet J Rare Dis*. 2018;13:50. **2.** Patterson MC et al. Mol Genet Metab. 2012;106:330-344. **3.** Patterson MC, et al. *Neurology*. 2025;105(1):e213589.

# MIPLYFFA Has Convenient Dosing and Flexible Administration Options

## Dosing is available in 4 different strengths and is based on body weight

**Recommended MIPLYFFA dose for patients aged 2 years and older**

| Body weight | 18-33 lb (8-15 kg) | >33-60 lb (>15-30 kg) | >60-121 lb (>30-55 kg) | >121 lb (>55 kg) |
|---|---|---|---|---|
| Recommended dose* (3 times per day) | 47 mg | 62 mg | 93 mg | 124 mg |

*Capsules shown not actual size.

## Administration†

**One capsule**


**3x per day**
with or without food

†For administration considerations, please refer to the full Prescribing Information.

MIPLYFFA Full Prescribing Information. Celebration, FL, US, Zevra Therapeutics Inc.; 09/2024.

# MIPLYFFA Is Ordered and Sent Directly to Patients Through the AmplifyAssist™ Program

## AmplifyAssist is a support program for caregivers and patients living with NPC and taking MIPLYFFA

- Clinical support*
- Coverage support
- Prescription support

AmplifyAssist™
Your ally in what's ahead.

To learn more about AmplifyAssist, please visit the Zevra table during exhibit hours

*Information provided by the clinical support team is intended to be educational and not replace the advice of a patient's healthcare provider.

MIPLYFFA Full Prescribing Information. Celebration, FL, US, Zevra Therapeutics Inc.; 09/2024.

# Summary

- First FDA-approved NPC treatment
- Clinically meaningful difference
- Proven robust and enduring outcomes
- Well-tolerated with no new safety signals
- Convenient dosing and flexible administration
- Support for patients and families

Scan the QR code for more information about MIPLYFFA

Learn more at **MIPLYFFA.com**.

ZEVRA THERAPEUTICS

# Thank You & Questions