MIPLYFFA®
arimoclomol capsules

HCP Fact Sheet
A guide for healthcare providers

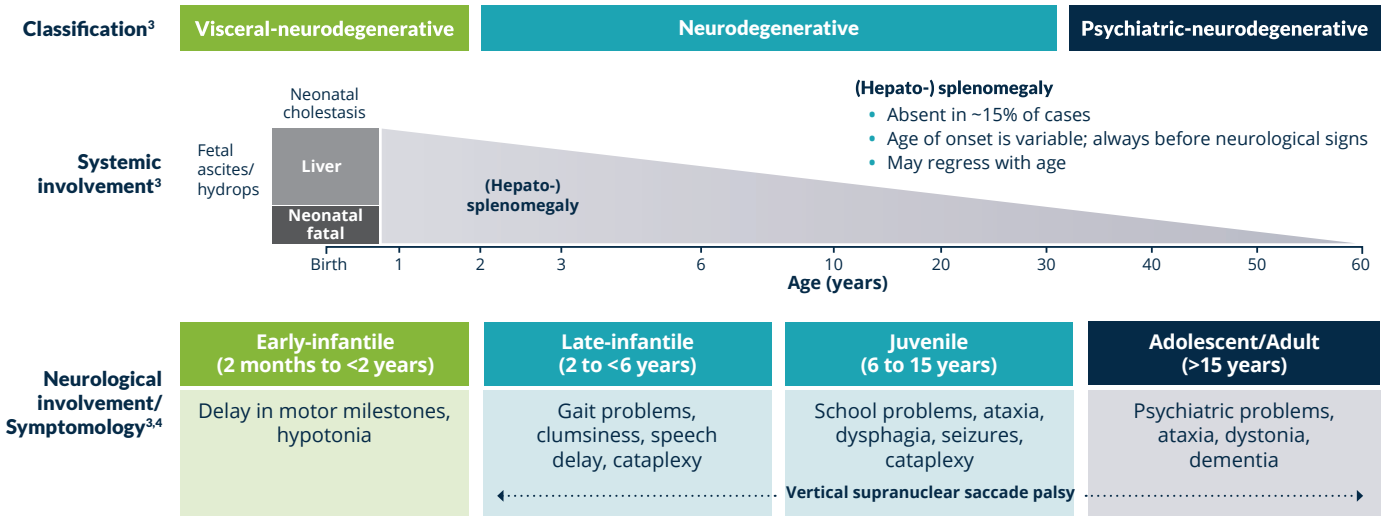
MIPLYFFA is the first FDA-approved treatment for Niemann-Pick disease type C (NPC)[1]

MIPLYFFA is indicated for use in combination with miglustat for the treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in adult and pediatric patients 2 years of age and older.

NPC is an ultra-rare, relentlessly progressive neurodegenerative disease[2]

- NPC is a genetic disease that results in dysfunction of lysosomal proteins[2]
  - In NPC, the accumulation of unprocessed lipids leads to dysfunction in the brain, liver, and spleen[2,3]
- NPC is difficult to diagnose and can affect patients at any age[2,4]
  - Patients aged >15 years could represent up to one-third of all patients with NPC[5]

Symptoms of NPC are progressive and may present differently depending on age[2]



SELECT IMPORTANT SAFETY INFORMATION

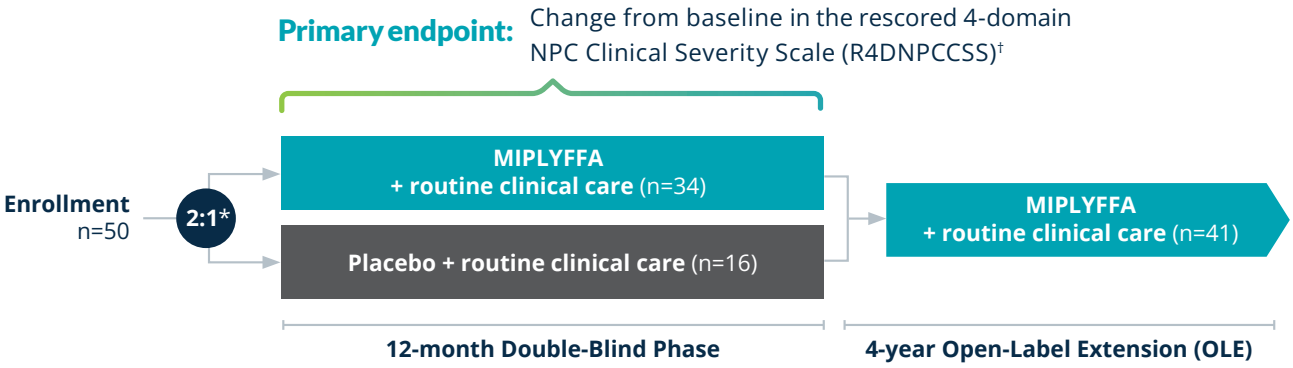
Hypersensitivity Reactions: Hypersensitivity reactions such as urticaria and angioedema have been reported in patients treated with MIPLYFFA during Trial 1: two patients reported both urticaria and angioedema (6%) and one patient (3%) experienced urticaria alone within the first two months of treatment. Discontinue MIPLYFFA in patients who develop severe hypersensitivity reactions. If a mild or moderate hypersensitivity reaction occurs, stop MIPLYFFA and treat promptly. Monitor the patient until signs and symptoms resolve.

Please see additional Important Safety Information throughout and in full on Page 7, and the full Prescribing Information, including Instructions for Use.

Trial 1 study design

Safety and effectiveness of MIPLYFFA were studied in a 12-month, multicenter, randomized, double-blind, placebo-controlled trial in patients with NPC aged 2 to 19 years[1,4]

In Trial 1, 76% of patients in the MIPLYFFA group and 81% of those in the 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.[1,6]



*Stratified for miglustat use.
†Observed values.

Basic demographics for Trial 1 subgroup of patients who also received miglustat (n=39)[1]

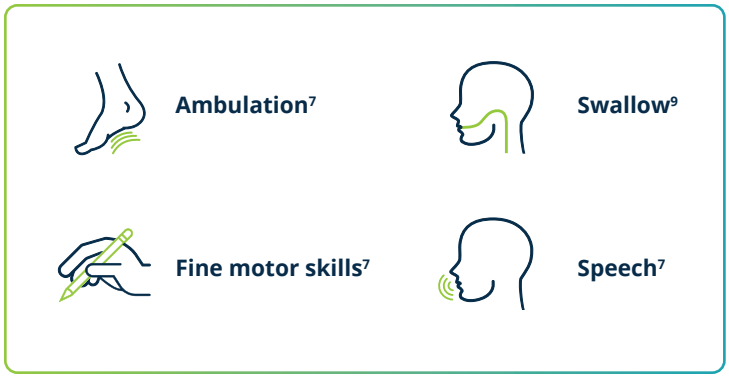
- Mean age was 11.6 years
- Mean time since first NPC symptom was 8.5 years
- Mean age at onset of first neurological symptom was 4.9 years
- Mean baseline score in the rescored 4-domain NPC Clinical Severity Scale (R4DNPCCSS) was higher in the MIPLYFFA group (8.9; n=26) than the placebo group (7; n=13), with an overall mean R4DNPCCSS score of 8.3

The treatment effect in Trial 1 was assessed as change from baseline on the R4DNPCCSS

R4DNPCCSS

The NPC Clinical Severity Scale is a clinician-reported outcome measure of disease severity and progression.[7] The R4DNPCCSS was revised to more accurately assess a specific group of heterogeneous patients over a 12-month period.[8]

Four key domains have been identified as **some of the most important** by NPC expert clinicians, caregivers, and patients, and allow for an assessment of NPC symptom progression.[7]



SELECT IMPORTANT SAFETY INFORMATION

Embryofetal Toxicity: MIPLYFFA may cause embryofetal harm when administered during pregnancy based on findings from animal reproduction studies. Advise pregnant females of the potential risk to the fetus and consider pregnancy planning and prevention for females of reproductive potential.

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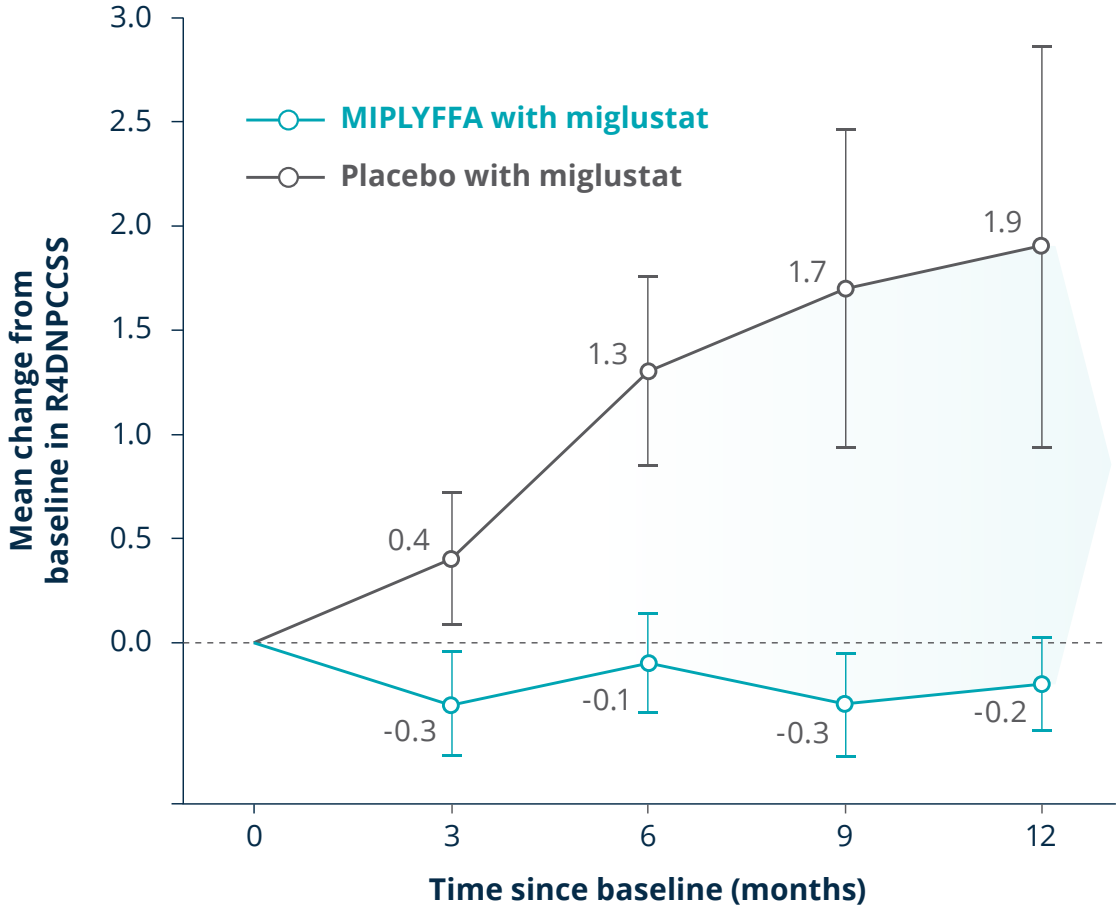
MIPLYFFA, in combination with miglustat, stopped disease progression at 12 months[1]

NPC symptom reduction at 12 months
as measured by the R4DNPCCSS score:
ambulation, speech, swallow, and fine motor skills



MIPLYFFA with miglustat (n)	26	26	23	23	22
Placebo with miglustat (n)	13	12	12	12	12

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

-2.2 pts.

There were insufficient data to determine the effectiveness of the use of MIPLYFFA without miglustat for the treatment of neurological manifestations in patients with NPC.

SELECT IMPORTANT SAFETY INFORMATION

Increased Creatinine without Affecting Glomerular Function: Across clinical trials of MIPLYFFA, mean increases in serum creatinine of 10% to 20% compared to baseline were reported. These increases occurred mostly in the first month of MIPLYFFA treatment and were not associated with changes in glomerular function.

During MIPLYFFA treatment, use alternative measures that are not based on creatinine to assess renal function. Increases in creatinine reversed upon MIPLYFFA discontinuation.

Please see additional Important Safety Information throughout and in full on Page 7, and the full Prescribing Information, including Instructions for Use.

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In a clinical study, MIPLYFFA was well-tolerated compared to placebo[1]

Common adverse reactions occurring in ≥8% of patients treated with MIPLYFFA and more frequently than in patients receiving placebo (subgroup who also received miglustat)

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)

*Upper respiratory tract infection: combined incidence of upper respiratory tract infection and rhinitis.
†Urticaria: includes 1 patient in which urticaria occurred alone (3%) and 2 patients who had urticaria with angioedema (6%).

Adverse events were generally of mild to moderate severity and very few led to withdrawal of treatment[1]

- Thrombocytopenia was observed in 3 patients during the trial, all of whom were receiving miglustat for 6 months or longer at the time of enrollment. In 2 of these patients, the thrombocytopenia was present at baseline and persisted throughout the trial. In the other patient, the thrombocytopenia developed and resolved during the trial
- Across the clinical trials, increases in serum creatinine (mean increase was 10% to 20%) occurred mainly within the first month of dosing and were reversible upon treatment discontinuation

SELECT IMPORTANT SAFETY INFORMATION

The most common adverse reactions in Trial 1 (≥15%) in MIPLYFFA-treated patients who also received miglustat were upper respiratory tract infection, diarrhea, and decreased weight.

Three (6%) of the MIPLYFFA-treated patients had the following adverse reactions that led to withdrawal from Trial 1: increased serum creatinine (one patient), and progressive urticaria and angioedema (two patients). Serious adverse reactions reported in MIPLYFFA-treated patients were hypersensitivity reactions including urticaria and angioedema.

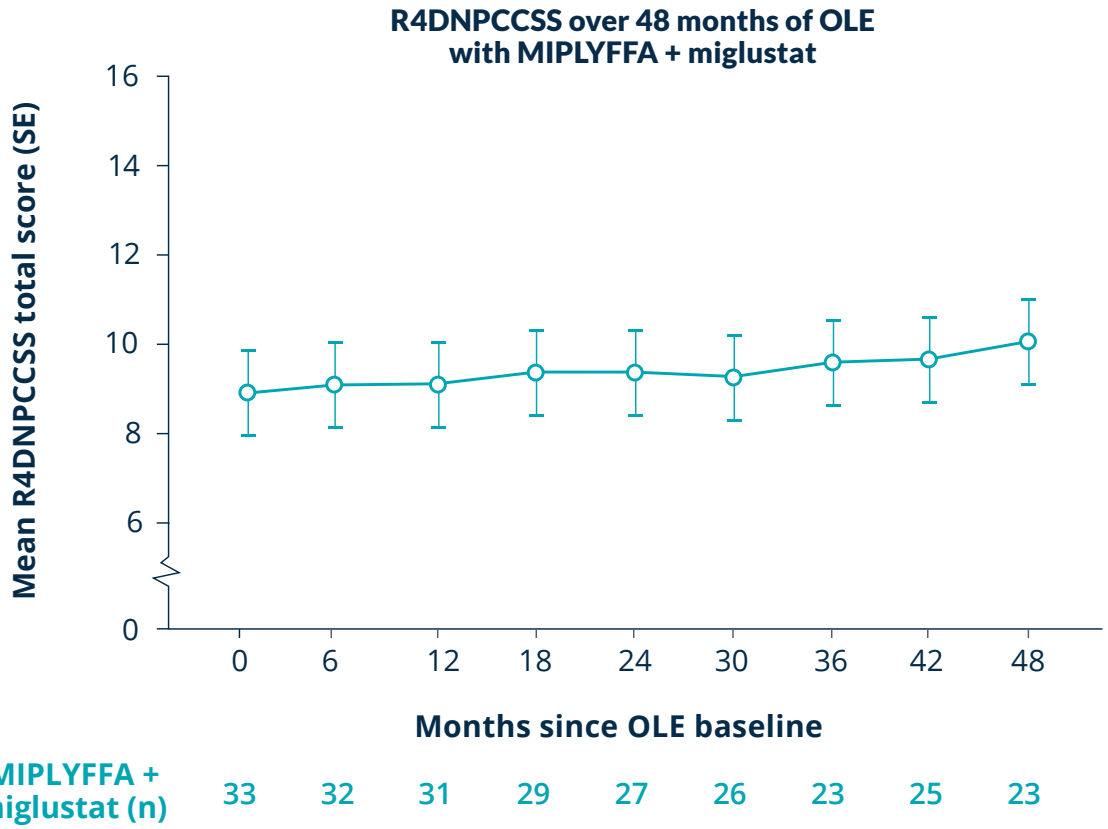
Please see additional Important Safety Information throughout and in full on Page 7, and the full Prescribing Information, including Instructions for Use.

MIPLYFFA® arimoclomol capsules

MIPLYFFA is the first FDA-approved NPC treatment that has demonstrated long-term effectiveness and safety data of up to 4 years[6]

Consistent effectiveness in open-label extension

During the OLE, the on-label population's sustained rate of disease progression was comparable to the double-blind phase. Observed disease severity progressed slowly over the 48 months, with a stepwise progression pattern.



MIPLYFFA was well-tolerated with no new safety signals observed over 4 years

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:	N=41 n (%)
Diarrhea	**10** (24.4%)
Upper respiratory tract infection	**10** (24.4%)
Nasopharyngitis	**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; SE=standard error.

SELECT IMPORTANT SAFETY INFORMATION

Drug Interaction(s): Arimoclomol is an inhibitor of the organic cationic transporter 2 (OCT2) transporter and may increase the exposure of drugs that are OCT2 substrates. When MIPLYFFA is used concomitantly with OCT2 substrates, monitor for adverse reactions and reduce the dosage of the OCT2 substrate.

Please see additional Important Safety Information throughout and in full on Page 7, and the full Prescribing Information, including Instructions for Use.

MIPLYFFA® arimoclomol capsules

MIPLYFFA has convenient dosing and flexible administration options and can be taken at home

One capsule 3X per day with or without food[1]

For administration considerations, please refer to the **full Prescribing Information, including Instructions for Use**.

Dosing comes in 4 different strengths and is based on body weight. MIPLYFFA is only recommended for patients aged 2 years and older[1]

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

In patients with renal impairment with an eGFR ≥15 mL/minute to <50 mL/minute, it is recommended to reduce frequency of dosing.

Getting your patients started on MIPLYFFA

MIPLYFFA is sent directly to patients through a specialty pharmacy

- Download the **enrollment form** at **MIPLYFFA-HCP.com**
- Send the completed form to AmplifyAssist™ to initiate the prescription
- The prescription will be completed, and once approved, MIPLYFFA will be mailed to patients at home
- Other questions about MIPLYFFA? Call AmplifyAssist Monday through Friday at **888-668-4198** from 8:00 AM to 6:00 PM (CT). You can also fax us at **888-668-2143**

Support for your patients

AmplifyAssist is available to help support your patients throughout the treatment journey, offering educational resources as well as financial and insurance assistance to eligible patients.

AmplifyAssist™
Your ally in what's ahead.

SELECT IMPORTANT SAFETY INFORMATION

Use in Females and Males of Reproductive Potential: Based on animal findings, MIPLYFFA may impair fertility and may increase post-implantation loss and reduce maternal, placental, and fetal weights.

Please see additional Important Safety Information throughout and in full on Page 7, and the full Prescribing Information, including Instructions for Use.

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INDICATIONS AND USAGE

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To report SUSPECTED ADVERSE REACTIONS, contact Zevra Therapeutics, Inc. at toll-free phone 1-844-600-2237 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Drug Interaction(s): Arimoclomol is an inhibitor of the organic cationic transporter 2 (OCT2) transporter and may increase the exposure of drugs that are OCT2 substrates. When MIPLYFFA is used concomitantly with OCT2 substrates, monitor for adverse reactions and reduce the dosage of the OCT2 substrate.

Use in Females and Males of Reproductive Potential: Based on animal findings, MIPLYFFA may impair fertility and may increase post-implantation loss and reduce maternal, placental, and fetal weights.

Renal Impairment: The recommended dosage of MIPLYFFA, in combination with miglustat, in patients with an eGFR ≥15 mL/minute to <50 mL/minute is lower than the recommended dosage (less frequent dosing) in patients with normal renal function.

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

Before prescribing MIPLYFFA, please read the full Prescribing Information, including Instructions for Use.

References: 1. MIPLYFFA Full Prescribing Information. Celebration, FL, US, Zevra Therapeutics, Inc.; 09/2024. **2.** Mengel E, Patterson MC, Chladek M, et al. Impacts and burden of Niemann pick type-C: a patient and caregiver perspective. *Orphanet J Rare Dis*. 2021;16(1):493. doi:10.1186/s13023-021-02105-8 **3.** Vanier MT. Niemann-Pick disease type C. *Orphanet J Rare Dis.* 2010;5(16):1-18. doi:10.1186/1750-1172-5-16 **4.** Patterson MC, Hendriksz CJ, Walterfang M, et al. Recommendations for the diagnosis and management of Niemann-Pick disease type C: an update. *Mol Genet Metab*. 2012;106(3):330-344. doi:10.1016/j.ymgme.2012.03.012 **5.** Geberhiwot T, Moro A, Dardis A, et al. Consensus clinical management guidelines for Niemann-Pick disease type C. *Orphanet J Rare Dis.* 2018;13(1):1-19. doi:10.1186/s13023-018-0785-7 **6.** Mengel E, Patterson M, Guenther S, Dali Cí. Long-term efficacy and safety evaluation of arimoclomol treatment in patients with Niemann-Pick disease type C - Data from a 48-month open-label trial. Poster presented at 21st Annual World*Symposium*; February 3-7, 2025; San Diego, CA. **7.** Patterson MC, Lloyd-Price L, Guldberg C, et al. Validation of the 5 domain Niemann-Pick type C Clinical Severity Scale. *Orphanet J Rare Dis*. 2021;16(1):79. doi:10.1186/s13023-021-01719-2 **8.** Mengel E. Efficacy results from a 12-month double-blind randomized trial of arimoclomol for treatment of Niemann-Pick disease type C (NPC): presenting a rescored 4-domain NPC Clinical Severity Scale. *Mol Genet Metab*. (Submitted manuscript). **9.** Berry-Kravis EM, LaGorio L, Dali Cí, Gallo D. Qualitative assessment of the validity and standardization of the swallow domain in the 5-domain Niemann-Pick disease type C (NPC) Clinical Severity Scale (5DNPCCSS). Poster presented at: The Child Neurology Society Annual Meeting; November 11-14, 2024; San Diego, CA.

MIPLYFFA® arimoclomol capsules

MIPLYFFA: Because every moment matters

First FDA-approved NPC treatment

Proven disease-modifying effects with 5 years of experience[1,6]

Clinically meaningful difference

Using the validated rescored NPC Clinical Severity Scale[1]

Proven robust and enduring outcomes

In a year-long clinical trial and additional 4 years of long-term effectiveness data[1,6]

Well-tolerated with no new safety signals

Observed long-term over 4 years of use[6]

Convenient dosing and flexible administration

Patients can take one capsule 3× a day at home, with or without food[1]

Support for your patients

With AmplifyAssist™, MIPLYFFA is sent directly to patients through a specialty pharmacy for easy access

Scan the QR code for more information about MIPLYFFA

Learn more at **MIPLYFFA-HCP.com**.

ZEVRA THERAPEUTICS

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