Request for Educational (RFE)
Reference # *RFE-24-IME-1*

The Ultragenyx Global Medical Education and Grants program is committed to improving global health outcomes for patients with rare and ultra-rare genetic disorders.

Ultragenyx's competitive grant program involves a publicly posted general Request for Education (RFE) related to a perceived educational gap. Decisions are not based on, or influenced by, commercial interests. External organizations are invited to submit an application addressing the knowledge gap as outlined below.

For all independent medical education grants, the grant requester is responsible for the design, implementation, and conduct of the independent initiative supported by the grant. Ultragenyx will not be involved in any aspect of the project, development, or faculty selection. Each request will be evaluated independently and on its own merits by a formal committee and Ultragenyx will not provide any guidance about the evaluation of a request.

Ultragenyx recognizes that a healthcare gap exists in the **current dosing and administration strategies** surrounding **long-chain fatty acid oxidation disorders (LC-FAODs)**. Many clinicians lack awareness on the optimized approach to dosing and administration, particularly for patients who may present as mild, moderate, and/or non-symptomatic. Undertreated patients may be at risk for major clinical events (MCEs).

- We welcome submissions for independent medical education grants from educational providers who can meet the time-sensitive grant submission window and launch an educational program in Q3 or Q4 2024.
- Submitted applications should be accompanied by a letter of request and a detailed grant proposal that includes;
    - Clearly stated format(s)
    - Educational Objectives
    - Expected Outcomes Level
    - Needs Assessment
    - Proposed Agenda
    - Minimum number of learners
    - Comprehensive Budget

Submission Deadline:	15 May 2024, 5PM PT
Therapeutic Area:	Long Chain Fatty Acid Oxidation Disorders (LC-FAODs)
Topic:	Comprehensive approach to dosing and administration for patients living with LC-FAODs by; • Understanding the unique metabolic requirements of a patient through;

	○ Estimated energy requirement (EER) ○ Macronutrient distribution • Assessing target daily dosage of triheptanoin (up to 35% of the patient's total prescribed daily caloric intake divided into at least four doses) and the role of initiation and titration • Recognizing strategies to achieve patient adherence and tolerance in instances of GI side effects
Learning Format(s) Considered:	• Innovative online enduring activities • Interactive case studies and/or treatment simulations • Regional series at IEM clinics • Programs that incorporate a downloadable point-of-care resource for IEM clinics and care teams
Target Audiences:	HCPs working in **Inborn Errors of Metabolism (IEM) clinics**; • Metabolic Dieticians (primary focus) • NPs, Nurses, Physicians
Target Regions:	Primary: US Secondary: Canada
Available Budget:	The maximum amount of funding available is **$150,000 USD**.

Disease Background:

LC-FAODs are rare, life-threatening, autosomal recessive disorders caused by mutations in the genes that encode the proteins involved in either the transport or catabolism of long-chain fatty acids.

Common clinical findings of LC-FAODs are rhabdomyolysis, hypoketotic hypoglycemia, and cardiomyopathy. Other symptoms include hepatomegaly, Reye-like syndrome, peripheral neuropathy, retinopathy, arrhythmias, and GI distress. Individuals with LC-FAODs can present with muscle weakness, myalgia, muscle cramps, and exercise fatigue. Many of these symptoms are often accompanied by signs of general impairment (fatigue, headache, nausea, vomiting) and are triggered by specific conditions such as exercise, change in temperature, emotional stress, and others (illness and fasting).

Submission Instructions:

- Applications should be formally submitted through the Request Management System (RMS) using the Medical Education application and include Reference **RFE-24-IME-1** in request title.
- Applications must be received by **5pm PT on 15 May 2024.** Late or incomplete submissions will be rejected without review.

- Applicants may be asked to provide additional information or clarification during the review period.
- All applicants will be notified of a decision via RMS system email no later than 15 June 2024.
- If accepted, applicant must agree to the terms, conditions, and purposes of grant as described in the Ultragenyx Letter of Agreement.

Questions regarding this RFE should be directed in writing to: grants@ultragenyx.com.

References:

1. Vockley J et al. Dietary management and major clinical events in patients with long-chain fatty acid oxidation disorders enrolled in a phase 2 triheptanoin study
2. Roe CR et al. Anaplerotic treatment of long-chain fat oxidation disorders with triheptanoin: review of 15 years experience. Mol Genet Metabol 2015;116:260-8.
3. Gillingham MB et al. Effects of higher dietary protein intake on energy balance and metabolic control in children with long-chain 3-hydroxy acyl-CoA dehydrogenase (LCHAD) or trifunctional protein (TFP) deficiency. Mol Genet Metabol 2007;90:64-9.
4. Terrone G et al, Ruoppolo M, Brunetti-Pierri N, Cozzolino N, Scolamiero E, Parenti G, Romano A, Andria G, Salvatore F, Frisso G. Child Neurology: Recurrent rhabdomyolysis due to fatty acid oxidation disorder. 2014.
5. Vockley J, Longo N, Madden M, Dwyer L, Mu Y, Chen C, Cataldo J. Dietary management and major clinical events in patients with long-chain fatty acid oxidation disorders enrolled in a phase 2 triheptanoin study. 2020. PMC - PubMed
6. Baker J, Burton B. Diagnosis and Clinical Management of Long-chain Fatty-acid Oxidation Disorders: A Review. 2021. PMC - PubMed
7. Vockley J. Long-chain fatty acid oxidation disorders and current management strategies. 2020. AJMC – PubMed
8. Williams-Hall R, Tinsley K, Kruger E, Johnson C, Bowden A, Cimms T, Gater A. Qualitative evaluation of the symptoms and quality of life impacts of long-chain fatty acid oxidation disorders. 2022. PMC – PubMed.