ARBOR RESEARCH

Unlocking the Power of Evidence for Better Health

Request for Information (RFI)

Arbor Research Collaborative for Health
PAn-european Registry Addressing Difelikefalin In Goal-oriented Medical treatment for dialysis-related pruritus (PARADIGM),

Issue Date: July 14th, 2025
Submission Deadline: July 25th, 2025

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A. BACKGROUND

The **PA**n-european **R**egistry **A**ddressing **D**ifelikefalin **I**n **G**oal-oriented **M**edical treatment for chronic kidney disease-associated pruritus (PARADIGM) study is an observational treatment registry which aims to address the gap in real-world data on the use of difelikefalin (DFK), the only FDA/EMA-approved treatment for CKD-associated pruritus (CKD-aP) in hemodialysis (HD) patients. While clinical trials have shown DFK's efficacy in reducing pruritus and improving quality of life, limited information exists on its long-term safety, dosing patterns, and treatment modifications in everyday clinical practice. By collecting real-world data, this study will enhance understanding of DFK's effectiveness, safety, impact on patient reported outcomes (PROs), and healthcare resource utilization (HCRU), helping to optimize its use and support informed clinical decision-making.

B. THE OPPORTUNITY

Objective
This RFI is intended to solicit Information from qualified companies to participate in the PARADIGM study as the regulatory partner for Ethical Review Board (Ethics Committee) Submission and coordination in the UK.

Scope of Work
The primary objective of the partner is to manage the submission of and secure all necessary regulatory and ethical approvals for the PARADIGM study within the United Kingdom and provide coordination of the UK arm of the registry.

- Pre-study set up activities, including:
    - Provide a comprehensive regulatory landscape assessment to identify applicable regulations
    - Determine specific submission requirements and pathways
    - Prepare and submit applications to relevant Ethical Committee (EC) and regulatory agencies
    - Prepare and submit all regulatory documentation required
    - Address all regulatory and EC queries and requests for additional information
    - Obtain all necessary ethical approvals
    - Provide scientific oversight for the PARADIGM registry and advise on UK clinical context.
- Ongoing study support, including:
    - Maintain regulatory compliance throughout the project lifecycle
    - Manage variations, amendments, and renewals
    - Maintain thorough records of all submissions, approvals, and communications

Preferred Qualifications
Partners who can best demonstrate not only technical capacity to carry out the responsibilities described above but can also speak to the following points will be more favorably regarded in our selection process:

- Demonstrated strong understanding of local regulatory requirements
- Excellent local reputation
- Strong understanding of the local context
- Experience in CKD-aP and familiarity with NIHR processes

Estimated Budget Ceiling and Projected Period of Performance

The estimated total budget ceiling for this implementation is $100,000 USD over a three (3) year period, to begin no sooner than July 2025.

C. ABOUT THE PROJECT

Project Overview

The primary aim of this study is to design and implement a registry that captures real-world data on the treatment of CKD-aP with DFK in adult patients on chronic hemodialysis. The registry will collect information on patient profiles, treatment patterns, effectiveness, safety, and HCRU to better understand DFK utilization and its impact on the management of itch severity.

The PARADIGM study is a prospective treatment registry designed to assess the real-world treatment patterns, safety, and effectiveness of DFK for CKD-aP. The study will collect data from approximately 80 HD facilities across 5 European countries (France, Germany, Italy, United Kingdom, Spain), starting in the second quarter of 2025. Participants will be adult patients aged 18 or older, scheduled to initiate DFK treatment for CKD-aP, and undergoing in-center dialysis. Participants will be followed for at least 12 months or until the administrative study end in October 2028. Initial target enrollment is 400 DFK initiators, with the potential to grow into a larger treatment registry.

Data will be collected by participating study sites from patient medical records, patient-facing questionnaires, and dialysis facility questionnaires. Study Site Coordinators (SSC) will complete Baseline and Follow-Up Assessments using information from medical records, with the Baseline Assessment also including patient-reported sociodemographic data when necessary.) PRO Questionnaires will be administered at various time points, including before DFK treatment begins and at follow-up intervals (1, 3, 6, and 12 months). SSCs will monitor patient records for DFK treatment discontinuation and promptly complete a DFK Discontinuation Form when necessary. All data will be entered directly into PARADIGMLink, Arbor Research's proprietary web-based data collection and management system.

D. SUBMISSION REQUIREMENTS

INSTRUCTIONS FOR SUBMISSION

Your response must include the following:

1. Organization History *(1 page maximum)*

- Mission statement
- A brief history of your organization including years of operation, core competencies and organizational structure
- Describe your organization's current programs and services
- Provide information on any awards, successes and relevant impact statistics

2. Statement of Interest and Experience *(4 pages maximum)*

- Why is your organization interested in this project?
- How are your organization's service(s) or practice(s) relevant to this project? Please provide information supporting your organization's experience under the following criteria, specifically in the UK:
    - Study management
    - Local reputation
    - Strong understanding of the local context

- Demonstrated strong understanding of local regulatory requirements

3. Financials

- Please provide your organization's most recent audited financial statements or other evidence to support your financial capacity to perform the work

QUESTIONS AND COMMENTS

If you have questions or comments on the RFI, please submit them via email to PARADIGM-Registry@arborresearch.org no later than July 18th, 2025.

SUBMISSION DEADLINE

Please submit your response via email to the distribution listed below, no later than July 25th, 2025.

PARADIGM-Registry@arborresearch.org

E. ABOUT ARBOR RESEARCH

Arbor Research empowers our government, the pharmaceutical industry, and private foundations with evidence-based insights that drive the delivery of improved policies, programs, services, and products.

Our distinctive organizational structure positions us as a valuable partner for the government and large businesses, by helping to achieve their small business goals.

At Arbor Research, we are fueled by the belief that collaboration, innovation, and evidence-based solutions have the power to transform the landscape of health care. Join us in shaping a future where data-driven insights pave the way for remarkable advancements that make a lasting difference in the lives of individuals and communities. Our decades of experience providing technical assistance to strengthen core health system functions allows us to provide guidance on global best practices while helping implement innovative solutions tailored to each country. Our collaborations with public and private sector partners in more than 50 countries have produced meaningful and measurable change: more effective and equitable health systems; higher-quality health care services; and better health.

F. TERMS & CONDITIONS

Please see Attachment A for standard Terms & Conditions. Offerors must detail any exceptions in their submission

ATTACHMENT A
STANDARD TERMS & CONDITIONS

Representations & Warranties required from Contractor

(a) Contractor has not been placed on the List of Excluded Individuals/Entities ("LEIE") issued by the Office of Inspector General of the Department of Health and Human Services Office pursuant provisions of or similar laws in other countries nor has it been excluded from government contracts by the General Services Administration ("GSA"). Further, if during the term of this Agreement, Contractor or any of its employees or are placed on the LEIE or excluded from government contracting, Contractor shall notify Arbor Research in writing as soon as is practicable of such event and Arbor Research shall have the right terminate this Agreement upon notice to Contractor.

(b) No Deliverables will contain any material from other copyrighted works without the express written consent of the owner of such copyrighted materials and that Deliverables will not knowingly infringe any copyright, violate any property rights or rights of privacy or publicity or any other rights of any third party and does not contain any scandalous, libelous or unlawful material.

(c) Contractor is aware of no known actual or perceived conflicts of interest or any other fact, circumstance or condition that would delay or interfere with its ability to perform the work contemplated under the Agreement. As a condition of award, Contractor agrees to avoid any actual or perceived conflict of interest during the term of this Agreement. Contractor agrees to immediately disclose to Arbor Research, any actual or perceived conflict of interest that may arise as a result of its involvement in this Agreement. The provisions of this clause shall survive expiration or termination of this Agreement.

(b) Contractor is qualified to perform the work required under this Agreement. All information that Contractor has provided to Arbor Research with respect to its qualifications, experience, affiliations, or financial records is accurate and complete.

(c) Contractor will not assign or subcontract any of the services required under this Agreement without the prior written consent of Arbor Research.

(d) Contractor is an independent Contractor and is engaged in its own business. Nothing contained in this Agreement shall be construed to create a joint venture, agency relationship or partnership between the parties. Contractor and its employees are not entitled to receive any benefits that Arbor Research may provide to its employees, including but not limited to insurance, vacation or retirement benefits. Contractor represents that it will obtain and maintain any workers' compensation that is legally required for Contractor or its employees.

(e) Contractor and its employees, as applicable to the Services, will comply with: all applicable laws and regulations, particularly including the requirements of the HIPAA, European General Data Protection Regulation (GDPR) and other data privacy laws and also all applicable GxP and ICH standards. Without limiting the generality of the foregoing, the Contractor represents that it is entitled to use the patient-level data in its databases and registries pursuant to the patients' informed consent and that it has obtained any requisite ethical approvals; all applicable regulatory requirements; Guidelines on Good Publication Practice (GPP Guidelines), if a publication and/or a presentation is made based on the findings of the research/study; and the agreed research Proposal.

(f) During the term of this Agreement and after its termination for the purpose of the Project and the consecutive ICH obligation, the Contractor shall maintain all material and all other data obtained or generated by Contractor in the course of performing this Agreement, including all computerized records and files, in a secure area reasonably protected from fire, theft and destruction.

(g) Compensation provided under this Agreement is consistent with fair market value in an arm's length transaction and are not being given in exchange for any explicit or implicit agreement by Contractor to recommend or prescribe any of Client's products.

(h) Services to be performed under this Agreement do not and will not involve the counselling or promotion of any unlawful business arrangement or other activity that violates any applicable law.

(i) Contractor's performance of the Services does not, and will not, breach any agreement to keep confidential any information of another entity acquired by Contractor in trust or confidence.

(j) Contractor has not entered into any agreement, whether written or oral, which would conflict with the Services and there are no conflicts of interest between any professional duties and the Services.

(k) Contractor has no financial or personal interests in Arbor Research or Client, any affiliated thereof, and/or in any Client product that would prevent Contractor from completing the Services under this Agreement.

(l) Contractor will not use business cards mentioning a capacity as private consultant to Arbor Research or Client and will not use Arbor Research or Client's name on stationery.

(m) Contractor it will declare that it provides Services to Arbor Research and Client whenever speaking in public about a matter that is the subject of the Services, while it agrees not to make any statement on Arbor Research or Client's behalf or concerning Arbor Research or Client to the press, media, investors, brokers, banks, financial analysts and/or any other person. If applicable, it shall be responsible for (i) reporting immediately to the Arbor Research Project Manager and Responsible Officer any adverse events, adverse drug reactions (including pregnancy or lactation exposure, medication abuse, medication misuse, medication overdose, medication errors, off-label use, occupational exposure, drug interaction, unexpected benefit, lack of efficacy) or any other potential risk in connection with or arising out of the application of the products it has been made aware of in the course of rendering the Services and (ii) will further conform to any additional instructions (e.g. follow-up, reconciliation requests) received from Arbor Research or Client in that respect.

(n) Neith Contractor nor any of Contractor's affiliates and/or employees are under investigation by the United States Food & Drug Administration ("FDA") or any other competent regulatory authority for debarment action or is presently debarred pursuant to the Generic Drug Enforcement Act of 1992 or similar laws and that Contractor shall notify Arbor Research as soon as is practicable upon being made aware of any inquiry or the effective date of any such proceeding concerning Contractor or any of Contractor's affiliates and/or employees.

<u>General Provisions</u>

(a) Arbor Research shall have the right to make unilateral no-cost extensions to the Schedule as may be required. Other proposed changes or any waiver of any provision of this Agreement will

be enforceable only if mutually agreed to in writing by authorized representatives of Arbor Research and Contractor.

(b) All information and data provided by Arbor Research to Contractor shall be deemed to be Confidential, and Contractor agrees that this information and data: (1) will be used by Contractor only for purposes of performing this Agreement; (2) will not be disclosed to any third party without the express written permission of Arbor Research, and (3) will be protected by Contractor through implementation of procedures sufficient to prevent disclosure. The foregoing shall not prevent use or disclosure of information and data that: (1) are in the public domain or become publicly known through no fault of Contractor; (2) are approved for use or disclosure in writing by an authorized Arbor Research representative; or (3) are legally compelled to be disclosed by a court of competent jurisdiction.

(c) The Contractor shall not publish or otherwise disclose, except to Arbor Research, any Confidential reports, data or information generated or obtained in the course of performing this Agreement (including without limitation, information or data obtained hereunder concerning private individuals protected by Privacy Act, GDPR, or HIPAA regulations, organizations, or public agencies or any other source under promise of confidentiality), without the prior written consent of an authorized Arbor Research representative.

(d) All Deliverables as defined in this Agreement and related information that is prepared, stored, purchased or developed by Contractor or its designees as a result of Contractor's performance of the Services shall be the property of Arbor Research and Contractor hereby assigns to Arbor Research all rights, title and interest to such Deliverables together with all goodwill associated therewith. Contractor warrants and represents that these Deliverables shall be transferred without encumbrances or remaining third party rights and then Service Provider shall indemnify Arbor Research in case of third party actions.

(e) Contractor agrees to indemnify and hold harmless Arbor Research, its officers, directors, and employees, against any loss or damage caused by Contractor's negligent or willful acts or omissions in the performance of this Agreement. The provisions of this paragraph shall survive expiration or termination of this Agreement.

(f) Arbor Research may at any time, by written notice, terminate this Agreement for default, in whole or in part, if Contractor fails to perform as required by the Agreement and such failure is not corrected within ten days from the date of receipt of written notice from Arbor Research. In addition to any other rights and remedies provided by law, Arbor Research shall be entitled to purchase replacement services from an alternative source, and Contractor shall be liable to Arbor Research for any excess costs for such replacement services. Further, Arbor Research may, by written notice, terminate this Agreement for its convenience. Upon termination for convenience, Contractor shall be entitled to recover reasonable and allocable costs incurred as mutually agreed for services performed by Contractor prior to the date of termination.

(g) This Agreement shall be construed and governed in accordance with the laws of the State of Michigan.

(h) This Agreement, together with all attachments constitutes the entire agreement between the parties and supersedes all previous and contemporaneous agreements or representations whether written or oral. This Agreement is binding on and shall inure to the benefit of the assigns, successors, and the legal representatives of the parties.

(i) In the event that any one or more of the provisions of this Agreement should be held to be unenforceable, such determination shall not affect any of the other provisions of this Agreement.

(j) Arbor Research' total aggregate liability howsoever arising from or connected with this Agreement, whether in contract, warranty or tort shall in no event exceed the net amounts paid to Contractor by Arbor Research for the Services under this Agreement. Whether in contract, warranty or tort, in no event shall Arbor Research, its employees, affiliates, or agents be liable for any special, incidental or consequential damages of any nature arising out of or in connection with this Agreement.

(k) Contractor will be responsible for the payment of any social security, income tax, VAT tax, or similar payments required by law to be made in relation to this Agreement

(l) In the event access to Arbor Research' internal network systems will be needed by Contractor to fulfill the requirements of this Agreement, Contractor will be required to sign a separate Non-Disclosure Agreement with applicable protection provisions.

(m) Neither the confidentiality provision contained in this Agreement, nor confidentiality provisions contained in any existing agreement with Arbor Research shall be construed to prohibit or otherwise restrict lawful reporting of waste, fraud, or abuse to a designated investigative or law enforcement representative of a federal department or agency authorized to receive such information.

Dispute Resolution

All disputes arising in connection with this Agreement that cannot be resolved within a reasonable time following good faith attempts by the parties shall be finally settled in accordance with the Commercial Industry Rules of the American Arbitration Association, before a single arbitrator. Such arbitration shall be held in Detroit, Michigan.

Judgment upon any award rendered may be entered in any court of competent jurisdiction; provided, however, that the arbitrator shall have no authority to add, modify, change or disregard any lawful terms of this Agreement or to provide any relief or award not provided for or consistent with the laws of the State of Michigan.