Breakthrough T1D Request for Applications:

Development of Continuous C-Peptide Monitoring Technologies

October 2025

Summary

- Breakthrough T1D invites applications to develop continuous C-peptide monitoring (CCPM) technologies.
- Applications focused on early-stage development of sensor technologies, preclinical/feasibility studies and early-stage clinical evaluation of CCPM technologies will be considered.
- Applications may request up to $900,000 in total funding over a maximum period of three years. Applications of increased scope (time and/or budget) will be considered where there is a strong justification. Interested applicants should discuss with the Breakthrough T1D scientific contact, aghavami@breakthrought1d.org

Funding Opportunity Description

Breakthrough T1D is the world's leading non-profit organization dedicated to curing and improving the lives of people with type 1 diabetes (T1D) by accelerating breakthroughs for T1D. T1D is a chronic autoimmune condition characterized by the destruction of insulin-producing beta cells in the pancreas, resulting in hyperglycemia and dependence on exogenous insulin. C-peptide, a byproduct of endogenous insulin production, is widely recognized as a biomarker of beta cell function. However, current monitoring methods—such as stimulated tests (e.g., glucagon stimulation) and point-of-care (POC) assays that assess basal levels without stimulation—are invasive, time-consuming, and limited to single time-point measurements in clinical settings1. These approaches are poorly suited to capturing the dynamic nature of C-peptide secretion, and they offer limited utility for real-world, longitudinal monitoring. In particular, they are not well suited for detecting early beta cell changes following interventions such as disease modifying therapies (immunotherapies or beta cell preservation agents) or beta cell replacement. For example, they may fail to reliably detect early engraftment or subtle graft dysfunction following cell implantation. To address these limitations, Breakthrough T1D invites applications to develop continuous C-peptide monitoring (CCPM)

technologies. These efforts aim to expand capabilities in research and care by enabling more detailed, real-time, and user-friendly assessments of beta cell function over time. CCPM has the potential to improve our understanding of T1D progression and to support the development and evaluation of disease-modifying and cell-based therapies.

Background

Across all stages of T1D—from pre-symptomatic autoimmunity to established insulin dependence—C-peptide is widely accepted as an appropriate biomarker for quantifying residual beta cell function. In Stage 1, individuals have two or more islet autoantibodies with normal glucose levels, marking the start of immune-mediated beta cell destruction. In Stage 2, dysglycemia becomes detectable as beta cell function declines. Longitudinal C-peptide monitoring during these early stages could provide a more sensitive and dynamic assessment of disease progression, improving risk stratification and informing trial design. In Stage 3, with clinical diagnosis and insulin dependence, C-peptide remains a key marker: even low levels are associated with reduced glycemic variability, fewer hypoglycemic events, and delayed complications [2]. In the new-onset stage and established T1D disease (Stages 3 and 4), preserving or restoring C-peptide is a major goal of emerging therapies, and the U.S. Food and Drug Administration (FDA) considers C-peptide a "reasonably likely surrogate endpoint" for evaluating beta-cell function in clinical trials.

C-peptide secretion is inherently dynamic, influenced by food intake, physical activity, circadian rhythms, and other physiological factors. Current testing strategies do not account for this variability. A single measurement may overestimate or underestimate true beta cell function depending on transient metabolic conditions. In contrast, CCPM could distinguish between short-term fluctuations and sustained changes in secretion patterns, providing a more accurate and actionable picture of beta cell status. CCPM would enable high-resolution, real-time assessment of beta cell activity. This capability could support earlier detection of functional recovery or deterioration, improve characterization of therapeutic effects, and enhance clinical and research decision-making. In cell therapy applications, where engraftment and functional recovery can take weeks to months and vary across individuals, CCPM could facilitate timely identification of graft failure or immune rejection and guide adjustments to immunosuppressive therapy. Similarly, in trials of immunotherapies or beta cell–protective agents, continuous monitoring could improve endpoint sensitivity, help differentiate responders from non-responders, and reduce reliance on burdensome stimulation protocols.

This RFA aims to advance the development of technologies for continuous C-peptide monitoring, primarily through early-stage and preclinical studies, with potential application across the stages of T1D. We seek sensor platforms capable of detecting C-peptide at physiological concentrations with sufficient sensitivity, specificity, and stability for real-world, longitudinal use. While the primary focus is on continuous monitoring, proposals that enable high-frequency or at-home testing will also be considered, provided they represent clear improvements over existing methods and support practical, scalable assessment of beta cell function. Depending on the context and maturity of the

technology, CCPM platforms developed under this RFA may ultimately serve as: (1) improved tools for clinical care, (2) investigational tools to accelerate development of disease-modifying therapies, or (3) companion diagnostics to guide or monitor response to therapies such as immunotherapy or cell therapy.

Objectives

Letters of Intent (LOIs) are sought from academic and industry applicants with innovative approaches to develop CCPM technologies. Examples of research appropriate for this RFA include, but are not limited to:

- Early-stage development of sensor technologies capable of continuous or high-frequency C-peptide detection in biological fluids such as plasma or interstitial fluid.
- Preclinical development and validation of CCPM systems.
- Feasibility studies and early-stage clinical evaluation of CCPM technologies.

Deliverables

Proposals must define clear, realistic goals and milestones aligned with the maturity of the technology. Proposals must be designed to reach key inflection points that will determine whether further development is warranted. Examples include:

- In vitro characterization of sensor performance (e.g., sensitivity, specificity, stability, dynamic range).
- Demonstration of detection in relevant biological fluids under physiological conditions.
- Initial validation in animal models or early clinical feasibility studies.
- Integration of biosensors into user-friendly, wearable, or at-home platforms.

Applicants are encouraged to consult with the Breakthrough T1D scientific staff below to discuss the alignment of their proposal to this RFA and to develop the projected study concept. Breakthrough T1D follows U.S. National Institutes of Health (NIH) Public Health Service Policy guidelines for the humane care and use of animals in research and the U.S. Department of Health and Human Services (HHS) regulations for the protection of human subjects in research (45 CFR 46). Breakthrough T1D requires the Grantee Institution to comply with these guidelines.

Critical considerations

- Innovative sensing technologies—such as aptamer-based, antibody-based, enzymatic, optical, or protein-binding mechanisms, as well as other novel recognition and transduction platforms—are of interest, provided they offer high sensitivity, selectivity, and scalability.
- Sensitivity to very low C-peptide concentrations must be demonstrated, as levels in people with T1D can fall into the picomolar range.
- Minimally invasive approaches or integration with commercially available CGM platforms are preferred. Implanted devices may be considered if accompanied by strong justification and demonstrated potential for clinical utility.
- Minimizing on-body burden and ensuring usability across diverse populations should be a priority in device design.
- User-friendly formats—such as wearable, at-home, or minimally invasive solutions—are encouraged to support real-world use and adoption.
- Proposals may describe how CCPM data could be used to complement existing diabetes technologies and biomarkers (e.g., proinsulin:C-peptide ratio) or to inform key research questions in therapeutic development.
- Collaboration between sensor developers and clinical experts is strongly encouraged to ensure clinical relevance, appropriate study design, and translational potential.
- Applicants must outline a clear plan for next steps beyond the funding period, including pathways for further development, validation, or regulatory engagement.
- Breakthrough T1D will consider additional funding to support independent third-party validation of preclinical or early clinical results.

Applications are welcome from academic institutions, industry, or cross-sector collaborations.:

Eligibility

- Applications may be submitted by domestic and foreign non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of state and local governments, and eligible agencies of the federal government. Applicants must hold an M.D., D.O., D.M.D., D.V.M., Ph.D., or equivalent and have a faculty position or equivalent at a college, university, medical school, or other research facility.

- To assure continued excellence and diversity among applicants and awardees, Breakthrough T1D welcomes proposals from all qualified individuals and encourages proposals from a broad cross section of researchers and scientists

Funding Mechanisms

In response to this announcement, applications may request up to a **total of $900,000 USD for up to three years**.

- The level of funding will vary depending on the scope and overall objectives of the proposal. Breakthrough T1D may consider applications with increased scope (time, budget) where there is a strong justification, and applicants interested in such should discuss with the Breakthrough T1D scientific contact below.
- Note that the above budget figure is a maximum, and Breakthrough T1D will also consider projects with substantially smaller budgets. In all cases, the level of requested funding should be commensurate with the studies proposed and non-Breakthrough T1D resources (funds, personnel, other) available to successfully complete the project. Appropriateness of budget in relation to scope will be considered as part of the review criteria.

Letters of Intent (LOI) can be submitted under the following mechanism(s):

Strategic Research Agreement (SRA)

Strategic Research Agreements are intended for support of research activities at non-for-profit entities such as academic institutions. For more information on the SRA grant mechanism please refer to the Grant Handbook. SRA applications may include up to 10% indirect costs as part of the total request.

Industry Discovery and Development Partnerships (IDDPs)

For-profit entities may apply under Breakthrough T1D's Industry Discovery & Development Partnership (IDDP) funding mechanism, which entails additional requirements including company matching funds.

If you would like to submit an IDDP project LOI to this RFA, please see our Grant Handbook for additional information and contact Dr. Courtney Ackeifi (cackeifi@breakthroughT1D.org) to discuss proposed scope and budget prior to submitting an application. Indirect costs are not permitted on IDDP applications. IDDP applications that are invited to a full proposal will receive their own timeline for completion of due diligence and finalization of an agreement.

Letter of Intent (LOI)

Prospective applicants should submit a letter of intent (LOI) using the template provided online via RMS360. The LOI should be 2 pages and submitted online to be considered for a full proposal invitation.

Proposal

An approved LOI is required prior to the submission of a full proposal. Upon notification of a request for a full proposal, the application must be completed using the templates provided in RMS360. Complete information should be included to permit a review of each application without reference to previous applications.

Clinical studies

- Note that all applications involving human subject research must include supplemental information to address subject safety, study design, and investigational product information.
- Breakthrough T1D follows U.S. National Institutes of Health (NIH) Public Health Service Policy guidelines for the humane care and use of animals in research and the U.S. Department of Health and Human Services (HHS) regulations for the protection of human subjects in research (45 CFR 46). Breakthrough T1D requires the Grantee Institution to comply with these guidelines.
- More details can be found in the Human Subject Research Guidelines section of the Grant Handbook.

Review Criteria

Applications will be evaluated based on Breakthrough T1D's standard confidential award policy and according to the following criteria:

- Significance

- Relevance
- Approach
- Innovation
- Environment
- Clinical translation roadmap

Projected Timeline

Milestone	Date
LOI Deadline	December 04, 2025
Notification of LOI Outcome	January 08, 2026
Full Proposal Deadline	February 12, 2026
Award Notification	July 2026
Earliest Anticipated Start	September 2026

Program Contacts

Strategic Fit and Scientific Inquires

Amin Ghavami Nejad, Ph.D.
Senior Scientist
aghavami@breakthrought1d.org

Administrative Inquiries

Madhu Prakash, MSW
Program Administrator
mprakash@breakthrought1d.org

If you have any system questions as you work within RMS360, please contact the administrative contact listed above.

1 Leighton, E., Sainsbury, C. A. & Jones, G. C. A Practical Review of C-Peptide Testing in Diabetes. *Diabetes Ther* **8**, 475-487 (2017). https://doi.org:10.1007/s13300-017-0265-4

2 Marinac, M. *et al.* Future Directions and Clinical Trial Considerations for Novel Islet β-Cell Replacement Therapies for Type 1 Diabetes. *Diabetes* **74**, 1452-1463 (2025). https://doi.org:10.2337/dbi24-0037