Breakthrough T1D Request for Applications: Supportive Technologies for the Scaling of Manufactured Islet Replacement Therapies

April 2025

Summary

- The goal of this funding opportunity is to improve the efficiency of scaling protocols for manufactured islet cell therapies for type 1 diabetes (T1D) via development of supportive technologies tackling one or more of the barriers associated with implementation and expansion of next-generation beta cell replacement therapies.

- This initiative will award grants to academic investigators and industry partners of up to $600,000.00 over 2 years.

Background

The ultimate goal of Breakthrough T1D's Cell Therapy program is to have an islet replacement therapy that is suitable and accessible for everyone living with T1D. (Link to Strategy Document Here). Current clinical islet transplantation is efficacious in improving glycemic control and quality of life but is restricted to individuals with severe hypoglycemia and hypoglycemia unawareness. Further advancements are required to expand the benefits of islet transplantation for broader patient populations. There are several barriers to consider for the expansion of these next generation therapies, namely the supply of a manufactured insulin producing cells, the limited survival and engraftment of transplanted cells, and the need for lifelong broad immunosuppressive medication to prevent rejection. The major barriers and progress toward addressing these barriers are reviewed here (Grattoni et al. 2024, Nature Rev Endo).

Thanks to the efforts of Breakthrough T1D funded researchers, industry partners, and others, there are multiple late preclinical and early clinical programs advancing toward the dismantling of one or more of these barriers. However, as these products move from late preclinical and early clinical stages, significant technological advancements in processes,

storage, and access will be required in order to enable the deployment of these therapies at later stages of development and larger scale.

For example, considerations for the differentiation processes to generate manufactured islets from pluripotent cells include cost of goods and labor-intensive protocols. These cells display an immature phenotype compared to bona fide primary islets, requiring a period of *in vivo* maturation to reach fully functional maturity and provide benefit to patients. Increasing the efficiency for generating high quality cells would better support the expanded T1D patient population for next generation therapies. For example, early critical quality attributes that predict successful differentiation are limited. In addition, the banking and storage of manufactured islet cells at late stages of differentiation remains challenging owing to the fragile nature of insulin producing cells, leading to loss in either viability or function. Overall, while great progress has been made in developing promising islet cell therapies utilizing renewable cell sources, pro-engraftment strategies, and alternative immune protection schemes, there is a need to develop supporting technologies to enable the scaling of these next generation therapies.

Funding Opportunity Scope

Breakthrough T1D's role is to enable the scientific community to address these challenges with the ultimate goal of accelerating the development of safe and effective islet cell therapies that are available to all individuals living with established T1D. Therefore, Breakthrough T1D is soliciting Letters of Intent (LOI) from investigators in academic and industry settings aiming to develop supportive technologies tackling one or more of the barriers associated with adoption of next-generation beta cell replacement therapies and enable the scaling of islet cell therapies for expanded patient populations.

Prioritization will be given to projects developing good manufacturing practice (GMP) compatible technologies with a clear plan toward implementation in current workflows.

Examples of topics pertinent to this call include but are not limited to:

- Validation of novel differentiation processes resulting in shorter timelines to insulin-producing cells.
- Development of innovative culture systems for scalable production capacity of pluripotent cell differentiation (e.g., automation)
- Cell culture processes and technologies that reduce the cost of goods for generating insulin-producing cells.

- Demonstration of cryoprotective storage solutions for manufactured islets that preserve cell viability and glucose responsive insulin secretion.
- Identification and validation of critical quality attributes at early stages of differentiation that can predict a successful manufactured run or the applicability of a given protocol to a new cell source.

Topics out of scope for this funding opportunity:

- Discovery stage research on immune protection or pro-engraftment strategies
- Derivative improvements of current protocols at small scale. Projects must demonstrate improvement is transferable to larger scales (e.g., ~$1x10^9$ cells per batch).

Eligibility

Applications may be submitted by domestic and foreign non-profit organization, public and private, such as universities, colleges, hospitals and laboratories, units of state and local governments and eligible agencies of the federal government, for-profit entities, or industry collaborations with academia. Applicants must hold an M.D., 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.

Please note that applications from for-profit entities or industry collaborations with academia may be submitted in response to this RFA. Additional information will be requested from for-profit entities if invited to submit a full proposal.

There are no citizenship requirements for this program. To assure continued excellence and diversity among applicants and awardees, Breakthrough T1D welcomes applications from all qualified individuals and encourages applications from persons with disabilities, women, and members of minority groups underrepresented in the sciences.

Funding Mechanisms

In response to this announcement, Letters of Intent (LOI) can be submitted under the following mechanism(s):

Strategic Research Agreements (SRAs)

Strategic Research Agreements are intended for support of research activities at non-for-profit entities such as academic institutions. For SRAs, proposed budgets for projects should not exceed $600,000.00 USD (including 10% indirect costs) total costs for up to two (2) years. The level of funding will vary depending on the scope, data available, need to perform additional laboratory assays, access to samples, degree of data analysis to be performed, and overall objectives of the proposal. If your project budget and/or timeline exceeds $600,000.00 and/or 2 years, please discuss with Breakthrough T1D staff (contact information below). For more information on the Strategic Research Agreement (SRA) grant mechanism please refer to our grant handbook.

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 and typically has a modest royalty payback to Breakthrough T1D. If you would like to submit an Industry Discovery and Development Partnership (IDDP) project LOI to this RFA, please check our grant handbook for additional information and contact Dr. Nicholas Mamrak (nmamrak@BT1D.org) to discuss proposed scope and budget prior to submitting an application. Indirect costs are not permitted on IDDP applications.

Letter of Intent

Applicants should submit an LOI, [2 pages maximum] online via RMS360 to be considered for a full proposal request. The LOI template provided on the RMS360 website must be used to complete the application to be considered for a full proposal request. The LOI template provided on the RMS360 website must be used to complete the application.

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. Proposal section templates in Microsoft Word, [10 pages maximum] should be type-written, single-spaced, and in typeface no smaller than 10-point font and have no more than six vertical lines per vertical inch. Margins, in all directions, must be at least ½ inch. Complete information should be included to permit a review of each application without reference to previous applications.

Note that all applications involving human subject research must include supplemental information to address subject safety, study design, and investigational product information. More details can be found in the Human Subject Research Guidelines section of the grant handbook.

Breakthrough T1D follows the U.S. National Institutes of Health (NIH) guidelines for studies including human subjects, including the Common Rule changes.

Review Criteria

Applications will be subjected to confidential external scientific review evaluated on the following:

- Significance
- Relevance
- Approach
- Environment
- Resource sharing plan

Projected Timeline

Milestone	Date
LOI deadline	May 28, 2025
Notification of LOI Outcome	June 16, 2025
Full proposal deadline	July 16, 2025
Award notification	September 2025
Earliest anticipated start	December 2025

Program Contacts

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