JDRF Request for Applications: Clinical Trials and Mechanistic Clinical Studies to Advance Adjunctive Therapies for Glucometabolic Control in Type 1 Diabetes

April 2022

Purpose

JDRF is committed to accelerating the development of therapies that can complement insulin (i.e., adjunctive therapies) to improve glucose and metabolic outcomes in people with type 1 diabetes (T1D). To this end, we invite applications that propose (1) clinical trials to evaluate glucometabolic therapies in people with T1D or (2) mechanistic clinical studies to advance our knowledge of glucometabolic control in T1D toward the goal of future therapy development.

Background

Insulin is required for all people with T1D. However, for most people, insulin monotherapy is insufficient for optimal glucose control. Further, a growing body of evidence is demonstrating the contribution of non-glucose metabolic imbalances like insulin resistance and obesity to long-term complications in T1D. Since insulin is powerless to address these and other challenges, adjunctive therapies must be developed to address both glucose and broader metabolic control. Despite the urgent need, only one adjunctive therapy (pramlintide) currently has regulatory approval in the US. Barriers to the development of adjunctive therapies for T1D glucometabolic control include an evidence gap for how existing and emerging therapies for type 2 diabetes, obesity, and other indications affect outcomes in T1D, lack of knowledge about specific mechanisms underlying glucometabolic imbalances in T1D, and limited commercial investment. This RFA is intended to support (1) clinical trials testing therapies—novel or repositioned, approved or in clinical development— for glucometabolic control in T1D, or (2) mechanistic clinical research to inform a better understanding of T1D glucometabolic imbalances to enable future therapy development.

Objectives

Letters of intent (LOIs) are sought from academic or industry applicants to advance adjunctive therapies for glucometabolic control in T1D.

Examples of research appropriate for this RFA include, but are not limited to:

- Clinical trials testing novel therapies in T1D
- Clinical trials testing drugs that are approved or in development for type 2 diabetes, obesity, and other indications, such as GLP-1 based mono-, di-, and tri-agonists and novel amylin analogs, or others
- Clinical trials testing drugs approved or in development for non-metabolic diseases where there is a credible hypothesis for efficacy in T1D glucometabolic control
- Clinical trials testing drug combinations or co-formulations
- Registrational clinical trials for a novel or expanded T1D indication

- Experimental medicine trials exploring mechanism of action and/or proof-of-concept in T1D
- Mechanistic clinical studies exploring druggable pathways for glucometabolic control in T1D
- Clinical studies to identify novel therapeutic targets or investigate existing targets
- Analysis of real-world data to assess efficacy and safety of therapies in T1D, including clinical trial emulations, EMR data, or other innovative methods

Examples of research not covered by this RFA include:

- Studies focused on beta cell protection or function
- Studies focused on T1D prevention
- Development of insulin therapeutics
- Nonclinical studies except in exceptional cases where they contribute directly to clinical development efforts
- Studies focused on hypoglycemia unawareness
- Studies focused on natural history of pathogenesis
- Clinical trials evaluating lifestyle interventions such as diet and exercise

Deliverables

- Successful clinical trials should provide safety and efficacy data to support next steps in a path toward further clinical development, regulatory approval and/or changes to clinical guidelines
- Successful mechanistic clinical studies will provide data that can be used to inform future therapy development efforts

Applicants are encouraged to consult with the JDRF Scientific Staff below to discuss the alignment of their proposal to this RFA and to develop the projected study concept.

Critical Considerations

- Clinically relevant glucose control outcomes include HbA1c, severe hypoglycemia, level 1 and 2 hypoglycemia, time-in-range, glycemic variability, and others
- Clinically relevant metabolic control outcomes include insulin resistance, weight/adiposity, lipids, ketones, and others
- Trials in sub-populations of T1D may be considered, such as people with T1D and overweight/obesity or high HbA1c, people in vulnerable age groups, and others
- Expectation of direct benefits on long-term complications is encouraged, but not required, in selection of therapeutic intervention
- Mechanistic clinical studies must be designed to inform further therapy development efforts
- JDRF strongly encourages applications from industry
- JDRF supports collaborative approaches, including between academic applicants and industry partners
- JDRF encourages proposals that seek to leverage existing or planned projects (e.g., proposals that add resources to projects with funding from other sources)
- JDRF encourages proposals to include people with T1D in existing or planned trials predominantly featuring other populations (e.g., people with type 2 diabetes or obesity)

- It is the responsibility of the applicant to obtain drugs for their study. JDRF funding will be contingent on a written commitment from the drug manufacturer to provide study drug and placebo.
- Insulin requiring non-T1D populations may be included in research plan as appropriate, but primary focus on T1D is required

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.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 to this RFA; however, additional information will be requested from for-profit entities if a full application is invited.
- There are no citizenship requirements for this program. To assure continued excellence and diversity among applicants and awardees, JDRF welcomes applications from all qualified individuals and encourages applications from persons with disabilities, women, and members of minority groups underrepresented in the sciences.

Funding Mechanism

In response to this announcement, LOI's can be submitted to JDRF's Strategic Research Agreement (SRA) or Industry Discovery and Development Program (IDDP) grant mechanisms. For more information on these mechanisms, please refer to our website:

- **Strategic Research Agreements:** http://grantcenter.jdrf.org/information-for-applicants/grant-mechanism-descriptions/strategic-research-agreements/
- **Industry Development and Discovery Program:** https://grantcenter.jdrf.org/industry-discovery-development-partnerships/ For IDDP applications, applicants are required to contact the JDRF scientific contact below prior to submitting a LOI.

Each application proposing a clinical trial may request up to a total of $2,000,000 over a maximum of three years. Each application proposing a mechanistic clinical study may request up to a total of $1,000,000 over a maximum of two years. SRA totals can include up to 10% indirect costs; IDDP applications do not permit indirect costs. JDRF may consider applications with increased scope (time and/or budget) where there is a strong justification, and interested applicants should discuss with the JDRF scientific contact below.

Letter of Intent

Prospective applicants should submit a LOI 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. Applicants will be notified according to the timeline below if they have been approved to submit a full application.

Letters of intent should use the template provided and include the following information:

- Background/rationale, preliminary data and references to relevant publications, specific aims, project deliverables, collaborative framework if applicable
- For clinical trials, expected benefits and risks of proposed therapy in T1D
- For mechanistic clinical studies, an explanation of how successful completion of the study will enable therapy development
- Plan for acquiring drugs and placebo/controls used in the study, if applicable
- Intellectual property or commercial efforts associated with the current application, including a list of existing business partnerships relevant to the proposed work
- Estimated budget (total and yearly)

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 on the RMS360. 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.

JDRF 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
- Innovation
- Investigator experience
- Environment

Projected Timeline

Milestone	Date
LOI deadline	Tuesday, June 21, 2022
Notification of LOI Outcome	Tuesday, July 12, 2022
Full proposal deadline	Tuesday, August 23, 2022
Award notification	February 2023
Earliest anticipated start	April 2023

Program Contacts

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