**REQUESTS FOR LETTERS OF INTENT (LOI):**

# CLINICAL AND PRECLINICAL STUDIES TO SIGNIFICANTLY REDUCE THE INCIDENCE OF HYPOGLYCEMIA BY PRESERVING OR RESTORING HYPOGLYCEMIA AWARENESS AND/OR THE COUNTER-REGULATORY RESPONSE IN INDIVIDUALS WITH T1D

## PURPOSE

JDRF aims to accelerate the discovery and translation of therapies to prevent or treat hypoglycemia unawareness in people with T1D as this complication significantly increases the risk of severe hypoglycemia that can lead to seizure, coma, cardiac arrhythmias and increased mortality. To this end, JDRF is soliciting letters of intent for research with the potential to translate into novel therapeutic strategies that will significantly reduce the incidence of hypoglycemia by maintaining or restoring awareness of potentially life-saving hypoglycemia warning symptoms in individuals with T1D.

## BACKGROUND

Iatrogenic hypoglycemia is responsible for 4-10% of the mortality rate and is the chief barrier to optimal glucose control in people with T1D. Frequent hypoglycemia has been shown to reduce the glycemic threshold for activation of the counter-regulatory response needed to restore euglycemia during a subsequent hypoglycemic episode (hence, “hypoglycemia begets hypoglycemia”). As a result, some individuals develop hypoglycemia-associated autonomic failure (HAAF) and do not experience and respond to the potentially life-saving warning symptoms, and are at increased risk of seizures, coma and death. It is estimated that up to 25-40% of individuals with T1D have some level of impaired awareness of hypoglycemia. Progress in closed-loop artificial pancreas systems and beta cell replacement therapies hold great promise for the mitigation and ultimate elimination of hypoglycemia. JDRF seeks to complement this progress with novel therapeutic approaches in order to provide the broadest range of treatment alternatives to people with T1D.

## OBJECTIVES

JDRF is seeking letters of interest with innovative approaches to treat, prevent and diagnose hypoglycemia unawareness and/or HAAF. Examples might include, but are not limited to:

- Strategies to restore or prevent loss of glucagon and/or epinephrine responses in hypoglycemia
- Strategies to restore or prevent loss of symptomatic awareness of hypoglycemia
- Clinical and preclinical studies to support the repurposing of existing drugs
- Biomarkers that may predict hypoglycemia unawareness and/or HAAF development or response to therapy

Preference will be given to clinical study proposals linking a pathway or target to hypoglycemia unawareness or HAAF with line of sight into therapy development. Device-based or beta-cell replacement/regeneration/survival approaches will not be considered in this RFA.

## MECHANISM

In response to this announcement, LOI’s can be submitted to our **Strategic Research Agreement (SRA)** or **Industry Development and Discovery 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*:* http://grantcenter.jdrf.org/industry-partnerships/

Up to a maximum of $300,000 USD per year including 10% indirect costs for up to 3 years may be requested. The level of funding and duration may vary depending on the scope and overall objectives of the proposal, and

applicants are encouraged to consult with JDRF scientific staff as needed. Applications whose budget and/or timeline exceeds the above specified guidelines, must obtain JDRF staff approval prior to submitting an LOI.

Applications that are not funded in this competition may be resubmitted to other JDRF grant mechanisms according to the deadlines and guidelines described on the JDRF website: http://grantcenter.jdrf.org/rfa/

## 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 LOI, however, additional information will be requested from for-profit entities if a full application is invited.

For clinical studies, applicants must hold an appointment or joint appointment in a subspecialty of clinical medicine, and conduct human clinical research.

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.

## LETTER OF INTENT

Prospective applicants should submit a Letter of Intent on line via RMS360 (http://jdrf.smartsimple.us) 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 approximately eight weeks after the LOI deadline date if they have been approved to submit a full application.

Please see below for complete instructions. Letters of intent should use the template provided and include the following information:

- Background /Rationale and Specific Aims of overall project
- Overview of hypotheses, goals, deliverables and collaborative framework as applicable
- Title, lead investigator and brief description and specific aims of individual projects (if collaborative/network)
- Expected deliverables and impact of the proposed study with potential next steps
- Intellectual Property or commercial efforts associated with the current application
- Total budget / budget by year by project
- Biosketches for all Principal Investigators

## PROPOSAL

**An approved Letter of Intent is required prior to 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 (http://jdrf.smartsimple.us). Proposal section templates in MS Word [**10 page 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 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:
http://grantcenter.jdrf.org/wp-content/uploads/2012/12/JDRF_Scientific_Guidelines_final-Aug2015.pdf

## ANNOUNCEMENT INTRODUCTION AND PUBLIC Q&A

JDRF will hold announcement introduction meeting via web and teleconference on **Tuesday October 4th, 2016 at 11:00am** US Eastern Standard Time, to which all interested prospective applicants are invited. JDRF scientists will give an overview of the goals of this initiative, explain the application process and answer initial questions on applications. A brief introduction on JDRF's new grant application portal (RMS360) will also be

given.

**Click here to Join WebEx meeting**
Meeting number: 732 792 304
Meeting password: jdrf2016

**Join by phone**
Dial in (US): 1-877-261-5012
Dial in (International): https://www.intercallonline.com/listNumbersByCode.action?confCode=5908746746
Conference Code: 361-854-0279

## DEADLINES

- **RFA Release Date** Friday September 23rd, 2016
- **Letter of Interest Deadline** Tuesday November 8th, 2016
- **Notification of Full Application Request** Tuesday November 22nd, 2016
- **Application Deadline** Tuesday January 24th, 2016
- **Response to Applicants** June 2017
- **Earliest Anticipated Start Date** July 2017

## SUBMISSION INSTRUCTIONS

Applicants should register and submit their completed LOI in RMS360 (http://jdrf.smartsimple.us).

## REVIEW CRITERIA

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

- Significance
- Relevance
- Approach
- Innovation
- Investigator Experience
- Environment

## CONTACTS

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

For any **non-grant-specific** inquiries or issues, please contact SmartSimple Support Services via email support@smartsimple.com or phone (866) 239-0991. Support hours are Monday through Friday between 5:00am and 9:00pm US Eastern Standard Time.