JDRF REQUESTS LETTERS OF INTENT FOR:
NOVEL THERAPEUTIC STRATEGIES TO PREVENT OR DELAY PROGRESSION OF EARLY STAGE DIABETIC NEPHROPATHY

PURPOSE

JDRF is the world's leading non-profit organization with the mission to accelerate life-changing breakthroughs to cure, prevent and treat type 1 diabetes (T1D) and its complications. To this end, JDRF is soliciting letters of intent for therapeutic strategies to prevent or delay progression of diabetic nephropathy (DN) at the earliest possible stages.

BACKGROUND

Diabetic nephropathy develops in approximately 30% of individuals with T1D and is the leading cause of mortality in this population. While there are encouraging signs that end-stage renal disease (ESRD) may be declining, this seems to reflect better glucose control and slower progression of established DN rather than prevention of early DN per se. Indeed, the majority of patients succumb to cardiovascular disease before needing kidney replacement therapy - underscoring the critical need for effective interventions at the earliest stages in people with T1D, well before the onset of ESRD.

The mortality risk from DN can be substantially reduced with improved management of glucose control, blood pressure and other cardiovascular risk factors, such as lipids. However, optimal control does not abolish the risk and novel therapeutic strategies are critically needed. Furthermore, only about one-fifth of people with T1D are achieving recommended glucose control targets.

DN is characterized by a long clinically silent period without signs or symptoms of disease. By the time clinical manifestations such as micro- or macroalbuminuria or GFR decline becomes apparent, renal structural changes are well established. As such, disease-modifying interventions are needed at the earliest stages when these lesions might be most responsive to therapy.

Recent landmark trials with SGLT2 inhibitor and GLP-1 drugs have demonstrated impressive cardiorenal protection in people with T2D. Unfortunately, T1D was largely excluded from these studies and remains an exclusion criterion in the majority of diabetic nephropathy clinical trials. Trials of promising novel or repurposed therapies in people with T1D, whether small mechanistic or large pivotal, are essential to bring urgently needed renoprotection, and by extension cardioprotection, to this underserved population.

Recent data from Joslin T1D Medalists, individuals who have lived with T1D for over 50 years and have not developed major complications, suggests the presence of endogenous mechanisms that protect against DN and other complications. Therapeutic strategies to enhance these protective effects may ultimately lead to novel treatments that prevent onset and progression of DN in people with T1D as well as T2D.

OBJECTIVES

JDRF is soliciting letters of intent (LOIs) for clinical studies that address a key research/knowledge gap for translation of novel therapies to prevent or delay DN pathology at the earliest possible stages in people with T1D.

Academic or industry applicants, preferably multidisciplinary teams, with innovative disease-modifying approaches are encouraged to apply.

Examples of clinical studies include but are not limited to:

- Mechanistic studies supporting the repurposing of existing drugs approved for other indications

- Clinical evaluation of novel therapies that prevent or reverse diabetic nephropathy by targeting the underlying pathogenic mechanisms
- Drugs that enhance the action of endogenous protective mechanisms and pathways

This call excludes preclinical studies. The tolerable risk and user burden for chronic renoprotective therapies is necessarily low and applicants should take drug safety profiles and treatment regimens into consideration. Applicants will also be responsible for procuring the necessary drug(s) for their studies.

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

CLINICAL STUDIES

- JDRF follows the U.S. National Institutes of Health (NIH) guidelines for studies including human subjects, including the common rule changes: https://nexus.od.nih.gov/all/2019/01/07/nih-implementation-of-the-final-rule-on-the-federal-policy-for-the-protection-of-human-subjects-common-rule/
- JDRF endorses the use of outcomes beyond A1c. Please review Section 6.3 of JDRF's Award Terms & Conditions: http://grantcenter.jdrf.org/wp-content/uploads/2019/07/JDRF-Terms-and-Conditions-7.2.2019.pdf

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: http://grantcenter.jdrf.org/industry-discovery-development-partnerships/

Each application may request up to $600K (including up to 10% indirect costs) for a project lasting up to 3 years. Applicants should discuss with JDRF Scientific Staff (see below) when proposing projects with increased scope (time, budget).

For-profit entities interested in submitting an IDDP LOI are requested to contact JDRF prior to submitting an LOI. The IDDP application entails additional requirements including matching funds from the company and administration of the award by contract agreements. Projected timelines for IDDP submissions will be determined ad hoc by JDRF and communicated to the Principal Investigator at the time of invitation to submit a full IDDP proposal.

For-profit entities whose business models do not lend themselves to JDRF's standard IDDP terms (e.g. fee-for-service models) are encouraged to submit LOI's in conversation with JDRF Scientific Staff.

Applications that are not funded through this RFA 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 a faculty position or equivalent at a college, university, medical school, industry setting 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. Submissions from for-profit entities or collaborations involving for-profit entities will be reviewed by the JDRF T1D Fund (t1dfund.org) in addition to JDRF 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 LOI online 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, scientific approach, published or preliminary data, hypotheses, specific aims, deliverables of project, collaborative framework if applicable
- Description of potential for translating project deliverables into therapies, including short and long-term development goals
- Plan for acquiring drugs used in the study, if applicable
- Indication of whether research will include human subjects
- Intellectual property or commercial efforts associated with the current application
- Estimated budget (total and yearly)

PROPOSAL

An approved LOI (2 page maximum) 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-Aug20151.pdf

ANNOUNCEMENT INTRODUCTION AND PUBLIC Q&A

JDRF will hold an announcement introduction meeting via web and teleconference on **Wednesday November 20, 2019 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.

Click here to Join WebEx meeting
Meeting number: 730 125 928
Meeting password: pyuqXZa9

Join by phone
Dial in (US): 1-650-429-3300
Dial in (International): Global Call in Numbers
Conference Code:730 125 928

DEADLINES

- **RFA release date** November 08, 2019
- **LOI deadline** December 10, 2019
- **Notification of full application request** December 16, 2019

- **Application deadline** January 27, 2020
- **Response to applicants** July 2020
- **Earliest anticipated start date** September 2020

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 to T1D
- Approach
- Innovation
- Investigator experience
- Environment

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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.