JDRF REQUESTS LETTERS OF INTENT FOR: REPOSITIONING DRUGS TO IMPROVE METABOLIC CONTROL IN ESTABLISHED TYPE 1 DIABETES

PURPOSE

JDRF is committed to accelerating the development of therapies that can complement insulin (i.e. adjunctive therapies) to improve metabolic outcomes in people with type 1 diabetes (T1D). A promising strategy to advance new therapies for T1D is to reposition drugs from other indications. To this end, we invite applications to identify or validate drugs with regulatory approval for non-T1D indications, or in advanced clinical development for non-T1D indications, to be repositioned as adjunctive therapies for established T1D, i.e. insulin-requiring T1D.

BACKGROUND

Insulin is necessary but not sufficient for most people with T1D to achieve optimal glycemic control and other metabolic outcomes. Adjunctive therapies (e.g. pramlintide, SGLT inhibitors, GLP-1 receptor agonists) improve outcomes, but few such therapies are currently approved for T1D. The barriers to bringing forward adjunctive therapies include the long duration and high cost of drug development, as well as the unknown safety profiles of novel drugs. These challenges can be substantially mitigated by repositioning (aka repurposing) drugs that are already approved or in clinical development for other indications such as type 2 diabetes or diseases seemingly unrelated to T1D. This RFA is intended to advance repositioning efforts to expand the armamentarium of T1D adjunctive therapies.

OBJECTIVES

Letters of intent (LOI's) are sought from academic or industry applicants with innovative approaches to 1) identify drugs, either approved or in clinical development, to be repositioned as T1D adjunctive therapies, or 2) validate such drugs in preclinical T1D models or clinical studies. Desired outcomes for metabolic control in T1D include improved glycemia (HbA1c, time-in-range, prandial glucose excursions, hypoglycemia, etc.) and improvement of non-glycemic imbalances relevant to T1D (e.g. insulin resistance, hyperketonemia, dyslipidemia, obesity, pathologies associated with development of long-term complications).

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

- In silico approaches to identify drugs likely to show efficacy for metabolic control in T1D. Such approaches may take advantage of any relevant data (e.g., "omics" datasets, molecular structures, health records, published screens, etc.) and technology (e.g., network-based approaches, machine learning, etc.);
- In vitro or in vivo screens to identify drugs likely to show efficacy as therapies for T1D metabolic control;
- Preclinical or clinical validation studies of drugs already identified as candidates for repositioning for T1D metabolic control.

This RFA will not support applications primarily focused on the following areas that are being funded by JDRF by other mechanisms:

- Identifying novel biological targets for T1D metabolic control as an end in itself; target identification and other mechanistic analyses may be intermediate steps in the study, but identification of drugs must be the end goal;
- Repositioning drugs to prevent beta cell depletion either by promoting beta cell survival/regeneration or by modulating the autoimmune attack on beta cells;
- Investigating drugs already being validated for T1D metabolic control (e.g. GLP-1 receptor agonists, SGLT inhibitors, metformin, etc.).

Deliverables

- Successful grants will either 1) identify one or more drugs to be validated for T1D metabolic control in future studies, or 2) complete preclinical or clinical validation studies to support repositioning of one or more drugs for T1D metabolic control.

CRITICAL CONSIDERATIONS

- The target population for repositioned drugs is people with established T1D, and strategies to identify or validate drugs for repositioning should be designed with this population in mind;
- The tolerable risk and user burden for T1D adjunctive therapies are low; strategies to identify candidates for repositioning should consider drug safety profiles and treatment regimens;
- As drug repositioning for T1D will benefit from multiple areas of expertise (e.g. data science, pharmacology, endocrinology, etc.), we encourage collaborative applications;
- We encourage creative approaches that can take advantage of available data on metabolic control in established T1D;
- Since an important goal of improving metabolic control in T1D is prevention of long-term diabetic complications, we encourage identification of drugs for repositioning that can both improve metabolic control and reduce long-term complications independent of glycemia (as is currently being investigated in T2D with GLP-1 receptor agonists and SGLT2 inhibitors);
- For validation studies, it will be the responsibility of the applicant to procure the necessary drug(s).

Applicants are 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 $400,000 (including up to 10% indirect costs) for a project lasting up to two years. Substantially shorter projects are welcome. Applicants should discuss with JDRF 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 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 **Monday August 19, 2019 at 1:30pm** 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: 735 512 151
Meeting password: jdrf2019

Join by phone
Dial in (US): 1-650-429-3300
Dial in (International): Global Call in Numbers
Conference Code: 735 512 151

DEADLINES

- **RFA release date** July 30, 2019
- **LOI deadline** September 26, 2019
- **Notification of full application request** October 11, 2019
- **Application deadline** November 14, 2019
- **Response to applicants** March 31, 2020
- **Earliest anticipated start date** July 1, 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

CONTACTS

SCIENTIFIC
Jonathan Rosen, Ph.D.
Scientist, Research
JDRF
26 Broadway, 14th Floor
New York, NY 10004
☎ +1-212-859-7896
💻 jrosen@jdrf.org

ADMINISTRATIVE
Nikki Carpenter
Senior Program Administrator
JDRF
26 Broadway, 14th Floor
New York, NY 10004
☎ +1-212-479-7643
💻 ncarpenter@jdrf.org

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.