JDRF REQUESTS LETTERS OF INTENT FOR: DEVELOPMENT OF CGMS WITH CONTINUOUS KETONE MONITORING FUNCTIONALITY FOR DKA PREVENTION IN T1D

PURPOSE

JDRF is committed to the development of devices to improve health outcomes in people with type 1 diabetes (T1D). Diabetic ketoacidosis (DKA) is a dangerous acute complication of T1D that is insufficiently addressed or even sometimes exacerbated by current therapeutic options. To fill this gap, JDRF invites applications to develop continuous ketone monitor (CKM) functionality in continuous glucose monitor (CGM) devices to warn users of impending DKA events and allow preventive actions to be taken.

BACKGROUND

DKA is an acute complication of T1D in which insulin deficiency leads to elevated blood ketones and acidosis, sometimes resulting in diabetic coma or even death. A cause of morbidity and mortality for people with T1D, DKA also imposes significant costs to healthcare systems due to associated hospitalizations. Avoidance of DKA requires symptom recognition and self-monitoring of ketones using commercially available blood or urine strips, tools that are poorly adopted and sometimes cost-prohibitive. Continuous, automatic monitoring of ketones is expected to identify more approaching DKA events than the current ketone testing regimens. This RFA is intended to drive development of combined CGM-CKM devices, i.e. CGMs that also continuously measure ketones. This functionality will allow for continuous testing of ketones with no additional on-body burden. We envision CGM-CKM devices that alert users when ketones have reached an elevated but subclinical threshold, allowing them to administer conventional self-care before a DKA event is imminent or contact a health care provider when needed. At the same time, to optimize user experience, we recommend CGM-CKMs that require minimal user engagement with ketone readings during periods of normal ketone levels.

While people with T1D are generally at an elevated risk for DKA relative to people with type 2 diabetes or non-diabetic people, some subgroups of people with T1D are at an even higher relative risk. These groups include adolescents, women, African Americans, and people with a history of DKA. Triggers of DKA include missed insulin doses or problems with insulin administration, acute illness, and reduced carbohydrate intake. Importantly, elevated DKA risk has been observed in people with T1D using drugs in the SGLT inhibitor class. SGLT inhibitors have demonstrated benefits for people with T1D, including reduction in HbA1c, increased time spent in target glucose ranges, and reductions in postprandial glucose excursions and glycemic variability. Moreover, SGLT2 inhibitors offer renal and cardiac protection in non-T1D populations, long-term benefits that have not been tested in people with T1D but may be expected *a priori* to extend to people with T1D as well. However, the increased risk of DKA, including euglycemic DKA, is a major barrier to the use of SGLT inhibitors by people with T1D; while several SGLT inhibitors are approved for T1D in Europe and Japan as adjunctive therapies to insulin, none are yet approved for T1D in the United States. Development of CGM-CKM devices that can warn users of approaching DKA and provide mitigation strategies to avoid it (such as administration of insulin and intake of carbohydrates) may enable safe, effective use of SGLT inhibitors in people with T1D.

This RFA is intended to solicit proposals to develop CGM-CKM devices to reduce DKA risk in all people with T1D.

OBJECTIVES

Letters of intent (LOIs) are sought from academic or industry applicants with innovative approaches to develop CGM-CKM devices.

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

- Early stage development of ketone monitoring technology with a clear line of sight to integrated CGM-CKM devices
- Preclinical CGM-CKM device development
- Clinical validation of CGM-CKM devices in development

Deliverables

- Project plans should be developed to reach clear inflection points appropriate to the maturity of the product being developed (e.g. achievement of proof of concept for a new ketone monitoring technology, completion of animal studies or a clinical trial, submission for regulatory approval, etc.)

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

- The CGM-CKM should be designed to have optimal device user interface (reduced on-body burden, minimal user interaction during periods of healthy ketone levels, matching durability of glucose and ketone sensors, etc.)
- JDRF strongly encourages applications from industry
- JDRF supports collaborative approaches, including between academic applicants and industry partners
- Applicants are encouraged to take advisement from clinicians and people with T1D in the development and execution of their project plans

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/

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 may request up to $200,000 per year (including up to 10% indirect costs), for up to two years. JDRF will consider applications with increased scope (time, budget), especially in grants with clinical research. Applicants proposing grants with increased scope should discuss with the JDRF scientific contact below.

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 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.

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.

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
- Development plan with timeline for advancing the CGM-CKM through pre-clinical and clinical development, including previous and planned future interactions with CGM manufacturers, if applicable
- 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, 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 submission of a full proposal. Upon notification of a request for a full proposal, the application must be completed using the templates provided on RMS360 (http://jdrf.smartsimple.us). 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

DEADLINES

- **RFA release date:** **June 1, 2021**
- **LOI deadline:** **July 29, 2021**
- **Notification of full application request** **August 19, 2021**
- **Application deadline** **September 30, 2021**
- **Response to applicants** **March 2022**
- **Earliest anticipated start date** **May 2022**

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
- Approach
- Innovation
- Likelihood of ultimate regulatory approval, commercialization, and adoption
- Investigator experience
- Environment

CONTACTS

SCIENTIFIC
Jonathan Rosen, Ph.D.
Associate Director, Research
JDRF
200 Vesey Street, 28th Floor
New York, NY 10281
jrosen@jdrf.org

ADMINISTRATIVE
Tamara Croland, MPA
Associate Director, Program Administration
JDRF
200 Vesey Street, 28th Floor
New York, NY 10281
tcroland@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.