JDRF REQUESTS LETTERS OF INTENT FOR:
GLUCOSE RESPONSIVE INSULIN DISCOVERY AND VALIDATION

PURPOSE

JDRF, the world's leading non-profit organization with the mission to cure, treat and prevent type 1 diabetes (T1D), invites Letters of Intent (LOI) for the discovery and validation of novel glucose responsive insulin (GRI) drugs for better treatment of insulin-dependent diabetes mellitus (IDDM) and reducing the burden of daily management of the disease, particularly T1D.

BACKGROUND

Since its discovery in 1921, insulin has been the lifeline for people with IDDM, such as T1D. Yet almost 100 years later, controlling blood glucose in T1D remains unconquered. Despite the advent of better insulins, automated devices and diligent self-care, the disease remains challenging to manage, is a huge burden on both the affected individual and the caregiver, is unpredictable from day to day even in the same individual and does not eliminate the risks, fear or consequences of extreme blood glucose values. This is evidenced by results from numerous clinical and epidemiological studies demonstrating prevailing high HbA1c levels, frequency of hypoglycemia and ketoacidosis, more than 70% time spent outside of target glucose values, as well as long term complications of the disease mostly arising from years of dysglycemia.

In an effort to reduce the burden of living with TID, JDRF has prioritized the development of a glucose-responsive insulin, a drug that could transform the lives of people with TID, and those with type 2 diabetes who are insulin-dependent. Unlike current insulin therapies, glucose-responsive insulins would act like a surrogate pancreas, delivering insulin to the body's tissues and organs precisely when and where it is needed, in precisely the right amounts – thus avoiding the risks of extreme blood glucose levels. The drug would only need to be taken once a day or less frequently, and would not have to be calibrated with carbohydrates, exercise, and blood glucose testing. And since glucose-responsive insulins could be device-free—limiting finger sticks, replacing pumps, and reducing human intervention—it would drastically reduce the daily burden of managing the disease thereby improving therapeutic adherence and leading to improved outcomes.

OBJECTIVES

Letters of intent are sought from academic or industry applicants with innovative approaches to discover and provide validation (proof-of-concept) for insulin delivery proportional to circulating real time levels of blood glucose in animal models of T1D. Early concepts with limited preliminary results may be considered at reduced scope, budget and timelines based on strength of hypothesis and feasibility of approach. Designing glucose-responsive insulins may require a concerted effort from various areas of expertise. Therefore, applications from a network of investigators and/or collaborations leveraging expertise in protein biochemistry, pharmacology, drug delivery, formulation sciences, bioengineering and other fields, as applicable, will be given a high priority. Alternately, JDRF Staff may suggest collaborations between two or more applicants based upon complementarity to form a network.

Expected outcomes from project proposals would demonstrate but be not limited to:

- Insulin release and blood glucose lowering proportional to circulating levels of glucose
- Improvements in glycemic parameters – glucose tolerance, reduced hypoglycemia, etc.
- Reversibility of mechanism
- Safety and tolerability of biomaterials, excipients, etc.
- Pharmacokinetic and pharmacodynamic measures
- Evidence of elimination of biomaterials, if any

Applications should contain an analysis of the *projected* GRI product concept compared to standard-of-care, including:

- Target Product Profile and Target Patient Profile

- Reduced frequency of dosing (such as once-a-day)
- Reduced need for monitoring blood glucose levels
- Reduced risk for hypo and hyperglycemia
- Timelines for development
- Cost/benefit analysis
- Competitive landscape

Applicants are encouraged to consult with JDRF Scientific Staff to discuss the alignment of their proposal to this RFA and in developing the projected GRI product concept. Collaborations with industry and/or direct applications by companies are strongly encouraged.

MECHANISM

LOIs in response to this announcement can be submitted to the following mechanism:

- Academic groups would submit as Strategic Research Agreements (http://jdrf.org/grant-center/information-for-applicants/grant-mechanism-descriptions/strategic-research-agreements)
- Industry groups would submit as Industry Partnership program (http://jdrf.org/grant-center/industry-partnerships/)
- Project proposals of up to 36 months duration will be considered
- Proposals (supported by strong rationale and/or preliminary data) will be considered for a maximum budget of up to $500,000* per year for up to 3 years of funding (including 10% indirect costs)
    - *Applications whose budget and/or timeline exceeds the above specified guidelines, must obtain JDRF staff approval prior to submitting an LOI

PRE-APPLICATION MEETING

JDRF will hold a pre-application meeting via web and teleconference on **Thursday, May 29th at 10 AM USA ET,** 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. Please click here for the call information:
https://jdrfmeetings.webex.com/jdrfmeetings/j.php?MTID=ma99e4f9704a2e8212b7fae3375102b5a.

ELIGIBILITY

Applicants must hold an M.D., D.M.D., D.V.M., Ph.D., or equivalent academic degree and a faculty position or equivalent at a college, university, medical school, or comparable institution.

Applications may be submitted by for-profit entities as well as nonprofit organizations, public and private universities, colleges, hospitals, laboratories, units of state and local governments.

There are no citizenship requirements.

LETTER OF INTENT

An approved LOI is required prior to submission of a full proposal. 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

DEADLINES

• LOI Release Date	May 16, 2014
• Letter of Interest Deadline	July 11, 2014
• Notification of Full Application Request	August 1, 2014
• Application Deadline	September 19, 2014
• Response to Applicants	January 2015
• Earliest Anticipated Start Date	March 2015

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

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PROGRAMMATIC

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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.