JDRF REQUESTS EXPRESSIONS OF INTEREST FOR: EXPLORATORY CLINICAL TRIALS OF NON-INSULIN ADJUNCT THERAPIES IN TYPE 1 DIABETES

PURPOSE
JDRF, the world’s leading non-profit organization with the mission to cure, treat and prevent type 1 diabetes (T1D), invites Expressions of Interest (EOI) for clinical trials to evaluate non-insulin based adjunct therapies for improved glycemic and overall metabolic control of T1D.

BACKGROUND
While over the past two decades the advent of insulin analogs, infusion pumps and other devices allowing diligent monitoring have been shown to improve diabetes outcomes, a number of individuals with T1D are still not at target glycemic levels as exemplified by HbA1c higher than the recommended ADA guidelines and frequency of hypoglycemic and DKA events, both in the US and globally. Exacerbating the pathology are increasing trends in obesity, insulin resistance and other co-morbidities affecting individuals with T1D, with metabolic resemblance to T2D. Also, a significant number of individuals with long standing T1D have detectable levels of C-peptide, a marker of residual pancreatic beta cell function. Finally, increasing number of clinical studies are revealing the complex heterogeneity of T1D and challenging the previous paradigm of monogenic T1D and iatrogenic insulin monotherapy.

Future treatments for T1D are likely to be best realized by the utilization of non-insulin based adjunct therapies with complementary actions to insulin – such as but not limited to the use of T2D therapeutics – so as to elicit a glycemic balance and overall metabolic homeostasis, thus reducing or preventing long term complications of the disease.

OBJECTIVES
JDRF has an unprecedented opportunity to make progress in the clinical assessment of adjunctive therapies for T1D that move beyond an insulin-centric view of the disease. At present, several agents – mostly approved T2D therapies such as incretins, SGLT inhibitors, metformin – are under clinical investigation to assess the benefit: risk profile in T1D. However, a systematic clinical phenotyping of the heterogeneous disease to enable personalized interventions addressing specific dysfunctional pathways or an understanding of the mechanistic pathology is yet to be undertaken. It is our goal to de-convolute the T1D disease complexity such that subgroups of individuals can be identified and stratified to determine optimal therapeutic regimen of non-insulin adjunct therapies, thus maximizing the benefit: risk ratio for the patients.

JDRF wishes to solicit expressions of interest for clinical trials in established from academic and industry applicants T1D to test the safety, efficacy, and potential synergies of adjunct therapies that target multiple facets of the disease.

Research objectives could include but be not limited to addressing the following:
- Influence of clinical phenotype on treatments – weight/BMI, lipids, age, duration of T1D, age at diagnosis
- Contributions of target organs to the pathophysiology, such as pancreas, liver, adipose, skeletal muscle, etc.; ex: presence of C-peptide in influencing response to treatments
- Role of glucagon, glucagonemia or hyperglucagonemia on effect of treatments
- Studies in T1D sub-populations with unmet medical needs such as adolescents/young adults, high HbA1c, overweight/obese, non-obese insulin resistant, adults with slowly progressing disease (steady levels of C-peptide), others
- Comparative (mechanistic) analyses of two or more distinct adjunct therapeutics, such as DPP4 inhibitors vs. GLP1 agonists, DPP4 inhibitors vs. SGLT2 inhibitors, etc. to facilitate choice of personalized treatments
Desired clinical outcomes can include, but are not limited to:

- Improved glycemic measures – reduced HbA1c, fasted and prandial glucose, glycemic variability, hypoglycemia, and hyperglycemia, as well as increased time in-target
- Improved metabolic measures – reduced BW/BMI, lipids, HOMA-IR
- Improved hormonal balance as evidenced by levels of glucagon, GLP-1, GIP, PYY, leptin, others
- Reduced daily burden – reduced insulin dosing frequency and amounts, reduction/elimination of pre-prandial bolus, improved adherence to therapy compared to insulin monotherapy
- Potential impact on T1D clinical care, i.e., “effectiveness” of proposed interventions

Criteria:

- Proposed studies should be based on robust scientific hypothesis and have a clear plan for a regulatory path to allow the trial to be done; use pre-existing infrastructures for maximizing efficiency and provide a clear recruitment plan for timely execution of study
- Innovative trial designs, smaller number of subjects, interim endpoints, exploratory biomarker analyses are encouraged
- Collaborative efforts engaging investigators with complementary expertise and patient cohorts are highly encouraged. Likewise, JDRF Staff may propose collaborations between investigators submitting EOs based on the content therein; proposals may leverage or extend current studies
- Industry collaborations and direct applications from companies are strongly encouraged
- EOs should contain information regarding any industry collaborations, and any provisions for obtaining the agents for the proposed trial (at no-cost or at-cost) from the relevant companies
- Statistical analyses should be presented as necessary
- Investigators may propose a budget appropriate to the proposed research according to the general criteria below*

All academic and industry applicants are encouraged to consult with JDRF Scientific Staff to discuss the alignment of their proposal to this RFA.

MECHANISM

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

- Academic groups would submit as Clinical 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/)
- Clinical trials of up to 36 months duration will be considered
- Proposals (supported by strong preliminary data) will be considered for a maximum budget of $500,000* per year for up to 3 years of funding (including 10% indirect costs)
  - * Applications whose budget and/or timeline exceed the above specified guidelines, must obtain JDRF staff approval prior to submitting an EOI
- Under exceptional circumstances, proposals which also include preclinical studies may be considered if needed to obtain regulatory approval to move forward with the proposed clinical trial. Please contact Dr. Sanjoy Dutta to discuss studies in this area

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 Web site: http://www.jdrf.org/

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.
**EXPRESSIONS OF INTEREST**

Prospective applicants should submit an EOI on-line via RMS360 at [https://jdrf.smartsimple.us](https://jdrf.smartsimple.us). The EOI template located under the LOI Research Plan tab must be used to submit.

EOI submissions will undergo expedited review. Applicants will be notified if they have been approved to submit a full application. An approved EOI is mandatory prior to submission of a full proposal.

Expressions of Interest should be no more than 4 pages in length including the following information:

- Specific aims for the proposed study
- Background and rationale for the proposed study
- Brief description of research plan including preliminary data
- Description of cohort to be studied and inclusion/exclusion criteria
- Brief overview of statistical power, if relevant.
- Future plans if successful and potential translational impact of the proposed study
- Projected deliverables for the project if successful
- Intellectual Property or commercial efforts associated with the current application
- For collaborative projects, description of how the project will be led and coordinated
- References (no page limit)

**DEADLINES**

- EOI Release Date: May 16, 2014
- Expression 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

**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**

JDRF
26 Broadway, 14th Floor
New York, NY 10004

**PROGRAMMATIC**

Sanjoy Dutta, Ph.D.
Senior Director, Translational Development
📞+1-212-479-7668
✉️ sdutta@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.