F.M. KIRBY FOUNDATION SOLICITATION EVALUATION FORM

DATE: August 23, 2022 **REQUEST DATE:** July 2022
Last grant acknowledgment: Yes
Program Area: Health

APPLICANT:
JDRF International
28th Floor
200 Vesey Street
New York, NY 10281

SEND CHECK TO:
CDS
Attn: Jennifer Derry
2005 Lakewood Drive
Boone, IA 50036

CONTACT: Ms. Sarah Cunningham, Associate National Director, Leadership Giving
PHONE: (919) 847-2630
PAYEE OTHER THAN ADDRESSEE:

AMOUNT REQUESTED: $200,000 **NATURE OF REQUEST:** For support of the Center of Excellence in New England

GRANT HISTORY

SUPPORT: 2013 - 2021 **# OF GRANTS:** 9 **TOTAL DOLLARS:** $1,600,000

LAST GRANT DATE: 12/20/2021 **LAST GRANT AMOUNT:** $200,000
FYE DATE: 06/30/2021 **AFS DATE:** 12/23/2021

2017	$200,000	9/15/2017	Toward Beta Cell Restoration and Beta Cell Replacement research
2018	$200,000	9/17/2018	Toward Beta Cell Replacement research
2019	$200,000	12/16/2019	Toward Beta Cell Replacement research
2020	$200,000	9/14/2020	Toward Beta Cell Replacement research and Regeneration work
2021	$200,000	12/20/2021	Toward Beta Cell Replacement research and Regeneration work

LHV and AKH endorsements received.

DLK COMMENTS: This year's request regurgitated many paragraphs from last year, including the same 2021-2022 International Board of Directors list and 2021-2022 budget. It even reused a quote from Dr. Thomas Kay, so I was a bit disappointed in what is typically a concise but enlightening request. Update: I have received an updated budget from Sarah and have updated the financial analysis to reflect such.

We received more details on the BANDIT trial, which is repurposing baricitinib, a treatment for rheumatoid arthritis, as a potential Type 1 Diabetes (T1D) treatment. The trial is recruiting 85 participants, aged 12-30 years, who have recently been diagnosed with T1D and will test if baricitinib can slow the loss of insulin-producing beta cells.

There are multiple cell therapies in human clinical trials. We received an update on the Vertex clinical trial (a stem cell-based beta cell therapy) for VX-880. As of May 2022, Patient #1 is 100% insulin independent 270 days after receiving the therapy. He is on immunosuppressive therapy, but

no longer needs to administer insulin. Patient #2 also received a half dose of VX-880 and has had a 30% reduction in insulin requirements (150 days into the trial). A third patient has received the full dosage of VX-880. They are experiencing an increase in C-peptide and improving glycemic control after 29 days. Patient #3 will be more fully evaluated at their 90-day visit later this summer. There have been no serious adverse events with any of the three participants, meaning none have experienced a serious and undesirable experience because of VX-880. The request didn't mention that the FDA put a Clinical Hold on the trial due to "insufficient information to support dose escalation with the product." However, on July 5th, the FDA Clinical Hold was lifted. The trial will now be reopened for screening, enrollment, and dosing at multiple sites in the U.S.

CRISPR Therapeutics and ViaCyte announced the first-person dosed Phase 1 Clinical Trial of Novel Gene-Edited Cell Replacement Therapy (VCTX210) for Treatment of T1D in February. The first phase will assess its safety, tolerability, and immune evasion. If successful, it could offer a functional cure for people living with T1D and insulin-requiring type 2 diabetes without the need for immunosuppression! One must wonder how and if the U.S. Supreme Court's June 24 ruling ending federal abortion rights under Roe v Wade will impact stem cell research.

The request touched upon the "beta cell factory" that Jeffrey Millman, Ph.D. has developed. JDRF continues to fund the Advanced Regenerative Manufacturing Institute (ARMI) to attempt to automate and industrialize Millman's procedure, thus enabling the production of unlimited insulin-producing cells that could be used in research for the creation of cell replacement therapies.

There were also updates on 3D printing strategies to realize cell therapies. Bioengineered tissue therapeutics aim to provide insulin independence and control of blood sugar without the need for chronic immune suppression. Bioprinting technology aims to enhance the survival and function of transplanted islet cells. New hydrogel materials are being evaluated to ascertain whether they can induce new blood vessels, which are crucial to the survival and function of implanted cells. Dr. Daniel Zeve, at Boston Children's Hospital (another FMKF grantee), is rewiring gastrointestinal stem cells to turn them into stronger insulin-producing cells that can be used in T1D therapies.

Another key priority area for JDRF is Global Universal Screening for T1D. Most current screening programs only pertain to individuals who have relatives living with the disease. However, 85% to 90% of newly diagnosed cases do not have a direct family connection, which is why universal screening is important. One of JDRF's top-funded screening trials is **T1Detect**, a screening, education, and awareness program that will be piloted at Adams County Health Center in Iowa and University Hospital in New Jersey. Both pilot sites provide health care to medically underserved populations. **Autoimmune Testing of Kids (ASK)** is a large-scale, multiyear screening study in Colorado funded by JDRF to provide evidence in support of universal screening for both T1D and celiac disease. It is targeting children between the ages of 1 to 17 in the Denver metro area for these two most frequent autoimmune diseases of childhood.

This year's request focused on the research at the JDRF Center of Excellence in New England. There are five Centers (three in the U.S., one in Australia, and one in Canada). The intent of the Centers is to leverage resources, foster dynamic, nimble work, and remove the red tape that normally accompanies standard research grants. A keyword throughout the request was collaboration. The New England Center is working with researchers from Harvard, Dana-Farber Cancer Institute, The Jackson Laboratory, Joslin Diabetes Center, and UMass Medical Center. JDRF has targeted the investment in the Center at $20 million over five years, more than double the investment in any other center it has selected. The New England team will: 1) create better

laboratory models of T1D to study how immune cells recognize and respond to stem cell-derived islet cells and uncover the "alarm cells" within the islets that signal the immune system to destroy these cells, 2) determine how and what they can genetically modify in stem cell-derived islet cells to protect them and make them strong enough to withstand the immune reaction after transplantation, and 3) test the "inert" stem cell-derived islet cells for their ability to resist rejection by the immune system using improved laboratory models generated by the Center.

There have been more changes on the JDRF leadership team. Anne Gehring (interim CFO) was replaced by Rob King, Bala Balasubramanian is the Chief Information Officer, and Pam Morrisroe is the Chief Marketing Officer. Both the technology and marketing roles were not referenced in last year's request. There is no mention of Troy Lindloff, Chief Development Officer, so I'm assuming that is an open position.

Financial analysis of FY21 audit attached. Awaiting a reply from Sarah Cunningham regarding a FY23 budget. I recommend the budgeted $200K

JJK COMMENTS: While all of our medical research grants for chronic disease hope to one day boast of seeing a complete cure, it is exceedingly rare to hear of such a success. All the more reason that the Vertex trial for the product named VX-880 remains groundbreaking. Patient #1 received an infusion of stem cell cultured beta cells, and today, his body is automatically controlling his insulin and blood sugar levels (Patient #1 was later revealed as 64-year-old Brian Shelton: https://www.nytimes.com/2021/11/27/health/diabetes-cure-stem-cells.html. I'll note the article quotes at length Dr. Doug Melton, current Vertex Pharmaceutical fellow and former director of the New England Center of Excellence).

In other news, Vertex acquired last month ViaCyte, "with the goal of accelerating its potentially curative VX-880 programs in Type 1 Diabetes." (https://investors.vrtx.com/news-releases/news-release-details/vertex-acquire-viacyte-goal-accelerating-its-potentially). Complementing the insulin-producing, stem cell-derived islet cell therapy from Vertex, ViaCyte itself has been working a CRISPR-edited stem cell-derived cell replacement that would *not* require immunosuppression (while the aforementioned Vertex VX-880 does) because it would evade recognition from the immune system.

What's notable about all of this is the role that JDRF – and thereby the FMKF funding for beta cell restoration and replacement work which has been the target of our grants since 2014 – has played in getting the T1D community seemingly so close to a cure. To summarize, JDRF initially funded Melton at Harvard in 2004, as he attempted to make insulin-producing beta cells from stem cells. By 2015, Melton formed Semma Therapeutics to develop these cells into curative therapies; at that time the JDRF T1D Fund made a "catalytic" investment in Semma, which was acquired by Vertex a year later for $1B. The FA-approved VX-880 clinical trial is now open for screening, enrollment, and dosing at sites across the U.S.

I was surprised to see a request for a new area of focus here, in the New England Center of Excellence, considering our support has been concentrated on beta cell regeneration and replacement for so long. That said, the New England center has apparently been "ground zero" for the aforementioned work, and as the request suggests, the center will "leverage Dr. Melton's work creating beta cells and use advanced scientific technologies, such as CRISPR gene editing, to overcome the existing limitations of islet transplantation and to prevent the immune system from attacking the beta cells." Now that researchers know that these stem cell-derived beta cells can

create insulin, the primary target of the Center's research seems to be the immune system, in an effort to ensure the long-term survival of transplanted cells. Clearly, the goal is to remove the need for immunosuppression for VX-880-like therapies. By all accounts, it appears JDRF is playing a supportive role to organizations like Vertex in the development of these kinds of cells.

With the New England Center of Excellence engaged in the work of beta cell regeneration and replacement, I do not have an objection to the designation change. This is exciting work, as millions in the T1D community eagerly await to hear more. I recommend $200K for the Center of Excellence in New England.

APPLICANT: JDRF International

FM KIRBY FOUNDATION
Financial Statement Analysis

Grantee Name:	JDRF International	**Date:**	8/10/2022
Prepared By:	DLK		
Grant Request Amt.	$ 200,000	**Type of Financial Report Submitted**	Audit
Budgeted Amt.	$ 200,000	**Period Covered in Financial Report**	6/30/2021
Audit Firm	KPMG		
Opinion	Present Fairly	**Date of Report Issuance**	12/23/2021
Basis of Acctg.	GAAP		

Current Ratio (Liquidity Ratio/Working Capital Ratio)	3.86 Used Liquidity Note 4/CL	**Amount of Unrestricted Net Assets (Operating Reserve)**	**$ 193,001,000**

Note: A current ratio measures an organization's ability to pay short-term and long-term obligations. The higher the ratio, the more capable the organization is of paying its obligations. A ratio under 1 indicates that the organization's liabilities are greater than its assets.

Allocation of Functional Expenses	6/30/2021	**%**	Must Read Financial Statement Notes
A. Program Service Expenses	$ 73,831	64%	Ideally program expenses should be at least 70% of total budget.
B. Management and General	$ 17,952	16%	
C. Fundraising	$ 23,281	20%	
D. Total Expenses	$ 115,064	100%	
	(in thousands)		

Comments/ Notes:

FY23 Budget: The FY23 budget projects a $10.4M deficit vs $17.8M surplus for FY22. Total revenues are budgeted to grow by $33.6M (20%) over FY22, with core fundraising up $951K (0.5%) and other contributions up $33.6M (242%). Total expenses are budgeted to grow by $62.8M (40%), with operating expenses increasing by $34.8M (40%) and grant expenses increasing $28.0M (40%).

FY21 Audit: JDRF should move to January request/April Board approval so we are working with fresh financials. FY21 had an operating surplus of $126.9M vs a surplus of $17.9M for FY20. Total public support declined $13.5M (7%), with events revenue down $40.8M (32%) while contributions increased $14.9M (19%). Investment returns grew by $33.6M (243%) over FY20. Program expenses decreased by $62.7M (46%), with large decreases in both research and education/advocacy. Supporting services also declined, down $14.5M (26%) from FY20. JDRF had investments of $238.1M, of which $8.9M were endowment-related. Included within the investments are $66.4M invested in privately held companies with Type 1 diabetes-related projects (to directly fund research and development). As of June 30, 2021, ten donors represented 33% of the total outstanding contributions and other receivables. JDRF has a $5M line of credit and the line was used in FY20, with the full amount outstanding as of June 30, 2021. It was noted that JDRF received forgiveness for its 2020 funding from the CARES Act and it was recorded in other revenue. No amount was specified but other revenue increased from $1.7M in FY20 to $13.3M in FY21. Overall, there were no red flags as a result of my review. Laura's 2021 endorsement stated that JDRF would submit earlier in 2022 and it was included in the email notifying them of their 2021 grant award, so not sure what happened. Perhaps staffing changes in the development team?

APPLICANT: JDRF International

DISPOSITION:

( ) Declination

( ) Hold for review on/about**:**

( ) Approval for**: $200,000**

(xx) Hold for Board Review

(xx) Insert Information**: For: Support of the Center of Excellence in New England**

(xx) Other**: Include note in email requesting submission in Jan/Feb 2023 to better align with their audit schedule.**

Initials: JJK Date: 8/28/22

Check #:_____ Date:_____