Type 1 Diabetes

State of the Cure

Fall 2014

Juvenile Diabetes Cure Alliance

The Voice of the Donor For a Cure

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I. Introductory Letter

The past twelve months have brought some exciting news to the T1D community but have not yet brought us a Practical Cure. We at the JDCA will not stop working toward our mission to deliver a Practical Cure for type 1 diabetes until this goal is achieved. While we are heartened by some of the research progress in the past 12 months and fully believe we are closer to a cure for type 1 diabetes than ever before, we still have a long road ahead and not a moment to lose.

This year's *State of the Cure* report dives into the opportunities and hurdles that face the T1D community. We provide comprehensive summaries of our research and analysis from the last 12 months and also present brand new content, including updates on Practical Cure projects in human trials.

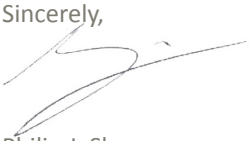
In the past year, several notable projects have been making their way into human trials, which warrants excitement and optimism, but misallocated donor funds remain a major stumbling block on the road to a Practical Cure. Leadership changes occurred at both the major T1D non-profits—announced well in advance by the American Diabetes Association, but coming as a total surprise from JDRF—which we hope will pave the way to a new, more cure-focused agenda.

One key takeaway from any cover-to-cover reading of this report is that there remains a stark lack of alignment between donors and the diabetes charities, which, if rectified, would greatly accelerate the delivery of a Practical Cure. As in prior years, the clear top priority of donors is to fund cure research, while, in contrast, only a minority of the money raised by the major T1D organizations is actually spent on cure research. We believe that the Boards of Directors of these organizations have a fiduciary duty to ensure that their organizations are fully aligned with donor priorities.

2014 has been a busy year for the JDCA. We visited leading research centers across the country and met with many of the T1D charity leaders. We put thousands of man hours into in-depth analysis of cure research projects and the operations of the major diabetes non-profits. We also initiated deeper coverage of commercial enterprises that are pursuing a Practical Cure and introduced flash reports on T1D current events to keep our readers informed. The JDCA continues to actively engage in social media with the T1D community, whose passion and interest in curing T1D inspire us every day.

We hope you will find this report both interesting and useful. It is written as a resource to inform and guide your giving decisions. But most importantly, it is written to help us all understand where to apply the right kind of pressure to accelerate a cure.

Sincerely,



Philip J. Shaw
Executive Director

II. Type 1 Diabetes Statistics and Background

Background

Type 1 diabetes is an autoimmune disease characterized by an inability to produce insulin, a hormone necessary to regulate blood sugar. For unknown reasons, the body's immune system turns against itself, attacking and killing the pancreatic beta cells that produce insulin. Consequently, people with type 1 diabetes must manually administer insulin on a daily basis, either through injections or an insulin pump. Management of T1D requires constant vigilance and relentless hours of planning and monitoring, due to the fact that blood sugar levels are affected by a number of often unpredictable factors, including meals, exercise, illness, and stress.

Number of People Impacted

Over 5 million Americans are directly impacted by type 1 diabetes. Although estimates vary as to the exact number of people living with the disease, a general estimate puts the figure at about 1.5 million people. An additional 4 million of those affected are immediate family members who are involved in the day-to-day routines of managing type 1.

Increasing Incidence

The number of people in the United States diagnosed with type 1 diabetes is rising at a pace that exceeds population growth. Children, in particular, have been diagnosed with type 1 at a higher rate in recent years (Exhibit A).

It is unclear why the incidence is rising. Scientists have proposed several hypotheses, but the academic community has not widely accepted any of them as the definitive explanation.[1]

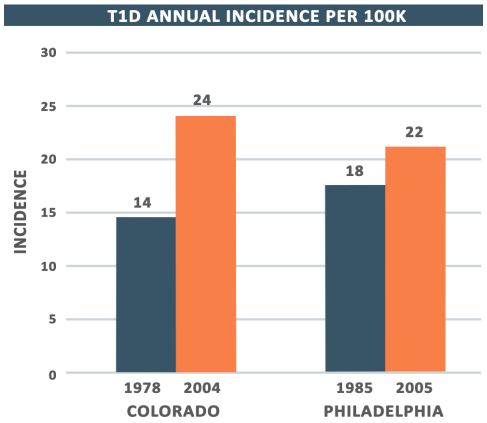
Mounting Costs of Type 1 Diabetes

In addition to health complications, type 1 diabetes poses a real dollar cost to patients, their families, and society at large. One commonly cited estimate puts the annual cost of diabetes in the United States at $14.5 billion per year, including both direct costs such as medical care and indirect costs such as loss of work.[2]

There are stark medical cost differences between diabetics and non-diabetics. A type 1 diabetic incurs $10,500 annually in direct costs, almost three times as much as a non-diabetic, who incurs $3,500 per year (Exhibit B). In addition, adults with T1D miss an average of 5.5 additional days of work while children miss 3.3 more days of school.[3]

When the annual cost of type 1 diabetes is extrapolated over the lifetimes of all those diagnosed, the cumulative cost reaches $450 billion. Accordingly, while there are tremendous emotional benefits to finding a Practical Cure, there is also a clear social imperative.

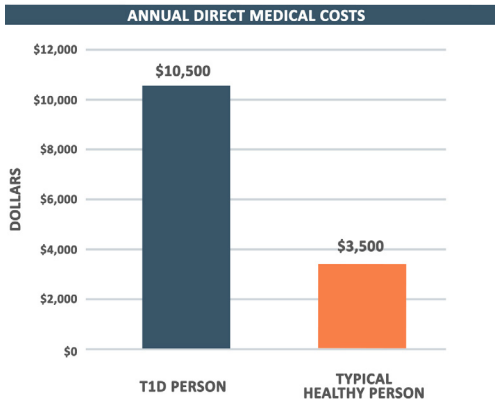
Exhibit A



SOURCE: Lipman, T. (2013). Increasing incidence of type 1 diabetes in youth: twenty years of the Philadelphia pediatric Diabetes Registry. Diabetes Care, 36 (6).

Vehik, K. (2007). Increasing incidence of type 1 diabetes in 0-17-year-old Colorado youth. Diabetes Care, 30 (3).

Exhibit B



SOURCE: Tao, B. (2012). Estimating the Cost of Type 1 Diabetes in the U.S.

1. For more information on these theories, see the JDCA report "Type 1 Diabetes: A Growing Concern," November 21, 2013.

2. Tao, B., Pietropaolo, M., Atkinson, M., Schatz, D., & Taylor, D. (2010). Estimating the Cost of Type 1 Diabetes in the U.S.: A Propensity Score Matching Method. PLoS ONE, 5(7): 1-11. doi:10.1371/journal.pone.0011501
Jasinski, C., Rodriguez-Monguio, R., Tonyushkina, K., Allen, H. (2013). Healthcare cost of type 1 diabetes mellitus in new-onset children in a hospital compared to an outpatient setting. BMC Pediatrics, 13(55). doi:10.1186/1471-2431-13-55

3. Ibid.

III. Type 1 Diabetes Research Funding Landscape

During 2014, nearly 1 billion dollars will be spent on type 1 diabetes research in the United States. This spending is funded by the government, donor contributions, and commercial investments.

Government Funding

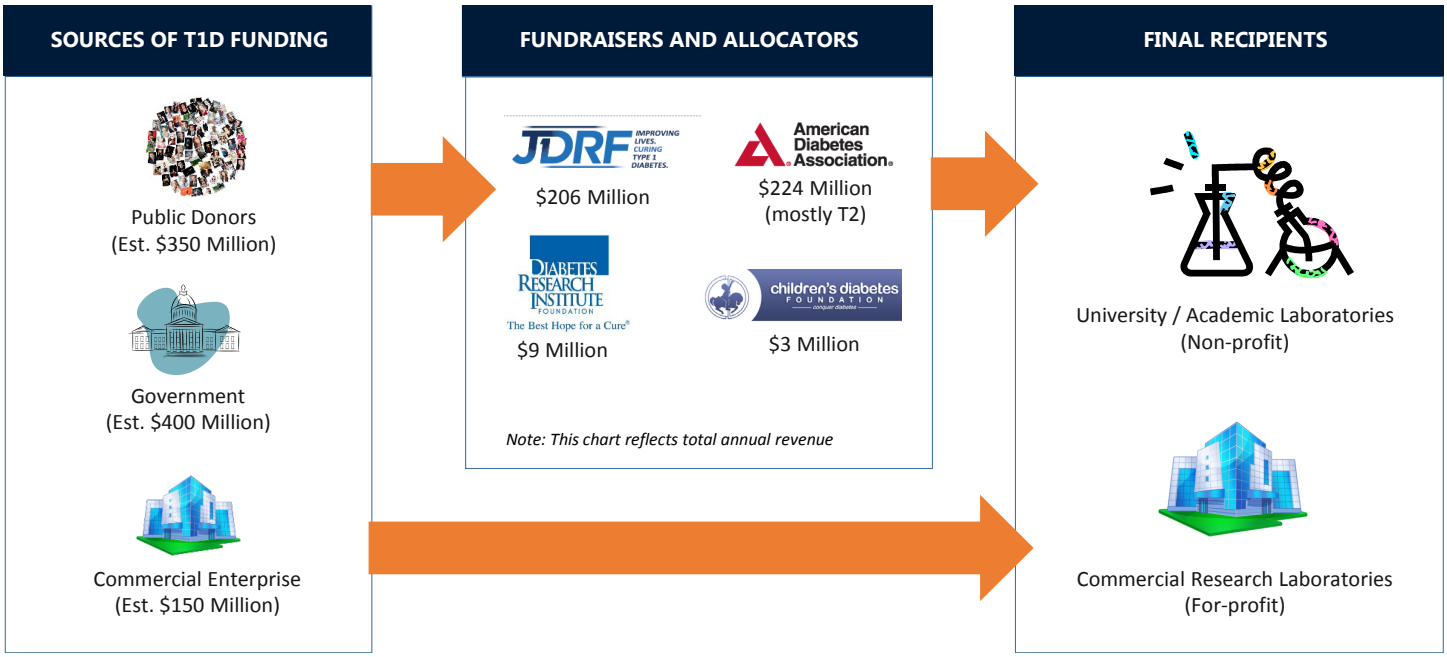
The primary gatekeeper of U.S. government funds is the National Institutes of Health (NIH), which is federally funded. A relatively small professional staff decides where the agency's budget will be allocated from year to year. The NIH often funds research projects that are in early stages of development via academic institutions and research centers. In fact, the largest T1D academic research centers in the nation receive the majority of their research budget from the NIH.

Donor Contributions

While a few private foundations support type 1 research, the largest portion of funding for T1D comes from donor-funded non-profits like the American Diabetes Association (ADA) and JDRF. JDRF and the ADA use donor contributions to fund research grants but do not actually conduct their own research. In addition to research, these organizations support a broad range of activities, including education, advocacy, and outreach.

Commercial Investments

The third important source of funding for T1D research is commercial enterprises. Large companies like Johnson & Johnson typically fund diabetes research through annual income from their ongoing operations, while smaller companies like Viacyte often rely on raising money from investors. On occasion, both large and small companies also receive funding from the major T1D non-profits. Since profit is a primary motive for commercial enterprises, they often focus on projects that have potential to make it to market in the near-term.



SOURCE: JDCA Estimates

IV. Practical Cure Defined

The Practical Cure Vision:
Imagine a world where stopping what you're doing to test your blood sugar is a thing of the past; where the scar tissue of countless insulin injections is no more; where you can go to bed at night without fear.

For over a century, researchers have pursued a perfect cure with little to no results. The last real game changer for type 1 diabetes was the discovery of insulin in 1922. We need a game changer for our generation: the kind that would reduce injections, eliminate complications, and keep blood sugars in check. This is a "Practical Cure."

Definition:
A Practical Cure describes any solution that can be widely available in the near future which enables people with established type 1 diabetes to live a near-normal lifestyle, free from daily disease management routines. There are four main characteristics of a Practical Cure:

> "A Practical Cure describes any solution that can be widely available in the near future which enables people with established type 1 diabetes to live a near-normal lifestyle..."

FOUR MAIN CHARACTERISTICS OF A PRACTICAL CURE:

Minimal Monitoring
- Does not require blood glucose monitoring beyond once a week
- A1C levels 5-7%

Sleep Worry Free
- Allows patients to sleep care free

Free Diet
- Does not restrict a patient's diet
- Does not require carb counting

Minimal Side Effects
- Best case: Zero side effects
- Acceptable case: Insignificant side effects

Practical Cure Defined Continued

The Unique Attributes of a Practical Cure:

1) A Practical Cure focuses on outcomes, not research pathways

In pursuit of a Practical Cure there is no bias for or against particular research types or methods. Any research project that has the potential to deliver the characteristics of a Practical Cure is welcome. The JDCA tracks a range of potential Practical Cure research projects, which are outlined in Section VII of this report.

2) A Practical Cure does not need to be a 'perfect' solution

A Practical Cure will revolutionize the quality of life for those living with type 1 diabetes, but it does not need to be a perfect solution that completely eliminates the disease. While reversing type 1 diabetes would be ideal, a Practical Cure is broad enough to accommodate periodic treatment or maintenance therapy. As a result, a Practical Cure initiative draws in a wide set of possible pathways and projects.

3) A Practical Cure has potential be achieved in the near-term

The JDCA is working to maximize the chances that a Practical Cure will be delivered in time to make an impact on the generations of people currently living with type 1 diabetes. We are not content with developing a cure that will only impact future generations. As a result, we often propose a target market date of 2025. Without such a time goal there is no mechanism to prioritize projects that have a chance to deliver results sooner over projects that are only likely to produce results much later. As a result we place great emphasis on projects that are already in human trials or are about to enter human trials.

Value of a Practical Cure:

The benefit of a Practical Cure is intuitive and overwhelmingly supported by the T1D community. Later sections of this report will demonstrate the continued support for a Practical Cure by both people living with type 1 and their families. On the other hand, this report will also show that the major T1D charitable organizations and research centers apply a relatively limited amount of effort to making a Practical Cure a reality.

By urging donors and charities to direct their money to Practical Cure projects, we aim to catalyze progress and create the best chance that a Practical Cure will be developed in the next 15 years.

V. Donor Priorities

As donors, we are the heart of the diabetes charities. We are the people with type 1 diabetes and the mothers, fathers, sisters, brothers, spouses, grandparents, and friends who share the challenges of living with type 1. We volunteer and fundraise to support the diabetes charities and make a difference for those living with the disease today.

The JDCA conducts multiple surveys throughout the year to track the opinions, values, and priorities of the T1D donor community. The objective of these surveys is to gain a deep and accurate understanding of areas of greatest importance among T1D donors at any given point in time. We also track any changes in priorities from one survey to the next.

Since 2012, the JDCA has conducted eight surveys of the type 1 community. During 2014 we received direct input from roughly 1,000 donors in three different surveys throughout the year. The surveys were conducted by a third party and were carefully monitored to follow best practices of market research and survey design. Statistical significance in all cases was 90% and the error range never exceeded +/- 10%.

Five insights consistently emerged from the data:

1. The T1D community is active and engaged

The overwhelming majority of the T1D community raises money for type 1 diabetes non-profits and research organizations. Nine out of 10 survey respondents have either donated directly to a diabetes charity or participated in a fundraising event over the past 12 months (Exhibit C). This level of support is consistent with previous JDCA surveys and demonstrates the ongoing commitment of the type 1 community. [4]

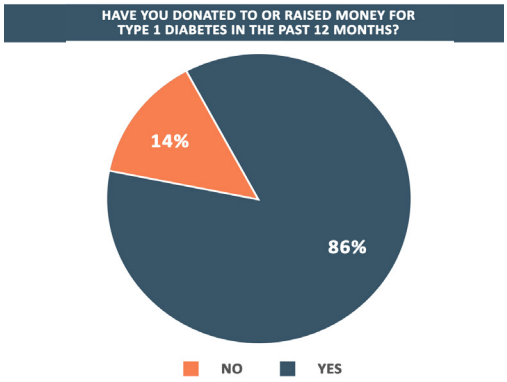
Fundraising events are the primary point of engagement for the type 1 community. This year 69% of T1D donors will participate in a fundraising event, such as a walk, gala, or ride. Many also give directly to their primary charity, with 46% of people indicating that they either donate online or mail personal checks. [5]

2. Cure research is donors' top priority

In each survey conducted by the JDCA during the past three years, **the number one priority of donors is to fund cure research.** When asked to indicate the top activity that they want their donation to fund, 9 out of every 10 donors indicates 'cure research' (Exhibit D). [6]

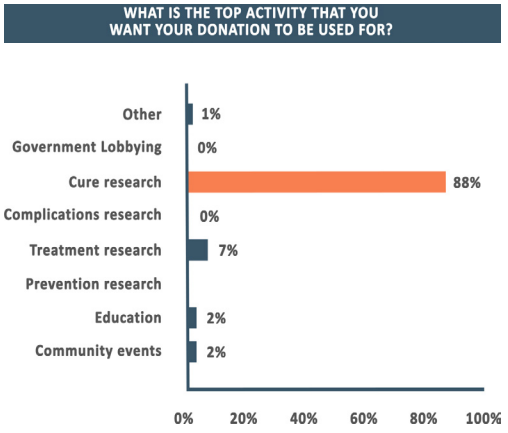
Furthermore, the primary reason people participate in fundraising walks, which are the highest grossing events for the major diabetes non-profits, is to fund a cure for type 1 diabetes (followed closely by supporting a loved one). [7]

Exhibit C



SOURCE: JDCA Survey, June 2014

Exhibit D



SOURCE: JDCA Survey, June 2014

4. JDCA Survey Report, "Donor Sentiment a Mixed Bag: Active in Fundraising, Weak In Confidence," June 2014.

5. Ibid.

6. Ibid.

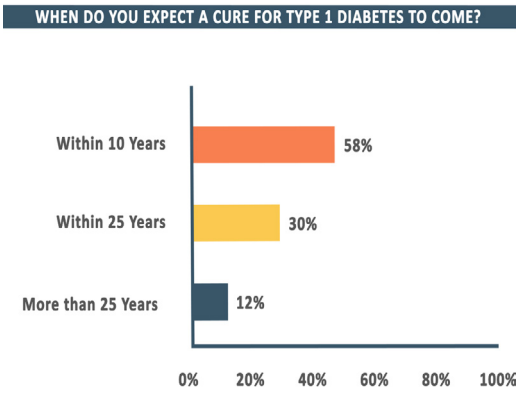
7. JDCA Survey Report, "Why Do We Walk?," Oct 2014.

Donor Priorities Continued

3. Donors expect a cure in the near future

Donors both want and expect a cure in the immediate future – within years not decades. Consistent with past survey findings, the JDCA's March 2014 survey showed that while nearly all respondents want a cure in the next 10 years, 6 out of 10 donors expect that the non-profit and research community will actually deliver a cure in the next 10 years (Exhibit E). These expectations amplify the responsibility of the organizations that are soliciting donations, as well as funding and conducting cure research, to focus resources on a near term solution.[8]

Exhibit E



SOURCE: JDCA Survey, March 2014

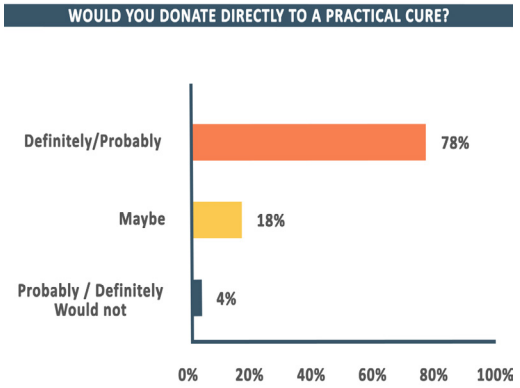
4. Donors choose a Practical Cure

Donors overwhelmingly state that a Practical Cure would greatly improve the quality of their life and, perhaps as a result, they believe its pursuit should be a priority. Over 80% of donors surveyed in each of the past three years consistently state that they would prioritize funding Practical Cure research over research that would take decades longer to produce a perfect cure. Yet, as we will see in the funding section of this report, only a very small portion of donor dollars actually make their way to Practical Cure research.

5. Donors want to give to Practical Cure research

Eight out of 10 respondents said they would donate to Practical Cure research projects if that option was made easily available to them (Exhibit F).[9] We believe that giving donors that option would be a win-win for donors and the major diabetes non-profits. For donors, it would ensure their money is being used for near-term cure research. For the non-profits, it would demonstrate alignment with donor interests, result in sustained fundraising growth, and ultimately enable more resources to be deployed in support of the most promising near-term solutions.

Exhibit F



SOURCE: JDCA Survey, March 2014

8. JDCA Survey Report, "Cure Attitudes and Trends Survey: Donors Value Speed and Focus," March 2014.

9. Ibid.

VI. Practical Cure Pathways

There are currently four broad research pathways in development that could yield a Practical Cure. While each of the four approaches has the potential to deliver a Practical Cure by itself, it is also possible that a full solution will require a combination of elements from different pathways. The four pathways are:

I. Islet Cell Transplantation

This pathway refers to transplanting insulin-producing islet cells into a person with type 1 diabetes.

Islet cell transplantation requires a sustainable and widely-available supply of islet cells. Historically, cadavers have been the only proven source of insulin-producing cells, but the availability of cadaver cells is very limited. In search of a more readily available source, researchers have tried to use cells from animals, particularly pigs, with only limited success. More recently, there have been advances toward deriving a sustainable cell supply from human stem cells.

Islet cell transplantation also requires a solution to protect the cells from the autoimmune attack after they have been implanted in the body. The primary approach to protection has been encapsulating islet cells in an implantable device that acts as a physical barrier between the islet cells and the autoimmune attack. The device material would have to be semi-permeable to allow the encapsulated cells to sense and respond to glucose levels in the surrounding tissue. Despite considerable time and energy, various encapsulation approaches have been tested with no breakthrough. However, advances in biomaterials have given rise to a new round of encapsulation work.

II. Device that Mimics the Pancreas

This type of device, sometimes referred to as an artificial pancreas, is under development at several commercial entities and academic research centers, but most are not advanced enough to deliver a Practical Cure. To be a Practical Cure, a mechanical device that mimics the pancreas would require an exceptionally reliable closed-loop system that is adaptive to each individual.

III. Glucose-Responsive Insulin (aka Smart Insulin)

Colloquially referred to as smart insulin, the intent of this pathway is to chemically engineer an insulin that is “smart” in the sense that it is activated only in response to rises in blood glucose levels. It would be injected subcutaneously and remain inactive until chemical compounds in or around the insulin sense that blood glucose has risen above a certain level. At that point, the smart insulin would quickly kick in to bring glucose levels down. The smart insulin would automatically become inactive again once blood glucose reached a normal level, thus avoiding low blood sugar. While there is considerable enthusiasm for this project in the T1D community, none of the research efforts has yet entered human trials.

Practical Cure Pathways Continued

IV. Modifying the Immune System

Stated simply, this pathway stops the body's immune system from attacking the insulin-producing beta cells. There are three basic approaches:

Blocking

A direct way to stop diabetes is to stop the autoimmune attack. This would include any approach that blocks the autoimmune attack without reducing the body's ability to fight disease and infection. In order for this to be a Practical Cure for established type 1 diabetics, there would have to be a sufficient amount of beta cells still in the body that could multiply and produce a sufficient amount of insulin after the attack was blocked. There is some evidence that even people with long-standing T1D have residual beta cells left, but if this is not the case, blocking the autoimmune attack would need to be combined with islet cell transplantation.

Balancing

Some researchers believe that T1D exists because the immune system has become unbalanced, meaning either the body is making too many killer T-cells which fight disease (and attack beta cells in type 1), or too few regulatory T-cells to keep the killer cells in check. Balancing the immune system would involve any approach that restores balance between killer T-cells and regulatory T-cells. To date there has only been limited progress along this path. Additionally, this approach faces the same islet cell supply issues as blocking.

Retraining

It may be possible to retrain the immune system not to attack beta cells. These approaches take immune system cells in the blood and retrain them not to attack the islet cells, either by ongoing exposure therapy (potentially through periodic injections) or by a mechanized process that removes, treats, and reinserts immune system cells in the blood.

VII. Practical Cure Projects in Human Clinical Trials

Each year the JDCA reviews all T1D projects that are active in human trials to identify the ones that have the potential to become a Practical Cure. We focus our analysis on projects in human trials because this is a critical milestone for all research, and given the 10-14 years that are required to get through all stages of clinical testing, we believe projects in human trials offer the best chance of delivering a Practical Cure in the near future.

In 2014, we reviewed 380 T1D projects that are currently in human trials. Only 8 of these projects are potential Practical Cure solutions. This year four projects are on the list for the first time, as described in the chart below. Since last year, two projects were removed from the list. The first one removed, a Sitagliptin/Lansoprazole drug combination run by Sanford Research, failed phase I testing. The second project removed, the 'Monolayer Cellular Device' run at the University clinical Hospital Saint-Luc in Brussels, completed testing more than 24 months ago but has not reported any results or communicated any status updates.

"In 2014 we reviewed 380 T1D projects that are currently in human trials. Only 8 are potential Practical Cure solutions."

PROJECT	ENTITY	DESCRIPTION	STATUS
VC-01 *(new)*	ViaCyte *San Diego, CA*	Supply source plus encapsulation device. Precursor cells, derived from an embryonic stem cell line, mature into functional beta cells when implanted under the skin. Cells are protected by an encapsulation device which requires replacement every 2 years.	➢ Currently recruiting for Phase I/II human trials.
Tolerion TOL-3021 *(new)*	Tolerion / Stanford *Portola Valley, CA*	Injectable drug. Unlike conventional vaccines, which act to stimulate the immune system, the reverse vaccine TOL-3021 is designed to selectively suppress specific elements of the immune system, stopping the attack on beta cells.	➢ Trial results released June 2013. Generally positive. ➢ Next step: Expand Phase II trials with a larger population and larger doses.
Bionic Pancreas *(new)*	Boston University / Ed Damiano *Boston, MA*	Bi-hormonal closed-loop pump + continuous glucose monitoring device. System delivers insulin and glucagon, and measures and adapts to each individual.	➢ Tested in both children and adults to positive results and user experiences. ➢ Now conducting additional testing to identify a pathway to commercialization.
Cyclosporine Lansoprazole *(new)*	Perle Bioscience *Charleston, SC*	Drug combination. Cyclosporine is supposed to combat autoimmunity while Lansoprazole is supposed to aid in re-growing beta cells.	➢ A trial in 130 people is scheduled to start in February 2015.
ßAir bio-artificial pancreas	Beta-O2 Technologies *Tel Aviv, Israel*	Islet cell encapsulation device. Islet cells encapsulated in a device slightly smaller than a hockey puck, which is implanted in the abdomen. The patient administers daily subcutaneous injections of oxygen into the device to keep the implanted cells alive.	➢ Just started recruiting for a Phase I clinical trial in Sweden. ➢ **Cautionary Notes: Daily user maintenance regime may be onerous; still being refined.**
Diabecell	Diatranz - Otsuka Ltd. *Auckland, New Zealand*	Encapsulated porcine islets. Porcine islets are encapsulated in alginate microcapsules and implanted in the abdomen.	➢ Phase IIB study in progress with an expected completion date of December 2014. ➢ **Cautionary Note: Mixed results to date.**
Stem Cell Educator	Tianhe Stem Cell Biotech *Hackensack, NJ*	Immune system retraining machine. Over several hours, a patient's blood continuously passes through a machine which exposes blood cells involved in the autoimmune attack to cord blood stem cells, which 'remind' the cells how to act properly.	➢ Phase II study has started. ➢ **Cautionary Note: May require a complex and frequent blood-processing procedure, TBD as testing progresses.**
BCG	Faustman Lab *Boston, MA*	Single drug. Tuberculosis vaccine repurposed to halt autoimmune attack and spur beta cell regeneration.	➢ Phase II scheduled to start May 2014. Completion date is May 2022. ➢ **Cautionary Notes:** ○ **Inconclusive Phase I trial results** ○ **Very long Phase II trial – 8 years** ○ **Very expensive trial for 120 people at $25MM**

VIII. Emerging Practical Cure Projects

While the JDCA focuses most closely on projects in human trials, we also monitor potential Practical Cure projects which are on the verge of human trials. These projects are funded by the major non-profits, the NIH, commercial ventures, and/or other governments around the world. A few projects worth following are presented in the chart below.

PROJECT	ENTITY	DESCRIPTION	STATUS
BioHub	Diabetes Research Institute *Miami, FL*	Multiple pathway initiative. Only one area is nearing human trials: Testing of a biodegradable scaffold, filled with human islets, to be inserted into abdominal lining called the omentum. The scaffold is a combination of a patient's own plasma and thrombin, a commonly used, clinical-grade enzyme. Immunosuppressant drugs will be used. Other projects underway test other insertion sites, other biological materials for the scaffold, and work to eliminate the need for immunosuppression. However, none of these projects are ready for human trials.	➢ Omentum / biodegradable scaffold testing to start Phase I/II November 1, 2014. ➢ Next wave human trials in discussion with FDA – no dates yet set.
DiaVacs	DiaVacs, Inc. *Edgewater, NJ*	Customized drug using patient's own cells. A patient's dendritic cells are extracted from the blood and modified through the use of small interfering oligonucleotides. The patient is injected with the modified cells, which are absorbed and trafficked to the pancreatic lymph nodes, where they induce tolerance to stop the autoimmune attack.	➢ Scheduled for Phase II trials in late 2014. ➢ Received orphan drug status from the FDA in January 2014.
SmartCells (SmartInsulin)	Merck *Whitehouse Station, NJ*	Responsive and adaptive insulin. Injected under the skin, unique chemical properties activate the insulin when blood sugars rise and halt insulin action when blood sugar drops. Regular injections are still required.	➢ Phase I to start soon. ➢ Not yet registered on the NIH clinical trial database, and there is no other public information about when the trial will begin.
Islet Cell Transplantation + Immunosuppression	Chicago Diabetes Project *Chicago, IL*	Transplantation + immunosuppression. Human islet cells transplanted into PWD. Transplanted cells are protected by a battery of immunosuppressants which is modified over time to become more focused and localized.	➢ About to start Phase III islet cell transplantation project with localized immunosuppressants.
T1D Cure Program	City of Hope *Los Angeles, CA*	Transplantation + immune modulation. Multi-pathway strategy that combines islet cell transplantation with immune modification to protect the islet cells. Encompasses a range of projects. Does not use encapsulation.	➢ Different projects on different timetables, with clinical trials for immune modification beginning in 2 years and clinical trials for renewable cell supply beginning in 5+ years.
Embryonic Stem Cell Line	Harvard University / Melton lab *Cambridge, MA*	Stem-cell line of fully functioning beta cells. Able to generate large amounts of fully functional beta cells from embryonic stem cells. They have shown that this works in animals, but still have more pre-clinical tests to run before it will be ready to start testing in people.	➢ Time to human trials unknown.

IX. Non-Profit Practical Cure Funding

JDRF and the ADA are the two principle fundraisers for diabetes. Together, they raise over $400 million per year, which represents 80% of all donor contributions to type 1 diabetes in the United States. Of that $400 million, only $6 million (1.5%) went to Practical Cure research in 2013, all from JDRF. The ADA did not fund any Practical Cure research at all (Exhibit G). Said differently, **only 1.5 cents of every donor dollar makes it to Practical Cure research.**

JDRF Highlights

Other than the U.S. government, JDRF remains the largest funder of type 1 diabetes research in the world. JDRF's exceptional fundraising success has, more than any other T1D organization, given its donors a unique sense of trust, hope, and expectations for progress. In return, we believe JDRF has a deep responsibility and obligation to meet the expectations of its donors to the best of its ability.

One way to determine where an organization places its focus is to look at how it utilizes its budget. Research funding is decreasing in both relative and absolute terms in the JDRF's recent budget strategy. Research grants as a portion of total spending have fallen to 51%, the lowest level in a decade. Compared to the peak five years ago, JDRF is spending $50 million dollars less on research grants, a 33% decline. At the same time, it has increased spending on all major non-research categories (Exhibit H). These facts raise a red flag because they suggest that JDRF is deprioritizing cure research.

The most important finding from the financial analysis is that JDRF dedicates a relatively small amount of their total budget to cure research. Only 15% of their total annual revenue is used for any kind of cure research, with only 3% directed to near-term Practical Cure research projects (Exhibit I).

JDRF's budget allocations do not reflect donor wishes. In the "Donor Priorities" section of this report, the data overwhelmingly demonstrate that donors consistently identify cure research as their top priority.

ADA Highlights

Though the ADA actually raises more money than JDRF—$225 million per year—it does not focus on type 1 diabetes or on research. Instead, the ADA focuses primarily on publishing, advocacy, and communication. Only 16% of their overall budget is used for research grants of any type, mostly related to type 2 diabetes.

Roughly 40% of ADA research grants are applied to type 1 diabetes-- with $4 million toward cure research and $10 million toward other types of T1D research. Most importantly, the ADA does not directly fund any Practical Cure research at all (Exhibit J).

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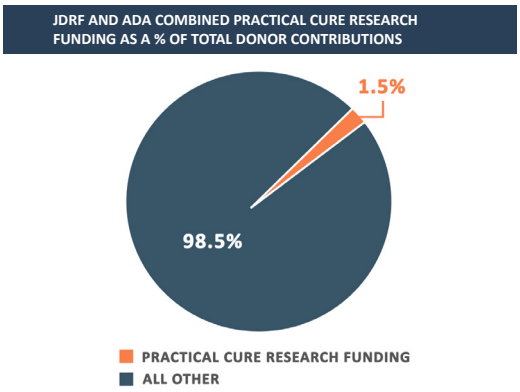
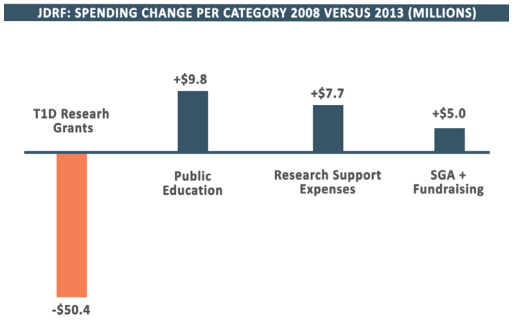
Exhibit G



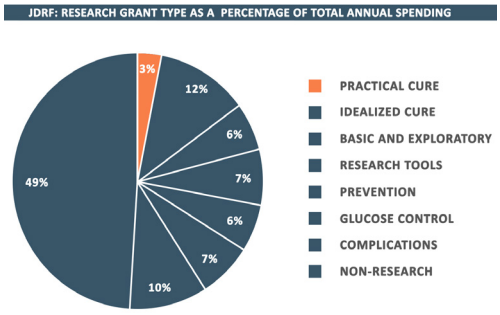
SOURCE: ADA and JDRF Online Research Databases and Annual Reports

Exhibit H



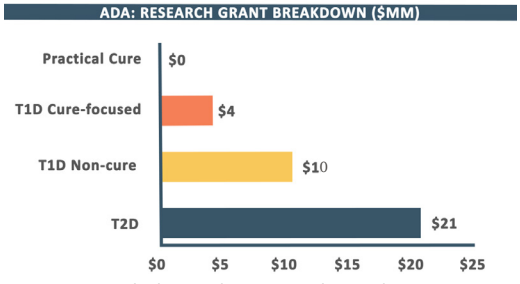
SOURCE: JDRF 2004-2013 Audited Financial Statements

Exhibit I



SOURCE: JDRF Online Research Database and 2013 Audited Financial Statements

Exhibit J

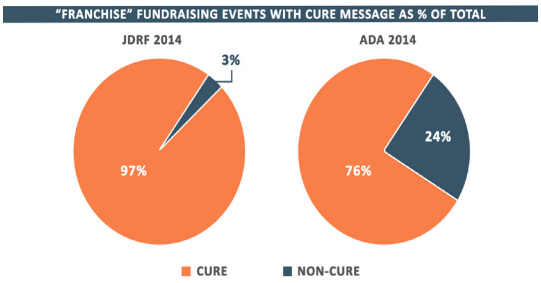


SOURCE: ADA Audited Financial Statements and Press Releases

X. Fundraising Events by the Major Non-Profits

In 2014 JDRF will host more than 140 nationally branded fundraising walks (e.g. Walk to Cure Diabetes), and the ADA will host over 100 similar events (e.g. Step Out: Walk to Stop Diabetes). These events are highly effective fundraising vehicles. Big fundraising walks attract several thousand people. If each walker individually raises an average of $500, an event with 2,000 participants will net $1 million in proceeds. As a result, these walks provide a major source of funding for both the ADA and JDRF. *But does the money raised by these events actually make it to cure research?*

Exhibit K



SOURCE: Chapter Websites and Press Releases

The Majority of Fundraising Events Promise to Fund Cure Research

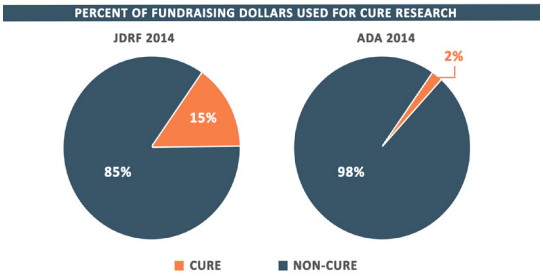
The majority of JDRF and the ADA's fundraising events promise that proceeds will be spent on a cure (Exhibit K). This comes as no surprise since, as noted earlier in this report, donors' top reason for giving is to support cure research.

Besides JDRF's Walk to Cure Diabetes and the ADA's Step Out: Walk to Stop Diabetes, other national events that use a cure message include the ADA's Tour de Cure, and JDRF's Ride to Cure Diabetes, Crossroads to a Cure Gala, and Promise Gala. In all cases, the promise of a cure is the major selling point for the event, and participants come away with the impression that their contributions will further cure research.

Only a Minority of Fundraising Event Proceeds are Actually Used for Cure Research

The previous section of this report showed that JDRF and the ADA spend a small minority of total annual revenue on cure research. Last year only 15% of JDRF's annual budget and 2% of the ADA's annual budget were allocated to T1D cure research (Exhibit L).

Exhibit L



SOURCE: Chapter Websites and Press Releases

Given that fundraising events are a major source of revenue for these organizations (1/3 of the ADA's annual revenue and 2/3 of JDRF's), it is clear that most of the proceeds from fundraising events are not used for cure. The rest of the money goes to other types of research, public education, government lobbying, publishing (in the case of the ADA), marketing, fundraising support, and overhead. If the non-profits want to maintain donor loyalty, it is in their best interest to make cure research their top priority and align with donors' wishes.

XI. Non-Profit Leadership

The JDCA tracks and comments on the actions of non-profit leadership, including board members and executives. These non-profit leaders have more ability than almost any other group of people to accelerate a cure for type 1 diabetes. They possess the authority to determine how their organizations' money and personnel are utilized, and can choose to shift resources toward Practical Cure research. Even small changes can significantly deepen the impact of the combined $400 million that JDRF and the ADA allocate each year.

"Non-profit leaders have more ability than almost any other group of people to accelerate a cure for type 1 diabetes."

We believe that each member of the Board of Directors has a fiduciary duty to ensure that their organization act in a way that reflects the wishes and desires of their donors. Donors overwhelmingly prioritize cure research but the non-profit boards and executives allocate only a minority of their budgets for that purpose.

Non-profits exist in a different sphere than for-profits, but the ADA and JDRF would benefit from some of the best practices that keep for-profit leadership accountable. Some of these practices would help align the goals of the non-profits with the donors who generously fund them.

These are five recommendations for non-profit leadership:

1) **Make the Board of Directors accountable to donors.** Currently, non-profit board members can be appointed or removed by fellow board members, a system that gives most donors no voice in the process. Non-profits would benefit from a structure that makes their board of directors directly accountable to the donors who fund them. We recommend a system where board members are nominated by leadership but ultimately elected by donors.

2) **Reduce board size to under 15.** The average size of a for-profit board is 9 members, large enough to represent a range of key skills but small enough to ensure engaged discussion. In comparison, the JDRF currently has 34 board members and the ADA has 38. We recommend reducing this number to a more manageable and appropriate size.

3) **Implement and communicate annual key performance metrics.** Every high-performing for-profit entity sets annual objectives for its most important areas of focus. These objectives give a focal point and give leadership the ability to evaluate whether or not real progress is made. Neither of the major T1D non-profits have set or published annual performance metrics for cure progress. We recommend implementing and communicating annual objectives for the evaluative capacity that they provide.

4) **Tie executive compensation to annual key performance metrics.** Tying an executive's personal compensation to positive performance metrics ensures that the organization stays focused and maintains consistent goals. We recommend using this effective compensation program to better direct non-profit objectives and ensure a responsible leadership.

5) **Publish a full annual report within 90 days of year end.** In general, the non-profits communicate with their donors much less frequently than for-profits do. Regular reporting by for-profit entities keeps shareholders informed and management accountable. Increased non-profit reporting would be a win-win – the transparency would keep donors informed while the non-profits would enhance donor trust. We recommend full annual reports and a higher level of communication between the non-profits and their donors.

XII. A Few Final Thoughts On Donor Action

With 2015 just around the corner, many of us will be setting goals for the year ahead. Our goal is clear: greatly accelerate progress to a Practical Cure. We will continue to track projects in human trials, encourage the major non-profits to adopt a Practical Cure initiative, and offer both constructive and critical suggestions about how the system can be better focused and aligned with donor interests. By the end of 2015, we hope that our efforts will result in more high quality Practical Cure projects entering human trials.

"Our goal is clear: greatly accelerate progress to a Practical Cure."

There are a number of things that members of the type 1 diabetes community can do to help move us toward a Practical Cure as quickly as possible. Whether you prefer to take a collaborative or confrontational approach to bring about change, select the CURE steps that are right for you.

Create Awareness

- ✓ Discuss what a Practical Cure would mean to you with friends and family.
- ✓ Take an active part in social media to express the importance of a near-term cure.
- ✓ Start a Practical Cure 'team' at your local fundraising walk or ride.
- ✓ Set a giving goal for the year and publicly share your progress.

Uncover the facts

- ✓ Read publications and mailings from the recipients of your donations.
- ✓ Sign up for the JDCA's email list to ensure you receive the latest reports on the T1D research landscape.
- ✓ Ask: "Where does the money go?" Without asking this basic question we don't really know how our gifts will be used. By asking, we communicate that we are engaged and have expectations for how the organizations use our donations.
- ✓ Other key questions we can ask are:
  1. *How will the money I raise be used? How much will go towards cure, treatment, advocacy, etc.?*
  2. *If I want my money to be used for something specific (most of us prioritize finding a cure), is there a way that I can ensure the money I raise is used for that? If not, why not?*
  3. *After I give, how and when do I get an update on the difference my gift has made?*

Request that a Practical Cure be made a top priority

- ✓ Write, call, or email local and national leaders of the organizations that you support, including the members of their Boards of Directors. (All this information is available on the organization's website)
- ✓ Join or start a petition for a Practical Cure. Send your results to JDRF, the ADA, etc.
- ✓ Ask that a certain portion of fundraising event proceeds be utilized for Practical Cure research.
- ✓ Follow and track the Practical Cure projects noted in this report and share the information with others.

Ensure that your donation is used for a Practical Cure

- ✓ Every time you make a gift to a T1D organization, include a letter stating that "*My gift is required to be used for Practical Cure research*." The receiving organization is legally obligated to use the gift only for the purpose you require or they must return the donation.
- ✓ Avoid giving online. It is so easy to make a donation online and, yet, by design, there is no way to give instructions about how an online donation should be used. Most charities would much rather have a "general" gift to use however they want than a gift that the donor has restricted for a specific use.
- ✓ Ensure that the proceeds your team raises for your local fundraising walk or special event be used for Practical Cure research.

Juvenile Diabetes Cure Alliance
The Voice of the Donor For a Cure

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Website: thejdca.org

About

The Juvenile Diabetes Cure Alliance is a non-profit organization that unites individuals who seek a Practical Cure for type 1 diabetes by 2025. We work with donors to ensure that their charitable contributions fund research with the best chance of delivering a Practical Cure. We conduct independent research that analyzes topics related to type 1 cure development with a focus on the major diabetes non-profits and report our findings to Alliance members and the donor community at large.