the plan to turn type one into type none
JDRF is the only global organization with a strategic research plan to end type one diabetes (T1D). Our plan ensures that there will be an ongoing stream of life-changing therapies moving from development through to commercialization that lessen the impact of T1D. We want to keep people with T1D healthy and safe today until we reach our ultimate goal of a cure and universal prevention of T1D.

One of JDRF’s founding mothers, Carol Lurie, established our mission more than 40 years ago. She helped build this organization from a few concerned parents into the leading global organization funding T1D research. While we mourn Carol’s passing away on February 15, 2013, we celebrate her tremendous contribution by renewing our commitment to our shared mission. As president and CEO of JDRF, I see that commitment everywhere. Our supporters—our donors, fundraisers, advocates, and volunteers—are our lifeblood. Every day I am more inspired by the energy and dedication they demonstrate—and motivate in others.

Decades of research have shown us that a cure for T1D will not come as the result of a single breakthrough. The best and most efficient way to fulfill our mission—best both from a scientific perspective and for patients—is to generate progress across a variety of strategically chosen therapeutic approaches. We will progressively remove the daily burden, side effects, and complications of T1D until the day we end the disease by advancing therapies through the research pipeline and holding ourselves accountable by setting measurable goals and embracing the highest standard of transparency.

In the following pages, you will read more about exactly how we are working to fulfill our mission, through our six priority research areas: artificial pancreas, complications, encapsulation, smart insulin, restoration, and prevention. And you will learn about the progress we made in research and advocacy programs in fiscal year 2013 from the newest member of JDRF’s executive team, Executive Vice President for Research and Advocacy David E. Wheaden, M.D. Dr. Wheaden’s depth of experience in drug development, translational research, regulatory and medical affairs, and patient advocacy are already providing expert guidance that will ensure JDRF’s most successful days lie ahead of us.

Thank you for your support in helping to make our vision of a world without T1D become a reality. One day in the future, we will declare victory and eliminate T1D entirely, and JDRF will have led the way. I know that together, we will turn Type One into Type None.
Artificial Pancreas

Currently, managing T1D is relentless. It requires people to constantly balance insulin delivery against the amount of food eaten, the amount of exercise, and even the stress of the workplace or school. Few people, regardless of age, can focus on this balancing act every moment of the day. But technology can.

Artificial pancreas (AP) systems will be the most revolutionary advance in diabetes care since the discovery of insulin. Like the body’s pancreas, AP systems will react to rising blood-glucose levels by combining monitoring technology with insulin pumps to provide the right amount of insulin at the right time. Not only will AP systems result in much tighter control, lowering the risk of health complications later in life, they will also reduce the constant worry about blood-sugar levels and what must be done to manage them.

In less than a decade, JDRF has transformed the AP field. The JDRF Artificial Pancreas Consortium—which brings the best researchers in the TID field together with some of the world’s leading engineers and mathematicians—has driven virtually every major advance in the AP field. Until we stepped in, companies and others were not heavily committed to developing this kind of device. The six-step roadmap JDRF laid out to create successively more sophisticated versions of the AP has since been embraced by manufacturers to guide their own R&D programs.

A first-generation system—operating low-glucose suspend technology, which will partially automate glucose control—was recently completed by Medtronic and approved by the U.S. Food and Drug Administration (FDA). JDRF is already driving progress forward on more sophisticated algorithms and improved glucose sensors so that we can achieve second- and third-generation devices. Treat-to-range devices will predict high and low blood-glucose levels and adjust insulin dosing accordingly to maintain blood glucose within a set range. Treat-to-target devices will be designed to maintain blood glucose not just within a range but at a target level. Eventually, we envision a fully automated, multihormonal, dual-chamber artificial pancreas system capable of keeping blood sugar at specific levels and of delivering, in addition to insulin, key pancreatic hormones that influence blood-glucose levels.

It is no exaggeration to say that without JDRF’s leadership, we would still be years away from seeing AP systems in the hands of people with TID. In addition to the research, JDRF’s advocacy arm worked closely with the FDA to develop regulatory guidance to help ensure that AP devices could move quickly to human clinical trials. Today, those trials are under way, and early results show they work.

Complications

Despite significant advances in blood-glucose monitoring and insulin therapy, people with TID still have to worry about the damaging effects of high blood-glucose levels, which can lead to life-threatening complications. JDRF is pursuing multiple strategies to resist and reverse conditions such as diabetic retinopathy (eye disease), diabetic nephropathy (kidney disease), and nerve damage. By supporting extensive studies and creating a platform for widespread collaboration, we are striving to better identify ways to predict, prevent, and treat these devastating complications.

The Joslin 50-Year Medalist Study is working to identify factors that may confer resistance or susceptibility to diabetic complications. The JDRF-supported study, which began in 1970, is constantly revealing new information about the long-term effects of TID in people who have lived with the disease for 50 years or longer without developing complications. Findings from the study are being used to further drug-discovery and measurement tools to predict risk or stage the progression of complications.

Since approximately one-third of people with TID develop diabetic nephropathy, JDRF formed the largest-ever international effort to investigate the genetics of kidney disease. The JDRF Genetics of Diabetic Nephropathy Collaborative Research Initiative is a three-year, $7-million initiative that brings together top scientists to expand previous research and share findings in an effort to identify possible ways to prevent and treat this life-threatening condition. The three initial key activities of the collaborative project include looking for genes that differ between people with TID who do and do not have diabetic nephropathy; identifying genes that predict how quickly a person with TID may develop kidney failure; and identifying genes that predict rapid progression of decline in kidney function.

Research on new therapies for all stages of diabetic eye disease—the leading cause of blindness in working-age adults—continues through our Healthy Eye Project. The project is focused on two main areas: understanding why some people with TID, even those who have lived with the disease for a long time, do not develop diabetic eye disease, as well as why some people respond to drug treatment while others do not; and clinical trials to identify and test molecular targets that improve the stability of blood vessels in the eye and/or address other risk factors for diabetic retinopathy. The findings are adding greatly to our understanding of the condition and may lead to new mechanism-based therapies to prevent, treat, and reverse diabetic eye disease.

Ending and preventing diabetic complications is essential to JDRF—and our research in this field has the potential to greatly improve quality of life for millions of people living with TID.
We’re the always moving forward type

**Encapsulation**

Beta cell encapsulation has the potential to virtually eliminate the relentless daily management burden for those living with TID: no need for multiple insulin injections or pump therapy, no more constant blood testing, and no more carb counting. People with TID would just go about their lives for extended periods of time, up to 24 months, as if they didn’t even have the disease.

Encapsulation is a therapy that involves putting insulin-producing beta cells in a protective barrier and implanting them beneath the skin. These encapsulated beta cells will sense a person’s glucose levels and produce insulin as needed, while the barrier shields the cells from the body’s autoimmune attack that triggered the onset of TID.

Encapsulation therapy overcomes two obstacles to earlier islet transplant procedures: a limited supply of donor islet cells; and the need for continued immunosuppressive drugs to prevent the immune system from destroying the newly introduced islets.

LCT has conducted small human trials and is still compiling the results. Preliminary results show the product has had a positive effect on reducing dangerous low blood sugar events.

JDRF investment has already helped bring one encapsulation product to early human testing, with several others heading to human trials in 2014.

- JDRF is partnering with biotechnology company ViaCyte to develop a first-of-its-kind encapsulation product that converts stem cells into immature pancreatic endocrine cells. The device maintained blood glucose at normal levels in diabetic mice. Human clinical trials are planned for 2014.
- JDRF supported a project conducted by Living Cell Technologies (LCT) involving the encapsulation of pig-derived islets for implantation into humans. Preclinical encapsulation trials have been encouraging.
- JDRF is co-funding investigators at the Diabetes Research Institute (DRI) at the University of Miami. The team seeks to create a device that can provide the optimal environment for islets to survive and function for a long time. DRI hopes to take part of this device to human clinical trials in 2014.

**Smart Insulin**

Eliminating virtually all of the daily burdens associated with mechanically managing TID would profoundly enhance and simplify the lives of people with the disease. Moreover, by improving overall blood-glucose controls, the risks of life-threatening complications would sharply diminish, leading to longer, healthier lives. Smart insulin is a drug designed to ensure perfect glucose control throughout any given day by turning on when it is needed and off when it is not—liberating people with TID from multiple daily insulin injections and the constant monitoring that accompanies the disease.

Smart insulin is a glucose-responsive insulin—insulin in a form that renders it essentially inert until it is needed. A person with TID would take a shot, or a pill, of this insulin—enough to cover the needs of a day—and the insulin would circulate in the body until blood-glucose levels start to rise. As glucose rises, the binding element of the insulin releases the insulin so it is free to do its job. As glucose levels return to normal, the release of insulin stops until it is needed again. Smart insulin would automatically activate or deactivate in response to the glucose in the blood, thus giving tighter control essentially as if the beta cells were working normally.

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Preclinical encapsulation trials have been encouraging. JDRF continues to work on identifying the best materials for a permeable barrier and to work on the design of implanted devices to hold beta cells without being intrusive. While this research progresses, JDRF is already taking encapsulation out of the lab and into the real world.

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**Smart Insulin**

Over the last decade, JDRF has been a leader in the smart insulin field. It was our early support of the company Smart Cells, Inc. at its riskiest stage that sustained the idea and validated the initial concept. And after this proof that smart insulin is a potential TID therapy, industry partners have made a financial commitment to take the concept further along the development pipeline. Beyond its support of Smart Cells, JDRF has continued to provide leadership, most recently through the Agnes Varis Glucose-Responsive Insulin (GRI) Grand Challenge Prize to stimulate the generation of novel ideas from a diverse array of disciplines to advance development of smart insulin.

Phase 1 of the challenge awarded prizes to three research projects in 2011 for their initial ideas on delivery and overdose prevention. Phase 2 will be the discovery phase, building on the winning ideas in Phase 1. This phase will provide experimental design and validation of potential smart insulin drugs, culminating in pre-clinical proof of principal studies in animal models. The final phase of the challenge will take the most promising drugs to human clinical trials.

While still years away from becoming a treatment, smart insulin will, with continued JDRF investment, become another life-changing therapy for those with TID.
We're the plan to change the future type

**Restoration**

A full biological cure is the ultimate and permanent solution to all the complexity and problems of TID. For a decade, JDRF has been exploring ways to restore the body’s ability to create new insulin-producing beta cells in the pancreas while preventing the autoimmune attack that triggers TID. Together, these areas of investigation will eventually yield a permanent cure for TID, and JDRF has made significant strides in both.

The JDRF Beta Cell Survival and Restoration Program is based on a simple principle: the body can heal itself. We believe the body can heal TID as well, though it needs help from science to do so. Our research is focused on:

- expanding the number of beta cells so normal insulin production can resume;
- extending the life and/or improving the health of underperforming beta cells; and
- delaying or preventing beta cell death.

A major focus in the program is to take existing drugs—approved for use for other conditions—and explore whether these drugs, alone or in combination with others, may have positive impact on either reducing beta cell stress and/or inducing beta cell survival. Another priority is to establish proof in human clinical studies that one or more of the repurposed drug candidates will indeed enhance beta cell survival and can be safely tolerated by patients. We’re also funding pioneering research to create new compounds and identify other molecules that might have a positive effect on beta cell health and restoration.

Identifying biomarkers, or indicators of disease progress and progression, is another key area that will facilitate early detection of subtle changes in beta cell health and function, giving us greater insight into beta cell stress and dysfunction.

Any effort to restore beta cells must also involve parallel efforts to tame the autoimmune attack. Successful restoration efforts must be combined with immune therapies that allow new and/or healthy beta cells to thrive and function normally. JDRF’s aggressive immunotherapy research program is developing therapies that promote tolerance to the beta cell autoantigens that trigger the attack on beta cells. Some of JDRF’s work in preventing TID, particularly our exploration into an antigen-specific TID vaccine, may also be applicable in the restoration field.

JDRF has set an ambitious goal to accomplish something never before done in biomedical research: reverse an autoimmune attack and restore the body to normal function. We are partnering with investigators, industry, and regulators so that we can advance a safe and effective therapy to people with TID as soon as it is discovered.

**Prevention**

Preventing TID from ever developing in anyone is the ultimate answer. Consider polio or smallpox—neither has been cured, but effective vaccines have largely eradicated these diseases. JDRF is pursuing both primary and secondary prevention strategies. Primary prevention means preventing the autoimmune attack so people never develop TID at all. Secondary prevention focuses on finding ways to prevent insulin dependence in individuals at risk or where the autoimmune attack on beta cells has already begun.

We know that the largest risk factor for TID is genetics. In fact, as a result of research funded by JDRF and the National Institutes of Health (NIH), we’ve now identified more than 50 genes that confer risk for TID. We understand TID genetics better than we did only a decade ago, and we have identified autoantibodies associated with the disease so we can more successfully screen those at risk.

But genes alone do not cause the disease, and scientists are now halfway through a longitudinal study called TEDDY (The Environmental Determinants of Diabetes in the Young) to identify the environmental factors that may trigger it. The study, funded by the NIH's Special Diabetes Program, a program in existence thanks in part to JDRF’s advocacy efforts, is exploring whether factors such as antibiotics, viruses, gut microbes, cow's milk, and/or deficiency of vitamin D or omega-3s are culprits in the onset of TID. Zeroing in on the causes of TID is fundamental to devising approaches to prevent the onset of the disease.

With our expanding knowledge, JDRF has intensified investigation into potential vaccines to prevent TID. JDRF is pioneering research into such vaccines, which might be used either before autoimmunity starts or after it starts but before total insulin dependence—or, ideally, a universal childhood vaccine to prevent TID, much like vaccines we administer to children to prevent measles, chicken pox, and other conditions.

JDRF is funding considerable research in other prevention strategies as well, including:

- The use of anti-inflammatory agents and other therapies to delay and prevent insulin dependence
- An approach that shows promise in suppressing the autoimmune response triggering TID without compromising the overall immune system’s ability to fight back

- A Phase II clinical trial studying whether orally delivered insulin can prevent TID onset in children at high risk
- A trial examining whether nasally delivered insulin can prevent TID onset where the autoimmune attack has already begun

Our research is ambitious, but so is our goal—to ensure that no one ever again needs to worry about being diagnosed with TID.
JDRF funds many of the leading type 1 diabetes (T1D) researchers across the globe. A discovery in the laboratory, however, is only the first step in bringing life-changing therapies to patients. To accelerate progress, we must shepherd potential therapies through every stage of the development pipeline. We must foster translational research—the “translation” of a laboratory discovery into a clinically viable therapy; guide clinical trials through the regulatory process; and work to ensure broad access to those therapies made available to patients.

Our numerous strengths make JDRF uniquely positioned to deliver on our mission. First, we maintain a “mountaintop view” of all the stages in the process. Second, we work collaboratively. The support we provide our researchers is about more than just funds. JDRF’s internal research and advocacy staff—expert scientists, physicians, and policy professionals—work closely with our funded investigators to ensure we reach established milestones. And we bring our funded researchers together into consortia, where the collective sharing of knowledge, data, and ideas pushes the research forward on all fronts.

Third, JDRF wields considerable influence in the industry, regulatory, and policy arenas. Several therapeutic innovations are currently in final phases of development precisely because JDRF put its name and funds behind the early-stage research others considered too risky. JDRF’s robust advocacy program has paved the path before us by helping secure: 1) clear regulatory guidance on artificial pancreas (AP) systems; and 2) Congressional reauthorization of the Special Diabetes Program, which provides $150 million per year for T1D research to the National Institutes of Health.

JDRF has played a central role in shaping the T1D research landscape. In fiscal year 2013 alone, we saw numerous advances, including:

- The FDA guidance on AP systems that JDRF helped shape had an astounding effect: real-world clinical testing is accelerating, and AP devices are steadily advancing through the pipeline. The recent FDA approval of Medtronic’s low-glucose suspend device represents successful attainment of the first step in JDRF’s six-step AP-development pathway. And we are continuing progress down this path by creating rigorous algorithms and improving glucose-sensing technology for AP systems.
- JDRF’s Encapsulation Consortium held its inaugural meeting this year. Scientists from 27 institutions are driving second- and third-generation approaches to beta cell encapsulation. Meanwhile, industry partner ViaCyte will conduct the first human studies of an encapsulation device in 2014.
- We now know that autoimmunity can be hormonally influenced and early-life exposure to gut bacteria may also play a role, indicating a potential prevention strategy that we are now exploring.

In other areas: JDRF formed the largest-ever international effort to investigate the genetics of diabetic nephropathy, or kidney disease, and research on other complications is encouraging. We are advancing exploration on biomarkers to identify disease stage and predict T1D progression. And we are pursuing the use of drugs approved for other indications to promote beta cell survival and regeneration.

JDRF’s approach is the most strategic way to turn Type One into Type None. Our research achievements this year—and our prospects for the future—are very exciting. To learn more, visit jdrf.org.

David E. Wheaton
Executive Vice President
Research and Advocacy
JDRF has a strategic research plan that will deliver a sustained stream of new, life-changing therapies.

LONG TERM
- PRIMARY: VACCINE
- RESTORATION: New beta cell growth protected from immune attack

MID TERM
- ARTIFICIAL PANCREAS: SMART INSULIN
  - Control
- ENCAPSULATION: Implantable Islets
- PREVENTION: Secondary Prevention

NEAR TERM
- ARTIFICIAL PANCREAS: Low Glucose Suspend
  - Treat-to-Range
- COMPLICATIONS: Diabetic Eye Disease
- TREATMENT: Prediabetes Diagnostics

This timeline is based on clinical delivery goals of identified therapies and will be updated as progress is achieved.

We’re the progress is inevitable type

Today, JDRF is the largest global funder of type 1 diabetes (T1D) research. We have accomplished what others only dreamed, and our future holds more promise than ever before—all because of you. You have made this organization what it is today. As donors, you give with an open heart, to help ensure our success. As fundraisers, you make a heroic impact, one donation at a time. As advocates, you tell your story where it matters most. As volunteers, you put yourselves out there, so the whole world may know our cause. You are the type that will stop at nothing. Your passion, your determination, your energy, and your generosity push us to ever greater heights of achievement, bringing us closer every day to the mission we all share—a cure for T1D.

We know that together, we will turn Type One into Type None. So from all of us at JDRF—THANK YOU.

Please visit jdrf.org/2013donors.

Thank you to our supporters
Message From the Chief Financial Officer

In the link below, we present the detailed financial statements of JDRF for the years ended June 30, 2013 and 2012. The graphics above illustrate a breakdown of functional expenses and public support and revenue in both real dollars and percentage. JDRF has continued the outstanding operating efficiency and transparency that led to our recognition as an accredited charity by the Better Business Bureau’s Wise Giving Alliance; our Gold-level ranking from GuideStar Exchange; our perfect score in accountability and transparency and three-star rating from Charity Navigator; and our top ranking 15 years in a row from the American Institute of Philanthropy’s CharityWatch.

This year, JDRF raised more than $181 million in public funds in the United States. Another $15.8 million was contributed by our international affiliates, and $9 million was generated through investment returns and other income. From these funds, we have been able to put more than $106 million to T1D research grants.

The strategic investments in organizational systems and infrastructure that JDRF has made in the last two years are beginning to yield positive return, and we continue to put our strongest efforts toward continued revenue increase for the year 2014 and beyond.

To JDRF’s donors, fundraisers, and partners, we thank you for your continuing support as we work to fund the research that will most quickly result in life-changing therapies and a cure for T1D. Together, we can turn Type One To JDRF’s donors, fundraisers, and partners, we thank you for your continuing support as we work to fund the research that will most quickly result in life-changing therapies and a cure for T1D. Together, we can turn Type One

Edward Sebald
Chief Financial Officer

To view the full Audited Financial Statement, please visit jdrf.org/2013financials.