

# JUVENILE DIABETES CURE ALLIANCE

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## Organizations Mentioned:

- American Diabetes Association (ADA)
- Diabetes Research Institute Foundation (DRIF)
- Joslin Diabetes Center
- Juvenile Diabetes Research Foundation International (JDRF)
- The Leona M. and Harry B. Helmsley Charitable Trust (Helmsley Trust)

## **Type 1 Diabetes Charitable Foundations**

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### Initiation of Coverage Report:

## **Breaking the Glass: Focusing the Effort on a Cure by 2025**

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### Conclusions:

- Under the existing system, it's unclear when, if ever, a practical cure will be developed
- Funding allocations and priorities of the major charities could be better aligned with the intentions of donors contributing for a cure
- To re-align funding allocations with donor intentions, it is incumbent upon donors to assert their desire to fund work that can result in a cure
- A coalition of cure-seeking donors can present a unified voice to ensure their requests are heard and drive the effort toward a cure

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## **Background**

Type 1 diabetes (“Type 1”) is a chronic and ravaging disease that touches the lives of a great many people in the US and across the globe. Progress toward the ultimate goal of a cure has been painstakingly slow and the long-heard promise of a “cure within five years” has rung hollow. A lack of focus on developing a cure as expeditiously as possible has thus far led to disappointing progress. The Juvenile Diabetes Cure Alliance (“JDCA” or “Alliance”) is addressing this issue. We will be advocating a more directed approach and more effective utilization of resources which will accelerate the timeline to a cure.

The work of Frederick Banting and Charles Best that led to the discovery of insulin combined novel thinking, determination, and urgency. That same sense of urgency is not being translated to current cure efforts. Within the existing system of Type 1 charitable organizations that fund cure development lies a fundamental disconnect between the desires of donors contributing for a cure and the resources being applied to the problem.

### **□ This report will focus on four central points:**

- Introducing the Alliance
- Presenting our major beliefs and findings
- Exploring the Type 1 research landscape
- JDCA’s relationship with donors and directing resources toward cure research

## **JDCA's Mission**

- **Our mission is to direct donor contributions to the research opportunities that provide the best chance of curing Type 1 diabetes by 2025**

The JDCA is solely focused on facilitating the development of a cure for Type 1 by 2025. We are forming a unique, paradigm-shifting coalition of donors who will work together to shift resources toward research opportunities that have the potential of meeting that goal.

**Ultimately creating the collective “voice of the donor for a cure” is of paramount importance to the JDCA.** It is our intent to develop a close relationship with donors through information sharing and donation advising. The JDCA will work diligently to become viewed as a Trusted Independent Advisor. By aligning donors who wish to contribute for a cure and advocating and creating a unified voice, resources will be shifted toward cure efforts and the chances of achieving the 2025 goal maximized.

## **Introduction and Summary**

**The JDCA is a new organization applying a business-like approach to assess progress toward the discovery of a cure for Type 1.** The Alliance was founded by and is staffed with parents of children with Type 1. Like most people involved with Type 1, the discovery of a cure is first and foremost in our minds. The JDCA is a self-funding 501 (c) (3) not-for-profit organization operating independently:

- The JDCA is not soliciting funds and will not be handling donor contributions
- The Alliance operates free from conflicts of interest
- We possess no prejudice regarding scientific approaches or research methodologies
- We are not beholden to any Type 1 charity or research organization

**We aim to become the recognized leader in providing objective and independent research on the Type 1 landscape and will conduct ongoing analysis of several major Type 1 research organizations.** Future reports will analyze the individual charities, progress toward a cure, and related Type 1 issues. Commentary will be framed within the context of achieving a cure by 2025. All information will be made available free of charge and can be accessed on the Alliance's website [www.thejdca.org](http://www.thejdca.org).

**Following extensive diligence on the Type 1 landscape, the Alliance discovered a variety of conflicts and inefficiencies within the charities and philanthropies that severely impact the urgency and effectiveness of cure development.** The JDCA concluded that none of the existing Type 1 charities allocate their funding in a manner that maximizes their chances for developing a cure by a date certain, if ever. Complicating this issue is the fact that none of the major Type 1 charities publicly state a definition of a cure.

**The JDCA believes the primary motivator of Type 1 donor support is the delivery of a cure.** However, charities operate within a framework that allows significant funding to be directed to non-cure initiatives. Funding is diverted to research that is too theoretical in nature or to non-research areas that are well-addressed by free market initiatives. Such strategies are misaligned with the intentions of most donors, in our view. Directing more donor support to cure research, and specifically to opportunities that have the potential to meet a 2025 timeline, is the goal of the JDCA.

**We believe that a cure that meets JDCA's definition will not be developed within the next ten years.** None of the drugs currently in U.S. clinical trials meet our definition of a practical cure. Considering that 10-15 years could potentially be required to commercialize a drug deemed to be a cure, setting a goal earlier than 2025 is ambitious.

**Establishing and building close relationships with donors is a high priority.** As the JDCA builds its capabilities, insight, and reputation, we will offer our advice to donors on how to specifically maximize their chances of directly contributing to a cure for Type1 by 2025. Assistance will also be provided to donors wishing to communicate with charities regarding their support for a cure.

## **Defining a Cure**

JDCA advocates the concept of a practical cure versus an “idealized cure.” A practical cure does not return the patient to a state as if they did not have diabetes. It seeks to deliver a result that most people and families would consider an acceptable cure-like lifestyle. This is important to distinguish because an “idealized cure” is extremely unlikely and rationalizes a substantial amount of funding as cure related when it would be practically judged idealized and exploratory by most donor’s standards.

Part of the problem in advancing cure research is that the largest charities and research institutions do not define a cure in their literature. Among the considerations involved in defining a practical cure are blood glucose monitoring, diet, side effects from the drugs or procedures administered as part of the cure itself, and mental well being.

### **□ Utilizing input from Type 1 diabetics and parents of children with Type 1, the JDCA is guided by the following definition of a practical cure:**

- For at least 1 year, a cure must:
  - Not require blood glucose monitoring beyond once a week
  - Not require carb counting
  - Not restrict a patient’s diet
  - Allow patients to sleep care free
  - Maintain A1c levels between 6-7
  
- A cure must be delivered through a treatment that:
  - If it is surgical, requires a full recovery time of less than 72 hours.
  
  - If it is pharmacological, requires no more than a reasonable pill and/or injection regimen
  
- A cure, which may include a drug regimen, must not have side effects, or pose longer term risks, greater than current complications of Type 1.

## **Beliefs and Findings**

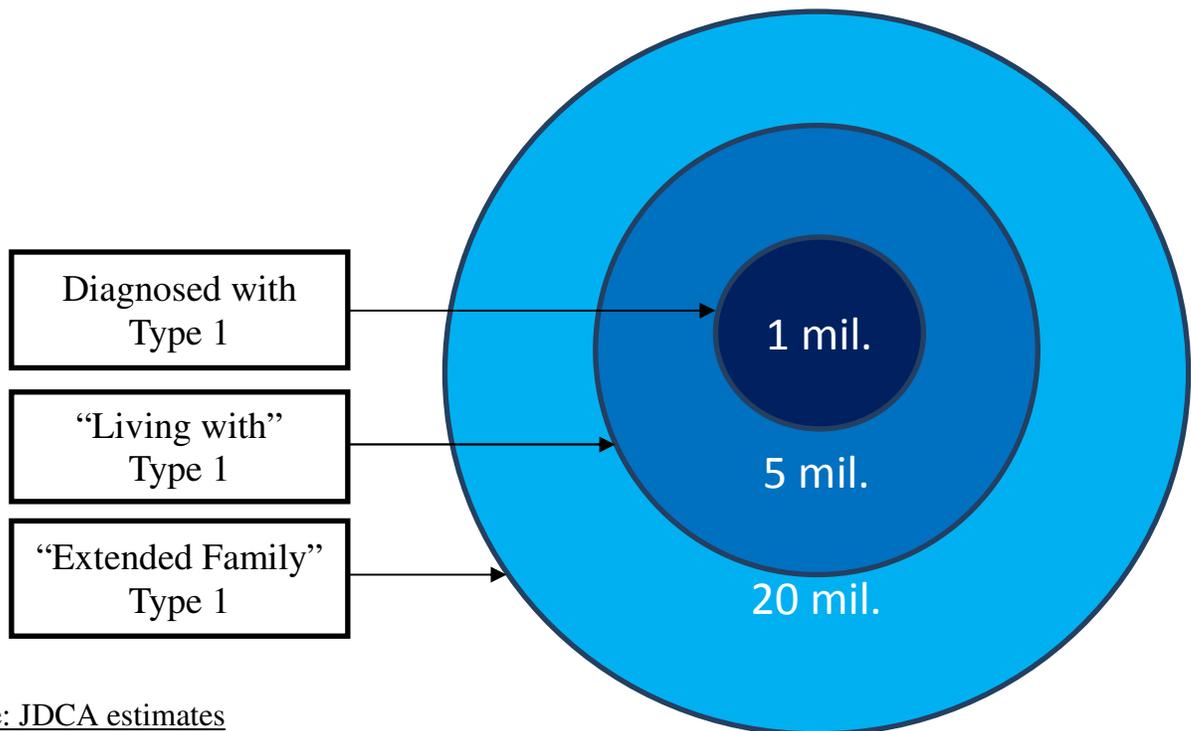
Great numbers of people are affected by Type 1, but accurate identification of the patient population is problematic due to insufficient data. As a result, estimates vary widely and we believe that some statistics provided by industry participants may be inflated and are somewhat self-serving. The following Type 1 population estimates should provide some parameters:

- JDCA estimates there are around 1 million people in the US with Type 1
- The Centers for Disease Control and Prevention (CDC) estimates there were around 26 million Type 1 and 2 diabetics in the U.S. in 2010 with Type 1 alone accounting for about 5% or 1.3 million
- CDC estimates that from 2002-5, 15,600 youth were newly diagnosed with Type 1 annually

Source: JDCA estimates and Centers for Disease Control and Prevention (CDC)

Broadening the scope of affected individuals to include immediate family members, the number increases to five million. Including grandparents and relatives close to a Type 1 diabetic, the number rises to twenty million.

### **Individuals in the U.S. Affected by Type 1**



Source: JDCA estimates

**□ We believe there is a sufficient universe of people to fund work capable of achieving a cure by 2025**

- Funding derived from 20 million supporters can result in a cure by 2025 if properly allocated
- Reorganizing research strategies and re-focusing energies specifically toward cure initiatives aligns those efforts with most donor’s intentions
- Care must be taken to avoid co-opting the Type 1 universe by Type 2 organizations not focused on our mission

**□ We do not believe that a cure that meets JDCA’s definition will be commercialized within the next ten years**

Through hope and optimistic characterizations, the current establishment has created a mindset that a cure is on the horizon. The JDCA’s independent analysis of the data indicates otherwise. In the U.S., the timeframe involved in discovering a new drug, conducting three different phases of human clinical trials, and obtaining final regulatory approval typically requires a range of seven to fifteen years with the upper half of that range most likely.

**Timeline for Type 1 Drug Development**

	Discovery	Phase I	Phase II	Phase III	Approval	Total
Years	1+	1-4	2-4	2-4	1-2	7-15

Source: JDCA estimates, with contributions from Joshua Levy

A realistic assessment of the earliest date for commercialization of a JDCA-defined cure suggests a minimum of ten years from today. Allowing time for advancement of existing early stage research projects or the development of potential new cure approaches implies a more achievable goal is 2025. Many industry observers, including Joshua Levy who independently monitors Type 1 cure progress, also believe that a cure satisfying JDCA’s definition is unlikely within the next decade. Please refer to Exhibit A for a chart tracking current U.S. clinical trials of Type 1 cure research.

**□ Examination of the projects listed in Exhibit A reveals that there are currently no drugs in U.S. clinical trials, with the results currently seen, that meet our definition of a practical cure**

- After 40 years and billions spent on Type 1 research the clinical trial pipeline is devoid of drugs that could be considered a practical cure
- This lack of tangible results validates the need to re-focus efforts on more targeted strategies, define what a cure is, establish a goal with a date certain, and properly fund those projects that have the potential to meet that goal

- The JDCA will support initiatives that have the prospect of developing into a cure by 2025

**□ Unless the goal of a cure with a date certain is set by donors, we will not have a focused response that is measurable**

None of the major philanthropic organizations publicly state a timeframe for developing a cure. The JDCA is resolute in its timetable of targeting the delivery of a cure by 2025 and will recommend directing contributions to organizations and projects that have both a commitment and the potential to meet that goal. Adoption of a date certain creates greater urgency and more acutely focuses resources on initiatives that can potentially meet that timeframe.

**□ We are scientifically agnostic**

- It is not our role to find a cure
- We are not scientists and will only subject the underlying science to “business level” strategy goal and performance level assessments
- Our role is to incentivize charities and research organizations to identify cure opportunities so that donor support can be directed to those initiatives

**□ The real source of Type 1 research funding is from people who are seeking a cure**

After completing considerable diligence on the Type 1 charity landscape, the JDCA concluded there is abundant passion for developing a cure. We believe people’s primary motivation for giving to charities is the delivery of a cure. This is evident by the overwhelming use of such messaging by charities in fundraising tactics, tools, and in their literature. The industry’s efforts, however, are clearly not aligned with that desire. Meaningful resources are diverted from cure projects into other areas such as education, prevention, and treatments. In fact, one major charity recently signaled its intention to divert funding away from existing cure efforts. It is the JDCA’s goal to direct more funding toward cure research.

**□ Funding and research for Type 1 should not align itself with the Type 2 disease and community**

These are totally different diseases. The idea that Type 1 initiatives benefit from Type 2 research because Type 2 is approximately twenty five times more prevalent is a myth. Making the connection between the two creates false hope and a false sense of progress. It provides justification for non-cure related pursuits and hinders progress toward a cure for Type 1. Research for Type 2 diabetes is well-funded from both government and private sources and should remain separate from Type 1 cure-related efforts. Some organizations publicly positioning themselves as both Type 1 and 2 through their messaging spend significantly more on Type 2 and allocate but a small percentage of their total budget to Type 1 cure research.

**□ If current and future donors, essentially the owners of these charities, exercised more of an ownership approach the cause would benefit**

People's innate gratitude and emotional predisposition to desire a cure sharply reduces or eliminates the need for accountability by charitable and philanthropic organizations. Donors are happy to contribute to the cause and are typically unwilling to ask the tough questions of charities that are normally accepted or required in commercial pursuits. As a result, charities are not as effective as they should or could be and are not held accountable to the same standards that exist in commercial enterprise.

**□ Fundraising is a core capability of many large charities**

- Many charities have developed sophisticated fundraising systems
- Events are professionally organized, perennially successful, and represent the largest source of financial support for some organizations
- Fundraising is a vital source of research funding and it is imperative this success be perpetuated
- Success in fundraising, however, has yet to be replicated in the process of allocating grants

**□ Charities do not have an objective measurement system with integrity to assess progress in finding a cure**

- Successful and systematized fundraising has not translated into similarly successful research progress measurement and tracking systems
- Charities have not developed a transparent and objective based system to measure cure progress
- JDCA's review of charities' annual reports and feedback from industry contacts reveals a clear need for more rigorous internal controls and reporting practices

**□ We believe the cure will come from overwhelming, urgent, and persistent support for a small select group of initiatives versus a modest level of support for a large number of unrelated projects**

- Major charities pursue far too many projects resulting in a dilution of efforts
- Charities generally employ a broad and shallow research strategy with some organizations funding several hundred research projects annually
- Effective business strategy results from setting clear goals and pursuing the opportunities most likely to achieve those goals, not from pursuing every opportunity which may eventually meet the target
- We believe that a narrow and deep strategy pursuing fewer, higher-conviction and better-funded research programs would more acutely focus resources on the most promising cure opportunities

## Major Funders of Type 1 Research

□ Most donor support of Type 1 research is channeled through larger charities/organizations

- Several major charities and foundations are key funders of Type 1 research
- The Juvenile Diabetes Research Foundation International (JDRF) is the largest with reported research grants of \$107 million in 2010
- Other major non-government Type 1 funding organizations are listed below

### Type 1 Funders of Research

<u>Organization</u>	<u>Focus Type</u>	<u>2010 (mm)</u>			
		<u>Total Expenses<sup>1</sup></u>	<u>Program Expenses<sup>2</sup></u>	<u>Research Grants<sup>3</sup></u>	<u>% Research<sup>4</sup></u>
Juvenile Diabetes Research Foundation:	1	\$ 191	\$ 157	\$ 107	56%
American Diabetes Association: *	1 + 2	204	149	34	16%
Joslin Diabetes Center: *	1 + 2	98	73	39	39%
Diabetes Research Institute Foundation:	1	13	10	9	69%
Helmsley Trust: **	1	127	N/A	30	24%
<b>Total:</b>		<b>\$ 633</b>	<b>\$ 389</b>	<b>\$ 218</b>	<b>34%</b>

\* Data for American Diabetes Association and Joslin are for the year ended 2009

\*\* Pursues other initiatives outside of Type 1 Diabetes

<sup>1</sup> Aggregate spending by charity

<sup>2</sup> Spending on the programs and services for which the charity exists

<sup>3</sup> Amounts expended exclusively for research projects (as reported)

<sup>4</sup> Research Grants as percent of Total Expenses

Source: Charity and Foundation Data

- **Total annual spending by these organizations is in excess of \$600 million**
- **The amount devoted exclusively to Type 1 research is a small percentage of the whole**
- **And allocations to Type 1 cure research are even less**

## **Coverage Universe**

**□ JDCA will conduct ongoing independent research on the following Type 1 charitable research foundations/organizations (“CRF”):**

- Juvenile Diabetes Research Foundation International (JDRF)
- American Diabetes Association (ADA)
- Joslin Diabetes Center (Joslin)
- Diabetes Research Institute Foundation (DRIF)
- The Leona M. and Harry B. Helmsley Charitable Trust (Helmsley)

## Donor Relations

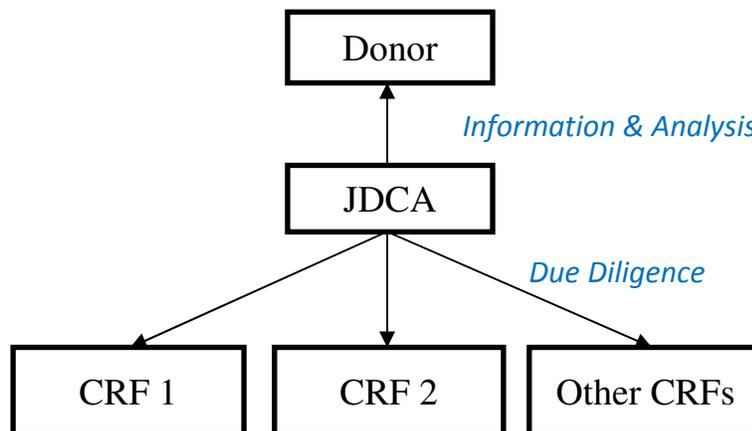
### □ Establishing and building a close working relationship with the donor community is vitally important

- JDCA will work hard to build its capabilities, insight, and reputation among the Type 1 donor community
- Donors can expect a steady flow of relevant and objective research
- Inquiries are welcome via our website [www.thejdca.org](http://www.thejdca.org) or e-mail: [info@thejdca.org](mailto:info@thejdca.org)
- As membership within the Alliance grows, the collective voice and influence of donors contributing for a cure will be leveraged

### □ JDCA information sharing through research and publishing:

- Due to the JDCA's independence and experience in research and analysis of commercial enterprises, we are uniquely positioned to comment on the Type 1 industry
- In-depth research reports on each of the CRFs will be published and will be followed by timely updates as news flow dictates
- Reports will also be published on topical cure-related issues and when material Type 1 information becomes public
- JDCA research and commentary will be provided to the public for free and available on our website at [www.thejdca.org](http://www.thejdca.org)

### JDCA Information Sharing and Analysis

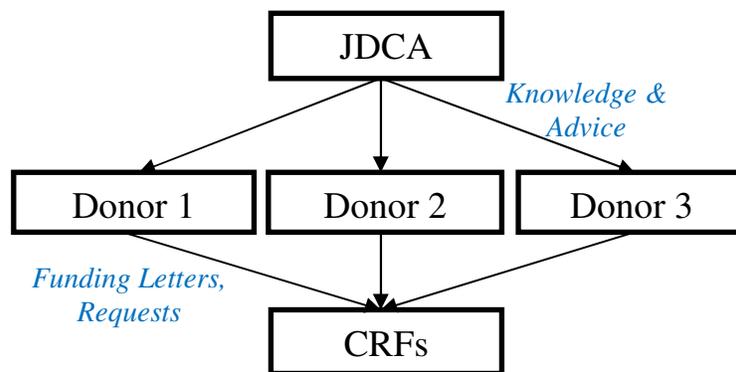


- **Donation Advising:** the Alliance will offer advice to both high net worth individuals and retail donors regarding contributions and provide assistance to those wishing to communicate with charities voicing their support for a cure

**Individual Donation Assistance:** The JDCA will advise individual donors on the stipulations they should require in exchange for ALL donations to maximize the donor’s effectiveness in directly leading to a cure by 2025. In addition, the JDCA will support individual donors as they request policy changes from Type 1 charities.

**Retail Donation Assistance:** The Alliance will provide average donors with letters and other materials to include with donations. This will allow donors to easily communicate their support for a cure by 2025.

### Donation Assistance



## **Conclusion**

We have presented an independent and objective analysis of the current Type 1 landscape and illustrated many inherent conflicts and inefficiencies therein. Donors may be surprised to learn how little of their contributions in many organizations is directed to Type 1 cure research and how much is directed to non-cure initiatives. Specifically, our findings conclude:

- Under the existing system, it's unclear when, if ever, a practical cure will be developed
- Funding allocations and priorities of the major charities could be better aligned with the intentions of donors contributing for a cure
- To re-align funding allocations with donor intentions, it is incumbent upon donors to assert their desire to fund work that can result in a cure
- A coalition of cure-seeking donors can present a unified voice to ensure their requests are heard and drive the effort toward a cure

The JDCA has developed a plan to build relationships, and is seeking to create a coalition of donors dedicated to the cure. We are operating with a sense of urgency and feel the time for donors to take action is now. If the system responds appropriately, funding for cure research will re-align with donors' intentions and disconnects within the system will self-correct. The result will be a more focused and productive research effort, and the chances of delivering a cure by 2025 significantly increased.

### **Analyst Certification**

The JDCA analyst responsible for the content of this report certifies that with respect to each organization covered in this report: 1) the views expressed accurately reflect his own personal views about the organizations; and 2) no part of his compensation was, is, or will be, directly or indirectly, related to the specific views expressed in this research report.

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# Exhibit A

## Overview of Clinical Trials Aimed At Curing Type-1 Diabetes Updated for May 2011

Clinical trials research studies done on people. They occur only after years of animal testing have established a basic level of safety and an expectation of success in people.

Because clinical trials take over 10 years to complete, this table offers a view into the future. Any possible cure for type-1 diabetes that will be available in the next ten year will need to be in clinical trials now.

Basic Approach to a Cure	Phase-I		
	Has Started	Fully Enrolled	Published Results
Stop the Autoimmune Attack		BCG by Faustman	BHT 3021 by Bayhill Therapeutics Etanercept by Amgen
Retrain the Immune System	Proleukin and Rapamycin Poly Tregs by Gitelman	Dendritic Cells by Trucco	IBC-VS01 by Orban
Encapsulated Transplanted Beta Cells	Monolayer Cellular Device at Hospital Saint Luc		Microcapsules
Combination Treatments: Stopping Immune Attack & Regrowing Beta Cells	ATG and GCSF	Diamyd, Sitagliptin, and Lansoprazole at the NIH	ATG etc. by Burt
Beta Cell Regeneration	GCSF		
Worked For Type 2s	Pioglitazone Sitagliptin & Lansoprazole Leptin	Abakirna	
Inflammation	Lisofylline by DiaKine AAT Rilonacept		
Basic Approach to a Cure	Phase-II		
	Has Started	Fully Enrolled	Published Results
Stop the Autoimmune Attack	NI-0401 by NovImmune Abtacept Alefacept		Abatacept by Orban Rituximab by Pescovitz
Retrain the Immune System	Thymoglobulin by Gitelman		Interferon by Brod
Encapsulated Transplanted Beta Cells	Diabecell by LCT		
Combination Treatments: Stopping Immune Attack & Regrowing Beta Cells			
Beta Cell Regeneration	Cord Ball by Haller	PROCHYMAL by Osiris	Exsulin by Exsulin
Worked For Type 2s		Atorvastatin by Willi Liraglutide by Madsbad	
Inflammation	Anakinra / Kineret at Steno	Canakinumab by Skyler Xoma 052 by Xoma	
Basic Approach to a Cure	Phase-III		
	Has Started	Fully Enrolled	Published Results
Stop the Autoimmune Attack		Diaprep 277 by Andromeda	
Retrain the Immune System			
Encapsulated Transplanted Beta Cells			
Combination Treatments: Stopping Immune Attack & Regrowing Beta Cells			
Beta Cell Regeneration			
Worked For Type 2s			
Inflammation			

Human research starts here → And moves through larger and longer trials → Until eventually it is found both safe and effective → And ready for marketing approval.

### Notes on this Table

This table was put together by Joshua Levy, who tracks all research which is in clinical trials and aimed at curing type-1 diabetes.

You can read his blog here:  
<http://cureresearch4type1diabetes.blogspot.com>

### Notes on Phases and Progress within Phases

**Phase-I**  
Generally between 4 and 20 people, and lasts 1 to 4 years. Often not blind, and sometimes there is no untreated, or "placebo", comparison group.

**Phase-II**  
Generally 50-150 people, and lasts 2-4 years. Usually double blind.

**Phase-III**  
Generally 300+ people, and lasts 2-4 years. Usually double blind.

The numbers and durations above are generally for type-1 diabetes. Different diseases have different requirements for the different phases of clinical trials. For example, phase-III trials for type-1 drugs are usually about 300 people. However, phase-III trials of drugs aimed at type-2 diabetes usually have more people enrolled.

**Has Started**  
This means that at least one patient has been accepted into the experiment protocol.  
(Some researchers mark this milestone when they start recruiting for the clinical trial.)

**Fully Enrolled**  
The clinical trial has enrolled all the patients that it needs to complete. This is an important milestone, because once this has happened, it is possible to know when all the data for the study will be gathered. The trial design will include how long data need to be gathered. For example, if the last person joins in Oct. 2008 and the protocol is to gather data for 15 months, then the study will be "data complete" in Jan. 2010.

**Published Results**  
Results for safety and effectiveness have been published, preferably in a peer reviewed journal.