The Voice of the Donor for a Cure

Juvenile Diabetes Cure Alliance

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An Update on Human Clinical Trials Progress

Conclusions:

- This report provides an overview of the Practical Cure research projects in human clinical trials.
- JDCA Fellow Joshua Levy contributed to the report. Joshua has been monitoring type 1 cure projects in pre-clinical and human clinical testing for the past ten years. He shares his findings on his highly regarded blog, *Current Research into a Cure for Type-1 Diabetes*.
- There are only seven Practical Cure projects in human clinical trials, out of a pool of 382 active human clinical trials related to type 1 diabetes.

Introduction

This report offers a comprehensive update on the human clinical trials that could provide a Practical Cure for type 1 diabetes. Due to the time outlay and high failure rate at each stage of testing from pre-clinical trials to market, research that has already entered human trials offers the best chance for a Practical Cure by 2025.

The seven human clinical trials on this year's list include five projects featured in last year's *State of the Cure* report, plus two new projects. Two additional projects are close to making the cut, but require additional development.

In compiling this list, the JDCA reviewed the U.S. National Institutes of Health's database of human clinical trials around the world (ClinicalTrials.gov), and consulted with numerous commercial enterprises and medical researchers.

The seven projects on our list represent less than 2% of the 382 type 1 diabetes projects in human clinical trials. It would significantly improve the chances of advancing a Practical Cure to market if the major diabetes non-profits and research centers directed more funding to Practical Cure initiatives, such that more than 2% of human trials focused on a Practical Cure.

Findings

The following pages review each candidate's progress and background, including the research pathway it is pursuing, as laid out in our last report on "Type 1 Diabetes Cure Platforms." We conclude with an overview of two close calls that did not make this year's list of Practical Cure projects in human testing but have strong potential to qualify in the future. (Turn to the last page to see the full chart)

When considering results from early phases of human testing, it is useful to keep a couple things in mind. The primary purpose of a Phase I trial is to establish the safety of a compound or procedure. Phase II trials establish safety as well as efficacy. Efficacy refers to how well the compound or procedure delivers beneficial results. For example, researchers might use measures like A1C readings or c-peptide levels. To this end, researchers often dose at lower levels in Phase I, so effectiveness results can look less robust than they would with increased dosages in Phase II, though higher dosing may also introduce a higher safety risk.

Living Cell Technology (LCT): Diabecell Encapsulated Beta Cells

Company Background: LCT was founded as Diatranz in 1987. After years of work, their technology, called Diabecell, progressed to Phase II human trials in the U.S. It was even approved for sale in Russia for a brief time. In 2011, LCT partnered with Otsuka Pharmaceutical Factory, Inc. to continue the development of Diabecell.

Research Pathway: Encapsulated Islet Cell Transplantation

Diabecell is an implanted device, sometimes called a "bio-artificial pancreas." Through a minor surgery, Diabecell replaces a person's beta cells with pig beta cells encapsulated in a special coating. The coating allows blood sugar in and insulin out, but does not allow the body's immune system to attack the implanted beta cells, thus eliminating the need for immune suppressing drugs.

Timeline: (extended timeline available on the web)

- Research started in the late 1980s.
- A Phase I trial began in 1996, but was canceled due to fears of xenotransplantation (i.e. transplantation of cells from another species) during the height of the mad cow disease scare.
- Phase I clinical trials restarted in mid-2007 in Russia, with data reported later in 2007 and 2009.
- Phase II studies started in 2009. No updates have been communicated regarding its progress.
- In in 2010, Diabecell was approved in Russia, but has never been sold there due to unknown issues with Russia's Ministry of Health.

Data: The most recent results are from August and November 2013:

- LCT reported on the results from their Phase I clinical study, an open-label (i.e. no placebo) trial on eight people. Four received a lower dose of Diabecell, and four received a higher dose. The results showed small improvements in the established type 1 diabetics, but nothing like cure level results:
  - A1C numbers dropped by 1.5-2% for patients who got the higher dose implant.
  - All but one patient used less insulin after the treatment, but it is not clear how much less.
  - Unaware hypoglycemic events and overall hypoglycemic events both dropped noticeably.
- LCT also reported that they were not going to attempt to start a Phase III trial based on these results, but would rework Diabecell to improve it, and test the improvements in a future Phase II trial.

Strengths:

1) Encapsulated beta cells could hypothetically cure any type 1 diabetic, no matter the duration of the disease.
2) The implant can be removed completely, if necessary, with minor surgery.
3) Since this treatment does not impact the immune system, it is unlikely to have any bad side effects, especially not in the way of a weakened immune system or heightened danger of future cancer or infections.

Challenges:

1) The technology does not appear to have worked yet. This research has been under active development by multiple groups and companies since the 1990s, and it is still not on the market.
2) LCT has done several clinical trials, while their nearest competitors have not completed one. However, they have not made obvious progress in the last several years.
3) Fears about beta cells from pig pancreases pose concerns, although pigs used for this purpose are developed on an isolated island near New Zealand and are not likely to get diseases that could transfer to humans.

Cliniques Universitaires Saint-Luc: Monolayer Cellular Device

Background: Investigators at the University Clinical Hospital St. Luke, in Brussels, are investigating the safety and efficacy of encapsulated human islets in a "Monolayer Cellular Device" for allogeneic (non-identical donor of the same species) islet transplantations in type 1 diabetic patients.

Research Pathway: Encapsulated Islet Cell Transplantation

Human islet cells are encapsulated in an alginate-based Monolayer Cellular Device (patch size of 1-3 cm) and will be transplanted subcutaneously. Investigators intend to use only one patch per patient, and do not anticipate re-transplantation.

Timeline:

- The Phase I trial, which began in 2008, was designed as a series of islet transplants for 15 adults with type 1.
- The last clinical trial record updates were posted in August 2011.
- The trial was projected to have completed Phase I testing in December 2013.

Data:
Preclinical trials in primates showed that pig islets encapsulated in the Monolayer Cellular Device controlled type 1 diabetes without immunosuppression for 6 months (which was the duration of the study). The Phase I trial may have concluded as of December 2013, but completion is not confirmed and results have not been published. The trial design was for 15 type 1 diabetics (ages 30-80), who are not producing any residual insulin (no c-peptides). The Device was tested in two phases. Phase 1A was administered in patients who are already on immunosuppressant drugs for a previous organ transplant (kidney, heart, liver, or unfunctioning pancreas). Phase 1B was administered in patients who are not on immunosuppressant drugs and are not eligible for a whole pancreas transplant.

Strengths:

1) Pre-clinical primate data showed 6 months of control without immunosuppression.
2) The procedure is minimally invasive.
3) Investigators are explicitly trying to develop a safe, simple, and functional procedure to control type 1 diabetes.

Challenges:

1) The Procedure would need to be repeated periodically, which could be onerous.
2) The lack of research updates since 2011 suggests progress may have stalled.
3) Lack of other scientific publications on the technology platform could imply a lack of support in the scientific community for this approach.

Tianhe: Stem Cell Educator

Background: Dr. Yong Zhao is a researcher at Hackensack University Medical Center and developer of the Stem Cell Educator, a device which he is testing as a cure for type 1 diabetes. Tianhe Stem Cell Biotechnologies, Inc. is a Chinese (PRC) company created by Dr. Zhao specifically to commercialize his Stem Cell Educator research.

Research Pathway: Training the Immune System

The Stem Cell Educator treatment removes immune cells from the patient, exposes the immune cells to umbilical cord stem cells, and puts the immune cells back in the patient. During exposure to the stem cells, the haywire immune cells seem to re-learn how to behave so that they cease the auto-immune attack on the pancreatic beta cells. Since the treated cells come from the patient's own body, this process theoretically eliminates the risk that the body would reject the modified cells as it would foreign cells.

Timeline: (extended timeline available on the web)

- Research started in the mid-2000s.
- NOD mice were cured in 2007.
- A Phase I Clinical trial started in 2010 and the first results were published in 2012.

Data:
Results from the first Phase I clinical trial of the Stem Cell Educator were published in January 2012. The study enrolled 15 participants who had had type 1 diabetes for an average of nine years: six had residual beta cell function ("Group A"), six had no residual beta cell function ("Group B"), and the remaining three functioned as a control group. In Groups A and B, C-peptide levels improved and remained steady at the 40-week follow up, indicating that their bodies were producing insulin. Twelve weeks after the study, Group A required 38% less daily insulin and saw a 1.06% reduction in their A1C levels, while Group B needed 25% less daily insulin and saw a 1.68% reduction in their A1C levels.

As of March 2014, there is one Phase II clinical trial being done on the Stem Cell Educator, which is expected to finish in September 2014. This trial is recruiting 100 people spread across several locations in China and Spain.

Strengths:

1) The Stem Cell Educator shows a strong, lasting effect in type 1 diabetics with no residual insulin production.
2) As opposed to most transplant procedures, the risk of an adverse immune response is reduced since cells are from the patient's own body.
3) In this benign procedure, patients are connected to the educator machine for several hours.

Challenges:

1) The treatment did not actually cure anyone in the Phase I trial.
2) There are potential recruitment issues since the treatment method is somewhat complicated and/or not intuitive, so it is harder to explain why someone should enroll in the trial.
3) So far, the only published human results have been from a trial in China. Many researchers (especially American researchers) may be reluctant to accept results from China.

Sanford Research: Sitagliptin/Lansoprazole

Background: Sanford Research in conjunction with the University of South Dakota is currently conducting a Phase II trial testing the combination therapy of oral sitagliptin and lansoprazole vs. placebo for preservation of pancreatic beta cells in patients with recent-onset type 1 diabetes. Dr. Alex Rabinovitch heads the project, which is also known as REPAIR-T1D.

Research Pathway: Blocking the Autoimmune Attack

Sitagliptin is commonly used to improve glycemic control in adults with type 2 diabetes by raising levels of glucagon-like peptide-1 (GLP-1). However, researchers have found that in mice with type 1 diabetes, sitagliptin both stimulates the remaining beta cells to secrete insulin, and generates new beta cells, in conjunction with lansoprazole. Lansoprazole raises levels of the hormone gastrin, which can cause pancreatic exocrine duct cells to transform into insulin producing beta cells. It appears that gastrin (raised by lansoprazole) works together with GLP-1 (raised by sitagliptin) to stop the autoimmune attack on the newly generated beta cells.

Timeline:

- Initial publications in 2011 suggested that sitagliptin could have a positive benefit in type 1 patients, after having previously been studied primarily in type 2 patients.
- Recent data was published in 2013 on a 141-subject trial that took place over 20 weeks.
- Sanford Research is currently running a Phase II trial which is being conducted at three sites in the U.S. (California, Minnesota, and South Dakota).

Data:
The Phase II trial will administer 50 mg of sitagliptin plus either a placebo or 30 mg of lansoprazole. The trial will enroll 54 people; 36 will receive the lansoprazole and 18 will receive placebo. Data reports are expected after 12 months of dosing. Collection of primary outcome measures is expected in May 2014, and results could be reported as early as September 2014.

Strengths:

1) The medicines are relatively inexpensive, readily available, and easily administered.
2) Investigators at Sanford are well funded with resources to pursue further development if Phase II is successful.
3) The compounds have a validated safety history.

Challenges:

1) The therapy is only being tested for newly diagnosed patients (diagnosis within 6 months).
2) Recent trials of a similar drug combination of sitagliptin and pantaprazole (aimed at stopping beta cell death and promoting the growth of new beta cells in conjunction with islet transplant) have not had long lasting results.
3) A paper published in 2013 found that sitagliptin use in type 1 diabetes did not change glucagon AUC, A1C, insulin dose, or weight despite post-meal rise in GLP-1 levels. The researchers also found that C-peptide positive subjects treated with sitagliptin had a slight trend in decreasing hyperglycemia, but it was not statistically significant. This study follows work by the same authors in 2011 that had found some initial benefits from sitagliptin.

Faustman Lab: BCG Vaccine

Background: BCG (Bacillus Calmette–Guérin) is a biologic (biological preparation) made from weakened live bovine tuberculosis bacteria which has been given to over a billion people in low doses as a tuberculosis vaccine, and is also approved in much higher doses as a bladder cancer treatment. It is a generic drug with a very long record of safety. Dr. Denise Faustman, a professor at Harvard University and researcher at Massachusetts General Hospital, is currently studying BCG as a potential cure for type 1 diabetes.

Research Pathway: Blocking the Autoimmune Attack

BCG may cure type 1 diabetes because it causes the body to generate TNF (Tumor Necrosis Factor). TNF in turn, selectively kills the auto-reactive, or "bad" killer T-cells (i.e. the immune cells that are attacking the body's own pancreas), while also not harming the "good" killer T-cells, those that are properly attacking foreign invaders. The hypothesis is that once the autoimmune attack stops, the body naturally regrows beta cells and the patient is cured. BCG is produced by many different companies all over the world. It is widely available and inexpensive.

Timeline: (extended timeline available on the web)

- The ideas that BCG might cure type 1 diabetes was developed in the late 1990s.
- Successful results from studies in mice were published in 2002 and 2003.
- Human tissue results were published in 2007.
- Results of Phase I clinical trials were published in 2013.
- As of March 4, 2014, Faustman Lab has filed paperwork for a Phase II trial of 120 patients with an expected completion date of May 2019

Data:
For the Phase I trial (3 patients), the experiment measured seven results. Of these, four were either not reported or showed no statistically significant change. The remaining results showed BCG to be safe, however the number of live "bad" killer T-cells was the same as the "good" ones (which could be interpreted multiple ways), and the C-peptide improvements were very small and were dependent on the exact comparison used. Dr. Faustman is now raising funds for the placebo-controlled Phase II trial of 120 people. She currently has $18 million of the total $25 million budget, which is enough to move forward. The ClinicalTrials.gov website estimates that the study will start in May 2014, with data collection in May 2019 for primary outcome measurements (improvement in A1C levels at 1, 2, 3, 4, and 5 years after BCG injection), and follow up in May 2022.

Strengths:

1) Dosing is as simple as getting a vaccine, an under the skin injection.
2) BCG is extremely safe; more people have taken BCG worldwide than have taken Tylenol or Aspirin.
3) The vaccine is inexpensive and widely available.

Challenges:

1) The results from the Phase I clinical trial of BCG are controversial. Some people believe they are an outright failure, while others believe they are a clear success and worthy of continued testing in Phase II. Comparing results to those of other researchers (including LCT) implies that the treatment was 100-400 times less impactful in terms of improvements in C-peptide generation. Others have also done studies with 4 times as many people, and over longer time periods.
2) There has been limited visible progress since publication of the first positive results in mice over ten years ago.
3) Significant funding to date ($10 million for Phase I) implies a higher per patient number (>$3 million) than other trials.

DiaVacs: DV-01

Background: DiaVacs is a private, Pennsylvania-based company focused on curing autoimmune diseases. In January 2014, the FDA granted DiaVacs' type 1 therapy (DV-0100) "orphan drug designation," which allows it to progress through the clinical trial process more quickly than normal.

Research Pathway: Training the Immune System

The platform is focused on inducing immune tolerance in children who have autoimmune diseases. The company will seek to reprogram dendritic cells to induce tolerance. They have optimized the protocol to take a patient's own dendritic cells from their blood, modify the cells, and vaccinate the patient. These modified cells are absorbed, trafficked to the pancreatic lymph nodes, and induce tolerance.

Timeline:

- The company formed in 2010 from research conducted at the University of Pittsburgh.
- A 10-patient Phase I clinical trial was completed in 2012.
- They are currently enrolling for an 80-patient Phase II trial.
- The FDA granted orphan drug designation in January 2014.

Data:
Prior data has shown the therapy to be safe and effective in those who have had type 1 diabetes for a significant time period as well as in the newly diagnosed. The prior Phase I trial showed that 4 of the 10 patients who had a beta cell mass of 0 produced some amount of c-peptides. The current Phase II clinical trial will dose 80 patients in two installments, beginning with 10 patients in 2014. The company will present six months of outcome data in January 2015. After this first group of 10 patients, the company intends to raise money to proceed with the next 70 patients.

Strengths:

1) The FDA's orphan drug designation provides a fast track to market.
2) They have the ability to tap capital markets to finish the Phase II study.
3) The management team is well regarded.

Challenges:

1) The company does not have sufficient funds to finish off the full 80-patient Phase II trial and will have to raise more money after the first 10 patients.
2) The Phase I trial's small data set poses unknowns for Phase II results.
3) The potential applicability across all diabetics (both honeymooners and established) is unclear after earlier tests showed a 40% success rate in longstanding diabetics.

Beta-O_2: BO_2

Background: Beta-O_2 Technologies is a private, Israel-based biomedical company developing a proprietary implantable bio-artificial pancreas called the BO_2. It was founded by two endocrinologists, Pnina Vardi and Constantine Birch, in collaboration with entrepreneur Yossi Gross.

Research Platform: Encapsulated Islet Cell Transplantation

The BO_2 is a device, implanted subcutaneously, that contains islets of Langerhans protected from the immune system by membranes covering the device. The islets can sense blood glucose and respond by secreting insulin and glucagon. The islets are embedded in alginate material housed in the space at the core of the device, which receives a continuous supply of oxygen to prevent cell death. Here is how the oxygenation process works. As part of the device, two ports are implanted just under the patient's skin. Tubing (also implanted within the patient's body) runs from the ports to the device. The patient uses a syringe to inject oxygen into a port every day. The oxygen travels down the tubing and passes through a gas chamber on the outside of the device into the core

Timeline:

- In 2007, an early model of the device was in animal testing with the hope of reaching market by 2011.
- Pre-clinical trials of the current model were completed in rats in 2012.
- In November 2013, Beta-O2 published results from a proof of concept case study in a single human.
- A Phase I clinical trial enrolling eight people began in February 2014 in Uppsala Hospital in Sweden and is expected to conclude in March 2016.

Data:
There has been encouraging data from animal testing and a single human case study. In pre-clinical trials, diabetic rats showed the ability to adjust blood glucose levels to normal levels after implantation with the device. A publication from August 2013 demonstrates the device's successful transplantation of islet cells from rats into diabetic mini-pigs without immunosuppressive therapy. In a case study, a human being (n=1) was implanted with islet cells (at 20% of the dose needed to cure someone) contained in the device and supplemented with the oxygen infuser. Researchers found that the test subject's c-peptide levels (an indicator of insulin production) remained consistent at 3, 6, and 9 months after implantation. The steady c-peptide levels indicate that the encapsulated islet cells continued to produce a consistent amount of insulin for the duration of the follow up, which is promising because in other encapsulation efforts, transplanted cells have deteriorated over time.

Strengths:

1) The case study showed positive results that were sustained for the duration of the follow-up period.
2) The implantation is convenient, minimally invasive, and safe.
3) Several venture capital funds are supporting the technology, as are government funding agencies in Israel, suggesting that the company would have funding for future development if trials are successful.

Challenges:

1) There is a lack of clear human data (n=1), which makes it unclear what efficacy and safety would look like at the right dosage and with more people.
2) The oxygen supply has to be replenished every day with a subcutaneous injection. It is unclear how quickly the encapsulated cells would die if the patient missed an oxygen dose.
3) The device is relatively large, at approximately 2 ¾ x 4 ⅓ inches.

Close Calls

There are two projects which almost made the list of Practical Cure work in human clinical trials. The first is VC-01, which consists of encapsulated islet cells. Although the technology and goals meet Practical Cure standards, the project has not yet registered for human clinical trials. If it registers for human trials later this year, as planned, it will likely become the eighth project on our list. The other close call is the dual chamber bionic pancreas, which has already gone through numerous human clinical trials. However, the bionic pancreas currently consists of four separate machines, three worn and one carried. If these distinct parts were streamlined into a single device, this project would likely constitute a Practical Cure as well.

Viacyte: VC-01

Background: Viacyte, based in California, is a private, venture-capital company founded as Novocell in 1999, and changed to Viacyte in 2010. Its regenerative medicine platform is focused on the goal of a "replacement endocrine pancreas."

Research Platform: Encapsulated Islet Cell Transplantation

The company has developed pioneering technology that uses a stem cell line to create pancreatic endoderm cells, which have been shown to mature into islet cells upon transplantation. These cells will be contained in a delivery system and encapsulation device called Encaptra. The Encaptra system's semipermeable barrier allows glucose, oxygen, and nutrients to reach the islet cells, but keeps the attacking immune cells out. The combined encapsulation system would be implanted subcutaneously, and the encapsulated islet cells would release insulin, glucagon, and other hormones into the body.

Timeline:

- A 2005 publication demonstrated the process by which Viacyte researchers directed human embryonic stem (hES) cells to differentiate to form human definitive endoderm (which gives rise to the pancreas).
- In 2008 they published results from a study in which pancreatic endoderm derived from hES cells was transplanted into mice, and generated glucose-responsive, insulin-producing cells *in vivo*.
- A paper published in 2011 established their process for isolating functional pancreatic progenitor cells from hES cells from a specific cell line. The progenitor cells protected against hyperglycemia in mice.
- A phase 1 study begun in 2005 stopped enrolling in 2006, and was officially terminated in January 2014.
- They plan to file an application with the FDA in 2014 to support initiation of a clinical trial for VC-01.

Data:
Previous pre-clinical data in mice showed treatment to be effective up to a year after dosing, with sufficient blood glucose control while on the product. Viacyte reports that is is currently preparing to initiate its Phase I/II trial later in 2014. The details of the trial have not yet been registered on ClinicalTrials.gov.

Strengths:

1) Viacyte has significant funding from numerous sources, including the California Institute for Regenerative Medicine, JDRF, and venture capital.
2) The management team is well regarded.
3) There is enthusiasm in the scientific community for the technology platform.

Challenges:

1) The cell therapy approach in general is largely unproven.
2) The capital intensive nature of funding may require further raises if results are successful.
3) There is a potential legislative risk in working with embryonic stem cells.

Boston University/Massachusetts General Hospital: Bionic Pancreas

Background: A group of engineers and doctors from Boston University and Massachusetts General Hospital is developing a closed loop bionic pancreas that is unique because it administers both insulin (to lower blood sugar) and glucagon (to raise blood sugar). Dr. Edward Damiano, associate professor of biomedical engineering at BU, heads the group in collaboration with Dr. Steven Russell, assistant professor of medicine at Harvard Medical School and endocrinologist at Mass General. In 2004 Dr. Damiano began working on the bionic pancreas. Dr. Russell joined the project in 2006. The goal is to get the product to market by the time Damiano's son, who was diagnosed with type 1 shortly before his first birthday, heads to college in 2017.

Technology: Device to Replicate the Pancreas

The patient wears a pump for insulin, a pump for glucagon, and a continuous glucose monitor. A smart phone app receives readings from the CGM every five minutes. Based on the patient's weight and CGM reading, the app uses an algorithm developed by Firas El-Khatib, a senior research scientist at BU, to activate the release of glucagon or insulin in the quantity appropriate to respond to changes in blood glucose levels.

Timeline:

- In 2005, Damiano and El-Khatib began testing in pigs.
- In 2009, the group completed a Phase I study in 11 adults testing an early version of the bionic pancreas that used a laptop computer over 24-hours.
- In 2011, they completed a 6-person study using a portable version of the bionic pancreas for 2 days.
- In 2013, they completed a 30-person study using a portable version of the bionic pancreas for 5 days, with patients eating, sleeping, and exercising outside the hospital.
- In 2013, they conducted a study in 32 children using the bionic pancreas at summer camp. A follow up summer camp study is planned for 24 children, ages 6-12, in 2014.
- In 2014 they are set to conduct a study in approximately 48 healthcare professionals with type 1, who will wear the device for almost two weeks at the hospital and at home.

Data:
Data from the six-person study, published in 2012, showed that despite high-carbohydrate meals and exercise, the bionic pancreas maintained blood glucose levels at an overall mean of 158 mg/dL. Mean nighttime blood glucose level was 123 mg/dL. There was only one instance of low blood sugar during the study. Data from the 30-person study appears to be more promising, but it has only been presented, not published.

Strengths:

1) The algorithm effectively responds to real-life scenarios like exercise and carbohydrate-heavy meals.
2) The system reliably avoids hypoglycemia.
3) Anecdotal evidence from participants in the studies has been overwhelmingly enthusiastic.

Challenges:

1) In its current formulation, glucagon is not stable, so the bionic pancreas' supply needs to be changed daily.
2) Wearing and carrying multiple machines is cumbersome and introduces increased potential for mechanical malfunction.
3) There is some delay in the uptake of insulin, which can vary based on the patient's body.

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

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Practical Cure Research Projects in Human Clinical Trials

Project Name	Location	Description	Research Pathway
LCT/DIABECELL	LCT living cell technologies	Transplanted porcine islets that are micro-capsulated	Encapsulated Islet Cell Transplantation
Monolayer Cellular Device	Cliniques universitaires Saint-Luc	A beta cell incapsulation approach that uses human islets	Encapsulated Islet Cell Transplantation
Tianhe: Stem Cell Educator Therapy	TIANHE STEM CELL BIOTECHNOLOGIES	An individual's blood is treated with stem cells which has the effect of reversing autoimmunity and stimulating beta cell growth	Training the Immune System
Sitagliptin/ Lansoprazole	SANFORD RESEARCH	Drug combination aimed at both stopping the auto immune attack and stimulating growth of beta cells	Blocking the Autoimmune Attack
Faustman: BCG Vaccine	faustmanlab.org	Drug that kills disease-causing autoimmune cells and restores pancreatic beta-cell function through regeneration	Blocking the Autoimmune Attack
DV-01	DiaVacs	Take out, retrain, and re-inject dendritic cells to stop autoimmune attack	Training the Immune System
Bo2	BETA-O2 TECHNOLOGIES LTD	Implanted bio-artificial pancreas with an oxygen infuser.	Encapsulated Islet Cell Transplantation

Sources:

1. Current Research into a Cure for Type 1 Diabetes Blog http://cureresearch4type1diabetes.blogspot.com/
2. Conversations with management
3. Public Documents
4. www.clinicaltrials.gov
5. NIH PubMed