ANNUAL REPORT

Prepared by:

CITR Coordinating Center
The EMMES Corporation
Rockville, MD

Sponsored by:
National Institute of Diabetes & Digestive & Kidney Diseases
National Institutes of Health
Bethesda, MD

July 1, 2006

NOTICE:

The CITR Annual Report details data received as of April 3, 2006 for all islet transplant recipients registered by December 31, 2005.

COLLABORATIVE ISLET TRANSPLANT REGISTRY
COORDINATING CENTER

July 1, 2006

M E M O R A N D U M

TO: CITR Islet Transplant Centers, Diabetes Research Community, and Interested Public

FROM: Mike Appel, PhD
Director, Islet Biology and Transplantation Research Program
NIDDK

Bernhard Hering, MD
CITR Medical Director, SAC Chair

SUBJECT: 2006 CITR Annual Report

The mission of the Collaborative Islet Transplant Registry (CITR) is to expedite progress and promote safety in islet/beta cell transplantation through the collection, analysis, and communication of comprehensive and current data on all islet/beta cell transplants performed in North America. This report is the compilation of numerous hours of scientific research, patient care and collection of information from islet transplant programs in North America. This third report builds upon the successes of the first and second reports and is a significant step towards furthering project goals. The report has been prepared by staff of The EMMES Corporation under the leadership of CITR Publications and Presentations Committee Chair, Dr. Rodolfo Alejandro, and CITR Coordinating Center Principal Investigator, Ms. Nicole Close, with support from a NIDDK contract.

Clearly, the success of this effort depends on the continued interest and efforts of the collaborating islet transplant programs and islet production facilities. We are pleased to present information on the combined efforts of 23 islet transplant programs. We thank them for their efforts and look forward to their continued participation along with all centers in the islet transplant community of North America.

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Scientific Summary

Background. Islets are clusters of insulin-producing cells located in the pancreas. In patients with Type 1 diabetes mellitus (T1DM) all islets are destroyed by an autoimmune attack and patients need to inject insulin every day to stay alive. The total prevalence of diagnosed T1DM in the United States (US) (all ages, 2004) is approximately 650,000-1,300,000 people. Exogenous insulin replacement therapy has been the only method of treatment for this disease. For patients with T1DM and poor kidney function, a whole pancreas transplant is sometimes performed. An alternative procedure uses insulin-producing cells (islets) extracted from a donor pancreas. These are implanted typically via the portal vein in the liver, so that the islets produce insulin as needed by the recipient.

Islet transplantation is an experimental procedure in the US that is regulated by the Food and Drug Administration (FDA). Approximately, 40 transplant programs in the US are conducting this procedure, or are in the process of starting a program. Typical patients eligible for this procedure include those who have T1DM for more than five years, are between 18 and 65 years of age, and have poor diabetes control despite intensive efforts being made in close collaboration with a qualified diabetes care team. Poor diabetes control can manifest as frequent episodes of critically low blood sugar levels (hypoglycemic episodes and insulin reactions) requiring the assistance of another person, wide swings of blood sugar levels (blood glucose lability), or consistently high HbA_{1C} levels ($>$ 8%).

Most ongoing studies differ minimally in the entry criteria for patients and in the types of immunosuppression therapy used to prevent rejection of the islet cells in the body. It is the goal of these studies to help determine if improvement in the glycemic control and/or reversal of insulin dependency can be achieved, to assess the long-term function of successful islet transplants and risks of associated immunosuppressive medication, and if the natural history of diabetes complications is altered. Each center publishes the results of their studies and provides information regarding their open and recruiting protocols through their own public website and through the National Library of Medicine's developed website www.clinicaltrials.gov.

To accumulate and compile the data from all completed and ongoing studies between 1999 and present, the National Institute of Diabetes & Digestive & Kidney Diseases funded the Collaborative Islet Transplant Registry (CITR). The mission of CITR is to expedite progress and promote safety in islet/beta cell transplantation through the collection, analysis, and communication of comprehensive and current data on all islet/beta cell transplants performed in North America. Each year the Registry provides a complete analysis of the cumulative data to date since 1999. The third report, published in 2006, summarizes information on patients who received one or more islet cell transplants between 1999 and 2005. All CITR reports are public and can be downloaded or requested in hard copy at www.citregistry.org.

Data contained in this summary must be interpreted cautiously. Even with the efforts of the 23 participating centers, the total number of reports is still small. As with any registry, a number of potential biases may exist, including selective reporting and differences in clinical care and decision-making. Islet transplant recipient data for this summary reflect cumulative data entered by the islet transplant centers on participants from January 1, 1999 through December 31, 2005. These data were reviewed by the CITR Coordinating Center for quality assurance, errors and data outliers. Data queries were identified and the database was updated by the islet transplant centers and closed for analysis on April 3, 2006 for the recipients that had been registered for CITR as the December 31, 2005 participant registration closure date.

Status of Islet Allograft Transplantation in North America. CITR collects basic information from all islet transplant centers in North America. Forty-two islet transplant programs were sent a questionnaire asking for information. All 42 programs responded and 31 of the 42 programs had been active during 1999-2005, performing at least one islet allograft transplant. The remaining programs (N=11) had not transplanted yet, or were in the process of starting their islet allograft transplant program. The table below displays the data collected from the 31 active islet transplant programs in North America for 1999-2005. To the knowledge of the Registry, this table is inclusive of all islet transplant programs in North America.

Exhibit A
Summary of North American Islet Allograft Transplantation Activity

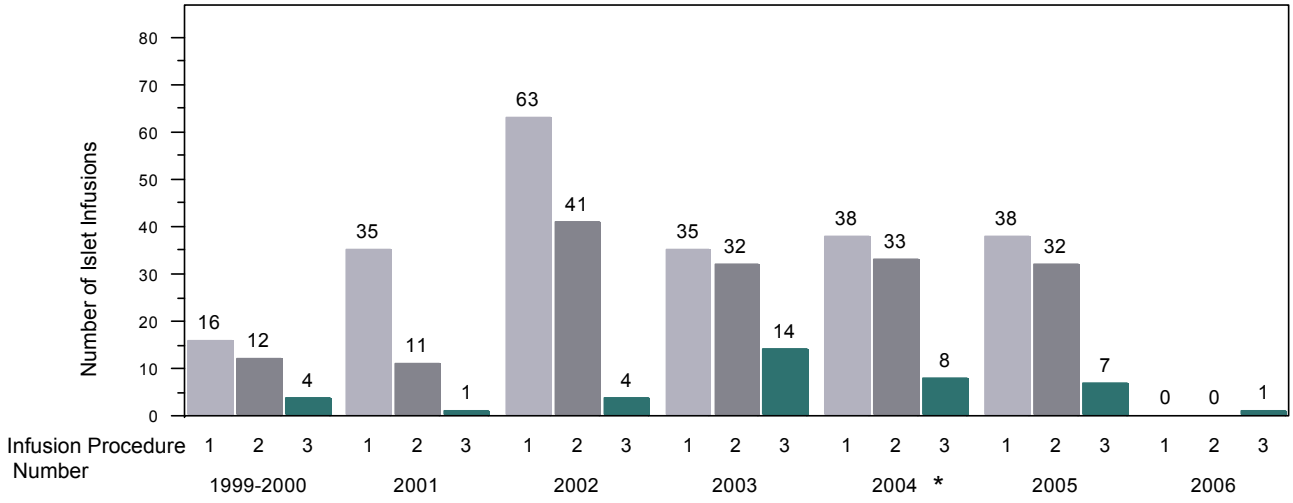
All Islet Transplant Programs in North America	Number of Human Islet Infusion Procedures Conducted	Number of Patients Receiving Their First Infusion
Total	593	319
1999	18	10
2000	32	21
2001	65	45
2002	142	82
2003	106	45
2004	110	53
2005	120	63

Registry Data Collection. The focus of the Registry is the collection and analysis of islet allograft transplants. From 1999-2005, 31 islet transplant programs have conducted 593 islet infusion procedures in 319 recipients (Exhibit A). CITR has information from 23 islet transplant programs on 225 of the 319 allograft recipients (71%) and 425 of the 593 infusion procedures (72%). Sixty-four of the recipients (28.4%) received just one islet infusion, 122 (54.2%) received two, 38 (16.9%) received three, and one (0.4%), received a total of four islet infusions. On average, recipients received a total of 814,378 (SD 368,620) total islet equivalents (IEQs), or 12,486 IEQs/kilogram body weight (SD 5,731).

Of the 225 recipients, 203 (89%) were recipients without a previous kidney transplant who received an islet infusion(s) (islet alone recipients), while 22 recipients (10%) had previously received a kindy transplant and received an islet infusion(s) after a kidney transplant. There were two recipients (1%) of an islet autograft for pancreatitis voluntarily reported to the Registry, even though the number of autografts performed in the US is much higher (>300 recipients ever receiving an islet autograft transplant).

Exhibit B summarizes the total number of islet allograft infusion procedures conducted and entered in the CITR database by year and by infusion procedure number. For example, in 2001, 35 participants received their first islet infusion, 11 received their second islet infusion, and one person received their third islet infusion.

Exhibit B
Total Number of Islet Allograft Infusion Procedures Conducted and Entered in the CITR Database by Year and by Infusion Procedure Number



*One person received a fourth infusion in 2004.

Participant Characteristics. The median age of the islet transplant participant is 42.3 years (range 23.0 to 65.1) and the median duration of diabetes is 29 years (range 4 to 51). The median weight of the participant is 65 kg (range 35.0 to 98.1) and the median body mass index (BMI) is 23.3 kg/m^2 (range 15.5 to 31.6). Over 68% of the participants are female and the participants have limited racial and ethnic diversity.

Approximately, 38% of the islet transplant participants were on an insulin pump prior to their first infusion and 92.6% of the participants were on the pump or were taking three or more insulin injections per day. At baseline, over 89% of the participants have a basal C-peptide < 0.5 ng/mL (C-peptide results at the time closest to transplant were used for this analysis and do not necessarily represent the typical value for the participant) and over 78% have an HbA_{1C} > 6.5%. The mean daily insulin requirement of participants prior to their first infusion procedure was 37.7 units (SD 14.0) and the subset on intensive insulin therapy had received intensive therapy for a mean of 18.3 years (SD 12.6). The mean fasting blood glucose for all participants was 169.7 mg/dL (SD 88.0), mean HbA_{1C} was 7.7% (SD 1.3), and their mean basal C-peptide was 0.1 ng/mL (SD 0.3).

Participant baseline characteristics prior to first infusion by the total number of infusions received were evaluated. On comparison, participants who had received a total of three infusions were younger, their duration of diabetes was shorter, they had a higher BMI, required a higher baseline daily insulin requirement, had a much higher fasting blood glucose and HbA_{1C} and had a lower PRA percentage than those participants who had one or two infusion procedures.

Donor Information. The median age of the deceased donor was 44 years (range 8 to 74) and the median body mass index was 28.2 kg/m^2 (range 13.3 to 59.8). The median time from cross clamp to pancreas recovery was 33 minutes (range 0 to 127) while the median cold ischemia time was 7.0 hours (range 1.1 to 27.0). Approximately 58% of the donors were male, 9% were Hispanic and 90% were white. Fifty-four percent of the donors had a cerebrovascular/stroke as cause of death while 31% experienced a head trauma. Approximately 31% of the donors had a history of hypertension and 17% had a history of alcohol dependency.

Thirty-six percent of the donors received a transfusion prior to organ procurement, while only 6% received a transfusion during the organ procurement surgery. Sixty-six percent of the donors received steroids and 39% of the donors had received insulin. Over 96% of the donors received at least one vasopressor during the donor's terminal hospitalization. There was a report of one donor testing positive for Anti HBC and this donor was used for a hepatitis B immunized recipient. The median serum creatinine of the donors is 1.0 mg/dL, total bilirubin 0.7 mg/dL, AST 37.0 IU/L, ALT 30.0 IU/L, serum lipase 27.5 IU/L and serum amylase 72.0 IU/L.

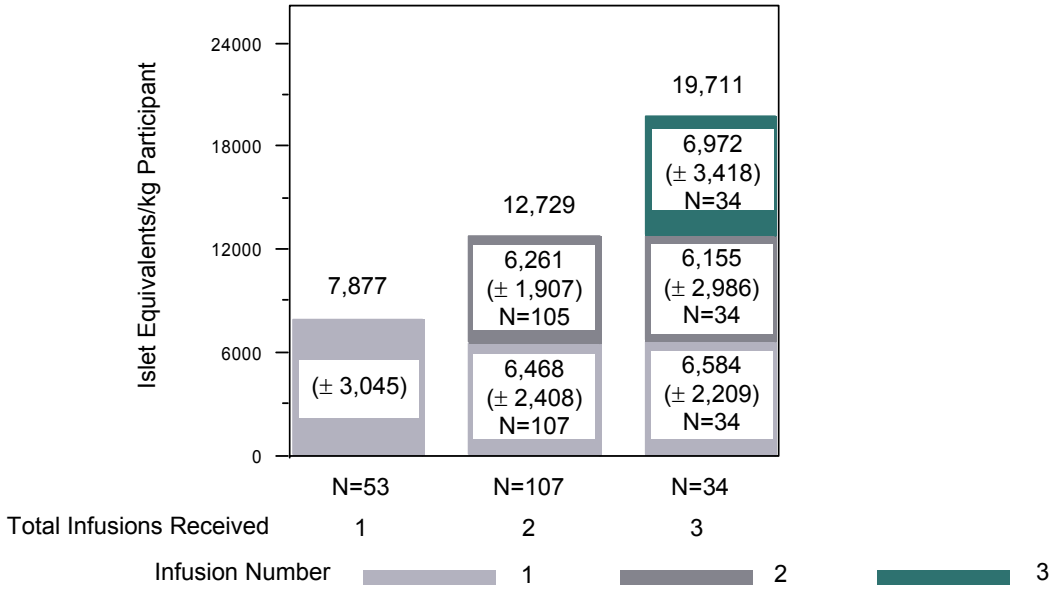
Pancreas Procurement. In over 62% of the pancreas procurement procedures, the pancreas procurement team was not related/affiliated with the processing/transplant team, while 88.5% of the processing procedures took place at the same institution as the islet transplant center. The median duration of cold ischemia was 7 hours (range 1.1 to 27.0). UW, Two Layer (UW and PFC, N=164; HTK and PFC, N=3), and UW followed by Two Layer were the most common methods used for pancreas preservation. Other preservation solutions used in conjunction or in absence of UW and/or PFC included HTK, Eurocollins, P Phase 2, and Lactated Ringer's solutions.

Liberase HI was the collagenase type used during most islet processing (95%) followed by Thermolysin plus Collagenase P (2%), and custom Liberase Blend (1%). All of the pancreata processed used a density gradient for islet purification. Almost 60% of the islet preparations were placed in culture for some period of time. The Registry defines "culture" as any specially prepared nutrient medium. The median culture time was 28 hours (range 1.5 to 84.0). Of the 418 preparations reported to CITR, six final preparations showed a positive aerobic culture (1.5%), four showed a positive anaerobic culture (1.4%) and three showed a positive fungal culture (0.8%).

Total islet equivalents in the final product were plotted versus cold ischemic time, donor body mass index, and donor age. Of these correlations, there is indication that donor body mass index has a statistically significant correlation with the total number of islet equivalents in the final product (Pearson correlation coefficient: $r=0.3133$, $p<0.0001$).

Exhibit C provides a summary of the total number of islet equivalents/kg participant weight for participants who received only one infusion (N=53), for those who received a total of two infusions (N=107) and for those who received a total of three islet infusions (N=34). Nine participants were excluded from this Exhibit, as they did not have islet equivalents reported and/or were missing a reported weight.

Exhibit C
Mean Number of Islet Equivalents/kg Participant (±SD) by Total Number of Infusions Received (Participants with a Total of 1 Infusion, 2 Infusions, and 3 Infusions)



Immunosuppression Therapy. The majority of the islet transplant alone recipients at the time of first infusion were on a Daclizumab, Sirolimus, and Tacrolimus immunosuppression regimen (61.1%). However, a number of other immunosuppression regimens (N=18) have been used by the islet transplant centers and are listed in Exhibit D.

Exhibit D
Immunosuppression Regimen at Time of First Infusion

	Overall	
	N	%
Total	203	100.0
Sirolimus + Tacrolimus + Daclizumab	124	61.1
Sirolimus + Tacrolimus + Daclizumab + Infliximab	17	8.4
Sirolimus + Tacrolimus + Daclizumab + Alemtuzumab	9	4.4

Exhibit D *(continued)*
Immunosuppression Regimen at Time of First Infusion

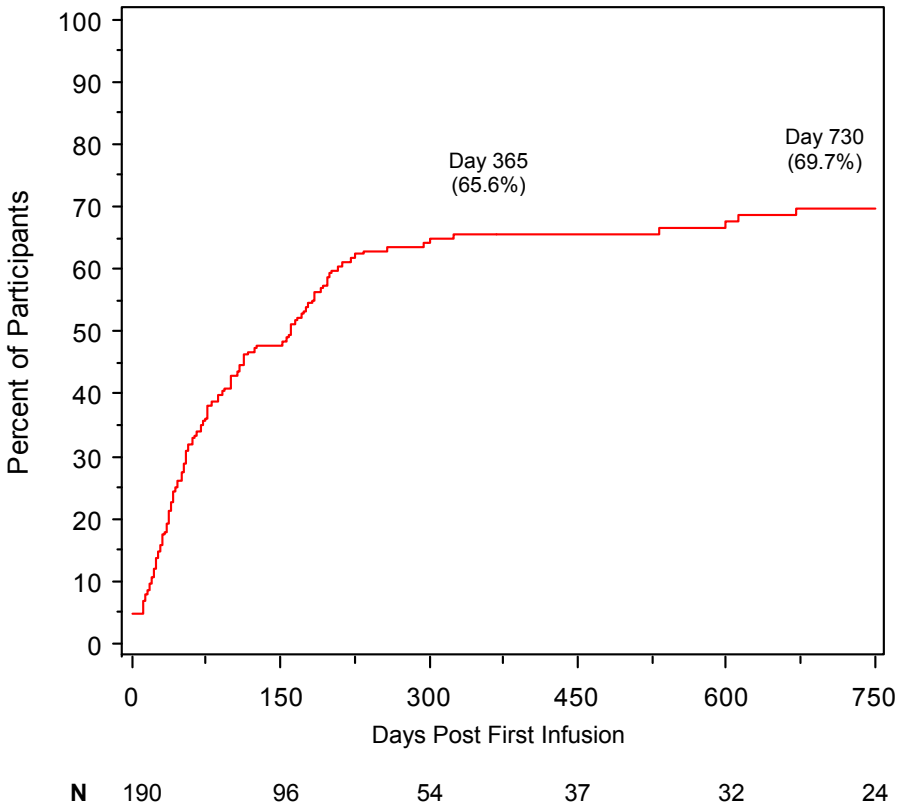
	Overall	
	N	%
Sirolimus + Tacrolimus + Basiliximab + Etanercept	9	4.4
Sirolimus + Tacrolimus + Daclizumab + 15-deoxyspergualin	5	2.5
Sirolimus + Tacrolimus + Daclizumab + MMF + Methylprednisolone + Anti-thymocyte Globulin + Etanercept	5	2.5
Neoral Cyclosporine + Methylprednisolone + Everolimus + Anti-thymocyte Globulin + Etanercept	4	2.0
Sirolimus + Tacrolimus + Daclizumab + Anti-thymocyte Globulin	3	1.5
Sirolimus + Tacrolimus + Daclizumab + MMF	3	1.5
Sirolimus + Tacrolimus + hOKT3γ-1 (Ala-Ala)	3	1.5
Sirolimus + Tacrolimus + Alemtuzumab + Etanercept	3	1.5
Other Immunosuppression Regimen Therapies	9	4.4
Missing Information on Immunosuppression	9	4.4

Medications and Adjunctive Therapy. Prior to the first infusion, almost 39% of the recipients were on at least one anti-hypertensive medication and over 24% were on a lipid lowering medication. By Year 1 post last infusion, these rates increased to over 48% and over 63%, respectively. Percentages are based on participants with complete medication information. For adjunctive therapies, at the time of their first infusion, over 98% of recipients used an antibiotic, 92.5% used antivirals, 88.9% used Heparin (including Heparin used during the infusion procedure), and 87.4% used vitamin supplements. The most common adjunctive therapies used during follow-up included vitamin supplements (11.9% at Month 6 and 11.0% at Year 1) and Pentoxifylline (9.3% at Month 6).

Graft Function. Following the first infusion procedure, 50.0% of participants were insulin independent six months later, with 49.4% insulin independent at one year following this first infusion. When analyzing insulin independence rates after the participant's last infusion procedure, 56.7% were insulin independent at six months, while this rate drops to 51.4% at one year. At six months and one year post the last infusion procedure, participants with a total of two infusions have the highest insulin independence rates of 60.2% and 54.4%, respectively, compared to those with only one islet infusion (52.1% and 50.0%) and those with three islet infusions (54.5% and 46.4%).

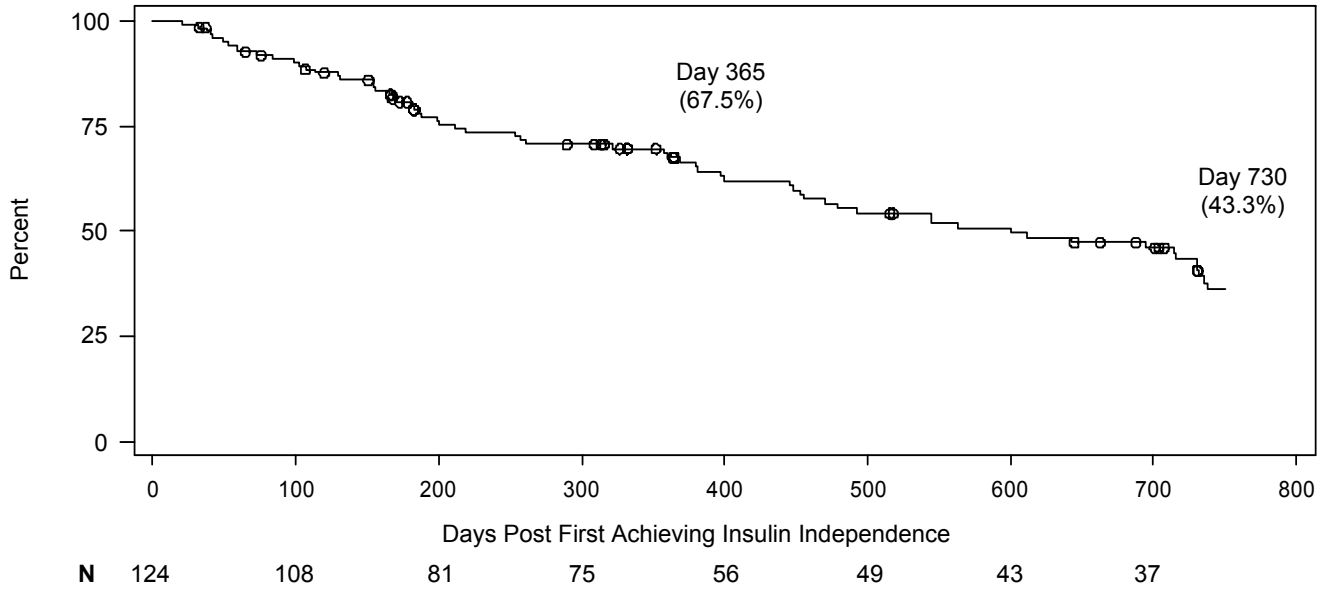
When determining if a participant ever achieves insulin independence (for 14 or more days) after receiving at least one islet infusion, at one year 65.6% of the participants have achieved insulin independence, and by year two this increases slightly to 69.7% (Exhibit E). However, no recipients have achieved insulin independence any longer than 200 days from the last infusion procedure. Stratified by the total number of infusions received when achieving insulin independence, rates at Day 75 were highest among those with two infusions (52.2%) and three infusions (46.6%). At Day 180, rates increase for all three groups to 56.1% for two infusions, 51.1% for three infusions, and 28.7% for recipients achieving insulin independence with one infusion.

Exhibit E
Percent of Participants Ever Achieving Insulin Independence



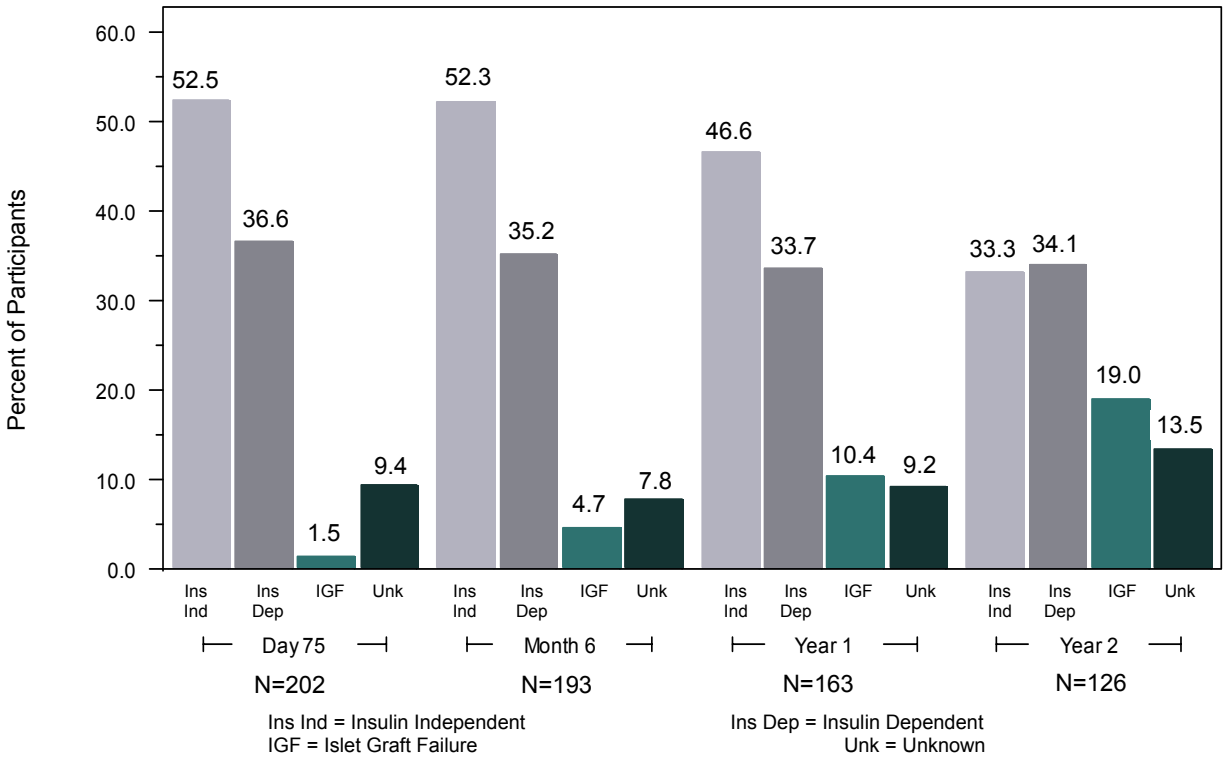
Over time there is a decrease in the sustainability of insulin independence. For all participants who have ever achieved insulin independence, only 67.5% have remained in this status one year after achieving it and this decreases to 43.3% at two years (Exhibit F). This decline is also seen by total number of infusion procedures conducted to achieve insulin independence.

Exhibit F
Time to Return to Insulin Dependence (≥ 14 Days of Insulin Use)
Among Insulin Independent Participants



A decrease in insulin independence and sustainability is also seen in Exhibit G, where at Day 75 post last infusion, rates are around 52%, then drop to 47% at one year and further drop to 33% at two years.

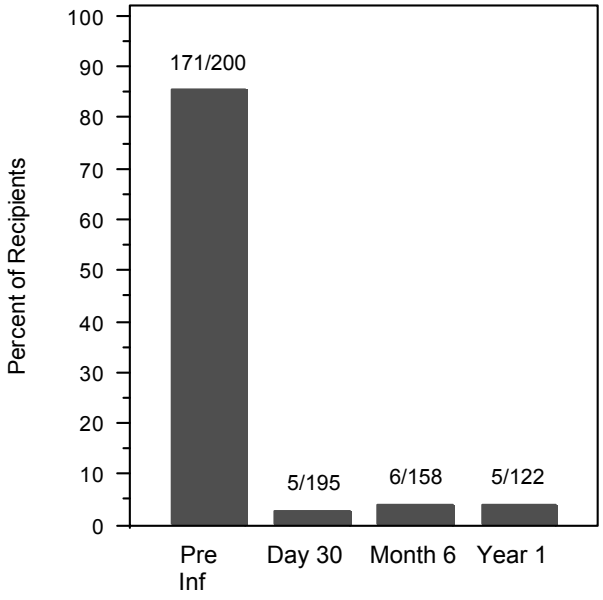
Exhibit G
Insulin Status (%) by Follow-up Visit Post Last Infusion



Changes In Islet Graft Function. For 121 participants with complete reporting of changes in islet graft function, there have been a total of 52 participants reported with one or more changes in their islet graft function (43.0%). Thirty-two participants (26.4%) have experienced islet graft failure. On average, complete loss of islet graft function occurred in these 32 participants 506 days (SD 429 days) after receiving their first islet infusion, while the median time to complete loss of islet function is 385 days.

Severe Hypoglycemic Events. As reported in last's year Annual Report, there continues to be a striking decrease in the number of severe hypoglycemic events that have occurred subsequent to the participant's first infusion procedure (Exhibit H). Over 85% of participants experienced one or more severe hypoglycemic events prior to their first infusion. This decreased to 2.6% up to 30 days post their first infusion and then to 3.8% in months 1-6 and 4.0% in months 6-12 post last infusion. All participants that experienced a severe hypoglycemic event during follow-up were on insulin at the time of the event.

Exhibit H
Percent of Participants with One or More Occurrences of Severe Hypoglycemic Episodes Pre First Infusion and Follow-Up Post First Infusion



Metabolic Measures. After the first infusion procedure, participant's fasting blood glucose values and HbA_{1C} decreased over time, while basal C-peptide values increased. This trend is seen within each of the cohort group of participants (with one, two and three infusions). At one year following the last infusion procedure, participants who ever achieved insulin independence have a mean fasting blood glucose of 111.5 mg/dL (SD 30.4), a basal C-peptide of 1.1 ng/mL (SD 0.65) and an HbA_{1C} of 6.0% (SD 0.8). Those who never achieved insulin independence have a higher fasting blood glucose (122.5 mg/dL, SD 61.0) and HbA_{1C} (6.5%, SD 1.0), and a lower C-peptide (0.41 ng/mL, SD 0.48).

Diabetes Related Secondary Complications. Diabetes related secondary complications experienced by the participants are captured prior to their first infusion procedure and at Registry follow-up intervals post their last infusion procedure. It is the goal of the Registry to continue to track the occurrence of these complications across time to determine any trends. At this time in the Registry, follow-up no observations can be made.

Elevated Laboratory Tests. Reports at the two times or greater than the upper limit of normal (ULN) at any of the specified follow-up time points (pre-subsequent infusion, 6 months, 1 year) were minimal for ALT (2.8%), AST (2.2%), alkaline phosphatase (2.2%) and for total bilirubin (0.5%). There were no reports at this level for total cholesterol and 8 reports (4.5%) for triglycerides. In addition, there were 10 reports (6.0%), of a participant with an increase in their serum creatinine of greater than 0.5 mg/dL of their baseline level.

Serious Adverse Events. Exhibit I presents the adverse event and serious adverse event rate for islet alone transplant recipients in Year 1 post their first islet infusion. Almost 72% of the recipients experienced at least one adverse event in Year 1, while over 47% experienced one or more serious adverse events in this same period. Of the 521 reported adverse events in Year 1 post first infusion, 32.8% were related to the immunosuppression therapy and 26.7% were related to the infusion procedure. Of the 186 reported serious adverse events in Year 1 post first infusion, 29.6% were related to the immunosuppression therapy and 41.9% were related to the islet infusion procedure.

Exhibit I
Summary of Adverse Events and Serious Adverse Events (SAEs) in Year 1 Post First Infusion (Participants, N=203)

	All Adverse Events (Including SAEs)			Serious Adverse Events		
		Related to Immunosuppression Therapy	Related to Infusion Procedure		Related to Immunosuppression Therapy	Related to Infusion Procedure
Number of Events	521	171 (32.8%)	139 (26.7%)	186	55 (29.6%)	78 (41.9%)
Number of Participants with 1 or More Events	146 (71.9%)	84 (41.4%)	75 (36.9%)	96 (47.3%)	35 (17.2%)	48 (23.6%)

A cumulative total of 236 serious adverse events (SAEs) were reported to the Registry. Of these 236 SAEs, 186 of the events (78.8%) were reported during the first year following their first infusion procedure, suggesting that most SAEs occur during this period. Of the 236 SAEs, 41.1% are classified as life threatening and 40.7% required an inpatient hospitalization. Over 33% of the serious adverse events were classified by the reporting CITR investigator as related to the islet infusion procedure and 25.0% related to the immunosuppression therapy. In 2.1% (N=5) of the reports the SAE was related to both the infusion procedure and to the immunosuppression therapy. Approximately 94% of the SAEs resolved with no residual effects.

The most commonly reported serious adverse events included elevated liver function tests (21.2%) (increased aspartate aminotransferase, alanine aminotransferase, and blood alkaline phosphatase), neutropenia (10.6%), procedural related bleeds/portal vein thrombosis (9.7%) and abdominal pain (5.5%). The 23 procedural-related bleeds consisted of hematoma (N=2), hemorrhage (N=14) and portal vein thrombosis (N=7) during, or immediately subsequent to, an islet infusion procedure. Currently, two recipients are on coumadin for their portal vein thrombosis, but all other procedural-related bleeds have resolved. The rate of reported bleeds ranged from 18.5% in 2003 to 1.6% in 2004.

Reported Deaths. There have been four reports of death to the Registry. The first is a viral meningitis attributed death occurring more than three years following the person's second islet infusion, a drug toxicity (acute methadone and diphenhydramine) 70 days post the person's third infusion, a stroke more than two years post the person's second infusion and a death due to unknown causes (discovered in obituaries) more than four years post the person's second infusion.

Conclusions. Islet transplantation continues to evolve and short-term benefits of islet transplantation such as normal or near normal HbA_{1C} levels in the absence of hypoglycemic episodes have been demonstrated by an ever-increasing number of transplant centers. The long-term safety and efficacy profile of islet transplantation and immunosuppression and the effects of islet transplantation on secondary complications are less well understood and are the focus of current research. With continued participation of the existing and new islet transplant programs, CITR expects, through expeditious analyses and Annual Reports, to assist the islet transplant community in the continued development of islet transplantation into a vital therapy for selected patients with T1DM.

Methods Summary

To accumulate and compile the data from all completed and ongoing studies between 1999 and present, the National Institute of Diabetes & Digestive & Kidney Diseases funded the Collaborative Islet Transplant Registry (CITR). The mission of CITR is to expedite progress and promote safety in islet/beta cell transplantation through the collection, analysis, and communication of comprehensive and current data on all islet/beta cell transplants performed in North America. Each year the Registry provides a complete analysis of the cumulative data to date since 1999. The third report, published in 2006, summarizes information on patients who received one or more islet cell transplants between 1999 and 2005. All CITR reports are public and can be downloaded or requested in hard copy at www.citregistry.org.

CITR implements a set of web-based forms to capture pertinent information necessary to achieve the primary objectives of the Registry. These data help characterize and follow trends in safety and efficacy of islet transplantation, with particular emphasis on islet processing, transplant techniques, and treatment protocols. The Registry compiles data that are normally collected by investigators for scientific evaluations and for reports to the multiple agencies and entities required by US Food and Drug Administration (FDA) regulated trials. Demographic information is collected only once at the time of the islet transplant recipient's registration. For each islet/beta cell infusion, information is collected on the pancreas donor(s), islet processing and testing of all pancreata used for the infusion procedure, and recipient status from screening through the early transplant period.

Follow-up data are collected for 6 months and 12 months post first infusion procedure for five main indicators (insulin status, severe hypoglycemic episodes, hemoglobin A_{1C}, fasting plasma blood glucose and C-peptide). Follow-up data are collected at six-months post infusion, one-year post infusion, and yearly thereafter. After recipients receive additional infusions, a new follow-up schedule is established such that a recipient is assessed at month 6 and annual anniversaries of the last infusion. There are also event driven data collection forms that gather information on adverse events, recipient's vital status, non-islet transplant and follow-up, islet graft dysfunction, loss to follow-up, and transfer of the islet transplant recipient to another islet transplant center. A copy of these data collection forms may be requested from the CITR Coordinating Center (citr@emmes.com).

Several key terms used by CITR that are represented in the Annual Report exhibits are listed below with their respective CITR definitions:

Abnormal tests: Liver function and lipid tests were analyzed as ≥ 1 times the upper limit of normal (ULN) and at ≥ 2 times the ULN. The ULN (Stedman's Medical Dictionary, 26th edition, Williams & Williams) for each of the tests are defined as the following:

ALT (alanine aminotransferase):	56 IU/L
AST (asparate aminotransferase):	40 IU/L
Alkaline phosphatase:	90 IU/L
Total bilirubin:	1.3 mg/dL
Total cholesterol:	240 mg/dL
Triglycerides:	150 mg/dL

Adverse Event: Grade 3-5 as classified by the Cancer Therapy Evaluation Program, Common Terminology Criteria for Adverse Events (CTCAE), Version 3.0, DCTD, NCI, NIH, DHHS. Adverse event relationships to the infusion procedure and to the immunosuppression regimen are determined by the local CITR Investigator.

Duration of cold ischemia: Duration of time from when the pancreas was placed in cold preservation solution until the heating up of the organ to start the digestion process.

Hypoglycemia status: Hypoglycemia status at baseline and during follow-up visits is determined by choosing one of the following categories that best describes the participant:

No occurrence: Participant was not diagnosed with hypoglycemia and/or signs and symptoms did not occur.

Having episodes and aware: Participant experiences episodes and has autonomic warning symptoms.

Partial awareness: Participant has a decreased magnitude of autonomic symptoms or an elevated threshold for autonomic symptoms with a lower glucose level.

Unawareness: Participant has a lack of autonomic warning symptoms, no warning symptoms, or a glucose level of < 54 mg/dL.

Insulin dependence: Insulin administered for a period of 14 or more consecutive days.

Insulin independence: Free from insulin use for 14 or more consecutive days.

Islet graft dysfunction: The number of episodes during the follow-up period (0 to 30 days post infusion, 30 days to 6 months post infusion, or 6 to 12 months post infusion).

In *insulin independent recipients* (after completion of induction immunotherapy), islet graft dysfunction will be suspected if the recipient displays, with no evidence of infection or drug toxicity, 3 blood glucose readings more than 2 hours post prandial over 180 mg/dL in any 1-week period OR 3 pre-prandial blood glucose readings over 140 mg/dL in any 1-week period.

In *insulin dependent recipients* (after completion of induction immunotherapy), islet graft dysfunction will be suspected if the recipient displays, with no evidence of infection or drug toxicity, a 50% increase in insulin requirements (with a minimum increase of 5 units per day) OR an increase of 10 units per day over a 1-2 week period.

Outcome of islet graft dysfunction: If a complete dysfunction was not experienced (islet graft failure), there may be:

Partial recovery: Recovery achieved but not to the functional level (as assessed by glycemic control, C-peptide level, and/or insulin requirements) prior to the change in islet graft function.

Full recovery: Recipient was able to obtain the same level of functioning (as assessed by glycemic control, C-peptide level, and/or insulin requirements) prior to the change in islet graft function.

PRA: Panel Reactive Antibody. Sensitization is reported as the percent PRA, which is the percentage of cells tested that were killed by the patient's serum.

Serious Adverse Event: Any adverse event involving death, life threatening event, inpatient hospitalization, prolongation of existing hospitalization, persistent or significant disability/incapacity or congenital anomaly/birth defect, regardless of the CTCAE grading. Serious adverse event relationships to the infusion procedure and to the immunosuppression regimen are determined by the local CITR Investigator.

Severe hypoglycemia: Hypoglycemic events requiring the assistance of another person to diagnose symptoms or administer treatment. Prior to the first infusion, this is defined as the number of episodes in one year prior to infusion. At follow-up, it is defined as the number of episodes during the follow-up period (0 to 30 days post infusion, 30 days to 6 months post infusion, or 6 to 12 months post infusion).

Time to first insulin use: Time to the first day insulin was required for 14 or more consecutive days.

CITR opened participation up to all North American centers early in the fall of 2002. The first Annual Report (2004) contained information on 86 islet transplant recipients, 173 deceased donors and 158 islet infusion procedures from twelve islet transplant centers. The Second Annual Report (2005) summarized information on 138 islet transplant recipients, 256 deceased donors and 266 islet infusion procedures. This Annual Report (2006) summarizes information on 227 islet transplant recipients, 469 deceased donors and 429 islet infusion procedures. This represents a 64.5% increase in the number of recipients, 83.2% increase in the number of donors, and a 61.3% increase in the number of infusion procedures that are reported in this Annual Report compared to last year's Report.

The focus of the Registry is data collection on all islet allograft transplants. Although islet autografts are conducted (> 300 procedures in North America) for other indications (pancreatitis), centers may voluntarily report these data also to the Registry. Only two such autograft transplants have been reported as of this report.

CITR adheres to strict quality control and assurance procedures. All data submitted are reviewed through several quality review processes. Islet transplant recipient data for this report reflect data entered by the islet transplant centers on participants from January 1, 1999 through December 31, 2005. These data were reviewed by the Coordinating Center for quality assurance, errors and data outliers. Any missing follow-up information on these participants were identified and conveyed back to the center for verification and correction. Any questions concerning specific data elements were also sent to the islet transplant centers for review and correction, if necessary. All islet transplant centers were provided ample time for completing any identified data discrepancies. The database was then updated and closed for analysis on April 3, 2006 based on the 227 recipients that had been registered for CITR at the December 31, 2005 participant registration closure date.

All participating islet transplant centers and the data they submit to the Registry are monitored and audited by the Registry's Coordinating Center. The schedule for monitoring includes an initial visit to the islet transplant center after the first three participants are submitted to the Registry, and then after every 10 participants are entered or two years since the last visit, whichever occurs first. Monitoring reports, with suggestions for improvement, data discrepancies, and all action items are sent both to the islet transplant center and CITR's sponsor, NIDDK.

CITR also collects basic information from all islet allograft transplant centers in North America, regardless of their participation with CITR. Forty-two islet transplant programs were sent a questionnaire asking for information. Information collected from each center included the number of islet transplant infusions performed at their islet transplant center as well as the number of recipients. All 42 programs responded and 31 of the 42 programs had been active during 1999-2005, transplanting at least one patient. The remaining programs (N=11) had not transplanted yet, or were in the process of starting their islet transplant program.

The table below displays the data collected from the 31 active islet allograft transplant programs in North America for 1999-2005. To the knowledge of the Registry, this table is inclusive of all islet allograft transplant programs in North America.

All Active Islet Transplant Programs in North America (N=31)	Number of Human Islet Allograft Procedures Conducted	Number of Patients Receiving Their First Allograft
Total	593	319
1999	18	10
2000	32	21
2001	65	45
2002	142	82
2003	106	45
2004	110	53
2005	120	63

In summary, this report includes data on 70.5% (225/319) of all islet transplant recipients in North America and 71.7% (425/593) of all islet allograft procedures conducted. As of this report, there have been nine consent refusals from recipients who do not wish to have their data contributed to the Registry.

Data contained in this report must be interpreted cautiously. Even with the efforts of the 23 participating centers, the total number of reports are still small. As with any registry, a number of potential biases may exist. First, not all islet transplant centers in North America participate in CITR (23/31; 74%). Second, those Centers reporting information to CITR have not reported on all of the islet transplant recipients at their Center yet or have not reported on all of the infusion procedures of their recipients. Those reported early from the Centers may constitute the most successful cases or they may not. Third, there is always the potential of hidden selection bias in a registry database. Since a registry is non-randomized and reflects the real world choices of islet transplant centers and physicians, some information may be selective based on the center's protocol (e.g. protocols limiting donor age <60 years). As the Registry progresses these biases may lessen.

Boxplots are used in the report to summarize data. The "star" (★) in the boxplot represents the mean value; and the whiskers represent the minimum and maximum value, while the lower line of the box represents the 25th percentile, the upper line of the box represents the 75th percentile and the middle line in the box represents the median (50th percentile). Total islet equivalents in the final product and donor characteristics were also plotted and Pearson correlation coefficients determined.

Statistical significance of analyses, not adjusted for repeated testing, is shown for a number of the Exhibits. These are provided to the reader for their own interpretation based on the report of 227 islet transplant recipients. Conclusions should recognize that the significance levels control for random variance, but not systematic biases in the data. It may be that statistical significance of the analyses in subsequent reports based on a greater sample size will vary from this year's report. However, these analyses do provide insight and direction for future questions and analyses.

This report is divided into four main sections representing a summary of the Registry data (Section 1), islet transplant alone recipient, donor and outcome information (Section 2), islet after kidney recipient, donor and outcome information (Section 3), and Registry data quality (Section 4). The focus of this year's report is the islet transplant alone recipient information and outcome data. As sample size increases for the islet after kidney recipients (N=22), additional tables and outcomes measures will be included for this section of the report.

Section 1
Registry Summary

Registry Summary

As of December 31, 2005, 23 North American islet transplant centers were activated for participation in the Collaborative Islet Transplant Registry (CITR). Exhibit 1 displays the locations of these centers. A complete listing of these centers and their staff is found in Appendix 1. Overall, there has been a steady increase in the number of islet transplant programs joining CITR and contributing information since the last Annual Report. There has been a 64.5% increase in the number of recipients reported to the Registry since the last Annual Report, as well as a 61.3% increase in the number of islet infusion procedures reported. Exhibit 2 displays the number of centers contributing to this report compared to those that were active islet transplant centers in the field conducting transplants during the same time period. For example, 13 of the 21 (61.9%) active islet transplant programs in 2005 contributed information to the Registry.

Exhibits 3 and 4 compare the total number of allograft participants and allograft infusions contained in this year's Annual Report to the overall number of allograft recipients and allograft infusions performed in all of North America. Overall, 225 of 319 allograft recipients (71%) and 425 of 593 (72%) of all allograft infusions performed in North America are included in this year's Annual Report.

A summary of the number of infusions entered in the Registry by year the islet infusion was performed is included in Exhibit 5. From this summary, there was a large number of first islet infusions conducted by the CITR centers in 2002 (N=63) as well as a large number of recipients receiving their second infusion in 2002 (N=41). In other years, first infusions ranged from 16-38 recipients.

Sixty-four participants (28.4%) have received just one islet infusion at the time of this report, 122 (54.2%) received a total of two infusions, 38 (16.9%) received three infusions, and one participant (0.4%) received a total of four islet infusions (Exhibit 6). Other sections of the report will not include the information for the recipient of four infusions, as to assure confidentiality for this one participant and center.

Of the 227 participants represented in this report, 203 (89%) are islet transplant alone (ITA) recipients, 22 (10%) are islet after kidney recipients (IAK), and 2 recipients (1%) received autograft transplants (Exhibit 7). The focus of the report will be for the 203 islet transplant alone recipients (Section 2), while a condensed section of analyses for the islet after kidney recipients (Section 3) are presented. The two autograft participants reported voluntarily to the Registry represent a very small percentage of the total number of autografts performed in North America ($<$ 1.5%). As additional autograft transplant reports are sent to the Registry, future Annual Reports may contain analyses for these participants.

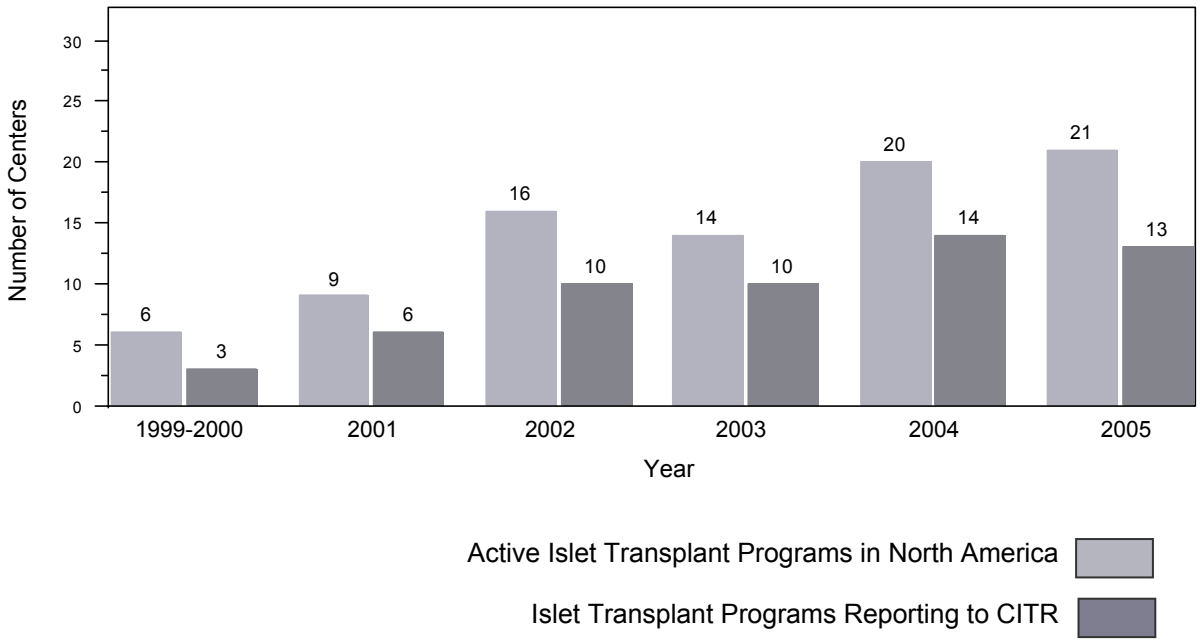
For ITA participants, there were 420 donors reported for 380 total infusions. Fifty-nine of 203 (29.1%) ITA participants received just one islet infusion, 108 (53.2%) received two infusions, 35 (17.2%) received three infusions, and one received four infusions (0.5%). For the 22 IAK participants, there were 49 donors reported for 45 total infusions. Two of 22 (9.1%) IAK participants received one infusion, 17 (77.3%) received two infusions and 3 (13.6%) received three infusions.

Exhibit 1
Contributing Islet Transplant Centers
(N = 23)

Islet Transplant Centers

CITR Coordinating Center

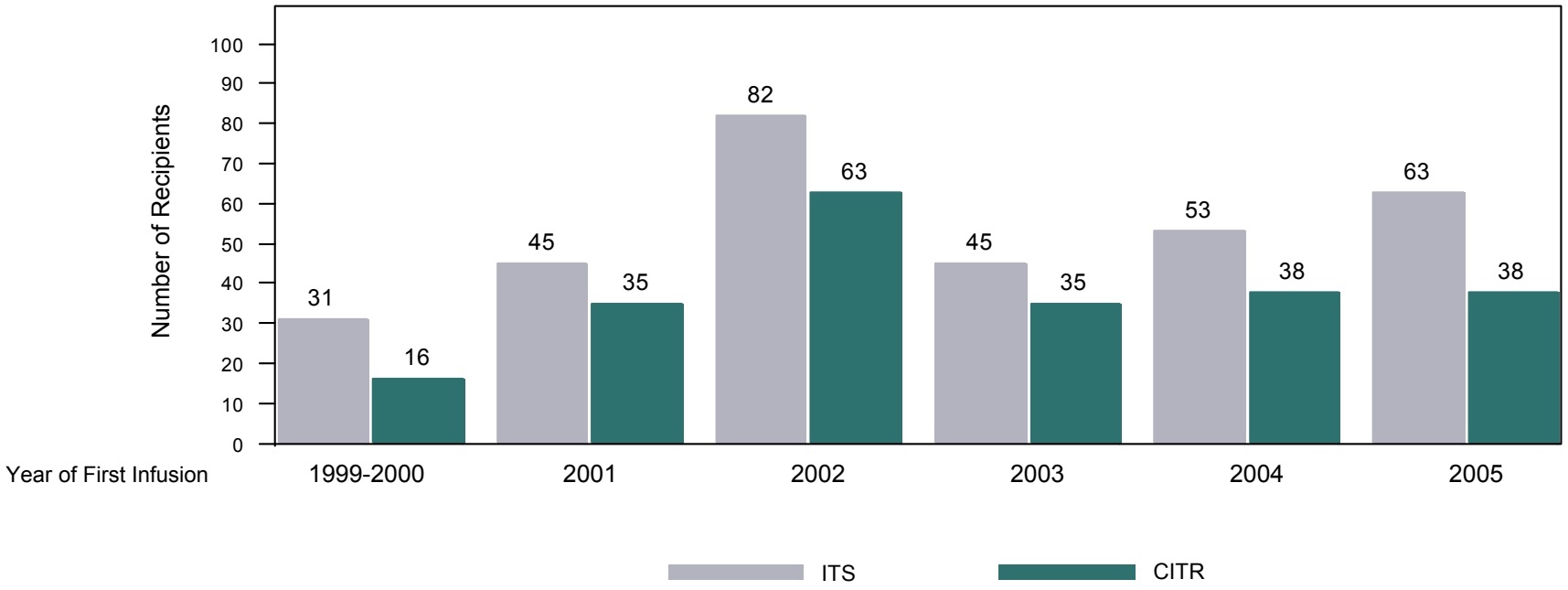
Exhibit 2
Number of Islet Transplant Programs Transplanting and Number Reporting Information to CITR by Year



CITR distributes an Islet Transplant Summary (ITS) questionnaire to all islet transplant programs in North America regardless of their participation in the Registry. The questionnaire captures information on the total number of pancreata processed and used for clinical islet transplant and the number of patients who received one or more islet infusions. Of 42 North American islet transplant programs polled, all have provided information through 2005.

"Active Islet Transplant Programs in North America" represents the number of programs that have reported performing at least one islet infusion procedure in the specified year. "Islet Transplant Programs Reporting to CITR" represents the number of islet transplant programs in the specified year that have contributed data for the analyses included in this Annual Report. Additional islet transplant programs may be participating in CITR, but data from these centers may have been excluded due to incompleteness or the center may not have conducted any infusion procedures as of the time of datafile closure.

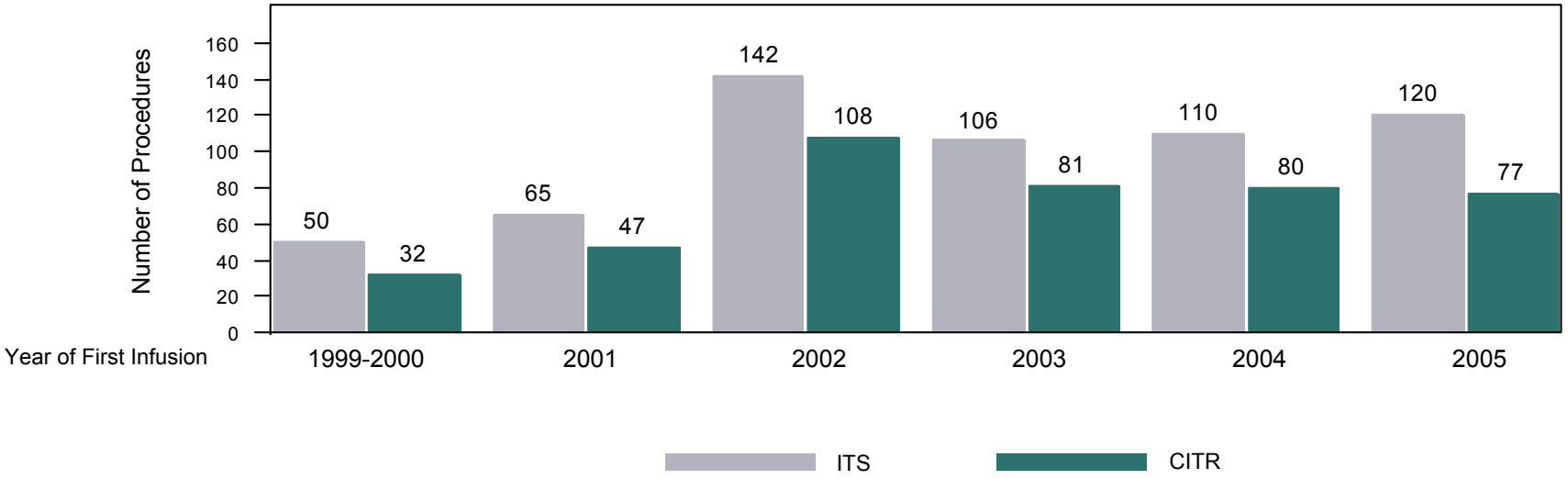
Exhibit 3
Total Number of Recipients Receiving Their First Islet Allograft Infusion in North America as Reported to the Registry and Number Contained in the Annual Report



The Islet Transplant Summary (ITS) questionnaire is completed by all North American islet transplant programs regardless of their participation in the Registry. Of 42 North American islet transplant programs polled, all have provided this information through 2005.

From 1999-2005, 319 patients with Type 1 diabetes mellitus have received at least one islet allograft infusion procedure. The Registry has received information on 225 of these recipients (71%) for analyses in this report.

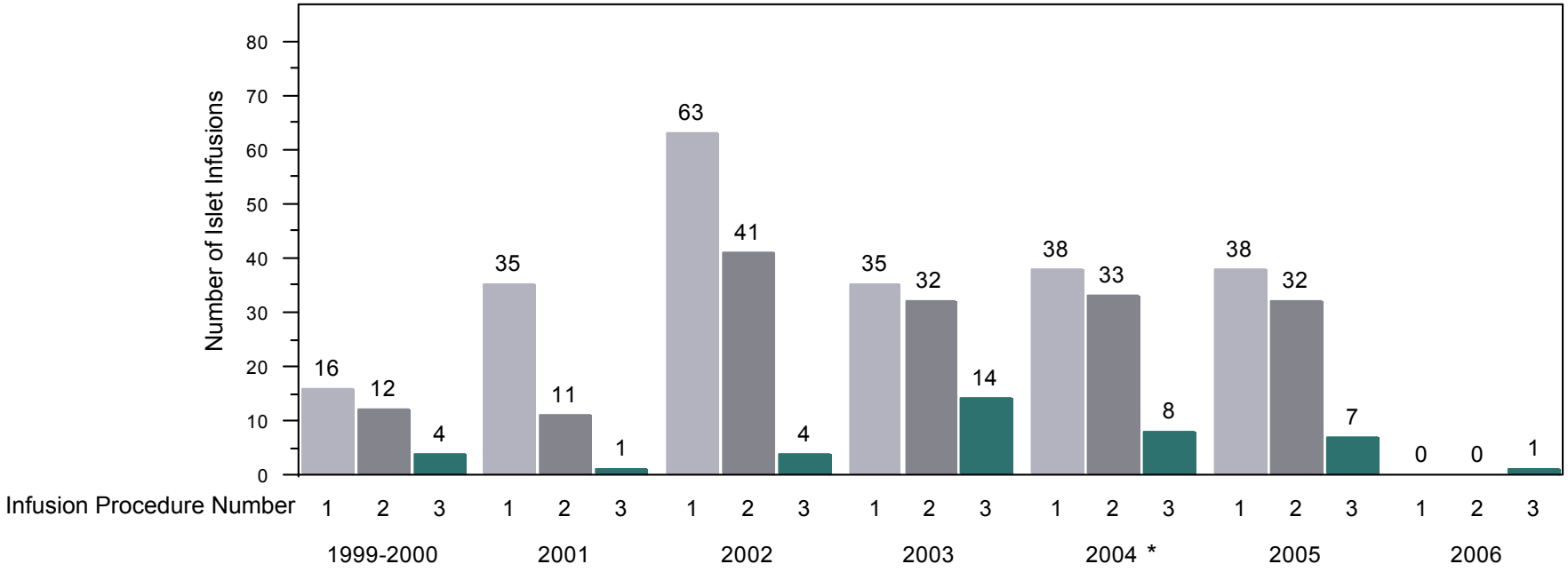
Exhibit 4
Total Number of Islet Allograft Infusion Procedures Performed
in North America as Reported to the Registry and Number Contained in the Annual Report



The Islet Transplant Summary (ITS) questionnaire is completed by all North American Islet Transplant Programs regardless of their participation in the Registry. Of 42 North American islet transplant programs polled, all have provided this information through 2005.

From 1999-2005, 319 patients with Type 1 diabetes mellitus have received a total of 593 allograft infusion procedures. The Registry has received information on 225 of these recipients (71%) and on 425 (72%) of the allograft infusion procedures for analyses in this report.

Exhibit 5
Total Number of Islet Allograft Infusion Procedures Conducted and Entered in CITR Database
by Year and by Infusion Procedure Number
(All Participants, N=225)



*One person received a fourth infusion in 2004.

Infusion procedure number is defined as the sequence number of the infusion procedures received by the recipient.

For example, in 2001, 35 participants received their first infusion, 11 received their second, while one person received their third infusion.

Exhibit 6
Total Number of Islet Allograft Infusion Procedures Received Per Participant
(All Participants, N=225)

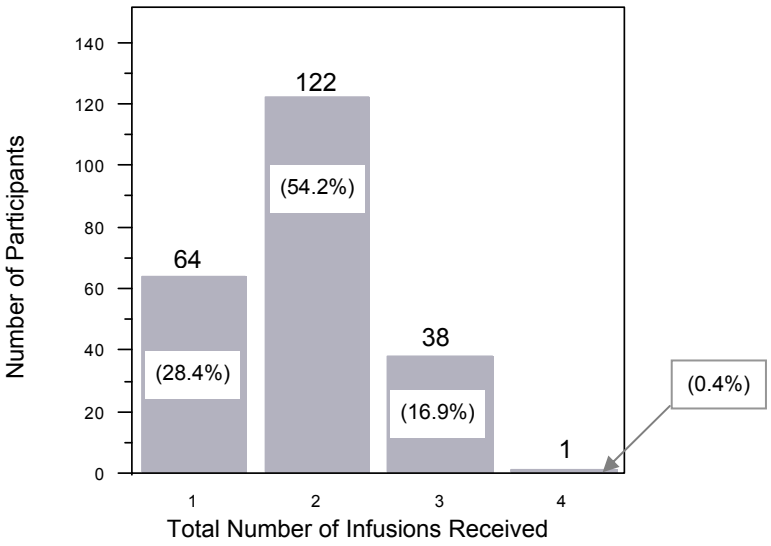
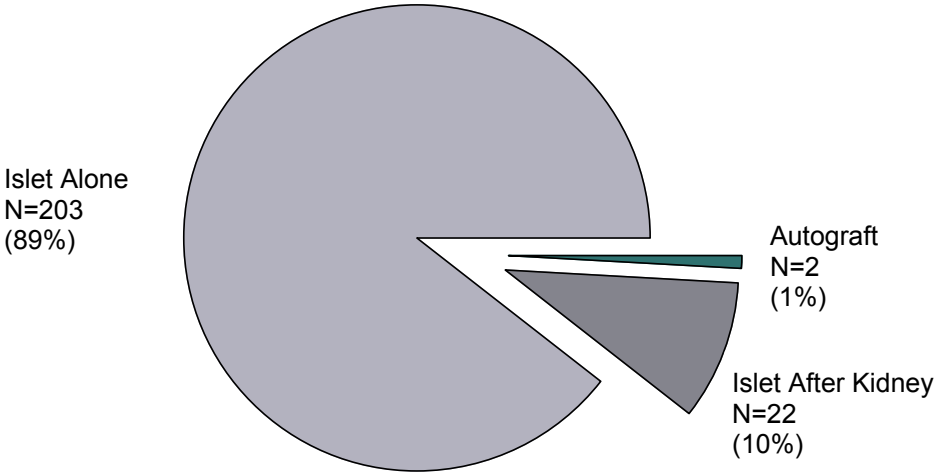


Exhibit 7
Summary of Transplant Types
(All Participants, N=227)



"Islet Alone" includes one participant who received a pancreas transplant subsequent to their islet transplant as well as one participant who received a bone marrow transplant in conjunction with their islet transplant. "Islet After Kidney" includes one participant who received two kidney transplants prior to their islet transplant as well as one participant who received a kidney transplant and a pancreas transplant prior to their islet transplant. The two autograft participants voluntarily reported to the Registry represent a very small percentage of the total number of autografts performed in North America (< 1.5%).

Section 2
Islet Transplant Alone Information

Chapter 1
Participant and Donor Characteristics

Participant and Donor Characteristics Summary

Registry information collected on islet transplant alone participants and the deceased donors are summarized in Chapter 1. This Annual Report represents information submitted by the twenty-three islet transplant centers trained and activated to conduct CITR registry procedures prior to December 31, 2005.

Recipient Information:

The median age of the islet transplant participant is 42.3 years (range 23.0 to 65.1) and the median duration of diabetes is 29 years (range 4 to 51). The median weight of the participant is 65 kg (range 35.0 to 98.1) and the median body mass index (BMI) is 23.3 kg/m^2 (range 15.5 to 31.6). Over 68% of the participants are female and the participants have limited racial and ethnic diversity (Exhibit 10).

At the time of their first infusion, 55.2% of the participants were employed full-time. Approximately 43% of the transplant procedures were funded through non-government research grants, 16% were funded from a US/State Government agency, and 17% were funded through a provincial government (Exhibit 11). Approximately, 38% of the islet transplant participants were on an insulin pump prior to their first infusion and 92.6% of the participants were on the pump or were taking three or more insulin injections per day (Exhibit 12). At baseline, over 76% of the participants have a basal C-peptide < 0.5 ng/mL and over 75% have an $HbA_{1C} > 6.5\%$ (Exhibit 12). The mean daily insulin requirement of participants prior to their first infusion procedure was 37.7 units (SD 14.0) and the subset on intensive insulin therapy had received intensive therapy for a mean of 18.3 years (SD 12.6) (Exhibit 9). The mean fasting plasma glucose for all participants was 169.7 mg/dL (SD 88.0), mean HbA_{1C} was 7.7% (SD 1.3), and their mean basal C-peptide was 0.1 ng/mL (SD 0.3).

Serology tests indicated that four participants tested positive for hepatitis B core antibodies, and three participants tested positive for hepatitis B surface antigen (Exhibit 13).

Exhibits 14 and 15 describe participant baseline characteristics prior to first infusion by the total number of infusions received. In comparison, participants who had received a total of three infusions were younger, their duration of diabetes was shorter, they had a higher BMI, required a higher baseline daily insulin requirement, had a much higher fasting plasma glucose and HbA_{1C} and lower PRA percentages than those participants who had one or two infusion procedures.

Islet Infusion Information:

Exhibit 16 summarizes the core infusion procedure characteristics by the infusion number. The mean number of islet equivalents infused was similar for each infusion (439,173, 405,232 and 441,492, respectively). On average, if a participant received a second infusion, they received this infusion 19.5 weeks following their first infusion, while those receiving a third infusion received this infusion 45.0 weeks after their initial one and 33.3 weeks post their second infusion. An increase in mean closure portal pressures was not seen across increasing infusion procedures (10.9, 11.5, and 11.0, respectively) (Exhibit 19).

Donor Information:

The median age of the deceased donor was 44 years (range 8 to 74) and the median body mass index was 28.2 kg/m^2 (range 13.3 to 59.8). The median time from cross clamp to pancreas recovery was 33 minutes (range 0 to 127) while the median cold ischemia time was 7.0 hours (range 1.1 to 27.0) (Exhibit 23). Approximately 58% of the donors were male, 9% were Hispanic and 71% were white. Race is currently missing on a large number of the donors in the database and with the missing removed from the calculation, 90% of the donors were white. Fifty-four percent of the donors had a cerebrovascular/stroke as cause of death while 31% experienced a head trauma. Approximately 31% of the donors had a history of hypertension and 17% had a history of alcohol dependency.

Thirty-three percent of the donors received a transfusion prior to organ procurement and only 4.8% received a transfusion during the organ procurement surgery. Thirty-six percent of the donors received steroids and 33.8% of the donors had received insulin (Exhibit 24). Over 92% of the donors received at least one vasopressor during the donor's terminal hospitalization (Exhibit 29).

Deceased donor serology is presented in Exhibit 30. There was a report of one donor testing positive for Anti HBC and this donor was used for a hepatitis B immunized recipient.

Deceased donor laboratory data are presented in Exhibit 31. The median serum creatinine of the donors is 1.0 mg/dL, total bilirubin 0.7 mg/dL, AST 37.0 IU/L, ALT 30.0 IU/L, serum lipase 27.5 IU/L and serum amylase 72.0 IU/L. Boxplots are presented for the donor laboratory values (Exhibits 32-40).

Exhibit 8
Participant Demographics

	Overall			
	N	Median	Min	Max
Age (yrs)	203	42.3	23.0	65.1
Duration of Diabetes (yrs)	203	29.0	4.0	51.0
Weight (kg)	201	65.0	35.0	98.1
Body Mass Index (kg/m^2)	198	23.3	15.5	31.6

Exhibit 9
Participant Summary Measures at First Infusion

	Overall		
	N	Mean	SD
Daily insulin requirement prior to infusion (units)	198	37.7	14.0
Duration of intensive insulin therapy (yrs)	136	18.3	12.6
Average daily insulin / kg participant body weight	198	0.6	0.2
Number of days on wait list for first infusion	198	292.1	306.0
Fasting plasma glucose (mg/dL)	191	169.7	88.0
Basal C-Peptide (ng/mL)	175	0.1	0.3
HbA_{1C} (%)	195	7.7	1.3
Most recent PRA (%)	182	2.9	9.9
Peak PRA (%)	153	4.2	12.3

Exhibit 10
Participant Characteristics

	Overall	
	N	%
Gender		
Male	64	31.5
Female	139	68.5
Race		
American Indian or Alaska Native	-	0.0
Asian	-	0.0
Black or African American	-	0.0
Indian Sub-Continent	-	0.0
Mideast or Arabian	-	0.0
Native Hawaiian or Other Pacific Islander	-	0.0
White	126	62.1
Missing*	77	37.9
Ethnicity		
Non Hispanic or Latino	124	61.1
Hispanic or Latino	2	1.0
Unknown*	77	37.9
Diabetes Type		
Type 1 Diabetes	203	100.0

*Race and Ethnicity are not collected outside of the United States, and are not reported to the Registry.

Exhibit 11
Participant's Primary Payer and Employment Status at Time of First Infusion

	Overall	
	N	%
Primary Payer		
US/State Government Agency	33	16.3
Private Insurance	1	0.5
Institutional Commitment	28	13.8
Non-Government Research Grant	88	43.3
Provincial Government	35	17.2
Missing	18	8.9
Employment status		
Working full time	112	55.2
Working part-time by choice	9	4.4
Working part-time due to disease	17	8.4
Working part-time, reason unknown	1	0.5
Not working by choice	9	4.4
Not working due to disease	24	11.8
Not working, reason unknown	2	1.0
Student	2	1.0
Retired	10	4.9
Employment status unknown	15	7.4
Missing	2	1.0

Exhibit 12
Participant Status at First Infusion

	Overall	
	N	%
Total	203	100.0
Use of insulin pump		
Yes	77	37.9
No	122	60.1
Unknown	4	2.0
Number of injections per day		
N/A-on pump	77	37.9
1-2*	7	3.4
3-5	110	54.2
6 or more	1	0.5
Unknown	8	3.9
Use of insulin pump or 3 or more injections per day		
Yes	188	92.6
No*	7	3.4
Unknown	8	3.9
Basal C-Peptide ≥ 0.5 ng/mL		
Yes	19	9.4
No	156	76.8
Unknown	28	13.8
$HbA_{1C} \leq 6.5\%$		
Yes	42	20.7
No	153	75.4
Unknown	8	3.9

*Six of seven participants administering two injections per day with a mean average daily insulin use of 38 units. One participant administering one injection per day with average daily insulin use of 25 units. All participants had experienced severe hypoglycemic episodes in the year prior to transplant.

"Hypoglycemia Status" categories are defined as follows: "Having Episodes and Aware" is defined as a participant experiencing hypoglycemic episodes and having autonomic warning symptoms. "Partial Awareness" is defined as a decreased magnitude of autonomic symptoms or elevated threshold for autonomic symptoms with a lower glucose level. "Unawareness" is defined as a lack of autonomic warning symptoms, no warning symptoms or glucose level of < 54 mg/dL.

Exhibit 12 *(continued)*
Participant Status at First Infusion

	Overall	
	N	%
Hypoglycemia Status		
Having Episodes and Aware	2	1.0
Partial Awareness	65	32.0
Unawareness	129	63.5
Unknown	7	3.4
Pre transplant autoantibody - GAD 65		
Positive	40	19.7
Negative	73	36.0
Not Done/Unknown	90	44.3
Pre transplant autoantibody - IA-2		
Positive	29	14.3
Negative	44	21.7
Not Done/Unknown	130	64.0
Pre transplant autoantibody - Insulin		
Positive	70	34.5
Negative	14	6.9
Not Done/Unknown	119	58.6
Total number of positive autoantibodies		
None	6	3.0
One	14	6.9
Two	8	3.9
All Three	3	1.5
Not Done/Unknown	172	84.7
Crossmatch for T-Cell		
Positive	-	0.0
Negative	92	45.3
Not Done/Unknown	111	54.7
Crossmatch for B-Cell		
Positive	2	1.0
Negative	86	42.3
Not Done/Unknown	115	56.7

Exhibit 13
Participant Serology at Screening

	Overall	
	N	%
Total	203	100.0
HIV screening		
Positive	-	0.0
Negative	196	96.6
Not Done/Unknown/Missing	7	3.4
CMV IgG		
Positive	82	40.4
Negative	111	54.7
Not Done/Unknown/Missing	10	4.9
CMV IgM		
Positive	-	0.0
Negative	94	46.3
Not Done/Unknown/Missing	109	53.7
HepB core antibody		
Positive	4	2.0
Negative	141	69.5
Not Done/Unknown/Missing	58	28.6
HepB surface antigen		
Positive	3	1.5
Negative	185	91.1
Not Done/Unknown/Missing	15	7.4
HepC antibody		
Positive	-	0.0
Negative	185	91.1
Not Done/Unknown/Missing	18	8.9
EBV IgG		
Positive	164	80.8
Negative	20	9.9
Not Done/Unknown/Missing	19	9.4

Exhibit 14
Participant Baseline Demographics Prior to First Infusion
by Total Number Infusions Received

	Total Number of Infusions Received								
	One Infusion			Two Infusions			Three Infusions		
	N	Mean	SD	N	Mean	SD	N	Mean	SD
Age (yrs)	59	42.5	9.4	108	42.8	9.6	35	39.9	8.2
Duration of Diabetes (yrs)	59	28.0	9.9	108	28.0	10.5	35	26.0	10.8
Weight (kg)	58	63.5	11.6	107	66.7	10.3	35	70.5	12.1
Body Mass Index (kg/m^2)	55	23.3	3.2	107	23.8	2.6	35	24.5	2.6
Daily Insulin Requirement (units)	56	32.8	11.2	106	38.7	13.6	35	42.9	16.9
Average daily insulin / kg participant body weight	56	0.5	0.1	106	0.6	0.2	35	0.6	0.2
Duration of Intensive Therapy (yrs)	36	19.4	14.6	75	18.9	12.0	24	14.8	11.2
Number of days on wait list for first infusion	58	320.9	331.2	104	312.8	318.7	35	189.5	188.9
Fasting Plasma Glucose (mg/dL)	56	162.7	84.5	102	169.3	85.5	32	186.1	101.7
Basal C-Peptide (ng/mL)	47	0.1	0.2	94	0.1	0.3	33	0.2	0.3
HbA_{1C} (%)	54	7.4	1.2	106	7.6	1.3	34	8.2	1.5
Most Recent PRA (%)	49	2.9	11.4	101	3.7	10.5	31	0.3	1.2
Peak PRA (%)	41	3.2	12.2	85	5.4	13.6	26	1.8	6.5

Exhibit 15
Participant Demographics Prior to First Infusion
by Total Number of Infusions Received

	Total Number of Infusions Received					
	One Infusion		Two Infusions		Three Infusions	
	N	%	N	%	N	%
Gender						
Male	12	20.3	38	35.2	14	40.0
Female	47	79.7	70	64.8	21	60.0
Pre transplant autoantibody - GAD 65						
Positive	11	18.6	24	22.2	5	14.3
Negative	13	22.0	48	44.4	12	34.3
Not Done/Unknown	35	59.3	36	33.3	18	51.4
Pre transplant autoantibody - IA-2						
Positive	8	13.6	13	12.0	8	22.9
Negative	9	15.3	26	24.1	8	22.9
Not Done/Unknown	42	71.2	69	63.9	19	54.3
Pre transplant autoantibody - Insulin						
Positive	10	16.9	53	49.1	7	20.0
Negative	4	6.8	10	9.3	-	0.0
Not Done/Unknown	45	76.3	45	41.7	28	80.0
Total number of positive autoantibodies						
None	1	1.7	5	4.6	-	0.0
One	5	8.5	8	7.4	1	2.9
Two	-	0.0	8	7.4	-	0.0
All Three	1	1.7	1	0.9	1	2.9
Not Done/Unknown	52	88.1	86	79.6	33	94.3

Exhibit 16
Infusion Summary by Infusion Sequence

	Infusion 1					
	N	Mean	SD	Median	Min	Max
Islet Equivalents infused	196	439,173	143,407	396,275	200,000	973,133
Islet Equivalents infused/kg participant body weight	195	6,730	2,337	6,238	2,949	18,768
Islet Equivalents infused/participant body mass index	192	18,585	5,936	17,212	7,455	38,531
Embedded islets (%)	133	14.3	15.7	10.0	0.0	85.0
Packed cell volume (mL)	189	4.0	2.0	3.7	0.8	15.0

	Infusion 2					
	N	Mean	SD	Median	Min	Max
Islet Equivalents infused	140	405,232	141,516	369,552	154,446	1,056,430
Islet Equivalents infused/kg participant body weight	138	6,268	2,287	5,888	2,758	18,599
Islet Equivalents infused/participant body mass index	136	17,681	6,531	16,481	7,256	52,245
Embedded islets (%)	100	16.4	18.8	10.0	0.0	80.0
Packed cell volume (mL)	136	3.5	1.6	3.2	0.8	9.0
Time since first infusion (weeks)	144	19.5	23.7	11.0	0.4	158.3

	Infusion 3					
	N	Mean	SD	Median	Min	Max
Islet Equivalents infused	36	441,492	180,140	405,501	212,234	1,122,400
Islet Equivalents infused/kg participant body weight	35	6,753	3,416	5,472	3,445	19,452
Islet Equivalents infused/participant body mass index	34	19,194	8,935	16,948	9,641	54,641
Embedded islets (%)	28	15.5	17.7	9.8	0.0	70.0
Packed cell volume (mL)	36	3.5	2.1	2.5	0.7	9.0
Time since first infusion (weeks)	36	45.0	32.5	33.8	6.3	118.0
Time since second infusion (weeks)	36	33.3	31.0	22.4	2.0	116.0

Exhibit 17
Pre Infusion Portal Pressure (mmHg) by Infusion Sequence

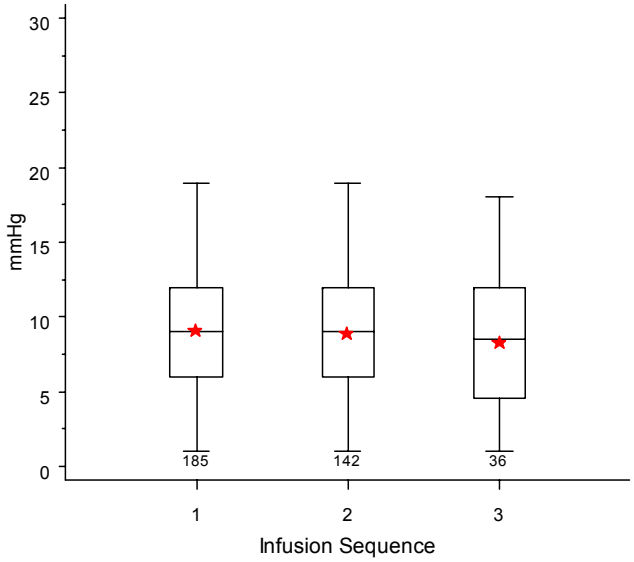


Exhibit 18
Peak Portal Pressure (mmHg) by Infusion Sequence

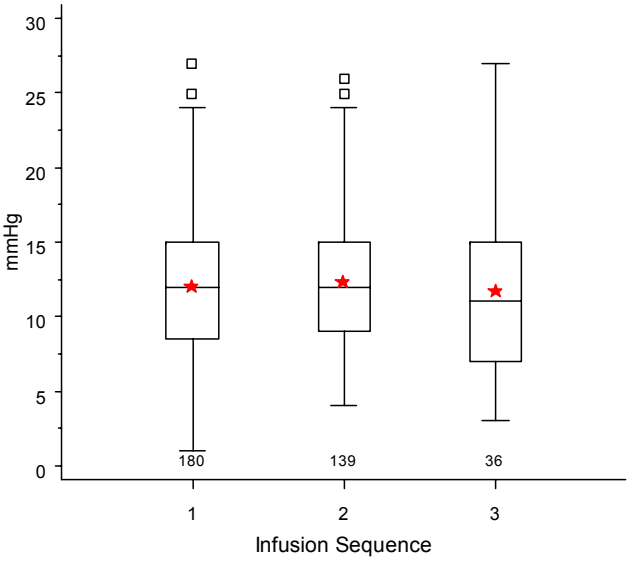


Exhibit 19
Closure Portal Pressure (mmHg) by Infusion Sequence

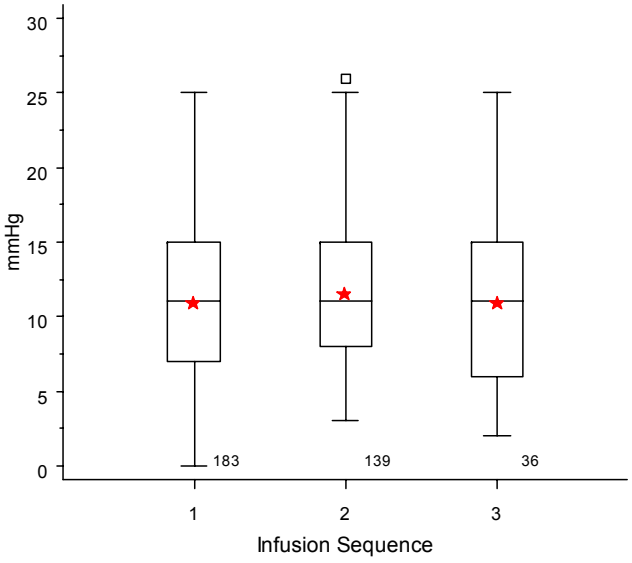


Exhibit 20
Change from Pre Infusion to Closure Portal Pressure (mmHg)
by Infusion Sequence

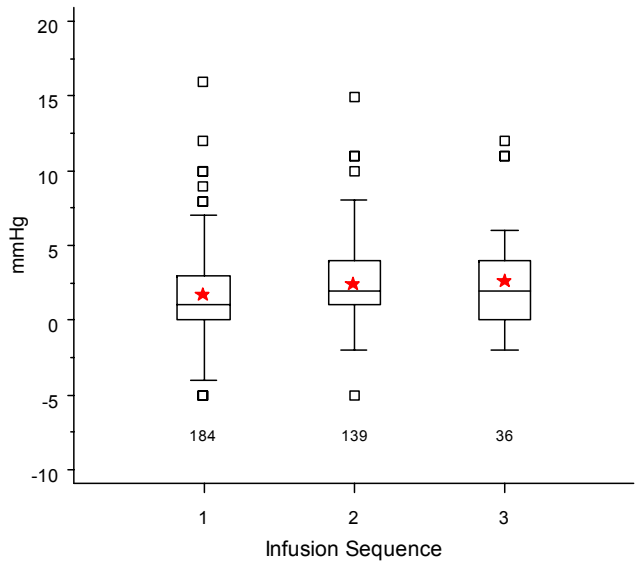


Exhibit 21
Change from Pre Infusion to Peak Portal Pressure (mmHg)
by Infusion Sequence

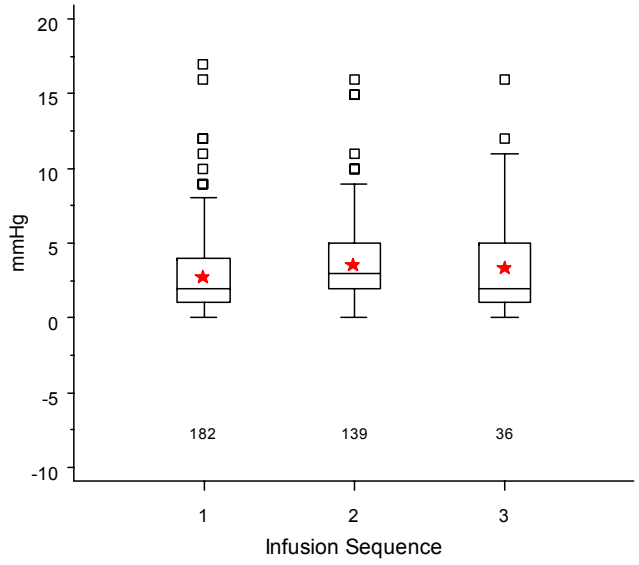


Exhibit 22
Packed Cell Volume (mL) Used During Infusion
by Infusion Year

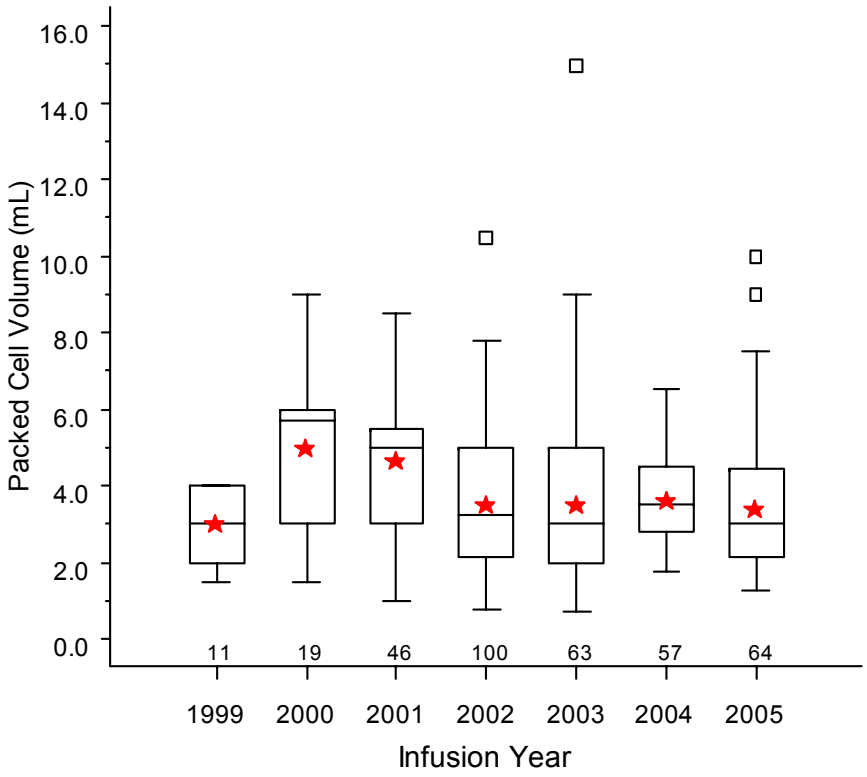


Exhibit 23
Donor Characteristics

	Overall			
	N	Median	Min	Max
Age (yrs)	418	44.0	8.0*	74.0
Weight (kg)	415	85.0	25.0*	200.0*
Height (m)	412	1.7	1.3	2.0
Body Mass Index (kg/m^2)	412	28.2	13.3	59.8
Time from admission to brain death (hrs)	319	26.0	-1.0*	602.0
Duration of cardiac arrest where cardiovascular death (mins)	26	20.0	1.0	60.0
Time from cross clamp to pancreas recovery (mins)	266	33.0	0.0	127.0
Time from brain death to pancreas recovery (hrs)	260	19.0	0.0	53.0
Cold ischemia time (hrs)	402	7.0	1.1	27.0

*Values verified by center as correct. Negative value for time from admission to brain death is verified as brain death confirmed prior to arrival at the hospital.

Time of brain death is defined as when a physician confirms the death and documents this per the medical chart. Time of cross clamp is defined as when the aorta was cross-clamped prior to organ retrieval. Duration of cold ischemia is defined as the time from when the pancreas was placed in cold preservation solution to the heating up of the organ to start the digestion process.

Exhibit 24
Donor Characteristics and Hospitalization Summary Information

	Overall	
	N	%
Total	420	100.0
Gender		
Female	172	41.0
Male	244	58.1
Missing	4	1.0
Race		
American Indian or Alaska Native	-	0.0
Asian	1	0.2
Black or African American	32	7.6
Indian Sub-Continent	2	0.5
Mideast or Arabian	-	0.0
Native Hawaiian or Other Pacific Islander	-	0.0
White	299	71.2
Missing*	86	20.5
Ethnicity		
Non Hispanic or Latino	249	59.3
Hispanic or Latino	37	8.8
Unknown*	134	31.9
Body Mass Index (kg/m^2)		
<25	110	26.2
25-27	89	21.2
28-30	59	14.0
>30	154	36.7
Missing	8	1.9

*Race and Ethnicity are not collected outside of the United States, and are not reported to the Registry.

Exhibit 24 *(continued)*
Donor Characteristics and Hospitalization Summary Information

	Overall	
	N	%
Donor ABO blood group		
A	142	33.8
A_1	21	5.0
A_2	-	0.0
AB	11	2.6
A_1B	1	0.2
A_2B	-	0.0
B	25	6.0
O	218	51.9
Missing	2	0.5
Cause of death		
Anoxia/cardiac arrest	16	3.8
CNS tumor	5	1.2
Cerebrovascular/stroke	227	54.0
Head trauma	130	31.0
Other	33	7.9
Missing	9	2.1
Mechanism of death		
Asphyxiation	7	1.7
Blunt injury	60	14.3
Cardiovascular	10	2.4
Death from natural causes	1	0.2
Drowning	3	0.7
Drug intoxication	5	1.2
Gunshot wound	33	7.9
Intracranial hemorrhage/stroke	278	66.2
None of the above	7	1.7
Missing	16	3.8

Exhibit 24 *(continued)*
Donor Characteristics and Hospitalization Summary Information

	Overall	
	N	%
History of hypertension		
Yes	128	30.5
No	247	58.8
Missing	45	10.7
-Hypertension duration		
0-5 years	53	41.4
6-10 years	10	7.8
>10 years	19	14.8
Missing	46	35.9
-Hypertension control-Diet		
Yes	15	11.7
No	27	21.1
Missing	86	67.2
-Hypertension control-Diuretics		
Yes	14	10.9
No	35	27.3
Missing	79	61.7
-Hypertension control-Other medications		
Yes	61	47.7
No	19	14.8
Missing	48	37.5
History of alcohol dependency		
Yes	70	16.7
No	289	68.8
Missing	61	14.5
-Alcohol use in past 6 months		
Yes	35	50.0
No	15	21.4
Missing	20	28.6

Exhibit 24 *(continued)*
Donor Characteristics and Hospitalization Summary Information

	Overall	
	N	%
History of diabetes		
Yes	-	0.0
No	417	99.3
Missing	3	0.7
Transfusions given prior to surgery		
0 units	251	59.8
0-5 units	100	23.8
6-10 units	23	5.5
>10 units	17	4.0
Missing	29	6.9
Transfusions given intraoperatively		
0 units	332	79.0
0-5 units	18	4.3
6-10 units	2	0.5
Missing	68	16.2
Steroids given		
Yes	153	36.4
No	78	18.6
Missing	189	45.0
Insulin given		
Yes	142	33.8
No	224	53.3
Missing	54	12.8

Exhibit 25
Donor Age (yrs)

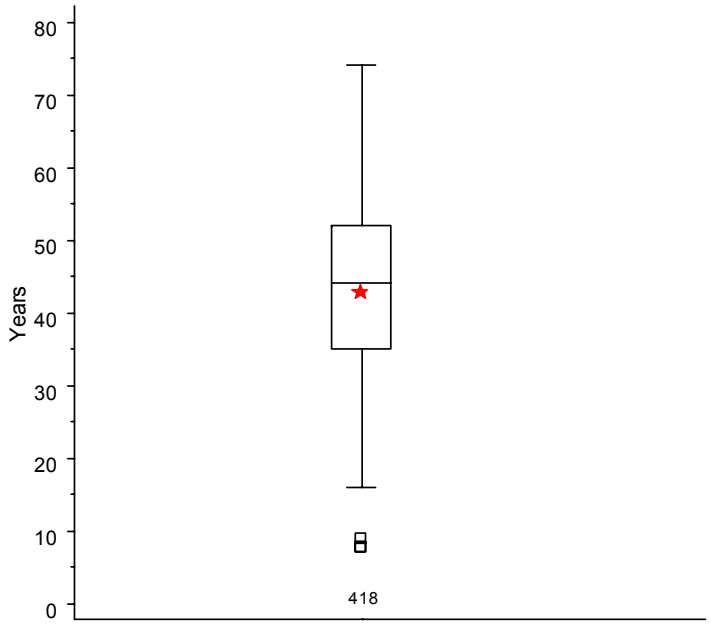


Exhibit 26
Donor Weight (kg)

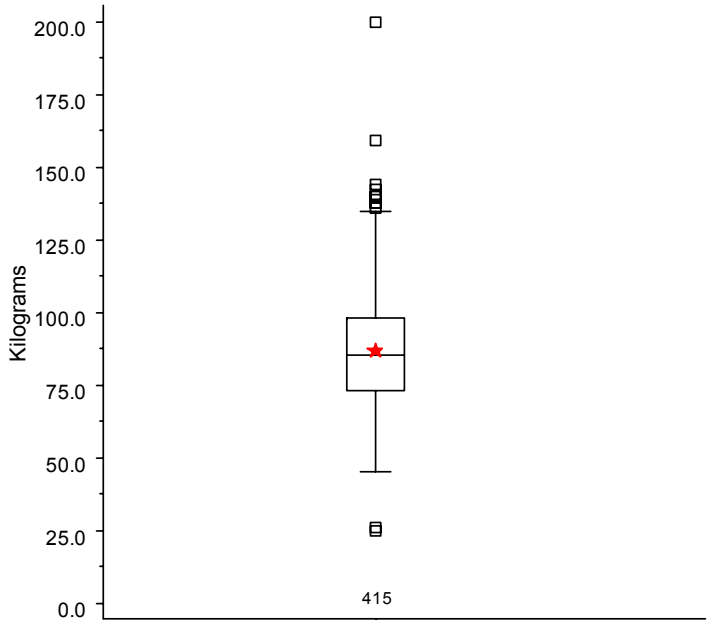


Exhibit 27
Donor Body Mass Index (kg/m^2)

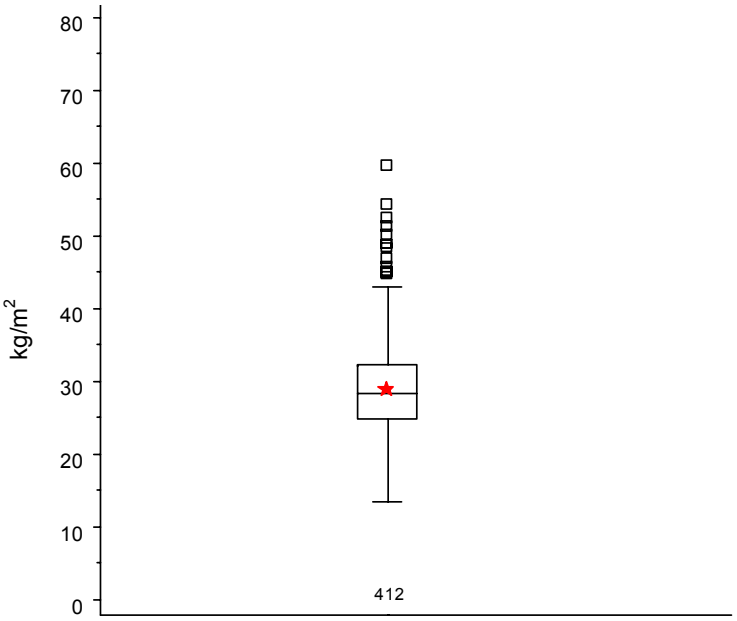
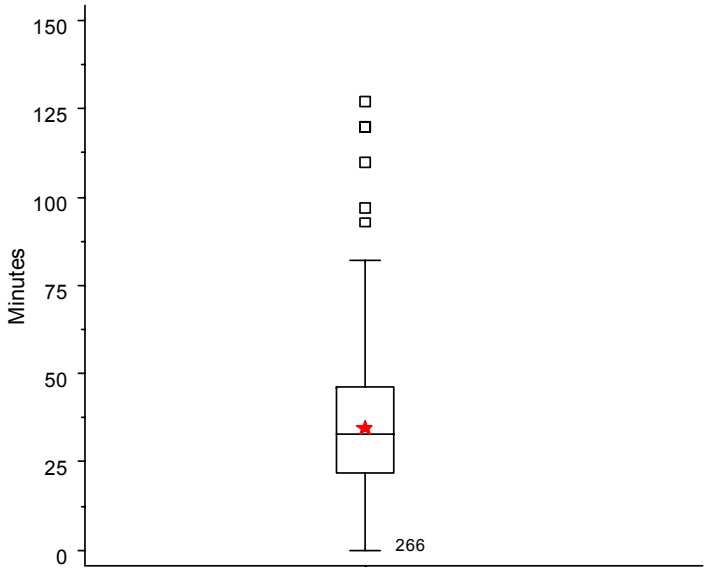


Exhibit 28
Time from Cross Clamp to Pancreas Recovery (mins)



Three values greater than 120 minutes were verified by center as correct.

Exhibit 29
Donor Characteristics: Use of Vasopressors

	Overall	
	N	%
Total	420	100.0
Vasopressors used		
Yes	390	92.9
No	14	3.3
Missing	16	3.8
Number of vasopressors used		
None	14	3.3
One	138	32.9
Two	160	38.1
Three	77	18.3
Four or More	15	3.5
Missing	16	3.8

Exhibit 30
Donor Serology

	Overall	
	N	%
Total	420	100.0
Anti HIV I/II		
Positive	-	0.0
Negative	417	99.3
Not Done/Unknown/Missing	3	0.7
Anti HTLV I/II		
Positive	-	0.0
Negative	398	94.8
Not Done/Unknown/Missing	22	5.2
RPR VDRL		
Positive	-	0.0
Negative	369	87.9
Indeterminate	2	0.5
Not Done/Unknown/Missing	49	11.7
Anti CMV		
Positive	231	55.0
Negative	182	43.3
Indeterminate	1	0.2
Not Done/Unknown/Missing	6	1.4
HBsAg		
Positive	-	0.0
Negative	411	97.9
Not Done/Unknown/Missing	9	2.1
Anti HBC		
Positive	1*	0.2
Negative	405	96.4
Not Done/Unknown/Missing	14	3.3
Anti HCV		
Positive	-	0.0
Negative	408	97.1
Not Done/Unknown/Missing	12	2.9

* Verified by center as correct. Donor was used for a hepatitis B immunized recipient.

Exhibit 31
Donor Laboratory Data

	Overall					
	N	Mean	SD	Median	Min	Max
Serum creatinine (mg/dL)	318	1.2	0.9	1.0	0.2	12.4
BUN (mg/dL)	247	14.8	8.3	13.0	3.0	55.0
Total bilirubin (mg/dL)	247	0.9	0.8	0.7	0.1	5.8*
AST (IU/L)	251	80.7	260.8	37.0	9.0	3,886.0*
ALT (IU/L)	255	61.4	213.5	30.0	5.0	3,318.0*
Serum lipase (IU/L)	334	73.3	126.4	27.5	0.0	840.0
Serum amylase (IU/L)	323	164.5	331.6	72.0	6.0	3,875.0*
Minimum pre-insulin blood glucose (mg/dL)	382	126.7	40.6	121.0	52.0	444.0
Maximum blood glucose (mg/dL)	343	242.7	94.2	225.0	84.0	700.0

*Values verified by center as correct.

Exhibit 32
Donor Serum Creatinine (mg/dL)

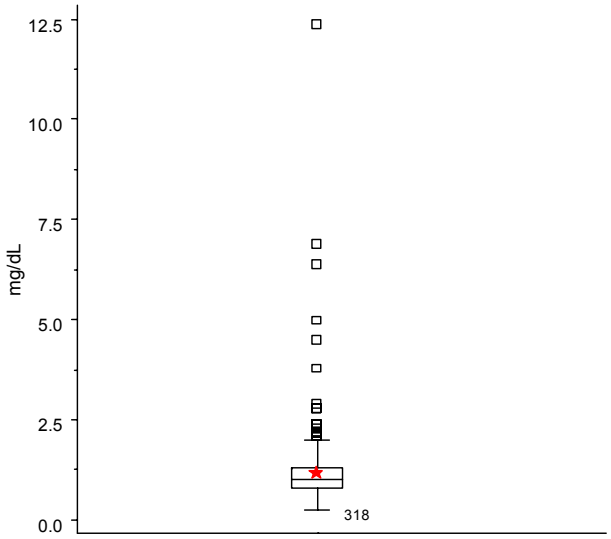


Exhibit 33
Donor BUN (mg/dL)

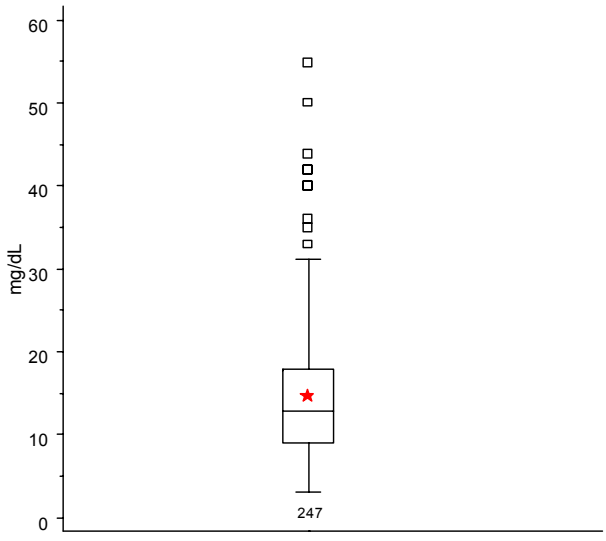


Exhibit 34
Donor Total Bilirubin (mg/dL)

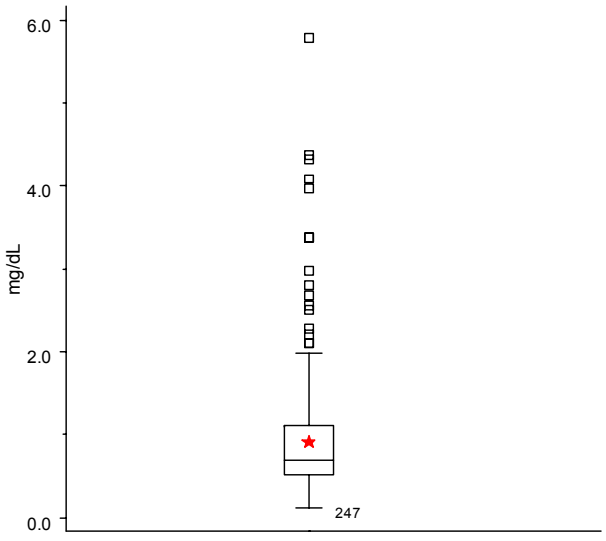
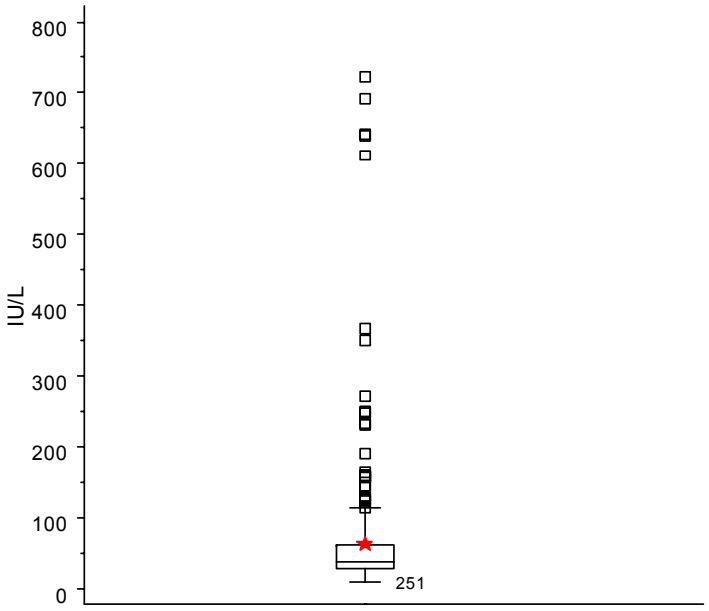
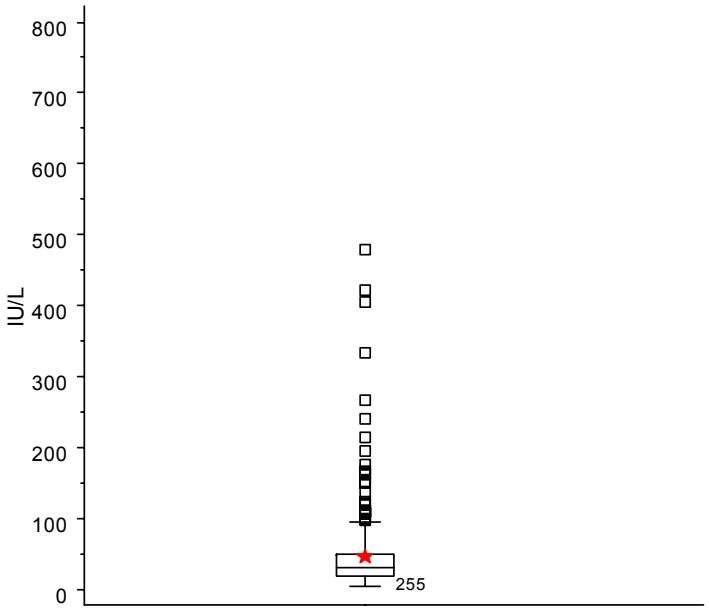


Exhibit 35
Donor AST (IU/L)



Data point 3886 IU/L excluded from graph for presentation, verified correct by center.

Exhibit 36
Donor ALT (IU/L)



Data point 3318 IU/L excluded from graph for presentation, verified correct by center.

Exhibit 37
Donor Serum Lipase (IU/L)

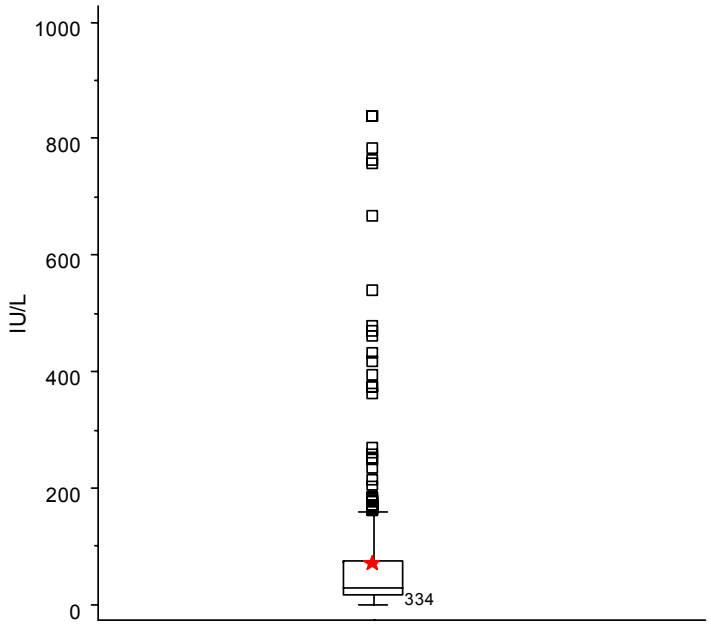
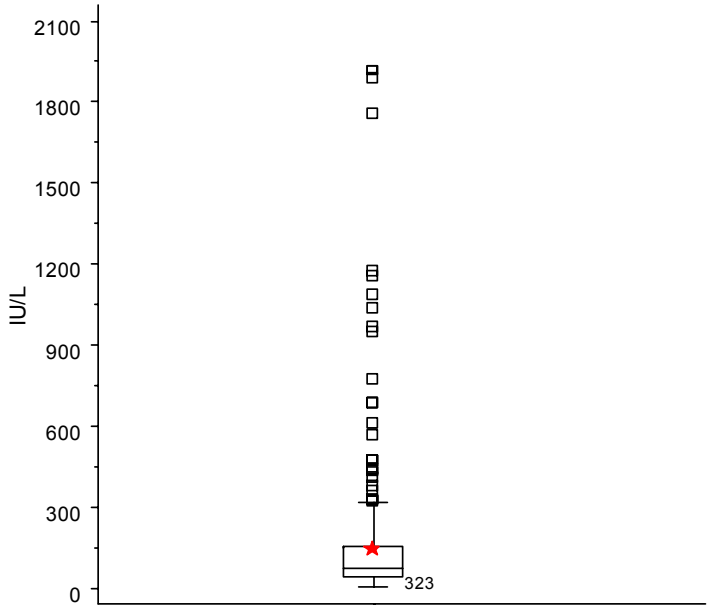


Exhibit 38
Donor Serum Amylase (IU/L)



Data point 3875 IU/L excluded from graph for presentation, verified correct by center.

Exhibit 39
Donor Pre-Insulin Blood Glucose (mg/dL)

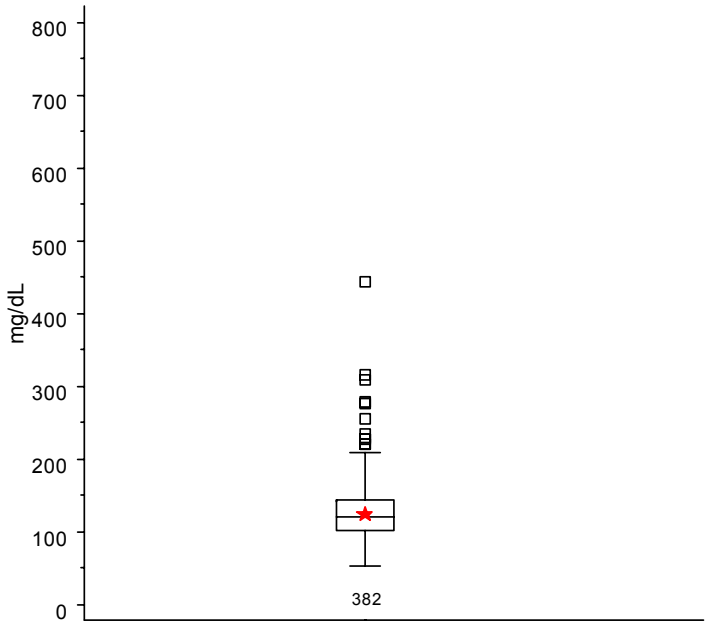
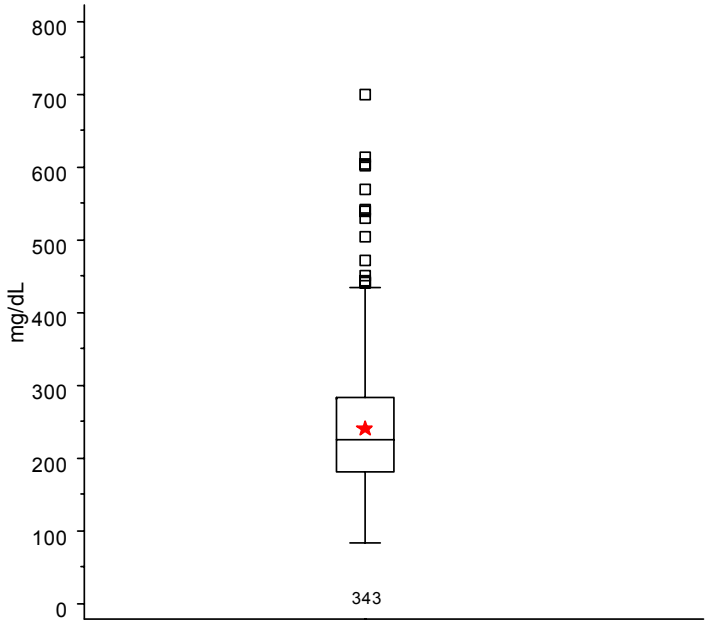


Exhibit 40
Donor Maximum Blood Glucose (mg/dL)



Chapter 2
Pancreas Procurement and Islet Processing

Pancreas Procurement and Islet Processing Summary

Summarized in this chapter are pancreas procurement and islet processing data reported to the Registry. Only pancreata used for clinical islet transplantation are reported to the Registry. Data for pancreata processed but not used for clinical islet transplantation are not collected by this Registry. In over 59% of the procedures, the pancreas procurement team was not related/affiliated with the processing/transplant team (Exhibit 41), while 86.6% of the processing procedures took place at the same institution as the islet transplant center. The median duration of cold ischemia was 7 hours (range 1.1 to 27.0) (Exhibit 42). UW, Two Layer (UW and PFC, N=164; HTK and PFC, N=3), and UW followed by Two Layer were the most common methods used for pancreas preservation (Exhibit 41). Other preservation solutions used in conjunction or in absence of UW and/or PFC included HTK, Eurocollins, P Phase 2, and Lactated Ringer's solutions.

Liberase HI was the collagenase type used during most islet processing (95.2%) followed by Thermolysin plus Collagenase P (2.2%), and custom Liberase Blend (1.0%). All of the pancreata processed used a density gradient for islet purification. Fifty-six percent of islets were placed in culture for some period of time. Culture is defined as any specially prepared nutrient medium. The median culture time was 28 hours (range 1.5 to 84.0) (Exhibit 42). Of the 418 preparations reported to CITR, six final preparations showed a positive aerobic culture (1.4%), four showed a positive anaerobic culture (1.0%) and three showed a positive fungal culture (0.7%).

An islet product characterization summary is located in Exhibit 44. Total islet equivalents in the final product were plotted versus cold ischemic time (Exhibits 45-47), donor body mass index (Exhibit 48), and donor age (Exhibit 49). Of these correlations, there is indication that donor body mass index has a statistically significant correlation with the total number of islet equivalents in the final product (Pearson correlation coefficient: $r=0.3133$, $p<0.0001$).

Exhibits 50 through 55 show the results of a series of contrasts for islet cell characteristics and preparation and donor characteristics. Total islet equivalents per kilogram donor weight, and the percent viability, as determined by fluorescein diacetate/propidium iodide, significantly decreased ($p<0.05$) as the time from cross clamp to pancreas recovery increased (Exhibit 50). In Exhibit 51, there was higher viability as determined by the same method above (94.4%) for pancreata preserved with a Two Layer method only as opposed to pancreata preserved with UW only (91.2%) ($p<0.05$). There was also a higher DNA content for the Two Layer method (9,309 µg) compared to UW alone (6,651 µg). However, the Two Layer method was associated with a decrease in total packed cell volume (3.6 mL) and in islet equivalents per kilogram donor weight (4,492 IEQ/kg) compared to UW alone (4.0 mL and 4,878 IEQ/kg). When examining cold ischemic time subgroups, there was a statistically significant difference among the groups for the number of islet equivalents/kg donor weight infused ($p<0.05$). There were also statistically significant differences between groups for DNA content and Stimulation Index.

When examining whether or not the islets were subjected to culture, islet particle count and islet equivalents/kg donor weight were higher in the non-cultured group ($p<0.05$). However, the number of beta cells, beta cells/kg donor weight, and DNA content were higher among the cultured group ($p<0.05$). When examining donor age, islet preparations from younger donors had a higher percentage of embedded islets and a higher DNA content. For donor body mass index (BMI), as BMI increases, islet equivalents/kg donor weight decreases, but the number of islet equivalents infused increases ($p<0.05$).

Exhibit 56 provides a summary of the total number of islet equivalents/kg participant weight for participants who received only one infusion (N=53), for those who received a total of two infusions (N=107) and for those who received a total of three islet infusions (N=34). Nine participants were excluded from this Exhibit, as they did not have islet equivalents reported and/or were missing a reported weight.

Exhibit 41
Islet Processing Summary

	Overall	
	N	%
Total	418	100.0
Pancreas procurement team		
Unrelated to processing/infusion team	250	59.8
Related to processing/infusion team	152	36.4
Unknown/Missing	16	3.8
Islet processing/testing center		
Same location as infusion center	362	86.6
Other location than infusion center	47	11.2
Unknown/Missing	9	2.2
Pancreas preservation		
UW	239	57.2
Two Layer	141	33.7
UW followed by Two Layer	26	6.2
Neither UW nor Two Layer	3	0.7
Unknown/Missing	9	2.2
Other preservation solutions used*		
HTK	13	3.1
Eurocollins	7	1.7
P Phase 2	2	0.5
Lactated Ringer's	1	0.2
Collagenase Type		
Liberase HI	398	95.2
Thermolysin + Liberase HI	3	0.7
Thermolysin + Collagenase P	9	2.2
Thermolysin + Liberase HI + Collagenase P	1	0.2
Serva + NB1	1	0.2
Custom Liberase Blend	4	1.0
Unknown/Missing	2	0.5
Islet purification		
Density gradient	416	99.5
Unknown/Missing	2	0.5

*Other preservation solutions used in conjunction with UW, Two Layer, both or neither.

Exhibit 41 *(continued)*
Islet Processing Summary

	Overall	
	N	%
Islet pretreatment		
None	179	42.8
Culture	236	56.5
Missing	3	0.7
Gram stain		
Positive	-	0.0
No organism seen	387	92.6
Missing	31	7.4
Aerobic culture		
Positive	6	1.4
No Growth	368	88.0
Not Done	18	4.3
Missing	26	6.2
Anaerobic culture		
Positive	4	1.0
No Growth	263	62.9
Not Done	18	4.3
Missing	133	31.8
Fungal Culture		
Positive	3	0.7
No Growth	363	86.8
Not Done	20	4.8
Missing	32	7.7
Mycoplasma		
Positive	-	0.0
Negative	327	78.2
Not Done	62	14.8
Missing	29	6.9

"Two Layer" is defined as any Two Layer solution and includes Two Layer solutions of UW and PFC (N=164) as well as HTK and PFC (N=3). Islet microbiology results represent the final culture results of the preparation.

Exhibit 42
Cold Ischemia Information

	Overall					
	N	Mean	SD	Median	Min	Max
Time from cross clamp to pancreas recovery (mins)	266	34.6	22.6	33.0	0.0	127.0
Duration of cold ischemia (hrs)	402	7.4	3.5	7.0	1.1	27.0
Time from brain death to pancreas recovery (hrs)	260	20.3	8.7	19.0	0.0	54.0
Culture time (hrs)	220	30.1	18.3	28.0	1.5	84.0

Time of brain death is defined as when a physician confirms the death and documents this per the medical chart. Time of cross clamp is defined as when the aorta was cross-clamped prior to organ retrieval. Duration of cold ischemia is defined as the time from when the pancreas was placed in cold preservation solution to the heating up of the organ to start the digestion process. Culture is defined as any time spent in a specially prepared nutrient medium.

Exhibit 43
Summary of Islet Equivalents and Timing of Count

	Total Islet Equivalents					
	N	Mean	SD	Median	Min	Max
Islet equivalents (IEQ) measured at:						
Post Digestion	6	736,448	318,819	730,304	314,290	1122400
Post Purification (Pre culture)	244	407,908	146,969	383,207	84,615	973,133
Post Culture	163	368,028	139,868	350,902	67,064	875,583
Timing Missing	1	339,217	-	339,217	339,217	339,217

This Exhibit represents the total Islet Equivalents (IEQs) measured from each individual pancreas at specified times of the count (eg., Post Digestion). Multiple pancreata are sometimes used for a single infusion procedure and will account for some of the counts in this Exhibit to be <100,000 IEQs.

Exhibit 44
Islet Product Characterization

	Overall					
	N	Mean	SD	Median	Min	Max
Total packed cell volume infused (mL)	394	3.8	1.9	3.5	0.7	15.0
Islet particle count	184	361,783	153,402	350,500	106,333	996,000
Embedded islets (%)	283	15.4	18.3	10.0	0.0	85.0
Islet equivalents/kg donor weight	406	4,705	1,918	4,455	713	16,987
Islet equivalents infused	404	432,934	147,339	397,335	154,446	1,122,400
Beta cells ($x10^6$)	171	268.2	218.6	193.0	4.0	954.0
Beta cells ($x10^6$)/kg donor weight	168	3.3	2.9	2.4	0.0	20.3
Insulin content (µgrams)	214	3,086	1,939	2,797	67	9,914
DNA content (µgrams)	212	7,602	8,969	4,882	83	55,111
Endotoxin units	336	23.4	44.7	6.9	0.0	540.6*
Endotoxin units/kg donor weight	334	0.3	0.6	0.1	0.0	6.6
Islet purity: Dithizone positive cells (%)	240	65.2	15.6	69.0	30.0	100.0*
Islet potency: Stimulation index	374	3.5	3.8	2.3	0.3	28.8
Islet Viability (%)						
Fluorescein Diacetate/Propidium Iodide	180	93.0	6.1	95.0	65.0	100.0*
Flourescein Diacetate/Ethidium Bromide	13	85.2	6.8	85.0	72.0	96.0
Trypan Blue	26	95.3	3.0	95.0	90.0	100.0*
Syto Green 13	117	85.7	7.2	87.0	63.0	98.0

*Values verified by center as correct.

Stimulation index is calculated by dividing the glucose-stimulated insulin release at high glucose by the glucose-stimulated insulin release at low glucose.

Exhibit 45
Total Islet Equivalents by Cold Ischemic Time (hrs)
All Pancreas Preservation Methods

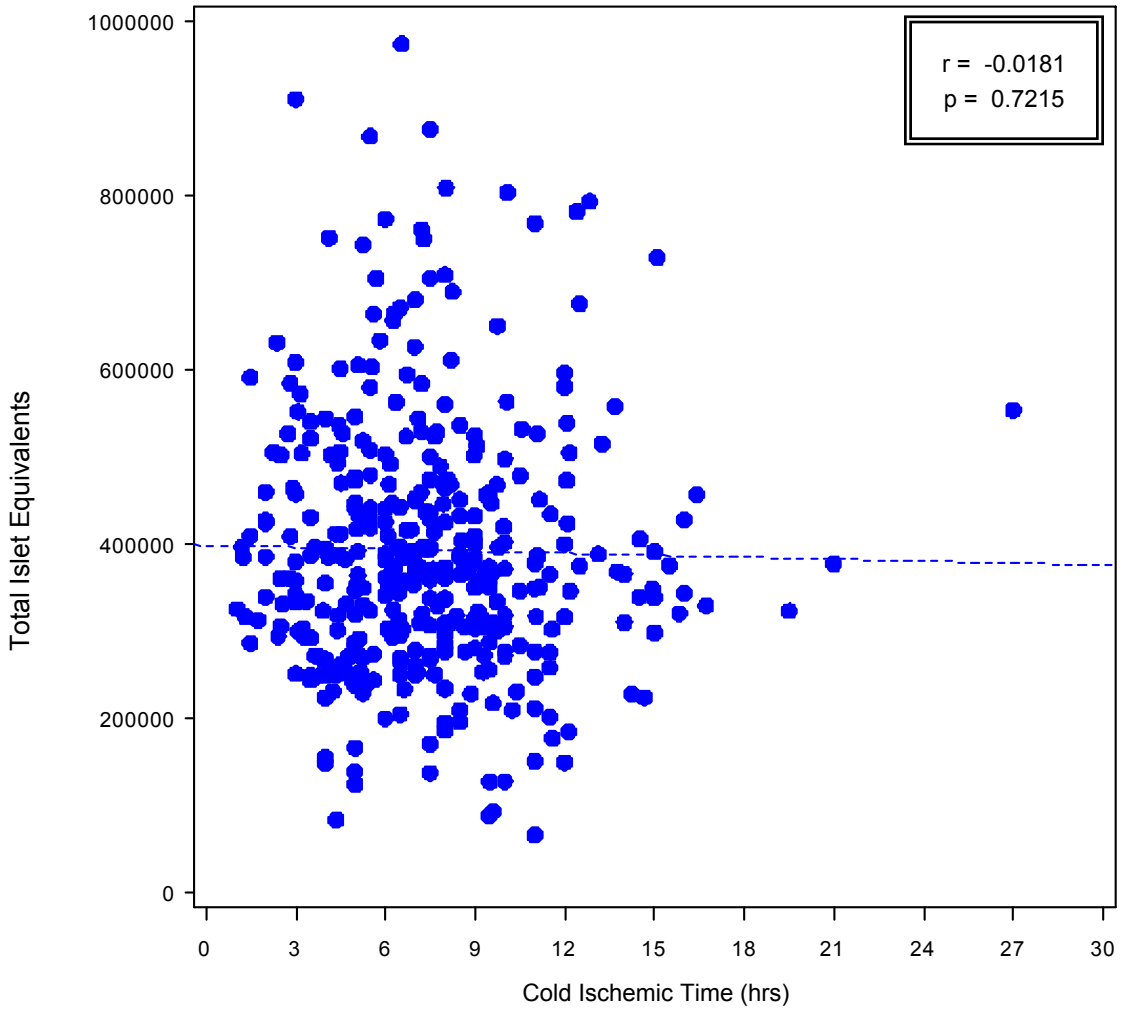


Exhibit 46
Total Islet Equivalents by Cold Ischemic Time (hrs)
Pancreata Preserved with UW Only

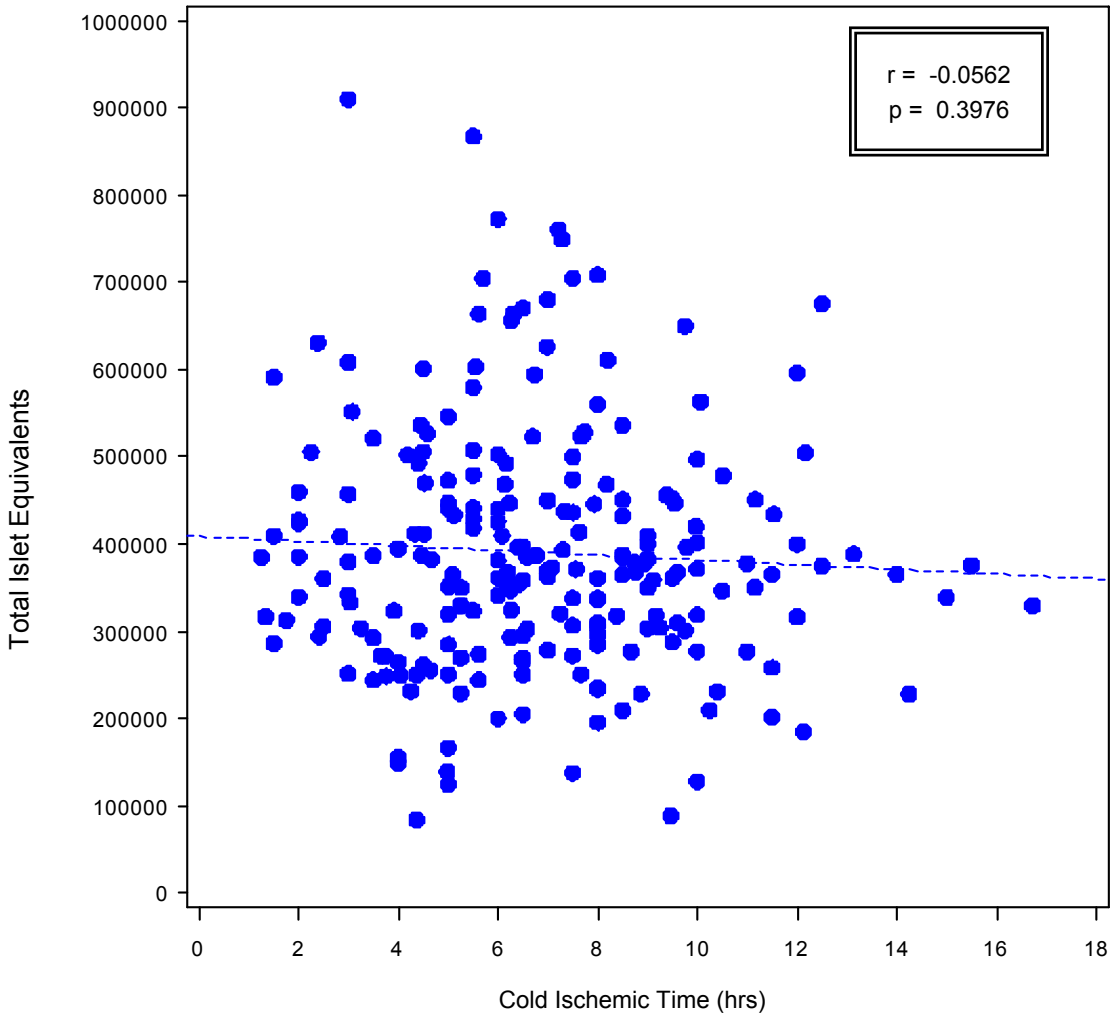


Exhibit 47
Total Islet Equivalents by Cold Ischemic Time (hrs)
Pancreata Preserved with Two Layer Only

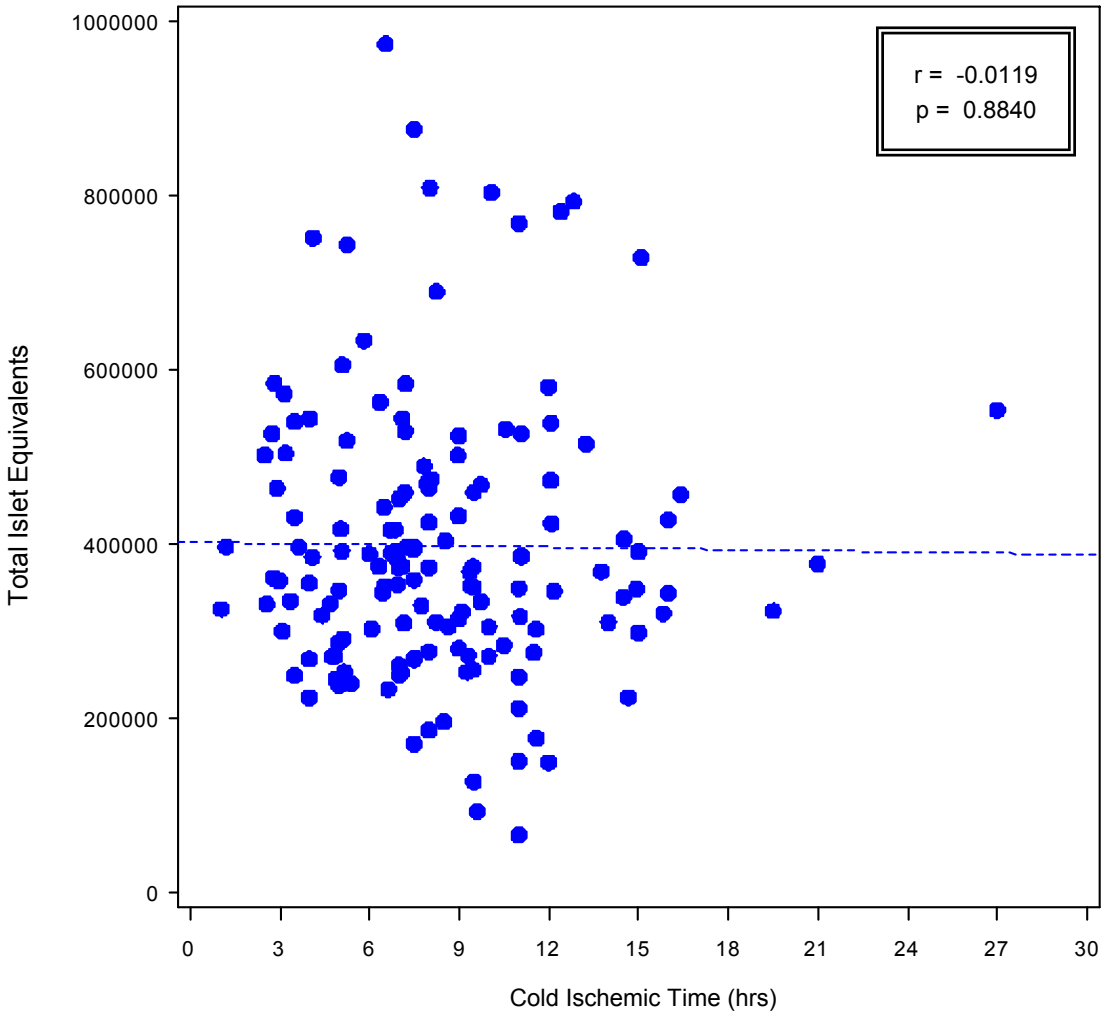


Exhibit 48
Total Islet Equivalents by Donor Body Mass Index (kg/m^2)

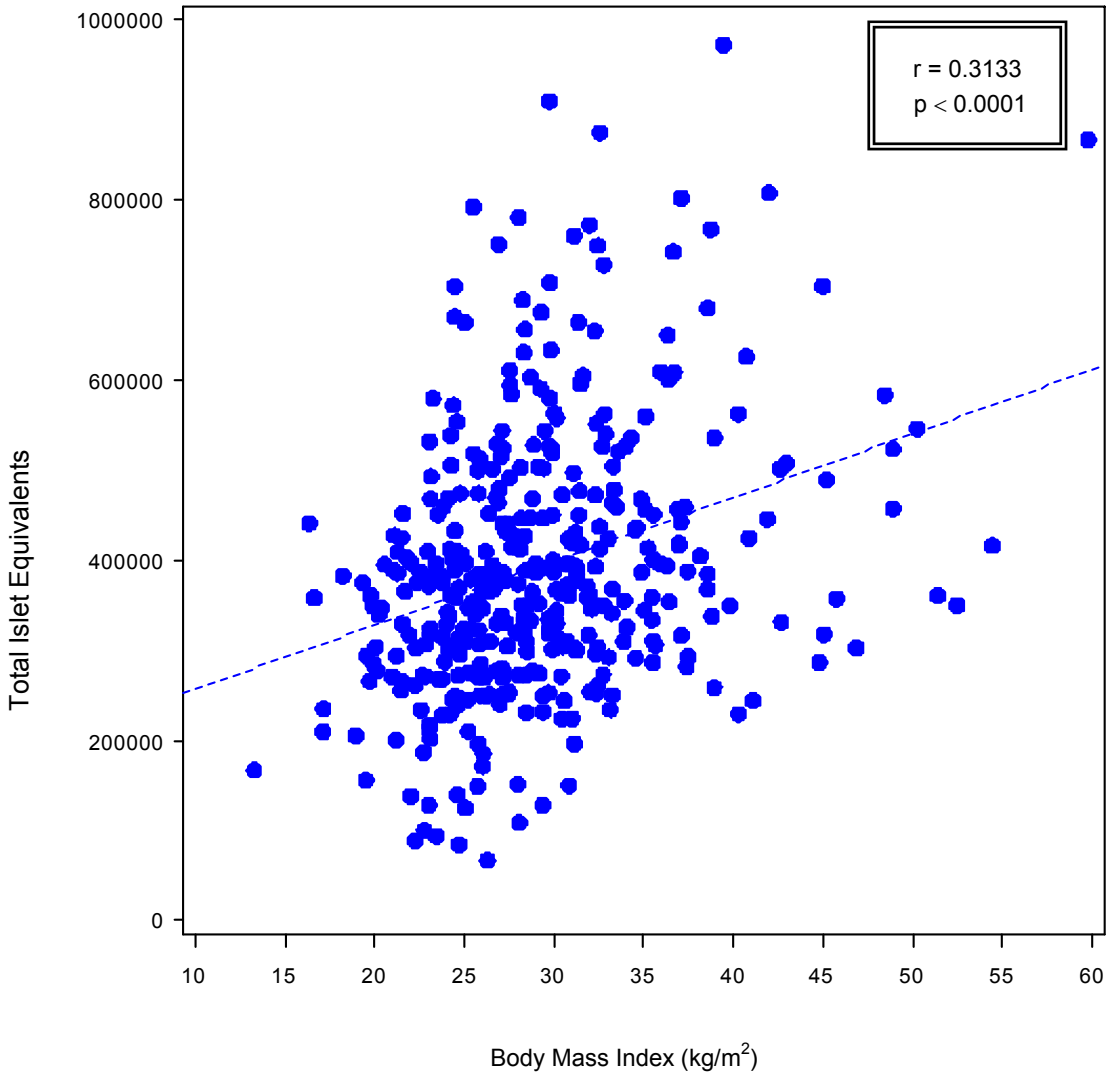


Exhibit 49
Total Islet Equivalents by Donor Age (yrs)

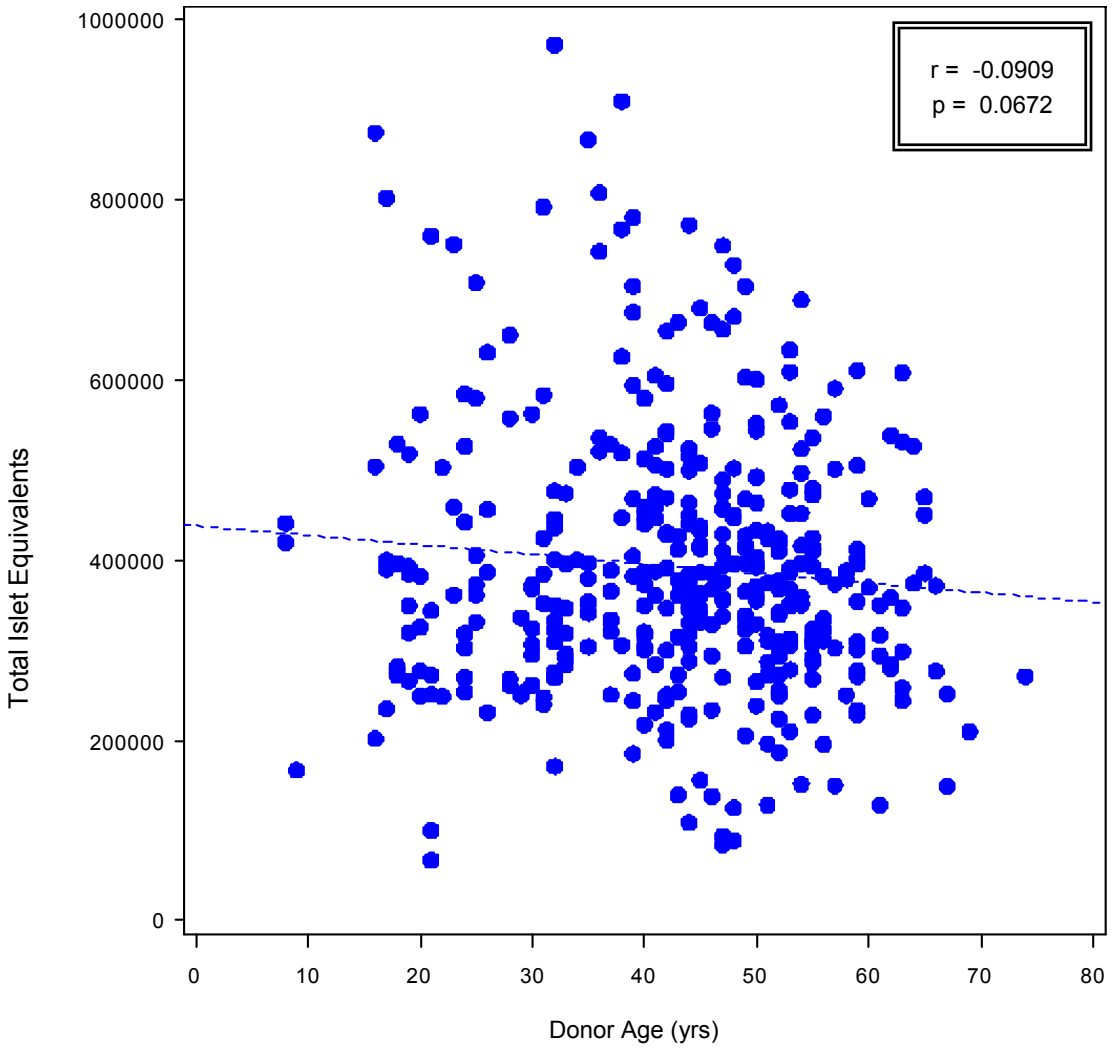


Exhibit 50
Islet Characteristics by Time from Cross Clamp to Pancreas Recovery

	Cross Clamp to Pancreas Recovery Time									Statistically significant at p < 0.05
	< 45 Minutes			45-60 Minutes			> 60 Minutes			
	N	Mean	SD	N	Mean	SD	N	Mean	SD	
Total packed cell volume infused (mL)	188	3.8	2.0	41	3.7	1.6	29	3.7	1.8	
Islet particle count	87	389,370	152,484	21	365,149	188,471	19	328,253	137,947	
Embedded islets (%)	135	17.5	19.0	31	16.4	16.2	19	20.9	27.2	
Islet equivalents/kg donor weight	193	4,815	1,802	42	4,289	2,077	30	3,983	1,481	*
Islet equivalents infused	190	440,122	147,573	41	385,348	114,570	29	423,220	125,191	
Beta cells ($x10^6$)	88	273.8	212.0	16	450.6	250.3	11	293.9	253.6	*
Beta cells ($x10^6$)/kg donor weight	88	3.5	3.1	16	4.8	2.7	11	3.3	3.1	
Insulin content (µgrams)	108	2,834	1,724	25	3,021	2,071	13	3,831	1,814	
DNA content (µgrams)	104	8,356	9,534	23	11,354	12,995	13	6,220	6,425	
Endotoxin units	166	20.6	32.4	36	23.9	45.3	27	17.1	40.2	
Endotoxin units/kg donor weight	165	0.3	0.5	36	0.3	0.4	27	0.2	0.5	
Islet purity: Dithizone positive cells (%)	122	66.1	14.6	27	63.4	17.1	19	61.3	19.4	
Islet potency: Stimulation index	175	3.5	3.9	37	3.8	4.7	27	3.0	3.2	
Islet viability: Fluorescein Diacetate/Propidium Iodide (%)	93	94.8	5.4	14	91.2	7.4	13	90.0	6.2	*
Islet viability: Syto Green 13 (%)	53	85.4	6.8	13	87.8	8.0	10	89.8	5.3	

Exhibit 51
Islet Characteristics by Pancreas Preservation Method

	Pancreas Preservation Method						Statistically significant at p < 0.05
	UW Only			Two Layer Only			
	N	Mean	SD	N	Mean	SD	
Total packed cell volume infused (mL)	229	4.0	2.0	159	3.6	1.7	*
Islet particle count	105	370,440	142,396	81	359,486	174,117	
Embedded islets (%)	170	13.9	17.5	112	17.4	19.0	
Islet equivalents/kg donor weight	236	4,878	2,063	161	4,492	1,683	*
Islet equivalents infused	229	425,932	134,622	163	434,150	149,231	
Beta cells ($x10^6$)	103	236.6	214.9	68	315.7	217.1	*
Beta cells ($x10^6$)/kg donor weight	101	3.1	2.7	67	3.8	3.1	
Insulin content (µgrams)	141	3,171	2,039	73	2,975	1,827	
DNA content (µgrams)	135	6,651	7,988	77	9,309	10,294	*
Endotoxin units	181	25.7	53.5	148	21.2	31.9	
Endotoxin units/kg donor weight	181	0.3	0.7	146	0.2	0.3	
Islet purity: Dithizone positive cells (%)	118	65.4	17.6	118	64.6	13.9	
Islet potency: Stimulation index	222	3.6	3.7	151	3.3	3.8	
Islet viability: Fluorescein Diacetate/Propidium Iodide (%)	77	91.2	6.4	100	94.4	5.5	*
Islet viability: Syto Green 13 (%)	72	84.7	7.5	44	87.3	6.4	

Two Layer is defined as any Two Layer solution and includes Two Layer solutions of UW and PFC (N=164) as well as HTK and PFC (N=3).

Exhibit 52
Islet Characteristics by Cold Ischemic Time (hrs)

	Cold Ischemic Time												Statistically significant at p < 0.05
	< 4 Hours			4-8 Hours			9-12 Hours			> 12 Hours			
	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	
Total packed cell volume infused (mL)	52	4.0	2.1	214	3.9	1.9	80	3.6	1.6	34	3.8	2.0	
Islet particle count	17	406,302	172,824	118	360,232	157,545	33	352,854	144,328	16	365,543	159,017	
Embedded islets (%)	47	18.0	19.7	145	16.1	17.8	58	11.6	17.7	23	9.7	12.9	
Islet equivalents/kg donor weight	55	5,141	2,701	225	4,748	1,810	78	4,172	1,408	33	5,333	1,843	*
Islet equivalents infused	49	405,207	128,141	219	433,733	144,688	82	422,330	136,634	34	456,866	144,965	
Beta cells ($x10^6$)	31	341.8	275.0	92	246.5	181.8	35	305.7	249.2	14	155.9	152.1	*
Beta cells ($x10^6$)/kg donor weight	31	4.0	3.9	92	3.1	2.4	33	3.8	3.0	13	2.3	2.5	
Insulin content (µgrams)	39	3,359	2,078	116	2,959	1,899	41	3,232	2,211	18	3,269	1,627	
DNA content (µgrams)	39	9,085	10,421	111	8,435	9,775	43	5,675	6,313	17	3,951	2,427	*
Endotoxin units	41	27.4	44.7	194	20.3	32.4	66	30.4	72.5	24	28.6	38.6	
Endotoxin units/kg donor weight	41	0.3	0.5	194	0.3	0.5	64	0.4	0.9	24	0.3	0.5	
Islet purity: Dithizone positive cells (%)	26	62.8	18.3	139	64.4	14.9	40	66.7	16.5	21	68.1	14.0	
Islet potency: Stimulation index	50	4.3	4.7	206	3.2	3.2	77	4.2	4.6	33	2.8	2.2	*
Islet viability: Fluorescein Diacetate/Propidium Iodide (%)	15	95.1	3.7	96	93.0	6.4	35	92.3	5.9	20	91.3	7.0	
Islet viability: Syto Green 13 (%)	19	86.8	6.9	62	85.4	6.8	31	85.6	7.3	5	85.8	12.7	

Exhibit 53
Islet Characteristics by Islet Pretreatment Method

	Islet Pretreatment Method						Statistically significant at p < 0.05
	None			Culture			
	N	Mean	SD	N	Mean	SD	
Total packed cell volume infused (mL)	172	4.0	1.8	220	3.7	1.9	
Islet particle count	83	402,383	164,794	104	335,383	143,330	*
Embedded islets (%)	122	13.4	16.0	163	16.8	19.5	
Islet equivalents/kg donor weight	176	5,002	1,998	233	4,470	1,817	*
Islet equivalents infused	172	430,350	144,513	227	428,280	136,809	
Beta cells ($x10^6$)	86	152.0	133.3	86	384.7	224.6	*
Beta cells ($x10^6$)/kg donor weight	83	2.0	1.9	86	4.7	3.1	*
Insulin content (µgrams)	114	3,057	1,938	101	3,168	2,001	
DNA content (µgrams)	110	5,608	6,465	103	9,708	10,632	*
Endotoxin units	118	24.9	40.1	221	22.3	46.8	
Endotoxin units/kg donor weight	118	0.3	0.4	219	0.3	0.6	
Islet purity: Dithizone positive cells (%)	105	65.8	16.8	138	64.6	14.9	
Islet potency: Stimulation index	160	3.2	3.6	217	3.7	3.9	
Islet viability: Fluorescein Diacetate/Propidium Iodide (%)	75	93.9	5.7	108	92.4	6.3	
Islet viability: Syto Green 13 (%)	17	86.1	7.8	100	85.7	7.1	

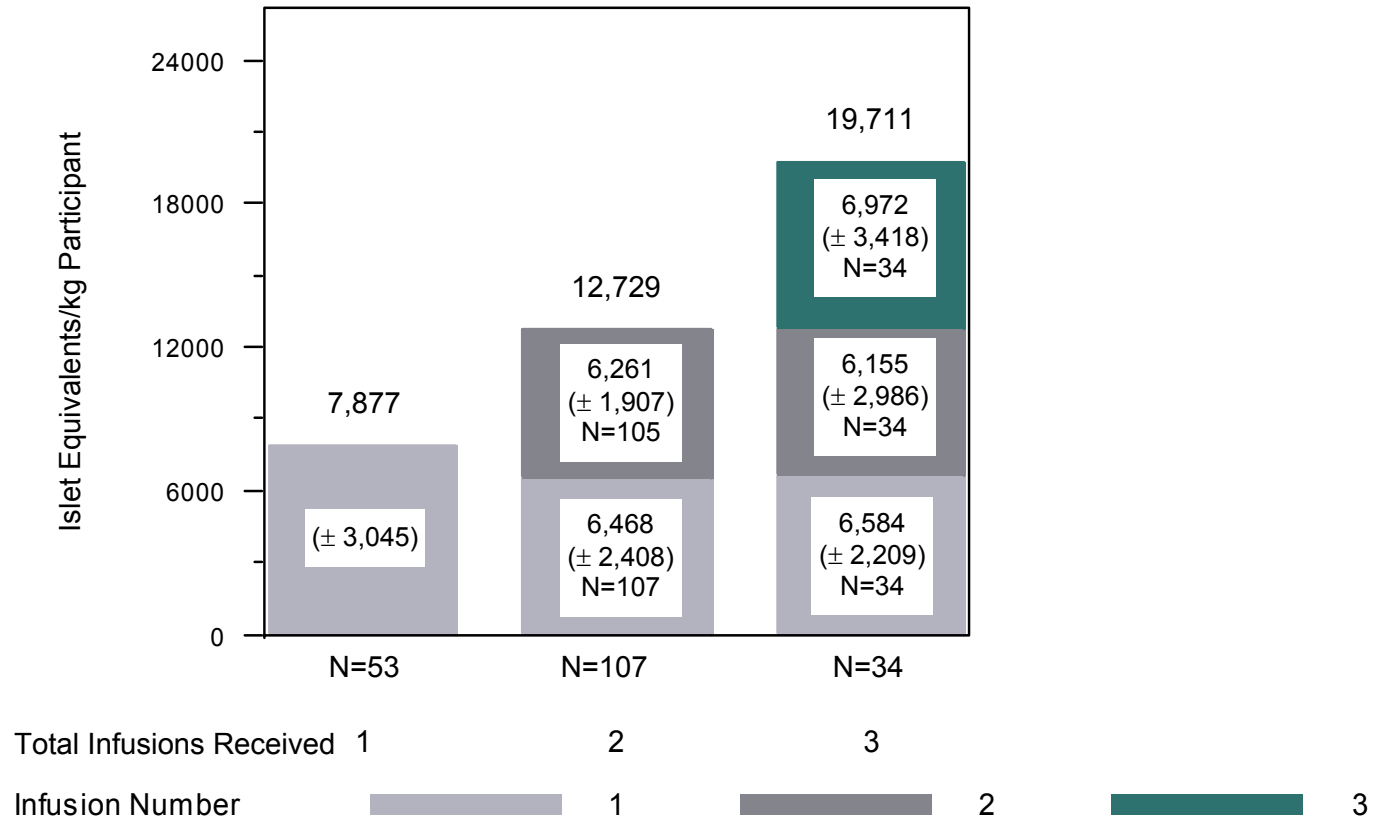
Exhibit 54
Islet Characteristics by Donor Age (yrs)

	Donor Age												Statistically significant at p < 0.05
	< 41 Years			41-50 Years			51-60 Years			> 60 Years			
	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	
Total packed cell volume infused (mL)	141	4.0	2.2	133	3.8	1.7	93	3.5	1.7	26	3.7	1.5	
Islet particle count	63	348,752	160,878	71	374,202	145,180	45	369,420	167,430	7	408,204	177,101	
Embedded islets (%)	94	19.7	21.1	99	15.0	18.1	71	12.2	14.7	20	7.9	8.5	*
Islet equivalents/kg donor weight	146	4,808	2,302	143	4,695	1,665	96	4,604	1,654	24	4,437	1,702	
Islet equivalents infused	143	439,392	163,192	137	443,168	130,771	94	402,666	114,749	26	395,854	113,306	
Beta cells ($x10^6$)	59	299.6	228.4	58	248.7	192.2	39	238.4	227.8	16	297.5	243.9	
Beta cells ($x10^6$)/kg donor weight	58	3.5	2.6	58	3.2	2.6	38	2.9	2.6	15	4.7	4.8	
Insulin content (µgrams)	73	2,890	1,929	72	3,297	1,826	52	3,085	1,950	18	3,318	2,657	
DNA content (µgrams)	73	9,505	11,962	73	7,762	7,837	49	5,627	5,420	18	4,474	3,515	*
Endotoxin units	120	20.3	36.8	117	29.7	60.0	80	20.3	29.8	20	15.3	24.9	
Endotoxin units/kg donor weight	120	0.3	0.5	117	0.3	0.7	80	0.2	0.3	20	0.2	0.3	
Islet purity: Dithizone positive cells (%)	92	66.8	15.7	87	64.3	15.9	55	63.8	15.6	7	68.9	15.4	
Islet potency: Stimulation index	136	4.0	4.8	125	3.4	3.3	92	2.8	2.3	22	3.3	4.0	
Islet viability: Fluorescein Diacetate/Propidium Iodide (%)	73	93.4	5.7	68	94.0	5.4	35	90.1	7.4	5	92.2	8.6	*
Islet viability: Syto Green 13 (%)	36	86.0	5.8	37	84.4	8.6	30	87.1	6.6	14	85.4	7.8	

Exhibit 55
Islet Characteristics by Donor Body Mass Index (kg/m^2)

	Body Mass Index												Statistically significant at p < 0.05
	< 26			26-30			31-35			> 35			
	N	Mean	SD	N	Mean	SD	N	Mean	SD	N	Mean	SD	
Total packed cell volume infused (mL)	136	3.9	2.1	130	3.7	1.8	74	3.8	1.8	47	3.9	1.4	
Islet particle count	51	343,900	150,387	69	353,166	123,521	39	410,654	193,157	27	374,010	179,352	
Embedded islets (%)	93	14.5	18.9	97	15.1	18.0	58	14.9	18.1	30	19.1	18.0	
Islet equivalents/kg donor weight	139	5,119	2,195	137	4,666	1,926	79	4,404	1,496	51	4,049	1,356	*
Islet equivalents infused	137	395,768	120,058	134	427,150	133,667	76	461,342	148,567	47	487,181	173,088	*
Beta cells (x10^6)	57	258.1	200.2	61	263.6	217.7	29	298.5	258.1	19	316.7	224.9	
Beta cells (x10^6)/kg donor weight	57	4.0	3.5	61	3.1	2.5	29	3.2	3.0	19	2.7	1.8	
Insulin content (µgrams)	73	2,834	1,588	77	3,045	1,865	37	3,257	2,446	22	3,696	2,516	
DNA content (µgrams)	69	7,621	7,494	76	8,559	11,394	39	5,382	4,607	23	9,000	9,916	
Endotoxin units	112	22.7	31.3	109	25.8	60.4	69	16.0	24.2	47	29.5	51.1	
Endotoxin units/kg donor weight	112	0.3	0.6	109	0.3	0.7	69	0.2	0.3	47	0.3	0.5	
Islet purity: Dithizone positive cells (%)	68	65.6	14.4	83	66.3	16.5	55	64.2	16.3	35	63.7	15.6	
Islet potency: Stimulation index	131	3.3	3.7	126	3.4	3.4	68	3.8	3.8	44	3.4	3.8	
Islet viability: Fluorescein Diacetate/Propidium Iodide (%)	52	91.9	6.8	63	93.2	5.0	43	94.0	6.2	23	93.0	7.3	
Islet viability: Syto Green 13 (%)	52	85.6	7.1	34	86.0	6.9	17	85.7	7.4	13	84.5	8.3	

Exhibit 56
Mean Number of Islet Equivalents/kg Participant (± SD) by Total Number of Infusions Received
(Participants with a Total of 1 Infusion, 2 Infusions, and 3 Infusions)*



* Nine participants were excluded from this Exhibit, as they did not have islet equivalents reported and/or were missing a reported participant weight.

Chapter 3
Immunosuppressive and Other Medications

Immunosuppressive and Other Medications Summary

Immunosuppressive, anti-hypertensive, and lipid lowering medications, as well as a summary of the administration of adjunctive therapies used by the islet transplant recipients are included in this chapter of the report. The majority of the islet transplant alone recipients at the time of first infusion were on a Daclizumab, Sirolimus, and Tacrolimus immunosuppression regimen (61.1%). A number of other immunosuppression regimens (N=18) have been used by the islet transplant centers and are listed in Exhibit 57.

A summary of T-cell antibodies used for the participant's first infusion is displayed in Exhibit 58. Daclizumab was the only T-cell antibody used in over 77% of first infusions. Dosing for the immunosuppressive medications at induction (dosing by mg/day and the mean total dose) are located in Exhibits 59 and 60. Maintenance therapy regimens and dosing information are located in Exhibits 61 and 62. Sirolimus and Tacrolimus trough levels at Day 30 for each infusion (1, 2, and 3), as well as trough levels at Month 6 and Year 1 post last infusion are presented as boxplots in Exhibits 63 and 64. There is one extreme Sirolimus trough level at Day 30 for the third infusion (61.8 ng/mL) that is explained by the center as the participant taking Sirolimus shortly before having labs drawn.

Prior to the first infusion, almost 39% of the recipients were on at least one anti-hypertensive medication (Exhibits 65 and 66) and over 24% were on a lipid lowering medication (Exhibits 67 and 68). By Year 1 post last infusion, these rates increased to over 48% and over 63%, respectively. Percentages are based on participants with complete medication information. For adjunctive therapies, at the time of their first infusion (Exhibit 69), over 98% of recipients used an antibiotic, 92.5% used antivirals, 88.9% used Heparin (including Heparin used during the infusion procedure), and 87.4% used vitamin supplements. The most common adjunctive therapies used during follow-up (Exhibit 70) included vitamin supplements (11.9% at Month 6 and 11.0% at Year 1) and Pentoxifylline (9.3% at Month 6).

Exhibit 57
Immunosuppression Regimen at Time of First Infusion

	Overall	
	N	%
Total	203	100.0
Sirolimus + Tacrolimus + Daclizumab	124	61.1
Sirolimus + Tacrolimus + Daclizumab + Infliximab	17	8.4
Sirolimus + Tacrolimus + Daclizumab + Alemtuzumab	9	4.4
Sirolimus + Tacrolimus + Daclizumab + Etanercept	1	0.5
Sirolimus + Tacrolimus + Daclizumab + 15-deoxyspergualin	5	2.5
Sirolimus + Tacrolimus + Daclizumab + Anti-thymocyte Globulin	3	1.5
Sirolimus + Tacrolimus + Daclizumab + MMF	3	1.5
Sirolimus + Daclizumab + MMF + Anti-thymocyte Globulin	1	0.5
Sirolimus + Tacrolimus + Daclizumab + MMF + Methylprednisolone + Anti-thymocyte Globulin + Etanercept	5	2.5
Sirolimus + Tacrolimus + Daclizumab + MMF + Methylprednisolone + Anti-thymocyte Globulin + Infliximab + Etanercept	2	1.0
Sirolimus + Tacrolimus	1	0.5
Sirolimus + Tacrolimus + hOKT3γ-1 (Ala-Ala)	3	1.5
Sirolimus + Tacrolimus + Basiliximab + Etanercept	9	4.4
Sirolimus + Tacrolimus + Alemtuzumab + Etanercept	3	1.5
Sirolimus + Tacrolimus + Anti-thymocyte Globulin + Intravenous Immunoglobulin	1	0.5
Sirolimus + MMF + Methylprednisolone + Anti-thymocyte Globulin	1	0.5
Neoral Cyclosporine + Everolimus + Anti-thymocyte Globulin + Etanercept	1	0.5
Neoral Cyclosporine + Methylprednisolone + Anti-thymocyte Globulin + Etanercept	1	0.5
Neoral Cyclosporine + Methylprednisolone + Everolimus + Anti-thymocyte Globulin + Etanercept	4	2.0
Missing Information on Immunosuppression	9	4.4

Exhibit 58
Summary of T Cell Antibodies Used During First Infusion for Induction Therapy

	N	%
Total	194	100.0
Daclizumab Alone	150	77.3
Anti-thymocyte Globulin and Daclizumab	11	5.7
Alemtuzumab and Daclizumab	9	4.6
Basiliximab Alone	9	4.6
Anti-thymocyte Globulin Alone	8	4.1
hOKT3γ-1(Ala-Ala) Alone	3	1.5
Alemtuzumab Alone	3	1.5
None	1	0.5

Exhibit 59
Immunosuppression Dosing (mg/day) at Time of Infusion by Infusion Sequence

	Infusion Sequence								
	Infusion 1			Infusion 2			Infusion 3		
	N	Mean	SD	N	Mean	SD	N	Mean	SD
Sirolimus (mg/day)	183	11.5	3.0	88	8.4	3.2	31	8.5	3.5
Tacrolimus (mg/day)	181	2.1	1.2	93	4.1	2.1	32	4.5	2.1
MMF (mg/day)	12	1270.8	779.4	9	1333.3	661.4	8	1125.0	744.0
Methylprednisolone (mg/day)	13	81.1	54.6	0	-	-	0	-	-
Neoral Cyclosporine (mg/day)	6	216.7	66.5	1	200.0	-	0	-	-
15-deoxyspergualin (mg/day)	5	117.6	9.5	4	111.0	14.3	2	107.0	9.9
Everolimus (mg/day)	5	3.0	0.0	4	2.3	0.5	0	-	-
Mycophenolic Acid (mg/day)	0	-	-	1	1440.0	-	1	1440.0	-

Exhibit 60
Induction Therapy at Time of Infusion by Infusion Sequence

	Infusion Sequence								
	Infusion 1			Infusion 2			Infusion 3		
	N	Mean Total Dose	SD	N	Mean Total Dose	SD	N	Mean Total Dose	SD
Daclizumab (mg/kg)	120	4.2	1.4	78	4.6	1.4	27	4.6	1.3
Etanercept (mg)	26	133.7	21.1	14	137.5	19.0	3	108.3	52.0
Anti-thymocyte Globulin (mg/kg)	15	5.8	0.6	0	-	-	0	-	-
Infliximab (mg/kg)	12	7.7	2.4	0	-	-	1	10.0	-
Basiliximab (mg)	9	37.8	6.7	4	40.0	0.0	0	-	-
hOKT3γ-1 (Ala-Ala) (mg/kg)	3	0.8	0.0	0	-	-	0	-	-
Alemtuzumab (mg)	3	33.3	11.5	2	40.0	0.0	0	-	-

Exhibit 61
Immunosuppression Therapy Use Post Last Infusion

	Follow-Up			
	1-6 Months		6-12 Months	
	N	%	N	%
Total	193	100.0	163	100.0
Sirolimus	1	0.5	-	0.0
Tacrolimus	3	1.6	-	0.0
Sirolimus + Tacrolimus	93	48.2	70	42.9
Sirolimus + Tacrolimus + Daclizumab	14	7.3	12	7.4
Sirolimus + Tacrolimus + MMF	15	7.8	13	8.0
Sirolimus + Tacrolimus + Anti-thymocyte Globulin	1	0.5	-	0.0
Sirolimus + MMF + Daclizumab	2	1.0	-	0.0
Sirolimus + MMF	3	1.6	6	3.7
Sirolimus + MMF + Anti-thymocyte Globulin + Daclizumab	1	0.5	-	0.0
Tacrolimus + MMF	12	6.2	10	6.1
Neoral Cyclosporine + MMF	-	0.0	-	0.0
Neoral Cyclosporine + Everolimus	4	2.1	2	1.2
Mycophenolic Acid + Neoral Cyclosporine	1	0.5	-	0.0
Mycophenolic Acid + Neoral Cyclosporine + Everolimus	1	0.5	-	0.0
No Immunosuppressant Medications Taken*	8	4.7	8	4.9
Missing Information on Immunosuppression**	34	17.6	42	25.8

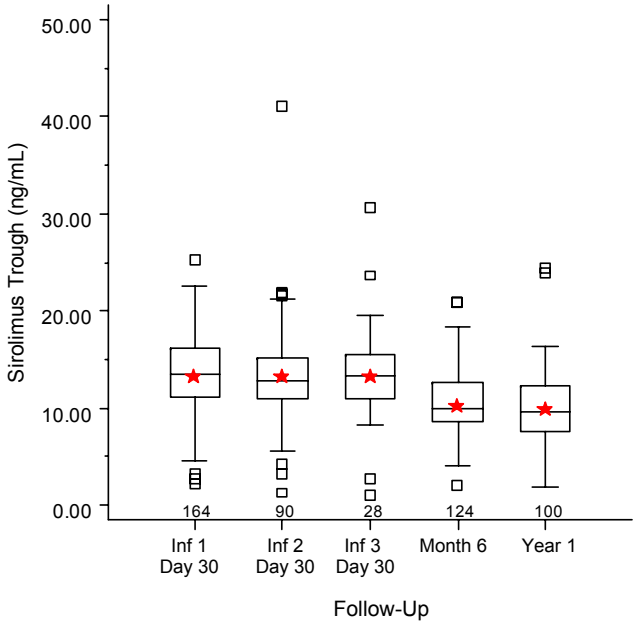
*One participant, C-Peptide status unknown, withdrew from therapy due to immunosuppression therapy side effects. All other participants were C-Peptide negative at time of follow-up.

**Majority of missing information due to unsubmitted follow-up forms to the Registry as of the datafile closure.

Exhibit 62
Immunosuppression Dosing Post Last Infusion

	Follow-Up								
	Day 30			Month 6			Year 1		
	N	Mean	SD	N	Mean	SD	N	Mean	SD
Sirolimus (mg/day)	137	7.9	3.4	129	7.1	3.2	101	6.6	3.1
Tacrolimus (mg/day)	139	3.7	1.8	137	3.6	1.9	105	3.5	1.6
MMF (mg/day)	22	1090.9	811.2	33	1363.6	667.6	29	1474.1	552.4
Methylprednisolone (mg/day)	9	0.0	0.0	0	-	-	0	-	-
Neoral Cyclosporine (mg/day)	6	295.8	158.4	6	341.7	100.8	2	300.0	70.7
15-deoxyspergualin (mg/day)	5	0.0	0.0	0	-	-	0	-	-
Everolimus (mg/day)	5	3.5	1.6	5	3.7	1.8	2	328.0	455.4
Daclizumab (mg/kg)	0	-	-	14	1.3	1.1	11	1.0	0.0
Mycophenolic acid (mg/day)	0	-	-	2	1440.0	0.0	0	-	-
Anti-thymocyte Globulin (mg/kg)	0	-	-	1	7.5	-	0	-	-

Exhibit 63
Sirolimus Trough Level (ng/mL) Post Last Infusion



Value of 61.8 ng/mL excluded from graph for presentation, verified correct by center.

Exhibit 64
Tacrolimus Trough Level (ng/mL) Post Last Infusion

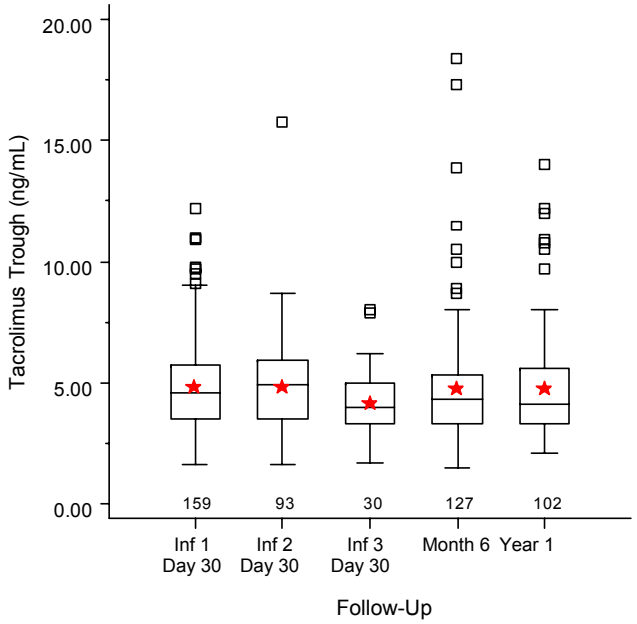


Exhibit 65
Use of Anti-Hypertensive Medications at Pre Infusion and Post Last Infusion

	Follow-Up					
	Pre Infusion 1		Month 6		Year 1	
	N	%	N	%	N	%
Total	203	100.0	193	100.0	163	100.0
ACE Inhibitors	65	32.0	57	29.5	47	28.8
Alpha Adrenergic Blockers	-	0.0	1	0.5	1	0.6
Angiotensin II Receptor Blockers	12	5.9	8	4.1	8	4.9
Beta Adrenergic Blockers	6	3.0	6	3.1	7	4.3
Calcium Channel Blockers	4	2.0	6	3.1	6	3.7
Diuretics	6	3.0	17	8.8	18	11.0
None	121	59.6	86	44.6	62	38.0
Missing Information on Medications	6	3.0	39	20.2	43	26.4

Exhibit 66
Percent of Participants Using Anti-Hypertensive Medications at Pre Infusion and Post Last Infusion

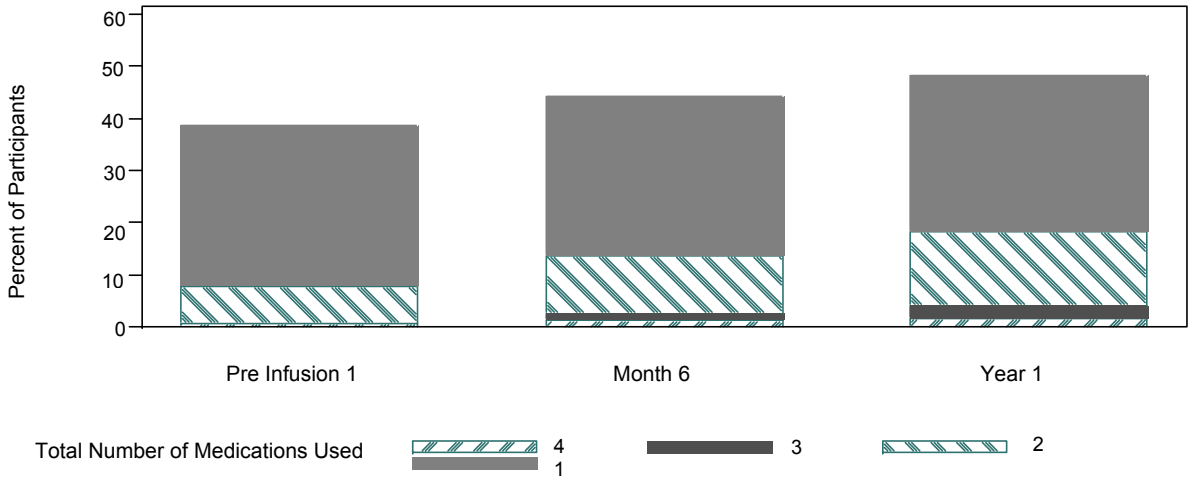


Exhibit 67
Use of Lipid Lowering Medications Pre Infusion and Post Last Infusion

	Follow-Up					
	Pre Infusion 1		Month 6		Year 1	
	N	%	N	%	N	%
Total	203	100.0	193	100.0	163	100.0
Bile Acid Sequestrants	-	0.0	2	1.0	1	0.6
Cholesterol Absorption Inhibitors	2	1.0	-	0.0	2	1.2
HMG CoA Reductase Inhibitors	48	23.6	79	40.9	70	42.9
Nicotinic Acid	-	0.0	6	3.1	4	2.5
None	148	72.9	72	37.3	44	27.0
Missing Information on Medications	6	3.0	38	19.7	43	26.4

Exhibit 68
Percentage of Participants Using Lipid Lowering Medications at Pre Infusion and Post Last Infusion

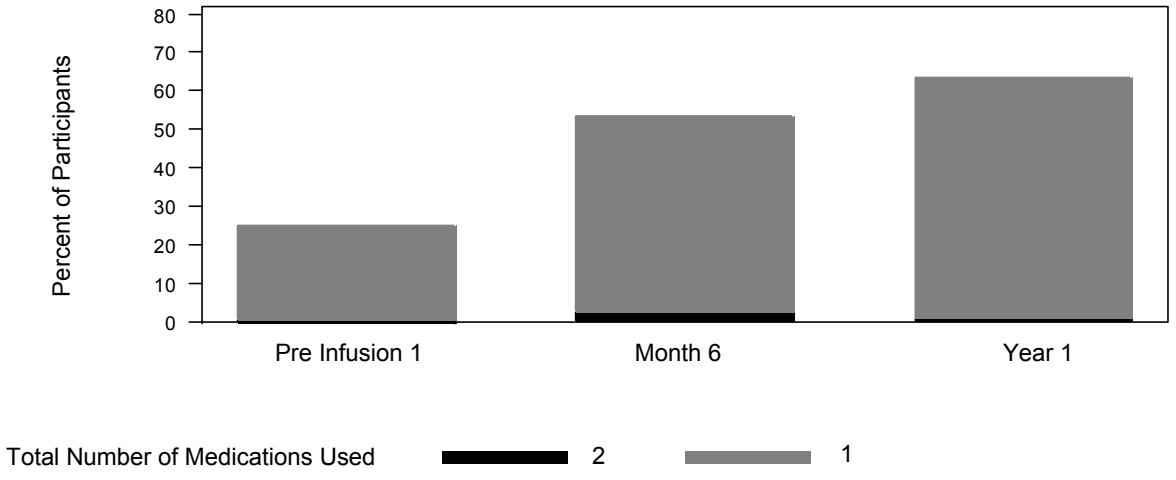


Exhibit 69
Adjunctive Therapy Used at Time of First Infusion

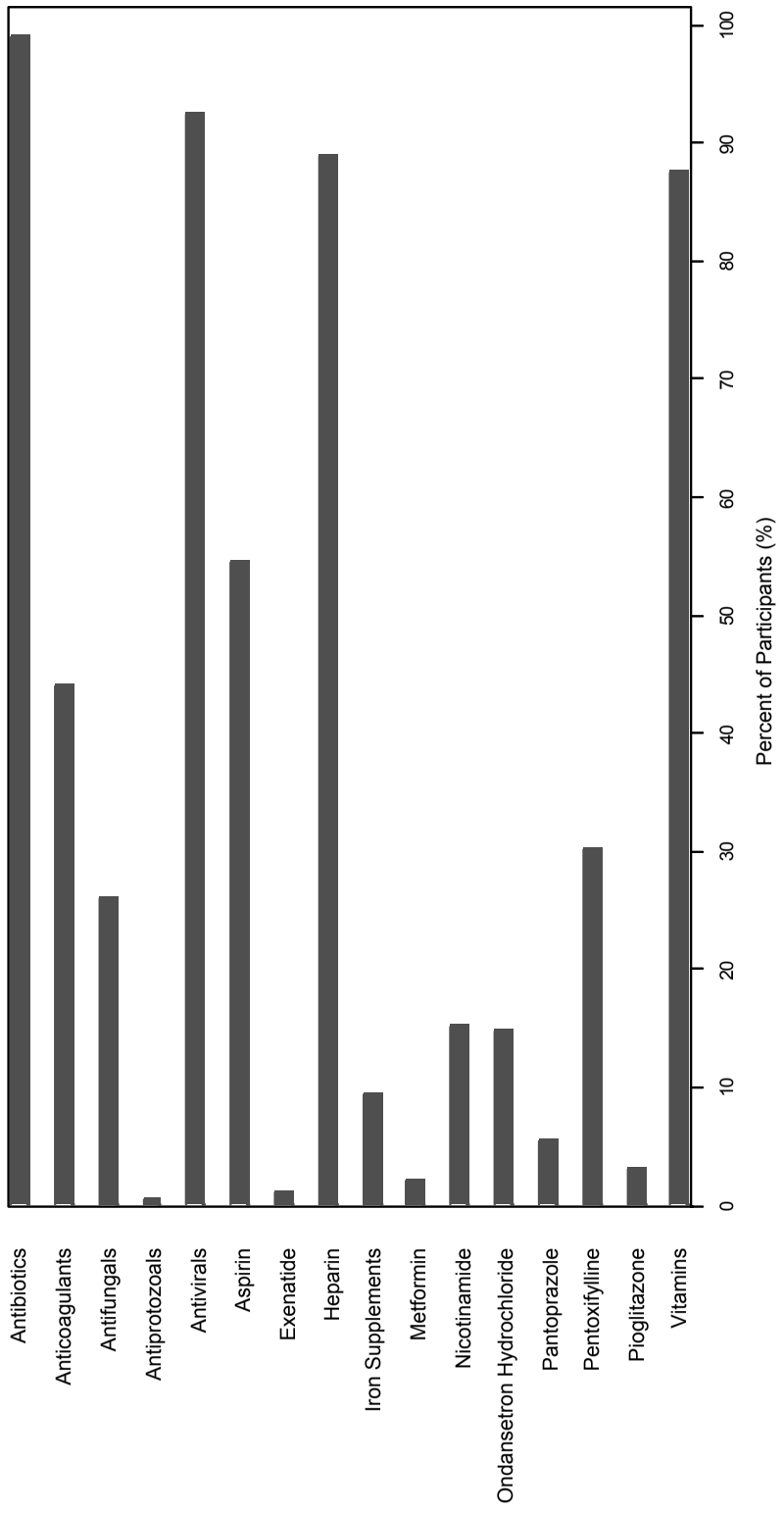


Exhibit 70
Adjunctive Therapy Used During Follow-Up
Post Last Infusion

	Follow-Up			
	Month 6		Year 1	
	N	%	N	%
Total	193	100.0	163	100.0
Chromium picolinate				
Yes	1	0.5	-	0.0
No	154	79.8	118	72.4
Unknown	38	19.7	45	27.6
Vitamins				
Yes	23	11.9	18	11.0
No	132	68.4	100	61.3
Unknown	38	19.7	45	27.6
Pentoxifylline				
Yes	18	9.3	-	0.0
No	137	71.0	118	72.4
Unknown	38	19.7	45	27.6
Rosiglitazone				
Yes	3	1.6	2	1.2
No	152	78.8	116	71.2
Unknown	38	19.7	45	27.6
Pioglitazone				
Yes	2	1.0	1	0.6
No	153	79.3	117	71.8
Unknown	38	19.7	45	27.6
Metformin				
Yes	7	3.6	1	0.6
No	148	76.7	117	71.8
Unknown	38	19.7	45	27.6

Exhibit 70 *(continued)*
Adjunctive Therapy During Follow-Up
Post Last Infusion

	Follow-Up			
	Month 6		Year 1	
	N	%	N	%
Iron				
Yes	3	1.6	5	3.1
No	152	78.8	113	69.3
Unknown	38	19.7	45	27.6
Magnesium				
Yes	-	0.0	2	1.2
No	155	80.3	116	71.2
Unknown	38	197	45	27.6

Chapter 4
Graft Function

Graft Function Summary

Chapter 4 includes information on the analysis of graft function for the 203 islet transplant alone participants reported to the Registry.

Insulin Independence:

Insulin status is collected from the day of the participant's first infusion procedure and throughout follow-up. Any changes in insulin status from going on insulin to coming off insulin are recorded. A change from insulin dependence to independence requires at least 14 consecutive days of insulin independence. A change from insulin independence to insulin dependence requires a minimum of 14 consecutive days of insulin use. Average daily insulin use is recorded for periods of insulin use before and after subsequent infusion procedures, changes in islet graft function, and all CITR follow-up visits.

This chapter evaluates insulin independence both post first infusion and post last infusion in several different ways:

- Summary of insulin independent participants at Month 6 and Year 1 post first infusion and post last infusion (Exhibit 71),
- Participant's insulin status post last infusion by the total number of infusions received (Exhibit 72),
- Percent of participants ever achieving insulin independence (Exhibits 73-74),
- Percent of insulin independent participants and their rate of return to insulin use (Exhibits 75-76),
- Percent of participants reaching defined outcome levels (Exhibit 77),
- By follow-up visit post last infusion (Exhibit 78),
- By insulin independence rate calculated each day post last infusion (Exhibits 79 and 80),
- Identifying differences in insulin independence rates by the participant's weight and average daily insulin use at baseline (Exhibits 86 and 87),
- Summarizing differences in insulin independence rates by the participant and donor characteristics (Exhibit 88),
- Summarizing differences in insulin independence rates by the participant baseline basal values of C-peptide, HbA_{1C}, and defined outcome levels (Exhibit 89-92),
- Summarizing differences in insulin independence rates by immunosuppression regimen used at first infusion (Exhibit 115) and for participants switching immunosuppression regimens during follow-up (Exhibit 116 and 117),
- Summarizing differences in immunosuppression trough level for insulin independent versus insulin dependent participants (Exhibits 118 and 119),

- Summarizing differences in fasting plasma glucose, HbA_{1C}, and basal C-peptide post last infusion for participants who ever achieved insulin independence versus those who did not (Exhibits 132-137),

- Summarizing differences in fasting plasma glucose, HbA_{1C}, and basal plasma C-peptide post first infusion for insulin independent participants compared to insulin dependent participants (Exhibits 138-146), and

- Summarizing differences in metabolic test results by insulin status (Exhibits 149-150).

After the first infusion procedure is performed, 50.0% of the participants were insulin independent six months later, with 49.4% insulin independent at one year following this first infusion. When analyzing insulin independence rates after the participant's last infusion procedure, 56.7% were insulin independent at six months, while this rate drops to 51.4% at one year (Exhibit 71). At six months and one year post the last infusion procedure, participants with a total of two infusions have the highest insulin independence rates of 60.2% and 54.4%, respectively (Exhibit 72), compared to those with only one islet infusion (52.1% and 50.0%) and those with three islet infusions (54.8% and 46.4%).

When determining if a participant ever achieves insulin independence after receiving at least one islet infusion, Exhibit 73 displays that at one year 65.6% of the participants have achieved insulin independence for at least 14 consecutive days, and by year two this increases slightly to 69.7%. Exhibit 74 stratifies these rates by the number of infusions the participant received to achieve this outcome. Over time there is a decrease in the sustainability of insulin independence. For all participants whoever achieved insulin independence, only 67.5% have remained in this status one year after achieving it and this decreases to 43.3% at two years (Exhibit 75). This decline is also displayed by total number of infusion procedures conducted to achieve insulin independence (Exhibit 76). A decrease in insulin independence and sustainability is also seen in Exhibit 78, where at Day 75 post last infusion, rates are around 52%, then drop to 47% at one year and further drop to 33% at two years.

A number of new clinical islet protocols are being initiated in 2006 by an NIH sponsored consortium and they have specified some common outcomes definitions. Using these definitions, Exhibit 77 and Exhibits 91-112 examine the percent of participants reaching these specified clinical outcomes, their insulin status by the outcomes and then stratified by several participant characteristics in relation to these outcomes. In future reports it will be appropriate to compare results of the Registry with the data produced from these clinical islet protocols.

Changes in Insulin Dosing:

Exhibits 81-82 show the changes in insulin dosing at six months and one year post the last infusion. For participants remaining on insulin at six months and one year, Exhibit 85 shows the distribution of their daily insulin use (units/kg).

Severe Hypoglycemic Events:

As reported in last year's Annual Report, there continues to be a striking decrease in the number of severe hypoglycemic events that have occurred subsequent to the participant's first infusion procedure (Exhibit 113). Over 84% of participants experienced one or more severe hypoglycemic events in a 12 month period prior to their first infusion. This decreased to 2.5% up to 30 days post their first infusion and then to 3.1% in months 1-6 and months 6-12 post last infusion. Further, all participants that experienced a severe hypoglycemic event during follow-up were on insulin at the time of the event.

Metabolic Measures:

Presented in this chapter are the participant's fasting plasma glucose, HbA_{1C}, and basal C-peptide values at baseline and post last infusion follow-up visits (Exhibits 120-146). Overall, as expected, fasting plasma glucose values and HbA_{1C} decreased over time, while basal C-peptide values increased. This trend is seen within each of the cohort group of participants (with one, two and three infusions). Some of these patterns disappear when examining them by the participants' insulin status at follow-up visits and whether or not they ever achieved insulin independence.

The ratio of participant C-peptide (ng/mL *1000) to fasting blood glucose (mg/dL) was compared over time. There was a notable rise in this ratio from baseline (mean 1.0, SD 2.98) to Month 6 (mean 14.8, SD 14.23) and Year 1 (mean 14.2, SD 9.85) time points post last infusion for all participants. The ratio was higher for insulin independent participants at Month 6 (mean 17.5, SD 13.16) and Year 1 (mean 16.8, SD 10.21) than for insulin dependent participants at Month 6 (mean 7.1, SD 6.23) and Year 1 (mean 4.6, SD 5.23) post last infusion. Participants who ever achieved insulin independence post infusion experienced an increased rise in this ratio from baseline (mean 1.3, SD 3.56) to Month 6 (mean 17.1, SD 10.71) and Year 1 (mean 15.5, SD 8.00) post last infusion. The rise in the ratio was less for participants who never achieved insulin independence. For these participants, the ratio at baseline was less (mean 0.6, SD 1.34) as were the ratios at Month 6 (mean 5.0, SD 5.90) and Year 1 (mean 4.5, SD 5.54) post last infusion.

A complete set of laboratory values are summarized by infusion sequence in Exhibit 147. Additional metabolic test summaries are located in Exhibits 148-150. The choice of which metabolic tests to perform varies from center to center.

Changes In Islet Graft Function:

Summary of changes in islet graft function is located in Exhibit 151. Six months following a participant's last infusion, 3.6% of the participants (N=6) experienced complete islet graft failure and this increases to 6.4% (N=8) by one year. For the 121 participants with complete reporting of changes in islet graft function, there have been a total of 52 (43.0%) participants with a change in their graft function, and often the participant has multiple episodes of a change in graft function reported (Exhibit 152). However, only two of the episodes reported had adverse events associated with them. At the time of this report, a significant number of episodes of change in graft function remain unreported to the Registry. Exhibit 153 includes the time from last infusion to complete islet graft failure (N=32). On average, complete loss of islet graft function occurred 506 days (SD 429 days) after receiving their first islet infusion, while the median time to complete loss of islet function is 385 days.

Diabetes Related Secondary Complications:

Exhibits 154-155 is a review of the diabetes related secondary complications experienced by the participants prior to their first infusion procedure and at Month 6 and Year 1 post their last infusion procedure. It is the goal of the Registry to continue to track the occurrence of these complications across time to determine any trends.

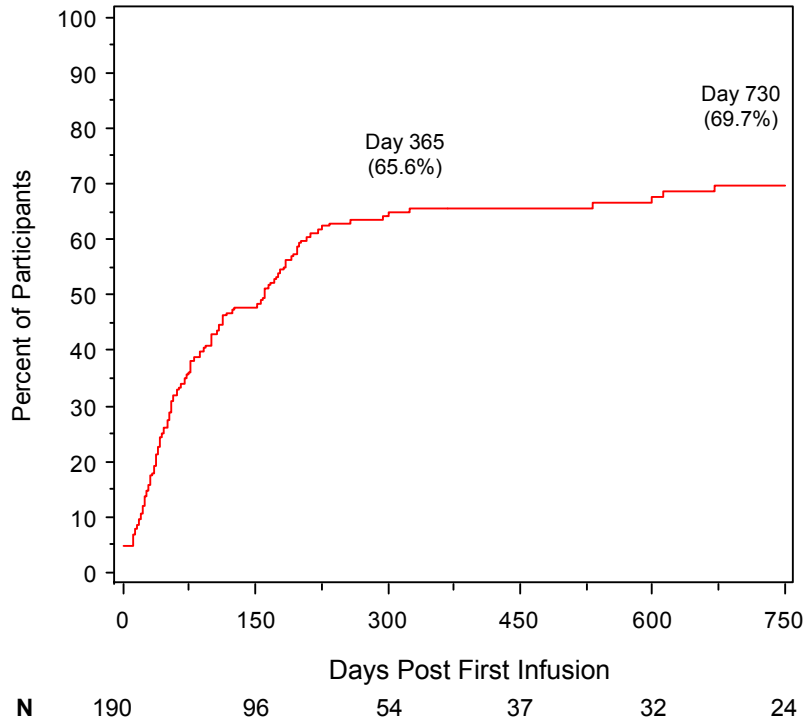
Exhibit 71
Participant's Insulin Status at Follow-Up
Post First and Last Infusion

	Follow-Up							
	Month 6				Year 1			
	Insulin Independent		Insulin Dependent		Insulin Independent		Insulin Dependent	
	N	%	N	%	N	%	N	%
Post First Infusion	94	50.0	94	50.0	83	49.4	85	50.6
Post Last Infusion	101	56.7	77	43.3	76	51.4	72	48.6

Exhibit 72
Participant's Insulin Status at Follow-Up Post Last Infusion
by Total Number of Infusions Received

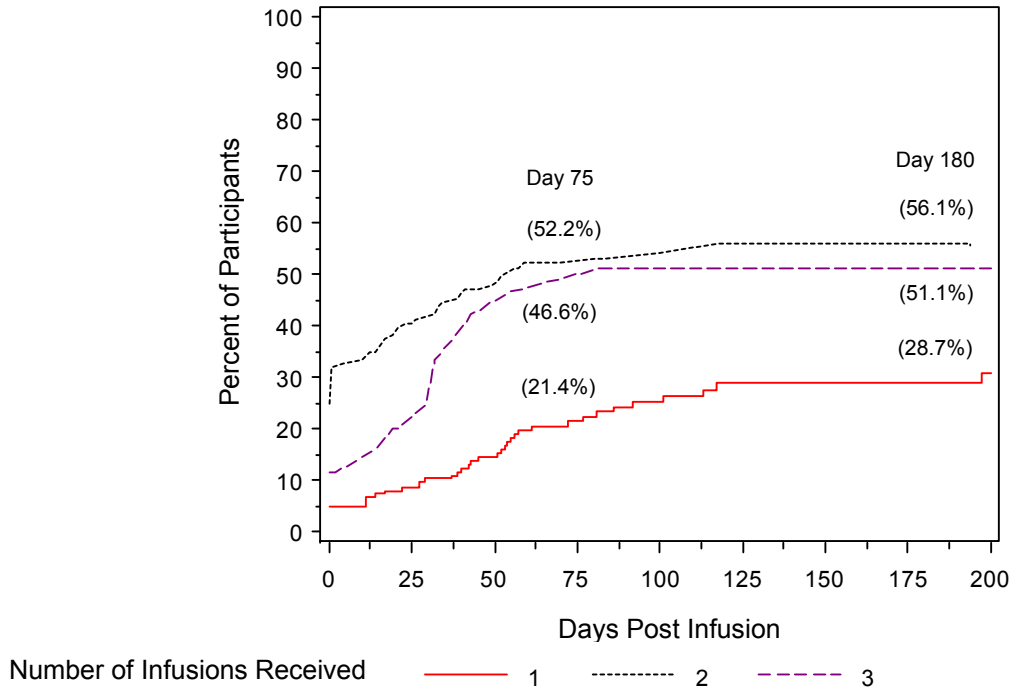
	Follow-Up							
	Month 6				Year 1			
	Insulin Independent		Insulin Dependent		Insulin Independent		Insulin Dependent	
	N	%	N	%	N	%	N	%
1 Infusion	25	52.1	23	47.9	20	50.0	20	50.0
2 Infusions	59	60.2	39	39.8	43	54.4	36	45.6
3 Infusions	17	54.8	14	45.2	13	46.4	15	53.6

Exhibit 73
Percent of Participants Ever Achieving Insulin Independence



This Exhibit displays the cumulative percent of participants who have ever achieved insulin independence after receiving their first islet infusion procedure. It does not represent the percentage of participants who remain insulin independent. A participant is counted as achieving insulin independence on the first day they achieve insulin independence and remain insulin free for 14 or more consecutive days. The day in which they became insulin independent is the first day of that insulin free span and that day is included in the analysis for this Exhibit. Five percent of the participants were reported as insulin independent on the day of their first infusion (Day 0).

Exhibit 74
Percent of Participants Ever Achieving Insulin Independence by the Infusion Received When Insulin Independence was Achieved



Timepoint	0	25	50	75	100	125	150	175	200
N1	190	161	115	89	68	55	51	43	34
N2	129	75	61	52	48	42	37	37	28
N3	26	18	13	12	11	11	11	11	11

This Exhibit displays the cumulative percent of participants who have ever achieved insulin independence stratified by the number of infusions the participant had received when insulin independence was first achieved. It does not represent the percentage of participants who remain insulin independent. A participant is counted as achieving insulin independence on the first day they achieve insulin independence and remain insulin free for 14 or more consecutive days. The day in which they became insulin independent is the first day of that insulin free span and that day is included in the analysis for this Exhibit. Some participants were reported as insulin independent on the day of infusion (Day 0). At the time of this analysis, none of the participants remaining on insulin were reported as insulin independent after 200 days post infusion procedure.

Exhibit 75
Time to Return to Insulin Dependence (≥ 14 Days of Insulin Use) Among Insulin Independent Participants

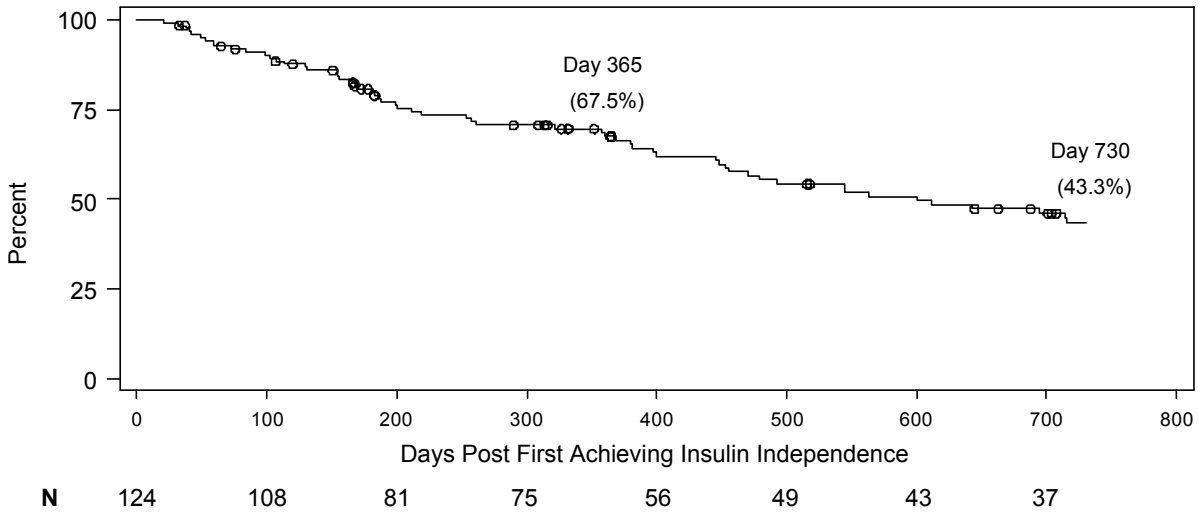
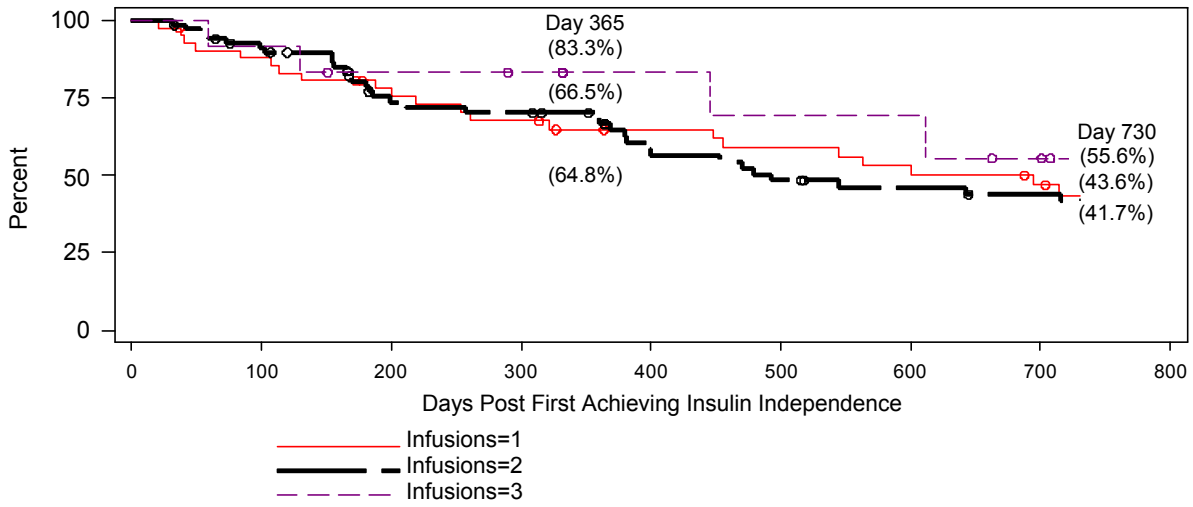


Exhibit 75 examines all insulin independent participants starting on the first day they achieve insulin independence for 14 or more consecutive days, and follows them over time noting if and when they return to insulin use (for 14 or more consecutive days). According to this analysis, by Day 365 after first achieving insulin independence, 67.5% of participants remain insulin independent and by Day 730, 43.3% remain insulin independent.

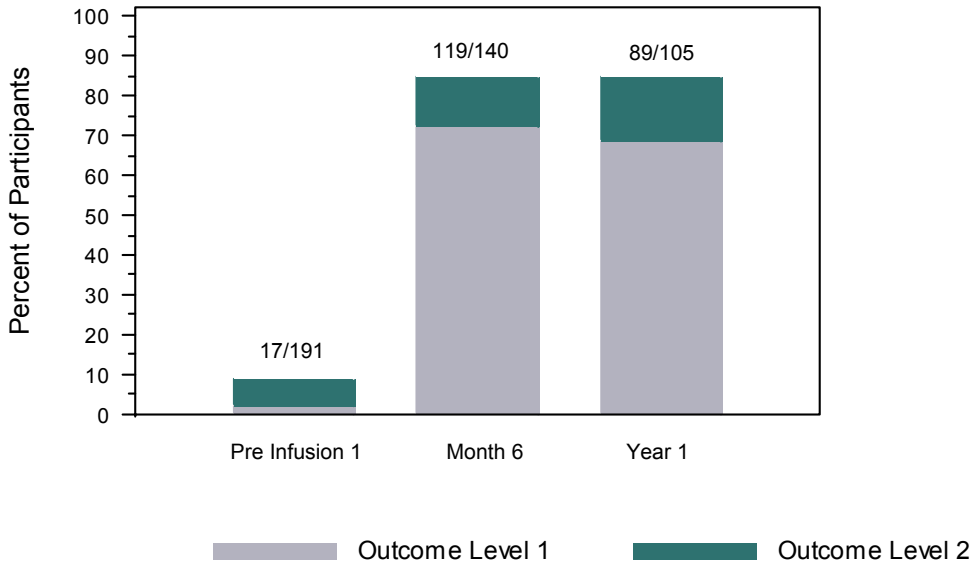
Exhibit 76
Time to Return to Insulin Dependence (≥ 14 Days of Insulin Use) Stratified by Total Number of Infusions Needed to First Achieve Insulin Independence Among Insulin Independent Participants



Timepoint	0	100	200	300	400	500	600	700
N1	42	36	29	26	22	20	17	15
N2	70	61	43	41	28	24	21	19
N3	12	11	9	8	6	5	5	3

Exhibit 76 is a similar analysis as was executed in Exhibit 75, but here sustainability of insulin independence is examined by the total number of infusion procedures required per participant to gain insulin independence. At Day 365, 83.3% of those who received three islet infusions remained insulin independent, while rates were similar for those who received one or two islet infusions (64.8% and 66.5%, respectively). By Day 730, sustainability of insulin independence drops to 55.6% for those who received three infusions, 43.6% for those with one infusion, and 41.7% for those who received two infusions. However, sample sizes are small for participants, especially those with three infusions, and the rates may be unstable.

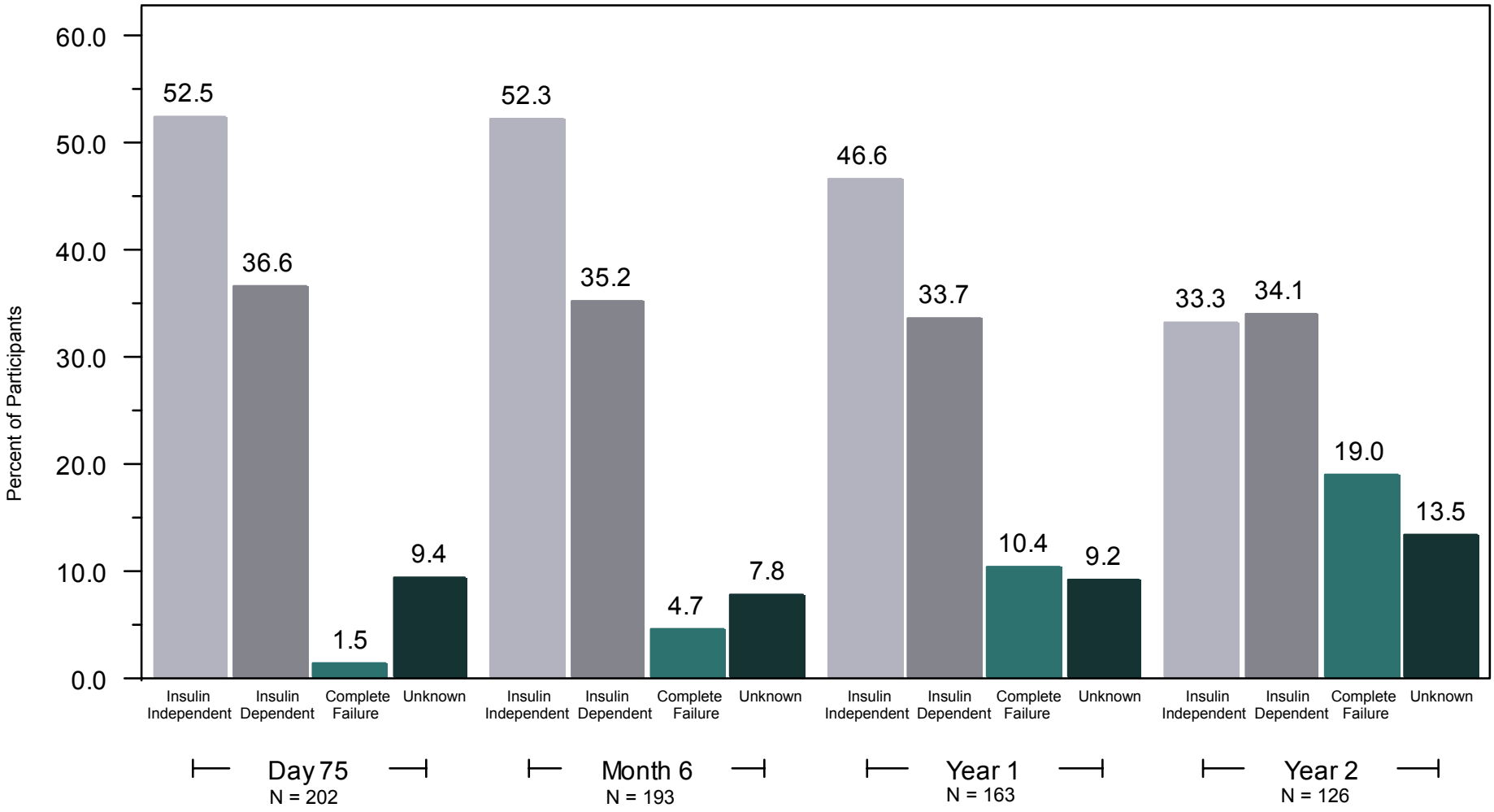
Exhibit 77
Percent of Participants by Outcome Level
at Follow-Up Post Last Infusion



Outcome Level 1 = No hypoglycemic episodes and $HbA_{1C} \leq 6.5\%$,
Outcome Level 2 = No hypoglycemic episodes and $6.5\% < HbA_{1C} \leq 7.5\%$

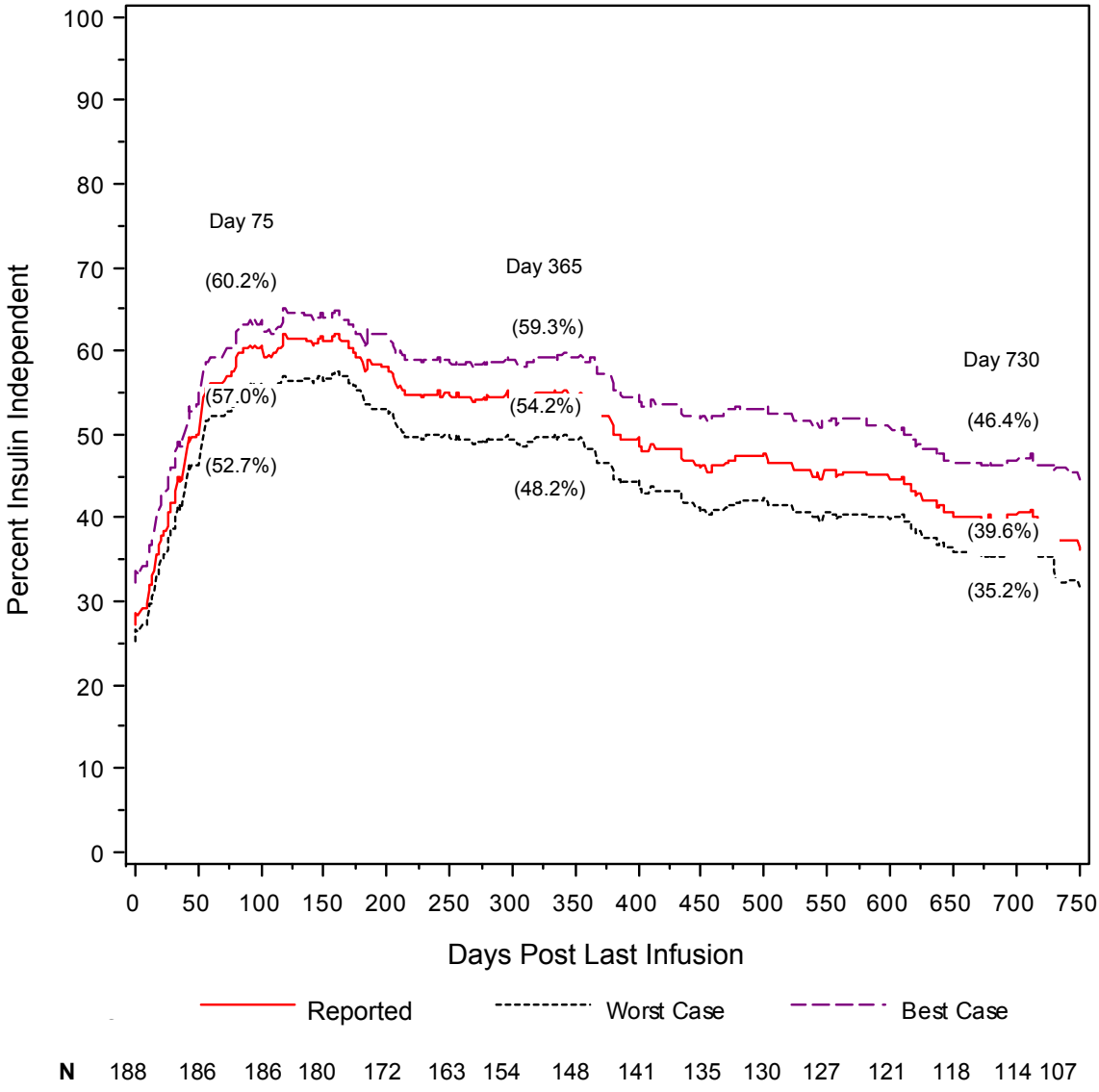
The outcome categories presented in this Exhibit do not represent goals of islet transplantation. The levels were constructed from categories defined in upcoming islet transplantation clinical trials sponsored by an NIH consortium and represent different degrees of glycemic control. Median follow-up time for islet alone participants is 12 months. Mean basal C-peptide for participants in Outcome Level One is 1.7 ng/mL (SD 1.23) at Month 6 and 1.6 ng/mL (SD 0.87) at Year 1. For participants in Outcome Level Two, mean basal C-peptide is 1.1 ng/mL (SD 0.88) at Month 6 and 0.9 ng/mL (SD 0.78) at Year 1.

Exhibit 78
Insulin Status (%) by Follow-Up Visit
Post Last Infusion



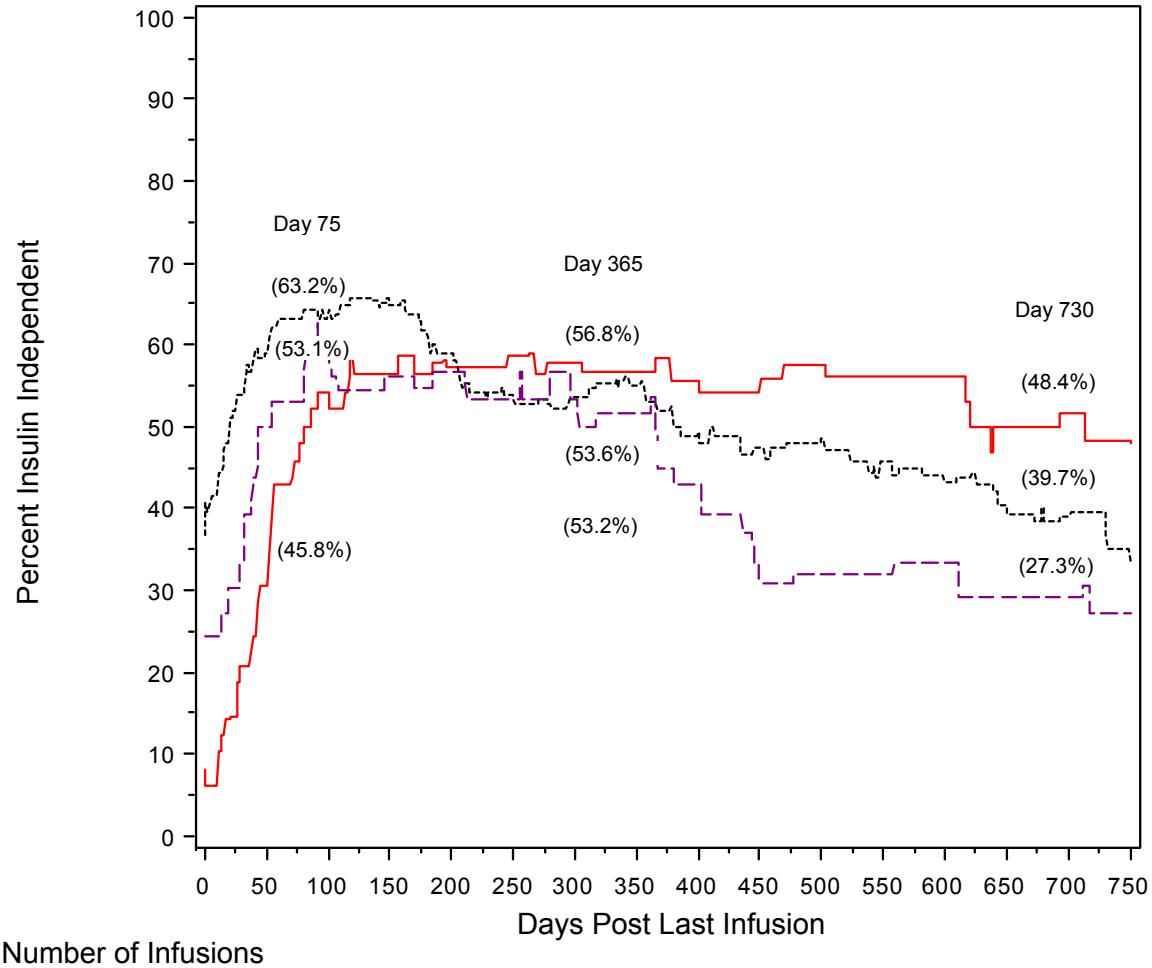
At the time of this report, the CITR database may be missing a significant number of islet graft failure reports.

Exhibit 79
Percent of Insulin Independent Participants Post Last Infusion



"Reported" is the percentage of participants that are insulin independent at the given time points post last infusion, based on the information provided to the Registry. "Best Case" is the representation where all missing data are classified as participants that are insulin independent. "Worst Case" is the representation where all missing data are classified as participants that are insulin dependent. For example, on Day 75 post last infusion procedure, 57% of the participants are insulin independent. However, this rate could be as high as 60.2% insulin independent or as low as 52.7% when all missing data are accounted for in subsequent analyses.

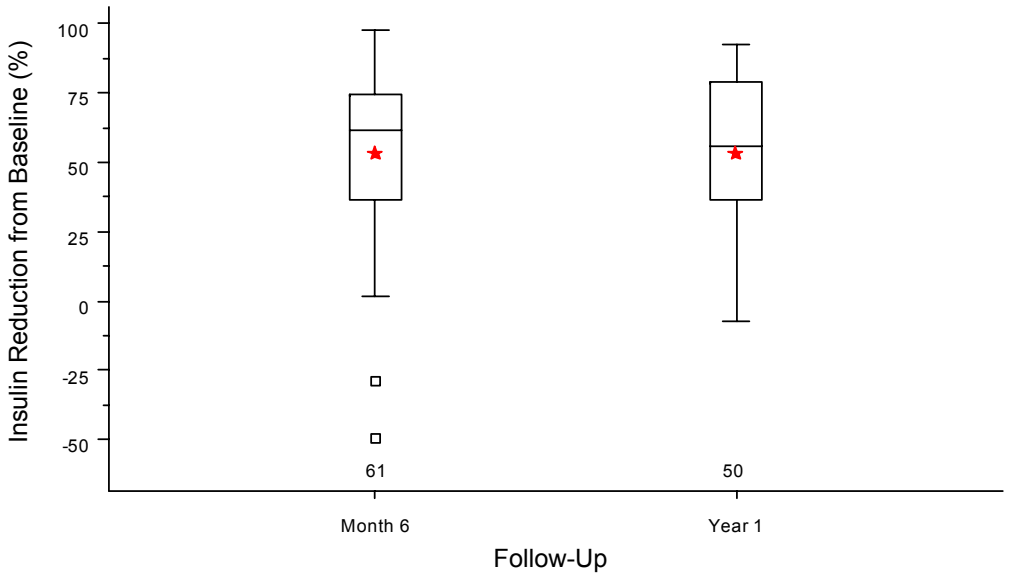
Exhibit 80
Percent Insulin Independent Participants Post Last Infusion by Total Number of Infusions Received



Timepoint	0	100	200	300	400	500	600	700
N1	49	48	42	38	36	33	32	31
N2	106	106	100	86	77	72	65	59
N3	33	32	30	30	28	25	24	24

This Exhibit summarizes the percent of participants that are insulin independent by time post their last infusion procedure. At Day 75, 63.2% of participants who received two islet infusions were insulin independent, while 53.1% with three infusions and 45.8% with one infusion were insulin independent. By Day 730, these rates drop to 48.4% for those with one infusion, 39.7% with two infusions and 27.3% with three infusions.

Exhibit 81
Reduction of Insulin (%) From Baseline to Follow-Up Post Last Infusion
Participants on Insulin



Negative insulin reduction from baseline values represents participants who were taking additional units of insulin after their islet infusion compared to at baseline (prior to their first infusion procedure). These values were verified as correct by the center.

Exhibit 82
Average Daily Insulin Use (Units) at Follow-Up Post Last Infusion
Participants on Insulin

	Average Daily Insulin Use (Units)					
	N	Mean	SD	Median	Min	Max
Follow-Up						
Month 6	62	18.2	13.9	13.8	2.0	71.0
Year 1	51	19.9	15.5	18.7	2.5	77.3

Exhibit 83
Percentage of Baseline Insulin Use at Follow-Up Post Last Infusion Participants Ever Achieving Insulin Independence

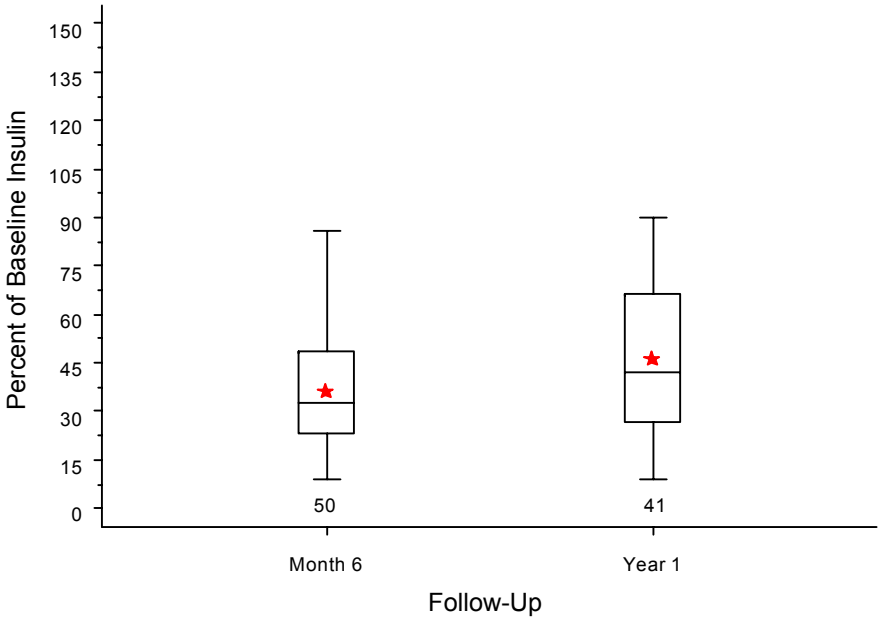


Exhibit 84
Percentage of Baseline Insulin Use at Follow-Up Post Last Infusion Participants Never Achieving Insulin Independence

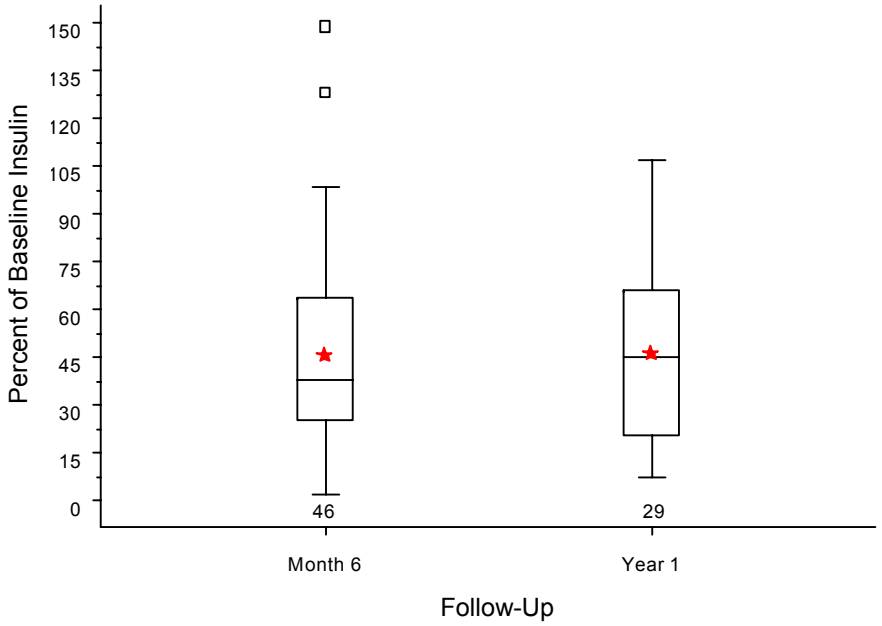


Exhibit 85
Average Daily Insulin Use (Units/kg) at Baseline and Post Last Infusion
Participants on Insulin

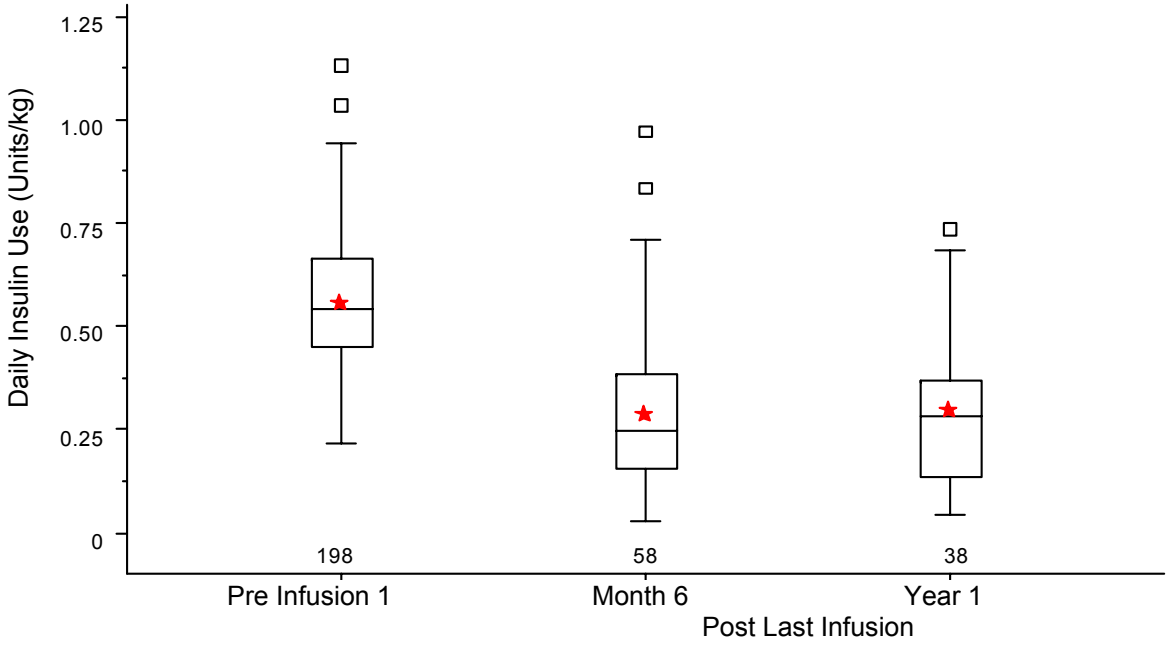


Exhibit 86
Insulin Independence (%) Year 1 Post First Infusion by Participant's Weight (kg) at Baseline

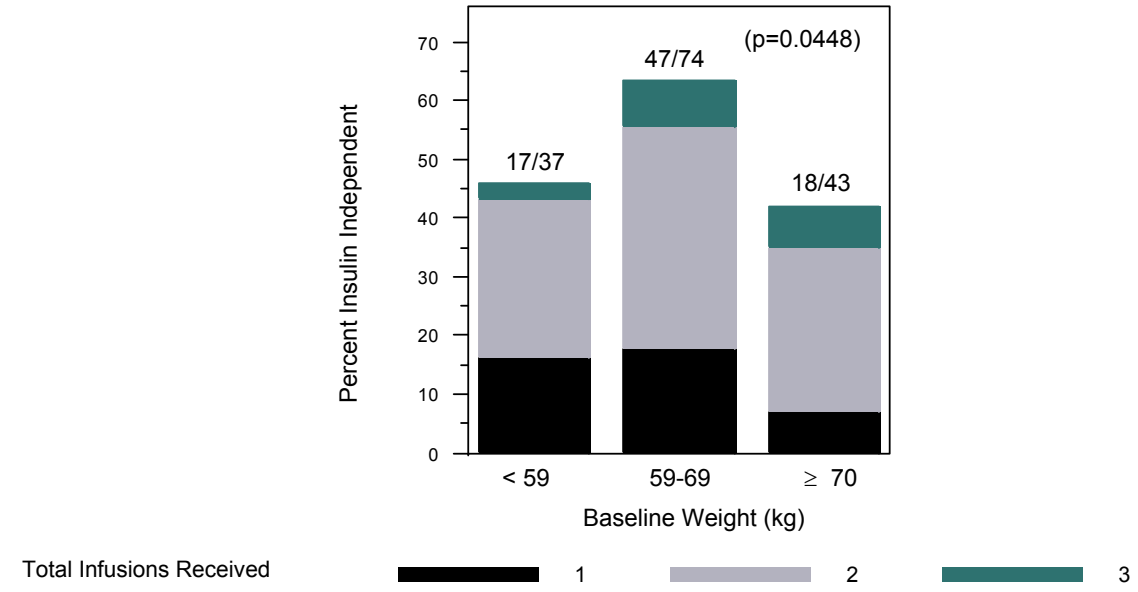


Exhibit 87
Insulin Independence (%) Year 1 Post First Infusion by Participant's Average Daily Insulin Use (Units/Day) at Baseline

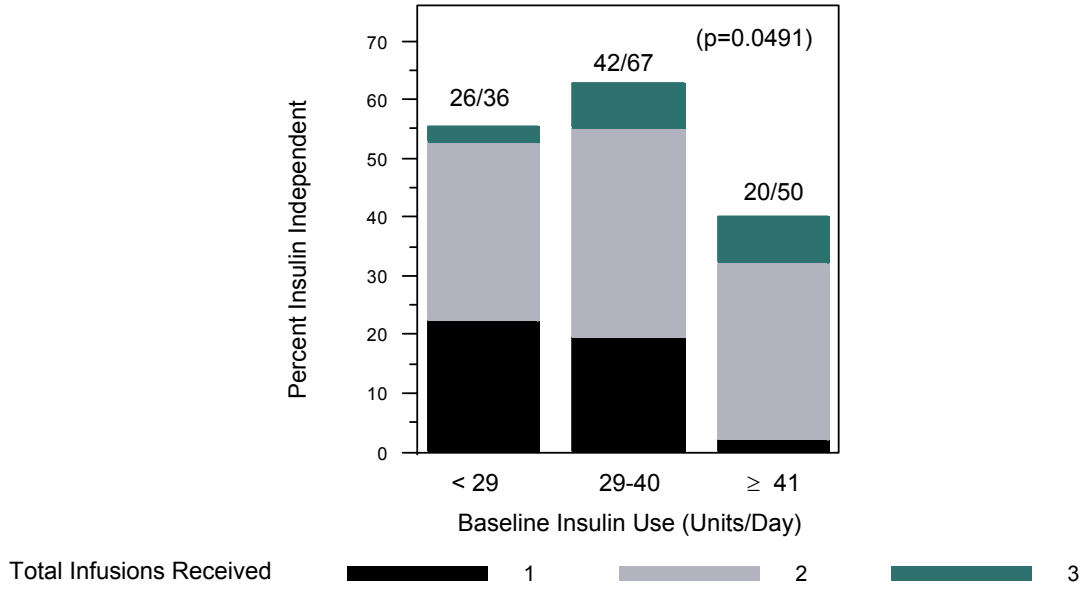


Exhibit 88
Insulin Independence at Month 6 and Year 1 Post Last Infusion by Donor and Participant Characteristics

	Follow-Up							
	Month 6				Year 1			
	Insulin Dependent		Insulin Independent		Insulin Dependent		Insulin Independent	
	N	%	N	%	N	%	N	%
Total	77	43.3	101	56.7	72	48.6	76	51.4
Participant Age (yrs)								
< 35	23	65.7	12	34.3	23	71.9	9	28.1
35 - 50	34	32.7	70	67.3	37	41.1	53	58.9
> 50	20	51.3	19	48.7	12	46.2	14	53.8
Duration of Diabetes (yrs)								
< 18	21	53.8	18	46.2	21	61.8	13	38.2
18 - 34	33	38.4	53	61.6	36	49.3	37	50.7
> 34	23	43.4	30	56.6	15	36.6	26	63.4
Participant Weight (kg)								
< 59	21	43.8	27	56.3	22	53.7	19	46.3
59 - 70	29	37.7	48	62.3	26	40.0	39	60.0
> 70	27	51.9	25	48.1	24	58.5	17	41.5
Unknown	-	0.0	1	100.0	-	0.0	1	100.0
BMI (kg/m^2)								
< 22	26	55.3	21	44.7	24	63.2	14	36.8
22 - 25	25	31.3	55	68.8	26	37.7	43	62.3
> 25	24	51.1	23	48.9	20	54.1	17	45.9
Unknown	2	50.0	2	50.0	2	50.0	2	50.0
Baseline Average Daily Insulin Use (Units/Day/kg)								
< 0.40	14	48.3	15	51.7	9	42.9	12	57.1
0.40 - 0.60	28	35.4	51	64.6	26	37.7	43	62.3
> 0.60	33	50.8	32	49.2	35	63.6	20	36.4
Unknown	2	40.0	3	60.0	2	66.7	1	33.3
Cultured Islets								
All Preparations	40	43.0	53	57.0	33	47.8	36	52.2
Some Preparations	10	66.7	5	33.3	9	81.8	2	18.2
No Preparations	27	38.6	43	61.4	30	44.1	38	55.9

Exhibit 88 *(continued)*
Insulin Independence at Month 6 and Year 1 Post Last Infusion by Donor and Participant Characteristics

	Follow-Up							
	Month 6				Year 1			
	Insulin Dependent		Insulin Independent		Insulin Dependent		Insulin Independent	
	N	%	N	%	N	%	N	%
Months from First to Second Infusion								
Only One Infusion	23	47.9	25	52.1	20	50.0	20	50.0
< 2 months	26	45.6	31	54.4	22	45.8	26	54.2
2 - 6 months	13	29.5	31	70.5	18	48.6	19	51.4
> 6 months	15	51.7	14	48.3	12	52.2	11	47.8
AE Definitely or Probably Related to Infusion Procedure (Prior to Follow-Up Assessment)*								
Yes	33	52.4	30	47.6	25	51.0	24	49.0
No	40	36.7	69	63.3	29	37.2	49	62.8
Unknown	4	66.7	2	33.3	18	85.7	3	14.3
Total Number of Pancreata Received								
1	16	44.4	20	55.6	14	46.7	16	53.3
2	38	40.9	55	59.1	36	46.8	41	53.2
3	14	41.2	20	58.8	13	46.4	15	53.6
4	6	50.0	6	50.0	6	60.0	4	40.0
Unknown	3	100.0	-	0.0	3	100.0	-	0.0
Abnormal Liver Function Test(s) (Prior to Follow-Up Assessment)								
Yes	23	56.1	18	43.9	17	56.7	13	43.3
No	50	38.2	81	61.8	37	38.1	60	61.9
Unknown	4	66.7	2	33.3	18	85.7	3	14.3
Preservation Solution Used on All Donors								
UW	31	40.3	46	59.7	30	44.8	37	55.2
Two Layer	21	47.7	23	52.3	18	50.0	18	50.0
UW and Two Layer	20	40.0	30	60.0	21	51.2	20	48.8
Other	5	71.4	2	28.6	3	75.0	1	25.0

*Adverse event relationship to infusion procedure is determined by the local CITR Investigator.

Exhibit 89
Basal C-Peptide ≥ 0.5 ng/mL at Month 6 and Year 1 Post Last Infusion by Donor and Participant Characteristics

	Follow-Up							
	Month 6				Year 1			
	< 0.5 ng/mL		≥ 0.5 ng/mL		< 0.5 ng/mL		≥ 0.5 ng/mL	
	N	%	N	%	N	%	N	%
Total	17	12.6	118	87.4	17	16.5	86	83.5
Participant Age (yrs)								
< 35	10	33.3	20	66.7	8	34.8	15	65.2
35 - 50	5	6.3	74	93.7	7	11.5	54	88.5
> 50	2	7.7	24	92.3	2	10.5	17	89.5
Duration of Diabetes (yrs)								
< 18	9	30.0	21	70.0	8	34.8	15	65.2
18 - 34	7	10.4	60	89.6	8	14.8	46	85.2
> 34	1	2.6	37	97.4	1	3.8	25	96.2
Participant Weight (kg)								
< 59	6	15.8	32	84.2	4	16.0	21	84.0
59 - 70	6	10.0	54	90.0	5	10.2	44	89.8
> 70	5	13.9	31	86.1	8	28.6	20	71.4
Unknown	-	0.0	1	100.0	-	0.0	1	100.0
BMI (kg/m^2)								
< 22	5	14.7	29	85.3	4	19.0	17	81.0
22 - 25	4	6.3	59	93.7	7	12.7	48	87.3
> 25	6	17.6	28	82.4	6	24.0	19	76.0
Unknown	2	50.0	2	50.0	-	0.0	2	100.0
Baseline Average Daily Insulin Use (Units/Day/kg)								
< 0.40	4	17.4	19	82.6	2	13.3	13	86.7
0.40 - 0.60	5	8.3	55	91.7	7	15.2	39	84.8
> 0.60	7	14.6	41	85.4	8	20.0	32	80.0
Unknown	1	25.0	3	75.0	-	0.0	2	100.0
Cultured Islets								
All Preparations	5	7.9	58	92.1	3	7.0	40	93.0
Some Preparations	3	30.0	7	70.0	3	37.5	5	62.5
No Preparations	9	14.5	53	85.5	11	21.2	41	78.8

Exhibit 89 *(continued)*
Basal C-Peptide ≥ 0.5 ng/mL at Month 6 and Year 1 Post Last Infusion by Donor and Participant Characteristics

	Follow-Up							
	Month 6				Year 1			
	< 0.5 ng/mL		≥ 0.5 ng/mL		< 0.5 ng/mL		≥ 0.5 ng/mL	
	N	%	N	%	N	%	N	%
Months from First to Second Infusion								
Only One Infusion	7	18.9	30	81.1	4	15.4	22	84.6
< 2 months	6	13.6	38	86.4	7	18.9	30	81.1
2 - 6 months	3	7.9	35	92.1	4	15.4	22	84.6
> 6 months	1	6.3	15	93.8	2	14.3	12	85.7
AE Definitely or Probably Related to Infusion Procedure (Prior to Follow-Up Assessment)*								
Yes	8	17.4	38	82.6	6	15.8	32	84.2
No	9	10.1	80	89.9	11	16.9	54	83.1
Total Number of Pancreata Received								
1	4	14.3	24	85.7	3	14.3	18	85.7
2	5	7.6	61	92.4	8	15.1	45	84.9
3	3	11.5	23	88.5	3	15.0	17	85.0
4	2	16.7	10	83.3	3	33.3	6	66.7
Unknown	3	100.0	-	0.0	-	0.0	-	0.0
Abnormal Liver Function Test(s) (Prior to Follow-Up Assessment)								
Yes	4	14.3	24	85.7	4	18.2	18	81.8
No	13	12.1	94	87.9	13	16.0	68	84.0
Preservation Solution Used on All Donors								
UW	8	12.9	54	87.1	11	19.0	47	81.0
Two Layer	2	6.3	30	93.8	3	15.0	17	85.0
UW and Two Layer	4	11.1	32	88.9	3	12.5	21	87.5
Other	3	60.0	2	40.0	-	0.0	1	100.0

*Adverse event relationship to infusion procedure is determined by the local CITR Investigator.

Exhibit 90
$HbA_{1C} \leq 6.5\%$ at Month 6 and Year 1 Post Last Infusion by Donor and Participant Characteristics

	Follow-Up							
	Month 6				Year 1			
	> 6.5%		≤ 6.5%		> 6.5%		≤ 6.5%	
	N	%	N	%	N	%	N	%
Total	30	20.7	115	79.3	26	24.1	82	75.9
Participant Age (yrs)								
< 35	12	40.0	18	60.0	13	65.0	7	35.0
35 - 50	12	14.0	74	86.0	9	13.2	59	86.8
> 50	6	20.7	23	79.3	4	20.0	16	80.0
Duration of Diabetes (yrs)								
< 18	11	34.4	21	65.6	10	45.5	12	54.5
18 - 34	15	21.4	55	78.6	13	22.8	44	77.2
> 34	4	9.3	39	90.7	3	10.3	26	89.7
Participant Weight (kg)								
< 59	9	22.5	31	77.5	4	14.3	24	85.7
59 - 70	11	16.9	54	83.1	13	26.5	36	73.5
> 70	10	25.6	29	74.4	9	30.0	21	70.0
Unknown	-	0.0	1	100.0	-	0.0	1	100.0
BMI (kg/m^2)								
< 22	9	24.3	28	75.7	6	24.0	19	76.0
22 - 25	11	16.2	57	83.8	11	20.4	43	79.6
> 25	9	25.0	27	75.0	9	33.3	18	66.7
Unknown	1	25.0	3	75.0	-	0.0	2	100.0
Baseline Average Daily Insulin Use (Units/Day/kg)								
< 0.40	5	20.8	19	79.2	3	18.8	13	81.3
0.40 - 0.60	10	15.4	55	84.6	7	14.3	42	85.7
> 0.60	14	26.9	38	73.1	16	39.0	25	61.0
Unknown	1	25.0	3	75.0	-	0.0	2	100.0
Cultured Islets								
All Preparations	13	18.1	59	81.9	8	16.0	42	84.0
Some Preparations	4	30.8	9	69.2	5	62.5	3	37.5
No Preparations	13	21.7	47	78.3	13	26.0	37	74.0

Exhibit 90 *(continued)*
$HbA_{1C} \leq 6.5\%$ at Month 6 and Year 1 Post Last Infusion by Donor and Participant Characteristics

	Follow-Up							
	Month 6				Year 1			
	> 6.5%		≤ 6.5%		> 6.5%		≤ 6.5%	
	N	%	N	%	N	%	N	%
Months from First to Second Infusion								
Only One Infusion	9	22.5	31	77.5	2	7.7	24	92.3
< 2 months	7	14.9	40	85.1	6	16.7	30	83.3
2 - 6 months	11	30.6	25	69.4	13	44.8	16	55.2
> 6 months	3	13.6	19	86.4	5	29.4	12	70.6
AE Definitely or Probably Related to Infusion Procedure (Prior to Follow-Up Assessment)*								
Yes	12	22.2	42	77.8	13	31.7	28	68.3
No	18	19.8	73	80.2	13	19.4	54	80.6
Total Number of Pancreata Received								
1	7	22.6	24	77.4	2	9.5	19	90.5
2	13	18.1	59	81.9	15	25.9	43	74.1
3	6	22.2	21	77.8	4	20.0	16	80.0
4	2	16.7	10	83.3	5	55.6	4	44.4
Unknown	2	66.7	1	33.3	-	0.0	-	0.0
Abnormal Liver Function Test(s) (Prior to Follow-Up Assessment)								
Yes	7	20.0	28	80.0	9	33.3	18	66.7
No	23	20.9	87	79.1	17	21.0	64	79.0
Preservation Solution Used on All Donors								
UW	18	26.9	49	73.1	18	32.1	38	67.9
Two Layer	1	2.9	33	97.1	1	4.3	22	95.7
UW and Two Layer	8	21.1	30	78.9	7	25.0	21	75.0
Other	3	50.0	3	50.0	-	0.0	1	100.0

*Adverse event relationship to infusion procedure is determined by the local CITR Investigator.

Exhibit 91
Outcome Levels at Month 6 Post Last Infusion by Donor and Participant Characteristics

	Month 6					
	Level 1		Level 2		Level 3	
	N	%	N	%	N	%
Total	101	72.1	18	12.9	21	15.0
Participant Age (yrs)						
< 35	13	46.4	5	17.9	10	35.7
35 - 50	68	81.9	9	10.8	6	7.2
> 50	20	69.0	4	13.8	5	17.2
Duration of Diabetes (yrs)						
< 18	16	53.3	6	20.0	8	26.7
18 - 34	52	76.5	9	13.2	7	10.3
> 34	33	78.6	3	7.1	6	14.3
Weight (kg)						
< 59	28	73.7	3	7.9	7	18.4
59 - 70	48	76.2	6	9.5	9	14.3
> 70	24	63.2	9	23.7	5	13.2
Unknown	1	100.0	-	0.0	-	0.0
BMI (kg/m^2)						
< 22	26	72.2	4	11.1	6	16.7
22 - 25	50	74.6	9	13.4	8	11.9
> 25	23	65.7	5	14.3	7	20.0
Unknown	2	100.0	-	0.0	-	0.0
Baseline Average Daily Insulin Use (Units/Day/kg)						
< 0.40	18	78.3	4	17.4	1	4.3
0.40 - 0.60	52	82.5	7	11.1	4	6.3
> 0.60	28	54.9	7	13.7	16	31.4
Unknown	3	100.0	-	0.0	-	0.0
Cultured Islets						
All Preparations	54	76.1	6	8.5	11	15.5
Some Preparations	6	46.2	3	23.1	4	30.8
No Preparations	41	73.2	9	16.1	6	10.7

Exhibit 91 *(continued)*
Outcome Levels at Month 6 Post Last Infusion
by Donor and Participant Characteristics

	Month 6					
	Level 1		Level 2		Level 3	
	N	%	N	%	N	%
Months from First to Second Infusion						
Only One Infusion	29	78.4	3	8.1	5	13.5
< 2 months	35	76.1	5	10.9	6	13.0
2 - 6 months	20	57.1	8	22.9	7	20.0
> 6 months	17	77.3	2	9.1	3	13.6
AE Definitely or Possibly Related to Infusion Procedure (Prior to Follow-Up Assessment)*						
Yes	33	61.1	7	13.0	14	25.9
No	68	79.1	11	12.8	7	8.1
Total Number of Pancreata Received						
1	23	74.2	3	9.7	5	16.1
2	51	71.8	8	11.3	12	16.9
3	19	73.1	5	19.2	2	7.7
4	8	66.7	2	16.7	2	16.7
Unknown	-	0.0	-	0.0	-	0.0
Abnormal Liver Function Test(s) (Prior to Follow-Up Assessment)						
Yes	23	65.7	4	11.4	8	22.9
No	78	74.3	14	13.3	13	12.4
Preservation Solution Used on All Donors						
UW	43	64.2	11	16.4	13	19.4
Two Layer	29	85.3	1	2.9	4	11.8
UW and Two Layer	27	75.0	5	13.9	4	11.1
Other	2	66.7	1	33.3	-	0.0

*Adverse event relationship to infusion procedure is determined by the local CITR Investigator.

Level 1 = No hypoglycemic episodes and $HbA_{1C} \leq 6.5\%$
Level 2 = No hypoglycemic episodes and $6.5\% < HbA_{1C} \leq 7.5\%$
Level 3 = Recipients failing to meet Level 1 or 2 criteria

Exhibit 92
Outcome Levels at Year 1 Post Last Infusion by Donor and Participant Characteristics

	Year 1					
	Level 1		Level 2		Level 3	
	N	%	N	%	N	%
Total	72	68.6	17	16.2	16	15.2
Participant Age (yrs)						
< 35	6	35.3	8	47.1	3	17.6
35 - 50	52	76.5	6	8.8	10	14.7
> 50	14	70.0	3	15.0	3	15.0
Duration of Diabetes (yrs)						
< 18	10	50.0	7	35.0	3	15.0
18 - 34	41	73.2	7	12.5	8	14.3
> 34	21	72.4	3	10.3	5	17.2
Participant Weight (kg)						
< 59	22	78.6	3	10.7	3	10.7
59 - 70	30	63.8	9	19.1	8	17.0
> 70	19	65.5	5	17.2	5	17.2
Unknown	1	100.0	-	0.0	-	0.0
BMI (kg/m^2)						
< 22	16	64.0	4	16.0	5	20.0
22 - 25	38	73.1	8	15.4	6	11.5
> 25	16	61.5	5	19.2	5	19.2
Unknown	2	100.0	-	0.0	-	0.0
Baseline Average Daily Insulin Use (Units/Day/kg)						
< 0.40	11	68.8	2	12.5	3	18.8
0.40 - 0.60	39	79.6	3	6.1	7	14.3
> 0.60	20	52.6	12	31.6	6	15.8
Unknown	2	100.0	-	0.0	-	0.0
Cultured Islets						
All Preparations	36	73.5	4	8.2	9	18.4
Some Preparations	3	42.9	3	42.9	1	14.3
No Preparations	33	67.3	10	20.4	6	12.2

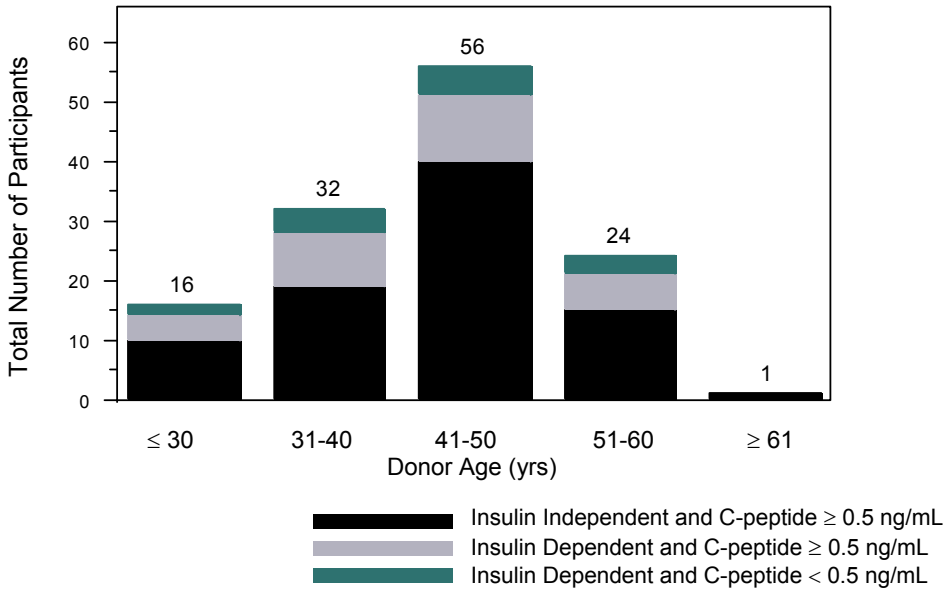
Exhibit 92 *(continued)*
Outcome Levels at Year 1 Post Last Infusion
by Donor and Participant Characteristics

	Year 1					
	Level 1		Level 2		Level 3	
	N	%	N	%	N	%
Months from First to Second Infusion						
Only One Infusion	24	92.3	1	3.8	1	3.8
< 2 months	26	74.3	5	14.3	4	11.4
2 - 6 months	12	42.9	8	28.6	8	28.6
> 6 months	10	62.5	3	18.8	3	18.8
AE Definitely or Possibly Related to Infusion Procedure (Prior to Follow-Up Assessment)*						
Yes	25	64.1	8	20.5	6	15.4
No	47	71.2	9	13.6	10	15.2
Total Number of Pancreata Received						
1	19	90.5	1	4.8	1	4.8
2	35	63.6	8	14.5	12	21.8
3	14	70.0	3	15.0	3	15.0
4	4	44.4	5	55.6	-	0.0
Unknown	-	0.0	-	0.0	-	0.0
Abnormal Liver Function Test(s) (Prior to Follow-Up Assessment)						
Yes	16	64.0	5	20.0	4	16.0
No	56	70.0	12	15.0	12	15.0
Preservation Solution Used on All Donors						
UW	34	63.0	12	22.2	8	14.8
Two Layer	19	82.6	-	0.0	4	17.4
UW and Two Layer	18	66.7	5	18.5	4	14.8
Other	1	100.0	-	0.0	-	0.0

*Adverse event relationship to infusion procedure is determined by the local CITR Investigator.

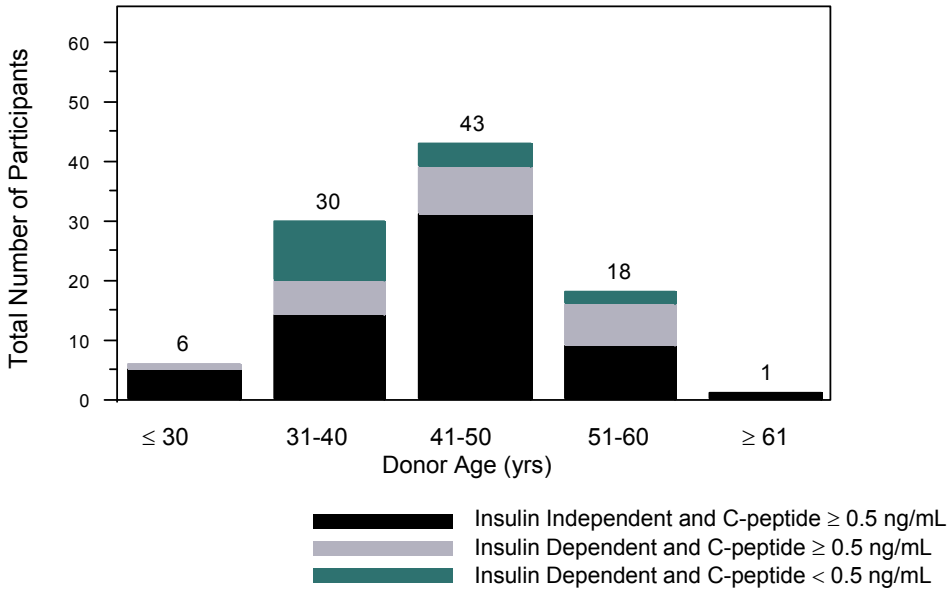
Level 1 = No hypoglycemic episodes and $HbA_{1C} \leq 6.5\%$
Level 2 = No hypoglycemic episodes and $6.5\% < HbA_{1C} \leq 7.5\%$
Level 3 = Recipients failing to meet Level 1 or 2 criteria

Exhibit 93
Participant Outcome at Month 6 Post Last Infusion
by Mean Donor Age Over All Infusions (yrs)



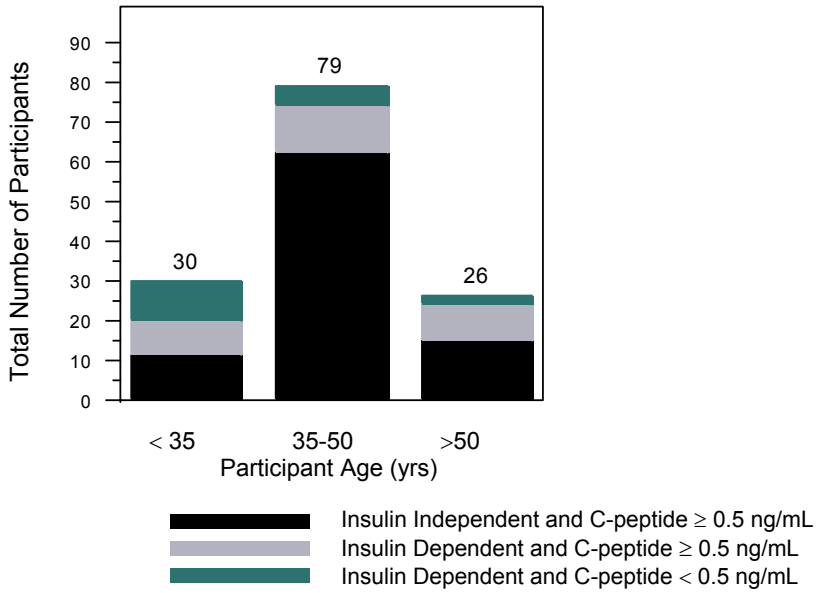
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by mean donor age is 62% (≤ 30 yrs), 59% (31-40 yrs), 71% (41-50 yrs), 62% (51-60 yrs), and 100% (≥ 61 yrs).

Exhibit 94
Participant Outcome at Year 1 Post Last Infusion
by Mean Donor Age Over All Infusions (yrs)



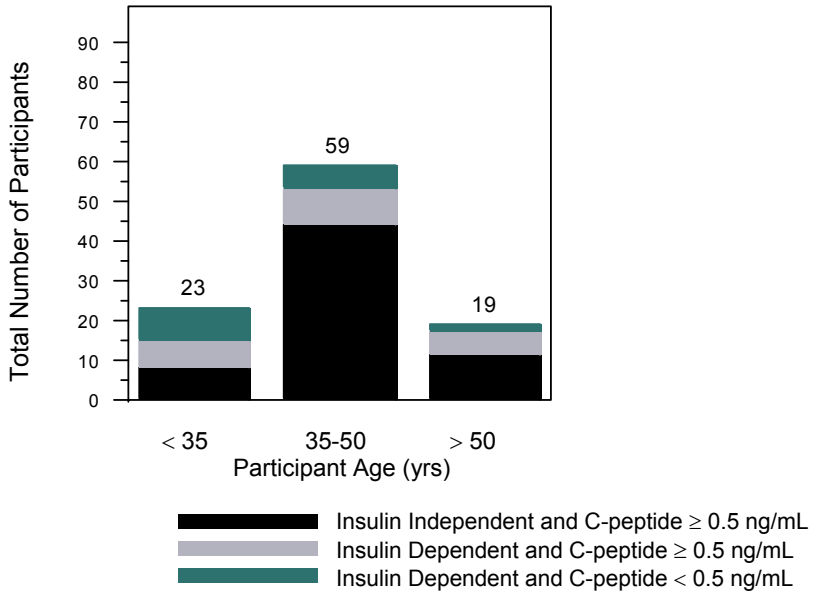
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by mean donor age is 83% (≤ 30 yrs), 47% (31-40 yrs), 72% (41-50 yrs), 50% (51-60 yrs), and 100% (≥ 61 yrs).

Exhibit 95
Participant Outcome at Month 6 Post Last Infusion
by Participant Age at Baseline (yrs)



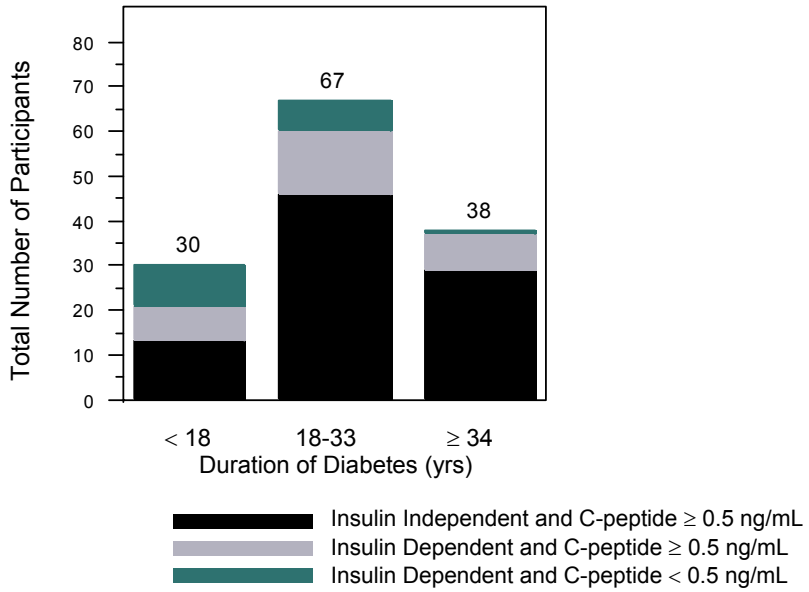
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by participant age is 37% (< 35 yrs), 78% (35-50 yrs), and 58% (> 50 yrs).

Exhibit 96
Participant Outcome at Year 1 Post Last Infusion
by Participant Age at Baseline (yrs)



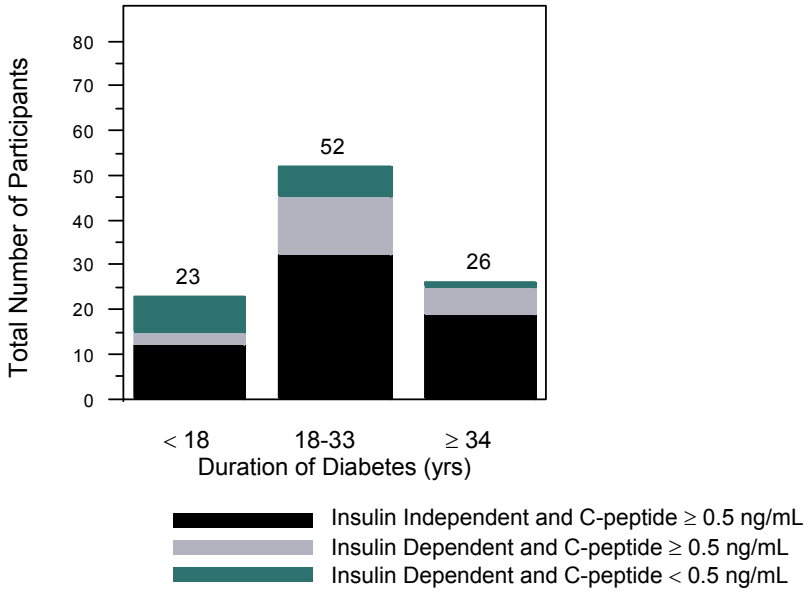
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by participant age is 35% (< 35 yrs), 75% (35-50 yrs), and 58% (> 50 yrs).

Exhibit 97
Participant Outcome at Month 6 Post Last Infusion
by Duration of Diabetes at Baseline (yrs)



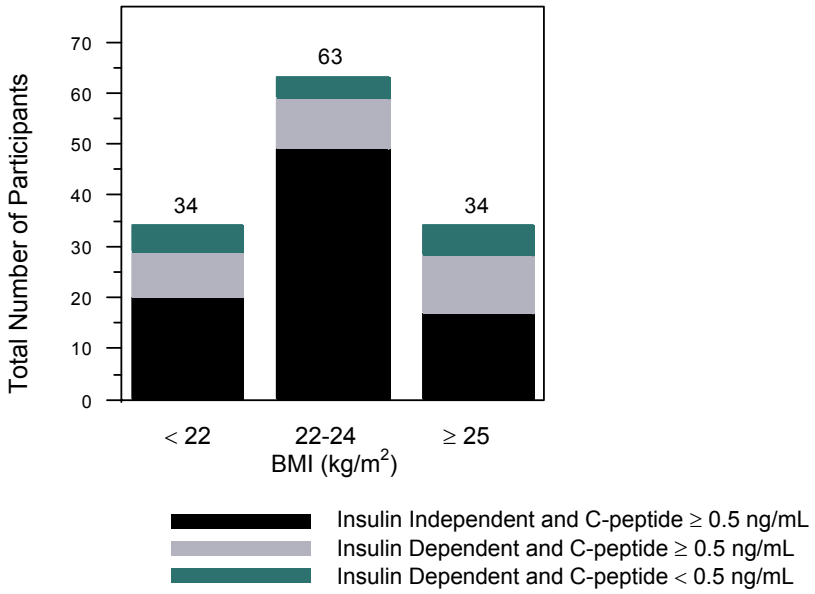
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by duration of diabetes is 43% (< 18 yrs), 69% (18-33 yrs), and 76% (≥ 34 yrs).

Exhibit 98
Participant Outcome at Year 1 Post Last Infusion
by Duration of Diabetes at Baseline (yrs)



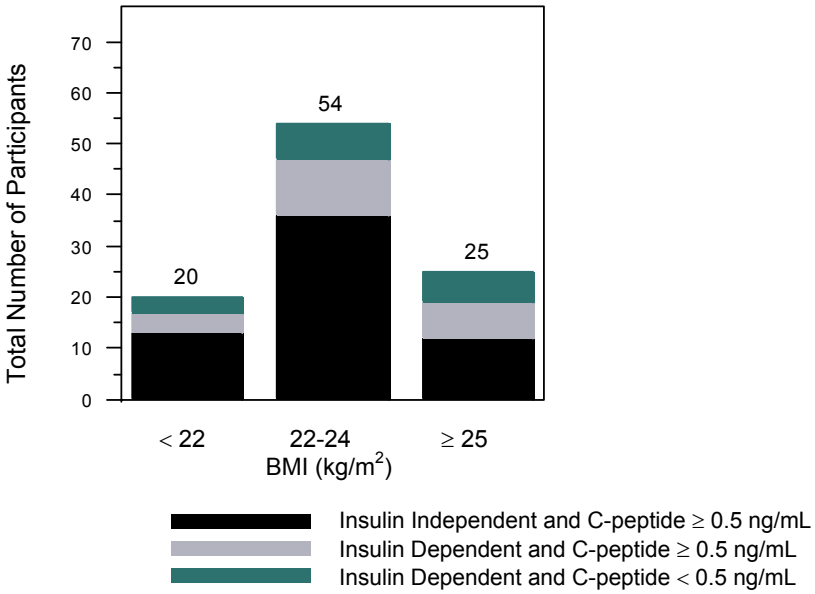
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by duration of diabetes is 52% (< 18 yrs), 62% (18-33 yrs), and 73% (≥ 34 yrs).

Exhibit 99
Participant Outcome at Month 6 Post Last Infusion
by Participant Body Mass Index (kg/m^2)



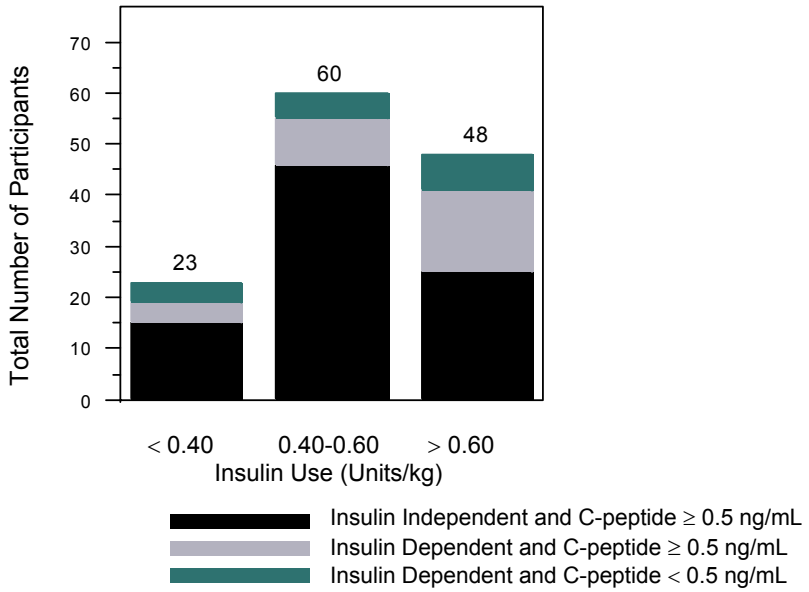
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by participant BMI is 59% (< 22 kg/m^2), 78% (22-24 kg/m^2), and 50% (≥ 25 kg/m^2).

Exhibit 100
Participant Outcome at Year 1 Post Last Infusion
by Participant Body Mass Index (kg/m^2)



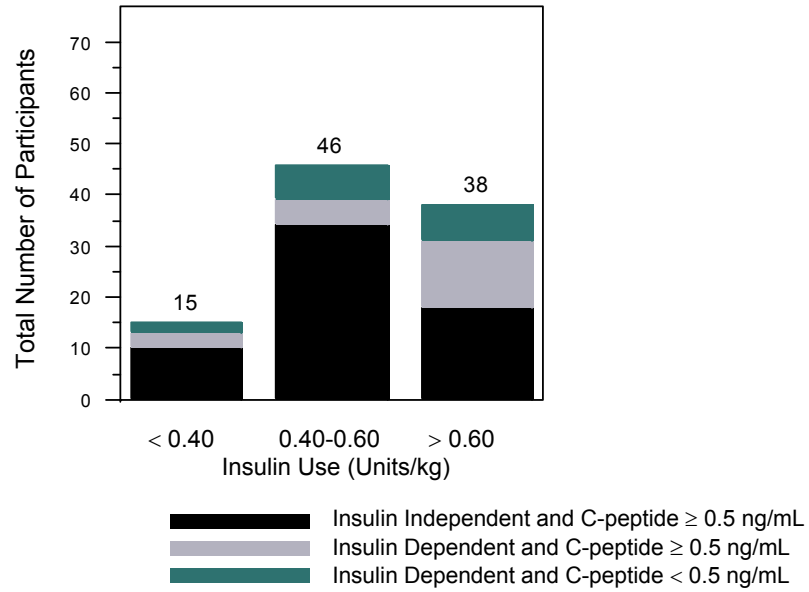
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by participant BMI is 65% (< 22 kg/m^2), 67% (22-24 kg/m^2), and 48% (≥ 25 kg/m^2).

Exhibit 101
Participant Outcome at Month 6 Post Last Infusion
by Insulin Use (Units/kg Participant Weight at Baseline)



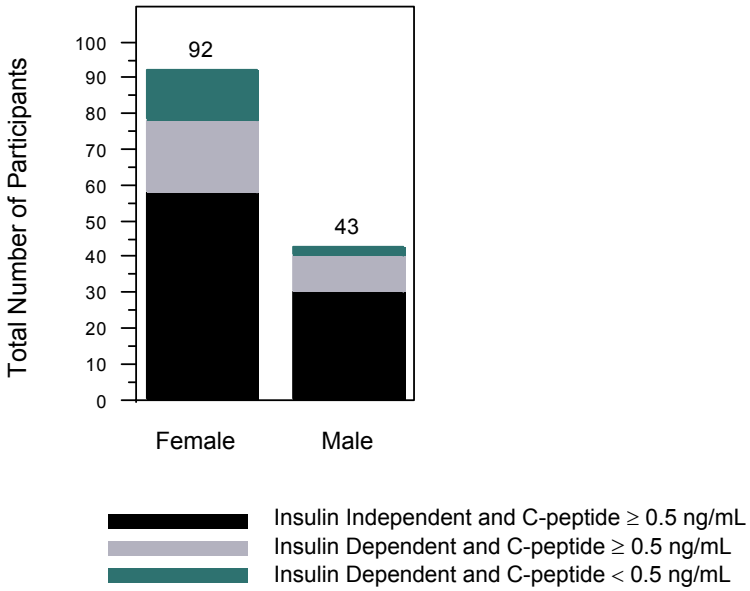
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by baseline insulin use is 65% (< 0.40 Units/kg), 77% (0.40-0.60 Units/kg), and 52% (> 0.60 Units/kg).

Exhibit 102
Participant Outcome at Year 1 Post Last Infusion
by Insulin Use (Units/kg Participant Weight at Baseline)



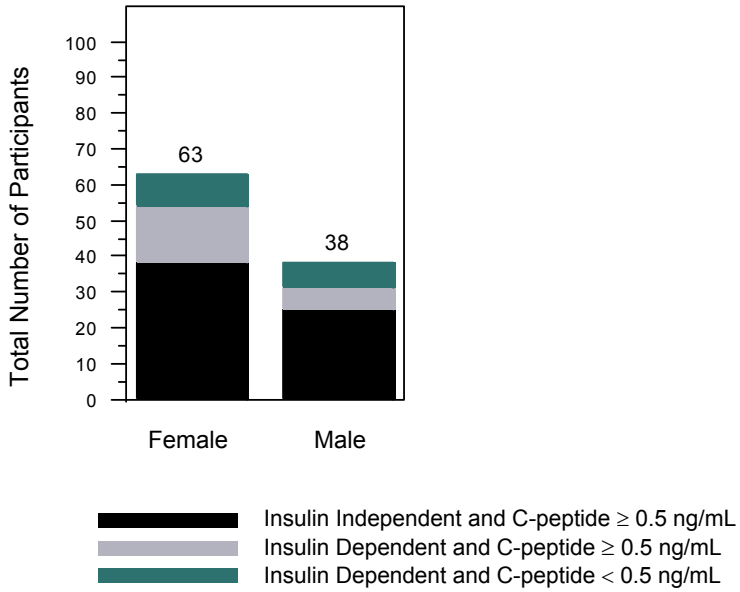
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by baseline insulin use is 67% (< 0.40 Units/kg), 74% (0.40-0.60 Units/kg), and 47% (> 0.60 Units/kg).

Exhibit 103
Participant Outcome at Month 6 Post Last Infusion
by Participant Gender



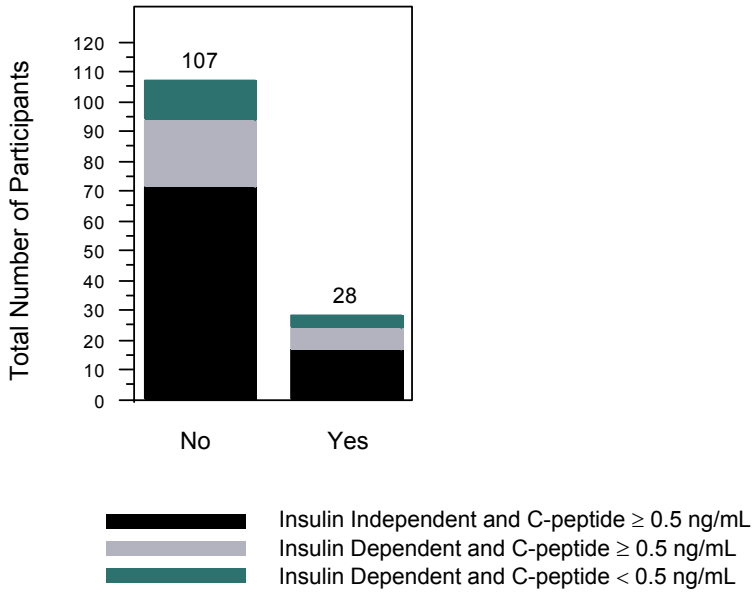
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by participant gender is 70% (Male) and 63% (Female).

Exhibit 104
Participant Outcome at Year 1 Post Last Infusion
by Participant Gender



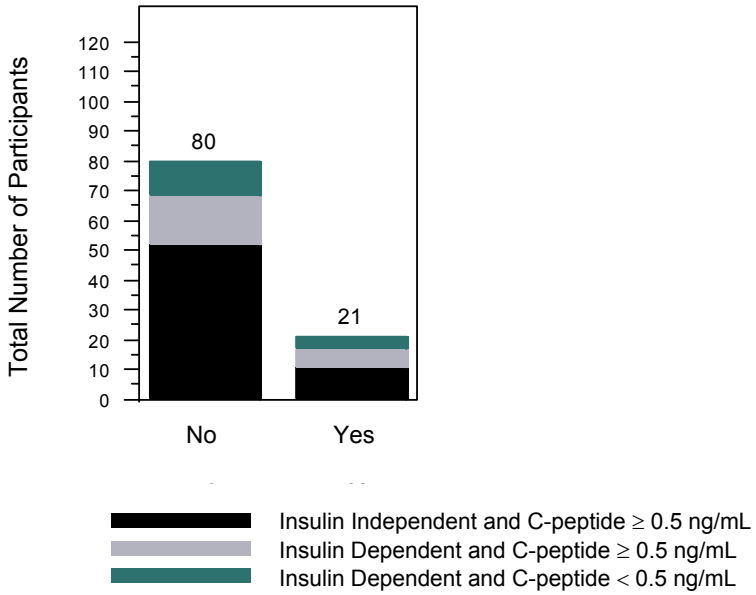
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by participant gender is 66% (Male) and 60% (Female).

Exhibit 105
Participant Outcome at Month 6 Post Last Infusion
by Any Elevated Liver Function Tests Prior to Assessment



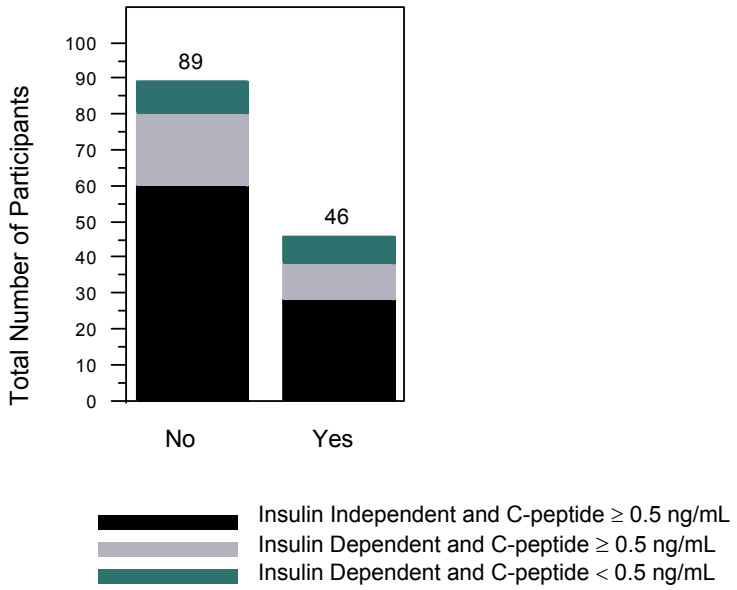
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by presence of elevated LFT is 66% (No elevated LFT reported) and 61% (Elevated LFT reported).

Exhibit 106
Participant Outcome at Year 1 Post Last Infusion
by Any Elevated Liver Function Tests Prior to Assessment



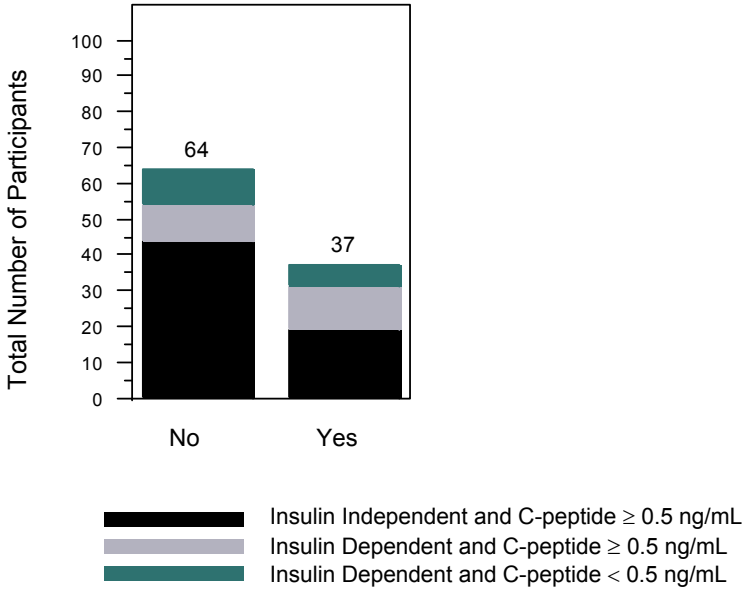
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by presence of elevated LFT is 66% (No elevated LFT reported) and 52% (Elevated LFT reported).

Exhibit 107
Participant Outcome at Month 6 Post Last Infusion
by Any Adverse Event Related to Infusion Prior to Assessment



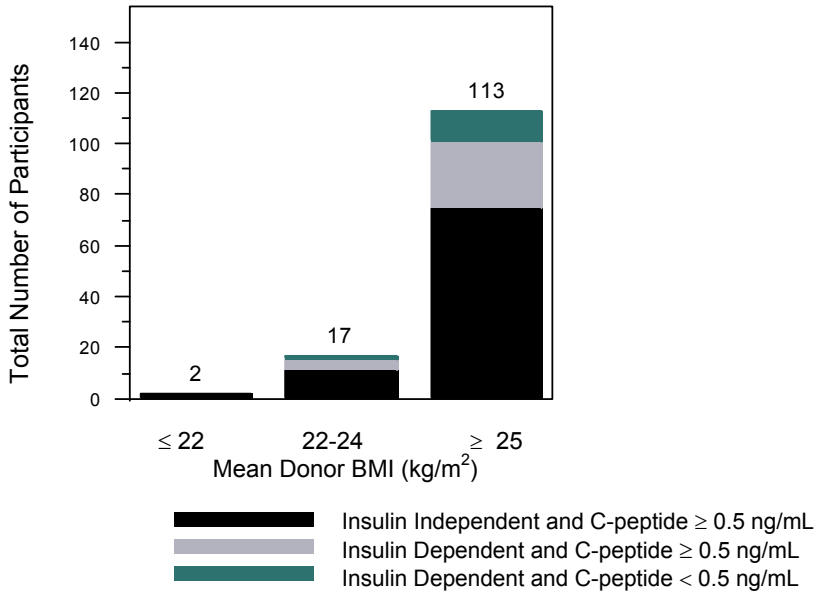
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by experience of infusion related adverse events is 67% (No infusion related AE reported) and 61% (Infusion related AE reported). Adverse event relationship to infusion procedure is determined by the local CITR Investigator.

Exhibit 108
Participant Outcome at Year 1 Post Last Infusion
by Any Adverse Event Related to Infusion Prior to Assessment



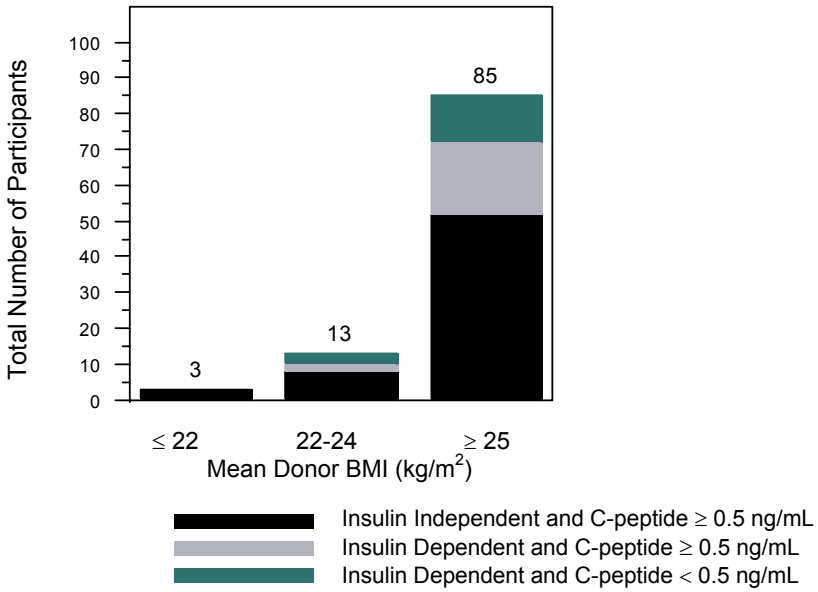
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by experience of infusion related adverse events is 69% (No infusion related AE reported) and 51% (Infusion related AE reported). Adverse event relationship to infusion procedure is determined by the local CITR Investigator.

Exhibit 109
Participant Outcome at Month 6 Post Last Infusion
by Mean Donor Body Mass Index (kg/m^2)



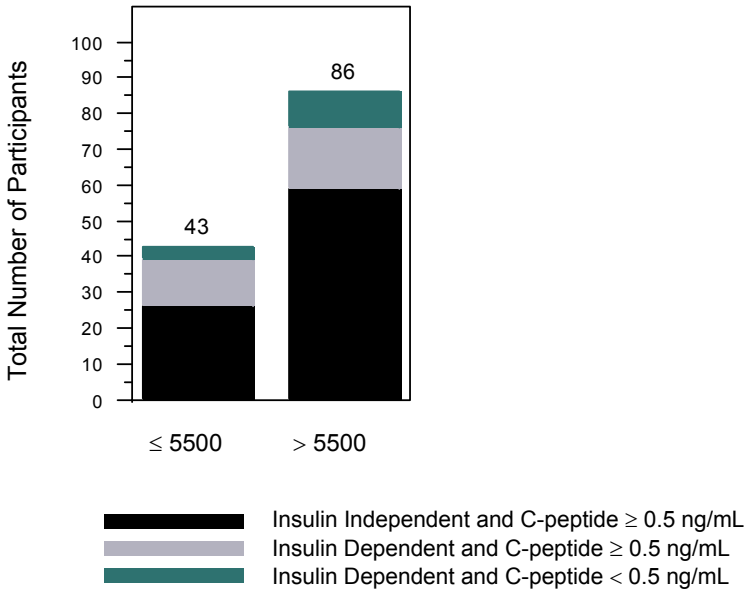
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by mean donor BMI is 100% (≤ 22 kg/m^2), 65% (22-24 kg/m^2), and 66% (≥ 25 kg/m^2).

Exhibit 110
Participant Outcome at Year 1 Post Last Infusion
by Mean Donor Body Mass Index (kg/m^2)



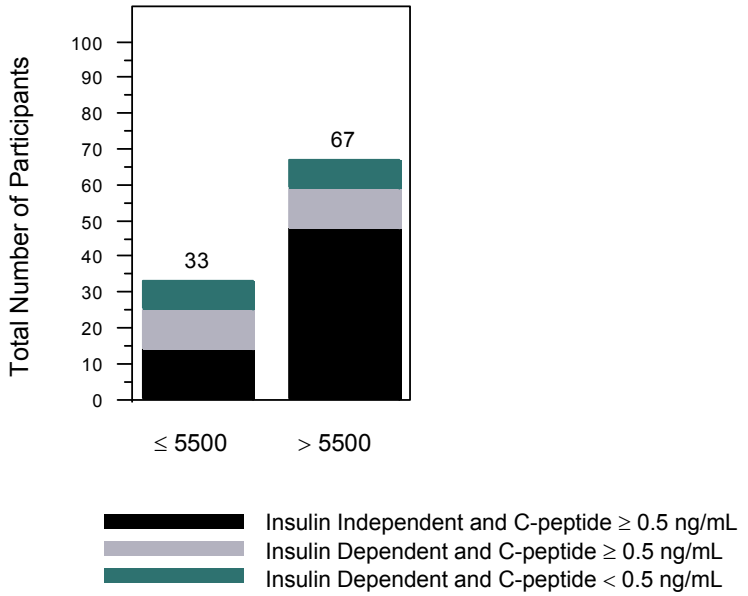
The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by mean donor BMI is 100% (≤ 22 kg/m^2), 62% (22-24 kg/m^2), and 61% (≥ 25 kg/m^2).

Exhibit 111
Participant Outcome at Month 6 Post Last Infusion by Islet Equivalents/kg Participant Weight



The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by IEQ/kg infused is 60% (≤ 5500 IEQ/kg) and 69% (> 5500 IEQ/kg).

Exhibit 112
Participant Outcome at Year 1 Post Last Infusion by Islet Equivalents/kg Participant Weight



The percentage of insulin independent participants with C-peptide ≥ 0.5 ng/mL by IEQ/kg infused is 42% (≤ 5500 IEQ/kg) and 72% (> 5500 IEQ/kg).

Exhibit 113
Summary of Severe Hypoglycemic Events Pre First Infusion and Follow-Up Post Last Infusion

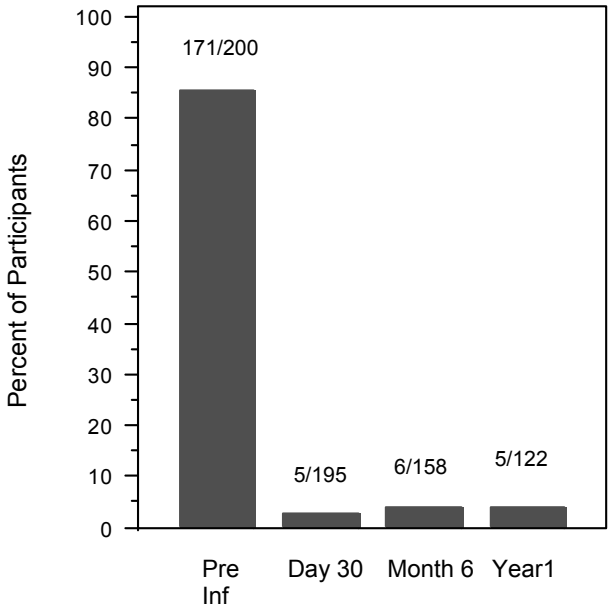
	Follow-Up							
	Pre First Infusion		Days 0-30 Post First Infusion		Months 1-6 Post Last Infusion		Months 6-12 Post Last Infusion	
	N	%	N	%	N	%	N	%
Total	203	100.0	203	100.0	193	100.0	163	100.0
Any Severe Hypoglycemic Episodes								
Yes*	171	84.2	5	2.5	6	3.1	5	3.1
No	29	14.3	190	93.6	152	78.8	117	71.8
Unknown	-	0.0	4	2.0	-	0.0	-	0.0
Missing**	3	1.5	4	2.0	35	18.1	41	25.2
Frequency of Severe Hypoglycemic Episodes								
None	29	14.3	190	93.6	152	78.8	117	71.8
1-2	19	9.4	2	1.0	-	0.0	1	0.6
3-5	14	6.9	1	0.5	-	0.0	-	0.0
6 or more	120	59.1	-	0.0	-	0.0	1	0.6
Unknown	17	8.4	2	1.0	6	3.1	3	1.8
Missing**	4	2.0	8	3.9	35	18.1	41	25.2

*All participants were using insulin at the time of hypoglycemic episodes.
**The majority of missing information is due to unsubmitted follow-up forms.

Mean HbA_{1C} for participants without hypoglycemic episodes is 7.6% (SD 1.2) pre first infusion, 7.2% (SD 1.2) at 30 days post first infusion, 6.1% (SD 1.0) at Month 6 post last infusion, and 6.1% (SD 0.8) at Year 1 post last infusion.

Mean HbA_{1C} for participants with hypoglycemic episodes is 7.7% (SD 1.4) pre first infusion, 7.4% (SD 0.6) at 30 days post first infusion, 6.2% (SD 0.8) at Month 6 post last infusion, and 5.7% (SD 0.1) at Year 1 post last infusion.

Exhibit 114
Percent of Participants with One or More Occurrences of Severe Hypoglycemic Episodes Pre First Infusion and Follow-Up Post Last Infusion



All participants experiencing a severe hypoglycemic event post infusion were using insulin at the time of the hypoglycemic episodes.

Mean HbA_{1C} for participants without hypoglycemic episodes is 7.6% (SD 1.2) pre first infusion, 7.2% (SD 1.2) at 30 days post first infusion, 6.1% (SD 1.0) at Month 6 post last infusion, and 6.1% (SD 0.8) at Year 1 post last infusion.

Mean HbA_{1C} for participants with hypoglycemic episodes is 7.7% (SD 1.4) pre first infusion, 7.4% (SD 0.6) at 30 days post first infusion, 6.2% (SD 0.8) at Month 6 post last infusion, and 5.7% (SD 0.1) at Year 1 post last infusion.

Exhibit 115
Insulin Independence by Immunosuppression Regimen

	Follow-Up Post Last Infusion							
	Month 6				Year 1			
	Insulin Dependent		Insulin Independent		Insulin Dependent		Insulin Independent	
	N	%	N	%	N	%	N	%
Overall	71	42.0	98	58.0	53	42.4	72	57.6
Sirolimus + Tacrolimus + Daclizumab	44	43.6	57	56.4	35	43.2	46	56.8
Other than Sirolimus + Tacrolimus + Daclizumab	27	39.7	41	60.3	18	40.9	26	59.1

Exhibit 116
Insulin Independence at Month 6 by Immunosuppression Regimen
All Participants on Sirolimus, Tacrolimus, and Daclizumab at Baseline

	Insulin Dependent		Insulin Independent	
	N	%	N	%
Overall	41	44.1	52	55.9
No Immunosuppressant Medications Taken*	8	100.0	-	0.0
Tacrolimus	1	50.0	1	50.0
Tacrolimus + MMF	5	50.0	5	50.0
Sirolimus + Tacrolimus	19	35.2	35	64.8
Sirolimus + Tacrolimus + Daclizumab	2	22.2	7	77.8
Sirolimus + Tacrolimus + MMF	6	60.0	4	40.0

*One participant withdrew from therapy due to immunosuppression side effects.
All other participants are complete islet graft failures prior to Month 6.

Exhibit 117
Insulin Independence at Year 1 by Immunosuppression Regimen
All Participants on Sirolimus, Tacrolimus, and Daclizumab at Baseline

	Insulin Dependent		Insulin Independent	
	N	%	N	%
Overall	30	40.5	44	59.5
No Immunosuppression Medications Taken*	3	100.0	-	0.0
Sirolimus + MMF	1	100.0	-	0.0
Tacrolimus + MMF	1	14.3	6	85.7
Sirolimus + Tacrolimus	18	36.7	31	63.3
Sirolimus + Tacrolimus + Daclizumab	2	28.6	5	71.4
Sirolimus + Tacrolimus + MMF	5	71.4	2	28.6

*All three participants experienced complete islet graft failure prior to Year 1.

Exhibit 118
Insulin Status at Post Last Infusion Follow-Up and Sirolimus Trough Level (ng/mL)

	Sirolimus Trough Level (ng/mL)*											
	Month 6						Year 1					
	N	Mean	SD	Median	Min	Max	N	Mean	SD	Median	Min	Max
Total	103	10.7	3.2	10.2	4.0	20.9	84	10.1	3.6	9.6	3.4	24.4
Insulin Independent	70	10.4	3.2	10.0	4.0	20.9	56	10.2	3.3	10.2	4.0	23.9
Insulin Dependent	32	11.5	3.3	11.0	6.7	20.9	28	9.7	4.3	8.7	3.4	24.4

* Target level is 10-12 ng/mL.

At Month 6, 62% of participants with a sirolimus trough level ≥ 10 ng/mL were insulin independent while 68% of participants with a sirolimus trough level < 10 mg/mL were insulin independent. At Year 1, 78% of participants with a sirolimus trough level ≥ 10 ng/mL were insulin independent while 54% of participants with a sirolimus trough level < 10 ng/mL were insulin independent.

Exhibit 119
Insulin Status at Post Last Infusion Follow-Up and Tacrolimus Trough Level (ng/mL)

	Tacrolimus Trough Level (ng/mL)*											
	Month 6						Year 1					
	N	Mean	SD	Median	Min	Max	N	Mean	SD	Median	Min	Max
Total	108	4.9	2.6	4.4	1.5	18.4	86	5.0	2.4	4.3	1.5	14.0
Insulin Independent	74	4.5	1.7	4.5	1.5	11.5	57	5.0	2.5	4.3	2.8	14.0
Insulin Dependent	33	5.7	4.0	4.1	1.5	18.4	29	4.9	2.3	4.0	1.5	10.8

* Target level is 3-6 ng/mL.

At Month 6, 68% of participants with a tacrolimus trough level ≥ 3 ng/mL were insulin independent while 58% of participants with a tacrolimus trough level < 3 mg/mL were insulin independent. At Year 1, 68% of participants with a tacrolimus trough level ≥ 3 ng/mL were insulin independent while 45% of participants with a tacrolimus trough level < 3 ng/mL were insulin independent.

Exhibit 120
Fasting Plasma Glucose (mg/dL)
Pre Infusion and Post Last Infusion

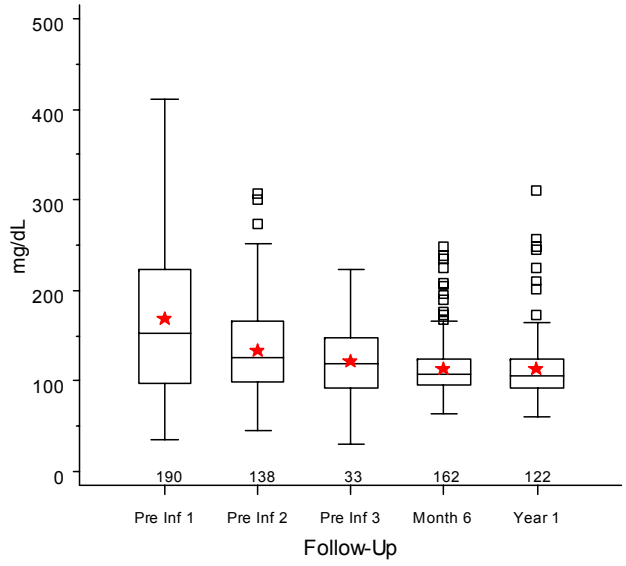


Exhibit 121
HbA_{1C} (%)
Pre Infusion and Post Last Infusion

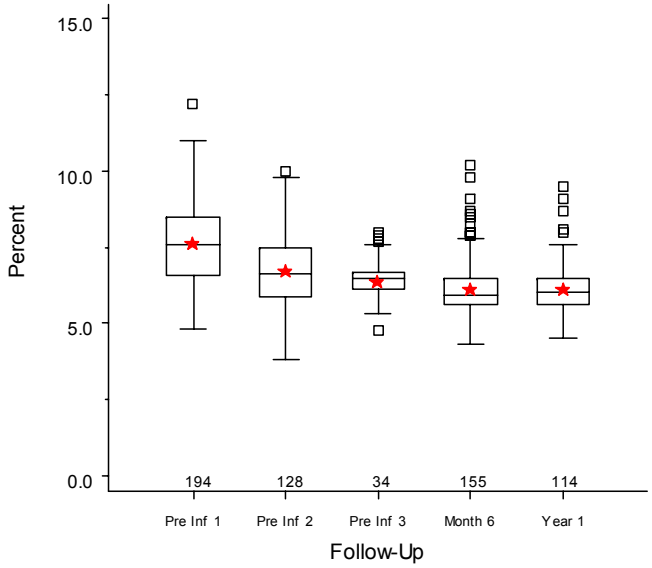
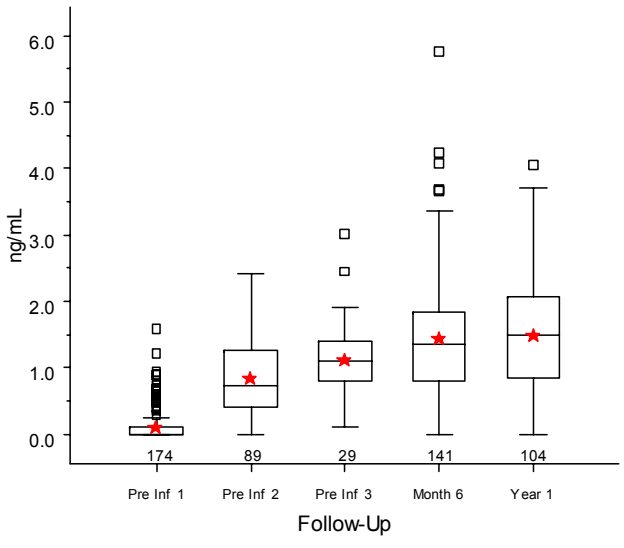


Exhibit 122
Basal Plasma C-Peptide (ng/mL)
Pre Infusion and Post Last Infusion



Values of 10.1 ng/mL and 6.1 ng/mL were removed from Month 6 for presentation, verified correct by center.

Exhibit 123
Fasting Plasma Glucose (mg/dL)
Pre Infusion and Post Last Infusion
Participants with One Infusion

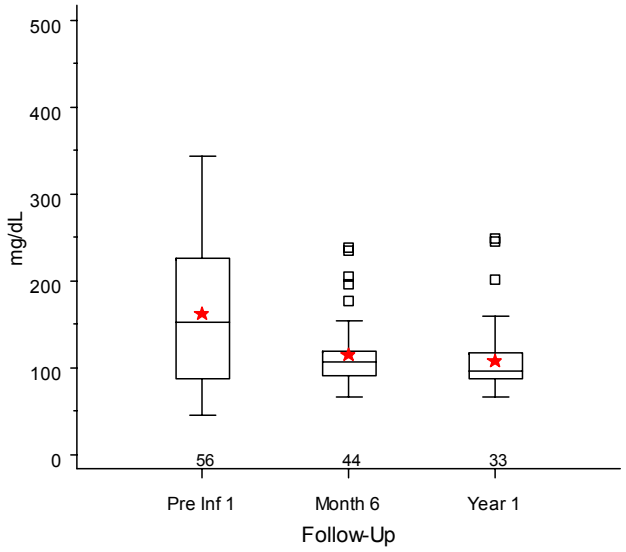


Exhibit 124
HbA_{1C} (%)
Pre Infusion and Post Last Infusion
Participants with One Infusion

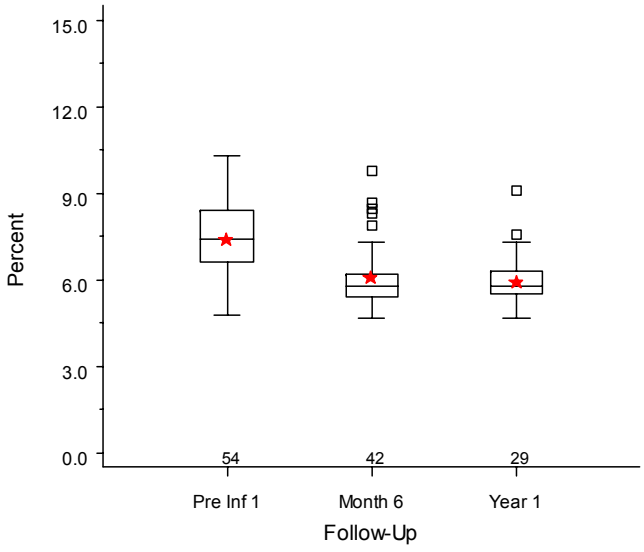


Exhibit 125
Basal Plasma C-Peptide (ng/mL)
Pre Infusion and Post Last Infusion
Participants with One Infusion

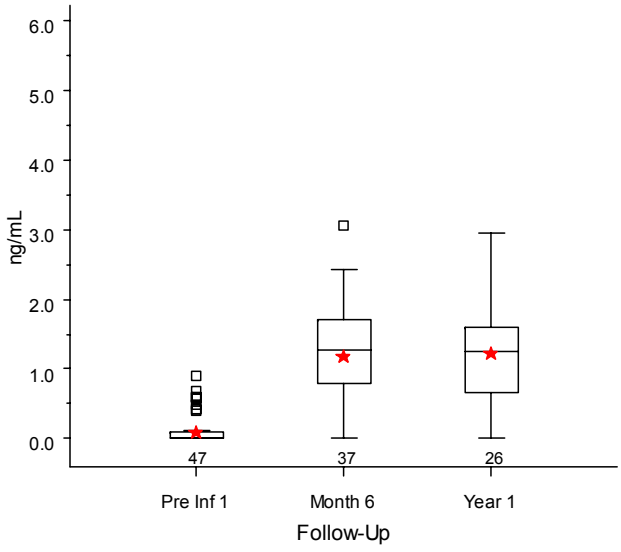


Exhibit 126
Fasting Plasma Glucose (mg/dL)
Pre Infusion and Post Last Infusion
Participants with Two Infusions

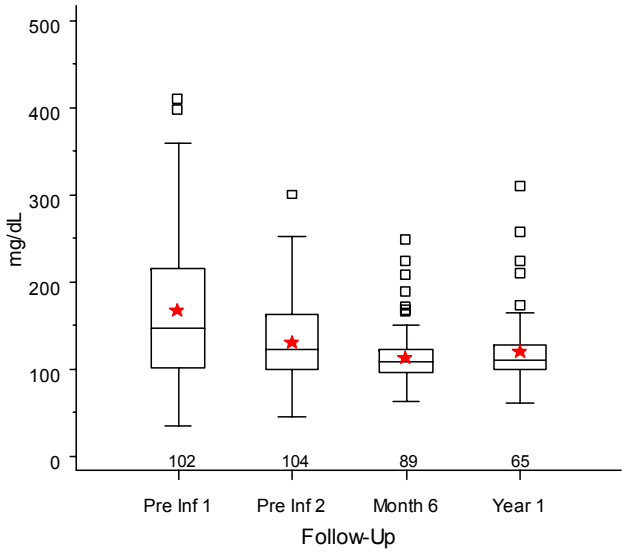


Exhibit 127
HbA_{1C} (%)
Pre Infusion and Post Last Infusion
Participants with Two Infusions

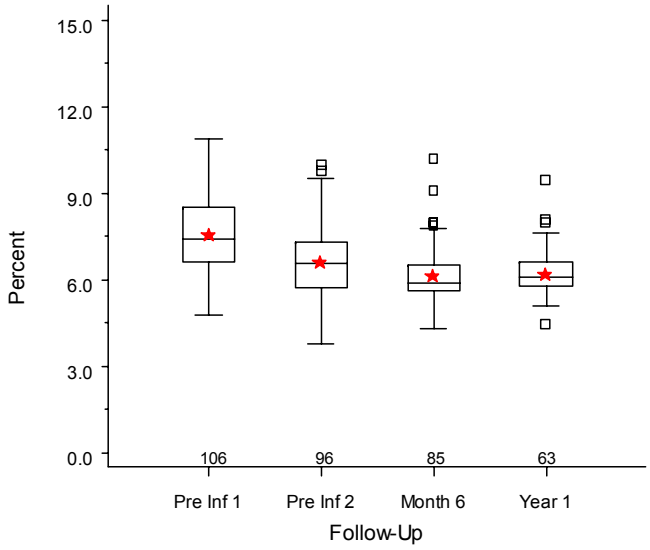
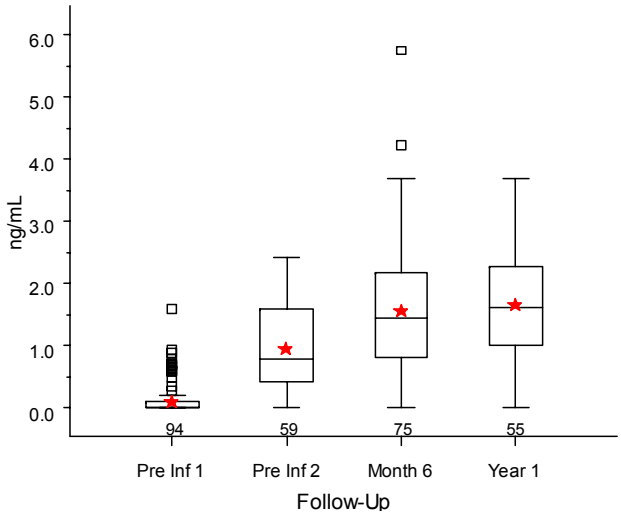


Exhibit 128
Basal Plasma C-Peptide (ng/mL)
Pre Infusion and Post Last Infusion
Participants with Two Infusions



Values of 10.1 ng/mL and 6.1 ng/mL were removed from Month 6 for presentation, verified correct by center.

Exhibit 129
Fasting Plasma Glucose (mg/dL)
Pre Infusion and Post Last Infusion
Participants with Three Infusions

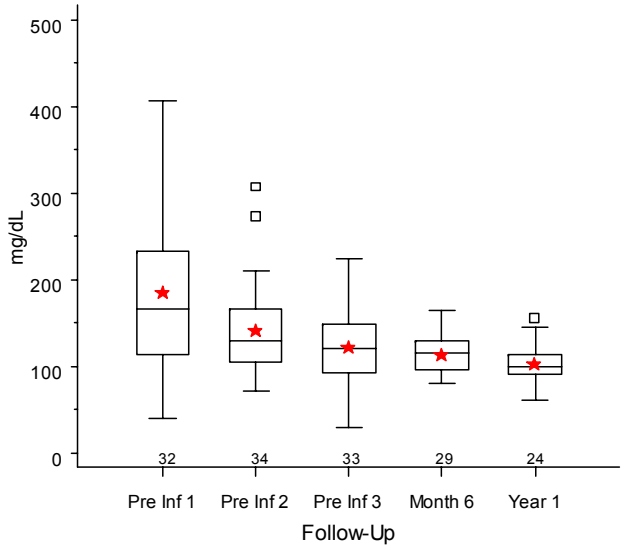


Exhibit 130
HbA_{1C} (%)
Pre Infusion and Post Last Infusion
Participants with Three Infusions

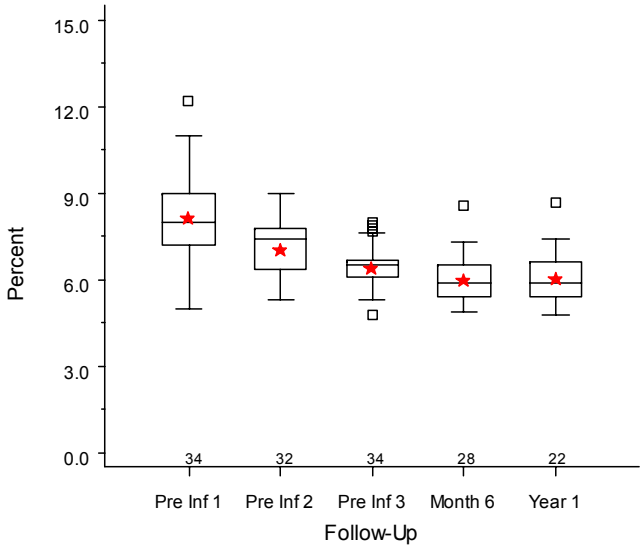


Exhibit 131
Basal Plasma C-Peptide (ng/mL)
Pre Infusion and Post Last Infusion
Participants with Three Infusions

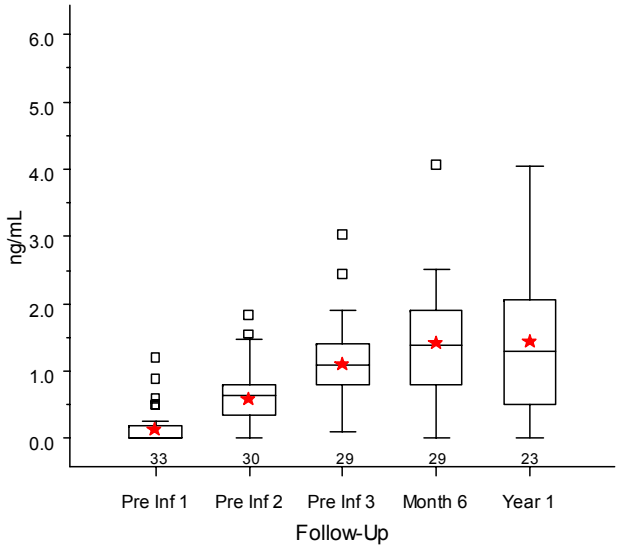


Exhibit 132
Fasting Plasma Glucose (mg/dL) Post Last Infusion
Participants Who Ever Achieved Insulin Independence

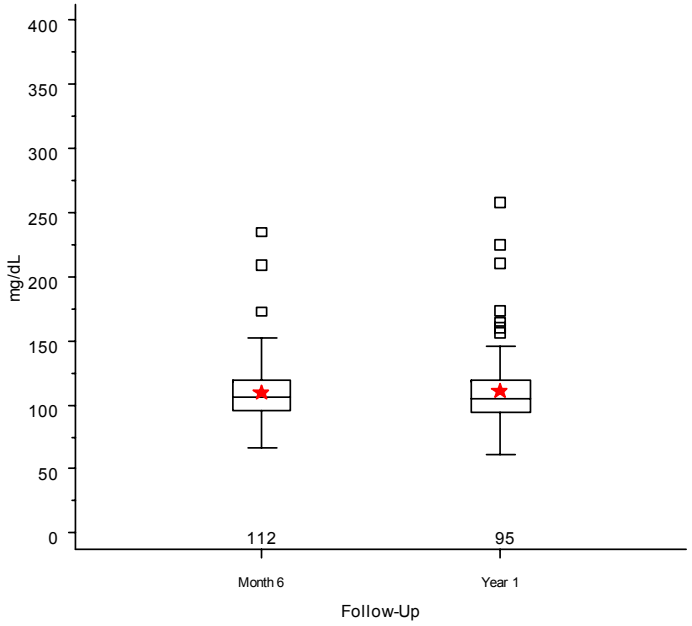


Exhibit 133
Fasting Plasma Glucose (mg/dL) Post Last Infusion
Participants Who Never Achieved Insulin Independence

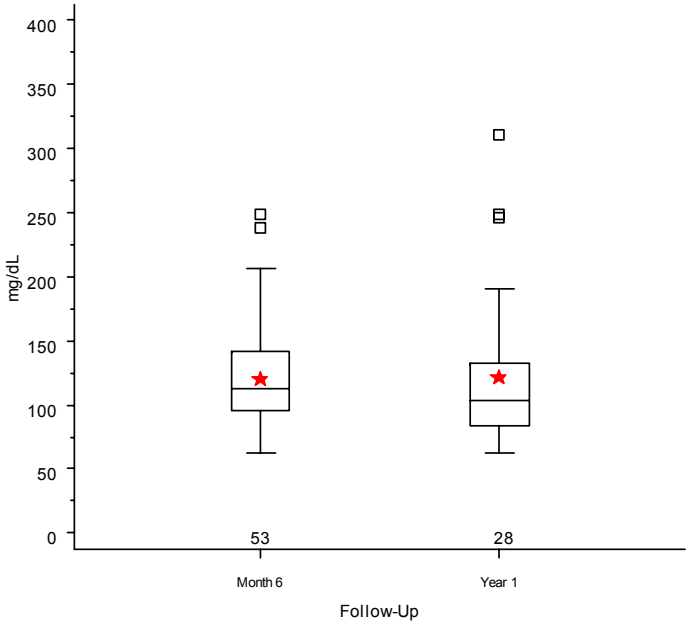


Exhibit 134
HbA_{1C} (%) Post Last Infusion
Participants Who Ever Achieved Insulin Independence

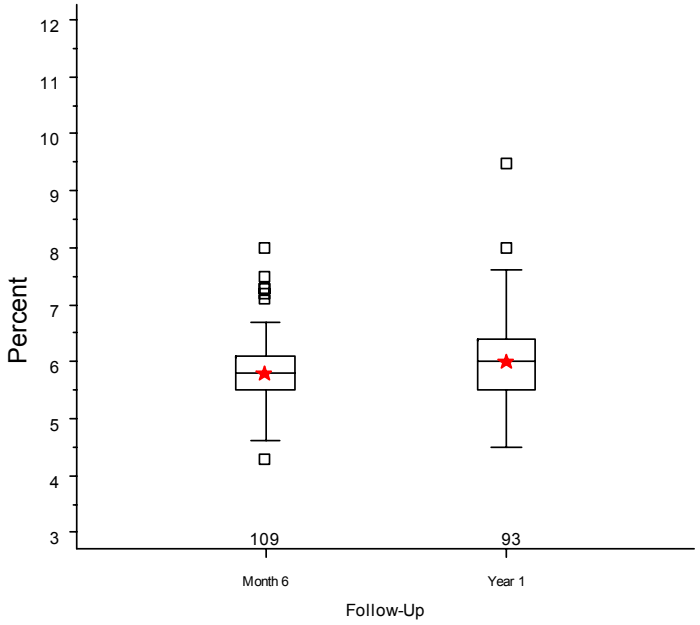


Exhibit 135
HbA_{1C} (%) Post Last Infusion
Participants Who Never Achieved Insulin Independence

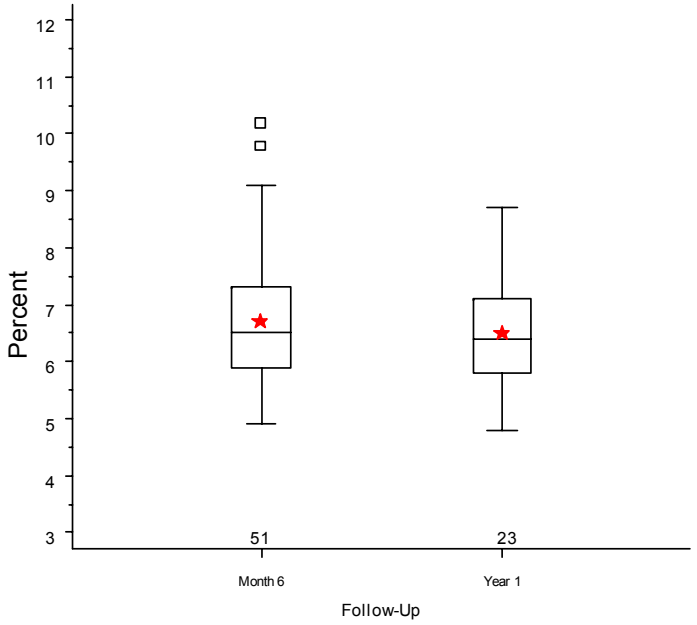
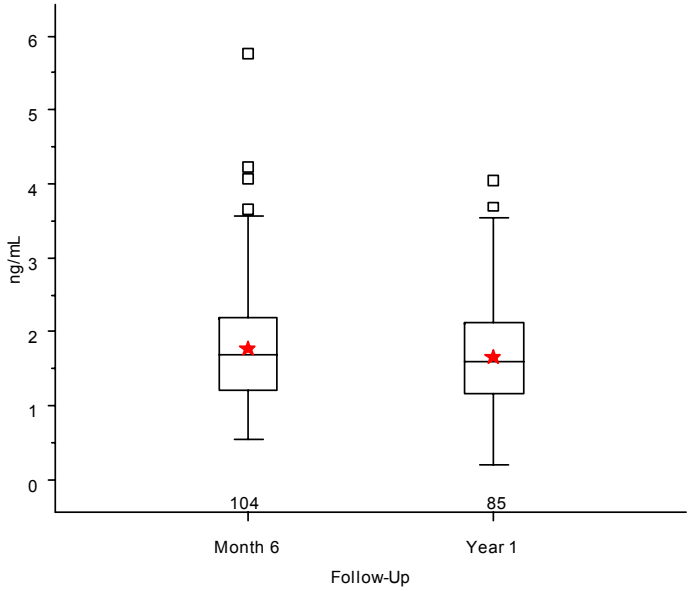


Exhibit 136
Basal Plasma C-peptide (ng/mL) Post Last Infusion
Participants Who Ever Achieved Insulin Independence



Values of 10.1 ng/mL and 6.1 ng/mL were removed from Month 6 for presentation, verified correct by center.

Exhibit 137
Basal Plasma C-peptide (ng/mL) Post Last Infusion
Participants Who Never Achieved Insulin Independence

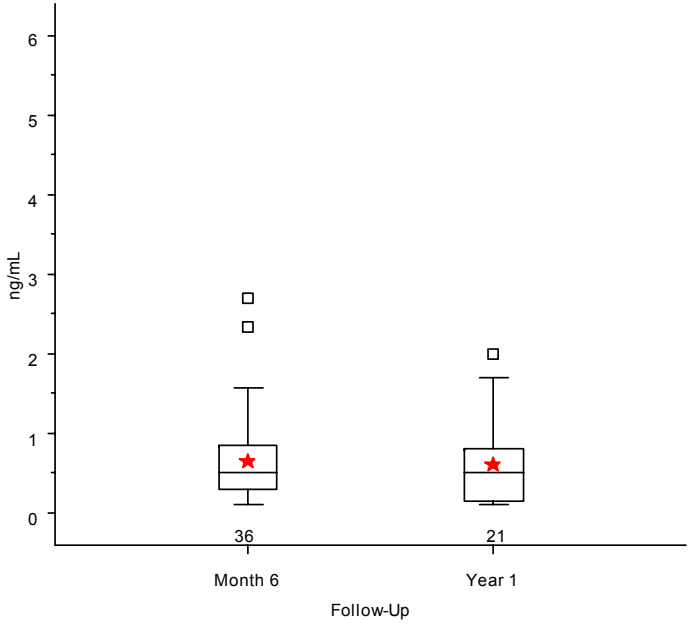


Exhibit 138
Fasting Plasma Glucose (mg/dL)
Pre and Post First Infusion
Insulin Independent Participants

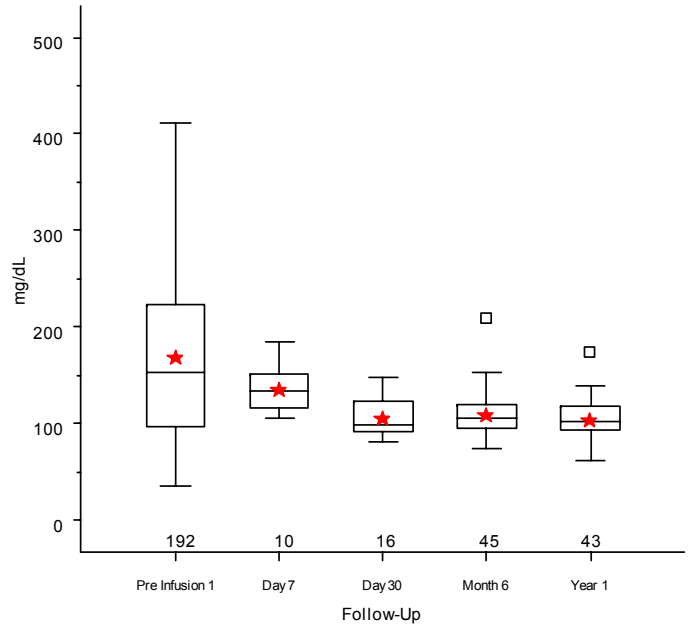


Exhibit 139
Fasting Plasma Glucose (mg/dL)
Pre and Post First Infusion
Insulin Dependent Participants

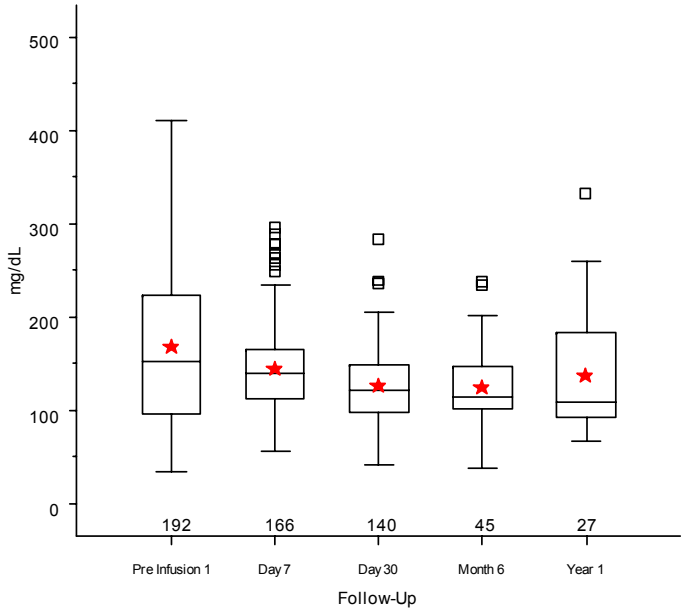


Exhibit 140
HbA_{1C} (%)
Pre and Post First Infusion
Insulin Independent Participants

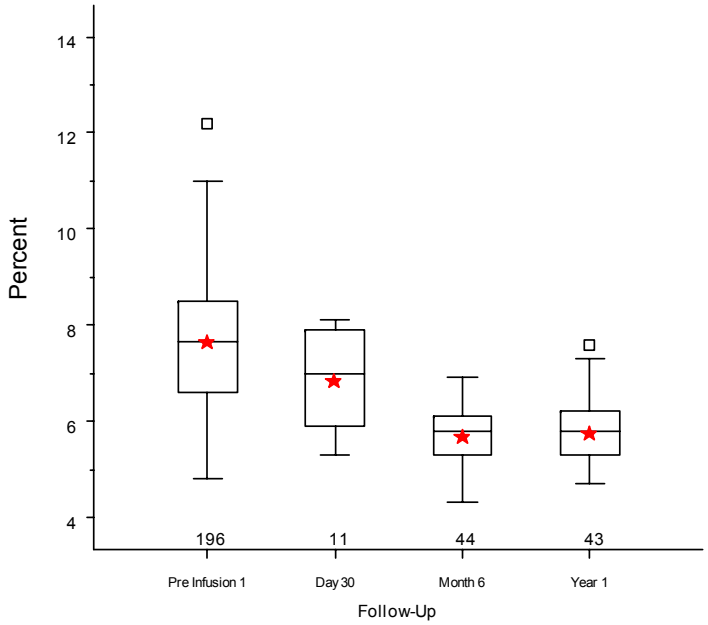


Exhibit 141
HbA_{1C} (%)
Pre and Post First Infusion
Insulin Dependent Participants

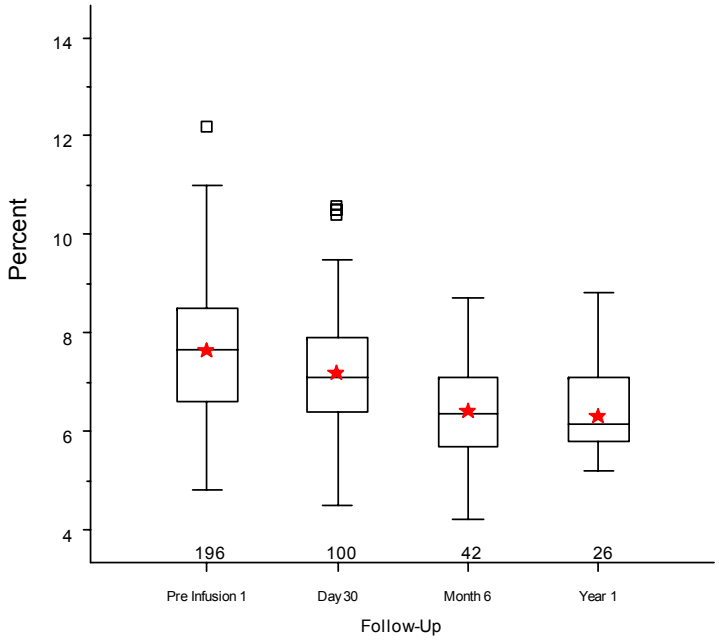
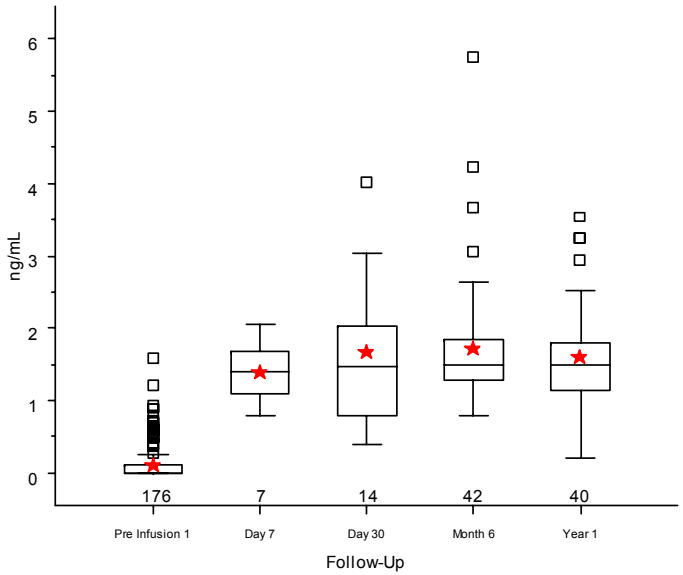


Exhibit 142
Basal Plasma C-Peptide (ng/mL)
Pre and Post First Infusion
Insulin Independent Participants



Values of 10.1 ng/mL at Month 6 and 6.1 ng/mL at Year 1 were removed for presentation, verified correct by center.

Exhibit 143
Basal Plasma C-Peptide (ng/mL)
Pre and Post First Infusion
Insulin Dependent Participants

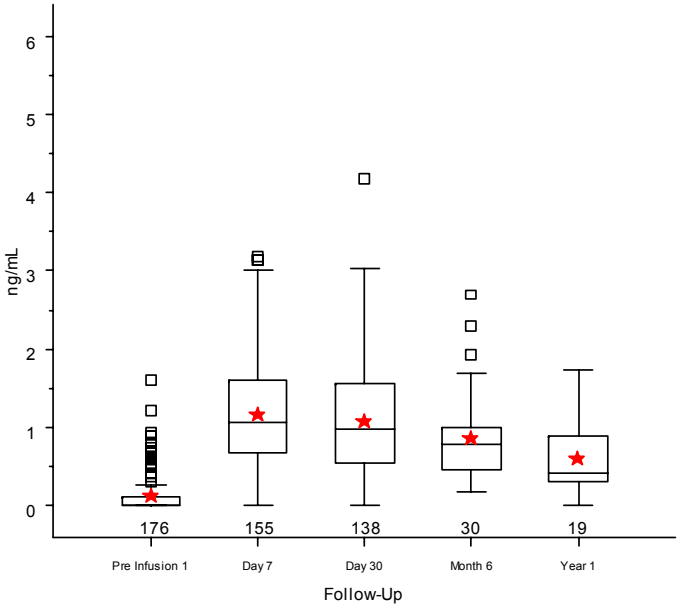
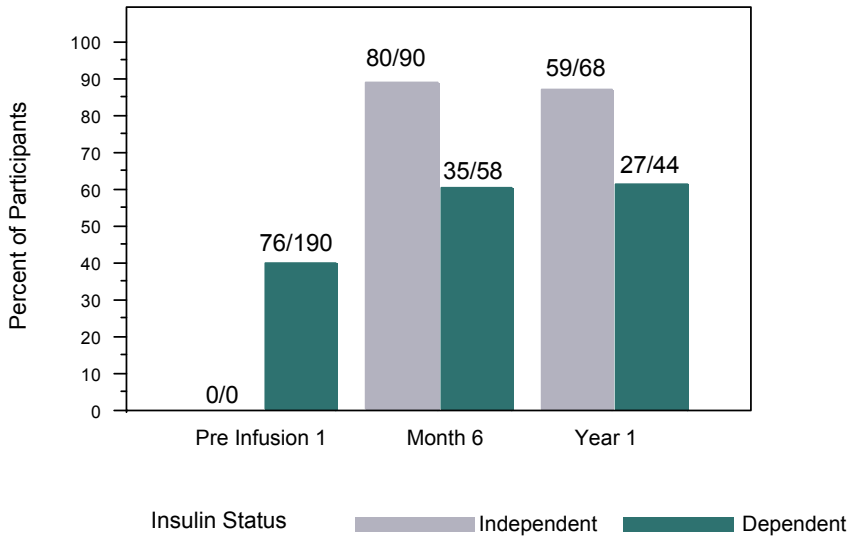
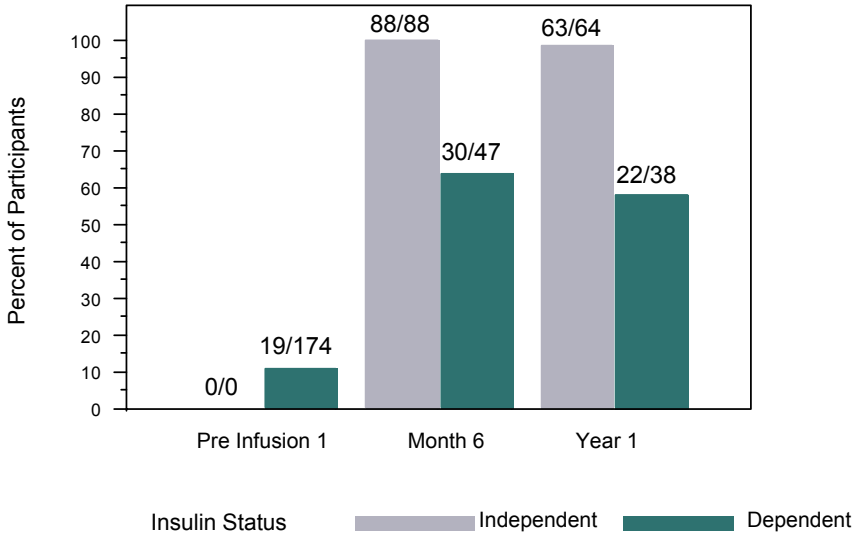


Exhibit 144
Participants with Fasting Blood Glucose < 126 mg/dL
Post Last Infusion
All Participants



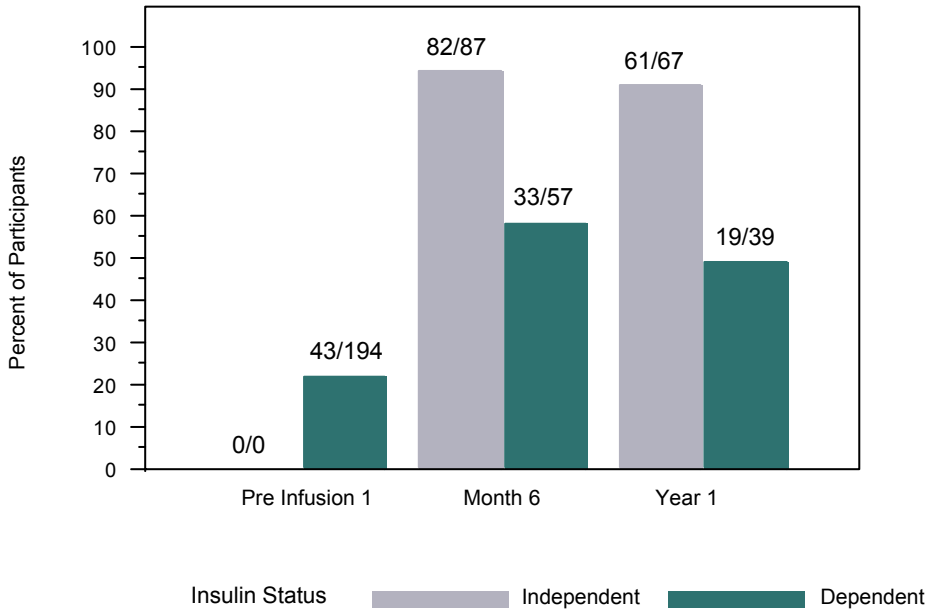
At Month 6, 77.9% of the participants had a fasting plasma glucose < 126 mg/dL while at Year 1 this drops to 58.9%

Exhibit 145
Participants with Basal C-Peptide ≥ 0.5 ng/mL
Post Last Infusion
All Participants



At Month 6, 77.6% of the participants had a basal C-peptide ≥ 0.5 ng/mL, while at Year 1 this drops to 58.6%. For comparison, this Exhibit was also run for participants with basal C-peptide ≥ 0.8 ng/mL at baseline and post last infusion. At baseline, 7 of 174 participants had basal C-peptide ≥ 0.8 ng/mL. For insulin independent participants, this rose to 85 of 88 participants at Month 6 and 61 of 64 participants at Year 1. For insulin dependent participants, the number of participants with basal C-peptide ≥ 0.8 ng/mL was 20 of 47 at Month 6 and 18 of 38 at Year 1.

Exhibit 146
Participants with $HbA_{1C} \leq 6.5$ %
Post Last Infusion
All Participants



At Month 6, 74.2% of the participants had an $HbA_{1C} \leq 6.5\%$, while at Year 1 this drops to 54.6%.

Exhibit 147
Pre Infusion Recipient Lab Summary by Infusion Sequence

	Infusion Sequence																	
	1						2						3					
	N	Mean	SD	Median	Min	Max	N	Mean	SD	Median	Min	Max	N	Mean	SD	Median	Min	Max
Fasting Plasma Glucose (mg/dL)	158	171.9	89.3	152.5	35.0	411.0	121	133.4	47.5	125.0	45.0	308.0	28	121.8	35.9	117.5	55.0	211.0
HbA_{1C} (%)	162	7.7	1.3	7.5	4.8	11.0	112	6.7	1.2	6.6	3.8	9.8	28	6.5	0.8	6.5	4.8	8.0
ALT (IU/L)	160	21.2	9.5	19.0	6.0	72.0	114	39.3	22.1	33.0	11.0	131.0	26	42.7	23.8	40.0	13.0	121.0
AST (IU/L)	165	23.9	7.7	23.0	6.0	58.0	122	33.7	12.4	32.0	17.0	87.0	29	36.1	14.6	33.0	15.0	77.0
Alkaline Phosphatase (IU/L)	159	69.6	21.7	65.0	24.0	150.0	119	70.5	24.4	65.0	32.0	161.0	29	80.7	32.6	73.0	37.0	175.0
Total Bilirubin (mg/dL)	160	0.6	0.4	0.5	0.1	2.7	120	0.5	0.2	0.4	0.1	1.7	28	0.4	0.2	0.4	0.1	0.9
Total Cholesterol (mg/dL)	165	169.2	29.3	169.0	96.0	282.0	109	182.8	34.2	183.0	78.0	262.0	28	183.0	33.9	183.5	116.0	278.0
HDL (mg/dL)	164	62.3	15.1	62.0	31.0	123.0	108	61.2	15.8	59.0	25.0	102.0	28	58.4	16.3	59.0	24.0	103.0
LDL (mg/dL)	164	93.8	24.0	93.0	44.0	173.0	109	101.5	27.6	98.0	46.0	163.0	27	101.9	33.9	100.0	50.0	181.0
Triglycerides (mg/dL)	165	65.7	35.8	54.0	16.0	256.0	108	102.5	63.3	85.0	32.0	379.0	28	120.6	82.5	90.0	50.0	399.0
Serum Creatinine (mg/dL)	167	0.9	0.2	0.9	0.1	1.8	124	0.9	0.2	0.9	0.6	1.7	29	0.9	0.2	0.9	0.7	1.3
Calculated Creatinine Clearance ($mL/min/1.73m^2$)	145	103.5	25.2	98.0	56.0	196.0	74	97.9	27.3	95.0	45.0	166.0	15	99.5	32.8	92.0	68.0	190.0
Basal Plasma C-peptide (ng/mL)	129	0.3	0.2	0.3	0.0	1.6	66	1.0	0.6	0.8	0.2	2.4	22	1.2	0.7	1.1	0.2	3.0

Exhibit 148
Metabolic Summary by Follow-Up Post Last Infusion

	Month 6			Year 1		
	N	Mean	SD	N	Mean	SD
Fasting Plasma Glucose (mg/dL)	138	112.4	26.8	106	110.6	31.3
HbA_{1C} (%)	132	6.0	0.9	99	6.1	0.8
Basal Plasma C-peptide (ng/mL)	99	1.0	0.6	76	0.9	0.6
Peak Stimulated C-peptide After Meal (ng/mL)	60	3.7	1.8	53	3.9	2.8
Basal Plasma C-peptide before IV Glucagon (ng/mL)	9	1.7	0.8	4	1.8	0.7
Peak Stimulated C-peptide After IV Glucagon (ng/mL)	9	2.8	1.3	4	3.1	2.0
Basal Plasma C-peptide Before IV Arginine (ng/mL)	57	1.6	0.8	45	1.6	0.8
Peak Stimulated C-peptide After IV Arginine (ng/mL)	56	2.6	1.2	45	2.6	1.2
Acute C-peptide Response to IV Arginine (ng/mL)	54	0.9	0.4	44	1.0	0.5
Acute Insulin Response to IV Arginine (µU/mL)	55	17.3	9.7	44	16.6	10.4
Basal Plasma C-peptide Before IV Glucose (ng/mL)	48	1.5	0.7	38	1.4	0.8
Peak Stimulated C-peptide After IV Glucose (ng/mL)	47	2.8	1.1	38	2.6	1.1
Acute C-peptide Response to IV Glucose (ng/ml)	46	0.8	0.8	37	0.8	0.6
Acute Insulin Response to IV Glucose (µU/mL)	45	17.2	12.8	40	13.9	10.7
AUC Insulin derived from 0.5 g/kg IVGTT (µU/mL x min)	14	397.6	206.9	13	507.0	298.9
KG-value derived from 0.5 g.kg IVGTT (KG Value)	37	0.2	1.1	31	0.3	0.9
2-hr 75g OGTT Plasma Glucose (mg/dL)	31	181.1	63.4	35	164.8	47.9
AUC C-peptide OGTT (ng/mL x min)	6	235.8	144.3	7	189.0	110.8
AUC C-peptide MMTT (ng/mL x min)	37	257.1	282.1	40	253.5	275.4
Mixed Meal Stimulation Index (pmol/mg)	12	1.0	0.8	15	1.0	0.9

Exhibit 149
Metabolic Summary Month 6 Post Last Infusion
by Insulin Status

	Insulin Independent			Insulin Dependent		
	N	Mean	SD	N	Mean	SD
Fasting Plasma Glucose (mg/dL)	86	107.2	19.8	45	117.9	31.6
HbA_{1C} (%)	84	5.7	0.5	41	6.6	1.1
Basal Plasma C-peptide (ng/mL)	65	1.2	0.6	28	0.5	0.4
Peak Stimulated C-peptide After Meal (ng/mL)	37	4.2	1.5	18	2.5	1.7
Basal Plasma C-peptide before IV Glucagon (ng/mL)	8	1.9	0.6	1	0.5	-
Peak Stimulated C-peptide After IV Glucagon (ng/mL)	8	3.1	1.0	1	0.6	-
Basal Plasma C-peptide Before IV Arginine (ng/mL)	48	1.7	0.7	9	1.2	1.5
Peak Stimulated C-peptide After IV Arginine (ng/mL)	47	2.7	0.9	9	1.7	2.0
Acute C-peptide Response to IV Arginine (ng/mL)	47	0.9	0.4	7	0.5	0.5
Acute Insulin Response to IV Arginine (µU/mL)	46	19.2	8.1	9	7.1	11.0
Basal Plasma C-peptide Before IV Glucose (ng/mL)	42	1.5	0.7	4	1.3	1.1
Peak Stimulated C-peptide After IV Glucose (ng/mL)	41	2.8	1.0	4	2.1	1.8
Acute C-peptide Response to IV Glucose (ng/ml)	40	0.8	0.8	4	0.4	0.6
Acute Insulin Response to IV Glucose (µU/mL)	39	17.3	12.3	4	11.7	15.4
AUC Insulin derived from 0.5 g/kg IVGTT (µU/mL x min)	10	422.7	204.3	2	161.7	1.0
KG-value derived from 0.5 g.kg IVGTT (KG Value)	32	0.2	1.2	3	0.2	1.4
2-hr 75g OGTT Plasma Glucose (mg/dL)	28	167.0	45.9	3	313.0	54.7
AUC C-peptide OGTT (ng/mL x min)	5	264.0	141.6	1	94.5	-
AUC C-peptide MMTT (ng/mL x min)	27	295.3	301.1	6	193.1	258.5
Mixed Meal Stimulation Index (pmol/mg)	11	1.0	0.8	1	0.7	-

Exhibit 150
Metabolic Summary Year 1 Post Last Infusion
by Insulin Status

	Insulin Independent			Insulin Dependent		
	N	Mean	SD	N	Mean	SD
Fasting Plasma Glucose (mg/dL)	62	104.0	16.7	38	114.7	41.8
HbA_{1C} (%)	60	5.8	0.5	33	6.6	0.9
Basal Plasma C-peptide (ng/mL)	44	1.1	0.5	26	0.6	0.6
Peak Stimulated C-peptide After Meal (ng/mL)	27	4.4	1.3	20	2.3	1.5
Basal Plasma C-peptide before IV Glucagon (ng/mL)	3	1.8	0.9	1	2.1	-
Peak Stimulated C-peptide After IV Glucagon (ng/mL)	3	3.3	2.4	1	2.4	-
Basal Plasma C-peptide Before IV Arginine (ng/mL)	38	1.6	0.7	7	1.3	1.0
Peak Stimulated C-peptide After IV Arginine (ng/mL)	38	2.7	1.1	7	2.0	1.5
Acute C-peptide Response to IV Arginine (ng/mL)	38	1.1	0.5	6	0.7	0.5
Acute Insulin Response to IV Arginine (µU/mL)	36	17.0	9.9	7	14.4	14.2
Basal Plasma C-peptide Before IV Glucose (ng/mL)	30	1.4	0.8	6	0.8	0.5
Peak Stimulated C-peptide After IV Glucose (ng/mL)	30	2.7	0.9	6	1.8	1.5
Acute C-peptide Response to IV Glucose (ng/ml)	29	0.9	0.6	6	0.5	0.4
Acute Insulin Response to IV Glucose (µU/mL)	31	14.8	10.6	6	10.5	10.3
AUC Insulin derived from 0.5 g/kg IVGTT (µU/mL x min)	10	531.4	306.5	1	133.0	-
KG-value derived from 0.5 g.kg IVGTT (KG Value)	24	0.4	1.0	5	-0.2	0.8
2-hr 75g OGTT Plasma Glucose (mg/dL)	32	166.3	48.7	3	148.3	41.7
AUC C-peptide OGTT (ng/mL x min)	6	185.1	120.8	1	212.4	-
AUC C-peptide MMTT (ng/mL x min)	25	273.7	257.9	10	285.5	364.8
Mixed Meal Stimulation Index (pmol/mg)	12	1.1	1.0	3	0.8	0.2

Exhibit 151
Change in Islet Graft Function and Recipient Survival Summary
Post Last Infusion

	Month 6		Year 1	
	N	%	N	%
Change in Islet Graft Function				
No Change Reported	139	82.7	93	74.4
One or More Changes Reported	5	3.0	6	4.8
Total Islet Graft Failure	6	3.6	8	6.4
Unknown or Not Reported on Change in Islet Graft Function Form	10	6.0	13	10.4
Missing	8	4.8	5	4.0
Participant Death				
Yes	1*	0.6	-	0.0
No	167	99.4	125	100.0

*One recipient died 70 days following their third islet cell infusion. The cause of death for this recipient was reported as acute methadone and diphenhydramine toxicity unrelated to both the infusion procedure and immunosuppression therapy. An additional recipient death has been reported which occurred after Year 3 post last infusion. The cause of death for this recipient was reported as viral meningitis possibly related to the immunosuppression therapy. Finally, a third death was reported which occurred after Year 4 post last infusion. The death was discovered in the obituaries and the cause of death is unknown.

At the time of this report, a number of episodes of change in islet graft function and forms remain unreported to the Registry.

Exhibit 152
Change in Islet Graft Function Summary

Recipient	Infusion Sequence	Total IEQs/kg to date	Days From Infusion to Change in Function	Primary Reason for Change in Function	Outcome*	Were any Adverse Events Associated
1	1	6,823	681	Islet exhaustion	Unknown	No
2	1	5,836	102	Islet exhaustion	Unknown	No
	2	13,720	523	Islet exhaustion	Unknown	No
3	1	7,745	30	Rejection	Partial recovery	No
4	1	6,723	789	Islet exhaustion	Unknown	No
5	1	16,142	1792	Islet exhaustion	Unknown	No
6	1	8,044	173	Rejection	Partial recovery	No
	1	8,044	230	Recipient discont. meds	Complete dysfunction	Unknown
7	1	8,553	777	Islet exhaustion	Unknown	No
8	1	5,918	1271	Islet exhaustion	Complete dysfunction	No
9	1	5,872	621	Islet exhaustion	Unknown	No
10	3	23,281	602	Islet exhaustion	Complete dysfunction	No
11	3	20,351	92	Islet exhaustion	Complete dysfunction	No
12	1	13,049	66	Unknown	Complete dysfunction	No
13	2	18,399	256	Unknown	Partial recovery	No
	3	24,923	80	Unknown	Partial recovery	No
	3	24,923	195	Unknown	Partial recovery	No
	3	24,923	651	Tx center discont. meds	Complete dysfunction	No
14	2	13,018	380	Unknown	Complete dysfunction	Unknown
15	2	13,450	1198	Unknown	Partial recovery	No
16	3	25,060	493	Islet exhaustion	Complete dysfunction	No
17	1	10,665	454	Islet exhaustion	Complete dysfunction	No
18	3	33,124	164	Rejection	Partial recovery	No
19	2	12,956	1232	Unknown	Partial recovery	No
20	2	18,500	149	Unknown	Partial recovery	No
	3	36,305	108	Unknown	Partial recovery	No
	3	36,305	174	Unknown	Partial recovery	No
	3	36,305	316	Unknown	Partial recovery	No
	3	36,305	396	Unknown	Partial recovery	No
	3	36,305	743	Unknown	Complete dysfunction	No

Exhibit 152 *(continued)*
Change in Islet Graft Function Summary

Recipient	Infusion Sequence	Total IEQs/kg to date	Days From Infusion to Change in Function	Primary Reason for Change in Function	Outcome*	Were any Adverse Events Associated
21	3	21,215	533	Unknown	Partial recovery	No
22	2	15,066	59	Unknown	Partial recovery	No
	2	15,066	132	Unknown	Partial recovery	No
	3	19,988	264	Unknown	Partial recovery	No
	3	19,988	353	Unknown	Partial recovery	No
	3	19,988	671	Unknown	Partial recovery	No
23	1	6,250	684	Unknown	Partial recovery	No
	1	6,250	982	Unknown	Partial recovery	No
24	1	12,269	830	Islet exhaustion	Partial recovery	No
25	2	14,409	347	Unknown	Partial recovery	No
26	2	13,185	828	Unknown	Partial recovery	No
	2	13,185	930	Unknown	Complete dysfunction	No
27	2	10,409	492	Insufficient islet mass	Unknown	No
28	1	5,262	301	Rejection	Complete dysfunction	No
29	2	11,905	119	Unknown	Complete dysfunction	No
30	2	14,553	564	Islet exhaustion	Complete dysfunction	No
31	2	13,125	307	Islet exhaustion	Complete dysfunction	No
32	2	13,962	769	Rejection	Complete dysfunction	No
33	3	18,187	576	Primary nonfunction	Complete dysfunction	No
34	1	13,553	888	Recipient discont. meds	Complete dysfunction	No
35	2	13,369	63	Unknown	Partial recovery	No
35	2	13,369	240	Other	Complete dysfunction	No
36	2	13,228	445	Islet exhaustion	Complete dysfunction	No
37	1	9,815	117	Primary nonfunction	Complete dysfunction	No
38	1	4,464	275	Rejection	Complete dysfunction	No
39	2	16,569	194	Recipient discont. meds	Complete dysfunction	No
40	1	10,256	421	Recipient discont. meds	Complete dysfunction	Unknown
41	1	8,283	268	Islet exhaustion	Complete dysfunction	No
42	3	Missing	612	Unknown	Complete dysfunction	No
43	2	11,931	643	Unknown	Partial recovery	No

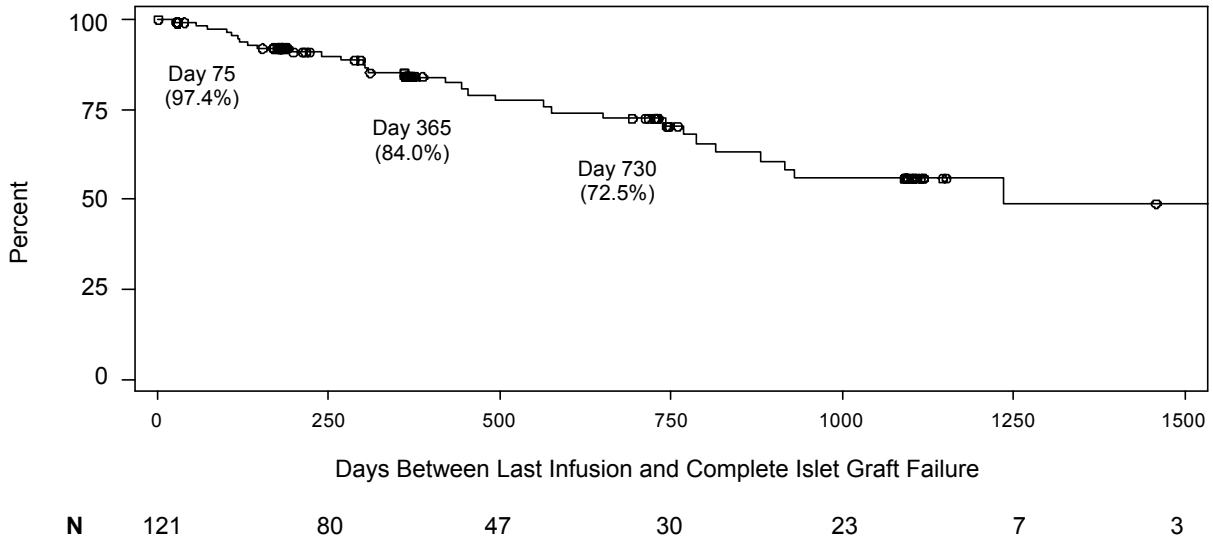
Exhibit 152 *(continued)*
Change in Islet Graft Function Summary

Recipient	Infusion Sequence	Total IEQs/kg to date	Days From Infusion to Change in Function	Primary Reason for Change in Function	Outcome*	Were any Adverse Events Associated
44	1	11,988	36	Primary nonfunction	Partial recovery	No
	2	30,587	31	Rejection	Partial recovery	No
45	2	15,086	181	Other	Unknown	No
46	1	9,652	313	Unknown	Partial recovery	No
47	1	Missing	108	Primary nonfunction	Complete dysfunction	No
48	1	Missing	102	Primary nonfunction	Complete dysfunction	No
49	1	6,382	27	Primary nonfunction	Complete dysfunction	Yes**
50	2	Missing	112	Tx center discont. meds	Complete dysfunction	Yes***
51	1	4,049	9	Primary nonfunction	Complete dysfunction	No
52	1	Missing	57	Primary nonfunction	Complete dysfunction	No

*Definitions of outcomes are included in the Methods section of the report.
**Experienced two lymphopenias and a leukopenia between infusion and complete dysfunction.
***Discontinued immunosuppression therapy after life-threatening infection.

A large number of reasons for dysfunction are listed as unknown due to the subjective nature of the question and the center choosing not to report a particular cause. Additionally, a number of episodes of changes in islet graft function remain unreported to the Registry at the time of this report.

Exhibit 153
Time to Complete Islet Graft Failure
All Participants from Centers Reporting Islet Graft Failures



For 121 participants with complete reporting of changes in islet graft function, 32 participants (26.4%) have experienced islet graft failure. On average, complete loss of islet graft function occurred in 506 days (SD 429) after receiving their first islet infusion, while the median time to complete loss of islet function is 385 days.

In this Exhibit, by Year 1 post last infusion 26% of participants have experienced islet graft failure.

Exhibit 154
Summary of Secondary Complications Pre First Infusion and Post Last Infusion

	Follow-Up					
	Pre First Infusion		Month 6		Year 1	
	N	%	N	%	N	%
Total	203	100.0	193	100.0	163	100.0
Hypoglycemia						
No occurrence	-	0.0	122	63.2	95	58.3
Partial awareness	65	32.0	14	7.3	8	4.9
Unawareness	129	63.5	1	0.5	4	2.5
Having episodes and aware	2	1.0	10	5.2	3	1.8
Unknown	7	3.4	46	23.8	53	32.5
Peripheral Neuropathy						
No occurrence	115	56.7	103	53.4	76	46.6
Asymptomatic	13	6.4	10	5.2	8	4.9
Symptomatic	66	32.5	26	13.5	20	12.3
Disabling	1	0.5	-	0.0	1	0.6
Unknown	8	3.9	54	28.0	58	35.6
Autonomic Neuropathy						
No occurrence	146	71.9	114	59.1	80	49.1
Asymptomatic	11	5.4	6	3.1	6	3.7
Symptomatic	32	15.8	22	11.4	14	8.6
Disabling	-	0.0	-	0.0	1	0.6
Unknown	14	6.9	51	26.4	62	38.0
Nephropathy						
No occurrence	150	73.9	111	57.5	79	48.5
Microalbuminuria	40	19.7	21	10.9	18	11.0
Macroalbuminuria	1	0.5	3	1.6	5	3.1
Stable allograft	1	0.5	1	0.5	1	0.6
Unknown	11	5.4	57	29.5	60	36.8
CAD						
Yes	11	5.4	9	4.7	5	3.1
No	184	90.6	140	72.5	106	65.0
Unknown	8	3.9	44	22.8	52	31.9

Exhibit 154 *(continued)*
Summary of Secondary Complications Pre First Infusion and Post Last Infusion

	Follow-Up					
	Pre First Infusion		Month 6		Year 1	
	N	%	N	%	N	%
CVA						
Yes	-	0.0	-	0.0	-	0.0
No	194	95.6	150	77.7	116	71.2
Unknown	9	4.4	43	22.3	47	28.8
PVD						
Yes	2	1.0	2	1.0	-	0.0
No	192	94.6	146	75.6	113	69.3
Unknown	9	4.4	45	23.3	50	30.7
Treated Hypertension						
Yes	67	33.0	59	30.6	51	31.3
No	130	64.0	93	48.2	67	41.1
Unknown	6	3.0	41	21.2	45	27.6
Foot Ulcers						
Yes	8	3.9	1	0.5	3	1.8
No	171	84.2	147	76.2	110	67.5
Unknown	24	11.8	45	23.3	50	30.7
Lower Limb Amputation						
Yes	1	0.5	-	0.0	-	0.0
No	191	94.1	156	80.8	118	72.4
Unknown	11	5.4	37	19.2	45	27.6
Foot Deformity						
Yes	2	1.0	2	1.0	1	0.6
No	182	89.7	147	76.2	112	68.7
Unknown	19	9.4	44	22.8	50	30.7
Dysesthesia						
Yes	29	14.3	14	7.3	9	5.5
No	143	70.4	126	65.3	100	61.3
Unknown	31	15.3	53	27.5	54	33.1

Exhibit 154 *(continued)*
Summary of Secondary Complications Pre First Infusion and Post Last Infusion

	Follow-Up					
	Pre First Infusion		Month 6		Year 1	
	N	%	N	%	N	%
Orthostatic Hypotension						
Yes	14	6.9	4	2.1	1	0.6
No	142	70.0	124	64.2	98	60.1
Unknown	47	23.2	65	33.7	64	39.3
Gastroparesis						
Yes	15	7.4	9	4.7	8	4.9
No	160	78.8	134	69.4	104	63.8
Unknown	28	13.8	50	25.9	51	31.3
Constipation						
Yes	17	8.4	9	4.7	3	1.8
No	160	78.8	137	71.0	111	68.1
Unknown	26	12.8	47	24.4	49	30.1
Diabetic Diarrhea						
Yes	6	3.0	6	3.1	5	3.1
No	171	84.2	128	66.3	101	62.0
Unknown	26	12.8	59	30.6	57	35.0
Fecal Incontinence						
Yes	-	0.0	-	0.0	-	0.0
No	177	87.2	147	76.2	115	70.6
Unknown	26	12.8	46	23.8	48	29.4
Diabetic Bladder Dysfunction						
Yes	2	1.0	2	1.0	1	0.6
No	173	85.2	143	74.1	113	69.3
Unknown	28	13.8	48	24.9	49	30.1
Sexual Dysfunction						
Yes	14	6.9	6	3.1	8	4.9
No	160	78.8	124	64.2	91	55.8
Unknown	29	14.3	63	32.6	64	39.3

Exhibit 155
Summary of Ocular Complications Post Last Infusion

	Follow-Up					
	Pre First Infusion		Month 6		Year 1	
	N	%	N	%	N	%
Total	203	100.0	193	100.0	163	100.0
Retinopathy						
None	93	45.8	65	33.7	54	33.1
Non Proliferative	47	23.2	33	17.1	23	14.1
Proliferative	50	24.6	20	10.4	13	8.0
Unknown	13	6.4	75	38.9	73	44.8
Diabetic Macular Edema						
None	182	89.7	122	63.2	93	57.1
Mild	3	1.5	-	0.0	-	0.0
Moderate	2	1.0	1	0.5	-	0.0
Severe	1	0.5	-	0.0	-	0.0
Unknown	15	7.4	70	36.3	70	42.9
Laser photocoagulation surgery performed for proliferative retinopathy						
Yes	68	33.5	5	2.6	2	1.2
No	126	62.1	148	76.7	113	69.3
Unknown	9	4.4	40	20.7	48	29.4
Laser photocoagulation surgery performed for diabetic macular edema						
Yes	9	4.4	-	0.0	1	0.6
No	179	88.2	153	79.3	114	69.9
Unknown	15	7.4	40	20.7	48	29.4
Vitrectomy						
Yes	19	9.4	-	0.0	1	0.6
No	174	85.7	152	78.8	115	70.6
Unknown	10	4.9	41	21.2	47	28.8
Other Surgery						
Yes	12	5.9	2	1.0	4	2.5
No	166	81.8	137	71.0	104	63.8
Unknown	25	12.3	54	28.0	55	33.7

Chapter 5
Participant's Laboratory Data

Participant's Laboratory Data Summary

This chapter provides a summary of reported abnormal laboratory liver function tests (Exhibit 156), abnormal lipid tests (Exhibit 161), and the percent of participants with a marked increase in serum creatinine from baseline (Exhibit 166). Abnormal has been defined as one or greater times the upper limit of normal (ULN) to up to two times the ULN for the test and two or greater times the ULN for the test.

Reports at the two times or greater than the ULN at any of the specified follow-up time points (pre-subsequent infusion, 6 months, 1 year) were minimal for ALT (2.8%), AST (2.2%), alkaline phosphatase (2.2%) and for total bilirubin (0.5%). There were no reports at this level for total cholesterol and 8 reports (4.5%) for triglycerides. In addition, there were 10 reports (6.0%), of a participant with an increase in their serum creatinine of greater than 0.5 mg/dL of their baseline level.

Summary measures for each laboratory value are also constructed prior to their first infusion and by Month 6 and Year 1 post the participant's last infusion procedure. For each of these laboratory tests, boxplots are displayed (Exhibits 157-160, 162-166, and 167-168). For a boxplot the "star" (★) represents the mean value. The whiskers of the plot represent the minimum value and the maximum value, while the lower line of the box represents the 25th percentile, the upper line of the box the 75th percentile and the middle line in the box represent the median (50th percentile).

Exhibit 156
Participants with Abnormal Liver Function Tests Post Infusion

	1-2X ULN		≥ 2X ULN	
	N	%	N	%
ALT	35	19.6	5	2.8
AST	56	30.3	4	2.2
Alkaline Phosphatase	42	23.1	4	2.2
Total Bilirubin	1	0.5	1	0.5

Upper Limit of Normal (ULN)

Values of liver function tests analyzed in this Exhibit are evaluated prior to each subsequent infusion and at Month 6 and Year 1 after the last infusion procedure occurs.

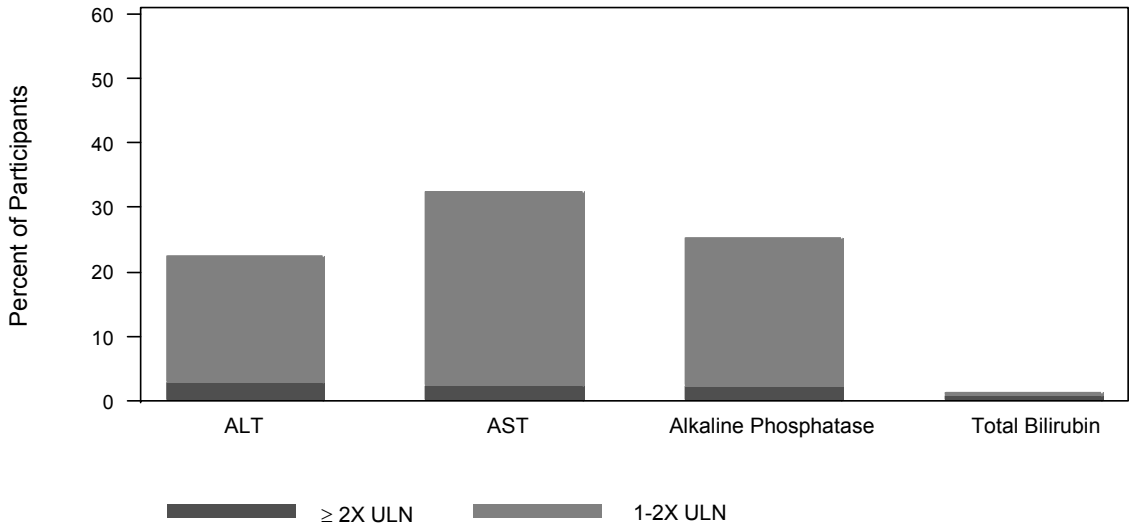


Exhibit 157
ALT (IU/L) Pre Infusion and Post Last Infusion

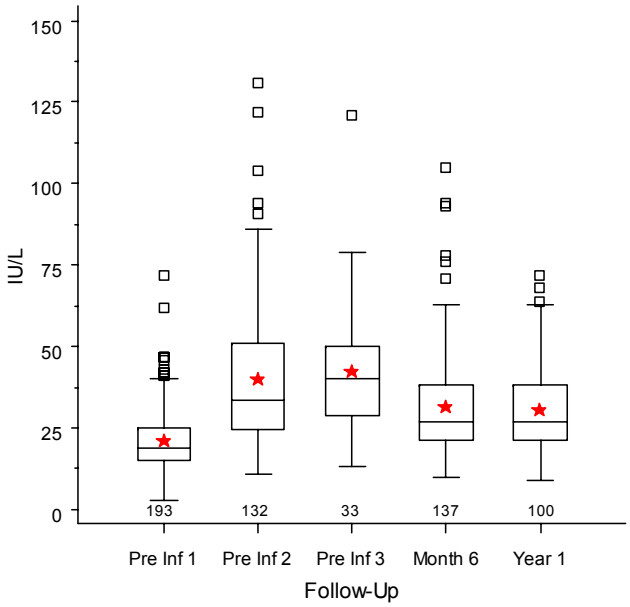


Exhibit 158
AST (IU/L) Pre Infusion and Post Last Infusion

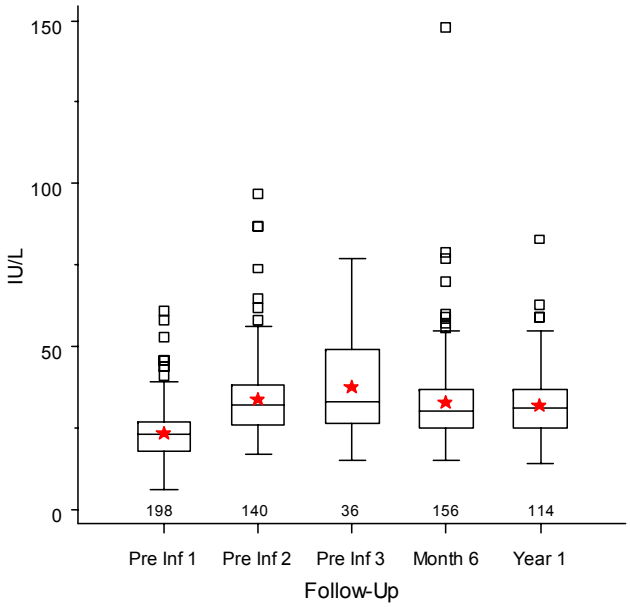


Exhibit 159
Alkaline Phosphatase (IU/L) Pre Infusion and Post Last Infusion

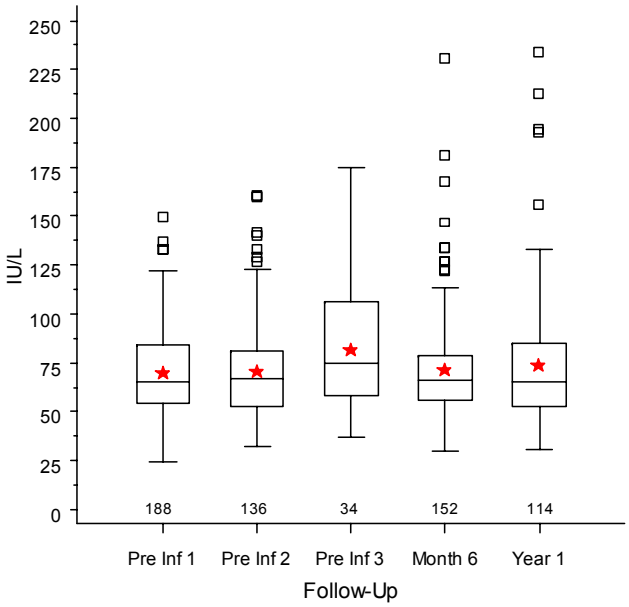


Exhibit 160
Total Bilirubin (mg/dL) Pre Infusion and Post Last Infusion

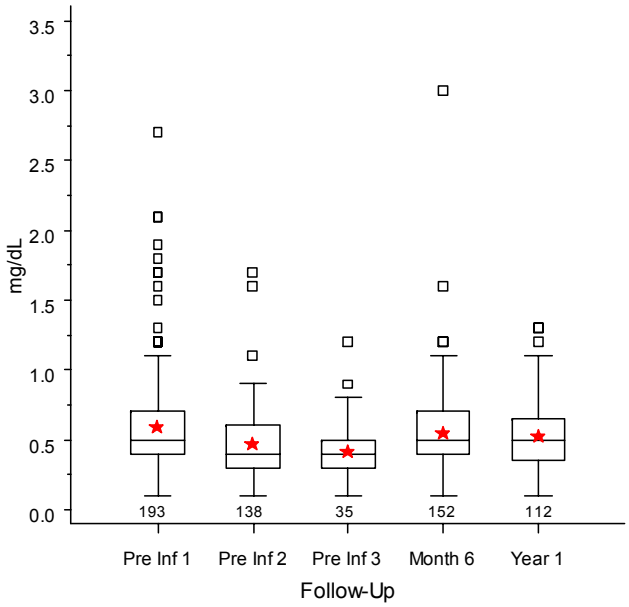


Exhibit 161
Participants with Abnormal Lipid Tests Post First Infusion

	1-2X ULN		≥ 2X ULN	
	N	%	N	%
Total Cholesterol	18	10.0	-	0.0
Triglycerides	32	17.9	8	4.5

Upper Limit of Normal (ULN)

Values of lipid tests analyzed in this Exhibit are evaluated prior to each subsequent infusion and at Month 6 and Year 1 after the last infusion procedure occurs.

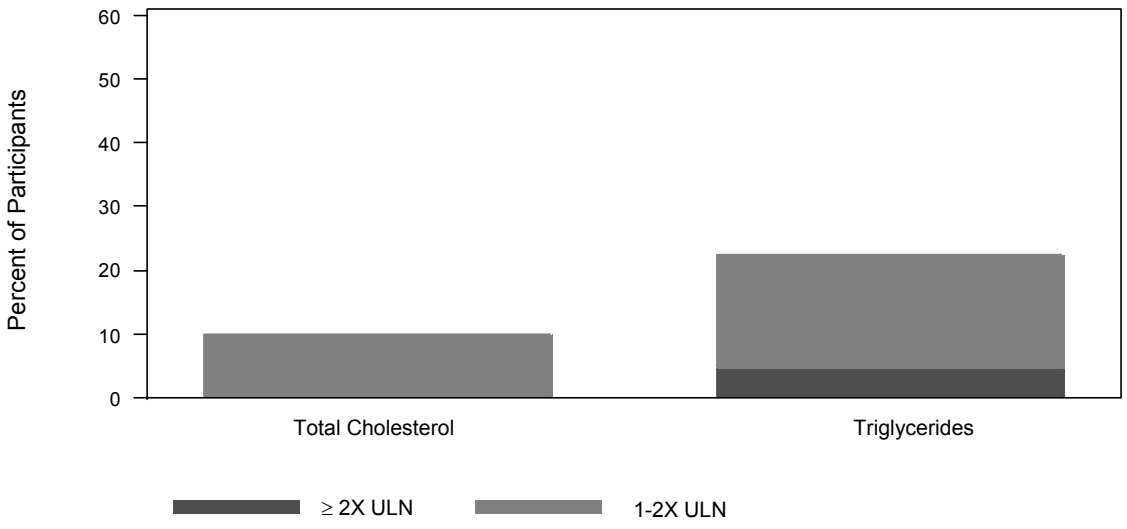


Exhibit 162
Total Cholesterol (mg/dL) Pre Infusion and Post Last Infusion

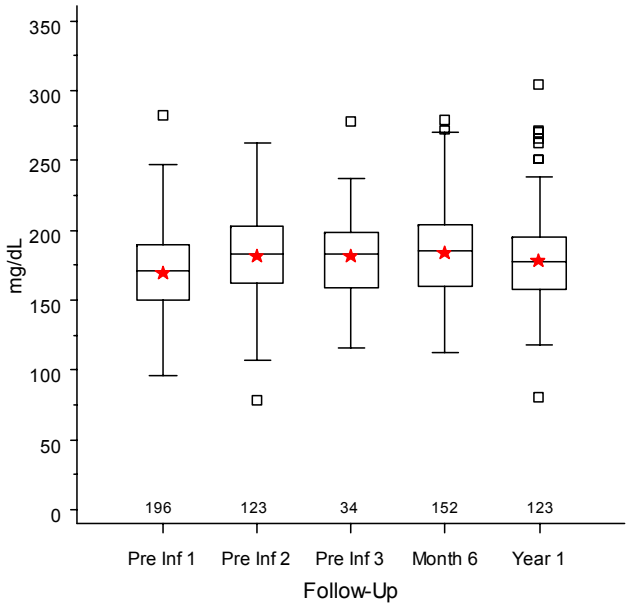


Exhibit 163
HDL (mg/dL) Pre Infusion and Post Last Infusion

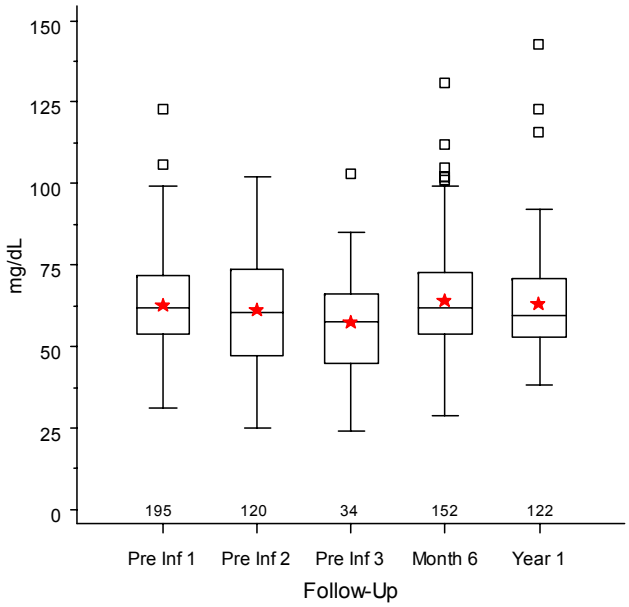


Exhibit 164
LDL (mg/dL) Pre Infusion and Post Last Infusion

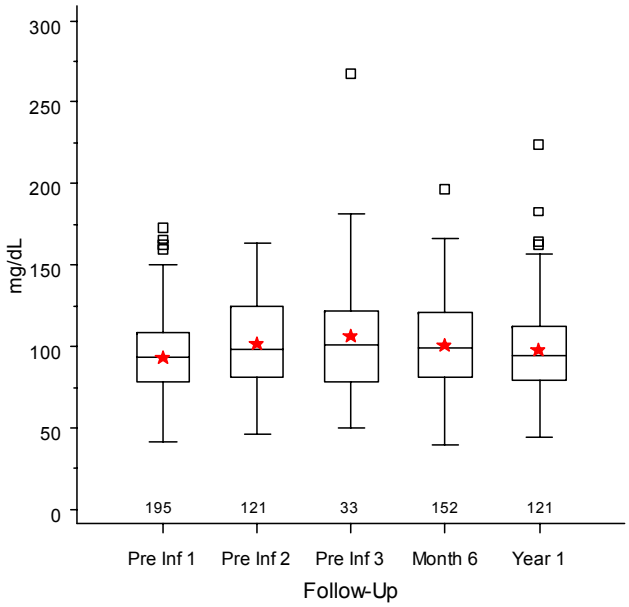


Exhibit 165
Triglycerides (mg/dL) Pre Infusion and Post Last Infusion

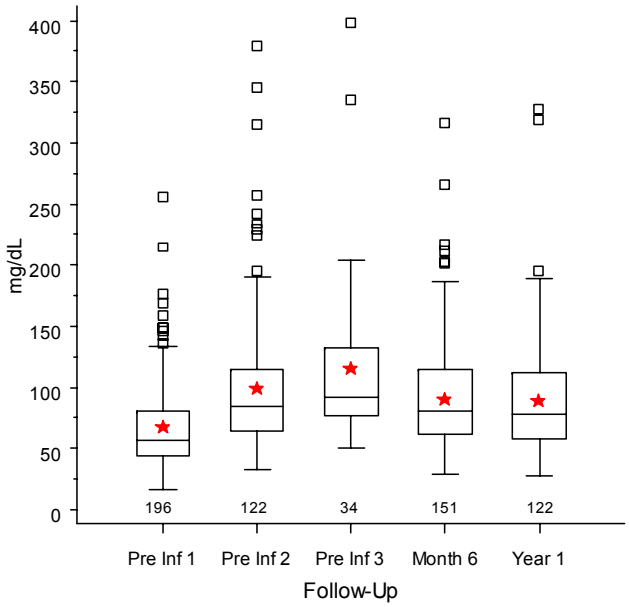


Exhibit 166
Percent of Participants with an Increase in Serum Creatinine (mg/dL) Greater Than 0.5 from Baseline

	Increase in Serum Creatinine > 0.5 mg/dL	
	N	%
Serum Creatinine	10	6.0

Values of serum creatinine analyzed in this Exhibit are evaluated prior to each subsequent infusion and at Month 6 and Year 1 after the last infusion procedure occurs.

Exhibit 167
Serum Creatinine (mg/dL)
Pre Infusion and Post Last Infusion

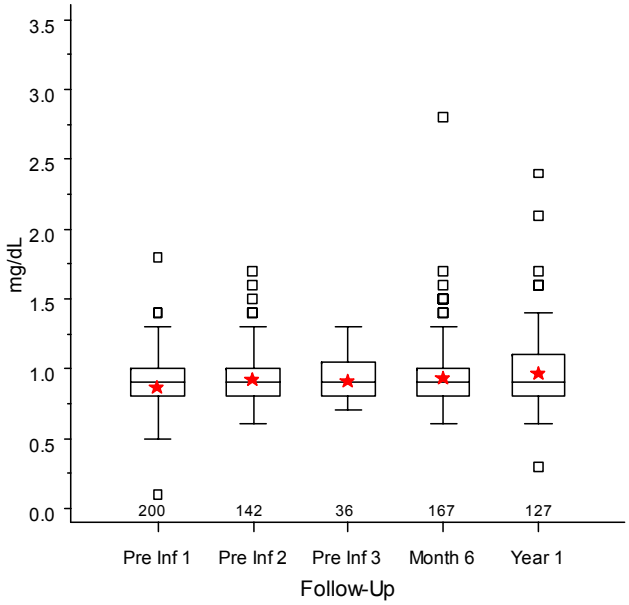
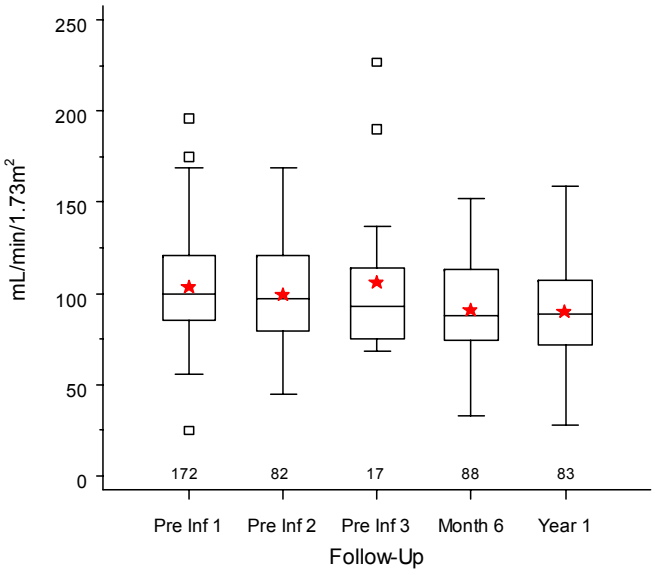


Exhibit 168
Calculated Creatinine Clearance (mL/min/1.73m^2)
Pre Infusion and Post Last Infusion



Chapter 6
Adverse Events

Adverse Events Summary

All grade 3, 4 and 5 adverse events, according to the Common Terminology Criteria for Adverse Events (CTCAE) of the National Cancer Institute, and all serious adverse events (regardless of grade) are reported to CITR. Respective CITR Principal Investigators currently determine the relationship of the adverse event to the immunosuppression therapy and to the islet infusion procedure at the time adverse event forms are completed. However, this procedure is being standardized and all relationship determination will be conducted by a committee using standard procedures.

Exhibit 169 presents the adverse event and serious adverse event rate for islet alone transplant recipients in Year 1 post their first islet infusion. Almost 72% of the recipients experienced at least one adverse event in Year 1, while over 47% experienced one or more serious adverse events in this same period. Of the 521 reported adverse events, 32.8% were related to the immunosuppression therapy and 26.7% were related to the infusion procedure. Of the 186 reported serious adverse events, 29.6% were related to the immunosuppression therapy and 41.9% were related to the islet infusion procedure. Exhibit 169-170 displays the number of serious adverse events reported and percent of participants with at least one reported serious adverse event in Year 1 post first infusion.

Overall, a total of 236 serious adverse events were reported to the Registry as of datafile closure, with 41.1% of them classified as life threatening and 40.7% requiring an inpatient hospitalization (Exhibit 171). Almost 79% (186 of 236) of serious adverse events occurred in the first year following the participants' first infusion procedure. Over 33% of the serious adverse events were classified by the reporting CITR investigator as related to the islet infusion procedure and 25.0% related to the immunosuppression therapy (Exhibit 171). Adverse event relationships to the infusion procedure and immunosuppression regimen are determined by the local CITR Investigator and do not necessarily represent scientific truth. In 2.1% (N=5) of the reports the SAE was related to both the infusion procedure and to the immunosuppression therapy. These events included increased alanine aminotransferase, increased blood alkaline phosphatase, leukopenia, and portal vein thrombosis. Approximately 94% of the serious adverse events resolved with no residual effects (Exhibit 172). Most of the reported serious adverse events were categorized as investigations (24.2%), gastrointestinal disorders (19.5%) and blood and lymphatic system disorders (17.4%) as classified by the MedDRA classifications system (Exhibit 173). The most common SAEs reported are summarized in Exhibit 174.

A summary of all serious adverse events reported to the Registry is listed in alphabetical order in Exhibit 175. This Exhibit contains information regarding the serious adverse event year, when it occurred related to the last infusion procedure date, its relationship to the islet infusion procedure and immunosuppression therapy as recorded by the local CITR Investigator, treatment required and the final outcome of the event.

A summary of reported neoplasms (N=4) are included in Exhibit 176. Duration of hospitalization for the infusion procedure is presented in Exhibit 177 and in Exhibit 178 hospitalizations experienced post the recipient's last infusion procedure are summarized.

Exhibit 169
Summary of Adverse Events and Serious Adverse Events (SAEs) in Year 1 Post First Infusion (Participants, N=203)

	All Adverse Events (Including SAEs)			Serious Adverse Events		
		Related to Immunosuppression Therapy	Related to Infusion Procedure		Related to Immunosuppression Therapy	Related to Infusion Procedure
Number of Events	521	171 (32.8%)	139 (26.7%)	186	55 (29.6%)	78 (41.9%)
Number of Participants with 1 or More Events	146 (71.9%)	84 (41.4%)	75 (36.9%)	96 (47.3%)	35 (17.2%)	48 (23.6%)

The Exhibit above represents all adverse events reported to CITR which occurred in the first year following the participant's first infusion procedure. It does not include adverse events reported to CITR after the first year following the participant's first infusion procedure. Subsequent Exhibits in this section are inclusive of all serious adverse events (SAEs) reported to CITR. This Exhibit summarizes the participant's transplant experience the first year following their first infusion procedure. It has been shown in previous reports and in this report that the majority of adverse events occur during the first year following the participant's first infusion procedure. Relationships of the adverse event to the immunosuppression therapy and to the infusion procedure are based on classification of "Probable" or "Definite" by the local CITR Investigator and do not necessarily represent scientific truth.

Exhibit 170
Percent of Participants with a Serious Adverse Event
in Year 1 Post First Infusion
by Year of First Infusion

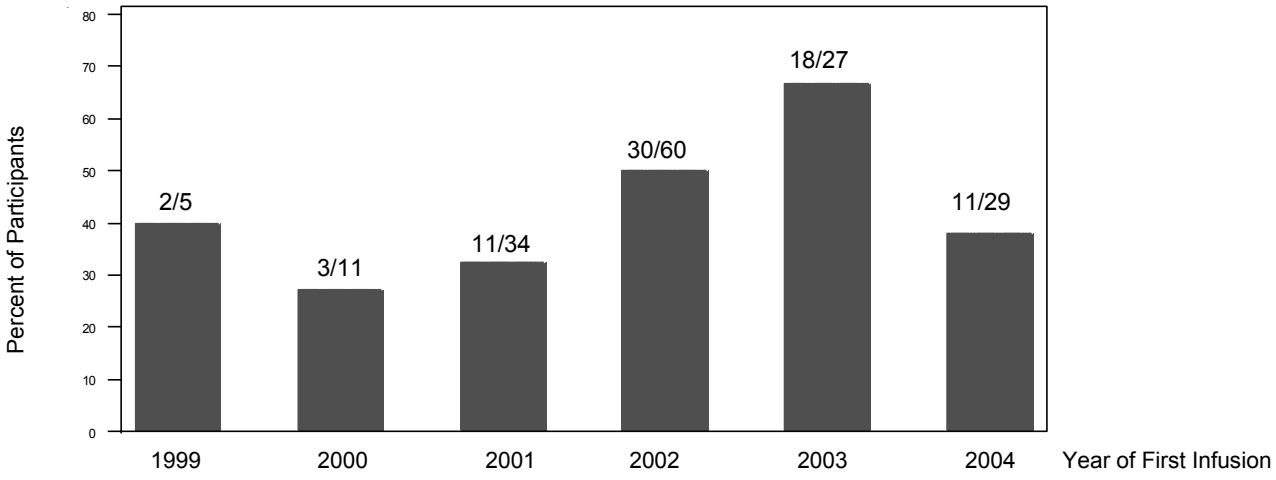


Exhibit 171
Summary of All Serious Adverse Events (SAEs) Reported by Type of SAE

	Relationship to Protocol								Overall	
	Related to Infusion Procedure		Related to Immunosuppression Therapy		Related to Both		Not Related			
	N	%	N	%	N	%	N	%	N	%
All Serious Adverse Events	78	33.1	59	25.0	5	2.1	94	39.8	236	100.0
Death	-	0.0	-	0.0	-	0.0	2***	100.0	2	0.8
Life Threatening	42	43.3	31	32.0	4	4.1	20	20.6	97	41.1
Inpatient Hospitalization	9	9.4	20	20.8	-	0.0	67	69.8	96	40.7
Prolongation of Existing Hospitalization	29	63.0	5	10.9	5	10.9	7	15.2	46	19.5
Persistent or Significant Disability/Incapacity	1*	12.5	4**	50.0	-	0.0	3	37.5	8	3.4
Congenital Anomaly/Birth Defect	-	0.0	-	0.0	-	0.0	-	0.0	-	0.0

Serious adverse event categories are not mutually exclusive.

*The event related to the infusion procedure was a portal vein thrombosis requiring continued anticoagulation.

**The four events related to immunosuppression therapy were a tongue ulceration, memory deficit, tacrolimus induced neurotoxicity, and diarrhea. All four events have since resolved with no residual side effects.

***One participant died 70 days following their third islet infusion procedure. The cause of death for this participant was reported as acute methadone and diphenhydramine toxicity unrelated to both the infusion procedure and immunosuppression therapy. An additional participant death has been reported which occurred after Year 3 post last infusion. The cause of death for this participant was reported as viral meningitis possibly related to the immunosuppression therapy. A third death was reported to the Registry after the database was locked. This death was discovered in the obituaries after Year 4 post last infusion and the cause of death is unknown.

Of the 236 serious adverse events, 186 (78.8%) occurred in the first year following their first infusion procedure. Relationships to immunosuppression therapy and to the infusion procedure are based on classification of “Probable” or “Definite” by the local CITR Investigator.

Exhibit 172
Summary of All Serious Adverse Events (SAEs) Reported and their Outcome

	Relationship to Protocol								Overall	
	Related to Infusion Procedure		Related to Immunosuppression Therapy		Related to Both		Not Related			
	N	%	N	%	N	%	N	%	N	%
All Serious Adverse Events	78	100.0	59	100.0	5	100.0	94	100.0	236	100.0
Outcome of Serious Adverse Event										
Resolved with No Residual Effects	77	98.7	53	89.8	5	100.0	86	91.5	221	93.6
Resolved with Sequelae	-	0.0	-	0.0	-	0.0	5	5.3	5	2.1
Persistent Condition, Recipient Alive	1*	1.3	2**	3.4	-	0.0	1	1.1	6	2.5
Death Caused by Adverse Event	-	0.0	-	0.0	-	0.0	2***	2.1	2	0.8
Missing Information		0.0	2	3.4	-	0.0	-	0.0	2	0.8

*The event related to the infusion procedure is a portal vein thrombosis requiring continued anticoagulation.

**The two events related to immunosuppression therapy are lymphopenia and papillary thyroid cancer.

***One participant died 70 days following their third islet infusion procedure. The cause of death for this participant was reported as acute methadone and diphenhydramine toxicity unrelated to both the infusion procedure and immunosuppression therapy. An additional participant death has been reported which occurred after Year 3 post last infusion. The cause of death for this participant was reported as viral meningitis possibly related to the immunosuppression therapy. A third death was reported to the Registry after the database was locked. This death was discovered in the obituaries after Year 4 post last infusion and the cause of death is unknown.

Relationships to immunosuppression therapy and to the infusion procedure are based on classification of “Probable” or “Definite” by the local CITR Investigator.

Exhibit 173
Summary of All Serious Adverse Events (SAEs) Reported by System Organ Class

	Relationship to Protocol								Overall	
	Related to Infusion Procedure		Related to Immunosuppression Therapy		Related to Both		Not Related			
	N	%	N	%	N	%	N	%	N	%
All Serious Adverse Events	78	100.0	59	100.0	5	100.0	94	100.0	236	100.0
System Organ Class*										
Blood and lymphatic system disorders	3	3.8	33	55.9	1	20.0	4	4.3	41	17.4
Cardiac disorders	-	0.0	-	0.0	-	0.0	1	1.1	1	0.4
Eye disorders	-	0.0	-	0.0	-	0.0	2	2.1	2	0.8
Gastrointestinal disorders	12	15.4	7	11.9	-	0.0	27	28.7	46	19.5
General disorders and administration site conditions	-	0.0	1	1.7	-	0.0	6	6.4	7	3.0
Hepatobiliary disorders	7	9.0	-	0.0	1	20.0	4	4.3	12	5.1
Immune system disorders	-	0.0	-	0.0	-	0.0	1	1.1	1	0.4
Infections and infestations	1	1.3	6	10.2	-	0.0	14	14.9	21	8.9
Injury, poisoning and procedural complications	11	14.1	1	1.7	-	0.0	3	3.2	15	6.4
Investigations**	43	55.1	4	6.8	3	60.0	7	7.4	57	24.2
Metabolism and nutrition disorders	-	0.0	1	1.7	-	0.0	8	8.5	9	3.8
Musculoskeletal and connective tissue disorders	-	0.0	-	0.0	-	0.0	1	1.1	1	0.4
Neoplasms benign, malignant and unspecified (including cysts and polyps)	-	0.0	1	1.7	-	0.0	2	2.1	3	1.3

Exhibit 173 *(continued)*
Summary of All Serious Adverse Events (SAEs) Reported by System Organ Class

	Relationship to Protocol								Overall	
	Related to Infusion Procedure		Related to Immunosuppression Therapy		Related to Both		Not Related			
	N	%	N	%	N	%	N	%	N	%
Nervous system disorders	-	0.0	1	1.7	-	0.0	2	2.1	3	1.3
Psychiatric disorders	-	0.0	1	1.7	-	0.0	1	1.1	2	0.8
Renal and urinary disorders	-	0.0	2	3.4	-	0.0	1	1.1	3	1.3
Reproductive system and breast disorders	-	0.0	1	1.7	-	0.0	2	2.1	3	1.3
Respiratory, thoracic and mediastinal disorders	-	0.0	-	0.0	-	0.0	4	4.3	4	1.7
Surgical and medical procedures	-	0.0	-	0.0	-	0.0	4	4.3	4	1.7
Vascular disorders	1	1.3	-	0.0	-	0.0	-	0.0	1	0.4

*MedDRA Classification (http://www.meddramsso.com/newweb2003/index.htm).
**MedDRA system organ class designation for lab procedures and test results. For example, elevated liver function tests are included in this category.

Relationships to immunosuppression therapy and to the infusion procedure are based on classification of “Probable” or “Definite” by the local CITR Investigator.

Exhibit 174
Most Common Serious Adverse Events (SAEs), Reported for All Participants
(Total SAEs, N=236)

	Relationship to Protocol								Overall	
	Related to Infusion Procedure		Related to Immunosuppression Therapy		Related to Both		Not Related			
	N	%	N	%	N	%	N	%	N	%
All Serious Adverse Events	78	100.0	59	100.0	5	100.0	94	100.0	236	100.0
Elevated Liver Function Tests*	41	52.6	-	0.0	3	60.0	6	6.4	50	21.2
Neutropenia	2	2.6	22	37.3	-	0.0	1	1.1	25	10.6
Abdominal pain	3	3.8	1	1.7	-	0.0	9	9.6	13	5.5
Leukopenia	-	0.0	7	11.9	1	20.0	-	0.0	8	3.4
Portal vein thrombosis	6	7.7	-	0.0	1	20.0	-	0.0	7	3.0
Hypoglycemia	-	0.0	-	0.0	-	0.0	6	6.4	6	2.5
Vomiting	-	0.0	2	3.4	-	0.0	4	4.3	6	2.5
Diarrhea	-	0.0	2	3.4	-	0.0	3	3.2	5	2.1
Peritoneal hemorrhage	5	6.4	-	0.0	-	0.0	-	0.0	5	2.1
Pneumonia	-	0.0	2	3.4	-	0.0	3	3.2	5	2.1
Post procedural hemorrhage	4	5.1	-	0.0	-	0.0	-	0.0	4	1.7

*Elevated Liver Function Tests include elevations in aspartate aminotransferase, alanine aminotransferase, and blood alkaline phosphatase.

Relationships to immunosuppression therapy and to the infusion procedure are based on classification of “Probable” or “Definite” by the local CITR Investigator.

Exhibit 175
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Abdominal hernia	2003	Inpatient hospitalization	299 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects
Abdominal hernia repair	2003	Inpatient hospitalization	39 days post 3rd Infusion	Yes	Severe (Grade 3)	Unrelated	Possible	No treatment or modification of treatment required for AE	Resolved, no residual effects
Abdominal pain	2002	Inpatient hospitalization	5 days post 1st Infusion	No	Severe (Grade 3)	Possible	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Abdominal pain	2002	Inpatient hospitalization	23 days post 1st Infusion	No	Severe (Grade 3)	Possible	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Abdominal pain	2002	Inpatient hospitalization	30 days post 2nd Infusion	No	Severe (Grade 3)	Possible	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Abdominal pain	2002	Inpatient hospitalization	52 days post 2nd Infusion	No	Severe (Grade 3)	Possible	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Abdominal pain	2004	Inpatient hospitalization	23 days post 2nd Infusion	Yes	Severe (Grade 3)	Unlikely	Possible	Required additional treatment for AE	Resolved, no residual effects
Abdominal pain	2004	Inpatient hospitalization	565 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Abdominal pain	2004	Inpatient hospitalization	909 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Possible	Required additional treatment and current treatment modified based on AE	Resolved, with sequelae
Abdominal pain	2005	Prolongation of existing hospitalization	0 days post 2nd Infusion	No	Missing	Definite	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Abdominal pain	2005	Inpatient hospitalization	1 day post 2nd Infusion	No	Severe (Grade 3)	Definite	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Abdominal pain	2005	Inpatient hospitalization	70 days post 1st Infusion	Yes	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects
Abdominal pain	2005	Prolongation of existing hospitalization	4 days post 1st Infusion	No	Severe (Grade 3)	Possible	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Abdominal pain	2005	Inpatient hospitalization	5 days post 2nd Infusion	No	Missing	Probable	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Abdominal pain	2005	Inpatient hospitalization	96 days post 1st Infusion	No	Severe (Grade 3)	Unlikely	Probable	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Alanine aminotransferase increased	2001	Life threatening	4 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Alanine aminotransferase increased	2001	Life threatening	5 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Alanine aminotransferase increased	2002	Prolongation of existing hospitalization	1 day post 2nd Infusion	Yes	Severe (Grade 3)	Definite	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Alanine aminotransferase increased	2002	Prolongation of existing hospitalization	2 days post 2nd Infusion	Yes	Severe (Grade 3)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Alanine aminotransferase increased	2002	Life threatening + Inpatient hospitalization	3 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Alanine aminotransferase increased	2002	Life threatening	3 days post 1st Infusion	No	Life threatening (Grade 4)	Definite	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Alanine aminotransferase increased	2002	Life threatening + Prolongation of existing hospitalization	3 days post 2nd Infusion	Yes	Life threatening (Grade 4)	Definite	Definite	No treatment or modification of treatment required for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Alanine aminotransferase increased	2002	Life threatening	4 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Alanine aminotransferase increased	2002	Life threatening	5 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Alanine aminotransferase increased	2002	Life threatening	6 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Alanine aminotransferase increased	2002	Life threatening	10 days post 1st Infusion	No	Life threatening (Grade 4)	Possible	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Alanine aminotransferase increased	2003	Life threatening	2 days post 2nd Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Alanine aminotransferase increased	2003	Life threatening	3 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Alanine aminotransferase increased	2005	Life threatening	11 days post 2nd Infusion	No	Life threatening (Grade 4)	Possible	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Alanine aminotransferase increased	2005	Life threatening	17 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Anaemia	2002	Life threatening	0 days post 3rd Infusion	No	Life threatening (Grade 4)	Unlikely	Possible	Required additional treatment for AE	Resolved, no residual effects
Anaemia	2003	Prolongation of existing hospitalization	5 days post 1st Infusion	Yes	Severe (Grade 3)	Definite	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Anaemia	2004	Life threatening + Prolongation of existing hospitalization	100 days post 1st Infusion	No	Life threatening (Grade 4)	Unlikely	Possible	Required additional treatment for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Anaemia postoperative	1999	Prolongation of existing hospitalization	0 days post 2nd Infusion	Yes	Severe (Grade 3)	Definite	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Anaphylactic reaction	2002	Inpatient hospitalization	250 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects
Appendicitis	2003	Inpatient hospitalization	54 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Possible	No treatment or modification of treatment required for AE	Resolved, no residual effects
Ascites	2002	Inpatient hospitalization	10 days post 2nd Infusion	No	Severe (Grade 3)	Probable	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2001	Life threatening	5 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2002	Life threatening	1 day post 1st Infusion	Yes	Life threatening (Grade 4)	Possible	Unlikely	No treatment or modification of treatment required for AE	Resolved, with sequelae
Aspartate aminotransferase increased	2002	Prolongation of existing hospitalization	1 day post 2nd Infusion	Yes	Severe (Grade 3)	Probable	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2002	Prolongation of existing hospitalization	1 day post 2nd Infusion	Yes	Severe (Grade 3)	Definite	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2002	Life threatening	2 days post 1st Infusion	No	Life threatening (Grade 4)	Definite	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2002	Life threatening + Inpatient hospitalization	3 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2002	Life threatening	3 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Aspartate aminotransferase increased	2002	Life threatening	3 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2002	Life threatening + Prolongation of existing hospitalization	3 days post 2nd Infusion	Yes	Life threatening (Grade 4)	Definite	Definite	No treatment or modification of treatment required for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2002	Life threatening	5 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2002	Life threatening	10 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2003	Life threatening	1 day post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2003	Life threatening	3 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2003	Life threatening	4 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2003	Life threatening	8 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2004	Life threatening	3 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2004	Life threatening	7 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Aspartate aminotransferase increased	2004	Life threatening	7 days post 2nd Infusion	No	Life threatening (Grade 4)	Possible	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Aspartate aminotransferase increased	2005	Life threatening	3 days post 2nd Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2005	Life threatening	6 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2005	Life threatening	9 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2005	Life threatening	9 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Aspartate aminotransferase increased	2005	Life threatening	11 days post 2nd Infusion	No	Life threatening (Grade 4)	Possible	Possible	No treatment or modification of treatment required for AE	Resolved, no residual effects
Back pain	2002	Inpatient hospitalization	119 days post 2nd Infusion	No	Severe (Grade 3)	Unlikely	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Benign neoplasm	2002	Inpatient hospitalization	1 day post 1st Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Blood alkaline phosphatase increased	2001	Life threatening	5 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Blood alkaline phosphatase increased	2002	Life threatening + Inpatient hospitalization	3 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Blood alkaline phosphatase increased	2002	Life threatening + Prolongation of existing hospitalization	3 days post 2nd Infusion	Yes	Life threatening (Grade 4)	Definite	Definite	No treatment or modification of treatment required for AE	Resolved, no residual effects
Blood alkaline phosphatase increased	2003	Life threatening	4 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Blood alkaline phosphatase increased	2004	Life threatening	4 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Blood alkaline phosphatase increased	2004	Life threatening	5 days post 2nd Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Blood alkaline phosphatase increased	2004	Life threatening	7 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Blood alkaline phosphatase increased	2005	Life threatening	3 days post 2nd Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Blood alkaline phosphatase increased	2005	Life threatening	4 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Blood alkaline phosphatase increased	2005	Life threatening	11 days post 2nd Infusion	No	Life threatening (Grade 4)	Possible	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Blood alkaline phosphatase increased	2005	Life threatening	13 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Blood alkaline phosphatase increased	2005	Life threatening	735 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	No treatment or modification of treatment required for AE	Resolved, no residual effects
Blood creatinine increased	2004	Prolongation of existing hospitalization	139 days post 2nd Infusion	No	Missing	Unlikely	Probable	Current treatment modified based on AE	Resolved, no residual effects
Cellulitis	2002	Inpatient hospitalization + Persistent or significant disability/incapacity	86 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects
Cellulitis	2003	Inpatient hospitalization	59 days post 2nd Infusion	No	Severe (Grade 3)	Possible	Possible	Required additional treatment for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Chagas disease antibody positive	2005	Missing	14 days post 1st Infusion	No	Mild (Grade 1) or Moderate (Grade 2)	Definite	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Chest pain	2002	Inpatient hospitalization	437 days post 1st Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Chest pain	2004	Inpatient hospitalization	711 days post 1st Infusion	No	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects
Chest pain	2005	Inpatient hospitalization	478 days post 2nd Infusion	No	Mild (Grade 1) or Moderate (Grade 2)	Unrelated	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Cholecystitis	2002	Inpatient hospitalization	211 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Cholecystitis	2003	Life threatening + Prolongation of existing hospitalization	0 days post 2nd Infusion	No	Life threatening (Grade 4)	Possible	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Cholecystitis acute	2005	Inpatient hospitalization	1205 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Cholelithiasis	2005	Missing	8 days post 1st Infusion	No	Severe (Grade 3)	Unlikely	Possible	Required additional treatment for AE	Resolved, no residual effects
Colitis	2005	Inpatient hospitalization	90 days post 2nd Infusion	No	Severe (Grade 3)	Unlikely	Possible	Current treatment modified based on AE	Resolved, no residual effects
Confusional state	2003	Inpatient hospitalization	113 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Crossmatch incompatible	2004	Inpatient hospitalization	20 days post 2nd Infusion	No	Missing	Definite	Unrelated	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Diarrhoea	2002	Inpatient hospitalization	30 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Possible	No treatment or modification of treatment required for AE	Resolved, no residual effects
Diarrhoea	2003	Persistent or significant disability/incapacity	8 days post 1st Infusion	No	Severe (Grade 3)	Unlikely	Probable	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Diarrhoea	2004	Inpatient hospitalization	621 days post 3rd Infusion	Yes	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects
Diarrhoea	2004	Inpatient hospitalization	697 days post 3rd Infusion	No	Severe (Grade 3)	Unrelated	Unlikely	Current treatment modified based on AE	Resolved, no residual effects
Diarrhoea	2005	Inpatient hospitalization	488 days post 1st Infusion	Yes	Severe (Grade 3)	Unrelated	Probable	Current treatment modified based on AE	Resolved, no residual effects
Drug toxicity	2002	Persistent or significant disability/incapacity	244 days post 2nd Infusion	Yes	Severe (Grade 3)	Unrelated	Probable	Current treatment modified based on AE	Resolved, no residual effects
Drug toxicity	2004	Death	70 days post 3rd Infusion	No	Fatal (Grade 5)	Unrelated	Unrelated	No treatment or modification of treatment required for AE	Death, related to AE
Dyspnoea	2005	Life threatening + Inpatient hospitalization	108 days post 1st Infusion	No	Life threatening (Grade 4)	Possible	Possible	No treatment or modification of treatment required for AE	Resolved, no residual effects
Elevated liver function tests (ALT and AST)	2005	Missing	3 days post 1st Infusion	Yes	Severe (Grade 3)	Definite	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Febrile neutropenia	2001	Inpatient hospitalization	62 days post 1st Infusion	Yes	Severe (Grade 3)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Foot fracture	2000	Inpatient hospitalization	401 days post 2nd Infusion	No	Mild (Grade 1) or Moderate (Grade 2)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Gallbladder perforation	2000	Prolongation of existing hospitalization	5 days post 2nd Infusion	Yes	Missing	Definite	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Gastroenteritis	2003	Inpatient hospitalization	94 days post 1st Infusion	No	Severe (Grade 3)	Missing	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Gastroenteritis	2005	Inpatient hospitalization	91 days post 1st Infusion	Yes	Severe (Grade 3)	Unrelated	Possible	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Gastroenteritis viral	2002	Inpatient hospitalization	44 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Gastroenteritis viral	2005	Inpatient hospitalization	81 days post 1st Infusion	No	Severe (Grade 3)	Unrelated	Possible	No treatment or modification of treatment required for AE	Resolved, no residual effects
Gastroenteritis viral	2005	Inpatient hospitalization	752 days post 1st Infusion	No	Severe (Grade 3)	Unrelated	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Gastrointestinal disorder	2003	Inpatient hospitalization	183 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Gastrointestinal disorder	2003	Inpatient hospitalization	510 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Haemoglobin decreased	2005	Life threatening	81 days post 1st Infusion	No	Life threatening (Grade 4)	Unlikely	Possible	Required additional treatment for AE	Resolved, no residual effects
Haemorrhoids	2003	Inpatient hospitalization	19 days post 1st Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Haemothorax	2003	Inpatient hospitalization	0 days post 3rd Infusion	No	Severe (Grade 3)	Definite	Possible	Required additional treatment for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Hematoma/Hemorrhage	2005	Prolongation of existing hospitalization	0 days post 2nd Infusion	No	Severe (Grade 3)	Probable	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Hepatic haematoma	2003	Prolongation of existing hospitalization	0 days post 3rd Infusion	Yes	Severe (Grade 3)	Definite	Possible	Required additional treatment for AE	Resolved, no residual effects
Hip fracture	2003	Inpatient hospitalization	396 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Hypoglycaemia	2002	Life threatening	59 days post 3rd Infusion	Yes	Life threatening (Grade 4)	Unrelated	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Hypoglycaemia	2002	Life threatening	230 days post 2nd Infusion	Yes	Life threatening (Grade 4)	Unrelated	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Hypoglycaemia	2004	Life threatening	296 days post 2nd Infusion	No	Life threatening (Grade 4)	Unrelated	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Hypoglycaemia	2004	Life threatening	360 days post 3rd Infusion	No	Life threatening (Grade 4)	Unrelated	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Hypoglycaemia	2005	Life threatening	673 days post 3rd Infusion	No	Life threatening (Grade 4)	Unrelated	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Hypoglycaemia	2006	Life threatening	318 days post 2nd Infusion	No	Life threatening (Grade 4)	Unrelated	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Hypokalaemia	2004	Missing	2 days post 1st Infusion	No	Missing	Missing	Possible	No treatment or modification of treatment required for AE	Resolved, no residual effects
Hypomagnesaemia	2005	Life threatening	68 days post 2nd Infusion	No	Life threatening (Grade 4)	Possible	Possible	Required additional treatment for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Hypophosphataemia	2005	Inpatient hospitalization	70 days post 1st Infusion	Yes	Life threatening (Grade 4)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Ileus	2001	Inpatient hospitalization	2 days post 1st Infusion	No	Missing	Possible	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Ileus	2004	Inpatient hospitalization	8 days post 2nd Infusion	No	Severe (Grade 3)	Possible	Possible	Required additional treatment for AE	Resolved, no residual effects
Infection	2005	Inpatient hospitalization	1215 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Inflammation	2003	Inpatient hospitalization	33 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Influenza	2003	Inpatient hospitalization	869 days post 2nd Infusion	Yes	Severe (Grade 3)	Unrelated	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Insomnia	2003	Life threatening	392 days post 2nd Infusion	Yes	Life threatening (Grade 4)	Unrelated	Definite	Current treatment modified based on AE	Resolved, no residual effects
Intestinal obstruction	2003	Inpatient hospitalization	88 days post 1st Infusion	No	Severe (Grade 3)	Possible	Possible	Required additional treatment for AE	Resolved, no residual effects
Intra-abdominal haemorrhage	2002	Prolongation of existing hospitalization	0 days post 1st Infusion	No	Severe (Grade 3)	Definite	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Intra-abdominal haemorrhage	2002	Prolongation of existing hospitalization	0 days post 2nd Infusion	No	Severe (Grade 3)	Definite	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Leukopenia	2002	Prolongation of existing hospitalization	1 day post 2nd Infusion	Yes	Severe (Grade 3)	Possible	Definite	No treatment or modification of treatment required for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Leukopenia	2002	Life threatening	56 days post 1st Infusion	Yes	Life threatening (Grade 4)	Unlikely	Definite	Required additional treatment for AE	Resolved, no residual effects
Leukopenia	2003	Missing	2 days post 1st Infusion	Yes	Severe (Grade 3)	Unlikely	Definite	No treatment or modification of treatment required for AE	Persistent condition, Alive
Leukopenia	2003	Missing	24 days post 1st Infusion	Yes	Severe (Grade 3)	Unlikely	Definite	Current treatment modified based on AE	Persistent condition, Alive
Leukopenia	2004	Life threatening + Prolongation of existing hospitalization	2 days post 1st Infusion	Yes	Life threatening (Grade 4)	Definite	Definite	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Leukopenia	2005	Missing	1 day post 1st Infusion	Yes	Severe (Grade 3)	Missing	Definite	Required additional treatment for AE	Missing
Leukopenia	2005	Missing	1 day post 1st Infusion	Yes	Severe (Grade 3)	Missing	Definite	Current treatment modified based on AE	Missing
Leukopenia	2005	Life threatening	2 days post 1st Infusion	Yes	Life threatening (Grade 4)	Unlikely	Definite	Required additional treatment for AE	Resolved, no residual effects
Localised infection	2005	Life threatening + Inpatient hospitalization	112 days post 2nd Infusion	No	Life threatening (Grade 4)	Unlikely	Probable	Required additional treatment for AE	Resolved, no residual effects
Lung infiltration	1999	Inpatient hospitalization	156 days post 2nd Infusion	No	Missing	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects
Lymphopenia	2005	Life threatening	1 day post 1st Infusion	Yes	Life threatening (Grade 4)	Unrelated	Definite	Current treatment modified based on AE	Resolved, no residual effects
Lymphopenia	2005	Life threatening	1 day post 1st Infusion	Yes	Life threatening (Grade 4)	Unrelated	Definite	No treatment or modification of treatment required for AE	Persistent condition, Alive

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Lymphopenia	2005	Inpatient hospitalization	70 days post 1st Infusion	Yes	Severe (Grade 3)	Possible	Probable	Required additional treatment for AE	Resolved, no residual effects
Memory impairment	2002	Persistent or significant disability/incapacity	193 days post 2nd Infusion	Yes	Severe (Grade 3)	Unrelated	Probable	Current treatment modified based on AE	Resolved, no residual effects
Meningitis aseptic	2002	Inpatient hospitalization	102 days post 1st Infusion	Yes	Severe (Grade 3)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Meningitis viral	2005	Death	1104 days post 2nd Infusion	No	Fatal (Grade 5)	Unrelated	Possible	Current treatment modified based on AE	Death, related to AE
Mouth ulceration	2004	Inpatient hospitalization	16 days post 1st Infusion	No	Severe (Grade 3)	Unrelated	Definite	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Myocardial infarction	2003	Life threatening + Prolongation of existing hospitalization	0 days post 1st Infusion	No	Life threatening (Grade 4)	Possible	Possible	Required additional treatment for AE	Resolved, with sequelae
Nausea	2002	Prolongation of existing hospitalization	0 days post 2nd Infusion	No	Missing	Possible	Possible	No treatment or modification of treatment required for AE	Resolved, no residual effects
Nausea	2005	Prolongation of existing hospitalization	0 days post 2nd Infusion	Unknown	Missing	Possible	Possible	Required additional treatment for AE	Resolved, no residual effects
Nausea	2005	Prolongation of existing hospitalization	1 day post 1st Infusion	No	Severe (Grade 3)	Possible	Possible	Required additional treatment for AE	Resolved, no residual effects
Nephrolithiasis	2000	Inpatient hospitalization	106 days post 1st Infusion	No	Severe (Grade 3)	Unrelated	Possible	No treatment or modification of treatment required for AE	Resolved, no residual effects
Neutropenia	2001	Life threatening	17 days post 2nd Infusion	Yes	Life threatening (Grade 4)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Neutropenia	2002	Prolongation of existing hospitalization	3 days post 1st Infusion	Yes	Severe (Grade 3)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Neutropenia	2002	Life threatening	8 days post 2nd Infusion	No	Life threatening (Grade 4)	Unlikely	Probable	Current treatment modified based on AE	Resolved, no residual effects
Neutropenia	2002	Life threatening	15 days post 1st Infusion	Yes	Life threatening (Grade 4)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Neutropenia	2002	Life threatening + Inpatient hospitalization	19 days post 2nd Infusion	Yes	Life threatening (Grade 4)	Unrelated	Definite	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Neutropenia	2002	Life threatening	42 days post 1st Infusion	Yes	Life threatening (Grade 4)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Neutropenia	2002	Life threatening	52 days post 1st Infusion	Yes	Life threatening (Grade 4)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Neutropenia	2002	Life threatening	75 days post 1st Infusion	Yes	Life threatening (Grade 4)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Neutropenia	2003	Life threatening	3 days post 1st Infusion	No	Life threatening (Grade 4)	Unlikely	Probable	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Neutropenia	2003	Life threatening	3 days post 1st Infusion	No	Life threatening (Grade 4)	Unlikely	Probable	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Neutropenia	2003	Life threatening	32 days post 2nd Infusion	Yes	Life threatening (Grade 4)	Unrelated	Definite	No treatment or modification of treatment required for AE	Resolved, no residual effects
Neutropenia	2003	Life threatening	83 days post 2nd Infusion	Yes	Life threatening (Grade 4)	Unrelated	Definite	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Neutropenia	2003	Life threatening	96 days post 2nd Infusion	Yes	Life threatening (Grade 4)	Unrelated	Definite	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Neutropenia	2003	Life threatening + Inpatient hospitalization	103 days post 1st Infusion	Yes	Life threatening (Grade 4)	Unrelated	Definite	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Neutropenia	2004	Life threatening	5 days post 1st Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	Current treatment modified based on AE	Resolved, no residual effects
Neutropenia	2004	Life threatening	33 days post 2nd Infusion	Yes	Life threatening (Grade 4)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Neutropenia	2004	Life threatening	764 days post 2nd Infusion	Yes	Life threatening (Grade 4)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Neutropenia	2005	Life threatening + Prolongation of existing hospitalization	2 days post 2nd Infusion	No	Life threatening (Grade 4)	Unlikely	Probable	Required additional treatment for AE	Resolved, no residual effects
Neutropenia	2005	Life threatening	8 days post 1st Infusion	No	Life threatening (Grade 4)	Unlikely	Probable	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Neutropenia	2005	Life threatening	21 days post 1st Infusion	No	Life threatening (Grade 4)	Unlikely	Probable	Current treatment modified based on AE	Resolved, no residual effects
Neutropenia	2005	Life threatening	22 days post 1st Infusion	No	Life threatening (Grade 4)	Possible	Probable	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Neutropenia	2005	Life threatening	68 days post 2nd Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Neutropenia	2005	Life threatening	494 days post 2nd Infusion	No	Life threatening (Grade 4)	Unlikely	Probable	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Neutropenia	2005	Life threatening	673 days post 2nd Infusion	No	Life threatening (Grade 4)	Unlikely	Probable	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Neutrophil count	2005	Life threatening	52 days post 2nd Infusion	No	Life threatening (Grade 4)	Unrelated	Probable	Current treatment modified based on AE	Resolved, no residual effects
Neutrophil count	2005	Life threatening	64 days post 2nd Infusion	No	Severe (Grade 3)	Unlikely	Probable	Current treatment modified based on AE	Resolved, no residual effects
Neutrophil count	2005	Inpatient hospitalization	99 days post 2nd Infusion	No	Severe (Grade 3)	Unlikely	Probable	Required additional treatment for AE	Resolved, no residual effects
Oedema peripheral	2004	Inpatient hospitalization	69 days post 2nd Infusion	Yes	Missing	Unrelated	Probable	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Operative haemorrhage	2003	Prolongation of existing hospitalization	0 days post 1st Infusion	No	Missing	Definite	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Operative haemorrhage	2003	Prolongation of existing hospitalization	0 days post 2nd Infusion	No	Missing	Definite	Unrelated	Current treatment modified based on AE	Resolved, no residual effects
Operative haemorrhage	2003	Prolongation of existing hospitalization	0 days post 2nd Infusion	No	Missing	Definite	Possible	Required additional treatment for AE	Resolved, no residual effects
Optic atrophy	2004	Persistent or significant disability/incapacity	61 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Possible	Required additional treatment and current treatment modified based on AE	Persistent condition, Alive
Ovarian cyst	2004	Inpatient hospitalization	12 days post 1st Infusion	No	Missing	Unlikely	Probable	Required additional treatment for AE	Resolved, no residual effects
Ovarian cyst	2005	Inpatient hospitalization	1322 days post 2nd Infusion	Yes	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Ovarian torsion	2004	Inpatient hospitalization	886 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects
Pancreatitis	2003	Inpatient hospitalization	542 days post 1st Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Papillary thyroid cancer	2003	Life threatening	656 days post 2nd Infusion	No	Life threatening (Grade 4)	Unrelated	Probable	Required additional treatment for AE	Persistent condition, Alive
Parvovirus infection	2002	Inpatient hospitalization	94 days post 1st Infusion	Yes	Severe (Grade 3)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Peritoneal haemorrhage	2002	Prolongation of existing hospitalization	2 days post 2nd Infusion	No	Severe (Grade 3)	Definite	Possible	No treatment or modification of treatment required for AE	Resolved, no residual effects
Peritoneal haemorrhage	2003	Prolongation of existing hospitalization	0 days post 2nd Infusion	No	Severe (Grade 3)	Definite	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Peritoneal haemorrhage	2003	Prolongation of existing hospitalization	1 day post 2nd Infusion	No	Missing	Definite	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Peritoneal haemorrhage	2003	Prolongation of existing hospitalization	1 day post 2nd Infusion	No	Severe (Grade 3)	Definite	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Peritoneal haemorrhage	2003	Prolongation of existing hospitalization	1 day post 3rd Infusion	No	Severe (Grade 3)	Definite	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Peritonitis	2002	Prolongation of existing hospitalization	1 day post 1st Infusion	No	Missing	Definite	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Persistent nausea and vomitting	2005	Inpatient hospitalization	5 days post 2nd Infusion	No	Mild (Grade 1) or Moderate (Grade 2)	Unrelated	Probable	No treatment or modification of treatment required for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Pneumonia	1999	Inpatient hospitalization	67 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects
Pneumonia	1999	Inpatient hospitalization	89 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, with sequelae
Pneumonia	2002	Inpatient hospitalization	164 days post 2nd Infusion	Yes	Severe (Grade 3)	Unrelated	Probable	No treatment or modification of treatment required for AE	Resolved, no residual effects
Pneumonia	2002	Inpatient hospitalization	247 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects
Pneumonia	2004	Inpatient hospitalization	62 days post 2nd Infusion	Yes	Severe (Grade 3)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Pneumonia aspiration	2001	Inpatient hospitalization	101 days post 1st Infusion	No	Severe (Grade 3)	Unrelated	Unlikely	Current treatment modified based on AE	Resolved, no residual effects
Portal vein thrombosis	2000	Inpatient hospitalization	1 day post 2nd Infusion	Yes	Severe (Grade 3)	Definite	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Portal vein thrombosis	2001	Prolongation of existing hospitalization	0 days post 3rd Infusion	Yes	Severe (Grade 3)	Definite	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Portal vein thrombosis	2002	Prolongation of existing hospitalization	1 day post 1st Infusion	No	Missing	Definite	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Portal vein thrombosis	2003	Persistent or significant disability/incapacity	5 days post 1st Infusion	No	Missing	Definite	Unrelated	Required additional treatment for AE	Persistent condition, Alive
Portal vein thrombosis	2003	Prolongation of existing hospitalization	6 days post 3rd Infusion	No	Severe (Grade 3)	Definite	Definite	Required additional treatment for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Portal vein thrombosis	2003	Life threatening	7 days post 2nd Infusion	No	Life threatening (Grade 4)	Definite	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Portal vein thrombosis	2005	Prolongation of existing hospitalization	1 day post 1st Infusion	No	Missing	Probable	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Post procedural haemorrhage	2002	Life threatening + Prolongation of existing hospitalization	0 days post 2nd Infusion	No	Life threatening (Grade 4)	Definite	Possible	Required additional treatment for AE	Resolved, no residual effects
Post procedural haemorrhage	2003	Prolongation of existing hospitalization	1 day post 1st Infusion	No	Missing	Definite	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Post procedural haemorrhage	2004	Prolongation of existing hospitalization	1 day post 2nd Infusion	Yes	Severe (Grade 3)	Definite	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Post procedural haemorrhage	2005	Life threatening + Prolongation of existing hospitalization	0 days post 1st Infusion	No	Life threatening (Grade 4)	Definite	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Post procedural pain	2005	Prolongation of existing hospitalization	0 days post 2nd Infusion	No	Severe (Grade 3)	Definite	Unrelated	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Postoperative infection	2004	Inpatient hospitalization	972 days post 2nd Infusion	Yes	Severe (Grade 3)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Pulmonary cavitation	2004	Inpatient hospitalization	136 days post 2nd Infusion	No	Severe (Grade 3)	Possible	Possible	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Pyrexia	2004	Inpatient hospitalization	960 days post 2nd Infusion	Yes	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Pyrexia	2005	Inpatient hospitalization	1184 days post 1st Infusion	Yes	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects
Renal failure acute	2004	Prolongation of existing hospitalization	0 days post 2nd Infusion	No	Severe (Grade 3)	Unlikely	Probable	Current treatment modified based on AE	Resolved, no residual effects
Renal failure acute	2004	Life threatening + Inpatient hospitalization	100 days post 1st Infusion	No	Life threatening (Grade 4)	Unlikely	Probable	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Retinal detachment	2002	Inpatient hospitalization	326 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Somnolence	2001	Inpatient hospitalization	101 days post 1st Infusion	No	Severe (Grade 3)	Unrelated	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Squamous cell carcinoma of skin	2004	Persistent or significant disability/incapacity	591 days post 2nd Infusion	Yes	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects
Surgery	2003	Inpatient hospitalization	133 days post 2nd Infusion	Yes	Severe (Grade 3)	Unrelated	Unrelated	Required additional treatment for AE	Resolved, with sequelae
Surgery	2006	Inpatient hospitalization	701 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Swollen tongue	1999	Inpatient hospitalization	148 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Possible	No treatment or modification of treatment required for AE	Resolved, no residual effects
Thrombocytopenia	2003	Inpatient hospitalization	14 days post 1st Infusion	Yes	Severe (Grade 3)	Unrelated	Possible	Current treatment modified based on AE	Resolved, no residual effects
Thyroidectomy total	2004	Inpatient hospitalization	770 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	Required additional treatment for AE	Resolved, no residual effects

Exhibit 175 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Tongue ulceration	1999	Persistent or significant disability/incapacity	58 days post 2nd Infusion	Yes	Severe (Grade 3)	Unrelated	Definite	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Tremor	2004	Inpatient hospitalization	8 days post 2nd Infusion	Yes	Mild (Grade 1) or Moderate (Grade 2)	Unrelated	Possible	Current treatment modified based on AE	Resolved, no residual effects
Vomiting	2003	Inpatient hospitalization	2 days post 3rd Infusion	No	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects
Vomiting	2004	Inpatient hospitalization	1135 days post 2nd Infusion	Yes	Severe (Grade 3)	Unrelated	Probable	No treatment or modification of treatment required for AE	Resolved, no residual effects
Vomiting	2005	Inpatient hospitalization	71 days post 1st Infusion	Yes	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects
White blood cell count decreased	2002	Life threatening + Inpatient hospitalization	28 days post 2nd Infusion	No	Life threatening (Grade 4)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects

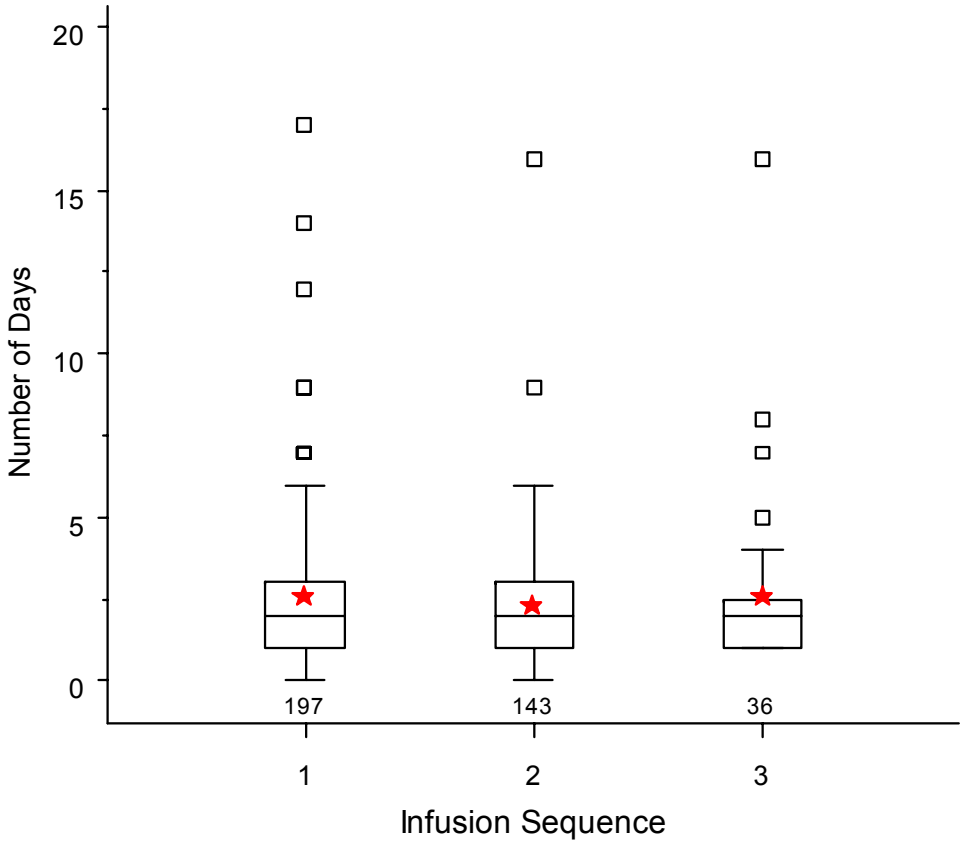
*Based on the Cancer Therapy Evaluation Program, Common Terminology Criteria For Adverse Events.
**Based on classification by local CITR Investigator.

"Serious Adverse Event (SAE)" name used in the first column is the preferred term derived from the MedDRA Classification System.

Exhibit 176
Summary of Reported Neoplasms (benign, malignant, unspecified)
All Participants

Reported Neoplasm	Timing	Relation to Islet Infusion Procedure	Relation to Immunosuppression Therapy	Outcome of Event
Benign neoplasm	1 day post first infusion	Unrelated	Unrelated	Resolved, no residual effects
Squamous cell carcinoma of skin	591 days post second infusion	Unrelated	Possible	Resolved, no residual effects
Squamous cell carcinoma of skin	640 days post first infusion	Unrelated	Probable	Resolved, no residual effects
Papillary thyroid cancer	656 days post second infusion	Unrelated	Probable	Persistent condition, Alive

Exhibit 177
Number of Days Hospitalized at Infusion (Admission to Discharge)
by Infusion Sequence



Serious adverse events which cause a prolongation of the inpatient hospitalization are summarized in Exhibit 171 and listed individually in Exhibit 175.

Exhibit 178
Hospitalizations Experienced Post Last Infusion by Total Number of Infusions Received

	Total Infusions Received											
	1				2				3			
	Month 6		Year 1		Month 6		Year 1		Month 6		Year 1	
	N	%	N	%	N	%	N	%	N	%	N	%
Total	43	100.0	34	100.0	92	100.0	64	100.0	30	100.0	26	100.0
Participants Requiring at Least One Hospitalization	6	14.0	-	0.0	19	20.7	7	10.9	2	6.7	3	11.5
Number of Hospitalizations												
0	31	72.1	29	85.3	64	69.6	53	82.8	26	86.7	22	84.6
1	5	11.6	-	0.0	14	15.2	6	9.4	2	6.7	3	11.5
2	-	0.0	-	0.0	4	4.3	1	1.6	-	0.0	-	0.0
3	1	2.3	-	0.0	1	1.1	-	0.0	-	0.0	-	0.0
Missing	6	14.0	5	14.7	9	9.8	4	6.3	2	6.7	1	3.8

Section 3
Islet After Kidney Transplant Information

Islet After Kidney Transplant Information Summary

Registry information collected on islet after kidney transplant recipients are included in this section. Currently, 22 recipients from five islet transplant programs were entered with initial infusions prior to December 31, 2005 and this report provides a description of these participants.

Recipient Information:

The median age of the islet after kidney transplant participants was 45.4 years (range 34.3 to 55.4) and the median duration of diabetes was 31.5 years (range 15 to 42). The median weight of the recipient was 60.2 kg (range 47.0 to 89.4) and the median body mass index (BMI) was 22.9 kg/m^2 (range 15.4 to 27.7) (Exhibit 179). Over 59% of the participants are female (Exhibit 180). Compared to islet alone recipients, islet after kidney recipients are older, weigh less and have a lower BMI.

At the time of the first infusion, 54.5% of the participants were employed full-time and for 68.2% of the transplant procedures the primary funding was through non-government research grants (Exhibit 181). Over 22% of the islet transplant recipients were on an insulin pump prior to their first infusion, while 86.4% of the participants were either on an insulin pump or were taking three or more insulin injections per day (Exhibit 182). The mean daily insulin requirement of participants prior to their first infusion procedure was 35.7 units (SD 13.8). Their mean fasting plasma glucose was 162.7 mg/dL (SD 100.8) and their mean HbA_{1C} was 8.0% (SD 1.3) (Exhibit 183).

Islet Infusion Information:

Exhibit 185 summarizes the main infusion procedure characteristics by infusion sequence. On average, second infusions were administered 14.7 weeks (SD 18.6) following first infusion (N=17) and third infusions were administered 70.8 weeks (SD 15.1) following first infusion (N=3).

Donor Information:

The median age of the deceased donor was 49 years (range 1 to 64) and the median body mass index was 28.4 kg/m^2 (range 20.2 to 68.9). The median time from cross clamp to pancreas recovery was 39 minutes (range 5 to 64) (Exhibit 186). Median time for islet alone recipients was 33.0 minutes (range 0 to 127). Approximately 51% of the donors were male, 12.2% were Hispanic and 85.7% were white. Over 71% of the donors had a cerebrovascular/stroke as cause of death while 20.4% experienced a head trauma. Thirty-seven percent of the donors had a history of hypertension and 31% had a history of alcohol dependency.

Twenty-seven percent of the donors received a transfusion prior to organ procurement and only one donor received a transfusion during the organ procurement surgery. Seventy-one percent of the donors received steroids and 37% of the donors had received insulin during the hospitalization leading to organ procurement (Exhibit 187). All but one donor received vasopressors during the hospitalization.

Donor serology is presented in Exhibit 189. Only one of the serology tests (except for Anti CMV) was positive, HBsAg. Donor laboratory data are presented in Exhibit 190. The median serum creatinine of the donors was 0.9 mg/dL, total bilirubin 0.7 mg/dL, AST 33.0 IU/L, ALT 33.0 IU/L, serum lipase 32.0 IU/L and serum amylase 61.0 IU/L. The median minimum pre-insulin blood glucose was 105.0 mg/dL and the median maximum blood glucose was 233.0 (mg/dL).

Pancreas Procurement and Islet Processing Information:

Also summarized in this section are pancreas procurement and islet processing data reported to the Registry. In 57.1% of the pancreas removal procedures, the procurement team was not related/affiliated with the processing/infusion team (Exhibit 191). In every case, islet processing occurred at the same institution where the islet infusion procedure was conducted. In all cases, Liberase HI was the collagenase preparation used, all used a density gradient for purification and 59.2% of the islet products processed utilized islet cell culture. Two of the final preparations were gram stain positive (4.1%), while one aerobic test (2.0%) and one anaerobic test (2.0%) were positive.

For the final preparations, the median duration of cold ischemia was 6.9 hours (Exhibit 194). An islet product characterization summary is located in Exhibit 194 and a summary of the mean number of islet equivalents/kg infused is summarized in Exhibit 195.

Immunosuppression Medications:

For 45.5% of the participants, a Daclizumab, Sirolimus, and Tacrolimus immunosuppression regimen was used. This same regimen was used for 61.1% of the islet alone recipients. A complete list of all immunosuppression regimens is included in Exhibit 196. Immunosuppression dosing at the time of infusion (Exhibit 197) and induction therapy (Exhibit 198) are presented by infusion sequence, and immunosuppression dosing post last infusion is displayed in Exhibit 200. Sirolimus and Tacrolimus trough levels at Day 30 for each infusion (1, 2, and 3), as well as trough levels at month 6, year 1, and year 2 post last infusion are presented as boxplots in Exhibits 201 and 202.

Graft Function:

As indicated in section 2 of this report, analyses for graft function includes only the most complete data. Given the small IAK sample size, analyses are limited this year.

Exhibit 203 displays insulin independence rates at month 6 and year 1 post both first and last infusions. Insulin independence rates drop from 46.7% to 42.9% between Month 6 and Year 1 post first infusion. This decrease is more pronounced post last infusion (46.7% to 33.3% from Month 6 to Year 1).

The boxplots in Exhibit 204 illustrate the percent reduction in insulin use from baseline to Month 6 and Year 1 post last infusion.

Severe Hypoglycemic Events:

Similar to the islet transplant alone recipients, there was a sharp decrease in the number of hypoglycemic events post first infusion from baseline (Exhibit 205). Over 54% of participants experienced one or more hypoglycemic events prior to their first infusion. This decreases to 4.5% (N=1) up to 30 days post infusion and to 0% at later intervals post their last infusion.

Laboratory Tests:

Exhibits 206-208 present summary data for fasting plasma glucose, HbA_{1C}, and basal plasma C-peptide values at pre infusion and post infusion and Exhibit 209 presents a summary of all laboratory values collected just prior to infusion.

Also included are a summary of reported abnormal laboratory liver function tests (Exhibit 210), abnormal lipid tests (Exhibit 215), and the percent of participants with a marked increase in serum creatinine from baseline (Exhibit 220). Abnormal has been defined as one or greater times the upper limit of normal to up to two times the ULN for the test and two or greater times the ULN for the test.

There were reports at the two times or greater than the ULN for AST (N=2) and ALT (N=1), but no reports for alkaline phosphatase or total bilirubin (Exhibit 210). There were no reports at two times or greater than the ULN for total cholesterol or for triglycerides (Exhibit 215). There were 2 reports (10.5%), of recipients with an increase in their serum creatinine of 0.5mg/dL or greater than their baseline level (Exhibit 220).

Summary measures for each laboratory value are also constructed prior to their first infusion and by month 6, year 1, and year 2 post the recipient's last infusion procedure. For each of these laboratory tests, boxplots are displayed (Exhibits 211-214, 216-219, and 221-222). For a boxplot the "star" (★) represents the mean value. The whiskers of the plot represent the minimum value and the maximum value, while the lower line of the box represents the 25th percentile, the upper line of the box the 75th percentile and the middle line in the box represent the median (50th percentile).

Adverse Events:

All grade 3, 4 and 5 adverse events, according to the Common Terminology Criteria for Adverse Events (CTCAE) of the National Cancer Institute, and all serious adverse events are reported to CITR. Respective CITR Principal Investigators determine the relationship of the adverse event to the immunosuppression therapy and to the islet infusion procedure at the time the adverse event forms are completed. Currently this procedure is being standardized and all relationship determination will be conducted by a committee using standard procedures.

Exhibit 223 presents the overall adverse event and serious adverse event rate for islet after kidney transplant recipients in Year 1 post their first islet infusion. Sixty-eight percent (N=15) of the recipients experienced at least one adverse event in Year 1, while 41% (N=9) experienced one or more serious adverse events in this same period. Of the 33 reported adverse events, 33.3% were related to the immunosuppression therapy and 42.4% were related to the infusion procedure. Of the 18 reported serious adverse events, 6 (33.3%) were related to the immunosuppression therapy and 6 (33.3%) were related to the islet infusion procedure.

Exhibit 224 displays the categories of serious adverse events by relation to the infusion procedure and immunosuppression therapy. At the time of this report, 30 serious adverse events have been reported for the 22 participants, with 60.0% of the serious adverse events requiring an inpatient hospitalization. Eighty percent of the serious adverse events were classified as unrelated to the islet infusion procedure with 63.3% unrelated to the immunosuppression therapy. Approximately 90% of the serious adverse events resolved with no residual effects (Exhibit 225). The most common serious adverse events were related to blood and lymphatic system disorders (N=6, 20.0% for each group), as classified by the MedDRA classifications system (Exhibit 226).

Exhibit 227 lists serious adverse events, the year when it occurred related to the last infusion date, its relationship to the islet infusion procedure, treatment required and the final outcome of the event. The number of hospitalization days for the islet infusion procedure is summarized in this section (Exhibit 228), as well as hospitalizations occurring during the post infusion follow-up period (Exhibit 229). Portal pressures, changes in portal pressures, islet equivalents infused, and islet packed cell volume are summarized in Exhibit 230.

Exhibit 179
Participant Demographics

	Overall			
	N	Median	Min	Max
Age (yrs)	22	45.4	34.3	55.4
Duration of Diabetes (yrs)	22	31.5	15.0	42.0
Weight (kg)	22	60.2	47.0	89.4
Body Mass Index (kg/m^2)	22	22.9	15.4	27.7

Exhibit 180
Participant Characteristics

	Overall	
	N	%
Gender		
Male	9	40.9
Female	13	59.1
Race		
American Indian or Alaska Native	-	0.0
Asian	-	0.0
Black or African American	1	4.5
Indian Sub-Continent	-	0.0
Mideast or Arabian	-	0.0
Native Hawaiian or Other Pacific Islander	-	0.0
White	21	95.5
Ethnicity		
Non Hispanic or Latino	22	100.0
Hispanic or Latino	-	0.0
Diabetes Type		
Type 1 Diabetes	22	100.0

Exhibit 181
Participant's Primary Payer and Employment Status at Time of First Infusion

	Overall	
	N	%
Primary Payer		
US/State Government Agency	6	27.3
Private Insurance	-	0.0
Institutional Commitment	-	0.0
Non-Government Research Grant	15	68.2
Provincial Government	-	0.0
Missing	1	4.5
Employment status		
Working full time	12	54.5
Working part-time by choice	2	9.1
Working part-time due to disease	1	4.5
Working part-time, reason unknown	-	0.0
Not working by choice	2	9.1
Not working due to disease	4	18.2
Not working, reason unknown	-	0.0
Student	-	0.0
Retired	-	0.0
Employment status unknown	1	4.5
Missing	-	0.0

Exhibit 182
Participant Status at First Infusion

	Overall	
	N	%
Total	22	100.0
Use of insulin pump		
Yes	5	22.7
No	16	72.7
Unknown	1	4.5
Number of injections per day		
N/A-on pump	5	22.7
1-2	1	4.5
3-5	13	59.1
6 or more	1	4.5
Unknown	2	9.1
Use of insulin pump or 3 or more injections per day		
Yes	19	86.4
No	1	4.5
Unknown	2	9.1
Pre transplant autoantibody - GAD 65		
Positive	-	0.0
Negative	6	27.3
Not Done/Unknown	16	72.7
Pre transplant autoantibody - IA-2		
Positive	-	0.0
Negative	6	27.3
Not Done/Unknown	16	72.7
Pre transplant autoantibody - Insulin		
Positive	5	22.7
Negative	-	0.0
Not Done/Unknown	17	77.3
Total number of positive antibodies		
One	5	22.7
Unknown	17	77.3

Exhibit 182 *(continued)*
Participant Status at First Infusion

	Overall	
	N	%
Positive crossmatch for B-Cell		
Positive	-	0.0
Negative	15	68.2
Not Done/Unknown	17	31.8
Positive crossmatch for T-Cell		
Positive	-	0.0
Negative	15	68.2
Not Done/Unknown	7	31.8

Exhibit 183
Participant Summary Measures at First Infusion

	Overall		
	N	Mean	SD
Daily insulin requirement prior to infusion (units)	21	35.7	13.8
Duration of intensive therapy (yrs)	1	10.0	-
Average daily insulin/kg participant body weight	21	0.6	0.2
Number of days on wait list for first infusion	22	366.7	348.2
Fasting plasma glucose (mg/dL)	22	162.7	100.8
Basal C-Peptide (ng/mL)	19	0.1	0.2
HbA_{1C} (%)	21	8.0	1.3
Most recent PRA (%)	18	0.4	1.3
Peak PRA (%)	16	3.0	9.3

Exhibit 184
Participant Serology at Screening

	Overall	
	N	%
Total	22	100.0
HIV screening		
Positive	-	0.0
Negative	22	100.0
Not Done/Unknown/Missing	-	0.0
CMV IgG		
Positive	10	45.5
Negative	11	50.0
Not Done/Unknown/Missing	1	4.5
CMV IgM		
Positive	-	0.0
Negative	8	36.4
Not Done/Unknown/Missing	14	63.6
HepB core antibody		
Positive	1	4.5
Negative	9	40.9
Not Done/Unknown/Missing	12	54.5
HepB surface antigen		
Positive	-	0.0
Negative	22	100.0
Not Done/Unknown/Missing	-	0.0
HepC antibody		
Positive	-	0.0
Negative	22	100.0
Not Done/Unknown/Missing	-	0.0
EBV IgG		
Positive	19	86.4
Negative	1	4.5
Not Done/Unknown/Missing	2	9.1

Exhibit 185
Infusion Summary by Infusion Sequence

	Infusion 1					
	N	Mean	SD	Median	Min	Max
Islet Equivalents infused	21	516,395	141,392	485,850	318,000	828,934
Islet Equivalents infused/kg participant weight	21	8,538	2,626	8,436	5,274	15,532
Packed cell volume (mL)	16	3.8	1.7	5.0	1.0	6.0

	Infusion 2					
	N	Mean	SD	Median	Min	Max
Islet Equivalents infused	14	424,383	88,616	400,892	298,200	600,000
Islet Equivalents infused/kg participant weight	13	7,254	1,649	6,920	5,117	10,926
Packed cell volume (mL)	11	3.4	1.5	3.5	1.0	5.0
Time since first infusion (weeks)	17	14.7	18.6	9.1	1.7	73.3

	Infusion 3					
	N	Mean	SD	Median	Min	Max
Islet Equivalents infused	1	492,708	-	492,708	492,708	492,708
Islet Equivalents infused/kg participant weight	1	7,049	-	7,049	7,049	7,049
Packed cell volume (mL)	1	5.0	-	5.0	5.0	5.0
Time since first infusion (weeks)	3	70.8	15.1	72.0	55.1	85.3
Time since second infusion (weeks)	3	64.5	15.9	67.9	47.1	78.4

Exhibit 186
Donor Characteristics

	Overall			
	N	Median	Min	Max
Age (yrs)	49	49.0	1.0	64.0
Weight (kg)	49	84.8	55.0	199.6
Height (m)	49	1.7	1.5	1.9
Body Mass Index (kg/m^2)	49	28.4	20.2	68.9
Time from admission to brain death (hrs)	47	35.0	2.0	276.0
Duration of cardiac arrest where cardiovascular death (mins)	4	7.5	1.0	25.0
Time from cross clamp to pancreas recovery (mins)	41	39.0	5.0	64.0

Time of brain death is defined as when a physician confirms the death and documents this per the medical chart. Time of cross clamp is defined as when the aorta was cross-clamped prior to organ retrieval.

Exhibit 187
Donor Characteristics and Hospitalization Summary Information

	Overall	
	N	%
Total	49	100.0
Gender		
Female	24	49.0
Male	25	51.0
Race		
American Indian or Alaska Native	-	0.0
Asian	1	2.0
Black or African American	4	8.2
Indian Sub-continent	-	0.0
Mideast or Arabian	-	0.0
Native Hawaiian or Other Pacific Islander	-	0.0
White	42	85.7
Missing	2	4.1
Ethnicity		
Non Hispanic or Latino	43	87.8
Hispanic or Latino	6	12.2
Body Mass Index (kg/m^2)		
<25	9	18.4
25-27	11	22.4
28-30	12	24.5
>30	17	34.7

Exhibit 187 *(continued)*
Donor Characteristics and Hospitalization Summary Information

	Overall	
	N	%
Donor ABO blood group		
A	15	30.6
A_1	4	8.2
A_2	1	2.0
AB	-	0.0
A_1B	-	0.0
A_2B	-	0.0
B	3	6.1
O	26	53.1
Cause of death		
Anoxia/cardiac arrest	3	6.1
CNS tumor	1	2.0
Cerebrovascular/stroke	35	71.4
Head trauma	10	20.4
Other	-	0.0
Mechanism of death		
Asphyxiation	-	0.0
Blunt injury	6	12.2
Cardiovascular	2	4.1
Death from natural causes	-	0.0
Drowning	-	0.0
Drug intoxication	-	0.0
Gunshot wound	3	6.1
Intracranial hemorrhage/stroke	37	75.5
None of the above	1	2.0

Exhibit 187 *(continued)*
Donor Characteristics and Hospitalization Summary Information

	Overall	
	N	%
History of hypertension		
Yes	18	36.7
No	30	61.2
Missing	1	2.0
-Hypertension duration		
0-5 years	9	50.0
6-10 years	2	11.1
>10 years	4	22.2
Missing	3	16.7
-Hypertension control-Diet		
Yes	2	11.1
No	5	27.8
Missing	11	61.1
-Hypertension control-Diuretics		
Yes	1	5.6
No	9	50.0
Missing	8	44.4
-Hypertension control-Other medications		
Yes	12	66.7
No	3	16.7
Missing	3	16.7
History of alcohol dependency		
Yes	15	30.6
No	32	65.3
Missing	2	4.0
-Alcohol use in past 6 months		
Yes	9	60.0
No	5	33.3
Missing	1	6.7

Exhibit 187 *(continued)*
Donor Characteristics and Hospitalization Summary Information

	Overall	
	N	%
History of diabetes		
Yes	-	0.0
No	49	100.0
Missing	-	0.0
Transfusions given prior to surgery		
0 units	35	71.4
0-5 units	10	20.4
6-10 units	2	4.1
>10 units	1	2.0
Missing	1	2.0
Transfusions given intraoperatively		
0 units	47	95.9
0-5 units	1	2.0
6-10 units	-	0.0
Missing	1	2.0
Steroids given		
Yes	35	71.4
No	13	26.5
Missing	1	2.0
Insulin given		
Yes	18	36.7
No	30	61.2
Missing	1	2.0

Exhibit 188
Donor Characteristics: Use of Vasopressors

	Overall	
	N	%
Total	49	100.0
Vasopressors used		
Yes	48	98.0
No	1	2.0
Missing	-	0.0
Number of vasopressors used		
None	1	2.0
One	15	30.6
Two	19	38.8
Three	11	22.4
Four	3	6.1
Missing	-	0.0

Exhibit 189
Donor Serology

	Overall	
	N	%
Total	49	100.0
Anti HIV I/II		
Positive	-	0.0
Negative	48	98.0
Not Done/Unknown/Missing	1	2.0
Anti HTLV I/II		
Positive	-	0.0
Negative	48	98.0
Not Done/Unknown/Missing	1	2.0
RPR VDRL		
Positive	-	0.0
Negative	48	98.0
Indeterminate	-	0.0
Not Done/Unknown/Missing	1	2.0
Anti CMV		
Positive	27	55.1
Negative	21	42.9
Not Done/Unknown/Missing	1	2.0
HBsAg		
Positive	1	2.0
Negative	46	93.9
Not Done/Unknown/Missing	2	4.1
Anti HBC		
Positive	-	0.0
Negative	48	98.0
Not Done/Unknown/Missing	1	2.0
Anti HCV		
Positive	-	0.0
Negative	48	98.0
Not Done/Unknown/Missing	1	2.0

Exhibit 190
Donor Laboratory Data

	Overall					
	N	Mean	SD	Median	Min	Max
Serum creatinine (mg/dL)	49	0.9	0.3	0.9	0.4	2.2
BUN (mg/dL)	49	13.3	6.5	13.0	4.0	29.0
Total bilirubin (mg/dL)	49	0.9	0.6	0.7	0.2	2.3
AST (IU/L)	49	48.8	48.3	33.0	17.0	269.0
ALT (IU/L)	49	42.2	39.9	33.0	14.0	262.0
Serum lipase (IU/L)	49	62.1	77.4	32.0	2.0	394.0
Serum amylase (IU/L)	48	138.5	192.2	61.0	18.0	797.0
Minimum pre-insulin blood glucose (mg/dL)	49	119.2	32.6	105.0	67.0	216.0
Maximum blood glucose (mg/dL)	49	252.8	91.1	233.0	117.0	581.0

Exhibit 191
Islet Processing Summary

	Overall	
	N	%
Total	49	100.0
Pancreas procurement team		
Unrelated to processing/infusion team	28	57.1
Related to processing/infusion team	18	36.7
Unknown/Missing	3	6.1
Islet processing/testing center		
CITR center, where infusion took place	49	100.0
Another facility not located or affiliated with the transplant center	-	0.0
Unknown/Missing	-	0.0
Pancreas preservation		
UW	38	77.6
Two Layer*	7	14.3
UW followed by Two Layer	4	8.2
Other	-	0.0
Collagenase Type: Liberase HI		
Yes	49	100.0
No	-	0.0
Islet purification		
None	-	0.0
Density gradient	49	100.0
Islet pretreatment		
None	20	40.8
Culture	29	59.2

Exhibit 191 *(continued)*
Islet Processing Summary

	Overall	
	N	%
Gram stain		
Positive	2	4.1
No organism seen	45	91.8
Missing	2	4.1
Aerobic culture		
Positive	1	2.0
No Growth	36	73.5
Not Done	9	18.4
Missing	3	7.1
Anaerobic culture		
Positive	1	2.0
No Growth	37	75.5
Not Done	8	16.3
Missing	3	6.1
Fungal culture		
Positive	1	2.0
No Growth	35	71.4
Not Done	9	18.4
Missing	4	8.2
Mycoplasma		
Positive	-	0.0
Negative	28	57.1
Not Done	18	36.7
Missing	3	6.1

*Two Layer is defined as any Two Layer solution and includes Two Layer solutions of UW and PFC (N=7).

Exhibit 192
Cold Ischemia Information

	Overall					
	N	Mean	SD	Median	Min	Max
Time from cross clamp to pancreas recovery (mins)	41	37.1	14.9	39.0	5.0	64.0
Duration of cold ischemia (hrs)	48	7.3	3.0	6.9	2.4	15.7
Time from brain death to pancreas recovery (hrs)	39	20.3	10.5	18.0	3.0	57.0
Culture time (hrs)	17	39.1	16.7	40.3	12.0	76.8

Time of brain death is defined as when a physician confirms the death and documents this per the medical chart. Time of cross clamp is defined as when the aorta was cross-clamped prior to organ retrieval. Duration of cold ischemia is defined as the time from when the pancreas was placed in cold preservation solution to the heating up of the organ to start the digestion process. Culture is defined as any time spent in a specially prepared nutrient medium.

Exhibit 193
Summary of Islet Equivalents and Timing of Count

	Total Islet Equivalents					
	N	Mean	SD	Median	Min	Max
Islet Equivalents (IEQ) measured at:						
Post Digestion	1	479,583	-	479,583	479,583	479,583
Post Purification (Pre Culture)	34	440,733	109,791	451,562	193,417	589,000
Post Culture	14	384,162	87,919	392,230	185,600	537,500

Exhibit 194
Islet Product Characterization

	Overall					
	N	Mean	SD	Median	Min	Max
Total packed cell volume infused (mL)	35	3.7	1.6	5.0	1.0	6.0
Islet particle count	43	381,546	131,872	379,950	102,500	728,333
Embedded islets (%)	22	13.9	14.3	10.0	0.0	50.0
Islet equivalents/kg donor weight	49	4,909	1,529	4,786	2,062	9,879
Islet equivalents infused	43	514,311	150,958	485,850	298,200	828,934
Beta cells ($x10^6$)	14	461.2	171.1	475.0	156.0	821.0
Beta cells/kg donor weight	14	5.3	1.8	5.5	2.3	7.8
Insulin content (µgrams)	15	3,186	2,631	2,960	19.0	8,200
DNA content (µgrams)	13	14,570	12,771	8,800	3,800	42,265
Endotoxin units	45	12.1	20.0	5.0	0.1	114.0
Endotoxin units/kg donor weight	45	0.1	0.2	0.1	0.0	0.9
Islet purity: Dithizone positive cells (%)	48	68.9	16.9	70.0	30.0	95.0
Islet potency: Stimulation index	32	3.2	3.2	2.2	0.9	17.0
Islet Viability (%)						
Fluorescein Diacetate/Propidium Iodide	29	91.0	6.7	91.0	76.0	100.0
Trypan Blue	15	93.2	2.7	95.0	88.0	95.0
Syto Green 13	0	-	-	-	-	-
Equivalent fluorochromes	1	80.0	-	80.0	80.0	80.0

Stimulation index is calculated by dividing the glucose-stimulated insulin release at high glucose by the glucose-stimulated insulin release at low glucose.

Exhibit 195
Mean Number of Islet Equivalents/kg (± SD) by Total Number of Infusions Received

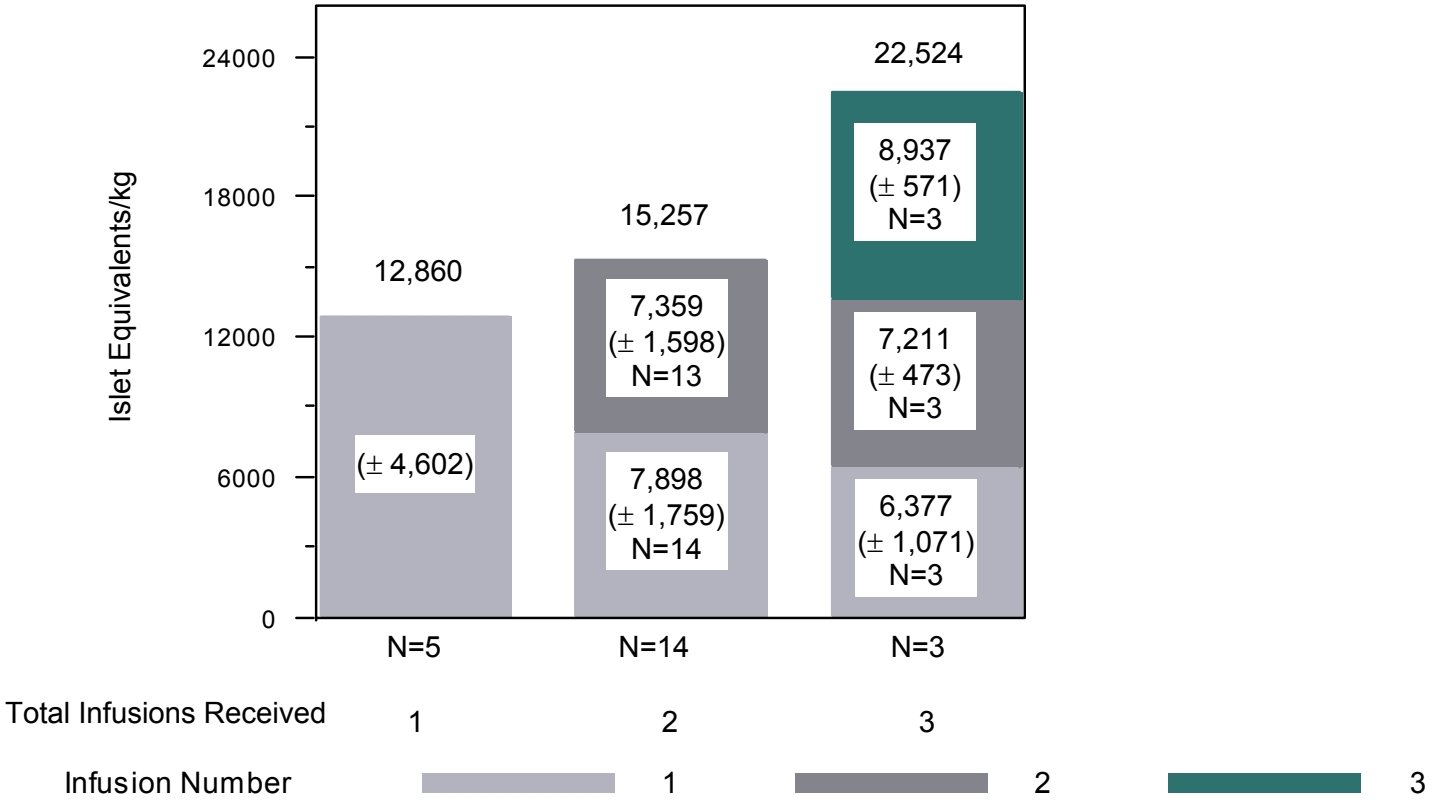


Exhibit 196
Immunosuppression Regimen at Time of First Infusion

	Overall	
	N	%
Total	22	100.0
Sirolimus + Tacrolimus + Daclizumab	10	45.5
Sirolimus + Tacrolimus + Daclizumab + MMF	1	4.5
Sirolimus + Tacrolimus + Daclizumab + MMF + Etanercept	1	4.5
Sirolimus + Tacrolimus + Daclizumab + Etanercept	1	4.5
Sirolimus + Tacrolimus + Daclizumab + Infliximab	2	9.1
Sirolimus + Tacrolimus + Daclizumab + MMF + Etanercept + Methylprednisolone	1	4.5
Sirolimus + Tacrolimus + Daclizumab + Prednisone	2	9.1
Tacrolimus + Daclizumab + MMF + Prednisone	4	18.2

Exhibit 197
Immunosuppression Dosing (mg/day) at Time of Infusion by Infusion Sequence

	Infusion Sequence								
	Infusion 1			Infusion 2			Infusion 3		
	N	Mean	SD	N	Mean	SD	N	Mean	SD
Sirolimus (mg/day)	17	5.3	2.8	14	8.3	1.9	2	8.0	1.4
Tacrolimus (mg/day)	21	3.1	1.6	16	3.6	1.2	3	4.7	1.2
MMF (mg/day)	7	678.6	278.2	3	750.0	250.0	1	500.0	-
Prednisone (mg/day)	6	5.0	0.0	4	5.0	0.0	1	5.0	-
Methylprednisolone (mg/day)	1	2.0	-	0	-	-	0	-	-

Exhibit 198
Induction Therapy (mg) at Time of Infusion by Infusion Sequence

	Infusion Sequence								
	Infusion 1			Infusion 2			Infusion 3		
	N	Mean Total Dose	SD	N	Mean Total Dose	SD	N	Mean Total Dose	SD
Daclizumab (mg/kg)	19	4.4	1.9	14	4.2	1.6	2	5.5	0.7
Infliximab (mg/kg)	2	10.0	0.0	1	10.0	-	0	-	-
Etanercept (mg)	3	150.0	0.0	2	150.0	0.0	0	-	-

Exhibit 199
Immunosuppression Therapy Use Post Last Infusion

	Follow-Up			
	Month 6		Year 1	
	N	%	N	%
Total	22	100.0	21	100.0
Sirolimus + Tacrolimus	8	36.4	5	23.8
Sirolimus + Tacrolimus + Daclizumab	1	4.5	1	4.8
Sirolimus + Tacrolimus + Prednisone	2	9.1	1	4.8
Sirolimus + Tacrolimus + Daclizumab + MMF	1	4.5	-	0.0
Sirolimus + Tacrolimus + Daclizumab + Prednisone	1	4.5	1	4.8
Sirolimus + Tacrolimus + Daclizumab + MMF + Methylprednisolone	1	4.5	-	0.0
Tacrolimus + MMF	1	4.5	2	9.5
Tacrolimus + Prednisone	1	4.5	1	4.8
Tacrolimus + MMF + Prednisone	1	13.6	2	9.5
Neoral Cyclosporine + MMF + Prednisone	-	0.0	1	4.8
No Immunosuppression Medications Taken	-	0.0	1*	4.8
Missing Information on Immunosuppression	3	13.6	6	28.6

*Participant did not take immunosuppression medications as instructed and their islet graft failed prior to Year 1.

Exhibit 200
Immunosuppressive Dosing Post Last Infusion

	Follow-Up								
	Day 30			Month 6			Year 1		
	N	Mean	SD	N	Mean	SD	N	Mean	SD
Sirolimus (mg/day)	16	7.6	3.1	12	6.7	2.6	7	6.0	1.0
Tacrolimus (mg/day)	20	3.8	1.4	16	3.4	1.3	12	4.0	1.4
Neoral Cyclosporine (mg/day)	0	-	-	0	-	-	1	250.0	-
MMF (mg/day)	7	928.6	449.9	5	1000.0	500.0	5	900.0	418.3
Prednisone (mg/day)	6	5.0	0.0	7	5.0	0.0	6	5.0	0.0
Methylprednisolone (mg/day)	1	4.0	-	1	4.0	-	0	-	-
Daclizumab (mg/kg)	0	-	-	3	1.0	0.0	2	1.0	0.0

Exhibit 201
Sirolimus Trough Level (ng/mL) Post Last Infusion

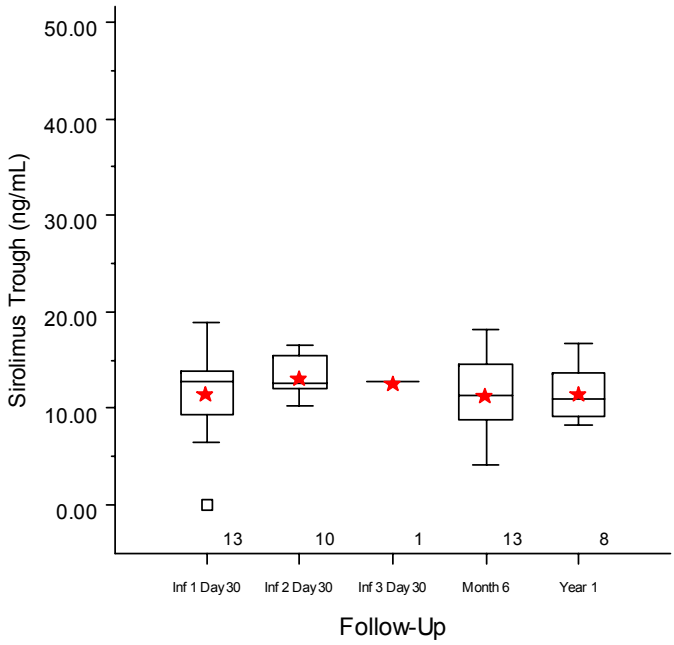


Exhibit 202
Tacrolimus Trough Level (ng/mL) Post Last Infusion

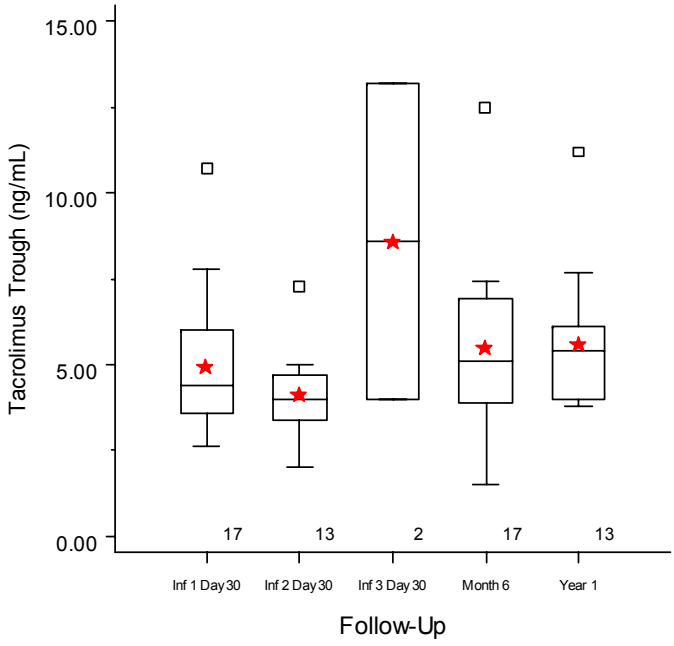


Exhibit 203
Participant's Insulin Status at Follow-Up
Post First and Last Infusion

	Follow-Up							
	Month 6				Year 1			
	Insulin Independent		Insulin Dependent		Insulin Independent		Insulin Dependent	
	N	%	N	%	N	%	N	%
Post First Infusion	7	46.7	8	53.3	6	42.9	8	57.1
Post Last Infusion	7	46.7	8	53.3	4	33.3	8	66.7

Exhibit 204
Reduction in Insulin (%) from Pre Infusion to Follow-Up Post Last Infusion
Participants on Insulin

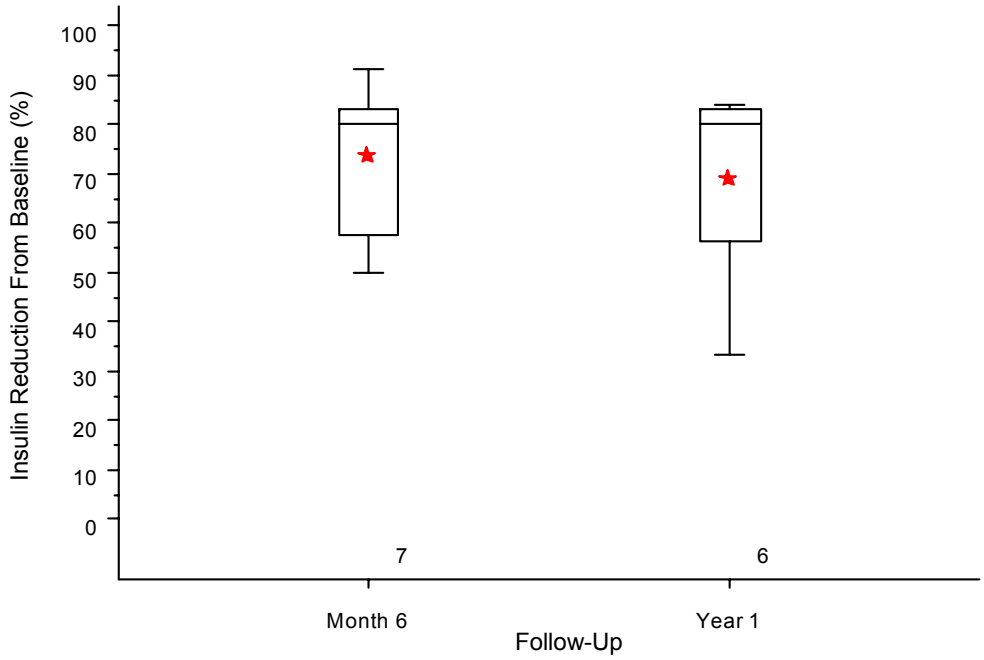


Exhibit 205
Summary of Severe Hypoglycemic Events by Pre Infusion and Follow-Up Post Last Infusion

	Follow-Up							
	Pre First Infusion		Days 0-30 Post First Infusion		Months 1-6 Post Last Infusion		Months 6-12 Post Last Infusion	
	N	%	N	%	N	%	N	%
Total	22	100.0	22	100.0	22	100.0	21	100.0
Any Hypoglycemic Episodes								
Yes*	12	54.1	1	4.5	-	0.0	-	0.0
No	10	45.5	21	95.5	19	86.4	15	71.4
Unknown	-	0.0	-	0.0	-	0.0	-	0.0
Missing	-	0.0	-	0.0	3	13.6	6	28.6
Frequency of Hypoglycemic Episodes								
None	10	45.5	21	95.5	19	86.4	15	71.4
1-2	4	18.2	1	4.5	-	0.0	-	0.0
3-5	1	4.5	-	0.0	-	0.0	-	0.0
6 or more	4	18.2	-	0.0	-	0.0	-	0.0
Unknown	3	13.6	-	0.0	-	0.0	-	0.0
Missing	-	0.0	-	0.0	3	13.6	6	28.6

*All participants on insulin at the time of the hypoglycemic episodes.

Exhibit 206
Fasting Plasma Glucose (mg/dL)
Pre Infusion and Post Last Infusion

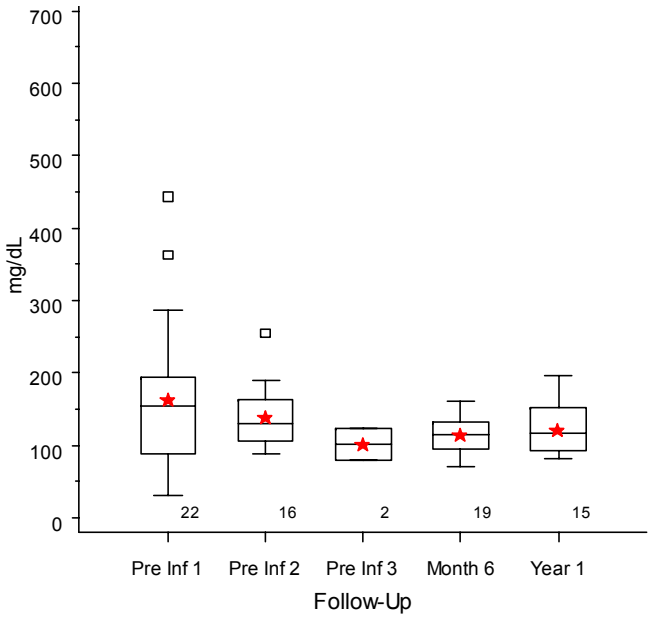


Exhibit 207
HbA_{1C} (%)
Pre Infusion and Post Last Infusion

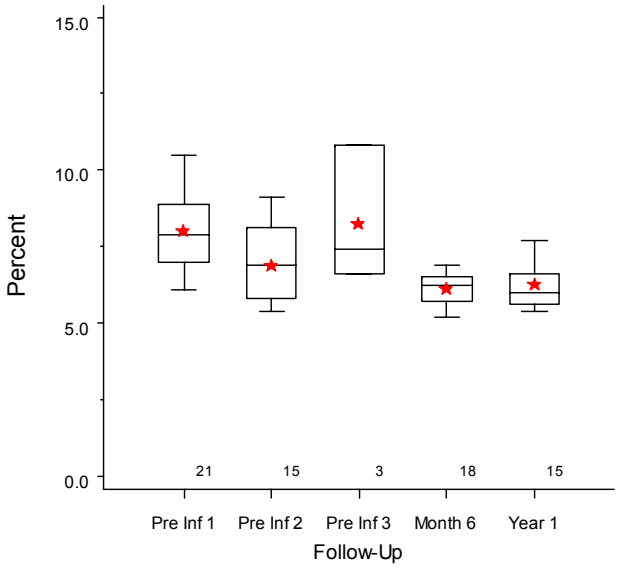


Exhibit 208
Basal Plasma C-Peptide (ng/mL)
Pre Infusion and Post Last Infusion

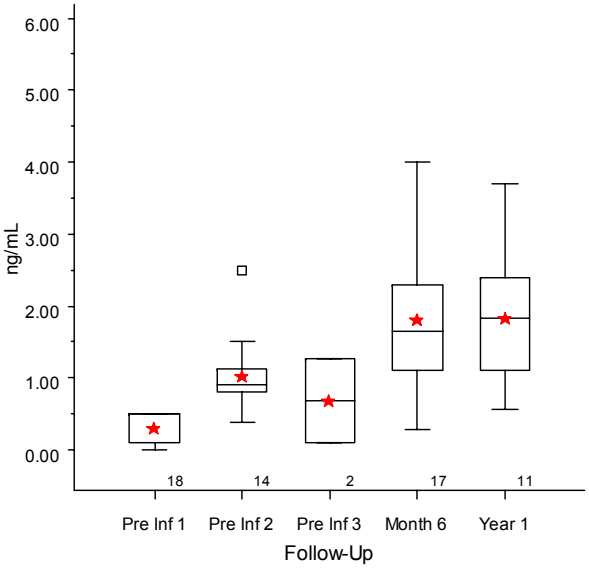


Exhibit 209
Pre Infusion Recipient Lab Summary by Infusion Sequence

	Infusion Sequence																	
	1						2						3					
	N	Mean	SD	Median	Min	Max	N	Mean	SD	Median	Min	Max	N	Mean	SD	Median	Min	Max
Fasting Plasma Glucose (mg/dL)	22	162.7	100.8	155.0	30.0	444.0	16	138.7	44.0	130.5	87.0	255.0	2	101.5	31.8	101.5	79.0	124.0
HbA_{1C} (%)	21	8.0	1.3	7.9	6.1	10.5	15	6.9	1.2	6.9	5.4	9.1	3	8.3	2.2	7.4	6.6	10.8
ALT (IU/L)	21	27.0	15.4	22.0	8.0	64.0	16	46.0	38.9	37.5	20.0	183.0	2	48.5	26.2	48.5	30.0	67.0
AST (IU/L)	22	30.7	14.2	25.0	16.0	80.0	16	41.5	24.6	31.0	17.0	113.0	2	40.0	12.7	40.0	31.0	49.0
Alkaline Phosphatase (IU/L)	21	77.2	25.8	74.0	40.0	134.0	16	70.7	26.2	63.5	40.0	144.0	2	104.0	58.0	104.0	63.0	145.0
Total Bilirubin (mg/dL)	22	0.5	0.3	0.4	0.1	1.2	16	0.4	0.2	0.4	0.1	0.8	2	0.8	0.1	0.8	0.7	0.8
Total Cholesterol (mg/dL)	21	191.0	22.9	180.0	155.0	240.0	10	179.0	20.7	180.5	150.0	206.0	1	189.0	-	189.0	189.0	189.0
HDL (mg/dL)	21	65.8	19.7	62.0	42.0	112.0	10	63.7	16.1	61.5	44.0	98.0	1	85.0	-	85.0	85.0	85.0
LDL (mg/dL)	21	101.8	22.5	100.0	66.0	143.0	10	95.3	14.2	96.0	75.0	114.0	1	92.0	-	92.0	92.0	92.0
Triglycerides (mg/dL)	21	108.7	45.9	106.0	34.0	217.0	10	99.4	45.7	98.5	38.0	188.0	1	60.0	-	60.0	60.0	60.0
Serum Creatinine (mg/dL)	22	1.2	0.4	1.2	0.5	2.0	16	1.3	0.3	1.3	0.7	2.0	2	1.1	0.1	1.1	1.0	1.2
Calculated Creatinine Clearance ($mL/min/1.73m^2$)	13	81.4	34.5	75.0	41.0	176.0	4	51.5	12.0	47.5	42.0	69.0	0	-	-	-	-	-
Basal Plasma C-peptide (ng/mL)	18	0.3	0.2	0.5	0.0	0.5	14	1.0	0.5	0.9	0.4	2.5	2	0.7	0.8	0.7	0.1	1.3

Exhibit 210
Participants with Abnormal Liver Function Tests Post Infusion

	1-2X ULN		≥ 2X ULN	
	N	%	N	%
ALT	6	30.0	1	5.0
AST	9	45.0	2	10.0
Alkaline Phosphatase	7	35.0	-	0.0
Total Bilirubin	1	5.0	-	0.0

Upper Limit of Normal (ULN)

Values of liver function tests analyzed in this Exhibit are evaluated prior to each subsequent infusion and at Month 6 and Year 1 after the last infusion occurs.

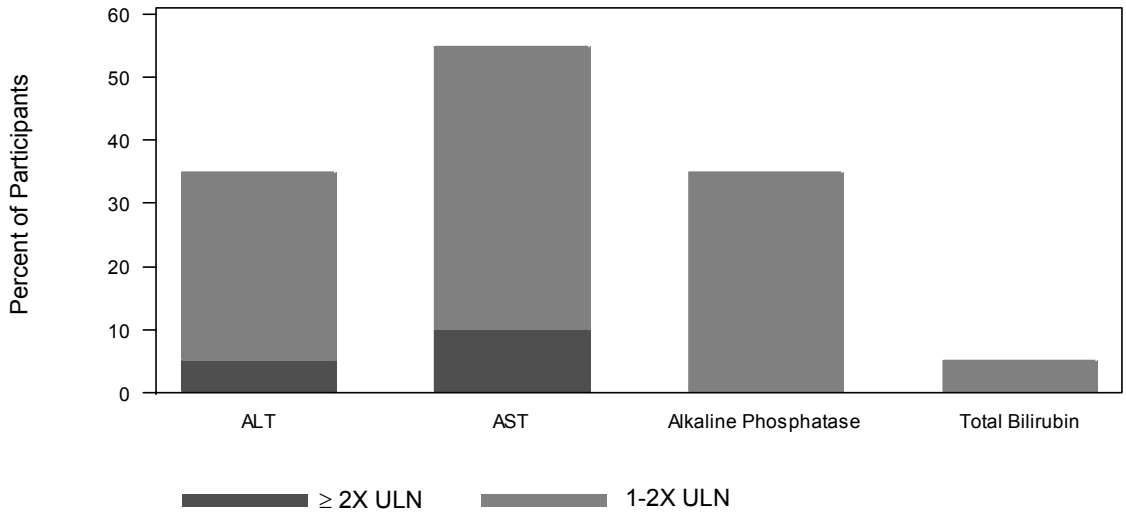


Exhibit 211
ALT (IU/L) Pre Infusion and Post Last Infusion

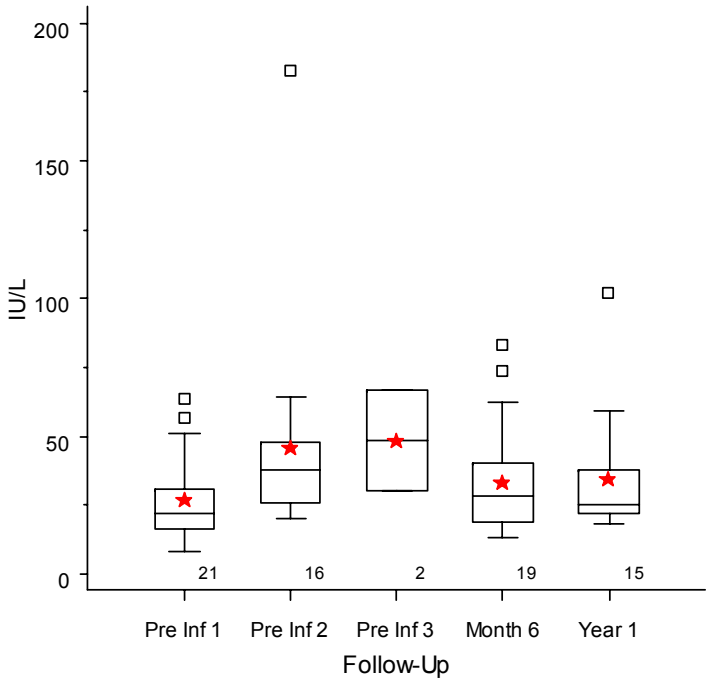


Exhibit 212
AST (IU/L) Pre Infusion and Post Last Infusion

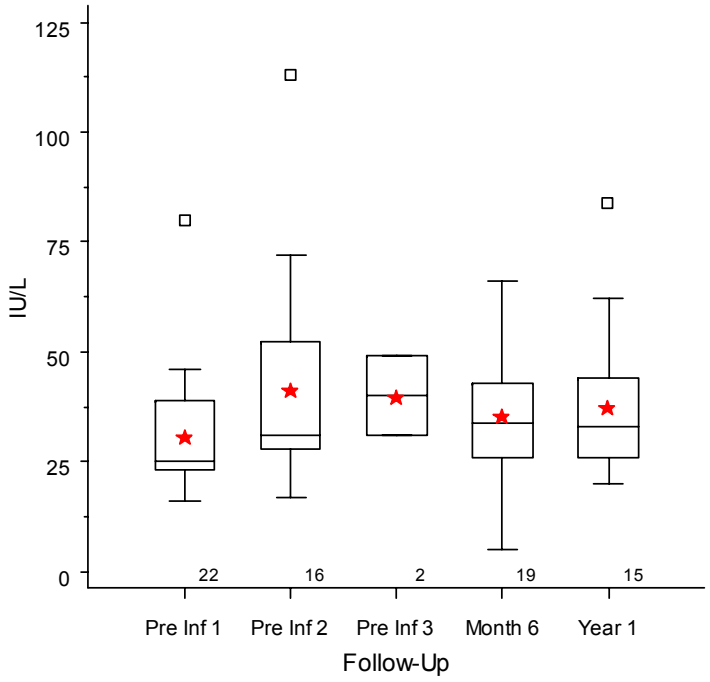


Exhibit 213
Alkaline Phosphatase (IU/L) Pre Infusion and Post Last Infusion

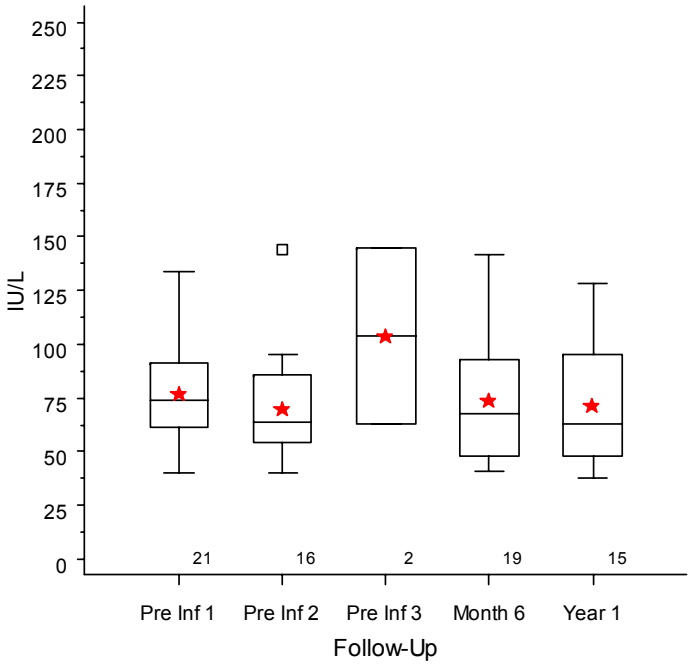


Exhibit 214
Total Bilirubin (mg/dL) Pre Infusion and Post Last Infusion

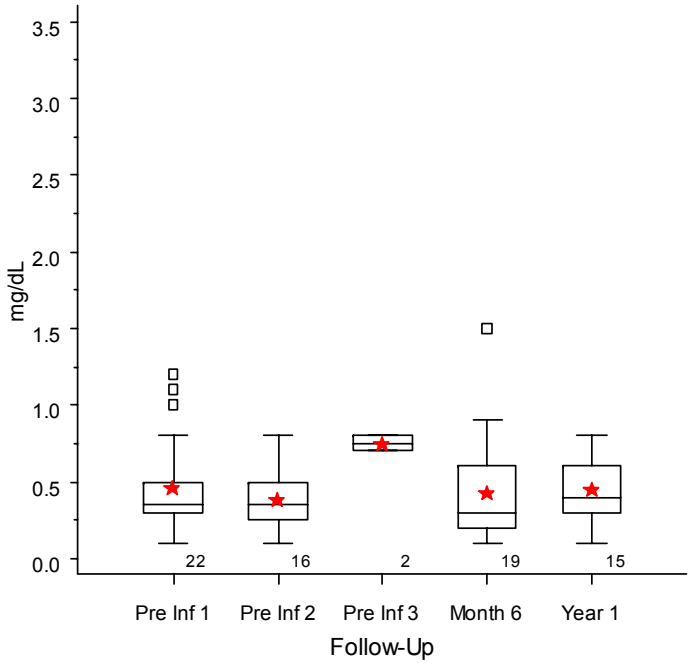


Exhibit 215
Participants with Abnormal Lipid Tests Post Infusion

	1-2X ULN		≥ 2X ULN	
	N	%	N	%
Total Cholesterol	-	0.0	-	0.0
Triglycerides	1	5.3	-	0.0

Upper Limit of Normal (ULN)

Values of lipid tests analyzed in this Exhibit are evaluated prior to each subsequent infusion and at Month 6 and Year 1 after the last infusion occurs.

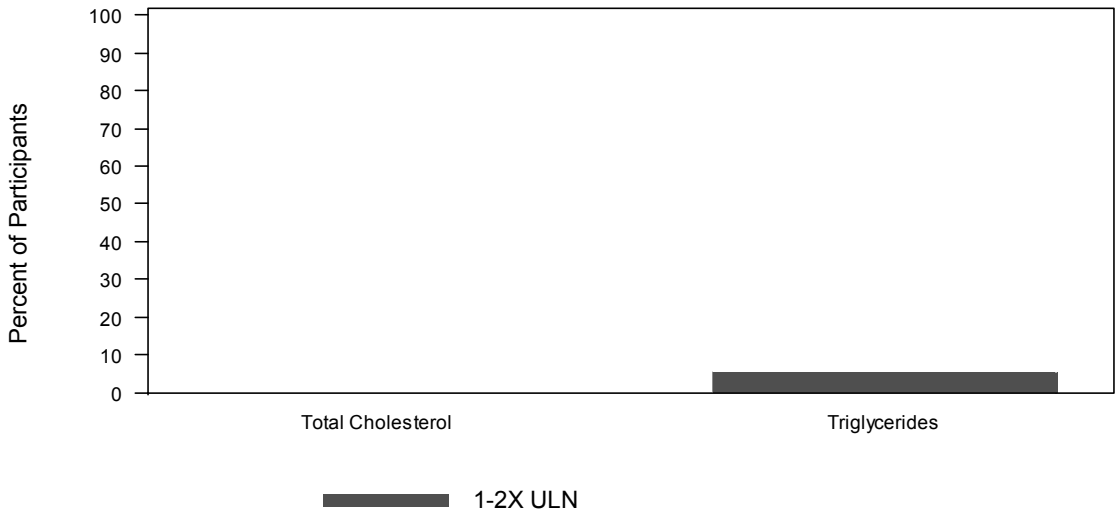


Exhibit 216
Total Cholesterol (mg/dL) Pre Infusion and Post Last Infusion

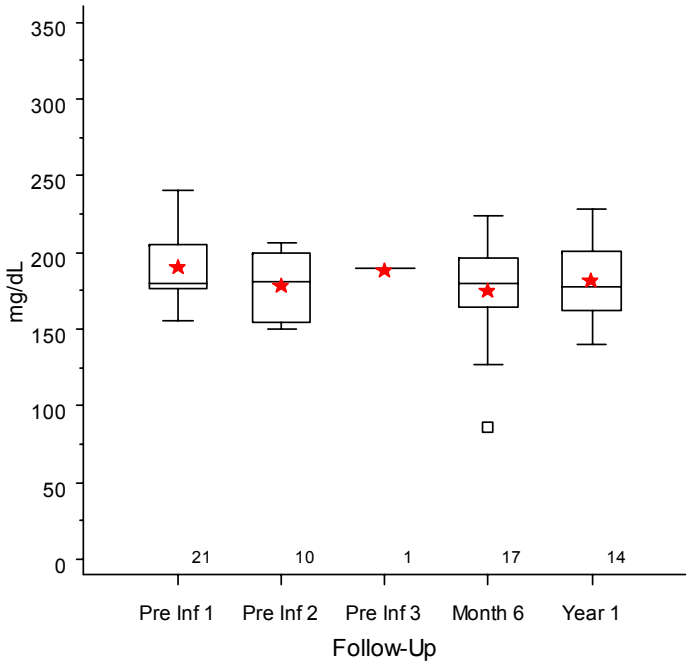


Exhibit 217
HDL (mg/dL) Pre Infusion and Post Last Infusion

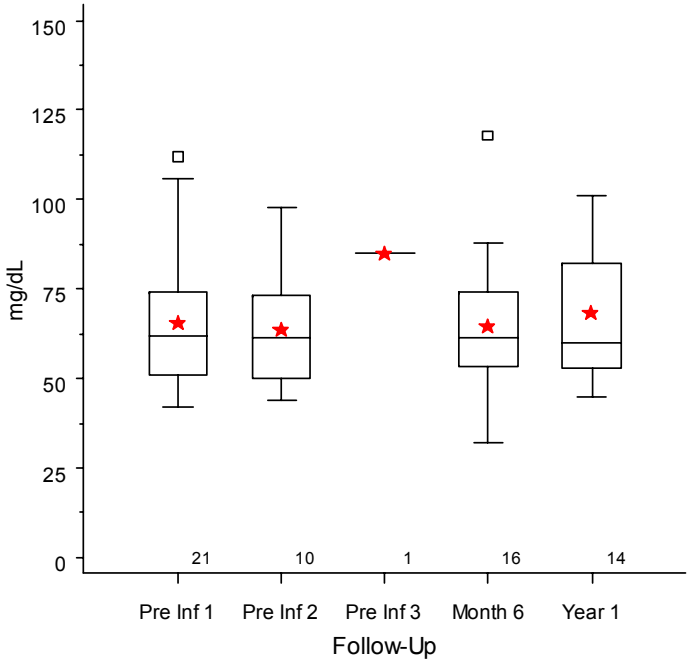


Exhibit 218
LDL (mg/dL) Pre Infusion and Post Last Infusion

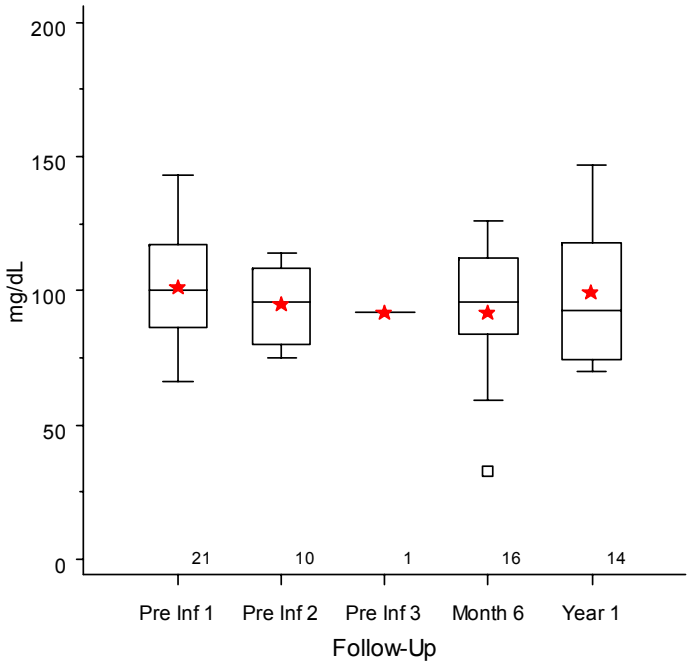


Exhibit 219
Triglycerides (mg/dL) Pre Infusion and Post Last Infusion

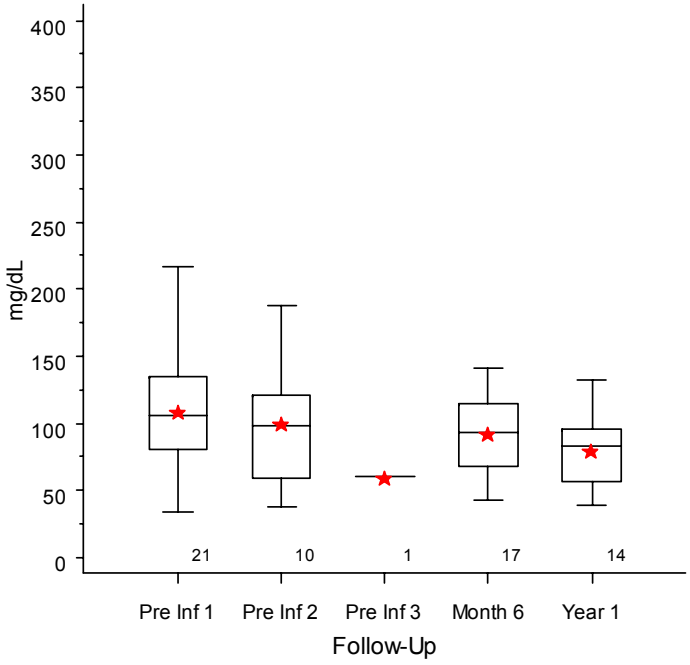


Exhibit 220
Percent of Participants with an Increase in Serum Creatinine (mg/dL) Greater Than 0.5 from Baseline

	Increase in Serum Creatinine >0.5 mg/dL	
	N	%
Serum Creatinine	2	10.5

Values of serum creatinine analyzed in this Exhibit are evaluated prior to each subsequent infusion and at Month 6 and Year 1 after the last infusion occurs.

Exhibit 221
Serum Creatinine (mg/dL) Pre Infusion and Post Last Infusion

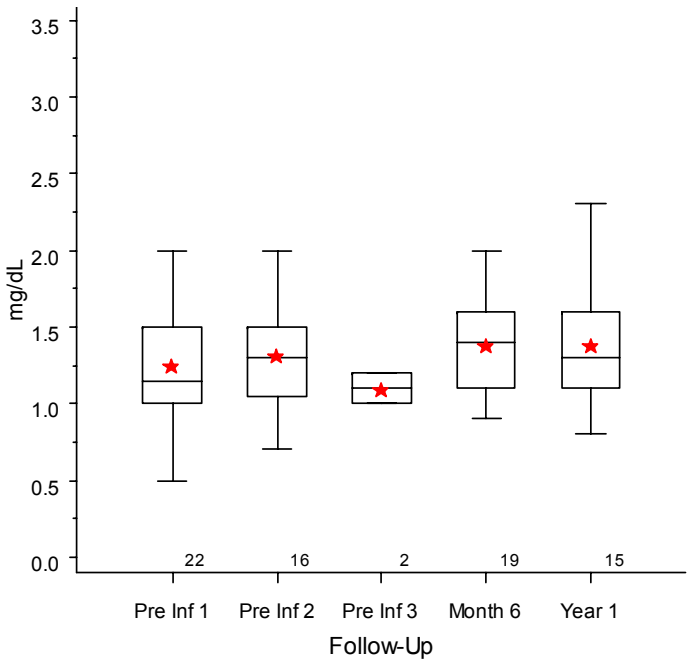


Exhibit 222
Calculated Creatinine Clearance (mL/min/1.73m^2)

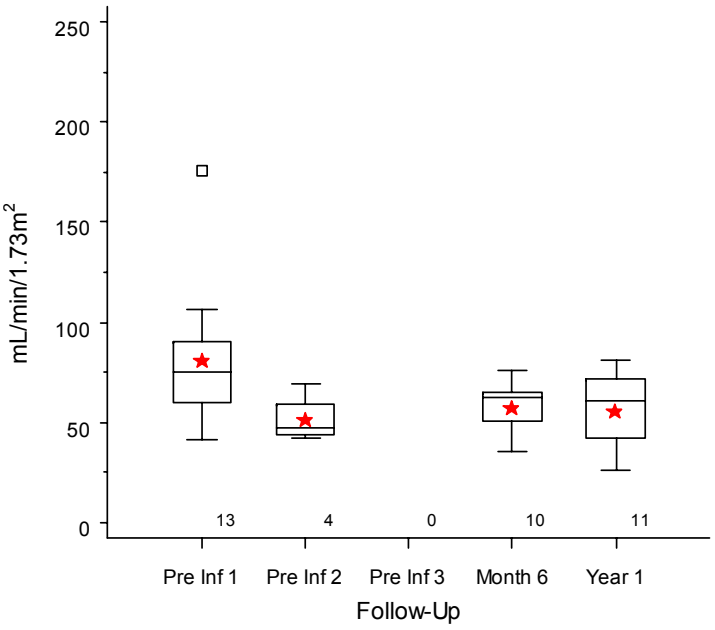


Exhibit 223
Summary of Adverse Events and Serious Adverse Events in Year 1 Post First Infusion (Participants, N=22)

	Adverse Events (Including SAEs)			Serious Adverse Events		
		Related to Immunosuppression Therapy	Related to Infusion Procedure		Related to Immunosuppression Therapy	Related to Infusion Procedure
Number of Events	33	11 (33.3%)	14 (42.4%)	18	6 (33.3%)	6 (33.3%)
Number of Participants with 1 or More Events	15 (68.2%)	6 (27.3%)	10 (45.5%)	9 (40.9%)	3 (13.6%)	5 (22.7%)

The Exhibit above represents all adverse events reported to CITR which occurred in the first year following the participant's first infusion procedure. It does not include adverse events reported to CITR after the first year following the participant's first infusion procedure. Subsequent Exhibits in this section are inclusive of all serious adverse events (SAEs) reported to CITR. Relationship to immunosuppression therapy and the infusion procedure are based on classification of "Probable" or "Definite" by the local CITR Investigator.

Exhibit 224
Summary of All Serious Adverse Events (SAEs)
by Type of SAE

	Relationship to Protocol								Overall	
	Related to Infusion Procedure		Related to Immunosuppression Therapy		Related to Both		Not Related			
	N	%	N	%	N	%	N	%	N	%
All Serious Adverse Events	6	20.0	11	36.7	-	0.0	13	43.3	30	100.0
Death	-	0.0	-	0.0	-	0.0	1*	100.0	1	3.3
Life Threatening	2	25.0	6	75.0	-	0.0	-	0.0	8	26.7
Inpatient Hospitalization	1	5.6	5	27.8	-	0.0	12	66.7	18	60.0
Prolongation of Existing Hospitalization	5	100.0	-	0.0	-	0.0	-	0.0	5	16.7
Persistent or Significant Disability/Incapacity	-	0.0	-	0.0	-	0.0	-	0.0	-	0.0
Congenital Anomaly/Birth Defect	-	0.0	-	0.0	-	0.0	-	0.0	-	0.0

*Participant died over two years post last infusion. The cause of death was reported as a hemorrhagic stroke unrelated to both the islet infusion procedure and immunosuppression therapy.

Relationship to immunosuppression therapy and the infusion procedure are based on classification of “Probable” or “Definite” by the local CITR Investigator.

Exhibit 225
Summary of All Serious Adverse Events (SAEs) Reported and their Outcome

	Relationship to Protocol								Overall	
	Related to Infusion Procedure		Related to Immunosuppression Therapy		Related to Both		Not Related			
	N	%	N	%	N	%	N	%	N	%
All Serious Adverse Events	6	100.0	11	100.0	-	0.0	13	100.0	30	100.0
Outcome of Serious Adverse Event										
Resolved with No Residual Effects	5	83.3	11	100.0	-	0.0	12	92.3	27	90.0
Resolved with Sequelae	-	0.0	-	0.0	-	0.0	-	0.0	-	0.0
Persistent Condition, Recipient Alive	1*	16.7	-	0.0	-	0.0	-	0.0	1	6.7
Death Caused by Adverse Event	-	0.0	-	0.0	-	0.0	1**	7.7	1	3.3

*The event related to the infusion procedure is a portal vein thrombosis requiring continued anticoagulation.
**Participant died over two years post last infusion. The cause of death was reported as a hemorrhagic stroke unrelated to both the the infusion procedure and immunosuppression therapy.

Relationship to immunosuppression therapy and the infusion procedure are based on classification of “Probable” or “Definite” by the local CITR Investigator.

Exhibit 226
Summary of All Serious Adverse Events (SAEs)
by System Organ Class

	Relationship to Protocol								Overall	
	Related to Infusion Procedure		Related to Immunosuppression Therapy		Related to Both		Not Related			
	N	%	N	%	N	%	N	%	N	%
All Serious Adverse Events	6	100.0	11	100.0	-	0.0	13	100.0	30	100.0
System Organ Class										
Blood and lymphatic system disorders	-	0.0	6	54.5	-	0.0	-	0.0	6	20.0
Cardiac disorders	-	0.0	-	0.0	-	0.0	1	7.7	1	3.3
Eye disorders	-	0.0	-	0.0	-	0.0	-	0.0	-	0.0
Gastrointestinal disorders	1	16.7	2	18.2	-	0.0	2	15.4	5	16.7
General disorders and administration site conditions	-	0.0	-	0.0	-	0.0	-	0.0	-	0.0
Hepatobiliary disorders	1	16.7	-	0.0	-	0.0	1	7.7	2	6.7
Immune system disorders	-	0.0	-	0.0	-	0.0	-	0.0	-	0.0
Infections and infestations	-	0.0	1	9.1	-	0.0	3	23.1	4	13.3
Injury, poisoning and procedural complications	1	16.7	-	0.0	-	0.0	2	15.4	3	10.0
Investigations	1	16.7	1	9.1	-	0.0	1	7.7	3	10.0
Metabolism and nutrition disorders	-	0.0	-	0.0	-	0.0	-	0.0	-	0.0
Musculoskeletal and connective tissue disorders	-	0.0	-	0.0	-	0.0	-	0.0	-	0.0
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	-	0.0	1	9.1	-	0.0	-	0.0	1	3.3

Exhibit 226 *(continued)*
Summary of All Serious Adverse Events (SAEs)
by System Organ Class

	Relationship to Protocol								Overall	
	Related to Infusion Procedure		Related to Immunosuppression Therapy		Related to Both		Not Related			
	N	%	N	%	N	%	N	%	N	%
Nervous system disorders	-	0.0	-	0.0	-	0.0	1	7.7	1	3.3
Psychiatric disorders	-	0.0	-	0.0	-	0.0	-	0.0	-	0.0
Renal and urinary disorders	-	0.0	-	0.0	-	0.0	-	0.0	-	0.0
Reproductive system and breast disorders	-	0.0	-	0.0	-	0.0	-	0.0	-	0.0
Respiratory, thoracic and mediastinal disorders	1	16.7	-	0.0	-	0.0	2	15.4	3	10.0
Surgical and medical procedures	-	0.0	-	0.0	-	0.0	-	0.0	-	0.0
Vascular disorders	1	16.7	-	0.0	-	0.0	-	0.0	1	3.3

* MedDRA Classification (http://www.meddramsso.com/newweb2003/index.html).
** MedDRA system organ class designation for lab procedures and test results.

Relationship to immunosuppression therapy and the infusion procedure are based on classification of “Probable” or “Definite” by the local CITR Investigator.

Exhibit 227
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity*	SAE Related to Infusion Procedure/ Infusion of Islets**	SAE Related to Immunosuppression Therapy**	Treatment Required	Outcome
Bacterial infection	2005	Inpatient hospitalization	802 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Blood creatinine increased	2004	Inpatient hospitalization	515 days post 1st Infusion	Yes	Life threatening (Grade 4)	Unrelated	Probable	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Cholecystitis	2003	Inpatient hospitalization	7 days post 2nd Infusion	Yes	Severe (Grade 3)	Possible	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects
Colitis	2004	Inpatient hospitalization	138 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	Current treatment modified based on AE	Resolved, no residual effects
Colitis	2004	Inpatient hospitalization	180 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects
Cough	2004	Inpatient hospitalization	319 days post 2nd Infusion	Yes	Severe (Grade 3)	Unrelated	Possible	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Diarrhoea	2004	Inpatient hospitalization	24 days post 1st Infusion	Yes	Severe (Grade 3)	Unrelated	Probable	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Gastrointestinal disorder	2005	Inpatient hospitalization	183 days post 2nd Infusion	Yes	Severe (Grade 3)	Unrelated	Probable	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Haematoma	2003	Prolongation of existing hospitalization	0 days post 2nd Infusion	No	Severe (Grade 3)	Definite	Unrelated	No treatment or modification of treatment required for AE	Resolved, no residual effects

Exhibit 227 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity *	SAE Related to Infusion Procedure/ Infusion of Islets **	SAE Related to Immunosuppression Therapy **	Treatment Required	Outcome
Haemoglobin decreased	2003	Life threatening + Prolongation of existing hospitalization	0 days post 2nd Infusion	No	Life threatening (Grade 4)	Probable	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Haemoglobin decreased	2004	Inpatient hospitalization	145 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Haemorrhagic stroke	2005	Death	750 days post 2nd Infusion	No	Fatal (Grade 5)	Unrelated	Unrelated	No treatment or modification of treatment required for AE	Death, related to AE
Haemothorax	2003	Prolongation of existing hospitalization	0 days post 2nd Infusion	No	Severe (Grade 3)	Probable	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Lung infiltration	2005	Inpatient hospitalization	781 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Neutropenia	2003	Life threatening	94 days post 1st Infusion	Yes	Life threatening (Grade 4)	Unrelated	Probable	No treatment or modification of treatment required for AE	Resolved, no residual effects
Neutropenia	2004	Life threatening	515 days post 1st Infusion	Yes	Life threatening (Grade 4)	Unrelated	Probable	Required additional treatment for AE	Persistent condition, Alive
Neutropenia	2004	Life threatening	581 days post 1st Infusion	Yes	Life threatening (Grade 4)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Neutropenia	2004	Life threatening	588 days post 1st Infusion	Yes	Life threatening (Grade 4)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects

Exhibit 227 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity*	SAE Related to Infusion Procedure/ Infusion of Islets**	SAE Related to Immunosuppression Therapy**	Treatment Required	Outcome
Neutropenia	2005	Inpatient hospitalization	77 days post 1st Infusion	Yes	Life threatening (Grade 4)	Unrelated	Probable	Required additional treatment and current treatment modified based on AE	Resolved, no residual effects
Neutropenia	2005	Life threatening	203 days post 2nd Infusion	Yes	Life threatening (Grade 4)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Pericardial effusion	2005	Inpatient hospitalization	351 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unlikely	Required additional treatment for AE	Resolved, no residual effects
Peritoneal haemorrhage	2001	Life threatening + Prolongation of existing hospitalization	0 days post 1st Infusion	Yes	Life threatening (Grade 4)	Definite	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Pneumonia	2005	Inpatient hospitalization	101 days post 1st Infusion	Yes	Life threatening (Grade 4)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Pneumonia	2006	Inpatient hospitalization	694 days post 1st Infusion	No	Mild (Grade 1) or Moderate (Grade 2)	Unrelated	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Portal vein thrombosis	2004	Inpatient hospitalization	35 days post 1st Infusion	No	Severe (Grade 3)	Probable	Unrelated	Required additional treatment for AE	Persistent condition, Alive
Right pleural effusion	2005	Prolongation of existing hospitalization	1 day post 2nd Infusion	Yes	Mild (Grade 1) or Moderate (Grade 2)	Probable	Unlikely	Incentive spirometry	Resolved, no residual effects

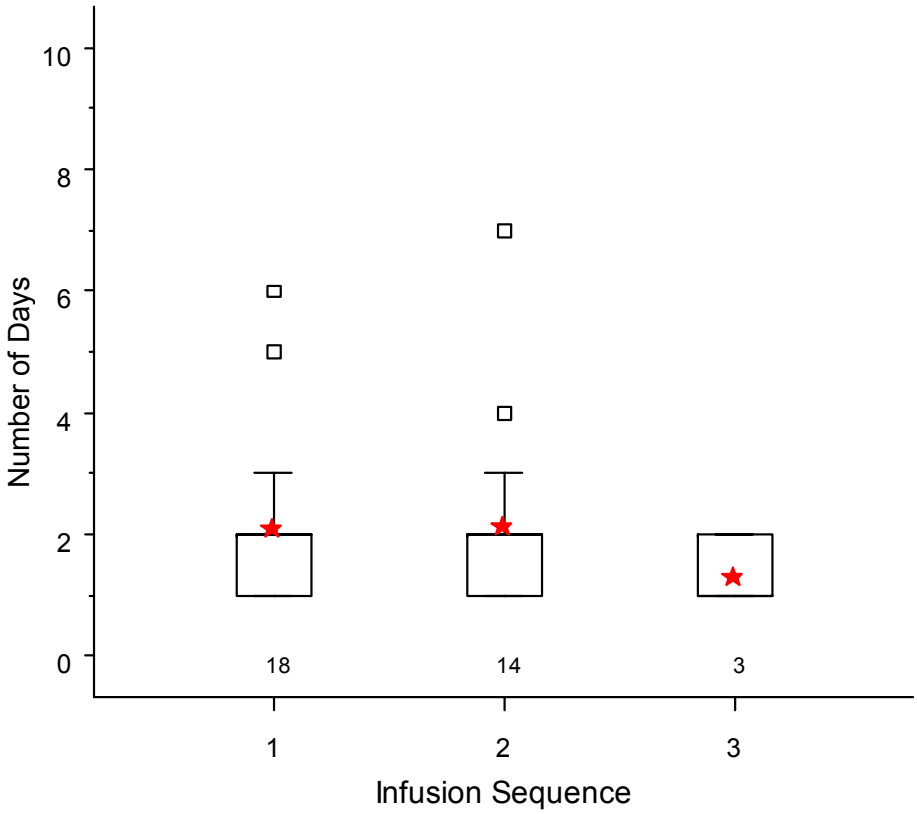
Exhibit 227 *(continued)*
All Serious Adverse Events (SAEs) Reported in Alphabetical Order

Serious Adverse Event (SAE)	SAE Year	Reason for Serious Adverse Event Classification	Timing	Expected	Severity*	SAE Related to Infusion Procedure/ Infusion of Islets**	SAE Related to Immunosuppression Therapy**	Treatment Required	Outcome
Rib fracture	2005	Inpatient hospitalization	53 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Squamous cell carcinoma of skin	2004	Life threatening	640 days post 1st Infusion	Yes	Severe (Grade 3)	Unrelated	Probable	Required additional treatment for AE	Resolved, no residual effects
Upper limb fracture	2004	Inpatient hospitalization	660 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Unrelated	Required additional treatment for AE	Resolved, no residual effects
Urinary tract infection	2004	Inpatient hospitalization	285 days post 2nd Infusion	No	Severe (Grade 3)	Unrelated	Possible	Required additional treatment for AE	Resolved, no residual effects

*Based on the Cancer Therapy Evaluation Program, Common Terminology Criteria For Adverse Events.
**Based on classification by local CITR Investigator.

Serious Adverse Event (SAE) name used in the first column is the preferred term from the MedDRA coding system.

Exhibit 228
Number of Days Hospitalized at Infusion (Admission to Discharge)
by Infusion Sequence



Serious Adverse Events which caused a prolongation of the inpatient hospitalization are summarized in Exhibit 226 and listed in Exhibit 229.

Exhibit 229
Hospitalizations Experienced Post Last Infusion
by Total Number of Infusions Received

	Total Infusions Received											
	1				2				3			
	Month 6		Year 1		Month 6		Year 1		Month 6		Year 1	
	N	%	N	%	N	%	N	%	N	%	N	%
Total	5	100.0	4	100.0	13	100.0	10	100.0	2	100.0	1	100.0
Participants Requiring at Least One Hospitalization	2	40.0	-	0.0	3	23.1	3	30.0	1	50.0	-	0.0
Number of Hospitalizations												
0	2	40.0	4	100.0	10	76.9	7	70.0	1	50.0	1	100.0
1	1	20.0	-	0.0	1	7.7	1	10.0	1	50.0	-	0.0
2	1	20.0	-	0.0	1	7.7	1	10.0	-	0.0	-	0.0
3	-	0.0	-	0.0	1	7.7	1	10.0	-	0.0	-	0.0
Missing	1	20.0	-	0.0	-	0.0	-	0.0	-	0.0	-	0.0

Exhibit 230
Changes in Portal Pressure (mmHg) and Infusion Summary by Infusion Sequence

	Infusion Sequence					
	1					
	N	Mean	SD	Median	Min	Max
Change in Portal Pressure from Pre Infusion to Peak Portal Pressure (mmHg)	16	3	1.4	2.0	0.0	5.0
Change in Portal Pressure from Pre to Post Infusion (mmHg)	19	1.4	2.0	2.0	-4.0	5.0
Islet Equivalents Infused	21	516,395	141,392	485,850	318,000	828,934
Islet Packed Cell Volume (mL)	16	3.8	1.7	5.0	1.0	6.0

	Infusion Sequence					
	2					
	N	Mean	SD	Median	Min	Max
Change in Portal Pressure from Pre Infusion to Peak Portal Pressure (mmHg)	14	1.6	1.4	2.0	0.0	5.0
Change in Portal Pressure from Pre to Post Infusion (mmHg)	16	0.3	2.2	0.0	-4.0	5.0
Islet Equivalents Infused	14	424,383	88,616	400,892	298,200	600,000
Islet Packed Cell Volume (mL)	11	3.4	1.5	3.5	1.0	5.0

	Infusion Sequence					
	3					
	N	Mean	SD	Median	Min	Max
Change in Portal Pressure from Pre Infusion to Peak Portal Pressure (mmHg)	2	1.0	1.4	1.0	0.0	2.0
Change in Portal Pressure from Pre to Post Infusion (mmHg)	3	2.3	3.2	1.0	0.0	6.0
Islet Equivalents Infused	1	492,708	-	492,708	492,708	492,708
Islet Packed Cell Volume (mL)	1	5.0	-	5.0	5.0	5.0

Section 4
Registry Data Quality Review

Registry Data Quality Review Summary

Data quality and assurance is an integral component of the Registry. Each islet transplant program that joins CITR and wishes to contribute data completes an application process that assures their compliance with current Good Clinical Practices (cGCP) and data integrity. In addition, each islet transplant center enters into an agreement with the CITR Coordinating Center indicating that they will submit data in a timely manner and respond to all queries and discrepancy reports. All centers are visited and trained periodically by CITR Coordinating Center staff. This training includes an initial detailed review of data collection forms, definitions, and CITR standards as well as timely and periodic training updates. Initial and continued training in data entry and navigation of the Internet based data collection system is conducted and monitored frequently.

Real time quality control and assurance programs and reports are implemented during data entry and monthly reports are generated and reviewed by the participating islet transplant centers. Each center is audited on-site with respect to their source documentation after three islet transplant recipients are entered in the CITR database. Subsequent data audits occur after an additional 10 recipients are registered or two years have passed since the last visit, whichever comes first.

Included in this section are summaries of the data collected and reported on for this Annual Report. Exhibit 231 is a summarization for all 227 participants and the number of CITR required forms that were submitted to the CITR Coordinating Center by the time of the final data lock on April 3, 2006. This summarization is separated by infusion sequence (1, 2 or 3) and an overall summary is provided. Submission form rates ranged from 89.7% (Induction Therapy Forms) to 99.3% (Pre Infusion Forms). The form submission rate of 100% for Infusion Forms is due to the fact that this was one of the criteria for closing the Annual Report analysis database (the participant had to have at least one Infusion Form submitted to be included in the analysis database).

Form submission for follow-up post the participant's first infusion procedure ranged from 87.9% at Month 6 to 79.9% at Year 1. Post the participant's last infusion procedure rates are similar for Month 6 (87.6%) and Year 1 (77.4%). However, the submitted forms for Year 2 drops to 46.4%, to 26.9% in Year 3 and only a quarter in Years 4 and 5 (Exhibit 232). The low submission rates for Years 2-5 are currently being reviewed by the CITR Scientific Advisory Committee and Compliance Committees.

A complete review of all local islet transplant protocols and patients were conducted to verify that all patients were approached to join the Registry and that there was not selective registration of participants for CITR. Source documents were reviewed and compared with data entered in the CITR database. Queries generated from the reviews included potential conflicts between source documentation and the CITR database, as well as errors that were identified on-site with data entry. In addition, the Registry sponsor reviews all audit reports.

Exhibit 231
Expected and Submitted Forms by Infusion Sequence
(All Participants, N=227)

	Infusion Sequence									Overall		
	1			2			3					
	Expected	Submitted	%	Expected	Submitted	%	Expected	Submitted	%	Expected	Submitted	%
Deceased Donor Forms	260	256	98.5	166	165	99.4	44	44	100.0	471	466	98.9
Islet Processing Forms	260	255	98.1	166	165	99.4	44	44	100.0	471	465	98.7
Pre Infusion Forms	227	226	99.6	161	159	98.6	39	39	100.0	428	425	99.3
Pre Infusion Lab Forms	227	224	98.7	161	158	98.1	39	39	100.0	428	422	98.6
Infusion Forms	227	227	100.0	161	161	100.0	39	39	100.0	428	428	100.0
Induction Therapy Forms	227	221	97.4	161	124	77.0	39	38	97.4	428	384	89.7

Exhibit 232
Expected and Submitted Follow-Up Forms Post Last Infusion

	Participant Follow Up Forms		
	Expected	Submitted	%
Post First Infusion			
Month 6	223	196	87.9
Year 1	204	163	79.9
Post Last Infusion			
Month 6	217	190	87.6
Year 1	186	144	77.4
Year 2	138	64	46.4
Year 3	98	29	29.6
Year 4	45	11	24.4
Year 5	16	4	25.0

Exhibit 233
Extent of Follow-Up Post Last Infusion
(All Participants, N=227)

	Extent of Participant Follow-Up Months Post Last Infusion					
	N	Mean	SD	Median	Min	Max
Follow Up Forms	227	15.3	12.9	12.0	1.0	60.0
Insulin Log Completion	227	19.7	17.1	12.1	0.0	72.0

Exhibit 234
Summary of All Participants Reported as Lost to CITR Follow-Up

Random Participant ID	Time Participant Reported Lost to CITR Follow-Up Post Last Infusion (months)
1	48.0
2	11.9
3	24.6
4	13.5
5	25.8
6	32.7
7	16.2
8	14.9
9	17.3
10	17.3
11	25.2
12	28.3
13	18.9
14	30.6
15	17.8
16	24.0
17	12.9
18	6.4
19	24.0
20	6.0
21	7.8
22	31.5
23	6.1
24	6.9
25	1.5
26	15.6
27	14.8

For the 27 participants reported as lost to follow-up, the average time post their last infusion procedure was 18.5 months.

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