The Company

A. Overview

Beta Bionics, Inc. ("Company") is a development stage biotechnology company developing a bionic pancreas system called the iLet™, a revolutionary fully integrated and wearable bionic pancreas medical device platform that automatically and autonomously manages blood sugar levels in people with type 1 insulin-dependent diabetes (T1D) 24/7, and thus reduces the burden and cost of diabetes care. Good, consistent management of blood sugar levels in people with T1D is essential to preventing and minimizing health complications but consistent management is oppressive – requiring the kind of vigilance that is unsustainable and impossible for many. What makes it different from all other diabetes medical devices that have come before it is that the iLet offers a holistic, fully automated systems approach to glycemic control, rather than just providing a component technology that addresses only one part of the glycemic control challenge (e.g. insulin infusion, glucose sensing, therapeutic dosing decisions, etc.).

The iLet integrates: (1) a glucose-sensing device that automatically and frequently estimates blood sugar levels; (2) decision software that automatically determines therapeutic dosing requirements; and (3) a single-hormone and dual-hormone configuration that automatically delivers insulin to lower blood sugar levels and glucagon (in the case of the dual-hormone system) to raise blood sugar levels. The iLet is designed to solve the four greatest concerns of T1D management: (1) it reduces mean glycemia in nearly everyone to levels that would meet or exceed the American Diabetes Association's goal for therapy, and would likely nearly eradicate long-term microvascular and neurological complications if implemented at the time of diagnosis; (2) it profoundly curtails mild hypoglycemia in everyone, and we expect it to dramatically reduce the risk of severe hypoglycemia; (3) it automates glycemic management, thus unburdening people with T1D of the relentless need to comply with therapy, as the bionic pancreas itself is the first technology to be entirely compliant with the patient's needs rather than the other way around; and (4) it unburdens people with T1D and their families of the emotional hardship that is, for now, part of everyday life, and of the constant fear of hypoglycemia, and of the worry and dread of long-term complications. A device that solves any one of these concerns would be groundbreaking; a device that simultaneously solves all four is without precedent and truly game changing.

No Basal. No Bolus. Just Be
… Be Bionic!©

Not only is our[1] technology innovative, but so too is our corporate structure. Our Company was formed on October 21, 2015 as a Massachusetts public benefit corporation, which is a relatively new corporate structure that allows, and, in fact, obliges, private companies to consider general and specific public benefit in its management decisions, in addition to considering the traditional corporate goals of maximizing profit for shareholders.

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[1] Unless otherwise indicated, we use "the Company," "Issuer," "we," "our" and "us" in Form C refer to the businesses of Beta Bionics, Inc.

Our bylaws establish the following four principles to guide us in the specific public benefit of improving human health for the T1D community:

1. To provide and to protect our turnkey solutions for safe and effective autonomous glycemic control;
2. To bring our technology to as many people with T1D as possible in an expeditious and responsible manner;
3. To continue to innovate and to offer the latest advances as expeditiously and responsibly as possible; and
4. To act in the best possible interest of the T1D community in connection with fulfilling our functions.

Since our incorporation, our primary activities have been the development of our business plan, negotiating strategic alliances and other agreements, and raising capital. In the first two-and-a-half months of our existence, we successfully negotiated and licensed the intellectual property related to the bionic pancreas technology from Boston University. Additionally, we successfully negotiated and secured an initial round of investment in the amount of $5,000,000.00 with Eli Lilly & Company to capitalize Beta Bionics and position itself to begin operations in 2016.

These foundational steps allow the Company to ultimately seek regulatory approval and, if achieved, commercialize the iLet. Information related to the iLet is preliminary and investigative. The iLet is not yet approved by the U.S. Food and Drug Administration (FDA). Regulatory approval of the iLet is critical to our success and ensuring that we meet our public benefit mission. To date, we have not generated any revenues from our operations and do not expect to do so in the near future.

B. Labor of Love

Dr. Edward R. Damiano, a Boston University professor of biomedical engineering, and senior research scientist Firas El-Khatib (at that time a student working with Ed in his lab) began their quest to develop a portable bionic pancreas not long after Ed's son, David, was diagnosed with T1D as an infant by his wife, Toby – a pediatrician. Managing David's blood sugar perfectly proved impossible, and the consequences of not being perfect can be extremely dangerous, and even acutely life threatening. Despite meticulous attention to detail, it was clear that David, himself, changed from day to day and even hour to hour, such that decisions made under seemingly identical circumstances the day before would have different outcomes the next day. The child grows, comes down sick, feels content or anxious, eats all of his food or doesn't, has a different mix of carbs, fats, and proteins in one meal compared to another, plays hard that day or doesn't, or the dose of insulin given is off by just a little bit. The result is a child who is fine, or hypoglycemic, combative or helpless, or hyperglycemic and heading to a lifetime of disability, including blindness, organ failure, and amputations. Furthermore, there is a tremendous amount of biological activity and hormonal variability from night to night, making blood sugar control a 24-hour-a-day, seven-day-a-week task.

Convinced that there should be a better solution to the management of insulin-dependent diabetes, Ed and his team embarked upon a journey to unburden himself, his son and so many parents, children and adults living with the burden of diabetes.

Recently, Ed was joined by another set of parents experiencing the similar challenges of caring for a child with diabetes. Another dad, also by the name of Ed, and his wife Serafina (two California based attorneys) experienced the familiar psychological trauma of having their seven-year-old son, Max, diagnosed with T1D in 2013. Ed and Serafina Raskin were initially volunteers with the bionic pancreas project, providing *pro bono* legal advice to the project through 2015. Then, in 2015, the Raskins formally joined the Company from inception. Serafina serves as the Company's General Counsel and Secretary and Ed serves on the Board of Directors as well as in the Benefit Officer function – ensuring that corporate strategy, management decisions and daily functions are designed and executed to maximize benefits to the T1D community.

Together with Jeff Hitchcock – the Company's Benefit Director – founder of Children with Diabetes and dad to adult daughter, Marissa (diagnosed in 1989), the Company is run by people with "skin in the game". While Gibb Clarke, the Company's Chief Operating and Financial Officer is not the parent of a child with T1D, he is a serial medical device entrepreneur. He also personally knew Ed and Serafina's son, Max, both before and after diagnosis. Gibb was deeply moved by how difficult and life changing Max's diagnosis was for the entire family, which motivated him to volunteer alongside Ed and Serafina beginning in 2015 and formally join the Company in 2016.

Ultimately, the entire team at Beta Bionics is deeply motivated to bring the iLet to someone they love and care for. It is a labor of love for all of us. We are building this for the T1D community – a community to which we all belong.

C. Market

Diabetes is a chronic, life-threatening disease for which there is no known cure. Diabetes is caused by the body's inability to produce or effectively utilize insulin, a life-sustaining hormone, to regulate the body's glucose levels.

In people with diabetes, blood glucose levels fluctuate from extremely high levels, a condition known as hyperglycemia, which is caused by too little insulin, to extremely low levels, a condition called hypoglycemia, which is caused by too much insulin.

Hyperglycemia may cause the individual with diabetes to feel thirsty or confused, but it can also be insidious and not noticed at all. However, it is not benign and over years, hyperglycemia causes devastating damage to the body, including damaging small blood vessels which leads to blindness, nerve damage and kidney failure, and also damaging larger blood vessels, which leads to coronary artery disease, stroke, heart attack, poor wound healing and amputation of the distal extremities. In its most severe form, hyperglycemia with ketosis (diabetic ketoacidosis) will cause death in a matter of hours to days without intervention. Medical management of acute DKA is itself risky, and deaths can occur from acute shifts in electrolytes and fluids.

All of this can be avoided by giving insulin, but the problem is that too much insulin leads to hypoglycemia, which causes confusion, combative irrational behavior, shakiness, feeling of extreme stress due to catecholamine release, loss of mental acuity, unconsciousness, seizure, coma and death.

The current state of the art for diabetes management has not proven adequate to balance the dangers of hyper- and hypoglycemia, although millions of people are compelled to try, day in and day out, with varying degrees of success.

We are profoundly grateful for the tools we do have, because without them our loved ones might not be alive today. However, soon we will all be able to do much better with less work and worry, with the iLet.

There are two main types of diabetes: type 1 (T1D) and type 2 (T2D).

- T1D is caused by an autoimmune response in which the body attacks and destroys the insulin-producing cells in the pancreas, called beta cells—hence the "Beta" in the name of our company. As a result, the pancreas' ability to produce insulin is almost entirely destroyed. T1D is most commonly diagnosed during childhood or adolescence, but adults may also develop T1D. According to estimates, between 1.5 and as many as 3 million Americans may have type 1 diabetes.

- T2D is caused by increasing resistance to the insulin produced by the beta cells. T2D has been most commonly thought of as a disease of middle and advanced age, but it is increasingly prevalent in children and adolescents. Over 29 million Americans have T2D (9.3% of the population) and 14% of those individuals need insulin.

D. Current Treatment Options

Currently, there is no system that automatically makes therapeutic decisions to administer insulin (or insulin and glucagon) in response to a continuous signal from a continuous glucose monitor ("CGM") has been FDA-approved or is commercially available. The current state-of-the-art in the management of T1D includes:

- The regular use of hand-held, in vitro blood glucose meters (BGM). These meters are capable of measuring the glucose concentration of small blood samples (~ 0.3-5 μl) in 5-30 seconds; the capillary blood sample is obtained by pricking the skin with a lancet.

- The use of rapid-acting human insulin analogs that can be adjusted to compensate for meals rather than making meal adjustments to match the insulin taken hours earlier, and, finally,

- Insulin pumps that can continuously deliver subcutaneous insulin at an infusion rate to suit metabolic insulin requirements, and by microburst infusion of insulin to treat carbohydrates consumed through user commanded dosing.

Although the key to managing diabetes is to maintain tight control of blood glucose levels, in practice, the management of T1D is extremely challenging, requiring perpetual vigilance and intervention with insulin or carbohydrates. Without a doubt, the iLet's automated insulin and glucagon administration would materially reduce the burden associated with managing the disease.

E. More About the iLet

The iLet is a wearable stand-alone Class III medical device intended to provide ambulatory autonomous care for insulin-dependent diabetes. The iLet consists of:

1. an integrated dual-chamber pump capable of delivering insulin alone or insulin and glucagon at microprecise doses and an integrated touchscreen user interface;
2. an integrated CGM;
3. a clinically tested suite of mathematical control algorithms that autonomously determine and command doses of insulin or glucagon based on CGM glucose data; and
4. a custom dual-cannula infusion set.

The iLet requires only the patient's weight for initialization and then autonomously adapts in real-time to changes in an individual's basal metabolic insulin need, acute (e.g. circadian hormonal fluctuations, intercurrent illness, physical activity, or emotional state), or gradual (e.g. hormonal changes that occur during puberty or menopause). Our adaptive meal dose controller eliminates the need for the user to set or know their "carbohydrate-to-insulin ratios", as it makes automatic adjustments based on dosing history for similar past meal announcements, and customizes its doses to the individual and time of day. The bihormonal configuration of our iLet also includes a proportional-derivative algorithm (based on the glucose level and rate of descent) governing subcutaneous micro-doses of glucagon to help prevent or reduce hypoglycemia beyond the capability of our insulin-only configuration.

Taken together, these mathematical algorithms provide a universal framework for a glycemic control strategy that requires no quantitative input from, or participation by, the user (besides entering body weight to initialize the iLet), but which automatically adapts insulin and glucagon dosing to meet each individual's needs. Another challenge we overcame is enabling our iLet to remain autonomous in managing insulin and glucagon delivery even when the CGM is offline by: (1) invoking the latest high-resolution "basal rate profile" it had converged upon when the CGM was online, (2) responding to meal announcements the same way, and (3) automatically responding to user-entered BG values by issuing a correction dose of insulin (or glucagon) based on its latest determination of the user's needs. Thus, our iLet never relies on, nor burdens the user, with determining subjective dosing decisions, which inevitably vary in quality and reliability over time or among different users. Indeed, our iLet provides a turnkey solution for people with T1D that

comprehensively manages glycemia across a broad range of individual needs and a large spectrum of circumstances and challenges.

In summary, the iLet's technology is pioneering because it:

- It is initialized only with the patient's body mass and comes online immediately with no run-in period;
- It provides a truly turnkey solution for both children and adults with T1D, and is able to cope with a wide range of insulin needs across all age groups.
- It uses no more insulin than under usual care, but distributes insulin doses more efficiently and optimally than under usual care, and thus dramatically improves mean glycemia and reduces hypoglycemia.
- It is designed to specifically refrain from stacking and overdosing insulin.
- It is completely autonomous in determining all dose deliveries, sparing the user to ever have to determine or set their so-called "basal-rate profiles", "correction factors", or "insulin-to-carbohydrate ratios".
- It continuously updates and stores a high-resolution "basal-rate" profile for insulin delivery (288 basal rate segments per day), which it dynamically adapts when the CGM is online, and automatically invokes when the CGM is offline.
- It autonomously doses insulin or glucagon for high or low glucose levels when the CGM is online and automatically corrects as necessary by dosing insulin or glucagon in response to user-entered BG values when the CGM is offline.
- It allows optional user-initiated (but system-calculated) meal-priming insulin doses, which adapt autonomously to user requirements and time of day (separately for "breakfast", "lunch", and "dinner" meals).
- It automatically shuts off insulin dosing, based on the glucose level and its trend, to prevent hypoglycemia.
- It allows the user to run a system-optimized dynamic glucose target or to set a permanent glucose target, or to temporarily raise the glucose target for added safety during activities such as exercising, driving, etc.
- It allows the user to trigger a (system-calculated) glucagon microburst dose, as an added safety measure prior to temporarily disconnecting from the BP, such as for showering, swimming, etc.
- It has been tested in C-peptide-negative as well as C-peptide-positive subjects in the outpatient setting.
- It has been tested under free-living conditions and without restrictions on exercise or other activities.

F. Licenses, Patents and Proprietary Rights

We have exclusive, worldwide sub-licensable licenses from the Trustee's of Boston University ("BU") to a portfolio of U.S. and international patents (both issued and pending) and a trademark that relate to iLet.

Under the terms of the licensing agreements, we are responsible for specified milestone and maintenance payments, as well as royalty payments on net sales once commercialized. We also

have the right to sublicense our rights under the license agreements but are required to pay a percentage of any sublicense income.

Additionally, under the terms of the licensing agreements, we must develop, manufacture, sell and market the technology pursuant to specified milestones and time schedule. In the event we fail to meet the milestones, BU is entitled to terminate the licensing agreements with prior written notice, provided we do not cure the breach. Upon termination, the intellectual property under the licenses would revert back to BU.

We believe that proprietary protection of our technologies is critical to the development of our business. Our intellectual property strategy includes protecting existing, and further developing, proprietary technology for the sourcing, scale up, and manufacturing of the iLet. This strategy includes expanding on technologies in-licensed to us as well as in-licensing additional technologies through collaborations with universities and biotech companies.

We rely upon trade-secret protection for certain confidential and proprietary information and take active measures to control access to that information. There is also substantial proprietary know-how surrounding the iLet development and manufacturing processes that remains a trade secret. We currently have confidentiality and non-disclosure agreements with all of our employees, consultants, vendors, advisory board members and contract research organizations.

G. Our Commitment to Good Business Practices and Our Public Benefit Mission

We benefit the public by providing education, support and eventually the bionic pancreas technology to alleviate the burdens of T1D management. We believe our status as a public benefit corporation, commitment to our public benefit mission, and focus on transparency, makes all the difference in the way we do business. We believe this will result in a healthier and happier T1D community.

Shortly upon incorporation, we selected B Lab (www.bcorporation.net), a non-profit organization that certifies benefit corporations via its B Impact Assessment and B Analytics to measure and manage positive impact. B Lab is the most widely recognized and rigorous third party standard for certifying and measuring corporate public benefit and sustainability performance.

We are working diligently to build a B Corporation-compliant enterprise that will excel according to the B Corporation Impact Assessment. Where other companies may focus only on return on investment, we are committed both to our shareholders and to the T1D community and will work diligently to ensure that the bionic pancreas technology is protected and available for your benefit. Beta Bionics is actively involved in the T1D community and is partnering with like-minded educational institutions, not-for-profit entities and socially minded companies to educate the public about T1D management and our bionic pancreas technology.

Our leadership strives to be ever mindful that it was founded by parents deeply affected by T1D to help not only their children, but all children and adults struggling to live with T1D and their loved ones who support them.

H. Performance of the Bionic Pancreas System in Trials

The bionic pancreas technology has been rigorously tested in inpatient and real-world outpatient and home-use studies in subjects with T1D in both the insulin-only and bihormonal configurations. The technology has evolved over the years from a laptop-driven system, to the first wearable iPhone-driven platform, to our current highly compact, fully integrated, mobile iLet.

A nine-year collaboration between Boston University (BU) and the Massachusetts General Hospital (MGH), resulted in 3 inpatient studies testing a laptop version of the bihormonal bionic pancreas in adults and adolescents with T1D in the clinical research center at MGH.

The iPhone version of the bihormonal bionic pancreas has also been tested in 4 outpatient studies. Although still somewhat cumbersome, the iPhone system was a mobile platform that could be tested in home-use environments, afforded unrestricted subject activity, and allowed for longer-duration experiments than was previously possible.

In 2013, the iPhone system was tested in five-day experiments in 20 adults with T1D in downtown Boston (the Beacon Hill Study). The Summer 2013 and 2014 studies, compared the iPhone system with insulin pump therapy in 5-day experiments in 51 children 6 to 20 years old with T1D at Camp Joslin and the Clara Barton Camp in central Massachusetts (the 2013 and 2014 Summer Camp Studies).

A collaboration between MGH, the University of Massachusetts Medical Center, Stanford University, and the University of North Carolina, Chapel Hill, resulted in the Bionic Pancreas Multicenter Study between 2014 and 2015, and compared the iPhone system with insulin pump therapy in a home-use study in 39 adults with T1D who used the device for 11 days at work and at home.

The mean CGM glucose levels obtained by the bihormonal bionic pancreas from the 2013 and 2014 Summer Camp Studies and the Bionic Pancreas Multicenter Study, were 141 ± 10 mg/dl in adults, 142 ± 12 mg/dl, in adolescents, and 137 ± 11 mg/dl in pre-adolescents. Based on these mean CGM glucose levels, we are able to project what the bionic pancreas is capable of achieving in terms of HbA1c in the three populations of ~ 6.5 ± 0.4%.

It is important to note that the bionic pancreas was able to achieve mean CGM glucose levels below the American Diabetes Association (ADA) goal for therapy in all three populations in nearly all subjects tested while simultaneously eliminating almost all hypoglycemia. On the bionic pancreas, CGM glucose levels fell below 60 mg/dl only 0.6% of the time in adults and 1.2–1.3% of the time in adolescents and pre-adolescents in a summer camp setting.

Our clinical collaborators at Stanford and at MGH have also conducted two home-use outpatient studies testing the iPhone-based bionic pancreas system in the insulin-only configuration and targeting different glycemic set-points. In the study conducted by the Stanford team, 16 adults with T1D compared the bionic pancreas in the insulin-only configuration with insulin pump therapy in one-week experiments at work and at home (with a glucose target of 130 mg/dl). In the study conducted by the MGH team, 20 adults with T1D compared our bionic pancreas in the insulin-

only configuration at a set-point of 130 mg/dl, with the bionic pancreas in the bihormonal configuration at glucose set-points of 100, 115, and 130 mg/dl, and with insulin pump therapy in 3-day experiments at work and at home.

The mean CGM glucose levels obtained by the insulin-only bionic pancreas with a glycemic set-point of 130 mg/dl was 161 ± 9 mg/dl in the Stanford Insulin-only Study and 160 ± 17 mg/dl in our MGH Set-Point Study, with CGM glucose levels falling below 60 mg/dl only 0.9% and 0.8% of the time, respectively. Based on these mean CGM glucose levels, we project that our insulin-only bionic pancreas would achieve an HbA1c in adults of 7.2 ± 0.5%, while simultaneously limiting CGM glucose levels below 60 mg/dl to less than 1% of the time.

Thus, we project that the insulin-only configuration of our bionic pancreas would result in HbA1c levels of ~ 7.3%. The bionic pancreas in the bihormonal configuration would obtain HbA1c of ~ 6.5%, which would effectively eradicate all long-term complications of T1D.

The academic team has also tested the first generation of our fully integrated iLet bionic pancreas in diabetic swine. Notably, results of the swine study showed no difference in the performance of our previous-generation iPhone-based bionic pancreas platform relative our iLet platform.

Despite challenging conditions, and no restrictions on diet, exercise and activity, the previous generations of the bionic pancreas technology have simultaneously lowered mean glucose and reduced hypoglycemia relative to comparator groups and demonstrated that the current iteration of the technology is ready to withstand the rigors of a Pivotal Trial.

I. Published Data related to the Bionic Pancreas Technology

For purposes of non-scientific summary, the following clinical data has been published by the academic team according to peer-review standards in the following highly regarded journals:

- The Lancet Diabetes and Endocrinology, 2016:
    - Background: The safety and efficacy of continuous, multiday, automated glycemic management has not been tested in outpatient studies of pre-adolescent children with type 1 diabetes. We aimed to compare the safety and efficacy of a bihormonal bionic pancreas versus conventional insulin pump therapy in this population of patients in an outpatient setting.
    - Methods: In this randomized, open-label, crossover study, we enrolled pre-adolescent children (aged 6–11 years) with type 1 diabetes (diagnosed for ≥1 year) who were on insulin pump therapy, from two diabetes camps in the USA. With the use of sealed envelopes, participants were randomly assigned in blocks of two to either 5 days with the bionic pancreas or conventional insulin pump therapy (control) as the first intervention, followed by a 3 day washout period and then 5 days with the other intervention. Study allocation was not masked. The autonomously adaptive algorithm of the bionic pancreas received data from a continuous glucose monitoring (CGM) device to control subcutaneous delivery of insulin and glucagon. Conventional insulin pump therapy was administered by the

camp physicians and other clinical staff in accordance with their established protocols; participants also wore a CGM device during the control period. The coprimary outcomes, analyzed by intention to treat, were mean CGM-measured glucose concentration and the proportion of time with a CGM-measured glucose concentration below 3.3 mmol/L, on days 2–5. This study is registered with ClinicalTrials.gov, number NCT02105324.

- Results: Between July 20, and Aug 19, 2014, 19 children with a mean age of 9.8 years (SD 1.6) participated in and completed the study. The bionic pancreas period was associated with a lower mean CGM-measured glucose concentration on days 2–5 than was the control period (7.6 mmol/L [SD 0.6] *vs* 9.3 mmol/L [1.7]; p=0.00037) and a lower proportion of time with a CGM-measured glucose concentration below 3.3 mmol/L on days 2–5 (1.2% [SD 1.1] *vs* 2.8% [1.2]; p<0.0001). The median number of carbohydrate interventions given per participant for hypoglycemia on days 1–5 (ie, glucose <3.9 mmol/L) was lower during the bionic pancreas period than during the control period (three [range 0–8] *vs* five [0–14]; p=0.037). No episodes of severe hypoglycemia were recorded. Medium-to-large concentrations of ketones (range 0.6–3.6 mmol/dL) were reported on seven occasions in five participants during the control period and on no occasion during the bionic pancreas period (p=0.063).

- The New England Journal of Medicine, 2014:
  - Background**:** The safety and effectiveness of automated glycemic management have not been tested in multiday studies under unrestricted outpatient conditions.
  - Methods**:** In two random-order, crossover studies with similar but distinct designs, we compared glycemic control with a wearable, bihormonal, automated, "bionic" pancreas (bionic-pancreas period) with glycemic control with an insulin pump (control period) for 5 days in 20 adults and 32 adolescents with type 1 diabetes mellitus. The automatically adaptive algorithm of the bionic pancreas received data from a continuous glucose monitor to control subcutaneous delivery of insulin and glucagon.
  - Results: Among the adults, the mean plasma glucose level over the 5-day bionic-pancreas period was 138 mg per deciliter (7.7 mmol per liter), and the mean percentage of time with a low glucose level (<70 mg per deciliter [3.9 mmol per liter]) was 4.8%. After 1 day of automatic adaptation by the bionic pancreas, the mean (±SD) glucose level on continuous monitoring was lower than the mean level during the control period (133±13 vs. 159±30 mg per deciliter [7.4±0.7 vs. 8.8±1.7 mmol per liter], P<0.001) and the percentage of time with a low glucose reading was lower (4.1% vs. 7.3%, P=0.01). Among the adolescents, the mean plasma glucose level was also lower during the bionic-pancreas period than during the control period (138±18 vs. 157±27 mg per deciliter [7.7±1.0 vs. 8.7±1.5 mmol per liter], P=0.004), but the percentage of time with a low plasma glucose reading was similar during the two periods (6.1% and 7.6%, respectively; P=0.23). The mean frequency of interventions for hypoglycemia among the adolescents

was lower during the bionic-pancreas period than during the control period (one per 1.6 days vs. one per 0.8 days, P<0.001).

- Journal of Clinical Endocrinology and Metabolism, 2014:
  - Background**:** The objectives of the study were to test the ability of a third-generation bihormonal bionic pancreas algorithm, initialized with only subject weight, to adapt automatically to the different insulin needs of adults and adolescents, and to evaluate the impact of optional, automatically adaptive meal-priming boluses.
  - Methods: This was a randomized controlled trial, conducted at an inpatient clinical research center with twelve adults and twelve adolescents with T1D. Subjects in each age group were randomized to automated glycemic control for 48 hours with or without automatically adaptive meal-priming boluses.
  - Results: The 48-hour mean PG values with and without adaptive meal-priming boluses were 132.9 vs 146.9 mg/dL (*P* .03) in adults and 162.6 vs 175.9 mg/dL (*P* .01) in adolescents. Adaptive meal-priming boluses improved mean PG without increasing time spent with PG less than 60 mg/dL: 1.4% vs 2.3% (*P* .6) in adults and 0.1% vs 0.1% (*P* 1.0) in adolescents. Large increases in adaptive meal-priming boluses and shifts in the timing and size of automatic insulin doses occurred in adolescents. Much less adaptation occurred in adults. There was nearly a 4-fold variation in the total daily insulin dose across all cohorts (0.36 –1.41 U/kg/d).

- Diabetes Care, 2012:
  - Background: To test whether safe and effective glycemic control could be achieved in type 1 diabetes using a bihormonal bionic endocrine pancreas driven by a continuous glucose monitor in experiments lasting more than two days and including six high-carbohydrate meals and exercise as challenges to glycemic control.
  - Methods: Six subjects with type 1 diabetes and no endogenous insulin secretion participated in two 51-h experiments. Blood glucose was managed with a bionic endocrine pancreas controlling subcutaneous delivery of insulin and glucagon with insulin pumps. A partial meal-priming bolus of insulin (0.035 units/kg/meal, then 0.05 units/kg/meal in repeat experiments) was administered at the beginning of each meal (on average 78 ± 12 g of carbohydrates per meal were consumed). Plasma glucose (PG) control was evaluated with a reference quality measurement on venous blood every 15 min.
  - Results: The overall mean PG was 158 mg/dL, with 68% of PG values in the range of 70–180 mg/dL. There were no significant differences in mean PG between larger and smaller meal-priming bolus experiments. Hypoglycemia (PG,70 mg/dL) was rare, with eight incidents during 576-h of closed-loop control (0.7% of total time). During 192-h of nighttime control, mean PG was 123 mg/dL, with 93% of PG values in the range of

70–180 mg/dL and only one episode of mild hypoglycemia (minimum PG 62 mg/dL).

- Science Translational Medicine, 2010
  - Background: Automated control of blood glucose (BG) concentration is a long-sought goal for type 1 diabetes therapy. We have developed a closed-loop control system that uses frequent measurements of BG concentration along with subcutaneous delivery of both the fast-acting insulin analog lispro and glucagon (to imitate normal physiology) as directed by a computer algorithm. The algorithm responded only to BG concentrations and incorporated a pharmacokinetic model for lispro.
  - Methods: Eleven subjects with type 1 diabetes and no endogenous insulin secretion were studied in 27-hour experiments, which included three carbohydrate-rich meals.
  - Results: In six subjects, the closed- loop system achieved a mean BG concentration of 140 mg/dl, which is below the mean BG concentration target of <_154 mg/dl recommended by the American Diabetes Association. There were no instances of treatment- requiring hypoglycemia. Five other subjects exhibited hypoglycemia that required treatment; however, these individuals had slower lispro absorption kinetics than the six subjects that did not become hypoglycemic. The time-to-peak plasma lispro concentrations of subjects that exhibited hypoglycemia ranged from 71 to 191 min (mean, 117 ± 48 min) versus 56 to 72 min (mean, 64 ± 6 min) in the group that did not become hypoglycemic (aggregate mean of 84 min versus 31 min longer than the algorithm's assumption of 33 min, P = 0.07). In an additional set of experiments, adjustment of the algorithm's pharmacokinetic parameters (time-to-peak plasma lispro concentration set to 65 min) prevented hypoglycemia in both groups while achieving an aggregate mean BG concentration of 164 mg/dl. These results demonstrate the feasibility of safe BG control by a bihormonal artificial endocrine pancreas.

In addition to the above, the academic bionic pancreas team has published multiple additional manuscripts on their pre-clinical studies, commentaries and other manuscripts related to blood glucose control and continuous glucose monitoring studies. Clinical data related to bionic pancreas multi-center study, during which subjects wore the system from eleven days to three weeks has been collected but not yet formally published. The data collected from those studies continues to show that the bionic pancreas system effectively lowers mean average blood glucose while simultaneously reducing hypoglycemia and substantially eases the psychological burdens of managing T1D.

All prior published clinical data is available online at:
http://sites.bu.edu/bionicpancreas/publications-2/.

J. The Pivotal Trial and Development Status

Our goal is to work with our clinical teams to initialize the Bionic Pancreas Pivotal Trial ("Pivotal Trial"), in the 2nd Quarter of 2017. Final trial design protocol is subject to change and is not in final format. However, as currently configured, we plan to enroll at least 600 subjects with T1D (initially in ages 13 and older with HbA1c levels of less than 11%, and later extending to infants) to test and qualify the iLet and to provide all of the clinical data necessary for a pre-market approval (PMA) application to the FDA for both the insulin-only and bihormonal configurations of the device.

We propose to achieve this objective with the following two specific aims:

1. to conduct the insulin-only arm, which we expect to take up to 9 months to complete, to test the safety and efficacy of the iLet in controlling glycemia in the insulin-only configuration and to evaluate the behavioral and psychosocial impact of the insulin-only configuration of the iLet relative to usual care,
2. to conduct the bihormonal arm, which we expect to take 12 months or more to complete, to test the safety and efficacy of the iLet in controlling glycemia in the bihormonal configuration, to evaluate the behavioral and psychosocial impact of the bihormonal configuration of the iLet relative to usual care, and to provide all safety data necessary and sufficient for a new chronic use indication for glucagon in this device.

Our ability to commence the pivotal trial in the 2nd Quarter of 2017 depends on securing FDA and IRB approvals for the trial and securing necessary funding, as well as completing shorter bridging studies to demonstrate feasibility of the fully integrated iLet to autonomously control blood glucose.

Our existing resources are not adequate to permit us to ensure that the pivotal trial is completed. In addition to one or more additional financings and grants, a funding request submitted through BU to the National Institute of Health, if funded, is expected to cover substantially all,current projected costs of running the Pivotal Trial. We are continuing to explore potential opportunities and alternatives to obtain additional resources that may be necessary to complete the planned pivotal trial and to support our operations in the interim time-frame. These opportunities and alternatives may include partnering arrangements with biotech or pharmaceutical companies. There can be no assurance that we will secure any grants, or that any such financings or partnering arrangements can be consummated on acceptable terms, if at all.

The pivotal trial we have designed will provide the essential clinical data necessary for a PMA submission for the iLet – a technology that will forever change the way in which T1D is managed and the effectiveness with which that care can be delivered. However, the true strength and promise of the grant application we now have in front of the NIH is found in the power of our technology, in the innovation that inspired it, in the strength of our clinical data, in the expertise of our national multi-center consortium, and in our commitment and dedication to bringing our solution to those suffering from T1D as expeditiously and responsibly as is possible.

K. Organizational History

We are a development-stage company and have a limited operating history. To date, we have not generated any commercial revenues from operations. As we continue to execute our business plan, we expect our development and operating expenses to increase substantially.

L. Manufacturing of the iLet

We do not have manufacturing facilities adequate to produce the iLet within Beta Bionics. We currently rely, and expect to continue to rely, on third-party contract manufacturers for the manufacture of the iLet. The iLet, is being built and manufactured as a Class III medical device by an FDA-registered ISO 13485 third-party contract manufacturing facility. The dual-cannula infusion set is being built and manufactured by a third-party facility that is fully compliant with relevant CFR 21, cGMP, ISO manufacturing protocols, and FDA standards. Eventually, we may decide to establish in-house manufacturing capabilities.

M. Sales and Marketing

We may choose to partner with large biotech or pharmaceutical companies for sales and marketing, if and when applicable, or alternatively develop our own sales force to market the iLet both inside and outside of the U.S. If we obtain CE Mark for the iLet, we anticipate initiating sales in the European market as well.

N. Collaboration Arrangements

From time to time we will enter into collaborative research agreements with academic and research institutions, including BU, to enhance our research and development capabilities. Typically, in industry, such agreements provide the industry partner with rights to license the intellectual property created through such collaborations. We may also enter into collaborative research agreements with other pharmaceutical companies when we believe such collaboration will support the development and commercialization of our technology.

O. Sublicenses to Third Parties

We currently do not have any sublicenses with third parties but we may, in the future decide to grant sublicenses for certain applications of our technologies.

P. Future Products/Indications for Use

Eventually, we may decide to seek an indication for use in T2D who require daily insulin therapy. There is also a potential for in-hospital use of our technology.

Q. Research and Development Expenditures

We have budgeted $3,788,00 in FY 2016 for research and development activities, not including direct labor costs.

R. Hiring of Additional Employees and Consultants

We intend to hire additional staff and to engage consultants in compliance, investor and public relations, and general administration. We also intend to engage experts in healthcare and in general business to advise us in various capacities.

S. Other Available Information

While information about Beta Bionics, Inc. is available on our website (www.betabionics.com), such information is not incorporated by reference into this Form C.