Statistical Analysis Plan

for

Evaluating the Safety and Effectiveness of the Omnipod Horizon™ Automated Glucose Control System in Children with Type 1 Diabetes Aged 2.0-5.9 Years: Preschool Cohort

SAP: version 1, dated 22 April 2020

Preschool Protocol: version 1.0, dated 24 April 2020

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1 PURPOSE

The purpose of this Statistical Analysis Plan (SAP) is to describe the statistical methodology that will be used to confirm the safety and effectiveness of the Omnipod Horizon™ Automated Glucose Control System in children with type 1 diabetes aged 2.0-5.9 years. Should there be any discrepancy between the preschool study protocol and this SAP, the content of the SAP shall prevail.

2 STUDY DESIGN

2.1 STUDY DESIGN OVERVIEW

This is a single-arm, multi-center, prospective clinical study. The study will be conducted in 6-12 clinical study sites in the United States. The study is expected to enroll up to 80 children, aged 2-5.9 in order to obtain 60 evaluable subjects. Subjects will be considered evaluable if they have at least 8 weeks of data during Phase 2 of hybrid closed-loop.

2.2 INVESTIGATIONAL DEVICE

The Omnipod Horizon™ Automated Glucose Control System ("Horizon™ System") is comprised of three primary components:

- Omnipod Horizon™ tubeless, insulin delivery alternate controller enabled (ACE) pump (Pod) with the Horizon™ algorithm
- Omnipod Horizon™ Personal Diabetes Manager (PDM) which is a Samsung J3 locked down Android device that operates the Omnipod Horizon™ App
- Dexcom G6 - Continuous Glucose Monitoring (CGM) system

In addition, the following non-investigational, commercially available devices will be used during the study:

- Contour® Next One blood glucose meter (Ascensia Diabetes Care, 5 Wood Hollow Road, Parsippany, NJ 07054 USA)
- Precision Xtra ketone meter (Abbott Diabetes Care Inc., 1360 South Loop Road, Alameda, CA 94502 USA)

2.3 STUDY SCHEDULE

The study will consist of a 14-day outpatient standard therapy (ST) outpatient phase (Phase 1), a 13-week outpatient hybrid closed-loop (HCL) phase (Phase 2), and a 6-month hybrid closed-loop extension phase (Phase 3). The sponsor intends to submit results from Phase 2 for marketing clearance after data collection for Phase 2 is complete.

The Horizon™ System has two modes. In Manual Mode, the system will function equivalently to the Omnipod DASH System. This includes delivering insulin at programmed basal rates and bolus amounts with the option to set temporary basal profiles. In Automated Mode, the system will support the use of multiple target glucose values. The

programmed basal rates, glucose targets and bolus calculator settings will inform the MPC (model predictive control) algorithm for insulin dosing parameters.

2.4 STUDY SUCCESS

The study will be deemed successful if the incidence rates of severe hypoglycemia and diabetic ketoacidosis during Phase 2 are considered acceptable compared to published rates.

2.5 RANDOMIZATION

This is a single-arm, multicenter, prospective clinical study where all eligible subjects will use the investigation device. Subjects will not be randomized.

2.6 POINT OF ENROLLMENT

A subject is enrolled in the study upon placement of the first study CGM. Subjects who do not meet the eligibility criteria will not continue in the study and will be considered screen failures.

3 STUDY OBJECTIVES AND ENDPOINTS

3.1 SAFETY OBJECTIVE AND ENDPOINTS

The safety objective is to evaluate the safety of the Omnipod Horizon™ Automated Glucose Control System in preschool patients with type 1 diabetes. The safety objective will be evaluated by summarizing the following events during Phase 2:

- Incidence rate of severe hypoglycemia (events per person months)
- Incidence rate of diabetic ketoacidosis (DKA) (events per person months)

3.2 PRIMARY EFFECTIVENESS OBJECTIVE AND ENDPOINTS

The primary effectiveness objective is to evaluate the effectiveness of the Omnipod Horizon™ Automated Glucose Control System. The primary effectiveness objective will be evaluated by analyzing the following endpoints:

- A1C at the end of Phase 2 compared to baseline A1C
- Percentage of time in range (70-180 mg/dL) during Phase 2 of the hybrid closed-loop phase compared to Phase 1 (standard therapy)

3.3 SECONDARY OBJECTIVE AND ENDPOINTS

The secondary objective is to evaluate additional glycemic measures of effectiveness of the Omnipod Horizon™ Automated Glucose Control System. The secondary objective will be evaluated based on the following per subject endpoints *with* prespecified hypotheses:

- Glucose metrics from system CGM during the hybrid closed-loop phase for Phase 2 will be compared to Phase 1 overall:
    - Percentage of time in range > 180 mg/dL
    - Percentage of time in range < 70 mg/dL

Additional per subject endpoints *without* prespecified hypotheses used to evaluate the secondary objective include:

- A1C:
    - A1C at the end of Phase 2 (Visit 13), 6 months (Visit 16) and the end of Phase 3 (Visit 19)
    - Change from baseline in A1C at the end of Phase 2 (Visit 13), 6 months (Visit 16) and the end of Phase 3 (Visit 19)
    - Proportion of subjects demonstrating an improvement from baseline in A1C at the end of Phase 2 (Visit 13), 6 months (Visit 16) and the end of Phase 3 (Visit 19)
- Glucose metrics from system CGM during the hybrid closed-loop phase for Phase 2 and Phase 3 will be compared to Phase 1 during the day, overnight, and overall:
    - Mean glucose
    - Percentage of time in range 70-180 mg/dL
    - Percentage of time in range 70-140 mg/dL
    - Percentage of time in range > 180 mg/dL
    - Percentage of time in range ≥ 250 mg/dL
    - Percentage of time in range ≥ 300 mg/dL
    - Percentage of time in range < 70 mg/dL
    - Percentage of time in range < 54 mg/dL
    - Standard deviation
    - Coefficient of variation
- Percentage of time in hybrid closed-loop as proportion of overall device usage time during Phase 2 and Phase 3
- Glucose management indicator (GMI) based on overall mean glucose during Phase 2 and Phase 3 will be compared to Phase 1
- Insulin requirements during Phase 2 and Phase 3 will be compared to Phase 1:
    - Total daily insulin (TDI) (units, units/kg)
    - Total daily basal insulin (units, units/kg)
    - Total daily bolus insulin (units, units/kg)
- Change from baseline in BMI (kg/m^2) at end of Phase 2 and Phase 3

4 ANALYSIS OF PRIMARY EFFECTIVENESS ENDPOINTS

There are two primary effectiveness endpoints. The primary effectiveness objective will be evaluated using the following endpoints:

- A1C at the end of Phase 2 compared to baseline A1C
- Percentage of time in range (70-180 mg/dL) during Phase 2 of the hybrid closed-loop phase compared to Phase 1 (standard therapy)

4.1 SAMPLE SIZE

This is a single-arm, multi-center, prospective study. The sample size and study duration were determined to allow for an adequate safety profile of the investigational device. The study will be claimed successful if the incidence rates of severe hypoglycemia and diabetic ketoacidosis are considered acceptable compared to published rates.

In addition, a statistically powered sample size was determined for the two primary effectiveness endpoints. Since each of the primary effectiveness endpoints will be evaluated separately, the significance level will be adjusted so that the overall type I error can be maintained at one-sided 2.5%, and each endpoint will be tested at one-sided 1.25%.

A1C

The sample size estimation is based on the following assumptions:

- Mean difference between paired observations of A1C at the end of Phase 2 compared to baseline is -0.5%
- Standard deviation of the difference between paired observations of A1C at the end of Phase 2 participation compared to baseline is 0.8%
- Power of 90% and one-sided significance level of 1.25%

The estimates for the mean difference and standard deviation of the difference between the paired observations were obtained from previous Omnipod studies, where subjects experienced a mean change in A1C of 0.38% over 3 months (standard pump therapy only), from 8.1 to 7.7%, n=85 (data on file). Based on the above assumptions, 35 subjects are required to provide evaluable data.

Percentage of Time in Range 70-180 mg/dL

The sample size estimation is based on the following assumptions:

- Mean difference between paired observations of percentage of time in range 70-180 mg/dL during Phase 2 of hybrid closed-loop compared to Phase 1 is 10%

- Standard deviation of the difference between paired observations of percentage of time in range 70-180 mg/dL during Phase 2 of hybrid closed-loop compared to Phase 1 is 10%
- Power of 90% and one-sided significance level of 1.25%

The estimates for the mean difference and standard deviation of the difference between the paired observations were obtained from recent Omnipod Horizon study, G170143, where twelve (12) subjects aged 3.4-5.9 years experienced a mean change in percentage of time in range 70-180 mg/dL of 13.2 ± 10.2%. Based on the above assumptions, 11 subjects are required to provide evaluable data.

To gather adequate safety and effectiveness data on the performance of the Omnipod Horizon™ System, the study plans to enroll up to 80 subjects to obtain a minimum of 60 evaluable subjects. Subjects will be enrolled across 6-12 clinical study sites. No single site should enroll more than 24 subjects.

4.2 PRIMARY ANALYSIS

There are two primary effectiveness endpoints. The primary effectiveness endpoints will not be used to support labeling claims.

A1C

The end of Phase 2 (~13 weeks) A1C will be compared to baseline A1C as measured by the core laboratory by calculating the change from baseline in A1C at Visit 13 (~13 weeks) for each subject.

The change in A1C is calculated as the A1C at Visit 13 minus baseline A1C. The null hypothesis associated with this endpoint states that the mean change in A1C is greater than or equal to zero. Rejection of the null hypothesis indicates that the observed data support the alternative hypothesis that the mean change in A1C is less than zero (indicating improved glycemic control). The hypotheses associated with the first primary effectiveness endpoint are defined as:

$H0: \mu \geq 0$
$H1: \mu < 0$

where μ is the mean of the per subject differences in A1C from baseline to Visit 13.

Percentage of Time in Range 70-180 mg/dL

The percentage of time in range (TIR) 70-180 mg/dL during Phase 2 of hybrid closed-loop will be compared to Phase 1 by calculating the change between the time in range percentages between Phase 2 and Phase 1 for each subject. The change is calculated as the percentage of time in range during Phase 2 minus the percentages of time in range

during Phase 1. The null hypothesis associated with this endpoint states that the mean change in percentage of time in range 70-180 mg/dL is less than or equal to zero. Rejection of the null hypothesis indicates that the observed data support the alternative hypothesis that the mean change in percentage of time in range 70-180 mg/dL is greater than zero. The hypotheses associated with the second primary effectiveness endpoint are defined as:

$H0: \mu \leq 0$
$H1: \mu > 0$

where μ is the mean of the per subject differences in percentage of time in range 70-180 mg/dL during Phase 2 (hybrid closed-loop) compared to Phase 1 (standard therapy).

Both primary effectiveness endpoints will be tested independently of each other for statistical significance using a paired t-test at a one-sided significance level of 1.25%.

The modified Intention to Treat (mITT) analysis set will be the primary analysis set used to analyze the primary effectiveness endpoints. The results based on the Per Protocol (PP) analysis set will be considered supportive.

4.3 SUBGROUP AND STRATIFIED ANALYSES

For the primary effectiveness endpoints, all data will be included in the primary analysis. Subgroup or stratified analyses may be presented. These may include but are not limited to:

- Day and night (daytime: 6AM to <12AM; nighttime as 12AM to <6AM)
- Length of time in HCL (e.g., Month 1, Month 2)
- Demographic measures (e.g., gender, race)
- Previous pump or CGM use
- BMI (≤25 vs >25 kg/m^2)

5 ANALYSIS OF SAFETY

All adverse events reported during the study will be reviewed and adequately reported to comply with applicable regulations. All reportable AEs will be assessed by the investigator who will determine whether the event is related to the study procedures or related to the study device and whether the event meets any of the criteria for seriousness. The event will be considered serious if the event meets at least one criterion for seriousness.

5.1 MEDICAL MONITOR

An independent Medical Monitor will be responsible for individual and timely review of adverse events. The Medical Monitor will also adjudicate all serious adverse events (SAEs), including events of severe hypoglycemia and diabetic ketoacidosis (as well as all

events reported by the investigator as being device-related) for seriousness, severity, relationship to study device and procedure, whether the event is anticipated or unanticipated, and event categorization. The adjudication decision by the Medical Monitor will be used for the final classification of adverse events for regulatory reports, product labeling, and publications or presentation.

5.2 RELATIONSHIP TO STUDY DEVICE AND PROCEDURE

The causal relationship to the study procedures and the investigational device for each adverse event will be rated as follows:

- Unrelated: The event is not related to the procedures or the investigational device.
- Possibly Related: The temporal sequence is such that the relationship is not unlikely or there is no contradicting evidence that can reasonably explain the subject's condition. There is a possibility of any relation between the event and the procedures or the investigational device.
- Related: The temporal sequence is relevant or the event abates upon completion of the procedure/ investigational device, or the event cannot be reasonably explained by the subject's condition or comorbidities. The event is related or most likely associated with the procedures or the investigational device.

For the purposes of dichotomizing the causal relationship in safety summaries, events that are "Related" or "Possibly Related" will be considered related.

5.3 SEVERITY

The severity of the adverse event will be rated based upon the following grades:

- Mild: Usually transient, requires no special treatment, and does not interfere with the participant's daily activities
- Moderate: Usually causes a low level of inconvenience, discomfort or concern to the participant and may interfere with daily activities, but is usually ameliorated by simple therapeutic measures and participant is able to continue in study
- Severe: Interrupts a participant's usual daily activities, causes severe discomfort, may cause discontinuation of study device, and generally requires systemic drug therapy or other treatment

5.4 ANALYSIS OF ADVERSE EVENTS

Safety summaries and analyses will be based on all subjects that are enrolled in the study (i.e., Intention to Treat analysis set). All adverse events reported over the course of the study will be summarized and tabulated by study phase, event category, seriousness, severity, and relationship to the study procedures and the investigational device. Except where indicated, a subject reporting the same adverse event more than once will be

counted once when calculating the number and percentage of subjects with that particular event.

Adverse events leading to death or to discontinuation from the study will be listed separately. A listing of all adverse events will be provided. The primary safety endpoints will be presented by existing Dexcom G6 use at the time of screening (users and non-users). No formal tests of hypotheses are proposed for the safety endpoints.

5.5 EVALUATION OF DEVICE DEFICIENCIES

Device deficiencies will be tabulated and listed in a manner similar to the methods described for adverse events. Any device deficiency leading to an adverse event or study termination will be listed separately.

6 ANALYSIS OF SECONDARY EFFECTIVENESS ENDPOINTS

The secondary effectiveness objective is to evaluate additional glycemic measures of effectiveness of the Omnipod Horizon™ Automated Glucose Control System. The secondary effectiveness objective will be evaluated based on the secondary effectiveness endpoints listed in Section 3.3 above.

6.1 ANALYSIS OF PERCENTAGE OF TIME IN RANGE

The analysis of secondary endpoints that summarize the percentage of time in range (TIR) will follow the analysis set forth for the primary effectiveness endpoint of TIR 70-180 mg/dL, with the range value updated as appropriate.

6.2 ANALYSIS OF PERCENTAGE OF TIME IN HYBRID CLOSED-LOOP

The percentage of time in hybrid closed-loop will be calculated as:

$$100 \times \frac{sum\ of\ gaps\ between\ consecutive\ CGM\ readings}{difference\ between\ the\ earliest\ and\ the\ latest\ CGM\ readings} = \%\ time\ in\ HCL$$

A gap is calculated as the difference in time (either minutes or seconds) between two consecutive CGM records as captured by the Horizon™ System. The gaps are then summed to obtain total time in HCL. As records are generally taken in about every 5 minutes, and to ensure that only confirmed HCL records are included, gaps greater than 7 minutes will be excluded from analysis. For the denominator, the chronologically earliest and latest CGM records during HCL as captured by the Horizon™ System will be used.

As opposed to the time in range endpoints, records with no glucose value in the Horizon™ System device output (such as due to an error or device deficiency during which the device does not record glucose readings) will be included in analysis. CGM records reported prior to the start of HCL or after the subject's discontinuation from HCL will be

excluded from analysis. This endpoint will also be reported separately for the manual and automated modes.

6.3 ANALYSIS OF GLUCOSE MEASURES

Mean glucose, glucose measurement indicator (GMI), standard deviation (SD) of glucose and coefficient of variation (CV) of glucose will be evaluated per subject based on CGM output. The GMI and CV are calculated as follows:

$$GMI\ (\%) = 3.31 + 0.02392 \times (mean\ glucose\ in\ mg/dL)$$

$$CV(\%) = \frac{SD\ of\ glucose}{mean\ glucose}$$

6.4 ANALYSIS OF INSULIN REQUIREMENTS

Insulin requirements (TDI, total daily basal insulin and total daily bolus insulin) during the hybrid closed-loop phase will be compared to the standard therapy phase. The insulin requirements will be collected at Visit 2 (start of ST phase) and compared to the data collected by the Horizon™ System during HCL:

- Total daily insulin: sum of basal and bolus insulin reported over the course of HCL, adjusted for 24-hour period
- Total daily basal insulin: sum of basal insulin reported over the course of HCL, adjusted for 24-hour period
- Total daily bolus insulin: sum of bolus insulin reported over the course of HCL, adjusted for 24-hour period. This will include only bolus insulin administered and recorded by the Horizon™ System.

Data will be summarized both in insulin units and units/kg to provide a weight-adjusted comparison.

6.5 ANALYSIS OF SECONDARY EFFECTIVENESS ENDPOINTS WITH PRESPECIFIED HYPOTHESES

There are two secondary effectiveness endpoints with prespecified hypotheses. The modified Intention to Treat (mITT) analysis set will be the primary analysis set used to analyze the secondary effectiveness endpoints. The results based on the Per Protocol (PP) analysis set will be considered supportive.

Percentage of Time in Range >180 mg/dL

The percentage of TIR >180 mg/dL during Phase 2 of hybrid closed-loop phase will be compared to standard therapy (Phase 1) by calculating the change between the time in range percentages between Phase 2 and Phase 1 for each subject. The change is

calculated as the percentage of time in range during Phase 2 minus the percentage of time in range during Phase 1. The null hypothesis associated with this endpoint states that the mean change in percentage of time in range >180 mg/dL is greater than or equal to zero. Rejection of the null hypothesis indicates that the observed data support the alternative hypothesis that the mean change in percentage of time in range >180 mg/dL is less than zero. The hypotheses associated with the second primary effectiveness endpoint are defined as:

$H0: \mu \geq 0$
$H1: \mu < 0$

where μ is the mean of the per subject differences in percentage of time in range >180 mg/dL during Phase 2 of hybrid closed-loop compared to the standard therapy phase (Phase 1).

Percentage of Time in Range <70 mg/dL

The percentage of TIR <70 mg/dL during Phase 2 of hybrid closed-loop phase will be compared to standard therapy (Phase 1) by calculating the change between the time in range percentages between Phase 2 and Phase 1 for each subject. The change is calculated as the percentage of time in range during Phase 2 minus the percentage of time in range during Phase 1. The null hypothesis associated with this endpoint states that the mean change in percentage of time in range <70 mg/dL is greater than or equal to zero. Rejection of the null hypothesis indicates that the observed data support the alternative hypothesis that the mean change in percentage of time in range <70 mg/dL is less than zero. The hypotheses associated with the second primary effectiveness endpoint are defined as:

$H0: \mu \geq 0$
$H1: \mu < 0$

where μ is the mean of the per subject differences in percentage of time in range <70 mg/dL during Phase 2 of hybrid closed-loop compared to the standard therapy phase (Phase 1).

If at least one of the primary effectiveness endpoints are found to be significant, the testing for secondary endpoints can commence. To maintain the family-wise error rate at one-sided 2.5% the testing will commence hierarchically, and Holm's correction will be applied as follows:

- A paired t-test will be applied to each of the secondary endpoints and the unadjusted p-values will be ordered from the smallest to largest.

- The hypothesis associated with the smallest unadjusted p-value will be tested for significance at a one-sided significance level of 2.5% / 2 = 1.25%.
- If the null hypothesis is rejected for the first hypothesis, the testing of the second hypothesis (with the higher unadjusted p-value) will commence, and the hypothesis will be tested for significance at a one-sided significance level of 2.5%. If the first null hypothesis is not rejected, the testing will stop.

6.6 ANALYSIS OF SECONDARY EFFECTIVENESS ENDPOINTS WITHOUT PRESPECIFIED HYPOTHESES

There are no pre-specified hypotheses associated with the other secondary effectiveness endpoints. The mITT analysis set will be the primary analysis set used to analyze the secondary effectiveness endpoints. The results based on the PP analysis set will be considered supportive. Summary statistics will be presented by age cohort for all endpoints, stratified by time points of interest (e.g., day, night, overall). All statistical comparisons will be conducted at a two-sided significance level of 5%, with no adjustment for multiple testing. If the assumptions for parametric tests are grossly violated, a non-parametric method such as Wilcoxon signed rank test may be used. Since the results of endpoint analyses will not be used to support clinical claims, no adjustment for multiplicity will be performed.

As described in this document, results will be stratified by phase of the study (ST and HCL), and time of day (daytime: 6AM to <12AM and nighttime: 12AM to <6AM). Results for other subgroups (e.g., demographics, previous pump or CGM use, length of time in HCL) may be presented as appropriate. Data at Visit 13 will be used for any parameters that are measured at end of Phase 2. Data at Visit 19 will be used for any parameters that are measured at end of Phase 3.

7 GENERAL STATISTICAL CONSIDERATIONS

7.1 ANALYSIS SETS

The following analysis sets are planned for the study and will apply to the endpoints through the end of Phase 2. There are no prespecified analysis sets for Phase 3; all available data will be used to summarize Phase 3 endpoints.

7.1.1 ITT (Intention to Treat) Analysis Set

The ITT analysis set includes all subjects that are enrolled in the study. All safety analyses (other than primary analysis for primary safety endpoints) will be based on the ITT analysis set.

7.1.2 mITT (modified Intention to Treat) Analysis Set

The mITT analysis set is a subset of the ITT analysis set. The mITT analysis set will consist of subjects who have entered the hybrid closed-loop phase of the study successfully. The mITT analysis set will be used as the primary analysis set for all primary and secondary endpoints (both safety and effectiveness), and other clinical outcome data.

7.1.3 PP (Per Protocol) Analysis Set

The Per-Protocol (PP) analysis set is a subset of the mITT analysis set. Subjects will be included in the PP analysis set if they have a minimum of 80% system use during Phase 2 inclusive of manual and hybrid closed-loop (automated) modes over a minimum duration of 10 weeks and have completed the study without major protocol deviations. The PP analysis set will be used as supportive analysis for the endpoints. The following will be considered major protocol deviations:

- Major inclusion/exclusion criteria deviation
- Significant protocol non-compliance that may confound the study objective data (e.g., use of prohibited medications)

The list of subjects excluded from the PP analysis set will be determined prior to analysis of Phase 2 endpoints. If the PP analysis set does not differ from the mITT analysis set, separate analyses will not be presented.

7.2 CONTROL OF SYSTEMATIC BIAS

Several measures are incorporated into the study design to help minimize study bias as follows:

1) This is a multi-center trial to help ensure that investigator or site or subject enrollment bias is minimized. Selection of subjects will be made from the Investigator's usual subject load. Consecutively eligible subjects should be enrolled into the study.
2) This document specifies appropriate statistical methodology to ensure that bias is minimized.
3) The effectiveness measures will be based on the direct output from the device or are analyzed at a NGSP certified central laboratory, ensuring objective reporting.
4) An independent Medical Monitor will adjudicate all SAEs and device-related adverse events; the Medical Monitor's assessment of adverse events will be used for regulatory reports, product labeling, and publications or presentation.

7.3 POOLING DATA ACROSS CENTERS

Up to 12 clinical sites will enroll subjects into the study. No single site should enroll more than 24 subjects. For the purposes of statistical analyses of primary effectiveness endpoints, data from all study centers will be pooled. The primary effectiveness endpoints

will also be presented by center. The appropriateness of pooling subjects across sites will be assessed graphically or utilizing an appropriate statistical test.

7.4 CALCULATION OF PERCENTAGE OF TIME IN RANGE

Several effectiveness endpoints involve calculation of percentage of time in a specific glycemic range. These endpoints will be based on the direct output from a device (either a CGM or The Omnipod Horizon™ Automated Glucose Control System). The percentage of time in range (TIR) will be calculated as:

$$100 \times \frac{\#\ of\ CGM\ readings\ in\ range}{\#\ of\ evaluable\ CGM\ readings} = TIR\%$$

The following CGM readings will be excluded from analysis, and therefore, from calculation of TIR endpoints:

- No glucose value is provided in the device output, such as due to an error or device deficiency during which the device does not record glucose readings
- CGM readings reported prior to start of standard therapy phase or after subject's discontinuation from HCL

7.5 HANDLING OF MISSING DATA

All practical monitoring and follow-up steps will be taken to ensure complete and accurate data collection. All analyses will be based on available data only; no imputation for missing data is planned.

7.6 EXPLORATORY ANALYSES

The following exploratory analyses will be considered. The analyses may be used for internal research purposes and/or scientific presentations and/or manuscripts and may not all be provided in a regulatory submission:

- Number of hypoglycemic and hyperglycemic events as measured by the system CGM during the hybrid closed-loop phase will be compared to Phase 1
- Glucose metrics from the system CGM during Phase 2 stratified by device mode
- Change from baseline in A1C and BMI at the last follow-up visit, given at least 8-weeks of participation in Phase 2
- Change from baseline in A1C at end of Phase 2, stratified by baseline A1C (e.g. A1C ≥7.5%, ≥9.0%)
- Proportion of subjects with A1C <7.0% at baseline and end of Phase 2; similar analyses using A1C cutoffs of <7.5%, <8.0% and <9.0%
- Proportion of subjects with change from baseline in A1C at end of Phase 2 of >0.5% and >1.0%

- Proportion of subjects who either had an improvement from baseline of >1.0% in A1C or A1C <7.0% at end of Phase 2
- Percentage of time the CGM was used during Phase 2
- Number of meal and correction boluses
- Compare glycemic outcomes (e.g., TIR <70 mg/dL, TIR >180 mg/dL) by bolus frequency per day
- Compare glycemic outcomes (e.g., TIR <70 mg/dL, TIR >180 mg/dL) by use of CGM informed bolus calculator (i.e., days with CGM informed bolus calculator used at least once and days without CGM informed bolus calculator use)
- Glycemic outcomes and other measures based on evaluable subjects (i.e., those subjects with at least 8 weeks of data during Phase 2)

The results of exploratory analyses will be presented using summary statistics. Data at Visit 13 will be used for any parameters that are measured at end of Phase 2 (data at Visit 19 will be used for any parameters that are measured at end of Phase 3). Any statistical testing will be performed at a two-sided significance level of 5% with no adjustment for multiple testing. If the observed data are found not to follow a normal distribution, non-parametric methods may be employed (such as Wilcoxon rank sum test as appropriate).

7.7 QUESTIONNAIRES

Various subject- and caregiver-completed questionnaires will be used to evaluate general and disease-specific quality of life, and device usability. These include, but are not limited to:

- Clarke Questionnaire on Impaired Awareness of Hypoglycemia (IAH)
- SUS (System Usability Scale)
- WHO-5 Well-Being Index
- PSQI (Pittsburgh Sleep Quality Index)
- Hypoglycemia Confidence Scale
- IDSS (T1) (Insulin Device Satisfaction Survey for subjects with Type 1 diabetes)
- PAID
- INSPIRE
- DTSQ
- Human Factors

For validated questionnaires, the prescribed scoring algorithm will be followed. The results will be presented using summary statistics. Any testing will be performed at a two-sided significance level of 5%, with no adjustment for multiple testing. If the observed data are found not to follow a normal distribution, non-parametric methods may be employed (such as Wilcoxon rank sum test) as appropriate.

7.8 OTHER DATA SUMMARIES

The distribution of each baseline characteristic or demographic parameter of interest (such as age, gender, medical history, etc.) will be presented. Data on all enrolled subjects will be presented. If a considerable number of subjects do not enter the HCL phase of the study, these results may also be presented for the mITT and/or PP analysis sets. Continuous variables will be summarized using count, mean, median, standard deviation, and range. Categorical variables will be summarized using counts and percentages.

7.9 STATISTICAL SOFTWARE

The statistical software package SAS® 9.4 or later will be used for all the data derivations, summarization, data listings and statistical analyses. Additional statistical software may be used for graphics or validation purposes as appropriate.

7.10 PERIODIC REVIEW OF CONTROLLER DATA

Following the upload of controller data into the database, the data will be made available to Sponsor representatives for periodic reviews. Reviews of the controller data will be conducted to identify any anomalies and to confirm the algorithm appears to be functioning as expected. Unless potential safety concerns are identified, the results of such reviews will not be shared with study sites or subjects and will not affect the data analyses.