SUPPLEMENTARY APPENDIX

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Brown, Forlenza, et al. Multicenter Trial of a Tubeless, On-Body Automated Insulin Delivery System with Customizable Glycemic Targets in Pediatric and Adult Participants with Type 1 Diabetes

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Supplemental Table S1. Eligibility and Exclusion Criteria

Inclusion Criteria

Subjects were required to meet the following criteria to be enrolled in the study:

1. Age at time of consent 6.0-70.0 years
2. Subjects aged < 18 years must be living with parent/legal guardian
3. Diagnosed with type 1 diabetes for at least 6 months. Diagnosis is based on investigator's clinical judgment
4. Deemed appropriate for pump therapy per investigator's assessment taking into account previous history of severe hypoglycemic and hyperglycemic events, and other comorbidities
5. Investigator has confidence that the subject can successfully operate all study devices and is capable of adhering to the protocol
6. Willing to use only the following types of insulin during the study: Humalog, Novolog, Admelog or Apidra during the study
7. Must be willing to travel to and participate in meal and exercise challenges during 5-days of the hybrid closed-loop phase
8. Willing to wear the system continuously throughout the study
9. A1C < 10% at screening visit
10. Must be willing to use the Dexcom App on the Omnipod Horizon™ PDM as the sole source of Dexcom data (with the exception of the Dexcom Follow App) during the hybrid closed-loop phase
11. Subjects scoring ≥ 4 on the Clarke Questionnaire must agree to have an overnight companion, defined as someone who resides in the same home or building as the study subject and who can be available overnight
12. Able to read and speak English fluently
13. Willing and able to sign the Informed Consent Form (ICF) and/or has a parent/guardian willing and able to sign the ICF. Assent will be obtained from subjects aged < 18 years per State requirements

Exclusion Criteria

Subjects who met any of the following criteria were to be excluded from the study:

1. A medical condition, which in the opinion of the investigator, would put the subject at an unacceptable safety risk
2. History of severe hypoglycemia in the past 6 months
3. History of Diabetic Ketoacidosis (DKA) in the past 6 months, unrelated to an intercurrent illness, infusion set failure or initial diagnosis
4. Diagnosed with sickle cell disease
5. Diagnosed with hemophilia or any other bleeding disorders
6. Plans to receive blood transfusion over the course of the study
7. Currently diagnosed with anorexia nervosa or bulimia
8. Acute or chronic kidney disease (e.g. estimated GFR < 45) or currently on hemodialysis
9. History of adrenal insufficiency
10. Has taken oral or injectable steroids within the past 8 weeks or plans to take oral or injectable steroids during the course of the study
11. Unable to tolerate adhesive tape or has any unresolved skin condition in the area of sensor or pump placement
12. Plans to use insulin other than U-100 insulin intended for use in the study device during the course of the study
13. Use of non-insulin anti-diabetic medication other than metformin (e.g. GLP1 agonist, SGLT2 inhibitor, DPP-4 inhibitor, pramlintide)
14. Current or known history of coronary artery disease that is not stable with medical management, including unstable angina, or angina that prevents moderate exercise despite medical management, or a history of myocardial infarction, percutaneous coronary intervention, or coronary artery bypass grafting within the previous 12 months
15. For subjects > 50 years old or with diabetes duration > 20 years, abnormal electrocardiogram consistent with increased risk of arrhythmia, ischemia, or prolonged QTc interval (> 450 ms)
16. Thyroid Stimulating Hormone (TSH) is outside of normal range with clinical signs of hypothyroidism or hyperthyroidism
17. Pregnant or lactating, or is a woman of childbearing potential and not on acceptable form of birth control (acceptable includes abstinence, condoms, oral/injectable contraceptives, IUD or implant)
18. Participation in another clinical study using an investigational drug or device within the preceding 30-days or intends to participate during the study period
19. Unable to follow clinical protocol for the duration of the study or is otherwise deemed unacceptable to participate in the study per the investigator's clinical judgment

Supplemental Table S2. Schedule of participant visits

Assessment Schedule	Screening	Standard Therapy 1	Standard Therapy 2	Automated Insulin Delivery Phase (AID)											EW[‖‖]
	Phase 1[‡]			Phase 2[#]											
Visit Number	1	2	3	4	5[‡]	6	7	8	9	10	11	12	13	UV[§§]	
Study Day/Visit Window[*]	-30 to -14d	-14d to AID start	-1d to AID start	1	2	3	10	24	38	52	66	80	94	N/A	
	AID start				±1d	±1d	±3d	±3d	±3d	±3d	±3d	±3d	±3d		
Telephone (T) or Office (O) Visit	O	O	O	O	T/O	T/O[‡‡]	T/O[‡‡]	T/O[‡‡]	T/O[‡‡]	T/O[‡‡]	T/O[‡‡]	T/O[‡‡]	T/O[‡‡]	T/O[‡‡]	O
Laboratory Assessments															
A1c	X												X		X
TSH	X														
Creatinine Level	X														
Pregnancy Test	X			X			X		X				X		
Clinical Assessments															
Informed Consent	X				X[††]										
Medical History (including demographics)	X														
Confirm Eligibility	X				X[††]										
Concomitant medications	X	X[§]		X[§]	X[§]	X[§]	X[§]	X[§]	X[§]	X[§]	X[§]	X[§]	X[§]	X[§]	X[§]
Average total daily insulin (~ 7 days)		X		X											
Average total basal insulin (~ 7 days)		X		X											
Average total bolus insulin (~ 7 days)		X		X											
Pump settings/MDI dosing		X		X											
Height	X												X		X
Weight	X												X		X
Vital signs	X						X		X				X		X
Electrocardiogram[†] (if applicable)	X														
Adverse events		X	X	X	X[§]	X[§]	X[§]	X[§]	X[§]	X[§]	X[§]	X[§]	X[§]	X[§]	X[§]
Questionnaires															
See Table 3 for specific questionnaires	X	X											X		X
Study Devices															

Training on Glucagon administration and information on treatment of hypo/hyperglycemia		X													
Horizon Data Portal initiation/discontinuation				X									X		X
Study device training		X‖		X**											
Dispense/Return		X											X		X
BG/Ketone meter, and CGM															
QC testing of BG/Ketone meter by site		X													
CGM sensor placement (as needed throughout)		X													
Assess CGM usage and data criteria has been met		X¶	X												
Dispense/Return Horizon System				X									X		X
Complaints/device deficiencies				X§	X§	X§	X§	X§	X§	X§	X§	X§	X§	X§	X§
Device uploads				X	X	X	X	X	X	X	X	X	X		X
Data review				X	X	X	X	X	X	X	X	X	X	X	X

*In the event of overlapping visit windows, no visits occurring during the automated insulin delivery phase are to occur on the same date, with the exception of challenge visit days. It is acceptable for a challenge visit to occur on the same date as an automated insulin delivery phase visit.

†Electrocardiogram required for subjects >50 years old or with diabetes duration >20 years.

‡Patients extending into the pivotal study from the pre-pivotal study will initiate their participation at Visit 5 of pivotal automated insulin delivery phase.

§Documentation only applicable if there are changes from previous assessment.

‖Study device training for the CGM, blood glucose and ketone meters.

¶Patients deemed exempt from wearing the study continuous glucose monitor for 14-days will be eligible to immediately commence the automated insulin delivery phase at Visit 4 and may skip Visit 3/Standard Therapy 2 (in which case, Visit 1, Visit 2/Standard Therapy1 and Visit 4 may all occur on the same day).

[#]Challenges can occur during any consecutive 5-days during automated insulin delivery phase of the automated insulin delivery phase. A follow up telephone visit will occur the following day after the conclusion of the challenge period.

[**]Study device training for the automated insulin delivery system.

[††]Pre-pivotal subjects extending into pivotal will be required to reconsent. If the original pre-pivotal screening is within 45 days prior to the start of the automated insulin delivery phase in the pivotal study, subjects will not require rescreening. All subjects must reconsent prior to commencing the extension phase (Phase 3) on or before Visit 13.

[‡‡]Visits identified as "T/O" can either be conducted in person at the clinical site or over the telephone. Visits identified as "O" can only be conducted in person at the clinical site. Vital signs, device uploads/data review from the blood glucose and Ketone meter, and pregnancy tests are not required at any visit conducted via telephone.

[§§]Unscheduled visits will serve as extra study visits, if needed. For unscheduled visits pertaining to a study pause and recommencement, sites should follow the assessments as defined in the protocol.

[‖‖]Early withdrawal visit will only be conducted for any subjects that started but did not complete the full study to include standard therapy and the automated insulin delivery phase.

Supplemental Table S3. Primary and secondary effectiveness outcomes for daytime for both children and adults*

	Children (6 to 13.9 years) (n=112)				Adults (14 to 70 years) (n=128)			
Parameter	**Standard Therapy Phase**	**Automated Insulin Delivery Phase**	**Change**	***p*-value‡**	**Standard Therapy Phase**	**Automated Insulin Delivery Phase**	**Change**	***p*-value‡**
Daytime (6:00-0:00)								
Primary Effectiveness Outcome, Percentage time 70-180mg/dL	51.5 ± 15.6 52.2 (40.3, 62.1)	64.6 ± 8.5 64.3 (59.5, 71.0)	13.1 ± 11.9 12.0 (5.4, 21.9)	<0.0001	64.8 ± 16.7 67.0 (51.4, 78.1)	72.5 ± 11.0 74.3 (66.3, 79.7)	7.8 ± 12.4 5.4 (-0.6, 14.9)	<0.0001
Mean sensor glucose, mg/dL	186 ± 33 184 (164, 203)	164 ± 16 165 (153, 174)	-21 ± 24 -16 (-38, -5)	<0.0001	162 ± 28 154 (140, 181)	155 ± 17 153 (144, 164)	-7 ± 21 -3 (-18, 9)	0.0047
Standard deviation of sensor glucose, mg/dL	70 ± 14 69 (60, 80)	62 ± 10 61 (55, 68)	-8 ± 9 -6 (-13, -2)	<0.0001	56 ± 14 54 (46, 66)	50 ±11 49 (43, 55)	-6 ± 9 -6 (-12, 1)	<0.0001
Coefficient of variation of sensor glucose, %†	37.7 ± 5.3 37.0 (34.1, 40.5)	37.6 ± 4.0 37.5 (34.8, 40.3)	-0.1 ± 4.2 -0.3 (-2.4, 2.5)	0.8938	34.6 ± 5.6 34.0 (30.7, 37.3)	32.0 ± 4.7 32.2 (28.8, 35.1)	-2.7 ± 4.1 -2.5 (-5.2, 0.4)	<0.0001
Percentage time in glucose range, %								
<54mg/dL	0.36 ± 0.68 0.11 (0.00, 0.37)	0.36 ± 0.37 0.25 (0.09, 0.48)	0.00 ± 0.52 0.05 (-0.05, 0.24)	0.0048	0.51 ± 1.19 0.20 (0.00, 0.63)	0.22 ± 0.26 0.16 (0.06, 0.29)	-0.29 ± 1.12 0.00 (-0.30, 0.07)	0.0014
<70mg/dL	2.13 ± 2.60 1.17 (0.43, 2.90)	1.98 ± 1.56 1.62 (0.78, 2.59)	-0.14 ± 1.88 0.22 (-0.60, 0.82)	0.2545	2.64 ± 2.92 1.91 (0.56, 3.57)	1.37 ± 1.14 1.08 (0.49, 1.93)	-1.27 ± 2.39 -0.66 (-1.89, 0.14)	<0.0001
>180mg/dL	46.4 ± 16.8 46.2 (34.4, 57.3)	33.4 ± 9.2 34.1 (26.7, 39.0)	-12.9 ± 12.5 -11.2 (-21.6, -4.7)	<0.0001	32.6 ± 17.3 29.2 (18.4, 46.6)	26.1 ± 11.3 24.2 (18.2, 32.8)	-6.5 ± 12.8 -4.5 (-13.9, 2.4)	<0.0001
≥250mg/dL	20.0 ± 13.5 17.5 (11.3, 26.4)	11.1 ± 5.9 10.5 (6.7, 14.2)	-8.9 ± 10.2 -5.7 (-14.9, -1.5)	<0.0001	10.0 ± 10.2 6.4 (2.2, 16.7)	6.1 ± 5.6 4.3 (2.3, 8.2)	-3.9 ± 7.9 -1.4 (-6.8, 0.6)	<0.0001
≥300mg/dL	9.2 ± 9.5 6.5 (2.7, 12.1)	4.0 ± 3.2 3.1 (1.7, 5.7)	-5.1 ± 7.6 -2.5 (-7.8, -0.2)	<0.0001	3.5 ± 5.0 1.3 (0.2, 4.9)	1.8 ± 2.6 0.8 (0.3, 2.2)	-1.7 ± 3.9 -0.3 (-2.9, 0.2)	<0.0001

[*]Plus–minus values are means ± SD. Unless otherwise indicated, remaining values are median (IQR). IQR denotes interquartile range. To convert the values for glucose to millimoles per liter, multiply by 0.05551.

[†] Coefficient of variation of sensor glucose is standard deviation divided by the mean.

[‡]*p*-value determined using unadjusted two-sided paired t-tests, unless otherwise specified. Two-sided Wilcoxon signed rank tests were used for mean sensor glucose and percent of time in glucose ranges: 70-180mg/dL for adults, <54mg/dL, <70 mg/dL, >180mg/dL for adults, ≥250mg/dL, ≥300mg/dL

Supplemental Table S4. Number of participants meeting consensus targets (1; 2) for glycemic control during the standard therapy phase and the 3-months of automated insulin delivery phase (study phase) for both children and adults

	Children (6 to 13.9 years) (n=112)		**Adults (14 to 70 years) (n=128)**	
Number of participants meeting target, n (%)	**Baseline† or Standard Therapy Phase**	**Follow-up† or Automated Insulin Delivery Phase**	**Baseline† or Standard Therapy Phase**	**Follow-up† or Automated Insulin Delivery Phase**
HbA1c* <7.0% (<53 mmol/mol)	26 (23%)	57 (53%)	58 (45%)	82 (66%)
HbA1c* <7.5% (<58 mmol/mol)	55 (49%)	83 (77%)	88 (69%)	103 (83%)
Time in range 70-180mg/dL >60%	34 (30%)	92 (82%)	80 (63%)	113 (88%)
Time in range 70-180mg/dL >70%	18 (16%)	47 (42%)	56 (44%)	88 (69%)
Time <70mg/dL <4%	95 (85%)	104 (93%)	92 (72%)	122 (95%)
Composite – Time in range >60% and time <70mg/dL <4%	24 (21%)	84 (75%)	55 (43%)	107 (84%)
Composite – Time in range >70% and time <70mg/dL <4%	12 (11%)	40 (36%)	40 (31%)	82 (64%)

To convert the values for glucose to millimoles per liter, multiply by 0.05551.

*Baseline HbA1c values were available for 112 children and 128 adults. Final HbA1c values were available for 108 children and 124 adults who completed the study

†Baseline and follow-up data were used for the primary effectiveness outcome of HbA1c, the remaining outcomes are described for the standard therapy phase and the automated insulin delivery phase.

Supplemental Table S5. Subgroup analyses of mean glycemic outcomes at baseline or during the standard therapy phase and the 3-months of automated insulin delivery phase ("study phase") for both children (6 to 13.9 years) and adults (14 to 70 years) stratified by baseline characteristics

	% Time in range 70-180mg/dL		**% Time below 70mg/dL**[‡]		**% Time above 180mg/dL**		**HbA1c (%) [mmol/mol]**	
Parameter	**Children** (n) standard therapy/study phase, p-value	**Adults** (n) standard therapy/study phase, p-value	**Children** (n) standard therapy/study phase, p-value	**Adults** (n) standard therapy/study phase, p-value	**Children** (n) standard therapy/study phase, p-value	**Adults** (n) standard therapy/study phase, p-value	**Children** (n) baseline/(n) follow-up, p-value	**Adults** (n) baseline/(n) follow-up, p-value
Overall	(112) 53/68, <0.0001[*]	(128) 65/74, <0.0001[†]	(112) 1.38/1.48, 0.8153[†]	(128) 2.00/1.09, <0.0001[†]	(112) 45/30, <0.0001[*]	(128) 32/25, <0.0001[†]	(112) 7.7 [61]/ (108) 7.0 [53], <0.0001[*]	(128) 7.2 [55]/ (124) 6.8 [51], <0.0001[†]
Standard Therapy								
Multiple daily injections	(13) 52/69, 0.0010[*]	(20) 60/72, 0.0006[*]	(13) 1.54/1.41, 0.8742[*]	(20) 2.38/0.79, 0.0006[†]	(13) 46/29, 0.0012[*]	(20) 36/27, 0.0051[*]	(13) 7.7 [61]/ (13) 6.7 [50], 0.0005[*]	(20) 7.6 [60]/ (19) 7.0 [53], 0.0046[*]
Pump	(99) 53/68, <0.0001[*]	(108) 65/74, <0.0001[†]	(99) 1.38/1.49, 0.7763[†]	(108) 1.93/1.16, <0.0001[†]	(99) 45/30, <0.0001[*]	(108) 32/24, <0.0001[†]	(99) 7.7 [61]/ (95) 7.0 [53], <0.0001[†]	(108) 7.1 [54]/ (105) 6.7 [50], <0.0001[†]
Previous pump use								
No	(12) 51/68, 0.0016[*]	(13) 59/73, 0.0059[*]	(12) 1.20/1.08, 0.9741[*]	(13) 1.82/0.74, 0.0171[†]	(12) 48/30, 0.0018[*]	(13) 37/26, 0.0237[*]	(12) 7.8 [62]/ (12) 6.8 [51], 0.0013[*]	(13) 7.6 [60]/ (13) 7.0 [53], 0.0243[*]
Yes	(100) 53/68, <0.0001[*]	(115) 65/74, <0.0001[†]	(100) 1.38/1.53, 0.7175[†]	(115) 2.03/1.15, <0.0001[†]	(100) 45/30, <0.0001[*]	(115) 32/25, <0.0001[†]	(100) 7.7 [61]/ (96) 7.0 [53], <0.0001[†]	(115) 7.1 [54]/ (111) 6.8 [51], <0.0001[†]
Previous continuous glucose monitor use								
No	(4) 34/63, 0.1250[†]	(2) 23/41, 1.0000[†]	(4) 0.74/0.76, 0.8750[†]	(2) 0.00/0.12, 0.5000[†]	(4) 65/36, 0.1250[†]	(2) 77/59, 1.0000[†]	(4) 8.7 [72], (4) 7.1 [54], 0.1250[†]	(2) 8.9 [74]/ (2) 7.9 [63], 0.5000[†]
Yes	(108) 53/68, <0.0001[*]	(126) 65/75, <0.0001[†]	(108) 1.39/1.53, 0.7538[†]	(126) 2.05/1.09, <0.0001[†]	(108) 45/30, <0.0001[*]	(126) 32/24, <0.0001[†]	(108) 7.6 [60]/ (104) 7.0 [53], <0.0001[*]	(126) 7.1 [54]/ (122) 6.8 [51], <0.0001[†]

Gender								
Female	(60) 53/69, <0.0001*	(78) 64/74, <0.0001†	(60) 1.05/1.16, 0.6467†	(78) 1.99/0.88, <0.0001†	(60) 45/29, <0.0001*	(78) 34/25, <0.0001†	(60) 7.7 [61]/ (58) 7.0 [53], <0.0001*	(78) 7.2 [55]/ (76) 6.8 [51], <0.0001†
Male	(52) 52/67, <0.0001*	(50) 66/74, <0.0001*	(52) 1.82/1.77, 0.9000†	(50) 2.00/1.38, <0.0001†	(52) 46/31, <0.0001*	(50) 31/24, <0.0001†	(52) 7.6 [60]/ (50) 7.0 [53], <0.0001*	(50) 7.1 [54]/ (48) 6.7 [50], <0.0001†
Body-mass index								
≤25 kg/m^2	(107) 53/68, <0.0001*	(56) 64/75, <0.0001†	(107) 1.38/1.49, 0.8241†	(56) 1.83/1.12, <0.0001†	(107) 45/30, <0.0001*	(56) 34/23, <0.0001†	(107) 7.6 [60]/ (103) 7.0 [53], <0.0001*	(56) 7.2 [55]/ (56) 6.8 [51], <0.0001†
>25 kg/m^2	(5) 40/61, 0.0625†	(72) 66/73, <0.0001†	(5) 1.57/0.77, 1.0000†	(72) 2.09/1.07, <0.0001†	(5) 59/38, 0.0625†	(72) 32/26, <0.0001†	(5) 8.7 [72]/ (5) 7.7 [61], 0.0625†	(72) 7.1 [54]/ (68) 6.8 [51], <0.0001*

To convert the values for glucose to millimoles per liter, multiply by 0.05551.

**p*-value determined using two-sided paired t-tests.

†*p*-value determined using two-sided Wilcoxon signed rank tests.

‡Values presented for % Time below 70mg/dL are medians, the remaining values in the table are means.

Supplemental Table S6. Glycemic outcomes during the 3-month automated insulin delivery phase when using a 110mg/dL glucose target overall (24 hours) and overnight (midnight to 6AM) for both children and adults*

	Children (6 to 13.9 years)				**Adults (14 to 70 years)**			
Parameter	**Standard Therapy Phase**	**Automated Insulin Delivery Phase**	**Change**	***p*-value‡**	**Standard Therapy Phase**	**Automated Insulin Delivery Phase**	**Change**	***p*-value‡**
Overall (24 hours)								
N	98	98			121	121		
Primary Effectiveness Outcome, Percentage time 70-180mg/dL	52.5 ± 15.7 53.5 (39.3, 63.1)	68.4 ± 9.1 68.8 (63.7, 74.6)	16.0 ± 11.9 16.4 (8.0, 22.9)	<0.0001	66.2 ± 15.3 68.6 (52.8, 78.0)	75.6 ± 9.9 76.9 (69.3, 82.1)	9.4 ± 11.4 8.5 (1.5, 16.0)	<0.0001
Mean sensor glucose, mg/dL	184 ±32 181 (163, 206)	159 ± 17 158 (147, 168)	-25 ± 23 -24 (-39, -8)	<0.0001	159 ± 25 154 (138, 177)	151 ± 15 149 (143, 160)	-7 ± 19 -6 (-16, 6)	0.0001
Standard deviation of sensor glucose, mg/dL	69 ± 14 68 (58, 79)	60 ± 10 59 (52, 65)	-9 ± 9 -8 (-14, -3)	<0.0001	56 ± 14 54 (46, 65)	48 ± 11 47 (41, 54)	-8 ± 9 -8 (-14, -1)	<0.0001
Coefficient of variation of sensor glucose, %†	37.5 ± 5.3 37.1 (33.6, 40.9)	37.5 ± 4.2 38.0 (34.7, 40.2)	0.0 ± 4.5 -0.1 (-2.8, 2.4)	0.9152	35.2 ± 5.8 34.6 (31.2, 37.8)	31.3 ± 4.9 32.0 (28.4, 34.4)	-3.9 ± 4.7 -3.8 (-6.7, -0.4)	<0.0001
Percentage time in glucose range, %								
<54mg/dL	0.41 ± 0.83 0.11 (0.00, 0.42)	0.33 ± 0.35 0.22 (0.06, 0.49)	-0.08 ± 0.70 0.04 (-0.13, 0.18)	0.1961	0.64 ± 1.27 0.22 (0.03, 0.76)	0.22 ± 0.28 0.16 (0.05, 0.26)	-0.42 ± 1.18 -0.09 (-0.49, 0.03)	<0.0001
<70mg/dL	2.23 ± 2.74 1.38 (0.42, 2.67)	1.85 ± 1.42 1.51 (0.76, 2.38)	-0.38 ± 2.08 0.22 (-0.70, 0.65)	0.8233	2.93 ± 3.07 2.07 (0.72, 4.01)	1.29 ± 1.15 0.99 (0.47, 1.67)	-1.64 ± 2.54 -0.99 (-2.30, -0.04)	<0.0001
>180mg/dL	45.3 ± 16.8 44.8 (35.3, 58.5)	29.7 ± 9.6 29.4 (22.6, 34.4)	-15.6 ± 12.6 -15.8 (-24.0, -7.3)	<0.0001	30.9 ± 15.8 28.6 (17.1, 44.6)	23.1 ± 10.2 21.9 (16.0, 29.8)	-7.7 ± 11.7 -6.9 (-13.8, 0.5)	<0.0001
≥250mg/dL	19.2 ± 13.3 16.3 (9.2, 26.3)	9.7 ± 5.8 8.9 (5.3, 12.8)	-9.5 ± 9.9 -7.0 (-15.3, -2.1)	<0.0001	9.0 ± 8.9 6.1 (2.2, 14.5)	5.1 ± 4.6 3.5 (1.8, 7.0)	-4.0 ± 6.6 -2.2 (-6.6, 0.2)	<0.0001
≥300mg/dL	8.7 ± 9.3 5.9 (2.3, 12.0)	3.6 ± 3.2 2.7 (1.3, 4.5)	-5.1 ± 7.3 -2.3 (-8.0, -0.3)	<0.0001	3.1 ±4.4 1.3 (0.2, 4.4)	1.4 ± 2.1 0.8 (0.2, 1.8)	-1.7 ± 3.3 -0.4 (-2.7, 0.2)	<0.0001

Overnight (00:00-06:00)								
N	87	87			119	119		
Primary Effectiveness Outcome, Percentage time 70-180mg/dL	55.1 ± 19.1 55.5 (41.1, 70.3)	79.8 ± 11.9 82.9 (71.4, 89.8)	24.7 ± 15.8 25.3 (15.0, 36.9)	<0.0001	66.0 ± 17.9 67.6 (52.6, 81.1)	79.6 ± 12.5 80.7 (70.5, 90.1)	13.5 ± 14.3 12.2 (5.2, 22.1)	<0.0001
Mean sensor glucose, mg/dL	177 ± 36 175 (153, 198)	144 ±19 142 (131, 155)	-33 ± 29 -33 (-51, -12)	<0.0001	156 ± 29 155 (132, 175)	147 ± 19 145 (134, 160)	-10 ± 22 -7 (-24, 5)	<0.0001
Standard deviation of sensor glucose, mg/dL	61 ± 16 61 (50, 72)	46 ± 13 45 (38, 56)	-15 ± 14 -15 (-23, -7)	<0.0001	55 ± 17 55 (42, 65)	43 ± 13 42 (33, 51)	-12 ± 12 -11 (-19, -4)	<0.0001
Coefficient of variation of sensor glucose, %†	34.7 ± 7.3 34.2 (28.1, 38.7)	31.8 ± 6.1 31.3 (27.7, 36.0)	-2.8 ± 7.9 -2.6 (-7.2, 2.7)	0.0012	34.9 ± 7.9 33.9 (29.7, 39.4)	28.6 ± 6.0 28.9 (25.1, 32.5)	-6.3 ± 7.5 -6.3 (-10.1, -1.3)	<0.0001
Percentage time in glucose range, %								
<54mg/dL	0.60 ± 1.63 0.00 (0.00, 0.30)	0.22 ± 0.34 0.08 (0.00, 0.29)	-0.38 ± 1.45 0.00 (-0.20, 0.09)	0.4978	0.99 ± 1.91 0.00 (0.00, 1.08)	0.24 ± 0.40 0.09 (0.00, 0.28)	-0.75 ± 1.79 0.00 (-0.90, 0.09)	<0.0001
<70mg/dL	2.57 ± 4.34 0.85 (0.00, 3.00)	1.23 ± 1.32 0.74 (0.36, 1.74)	-1.35 ± 3.77 -0.03 (-1.64, 0.48)	0.0269	3.66 ± 4.53 2.28 (0.50, 5.21)	1.20 ± 1.35 0.79 (0.29, 1.47)	-2.46 ± 4.05 -0.92 (-3.58, 0.15)	<0.0001
>180mg/dL	42.4 ± 20.1 40.8 (27.6, 57.7)	19.0 ± 12.0 15.9 (9.7, 26.7)	-23.4 ± 16.9 -24.1 (-36.1, -12.0)	<0.0001	30.3 ± 18.3 27.5 (15.2, 43.0)	19.2 ± 12.7 18.4 (8.5, 28.8)	-11.1 ± 14.5 -9.4 (-18.5, -2.1)	<0.0001
≥250mg/dL	16.4 ± 15.2 11.8 (5.4, 25.7)	4.9 ± 5.1 3.0 (1.5, 6.2)	-11.5 ± 12.9 -7.2 (-19.4, -3.1)	<0.0001	9.0 ± 9.8 5.5 (1.2, 14.8)	4.1 ± 4.8 2.3 (0.6, 6.2)	-4.9 ± 7.7 -1.7 (-8.9, 0.1)	<0.0001
≥300mg/dL	6.9 ± 9.8 3.7 (0.4, 10.0)	1.7 ± 2.3 0.7 (0.2, 2.3)	-5.3 ± 8.7 -1.8 (-6.9, 0.0)	<0.0001	3.2 ± 5.6 0.4 (0.0, 4.1)	1.2 ± 2.2 0.4 (0.0, 1.3)	-2.0 ± 4.7 0.0 (-2.5, 0.2)	0.0001

***** Plus–minus values are means ± SD. Unless otherwise indicated, remaining values are median (IQR). IQR denotes interquartile range. To convert the values for glucose to millimoles per liter, multiply by 0.05551.

† Coefficient of variation of sensor glucose is standard deviation divided by the mean

‡ *p*-value determined using two-sided paired t-tests. Two-sided Wilcoxon signed rank tests were used for mean sensor glucose (except for children overall), coefficient of variation for adults, and percent of time in glucose ranges: 70-180mg/dL for adults overall, <54mg/dL, <70 mg/dL, >180mg/dL for adults, ≥250mg/dL, ≥300mg/dL

Supplemental Table S7. HbA1c at baseline, before and after study pause, and at end of study for both children and adults with values at all four timepoints[*†]

	Children (6 to 13.9 years) (n=35)		**Adults (14 to 70 years) (n=60)**	
	HbA1c (%)	**HbA1c (mmol/mol)**	**HbA1c (%)**	**HbA1c (mmol/mol)**
Baseline	7.69 ± 1.01	61 ± 11	7.23 ± 0.78	56 ± 8.5
Before study pause [‡]	7.21 ± 0.79	55 ± 8.6	6.88 ± 0.58	52 ± 6.3
After study pause [§]	7.44 ± 1.08	58 ± 11.8	6.92 ± 0.85	52 ± 9.3
End of study [‖]	7.04 ± 0.71	53 ± 7.8	6.87 ± 0.68	52 ± 7.4

***** Plus–minus values are means ± SD.

[†] Data presented only for the participants that had values for all four time points (baseline, before study pause, after study pause, and end of study)

[‡] The median (interquartile range) number of days between baseline and study pause was 46 (36, 56) for children and 43 (30, 52) for adults

[§] The duration of the pause was approximately 97 days

[‖] The median (interquartile range) number of days between end of pause and end of study was 49 (38, 59) for children and 49 (41, 63) for adults

Supplementary Table S8. Glycemic outcomes for adults (14-70 years) during the standard therapy and automated insulin delivery (AID) phases when using various glucose targets*

Glycemic Outcomes	**Standard Therapy Phase**	**AID phase target 110mg/dL**	**AID phase target 120mg/dL**	**AID phase target 130mg/dL**	**AID phase target 150mg/dL with HypoProtect on**§
Sample size, n	**128**	**121**	**54**	**9**	**68**
Mean glucose, mg/dL	161 ± 28 156 (138, 178)	151 ± 15‡ 149 (143, 160)	156 ± 18 154 (144, 164)	172 ± 33 157 (151, 201)	141 ± 19‡ 138 (128, 150)
Percent time in range, %					
<54 mg/dL	0.62 ± 1.24 0.22 (0.00, 0.77)	0.22 ± 0.28 0.16 (0.05, 0.26)‡	0.26 ± 0.42 0.11 (0.00, 0.33)‡	0.01 ± 0.01 0.00 (0.00, 0.00)‡	0.73 ± 1.05 0.23 (0.00, 1.19)
<70 mg/dL	2.89 ± 3.07 2.00 (0.63, 4.06)	1.29 ± 1.15 0.99 (0.47, 1.67)‡	1.23 ± 1.21 0.91 (0.31, 1.68)‡	0.45 ± 0.57 0.26 (0.05, 0.63)‡	3.99 ± 3.48 2.75 (1.13, 6.33)‡
70-180 mg/dL	64.7 ± 16.6 67.1 (51.3, 77.6)	75.6 ± 9.9‡ 76.9 (69.3, 82.1)	73.4 ± 12.1† 74.4 (67.5, 82.4)	63.6 ± 25.9 76.4 (40.4, 79.0)	76.3 ± 11.9‡ 79.3 (69.3, 84.9)
>180 mg/dL	32.4 ± 17.3 28.9 (17.6, 46.6)	23.1 ± 10.2‡ 21.9 (16.0, 29.8)	25.4 ± 12.3† 24.5 (17.2, 30.3)	35.9 ± 26.1 23.4 (21.0, 58.9)	19.7 ± 12.7‡ 15.4 (11.4, 26.7)
≥250 mg/dL	10.1 ± 10.5 6.6 (2.3, 15.4)	5.1 ± 4.6‡ 3.5 (1.8, 7.0)	5.8 ± 6.4‡ 3.5 (1.6, 6.4)	9.6 ± 12.3 1.4 (1.0, 20.0)	3.4 ± 4.2‡ 1.7 (0.2, 4.6)
Cumulative number of person-days	1,792	9,278	1,827	178	220

*Plus–minus values are means ± SD. Remaining values are median (IQR). IQR denotes interquartile range. Results not shown for AID target of 140mg/dL or for 150mg/dL used without HypoProtect due to low sample size (n≤2). To convert the values for glucose to millimoles per liter, multiply by 0.05551.

†Significant difference from standard therapy phase with p-value <0.05. *p*-value determined using two-sided paired t-tests.

‡Significant difference from standard therapy phase with p-value <0.05. *p*-value determined using two-sided Wilcoxon signed rank test.

§HypoProtect™ is a feature that can be enabled by the user in times of increased risk of hypoglycemia, such as exercise, which automatically increases the target to 150mg/dL (3).

Supplementary Table S9. Glycemic outcomes for children (6-13.9 years) during the standard therapy and automated insulin delivery (AID) phases when using various glucose targets*

Glycemic Outcomes	**Standard Therapy Phase**	**AID phase target 110mg/dL**	**AID phase target 120mg/dL**	**AID phase target 130mg/dL**	**AID phase target 140mg/dL**	**AID phase target 150mg/dL with HypoProtect off§**	**AID phase target 150mg/dL with HypoProtect on§**
Sample size, n	**112**	**98**	**74**	**47**	**12**	**9**	**59**
Mean glucose, mg/dL	183 ± 32 181 (163, 205)	159 ±17† 158 (147, 168)	163 ± 16‡ 163 (152, 174)	169 ± 24† 167 (154, 181)	178 ± 24† 177 (156, 203)	184 ± 24 180 (178, 189)	148 ± 27† 146 (125, 168)
Percent time in range, %							
<54 mg/dL	0.41 ± 0.83 0.10 (0.00, 0.41)	0.33 ± 0.35 0.22 (0.06, 0.49)	0.26 ± 0.31 0.18 (0.05, 0.33)	0.19 ± 0.29 0.09 (0.00, 0.21)	0.17 ± 0.27 0.04 (0.00, 0.34)	0.09 ± 0.24 0.00 (0.00, 0.00)	1.44 ± 1.77 0.81 (0.00, 2.17)‡
<70 mg/dL	2.21 ± 2.66 1.38 (0.42, 2.67)	1.85 ± 1.42 1.51 (0.76, 2.38)	1.43 ± 1.29 1.16 (0.58, 1.94)	1.24 ± 1.65 0.71 (0.26, 1.63)	0.88 ± 0.95 0.59 (0.05, 1.52)	0.32 ± 0.56 0.12 (0.00, 0.21)	6.47 ± 5.54 5.24 (2.20, 9.59)†
70-180 mg/dL	52.5 ± 15.6 52.8 (39.3, 63.2)	68.4 ± 9.1† 68.8 (63.7, 74.6)	67.5 ± 9.7† 67.3 (60.6, 74.1)	64.2 ± 14.3† 65.2 (56.1, 71.3)	59.2 ± 16.9† 56.7 (42.9, 73.3)	53.3 ± 18.2 53.3 (40.2, 63.7)	66.9 ± 13.0† 68.8 (57.8, 78.3)
>180 mg/dL	45.3 ± 16.7 44.8 (35.2, 58.9)	29.7 ± 9.6† 29.4 (22.6, 34.4)	31.1 ± 10.0† 31.2 (24.2, 38.3)	34.5 ±14.8† 34.1 (24.3, 43.3)	39.9 ± 16.6† 42.0 (26.3, 55.1)	46.4 ± 18.0 46.6 (36.3, 58.6)	26.6 ± 15.5† 24.7 (14.7, 41.1)
≥250 mg/dL	19.1 ± 13.1 15.9 (9.7, 26.3)	9.7 ± 5.8‡ 8.9 (5.3, 12.8)	10.0 ± 6.3‡ 8.7 (5.4, 13.7)	11.8 ± 9.0† 9.6 (5.1, 16.1)	14.6 ± 11.1† 11.9 (5.4, 26.4)	13.3 ± 11.9‡ 10.2 (8.1, 16.6)	8.3 ± 7.6‡ 6.3 (2.6, 12.3)
Cumulative number of person-days	1,568	6,289	2,716	941	99	73	213

*Plus–minus values are means ± SD. Remaining values are median (IQR). IQR denotes interquartile range. To convert the values for glucose to millimoles per liter, multiply by 0.05551.

†Significant difference from standard therapy phase with p-value <0.05. *p*-value determined using two-sided paired t-tests.

‡ Significant difference from standard therapy phase with p-value <0.05. *p*-value determined using two-sided Wilcoxon signed rank test.

§HypoProtect™ is a feature that can be enabled by the user in times of increased risk of hypoglycemia, such as exercise, which automatically increases the target to 150mg/dL (3).

Supplemental Table S10. Insulin requirements during the standard therapy phase and the automated delivery phase for children and adults

	Children (6 to 13.9 years) (n=112)				**Adults (14 to 70 years) (n=128)**			
Insulin Requirement	**Standard Therapy Phase**	**Automated Insulin Delivery Phase**	**Change**	***p*-value***	**Standard Therapy Phase**	**Automated Insulin Delivery Phase**	**Change**	***p*-value***
Total daily insulin (U/kg)	0.85 ± 0.24 [0.82 (0.70, 1.00)]	0.92 ± 0.25 [0.88 (0.74, 1.08)]	0.07 ± 0.16 [0.07 (-0.02, 0.15)]	<0.0001	0.61 ± 0.22 [0.58 (0.48, 0.72)]	0.59 ± 0.21 [0.53 (0.45, 0.72)]	-0.02 ± 0.11 [-0.01 (-0.07, 0.03)]	0.02
Total daily basal insulin (U/kg)	0.36 ± 0.13 [0.35 (0.28, 0.42)]	0.47 ± 0.15 [0.44 (0.37, 0.56)]	0.10 ± 0.14 [0.10 (0.01, 0.18)]	<0.0001	0.31 ± 0.11 [0.31 (0.24, 0.37)]	0.30 ± 0.11 [0.28 (0.22, 0.38)]	-0.01 ± 0.08 [-0.01 (-0.05, 0.05)]	0.4
Total daily bolus insulin (U/kg)	0.48 ± 0.18 [0.46 (0.36, 0.57)]	0.45 ± 0.13 [0.45 (0.36, 0.53)]	-0.03 ± 0.13 [-0.02 (-0.09, 0.03)]	0.0023	0.31 ± 0.16 [0.28 (0.19, 0.39)]	0.29 ± 0.12 [0.27 (0.21, 0.35)]	-0.01 ± 0.09 [0.00 (-0.06, 0.03)]	0.2

Data are shown as mean ± SD [median (IQR)]. IQR denotes interquartile range.

*p-value determined using unadjusted two-sided paired t-tests, unless otherwise specified. Two-sided Wilcoxon signed rank tests were used for total daily insulin and total daily bolus insulin in both age groups.

Supplemental Table S11. Safety outcomes during the cumulative automated insulin delivery phase[*]

	Children (6 to 13.9 years) (n=112)	**Adults (14 to 70 years) (n=128)**	**Total (6 to 70 years) (n=240)**
Event Type			
Primary Safety Outcomes (events per 100 person-years) [†]			
Severe hypoglycemia	3.6	6.0	4.8
Diabetic ketoacidosis	3.6	0.0	1.2
Hypoglycemia, number of events (% of participants) [‡]	1 (0.9)	0 (0.0)	1 (0.4)
Severe Hypoglycemia, number of events (% of participants) [§]	1 (0.9)	2 (1.6)	3 (1.3)
Diabetic Ketoacidosis, number of events (% of participants)[‖]	1 (0.9)	0 (0.0)	1 (0.4)
Hyperglycemia, number of events (% of participants) [¶]	1 (0.9)	2 (1.6)	3 (1.3)
Prolonged Hyperglycemia, number of events (% of participants) [#]	13 (10.7)	5 (3.1)	18 (6.7)
Other, number of events (% of participants) [**]	8 (7.1)	8 (6.3)	16 (6.7)

[*] Cumulative automated insulin delivery phase was calculated from the start of the automated insulin delivery phase to study pause, plus from study recommencement to the end of the phase.

[†] Rates of severe hypoglycemia and diabetic ketoacidosis from the United States T1D Exchange were 25.2 and 10.8 per 100 person-years, respectively (4; 5).

[‡] Hypoglycemia resulting in a serious adverse event but otherwise not meeting the definition of severe hypoglycemia

[§] Severe hypoglycemia requiring the assistance of another person due to altered consciousness, and requiring another person to actively administer carbohydrate, glucagon, or other resuscitative actions

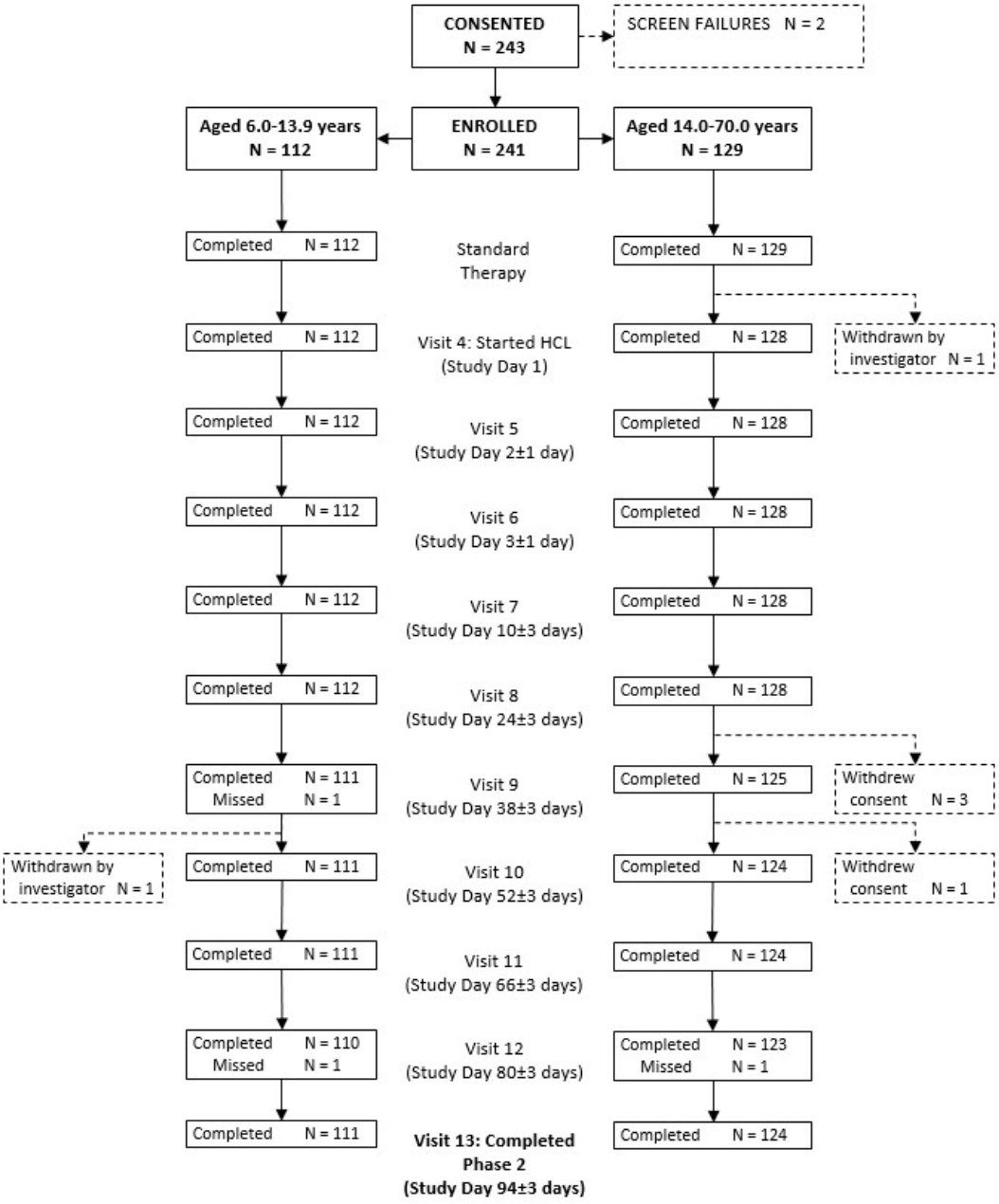
[‖] Hyperglycemia with the presence of polyuria, polydipsia, nausea or vomiting, serum ketones >1.5mmol/L or large/moderate urine ketones, either arterial blood pH <7.30, venous pH <7.24, or serum bicarbonate <15, and treatment provided in a health care facility. There was 1 additional case of diabetic ketoacidosis in a child during the study pause due to infusion site failure with their personal pump.

[¶] Hyperglycemia requiring evaluation, treatment or guidance from intervention site, or hyperglycemia resulting in a serious adverse event but otherwise not meeting the definition of DKA or prolonged hyperglycemia.

[#] Meter blood glucose measuring ≥300mg/dL and ketones >1.0mmol/L

[**] Other related, but non-glycemic adverse events included infection or irritation at infusion site (2 children, 2 adults). Other events unrelated to the study device included viral illnesses (e.g. cold and flu symptoms), a seizure disorder, gastroenteritis, chest pain, asthma, skin burn, removal of foreign body from a toe, bicycle injury, pain in arm and abnormal sensation, neck cancer.

Supplemental Figure S1. Flow of participants through the study



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