SUPPLEMENTARY DATA

Supplementary Table 1. Disposition of subjects in Stage I and Stage II.

Stage I

	Number (%) of Subjects			
	ITCA 650 20 mg/day	ITCA 650 40 mg/day	Ex-BID	Total
Randomized and received study drug in Stage I	51	51	53	155
Completed Stage I	47 (92.2)	48 (94.1)	47 (88.7)	142 (91.6)
Discontinued	4 (7.8)	3 (5.9)	6 (11.3)	13 (8.4)
Withdrew consent	2 (3.9)	1 (2.0)	2 (3.8)	5 (3.2)
Adverse event	1 (2.0)	2 (3.9)	2 (3.8)	5 (3.2)
Hyperglycemia	0	0	1 (1.9)	1 (0.6)
Elevated HbA1c	1 (2.0)	0	0	1 (0.6)
Other	0	0	1 (1.9)	1 (0.6)
Completed Stage I but not randomized to Stage II	4 (7.8)	1 (2.0)	3 (5.7)	8 (5.2)

Stage II

	Number (%) of Subjects						
	ITCA 650 20/20	ITCA 650 20/60	ITCA 650 40/40	ITCA 650 40/80	Ex-BID/ ITCA 650 40	Ex-BID/ ITCA 650 60	Total
Did not complete Stage I, randomized to Stage II but no drug given	0	0	0	0	0	1	1
Completed Stage I, randomized to Stage II, but no study drug given	2	0	0	1	0	0	3
Completed Stage I, randomized and given drug in Stage II	20	21	23	23	23	21	131
Completed Stage II	20 (100.0)	21 (100.0)	20 (87.0)	20 (87.0)	23 (100.0)	20 (95.2)	124 (94.7)
Discontinued	0	0	3 (13.0)	3 (13.0)	0	1 (4.8)	7 (5.3)
Adverse event	0	0	1 (4.3)	3 (13.0)	0	1 (4.8)	5 (3.8)
Withdrew consent	0	0	1 (4.3)	0	0	0	1 (0.8)
Other	0	0	1 (4.3)	0	0	0	1 (0.8)

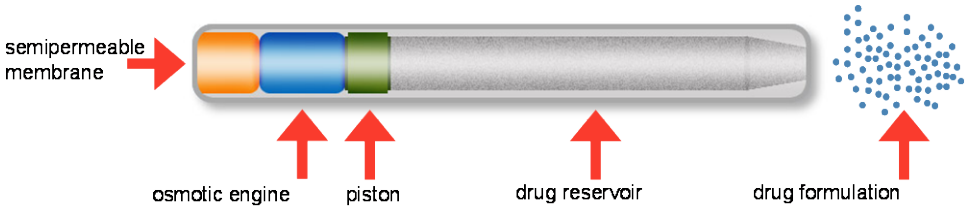
SUPPLEMENTARY DATA

Supplementary Table 2. Mean change from baseline for serum calcitonin, thyroid stimulating hormone (TSH), amylase, and lipase during Stage I and Stage II.

	Mean (SD) Change from Baseline			
	Calcitonin (pg/mL)	TSH (μIU/mL)	Amylase (U/L)	Lipase (U/L)
Stage I (0 - 12 weeks)				
ITCA 650 20 μg (n=51)	0.02 (0.892)	0.16 (0.964)	5.8 (16.27)	8.5 (35.84)
ITCA 650 40 μg (n=51)	0.14 (0.618)	0.12 (0.830)	10.5 (17.70)	19.4 (34.63)
Ex-BID (n=53)	0.31 (0.961)	-0.20 (1.100)	1.5 (24.77)	4.2 (61.77)
Stage II (12 - 24 weeks)				
ITCA 650 20/20 mg (n=20)	0.20 (1.246)	-0.02 (0.836)	3.2 (36.29)	14.4 (113.88)
ITCA 650 20/60 mg (n=21)	0.04 (0.956)	-0.29 (0.687)	1.9 (12.80)	0.8 (19.05)
ITCA 650 40/40 mg (n=23)	0.30 (1.910)	-0.18 (1.133)	2.4 (22.76)	5.2 (31.51)
ITCA 650 40/80 mg (n=23)	0.56 (2.059)	-0.34 (1.195)	-2.8 (22.42)	-11.0 (51.66)
Ex-BID/ITCA 650 40 mg (n=23)	-0.16 (0.812)	-0.10 (0.969)	2.8 (24.22)	-3.6 (58.51)
Ex-BID/ITCA 650 60 mg (n=21)	0.58 (1.732)	0.07 (0.814)	1.1 (19.16)	-3.8 (38.69)

SUPPLEMENTARY DATA

Supplementary Figure 1. ITCA 650 utilizes a novel drug delivery technology to provide continuous and controlled subcutaneous delivery of exenatide for as long as one year of treatment at a precise and predetermined rate. Initiating treatment with ITCA 650 involves the subcutaneous placement of a matchstick-size osmotic mini-pump done during a short office procedure that can be performed by a physician, physician's assistant or other licensed practitioner. The figure provides an illustration of ITCA 650. ITCA 650 consists of a cylindrical titanium alloy reservoir with external dimensions of 4 mm in diameter by 44 mm in length. The reservoir is capped at one end by a controlled-rate, semi-permeable membrane and capped at the other end by a diffusion moderator through which drug formulation is released from the drug reservoir. The drug formulation, piston and osmotic engine are contained inside the cylinder.



Schematic of ITCA 650

ITCA 650 releases drug at a predetermined rate based on the principle of osmosis. Water from the extracellular space enters through the semi-permeable membrane directly into the osmotic engine that expands to drive the piston at a slow and consistent rate of travel. Movement of the piston forces the drug formulation to be released through the orifice of the diffusion moderator.

The sterile ITCA 650 is placed in the horizontal plane subcutaneously into one of the four abdominal quadrants with a placement tool using sterile technique. The intended placement site is marked, cleaned with an antiseptic agent, draped and anesthetized. Once adequate anesthesia is achieved, a small (~5mm deep) incision is made. The tip of the cannula of the placement tool that has been loaded with the ITCA 650 is inserted into the incision. The tool is immediately leveled and advanced parallel to the surface of the skin to an indicator band on the placement tool. The cannula of the placement tool is then retracted into its handle, leaving the ITCA 650 in position directly under the skin. The incision is then closed with Steri-Strips™ and covered with a bandage.

Removal requires similar skin preparation and adherence to sterile technique as placement. The ITCA 650 is immobilized and a small (~5 mm) incision is made directly over one end of the device. The ITCA 650 is then gently pushed towards the incision and removed with a hemostat.

A new ITCA 650 can be placed in the same incision from which the old device has been removed. The incision is then closed with Steri-Strips™ and covered with a bandage.

Patients are instructed to keep the area clean and dry for 24 hours, to allow the Steri-Strips™ to fall off, and to avoid heavy lifting and strenuous physical activity for 48 hours.