

## SUPPLEMENTARY DATA

**Supplementary Table 1.** Other endpoints of interest, change from baseline at 26 and 52 weeks.

26 weeks			52 weeks			
	Dulaglutide 1.5 mg (n=269)	Dulaglutide 0.75 mg (n=270)	Metformin (n=268)	Dulaglutide 1.5 mg (n=269)	Dulaglutide 0.75 mg (n=270)	Metformin (n=268)
<b>Metabolic Parameters</b>						
Fasting insulin (pmol/L)	17.5 ± 9.7 <sup>#</sup>	35.4 ± 9.6 <sup>#</sup>	-20.5 ± 9.5	6.1 ± 9.5 <sup>#</sup>	31.5 ± 9.4 <sup>##</sup>	-23.0 ± 9.6
Fasting C-peptide (nmol/L)	0.07 ± 0.04 <sup>##</sup>	0.09 ± 0.03 <sup>##</sup>	-0.11 ± 0.03	0.06 ± 0.04 <sup>##</sup>	0.14 ± 0.04 <sup>##</sup>	-0.11 ± 0.04
Fasting proinsulin	-9.0 ± 2.1	-3.0 ± 2.1 <sup>##</sup>	-12.0 ± 2.1	-7.3 ± 2.0 <sup>#</sup>	-5.3 ± 2.0 <sup>#</sup>	-12.6 ± 2.0
HOMA2-%B	36.6 ± 3.4 <sup>##</sup>	29.0 ± 3.4 <sup>##</sup>	14.1 ± 3.4	30.0 ± 3.5 <sup>##</sup>	22.6 ± 3.5 <sup>#</sup>	9.8 ± 3.5
HOMA2-%S	0.12 ± 2.4 <sup>##</sup>	1.5 ± 2.4 <sup>#</sup>	9.1 ± 2.3	5.2 ± 2.4	2.7 ± 2.4 <sup>#</sup>	10.8 ± 2.4
Fasting proinsulin/insulin	-0.11 ± 0.03	-0.12 ± 0.03	-0.08 ± 0.03	-0.08 ± 0.02	-0.11 ± 0.02	-0.11 ± 0.02
Fasting proinsulin/C-peptide	-8.3 ± 1.2	-5.6 ± 1.2 <sup>#</sup>	-9.4 ± 1.2	-7.7 ± 1.0 <sup>#</sup>	-7.5 ± 1.0 <sup>#</sup>	-10.0 ± 1.0
Fasting glucagon (pmol/L)	-2.1 ± 0.44 <sup>##</sup>	-1.7 ± 0.44 <sup>##</sup>	0.2 ± 0.44	-2.1 ± 0.46	-2.2 ± 0.46	-1.4 ± 0.47
<b>Lipids Parameters, median % change from baseline [Q1,Q3]</b>						
Total cholesterol	-4 [-11, 5]	-2 [-10, 8]	-4 [-12, 5]	-2 [-11, 7]	-1 [-10, 8] <sup>#</sup>	-4 [-12, 6]
LDL cholesterol	-7 [-18, 8]	-3 [-15, 9] <sup>#</sup>	-9 [-20, 5]	-2 [-16, 9] <sup>#</sup>	-2 [-15, 11] <sup>#</sup>	-7 [-19, 4]
HDL cholesterol	2 [-4, 14]	4 [-6, 15]	6 [-3, 14]	5 [-5, 13]	2 [-5, 13]	4 [-7, 14]
Triglycerides	-2 [-22, 14] <sup>#</sup>	-2 [-22, 23]	3 [-16, 24]	-4 [-23, 19]	-1 [-22, 25]	2 [-22, 24]
<b>Pancreatic Enzymes, median [Q1,Q3] (U/L)</b>						
Lipase	7 [1,16] <sup>##</sup>	5 [0,13] <sup>##</sup>	1 [-4,8]	5 [-1,13] <sup>##</sup>	5 [0,12] <sup>##</sup>	1 [-4,6]
Total amylase	7 [2,13] <sup>##</sup>	6 [0,13] <sup>#</sup>	4 [-2,10]	6 [-1,13]	5 [-1,13]	4 [-2,9]
p-Amylase	5 [2,9] <sup>##</sup>	4 [1,7] <sup>##</sup>	1 [-1,5]	4 [1,7] <sup>##</sup>	3 [0,8] <sup>##</sup>	2 [-1,5]
<b>Patients with at least 1 TE abnormality (n, %)<sup>a</sup></b>						
Lipase	91 (37.6) <sup>#</sup>	76 (30.5)	61 (25.7)	109 (50.0) <sup>##</sup>	91 (41.7)	74 (34.7)
Total Amylase	28 (11.6)	24 (9.6)	14 (5.9)	34 (15.6) <sup>#</sup>	35 (16.1) <sup>#</sup>	16 (7.5)
p-Amylase	33 (13.7)	37 (14.9)	22 (9.3)	42 (19.3)	44 (20.3)	26 (12.2)
<b>Pancreatic Enzymes, n (%) of patients with &gt;3x ULN<sup>b</sup></b>						
Lipase	2 (0.9)	1 (0.4)	1 (0.5)	1 (0.5)	3 (1.5)	0 (0.0)
p-Amylase	2 (0.8)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)

<sup>a</sup>Cumulative number (%) of patients with at least one treatment emergent abnormality.

<sup>b</sup>Patients with a normal value at baseline and a value >3x ULN during the time period assessed.

All data are LS mean ± SE unless otherwise noted. <sup>#</sup> $P < 0.05$  vs metformin; <sup>##</sup> $P \leq 0.001$  vs metformin. Abbreviations: bpm = beats per minute; HOMA2-%B = updated homeostasis model beta cell function; HOMA2-%S = updated homeostasis model insulin sensitivity; p-amylase = pancreas-derived amylase; TE = treatment emergent; Q<sub>x</sub> = quartile number.

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**Supplementary Table 2.** Baseline HbA<sub>1c</sub> (%) and change from baseline in HbA<sub>1c</sub> (%) at 26 weeks in OAM-naïve patients and patients previously treated with one OAM.

	HbA <sub>1c</sub> (%)	Dulaglutide 1.5 mg	Dulaglutide 0.75 mg	Metformin	Total
No OAM	n	67	69	65	201
	Baseline	7.55 ± 0.95	7.46 ± 0.98	7.36 ± 0.71	7.46 ± 0.89
OAM	Change from baseline	-1.05 ± 0.77	-0.86 ± 0.78	-0.67 ± 0.80	-0.86 ± 0.79 <sup>#</sup>
	n	202	201	203	606
	Baseline	7.65 ± 0.90	7.62 ± 0.83	7.68 ± 0.84	7.65 ± 0.86
	Change from baseline	-0.58 ± 0.93	-0.50 ± 0.95	-0.40 ± 0.97	-0.50 ± 0.95

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**Supplementary Figure 1.** Baseline and 26 week eight-point SMPG profiles. Solid lines are baseline and dashed lines are 26 Week. ANCOVA using LOCF.

