SUPPLEMENTARY MATERIAL

Supplementary Table 1—Patient demographics and baseline clinical characteristics

Patient demographics	**Placebo (n = 187)**	**Rimonabant 20 mg (n = 179)**
Age, years	58.2±10.9	57.4±9.8
Gender, female/male, %	58.8/41.2	55.3/44.7
Race, %		
Caucasian	77.0	77.1
Black	10.7	8.9
Asian	7.5	7.8
Other	4.8	6.1
Weight, kg	95.26±20.38	97.63±21.13
Height, cm	166.62±9.91	166.91±10.06
Body mass index, kg/m^2	34.25±6.44	34.98±6.47
Waist circumference, cm	110.12±14.64	112.33±14.24
Time since diabetes diagnosis, years	15.0±8.1	13.7±7.3
Time since insulin initiation, years	6.4±5.2	5.9±4.6
HbA1c, %	9.12±1.51	9.13±1.55
FPG, mmol/l	11.03±3.77	11.40±3.68
Total daily insulin dose, U	83.46±52.57	83.56±48.56
HDL-C, mmol/l	1.32±0.40	1.32±0.32
Triglycerides, mmol/l	2.69±4.09	2.57±3.67
Total cholesterol, mmol/l	4.84±1.17	5.00±1.13
LDL-C, mmol/l	2.86±0.90	3.03±0.96
Total:HDL-C ratio	3.89±1.31	3.97±1.23

Data are mean±SD, unless otherwise stated.

Supplementary Table 2—Baseline values and changes from baseline in efficacy parameters at 48 weeks

Parameter	Placebo (n = 186)	Rimonabant 20 mg (n = 179)	P-value vs. placebo*
HbA_{1c}, %			
Week 48	8.85±1.48	8.24±1.51	
Change from baseline	-0.24±1.13	-0.89±1.34	<0.0001
Proportion of patients achieving HbA_{1c} target, %			
<7.0%	6.75	18.40	0.0012
<6.5%	1.23	8.55	0.002
FPG, mmol/l			
Week 48	10.33±3.89	9.75±3.69	
Change from baseline	-0.63±3.74	-1.85±3.82	0.0193
Total daily insulin dose, U			
Week 48	83.06±53.01	80.85±47.55	
Change from baseline	0.21±6.87	-2.71±8.57	0.0004
Proportion of patients receiving rescue medication, %	34.9	14.0	<0.0001
HDL-C, mmol/l			
Week 48	1.21±0.34	1.36±0.37	
% change from baseline	-7.14±13.39	3.14±13.49	<0.0001
Triglycerides, mmol/l			
Week 48	2.24±1.50	2.07±1.66	
% change from baseline	7.64±40.58	-3.99±52.99	0.0235
Total cholesterol, mmol/l			
Week 48	4.78±1.13	5.06±1.14	
% change from baseline	0.50±16.81	2.14±19.18	0.0888
LDL-C, mmol/l			
Week 48	2.82±0.91	3.00±0.96	
% change from baseline	3.68±37.21	1.77±26.32	0.6759
Total-cholesterol:HDL-C ratio			
Week 48	4.21±1.45	4.00±1.42	
Change from baseline	0.38±0.96	-0.01±0.98	0.0012
Body weight, kg			
Week 48	95.43±20.33	94.89±20.28	
Change from baseline	0.13±3.46	-2.49±4.01	<0.0001
Waist circumference, cm			
Week 48	109.96±14.37	109.29±13.42	
Change from baseline	-0.33±4.23	-2.95±5.47	<0.0001

*Least squares mean difference; data are mean±SD changes from baseline.

Supplementary Table 3—Patients treated for hypertension and breakdown of class of medications

	Placebo (N=187)	**Rimonabant 20 mg (N=179)**
Any concomitant medications for hypertension	152 (81.3%)	129 (72.1%)
Agents acting on the renin-angiotensin system	134 (71.7%)	112 (62.6%)
Diuretics	58 (31.0%)	57 (31.8%)
Beta blocking agents	48 (25.7%)	50 (27.9%)
Calcium channel blockers	44 (23.5%)	50 (27.9%)
Antihypertensives	7 (3.7%)	11 (6.1%)

Supplementary Table 4—Percentage of patients treated for lipid disorder

	Placebo (N=187)	**Rimonabant 20 mg (N=179)**
Lipid modifying agents	111 (59.4%)	97 (54.2%)

Supplementary Table 5—Percentage of patients receiving rescue medication

Rescue medication	**Placebo (N=186)**	**Rimonabant 20 mg (N=179)**	**P-value**
Any time during the study			
Yes	65 (34.9%)	25 (14.0%)	<0.0001
No	121 (65.1%)	154 (86.0%)	

Supplementary Table 6—Percentage of patients having insulin dose increase and or oral agents

Rescue medication	**Placebo (N=186)**	**Rimonabant 20 mg (N=179)**
	186 (100%)	179 (100%)
Yes	65 (34.9%)	25 (14.0%)
Insulin dose increase	57 (30.6%)	23 (12.8%)
Other anti-diabetic agents use	9 (4.8%)	2 (1.1%)
No	121 (65.1%)	154 (86%)

Supplementary Table 7—Day of initiation of rescue medication

Patients with introduction of rescue medication	**Placebo (N=186)**	**Rimonabant 20 mg (N=179)**
Day 1 - Day 28	8 (4.3%)	3 (1.7%)
Day 29 - Day 56	4 (2.2%)	3 (1.7%)
Day 57 - Day 84	4 (2.2%)	4 (2.2%)
Day 85 - Day 168	22 (11.8%)	4 (2.2%)
Day 169 - Day 252	17 (9.1%)	3 (1.7%)
Day 253 - Day 336	9 (4.8%)	7 (3.9%)
> Day 336	1 (0.5%)	1 (0.6%)

Supplementary Table 8—Overall incidence of treatment-emergent adverse

events (TEAEs), serious TEAEs, TEAEs leading to discontinuation, and commonly reported TEAEs

	Placebo (n = 187)	Rimonabant 20 mg (n = 179)
Overall (N [%])		
Patients with any TEAE	160 (85.6)	157 (87.7)
Patients with any serious TEAE	36 (19.3)	30 (16.8)
Death	2 (1.1)	0
Patients with any TEAE leading to discontinuation	15 (8.0)	31 (17.3)
Serious TEAEs that occurred in ≥1 of the rimonabant group		
Metabolism and nutritional disorders	3 (1.6)	4 (2.2)
Hypoglycemia	2 (1.1)	4 (2.2)
Psychiatric disorders	2 (1.1)	4 (2.2)
Depression	2 (1.1)	2 (1.1)
Post-traumatic stress disorder	0	1 (0.6)
Suicide ideation	0	1 (0.6)
Nervous system disorders	5 (2.7)	4 (2.2)
Cerebral ischemia	0	1 (0.6)
Ischemic stroke	0	1 (0.6)
Loss of consciousness	0	1 (0.6)
Presyncope	0	1 (0.6)
TEAEs that led to study discontinuation in ≥1% of any treatment group (N [%])[a]		
Psychiatric disorders	2 (1.1)	15 (8.4)
Anxiety	0	5 (2.8)
Depression	2 (1.1)	4 (2.2)
Insomnia	0	3 (1.7)
Depressed mood	0	2 (1.1)
Middle insomnia	0	2 (1.1)
Gastrointestinal disorders	2 (1.1)	9 (5.0)
Nausea	0	5 (2.8)
Nervous system disorders	3 (1.6)	8 (4.5)
Dizziness	1 (0.5)	2 (1.1)
General disorders and admin site conditions	0	4 (2.2)
Asthenia	0	2 (1.1)
TEAEs that occurred in ≥2% of patients receiving rimonabant 20 mg (N [%])		
Hypoglycemia	88 (47.1)	101 (56.4)
Anxiety	10 (5.3)	25 (14.0)
Nausea	3 (1.6)	20 (11.2)
Depression	8 (4.3)	18 (10.1)
Dizziness	15 (8.0)	18 (10.1)
Insomnia	6 (3.2)	14 (7.8)
Diarrhea	12 (6.4)	13 (7.3)
Influenza	20 (10.7)	13 (7.3)
Paresthesia	9 (4.8)	12 (6.7)
Nasopharyngitis	8 (4.3)	10 (5.6)

Headache	18 (9.6)	9 (5.0)
Fall	7 (3.7)	8 (4.5)
Depressed mood	6 (3.2)	7 (3.9)
Gastroenteritis	4 (2.1)	7 (3.9)
Vomiting	7 (3.7)	7 (3.9)
Bronchitis	9 (4.8)	6 (3.4)
Asthenia	4 (2.1)	5 (2.8)
Back pain	7 (3.7)	5 (2.8)
Fatigue	2 (1.1)	5 (2.8)
Hyperhidrosis	5 (2.7)	5 (2.8)
Muscular weakness	3 (1.6)	5 (2.8)
Neuropathy peripheral	0	5 (2.8)
Pain in extremity	3 (1.6)	5 (2.8)
Sinusitis	6 (3.2)	5 (2.8)
Muscle spasms	2 (1.1)	4 (2.2)
Panic attack	1 (0.5)	4 (2.2)
Skin ulcer	0	4 (2.2)
Upper respiratory tract infection	10 (5.3)	4 (2.2)
Vision blurred	6 (3.2)	4 (2.2)

[a]By system organ class and preferred term.

Supplementary Appendix: Scripted neurological and psychiatric questions

Neurological questions:

Since the last visit:

1. Have you had any loss of consciousness?
2. Have you had any dizziness or lightheadedness?
3. Have you had any problems seeing?
4. Have you had any problems hearing?
5. Have you had any problems with your ability to smell things?
6. Have you had any problems with your ability to taste things?
7. Have you had any problems with your ability to speak?
8. Have you had any trouble swallowing?
9. Have you had any problems with general movement?
10. Have you had any weakness of your arms or legs?
11. Have you had any numbness or tingling?
12. Have you had any problems walking?
13. Have you had any problems with your balance or coordination?

Psychiatric questions:

Since the last visit:

1. Have you had trouble falling or staying asleep, or have you awoken too early in the morning?
2. Have you been worried excessively or been anxious about several things?
3. Have you had spells or attacks when you suddenly felt anxious, frightened, or uneasy in situations where most people would not feel that way?
4. Have you had unexplained heart rate increase, sweating, or feelings of coming danger?
5. Have you felt sad, low, or depressed?
6. Have you felt a loss of energy or interest in your daily activities?

In case one or more of the above-mentioned questions is positive, add the following question:

7. Have you thought that life was not worth living or have you had urges to hurt yourself?