This report may include approved and non-approved uses, formulations, or treatment regimens. The results reported may not reflect the overall profile of a product. Before prescribing any product mentioned in this report, healthcare professionals should consult local prescribing information for the product approved in their country.

2. Synopsis

MERCK RESEARCH LABORATORIES MK-0364 taranabant, Soft Gel Capsule Prevention of Weight Regain in Obese Patients	**CLINICAL STUDY REPORT SYNOPSIS**

PROTOCOL TITLE/NO.: A Study to Assess Efficacy and Tolerability of Taranabant (MK-0364) in Maintaining Weight Loss Induced by Diet in Obese Patients Followed by a 1-Year Extension #012-10

INVESTIGATOR(S)/STUDY CENTER(S): Multicenter (35) sites: 21 sites in the US and 14 sites in 2 European countries

PRIMARY THERAPY PERIOD: 29-Nov-2006 to 14-Feb-2008; Extension study is ongoing

CLINICAL PHASE: III

DURATION OF TREATMENT: 52 Weeks

OBJECTIVE(S): **Primary**: In obese patients: (1) to compare the effects of taranabant versus placebo on weight regain and weight maintenance after low calorie diet (LCD)-induced weight loss after 52 weeks of treatment. (2) To assess the safety and tolerability of taranabant during base and extension studies. **Secondary:** In obese patients after 52 weeks of treatment: (1) To assess the proportion who maintain at least 75% of the weight loss that occurred in the LCD period. (2) To assess the proportion who maintain the loss of at least 5% of their initial (Week-6) body weight. (3) To assess the effects of taranabant on waist circumference. (4) To assess the effects of taranabant on biochemical markers, including fasting serum lipid profile, fasting plasma glucose, fasting insulin, and insulin sensitivity. (5) To assess the effects of taranabant on blood pressure. (6) To assess the effects of taranabant on quality-of-life and health economic patient-reported outcomes (PRO).

HYPOTHESES: **Primary:** In obese patients, daily administration of taranabant following low calorie diet (LCD)-induced weight loss. (1) produces less weight regain (or decreases body weight more) than treatment with placebo after 52 weeks of treatment. (2) is well tolerated. **Secondary:** (1) The proportion of obese patients who maintain at least 75% of the weight loss that occurred in the LCD period is higher in patients treated with taranabant than those treated with placebo after 52 weeks of treatment. (2) The proportion of obese patients who maintain the loss of at least 5% of their initial (Week-6) body weight is higher in patients treated with LCD followed by taranabant than those treated with LCD followed by placebo after 52 weeks of treatment.

STUDY DESIGN: Multicenter, double-blind, randomized, placebo-controlled study. The randomization ratio for this protocol was 1:1:1:1 for placebo or taranabant 0.5, 1 or 2 mg once daily for 52 weeks (plus continuing dietary/activity counseling in all groups). The duration of the study was approximately 63 weeks, with a one-week screening period, a 6-week low calorie diet (LCD) induced weight loss period that included single blind placebo during the last two weeks, a 52-week active treatment period, and a 28-day post-treatment follow up. Patients who discontinued from study drug were allowed to continue in the study off drug.

SUBJECT/PATIENT DISPOSITION:					
	Taranabant 0.5 mg N=196	Taranabant 1 mg N=196	Taranabant 2 mg N=196	Placebo N=196	Total N=784[†]
TOTAL SCREENED					1583
SCREENING FAILURES:					799
RANDOMIZED	196	196	196	196	784[†]
Female (age range)	142 (23-64)	145 (20-64)	160 (18-65)	153 (20-66)	600 (18-66)
Male (age range)	54 (25-64)	51 (22-66)	36 (20-64)	43 (25-66)	184 (20-66)
RANDOMIZED, NO TREATMENT[†]	1	0	1	2	4[†]
COMPLETED BASE STUDY	127 (65.1)	122 (62.2)	121 (62.1)	125 (64.4)	495 (63.5)
DISCONTINUED Study drug with follow-up:	22 (11.3)	27 (13.8)	35 (17.9)	17 (8.8)	101 (12.9)
Clinical adverse experience	18 (9.2)	23 (11.7)	32 (16.4)	10 (5.2)	83 (10.6)
Lack of efficacy	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
Patient moved	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.1)
Protocol deviation	2 (1.0)	1 (0.5)	2 (1.0)	2 (1.0)	7 (0.9)
Laboratory adverse experience	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.1)
Patient discontinued for other	1 (0.5)	3 (1.5)	1 (0.5)	3 (1.5)	8 (1.0)
DISCONTINUED Study drug without follow-up:	46 (23.6)	47 (24.0)	39 (20.0)	52 (26.8)	184 (23.6)
Clinical adverse experience	4 (2.1)	7 (3.6)	4 (2.1)	5 (2.6)	20 (2.6)
Lack of efficacy	2 (1.0)	3 (1.5)	0 (0.0)	2 (1.0)	7 (0.9)
Lost to follow up	16 (8.2)	15 (7.7)	7 (3.6)	16 (8.2)	54 (6.9)
Patient moved	1 (0.5)	1 (0.5)	3 (1.5)	1 (0.5)	6 (0.8)
Patient withdrew consent	16 (8.2)	18 (9.2)	21 (10.8)	24 (12.4)	79 (10.1)
Protocol deviation	2 (1.0)	2 (1.0)	1 (0.5)	2 (1.0)	7 (0.9)
Laboratory adverse experience	1 (0.5)	0 (0.0)	1 (0.5)[‡]	2 (1.0)[‡]	4 (0.5)
Patient discontinued for other	4 (2.1)	1 (0.5)	2 (1.0)	0 (0.0)	7 (0.9)

[†] There were seven hundred eighty four (784) patients randomized. [redacted]

[‡] [redacted]

This table is based on the first status data. [redacted]

DOSAGE/FORMULATION NOS.: One of 3 doses of taranabant (0.5, 1, or 2 mg) or placebo was administered orally (capsules) once daily for 52 weeks. The formulation numbers used for taranabant 0.5, 1 or 2 mg were [redacted] The formulation numbers used for matching placebo were [redacted] All formulations had the same image.

DIAGNOSIS/INCLUSION CRITERIA: Obese patients with a body mass index (BMI) between 30 kg/m^2 and 43 kg/m^2, inclusive, who were ≥18 and ≤65 years of age, had maintained a stable weight (+ 3 kg) for at least 3 months prior to study start, had lost at least 6% of initial body weight during the LCD period and who met other entry criteria were eligible to participate.

EVALUATION CRITERIA: **EFFICACY MEASUREMENTS**: Primary: Body weight. Secondary: waist circumference, fasting lipid profile (triglycerides, HDL-C, non-HDL-C, LDL-C and total cholesterol), fasting insulin and insulin sensitivity, fasting serum glucose (FPG), adiponectin, C-reactive protein, Patient-Reported-Outcomes (PRO) by questionnaires and. blood pressure. **SAFETY MEASUREMENTS**: Safety assessments included collection of adverse experiences, vital signs, and ECGs. Depression, suicidal ideation or behavior, mood, and cognitive/neuropsychomotor function were evaluated with validated questionnaires [Patient Health Questionnaire-9 (PHQ-9), Profile of Mood States Brief Form (POMSb)], and Digital Symbol Substitution Test (DSST)]. Laboratory safety assessment included blood chemistry, hematology and urinalysis. An external data safety monitoring committee (DSMC) was established to review and evaluate data across all studies in the taranabant Phase IIB/III program. Unblinded data are being provided to the DSMC every 3 to 6 months.

STATISTICAL PLANNING AND ANALYSIS:

Efficacy: The primary hypothesis was assessed by comparing the mean change from baseline in body weight at Week 52 between taranabant treatment groups and placebo using an analysis of covariance (ANCOVA) model that includes terms for treatment, region, baseline body weight, and weight change during LCD run-in. The proportion of patients who maintained at least 75% of the weight loss that occurred in the LCD period was analyzed using a logistic regression, with terms for treatment, region, baseline body weight, and weight change during LCD run-in. Comparisons between treatments were derived from the logistic model. The proportions of patients who maintained the loss of at least 5% of their initial (Week -6) body weight was analyzed similarly. Multiplicity adjustments were made for the primary and secondary efficacy hypotheses. For the primary hypothesis, if the comparison between taranabant 2 mg and placebo was significant, then the study would be declared positive from an efficacy perspective and the secondary efficacy endpoints would be assessed as well as the other comparisons associated with the primary hypothesis. For secondary efficacy hypotheses, multiplicity adjustments were made within families of endpoints using a closed testing procedure. Change (or percent change) in waist circumference, lipid parameters (HDL-C, non-HDL-C, LDL-C, TC), insulin, fasting plasma glucose, insulin sensitivity, blood pressures (systolic and diastolic), CRP, adiponectin, and patient-reported outcomes (SF-36v2, IWQoL) were analyzed using the similar ANCOVA model described for change in body weight. Percent change in triglycerides was assessed non-parametrically using Tukey's normalized scores of the percent change in triglycerides. The primary analysis population was an all-patients-treated (APT) population. The primary approach to handling missing data was the last observation carried forward (LOCF) method. For change in body weight, sensitivity analysis using repeated measures for handling missing data was performed. This study allows for following patients after having formally discontinued the test drug. Data collected after patients discontinued from treatment were not included in the primary analysis; an analysis that includes any available data collected after a patient discontinues was also performed.

With 150 patients per group this study had 90% (80%) power to detect a difference of 2.8 (2.5) kg between taranabant 2 mg or 1 mg or 0.5 mg versus placebo in weight change from baseline after 52 weeks of treatment. These calculations assume a standard deviation of 7.2 kg and a two-sided test at the 0.050 level of significance.

Safety: Safety and tolerability were assessed by a review of all safety parameters including adverse experiences (AEs), clinical and laboratory safety parameters, mood and cognition function and ECG data. A multitiered approach was used for the analysis of adverse experiences. For prespecified adverse experiences (Tier 1), inferential testing between treatment groups and the associated 95% confidence intervals were provided. For adverse experiences with an occurrence of ≥2% in 1 or more treatment groups (Tier 2), 95% confidence intervals between treatment groups were calculated. For uncommon adverse experiences (occurrence <2% in all treatment groups), tabulations are provided. The primary analysis of AEs only included those AEs that occurred on-drug or within 28 days of patient discontinuing from study therapy. For special safety endpoints constructed from DSST, POMSb and PHQ-9, analyses of change from baseline were performed via an ANCOVA model with terms similar to the model used for efficacy endpoints, with the addition of a term for the baseline safety parameter. LOCF method was used to impute missing data at Week 52. For other safety parameters, summary tabulations were provided. The number of patients exceeding predefined limits of change in key safety parameters was also evaluated.

For Tier 1 adverse experiences, when proportions of patients in each of the active treatment groups compared with placebo group were tested using Fisher's exact test and found to have a p-value that was <0.05, then the incidence is referred to as being either *"significantly higher"* or *"significantly lower."* Ninety-five percent confidence intervals were computed to help identify between-group differences that might be clinically meaningful and specific terminology was adopted for the use of 95% CI in the written text. If the 95% CI for the between-group difference excluded "0", the adverse experience was described as having a *higher or lower* incidence compared with the placebo group. Where incidences are numerically different and the 95% CI for the between-group difference included "0" or when groups were not formally compared but differences between groups might be clinically meaningful, e.g., differences between the incidences of adverse experiences in the 2-mg and 0.5-mg groups, the adverse experience was described as having a *numerically higher* or *numerically lower* incidence compared with the placebo group.

RESULTS: Efficacy: For the endpoints described in the primary and secondary hypotheses, the following table summarizes the key body weight results based on the All Patients Treated (APT) population. Following a 6-week LCD that resulted in a mean weigh loss of 9.6 kg, statistically significantly less weight regain (more weight loss) was observed in the taranabant 0.5-mg, 1-mg, and 2-mg dose groups compared to placebo at Week 52 and passed the multiplicity control. The proportions of patients who maintained at least 75% of the weight loss induced during the LCD run-in and the proportions of patients who maintained the loss of at least 5% of their initial body weight after 52 weeks of treatment in the taranabant 1-mg and 2-mg treatment groups were statistically significantly higher than the placebo group.

Change in body weight from baseline at Week 52				
Treatment	**N**	**Mean Change (SD)**	**LS Mean† Difference From Placebo (95% CI)**	**p-Value**
Taranabant 0.5 mg	188	-0.2 (7.1)	-1.8 (-3.1, -0.5)	0.007
Taranabant 1 mg	191	-0.6 (7.1)	-2.3 (-3.6, -1.0)	<0.001
Taranabant 2 mg	191	-1.3 (6.0)	-2.9 (-4.2, -1.6)	<0.001
Placebo	185	1.8 (5.9)	-	-
†: Least Squares Means based on an ANCOVA with terms for treatment, region, baseline body weight, LCD run-in weight change.				

Number (%) of patients who maintained at least ≥ 75% of the weight loss induced during LCD run-in at Week 52				
Treatment	**N**	**N (%)**	**Adjusted Odds Ratio‡ (95% CI)**	**p-Value**
Taranabant 0.5 mg	188	114 (60.6)	1.4 (0.9, 2.2)	0.088
Taranabant 1 mg	191	129 (67.5)	1.9 (1.3, 3.0)	0.002
Taranabant 2 mg	191	142 (74.3)	2.8 (1.8, 4.3)	<0.001
Placebo	185	94 (50.8)	-	-
Number (%) of patients who maintain the loss of ≥ 5% of initial (Week -6) body weight at Week 52				
Taranabant 0.5 mg	188	135 (71.8)	1.5 (1.0, 2.4)	0.074
Taranabant 1 mg	191	149 (78.0)	2.1 (1.3, 3.4)	0.003
Taranabant 2 mg	191	160 (83.8)	3.3 (2.0, 5.5)	<0.001
Placebo	185	115 (62.2)	-	-
‡: Compared to placebo and based on a logistic regression model with terms for treatment, region, baseline body weight, LCD run-in weight change.				

Body weight results at Week 52 were explored in a post-hoc analysis in the early responder and early non-responder subgroups defined by whether or not patients lost at least 1.5 kg of their baseline body weight at Week 4. The proportion of patients who were early responders was 53.7% in the 0.5-mg group, 58.2% in the 1-mg group, 64.9% in the 2-mg group, and 44.0% in the placebo group. Compared with placebo, the proportion of early responders at Week 4 was significantly higher in patients treated with taranabant 1-mg and 2-mg (Fishers exact test $p \leq 0.007$). All treatment groups including placebo in the early responders experienced mean weight loss at Week 52, whereas the early non-responders experienced mean weight gain at Week 52. In addition results from the ANCOVA model in the early responders showed a statistically significant reduction of 2.1, 2.4, and 1.8 kg from placebo in the taranabant 0.5-mg, 1-mg, and 2-mg groups. Consistent with findings of mean change in body weight, the proportion of patients who maintained at least 75% of the weight loss induced during LCD run-in in the early responders was 82.2%, 86.4%, 86.9% and 69.1% in the 0.5-mg,1-mg, 2-mg and placebo group respectively; whereas the proportion in the early non-responders was 35.6%, 43.0%, 53.0% and 36.9% in the 0.5-mg, 1-mg, 2-mg and placebo group respectively. The proportion of patients who maintained the loss of at least 5% of initial (Week -6) body weight at Week 52 in the early responders was 90.1%, 94.5%, 91.0% and 87.7% in the 0.5-mg, 1-mg, 2-mg and placebo group respectively; whereas the proportion in the early non-responders was 50.6%, 55.7%, 72.7% and 42.7% in the 0.5-mg, 1-mg, 2-mg and placebo group respectively.

Significant reductions in waist circumference from baseline at Week 52 were seen in all taranabant treatment groups compared to placebo. Compared to placebo, patients treated with taranabant 2 mg experienced statistically significant reductions in triglycerides (TG). These results are summarized in the table below. The effect of taranabant 2 mg on HDL-C, LDL-C, non-HDL-C, fasting plasma glucose, fasting plasma insulin and QUICKI did not reach statistical significance. Post-hoc analyses showed that the LS means of change from baseline in waist circumference (cm) at Week 52 in the early responders were -3.8, -5.6, -4.3 and -3.1 for the 0.5-mg, 1-mg, 2-mg and placebo groups respectively; whereas the LS means of change in the early non-responders were 1.5, 2.2, 2.1 and 3.7 for the 0.5-mg, 1-mg, 2-mg and placebo groups respectively.

Change in waist circumference from baseline at Week 52				
Treatment	**N**	**Mean Change (SD)**	**LS Mean† Difference From Placebo (95% CI)**	**p-Value**
Taranabant 0.5 mg	171	-1.6 (7.1)	-2.3 (-3.8, -0.7)	0.004
Taranabant 1 mg	180	-2.3 (8.1)	-3.0 (-4.5, -1.5)	<0.001
Taranabant 2 mg	169	-2.3 (8.3)	-3.1 (-4.6, -1.6)	<0.001
Placebo	173	0.5 (7.5)	-	-
†: Least Squares Means based on an ANCOVA with terms for treatment, region, baseline value, baseline body weight, LCD run-in weight change.				

Percent Change from Baseline	**Treatment**	**N**	**Median† Difference From Placebo (95% CI)**	**p-Value**
Triglycerides (median)	Taranabant 0.5 mg	182	-1.2 (-8.3, 6.0)	0.200
	Taranabant 1 mg	184	2.7 (-4.8, 10.2)	0.768
	Taranabant 2 mg	175	-6.5 (-13.3, 0.3)	0.012
†: Hodges-Lehmann estimate of the median difference between treatments with a corresponding distribution-free CI based on Wilcoxon's rank sum test.				

Safety: The table below summarizes the clinical adverse experiences for the 0.5-mg, 1-mg, and 2-mg and placebo groups over 52 weeks. The number (proportion) of patients with one or more clinical adverse experiences, and number of patients who had study drug discontinued due to drug-related adverse experiences, was higher in the taranabant 2-mg group compared with placebo. The incidence of drug-related adverse experiences was higher in all taranabant groups compared with placebo as shown in the table below. The incidences of serious adverse experiences were comparable across the treatment groups. The incidences of adverse experience leading to discontinuation of study drug were higher in the taranabant 1-mg and 2-mg groups compared with placebo. No deaths occurred in any treatment group. Fifteen (1.9%) patients had a laboratory adverse experience. The incidences laboratory adverse experiences and drug-related laboratory adverse experiences were comparable across treatment groups. One patient in the taranabant 0.5-mg group and one patient in the placebo group had study drug discontinued due to a laboratory adverse experience.

Clinical Adverse Experience Summary
(Treatment Phases Over 52 Weeks) All Patients as Treated Population

	Taranabant 0.5 mg (N = 195)		Taranabant 1 mg (N = 196)		Taranabant 2 mg (N = 195)		Placebo (N = 194)	
	n	(%)	n	(%)	n	(%)	n	(%)
Number (%) of patients:								
With one or more adverse experiences	161	(82.6)	162	(82.7)	172	(88.2)	157	(80.9)
With no adverse experience	34	(17.4)	34	(17.3)	23	(11.8)	37	(19.1)
With drug-related adverse experiences†	76	(39.0)	77	(39.3)	96	(49.2)	53	(27.3)
With serious adverse experiences	7	(3.6)	8	(4.1)	12	(6.2)	8	(4.1)
With serious drug-related adverse experiences	1	(0.5)	0	(0.0)	1	(0.5)	1	(0.5)
Who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Discontinued due to adverse experiences	22	(11.3)	30	(15.3)	36	(18.5)	15	(7.7)
Discontinued due to drug-related adverse experiences	17	(8.7)	23	(11.7)	26	(13.3)	13	(6.7)
Discontinued due to serious adverse experiences	2	(1.0)	4	(2.0)	5	(2.6)	1	(0.5)
Discontinued due to serious drug-related adverse experiences	1	(0.5)	0	(0.0)	1	(0.5)	1	(0.5)

† Determined by the investigator to be possibly, probably or definitely drug related.

No clinically significant changes were observed in any of the laboratory safety parameters measured, including ECG (QTc interval).

Tier I adverse experiences were prespecified based on adverse experiences that were identified in previous taranabant studies and/or deemed potentially related to the CB1R mechanism. Tier 1 adverse experiences encompass the relevant clinical adverse experiences in the Gastrointestinal (GI) Disorders, Nervous System Disorders, Psychiatric Disorders, Skin and Subcutaneous Tissue Disorders and Vascular Disorders System Organ Classes (SOCs). Tier 1 adverse experience terminology followed Medical Dictionary for Regulatory Activities (MedDRA) version 10.1. The term 'grouping' refers to MedDRA preferred terms that describe clinically related adverse experiences.

Treatment with 2-mg taranabant was associated with a significant increase in GI-related adverse experiences specifically nausea and diarrhea and a numerically higher incidence of vomiting compared with placebo. The incidence of adverse experiences in GI-related adverse experiences was comparable to placebo for the 0.5-mg and 1-mg groups. GI-related adverse experiences were predominantly mild to moderate in intensity, were mostly single episodes and were of limited duration. Despite the high incidence of GI adverse experiences (>25%), discontinuations due to GI-related adverse experiences were relatively low.

The incidences of nervous system-related adverse experiences were numerically higher in the taranabant groups compared with placebo. The incidences of the nervous system-related adverse experiences in the dizziness and motor disorder groupings were significantly higher in the taranabant 2-mg group compared with placebo. Nervous system-related adverse experiences were predominantly mild to moderate in intensity; however more patients in the taranabant groups compared with the placebo group had 2 or more episodes. Resolution of overall adverse experiences in the expanded Nervous System Disorders SOC occurred in approximately 75% of patients in the taranabant compared with approximately 90% in the placebo group. Discontinuations due to nervous system-related adverse experiences were infrequent and the incidences were comparable across the treatment groups.

The incidences of psychiatric-related adverse experiences were significantly higher in the taranabant 1-mg and 2-mg groups compared with the placebo group and numerically higher in the 0.5-mg group compared with the placebo group. Adverse experiences in the insomnia grouping and specific adverse experiences of irritability and anxiety were significantly higher in the 2-mg group compared with placebo. Adverse experiences within the Psychiatric Disorders SOC plus irritability were generally mild to moderate in intensity and predominantly single episodes. The incidence of discontinuations due to psychiatric-related adverse experiences was significantly higher in the 2-mg group compared with placebo, however more patients in the placebo group discontinued from the study due to their psychiatric related adverse experience. Resolution of the adverse experiences in the Psychiatric Disorders SOC plus irritability occurred in approximately 60% of patients by Week 52. There were 2 patients with a serious adverse experience in the taranabant 2-mg group: one of depression and one of anxiety. Neither was considered related to study drug and both patients had study drug discontinued. Both patients were experiencing concurrent psychosocial stressors. Adverse experiences of suicidal behavior or completed suicides were not reported; suicidal ideation was reported in 1 patient in the 0.5-mg group. Positive responses to PHQ-9 question 9 (which actively probes for suicidal ideation) were low and similar across treatment groups.

The overall incidences of adverse experiences within the Skin and Subcutaneous Disorders SOC minus hypoesthesia facial in the taranabant groups were comparable with placebo. The incidence of pruritis was numerically higher in the 2-mg group compared with placebo.

The overall incidences of adverse experiences within the Vascular Disorders SOC were numerically higher in the placebo group compared with the taranabant groups. The incidence of flushing, hot flush was numerically higher in the taranabant 2-mg group compared with placebo.

CONCLUSIONS: In obese patients following a low-calorie diet (LCD) induced weight loss: (1) Treatment with taranabant 0.5 mg, 1 mg, and 2 mg for 52 weeks results in statistically significantly less weight regain and statistically significant reduction in waist circumference compared with placebo. Weight loss after 4 weeks of treatment is a good predictor of Week 52 response. (2) Treatment with taranabant 1 mg and 2 mg for 52 weeks results in a statistically significantly greater proportion of patients who maintain (a) at least 75% of the weight loss induced during the LCD run-in period and (b) the loss of at least 5% of their initial body weight (Week -6) compared with placebo. (3) Treatment with taranabant 2 mg results in a statistically significant improvement in triglycerides compared with placebo at 52 weeks. (4) Treatment with taranabant 1 mg and 2 mg compared with placebo is associated with a higher incidence of psychiatric-related adverse experiences but not a higher incidence of discontinuations due to psychiatric-related adverse experiences. Treatment with taranabant 2 mg compared with placebo is associated with a higher incidence of adverse experiences in the insomnia grouping and specific adverse experiences of irritability and anxiety. The incidences of psychiatric-related adverse experiences are similar in early responders and early non-responders, and both groups have adverse experience profiles that are similar to the overall study population. (5) Treatment with taranabant 2 mg compared with placebo is associated with a higher incidence of gastrointestinal adverse experiences including specific adverse experiences of diarrhea, nausea. Treatment with taranabant 2 mg is associated with a higher incidence of specific adverse experiences, in the dizziness and motor disorder grouping (tremor). These adverse experiences are primarily mild to moderate in intensity and do not lead to discontinuation in the majority of patients. (6) Treatment with taranabant is not associated with significant laboratory safety test abnormalities compared with placebo.

AUTHORS: [redacted]