TABLE S1. Baseline Antidepressant Use[a]

	Number (%)			
ADT	**Placebo**	**ALKS 5461 2/2**	**ALKS 5461 8/8**	**Total**
Sertraline	31 (31.31)	6 (25.00)	9 (45.00)	46
Citalopram	24 (24.24)	7 (29.17)	3 (15.00)	34
Fluoxetine	12 (12.12)	5 (20.83)	4 (20.00)	21
Duloxetine	8 (8.08)	3 (12.50)	1 (5.00)	12
Escitalopram	5 (5.05)	1 (4.17)	2 (10.00)	8
Desvenlafaxine	7 (7.07)	0 (0.00)	0 (0.00)	7
Venlafaxine	5 (5.05)	2 (8.33)	0 (0.00)	7
Paroxetine	6 (6.06)	0 (0.00)	0 (0.00)	6
Buproprion	1 (1.01)	0 (0.00)	0 (0.00)	1
Total	99	24	19	142

[a] All patients continued on their current antidepressant therapy and on the same dose throughout the course of the study.

TABLE S2: Sensitivity Analysis Comparing 0.6:0.4 Weights to 0.5:0.5 Weights[a]

Assessment	Stage 1:Stage 2 Weights	Overall Study Placebo-adjusted LS Mean Change from Baseline LS Mean Difference (SE)	
		ALKS 5461 2/2	ALKS 5461 8/8
HAMD-17	0.6:0.4	-2.8 (1.2) *p*=0.014	-0.5 (1.2) *p*=0.699
	0.5:0.5	-3.0 (1.1) *p*=0.008	-0.7 (1.2) *p*=0.548
MADRS	0.6:0.4	-4.9 (1.7) *p*=0.004	-2.1 (1.8) *p*=0.233
	0.5:0.5	-5.2 (1.7) *p*=0.002	-2.2 (1.7) *p*=0.199

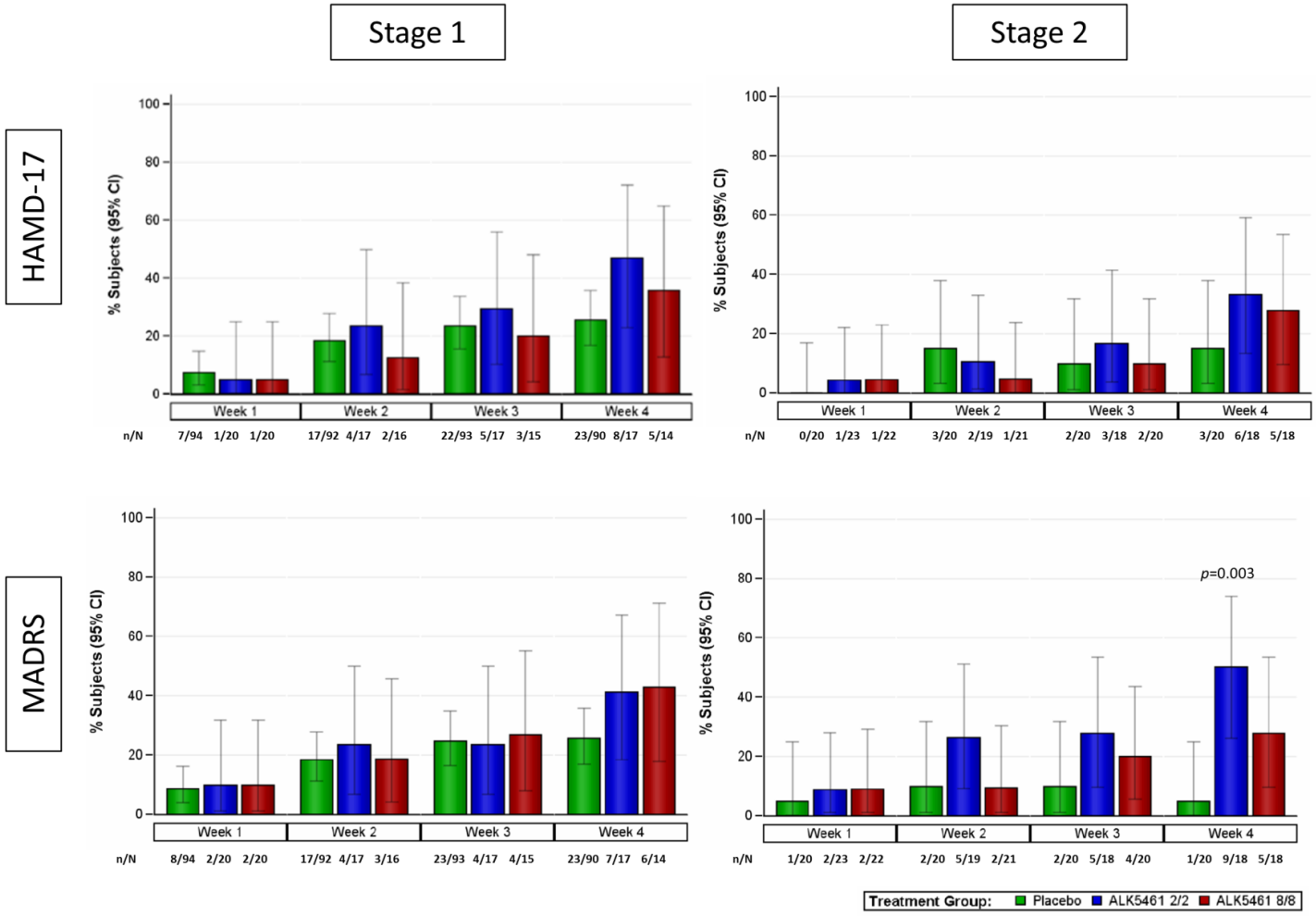
[a] Equal weights results in slightly larger treatment effects but did not affect the interpretation of results.

TABLE S3. Summary of 100 mm Visual Analogue Scale (VAS) and Addiction Research Center Inventory–Morphine Benzedrine Group (ARCI-MBG) Total Score During Treatment: Stage 1 and Stage 2 Randomized Safety Populations[a]

		VAS Total Score			ARCI-MBG Total Score		
		Treatment			Treatment		
	One hour Post-dose	**Placebo**	**ALKS 5461 2/2**	**ALKS 5461 8/8**	**Placebo**	**ALKS 5461 2/2**	**ALKS 5461 8/8**
Stage 1	Initial Dose						
	n	97	22	19	97	24	19
	Mean (SD)	49.4 (23.5)	48.6 (26.6)	53.0 (32.7)	3.3 (3.6)	5.9 (5.3)	4.8 (4.7)
	Median	50.0	50.0	50.0	2.0	4.5	3.0
	Week 1						
	n	94	18	15	94	19	15
	Mean (SD)	48.6 (25.3)	61.4 (24.8)	52.1 (30.6)	3.9 (3.7)	6.8 (4.5)	4.8 (4.6)
	Median	50.0	54.5	56.0	3.0	6.0	4.0
Stage 2	Initial Dose						
	n	20	23	21	20	23	22
	Mean (SD)	54.0 (22.5)	45.2 (25.8)	45.9 (31.0)	5.1 (5.7)	5.3 (4.9)	3.5 (4.1)
	Median	50.0	50.0	51.0	2.0	3.0	3.0
	Week 1						
	n	20	18	20	20	18	20
	Mean (SD)	61.5 (23.0)	39.6 (23.7)	42.8 (27.0)	5.6 (5.8)	5.4 (5.1)	3.5 (3.7)
	Median	50.5	45.0	47.0	2.5	5.0	2.0

[a] Summary of drug liking (100 mm VAS) and ARCI-MBG Total Score during treatment (Stage 1 and Stage 2 randomized safety populations). Generally neutral scores for Drug Liking were observed for all treatment groups (left). For the ARCI-MBG, inconsistent results were observed in Stages 1 and 2, with higher mean scores for the ALKS 5461 2 mg:2 mg group compared to the other treatment groups in Stage 1 but similar mean scores to placebo in Stage 2 (right).

FIGURE S1. HAMD-17 and MADRS Treatment Remission Rates[a]



[a] Rates are calculated as the number of patients meeting the criteria for remission (≤7 and ≤10 for HAMD-17 and MADRS, respectively) out of the total number of patients with a HAM-D17 or MADRS assessment at Week 4. Abbreviations: HAMD-17 = 17-item Hamilton Rating Scale for Depression; MADRS = Montgomery-Åsberg Depression Rating Scale.