

APPENDIX 5.1 - TABLE OF ALL STUDIES

GROUP 1 STUDIES (phase 2-3)	
Placebo-controlled, depressed patients, short-term ( $\leq$ 8 weeks)	
85A	Double-blind, randomized, parallel group, U.S.; citalopram 20-80 mg flexible x 4 weeks; outpatients with major depression or bipolar disorder, depressed; $n_c=89$ , $n_p=91$ .
91206	Double-blind, fixed dose, randomized, parallel group, U.S.; outpatients with moderate-severe depression; citalopram 10 mg (n=131), 20 mg (n=130), 40 mg (n=131), 60 mg (n=129), $n_p=129$ ; x 6 weeks.
86A	Incomplete, randomized, double-blind, parallel, U.S.; patients with major depression or bipolar disorder, depressed; citalopram 10, 20, 40, 60 mg fixed dose; n=20 each dose, $n_p=4$ ; x 4 weeks.
87A	Incomplete, randomized, double-blind, placebo- & imipramine-controls, flexible dose, x 6 weeks, U.S.; citalopram 20-80 mg, n=16 in each group.
86141	Double-blind, randomized, parallel group; citalopram 10 mg x 2 days, then 20 or 30 mg, x 6 weeks; depressed patients $\geq$ 65 with mild-moderate dementia; $n_c=98$ , $n_p=51$ .
89303	Double-blind, randomized, parallel group, fixed dose x 6 weeks; citalopram 20 mg (n=70), 40 mg (n=64), $n_p=66$ ; patients with moderate-severe depression.
89306	Double-blind, randomized, parallel group, fixed dose x 6 weeks; citalopram 20 mg (n=88), 40 mg (n=97), $n_p=89$ ; patients with moderate-severe depression
Placebo-controlled, depressed patients, long-term > 8 weeks	
89304	Initial 8-week flexible dose (20-60 mg) open phase (n=391), followed by double-blind, randomized, parallel group citalopram 20-60 mg, (fixed dose established in open phase) x 24 weeks; $n_c=152$ , $n_p=74$ .
89305	A continuation of some patients from 89303 & 89306: Placebo-control, double-blind, randomized, parallel group, fixed dose: 20 (n=48), $n_p=42$ or 40 mg (n=57), $n_p=60$ ; x 24 weeks

<b>Active-controlled, depressed patients</b>	
89422	Double-blind, randomized, parallel, x 6 weeks, fluvoxamine control (n=109); citalopram 20-40 mg, n=108; outpatients
91302	Double-blind, randomized, parallel, fixed dose x 8 weeks, fluoxetine control (n=158); citalopram 40 mg, n=158
92301	Double-blind, randomized, parallel, fixed dose x 8 weeks, fluoxetine control (n=184); citalopram 20 mg, n=173
88105	Double-blind, randomized, parallel group, imipramine-control, x 6 weeks; citalopram 10-30 mg, n=188, 20-60 mg, n=192, n <sub>i</sub> =92.
92302	Double-blind, amitriptyline-control, x 8 weeks; citalopram 20-40 mg, elderly patients; n <sub>c</sub> =179, n <sub>a</sub> =186.
93401	Ongoing double-blind, parallel, mianserin-control, x 12 weeks; citalopram 20-40 mg; elderly depressed ± dementia; n <sub>c</sub> =167, n <sub>m</sub> =178.
<b>Uncontrolled, depressed patients</b>	
8213	Open multicenter study in depressed and non-depressed patients; flexible dose (10-60 mg) for up to 12 months; n=993.
88A	Incomplete open study, includes ophthalmic evaluation, U.S.; citalopram 10-80 mg x 52 weeks; n=65
<b>Placebo-controlled, patients other than depression</b>	
91202	Double-blind, placebo- & clomipramine-controlled; panic disorder; citalopram 10-60 mg x 8 weeks; n <sub>c</sub> =283, n <sub>clom</sub> =98, n <sub>p</sub> =99; Continuation phase (up to 12 months): cit 10 or 15 mg (n=55), cit 20 or 30 mg (n=58), cit 40 or 60 mg (n=51), cit 60 or 90 mg (n=58), n <sub>p</sub> =21.
91203	Double-blind, dose-finding, x 12 weeks; Alzheimer's disease; 5 mg (n=31), 10 mg (n=28), 15 mg (n=28), 20 mg (n=30), 25 mg (n=29), 30 mg (n=28), 35 mg (n=29), 40 mg (n=30), n <sub>c</sub> (total)=233, n <sub>p</sub> =30.

**GROUP 2 STUDIES (Phase 1)****Bioequivalence/Bioavailability Studies**

90105	Single dose, two-way crossover study in 12 healthy males; oral (2 x 20 mg) and i.v. (40 mg).
83-N-0046	Single dose, two-way crossover comparison between 3 x 10 mg tablet and aqueous solution (30 mg) in 16 healthy subjects.
86112	Single dose, two-way crossover comparison (40 mg) in 14 healthy subjects.
91102	Single dose, two-way crossover comparison between 1 mL of 40 mg/mL citalopram solution and 1 x 40 mg tablet in 13 healthy subjects.
88117	Multiple dose, two-way crossover comparison between sugar-coated tablet (10 mg) and aqueous solution (40 mg/mL) in 11 depressed patients.

**Pharmacokinetics Studies (ADME)**

92103	Multiple dose (40 mg/day) for 29 days in 10 healthy subjects.
3120/816	Single p.o. dose (40 mg) with 30 $\mu$ Ci of <sup>14</sup> C-Citalopram in 4 healthy subjects.
90108	Multiple dose (40 mg/day) x 10 days in 25 volunteers, who were classified as extensive or poor metabolizers of sparteine or mephenytoin.

**Pharmacokinetics Studies; Effects of Age**

CIT-PK-01-000	Multiple dose (10 mg x 7 days, 20 mg x 7 days, and 40 mg x 21 days) study in 33 healthy elderly volunteers.
84-N-0082	Single dose (3 x 10 mg) study in 30 volunteers of different ages.
8306	Multiple dose, 20 mg study for 3-4 weeks in 11 elderly subjects with depression.

**Pharmacokinetics Studies, Special Populations**

90102	Single dose (20 mg) study in 10 subjects with impaired hepatic function.
90103	Single dose (20 mg) study in 8 subjects with impaired renal function.

**PK Studies; Drug Interaction with Food and Other Drugs**

83-N-0068	Single dose (30 mg), 3-way crossover in 15 healthy subjects that were fasting or after ingestion of high fat or non-fat meal.
93102	Multiple dose (days 1-21: 40 mg QD; days 22-29: 40 mg QD + cimetidine 400 mg BID) study in 12 healthy subjects.
94120	Multiple dose, two-way crossover study in 14 healthy subjects; 25 mg warfarin on day 15 of 21 days p.o. 40 mg citalopram.
93103	Multiple dose, 4-way crossover study in 13 healthy subjects; Day 1: 1 mg digoxin, Days 2-21: washout; Days 22 -50: 40 mg citalopram QD; Day 43: 1 mg digoxin.
95115	Multiple dose study in 17 healthy subjects ; Day 1: metoprolol 150 mg; Days 2-22: citalopram 40 mg; Day 23: metoprolol 150 mg + citalopram 40 mg.
94123	Multiple dose, two-way crossover in 16 healthy subjects; Days 1-3: carbamazine 100 mg BID; Days 4-6: CBZ 200 mg BID; Days 7-21: CBZ 400 mg CBZ; Days 22-35: CBZ 400 mg + citalopram 40 mg.
90106	Multiple dose, two-way crossover in 8 healthy subjects; Days 1-11: citalopram 40 mg; Days 12-20: washout; Days 21-25: lithium (30 mmol/day); Days 26-32: washout; Days 33-42: citalopram 40 mg/day; Days 35-39: lithium (30 mmol/day).
90107	Multiple dose, two-way crossover in 9 healthy subjects; Days 1-11: citalopram 40 mg; Days 12-24: washout; Day 25: imipramine (100 mg); Days 26-36: washout; Days 37-46: citalopram 40 mg/day; Day 43: imipramine (100 mg).
90109	Multiple dose, two-way crossover in 8 healthy subjects; Days 1-11: citalopram 40 mg; Days 12-24: washout; Day 25: levomepromazine (50 mg); Days 26-36: washout; Days 37-46: citalopram 40 mg/day; Day 43: levomepromazine (50 mg ).
84326	Multiple dose, 3-way crossover in 12 healthy subjects; citalopram: Days 1, 2, 7 (20 mg), Days 3, 4, 5, 6, 8 (40 mg); amitriptyline: Days 1, 2, 7 (37.5 mg), Days 3, 4, 5, 6, 8 (75 mg); placebo: Days 1-8: placebo 1 week washout between periods.
95103	Multiple dose study in 11 healthy subjects; 40 mg x 21 days.
7905	Citalopram: 40-60 mg QD x 4-8 weeks; During week 1, 2, and 3, nitrazepam, methotrimeprazine, and trimeprazine, respectively, were given concurrently with citalopram to 10 patients.

APPROVED FOR RELEASE  
2013

**Clinical Pharmacology Studies**

94303	Placebo- & dothiepin-controlled; 10, 20, 40 mg citalopram x 24 days; effects on psychomotor function; n=21 normal volunteers in each treatment group.
92104	Placebo-control, double-blind, multiple ascending dose, parallel group; citalopram 20-60 mg x 37 days; n=23 healthy males.
8109	Effects on psychomotor function; Part A: Single-dose, balanced-crossover, placebo- and amitriptyline-controls, double-blind; citalopram 20 mg, 40 mg; 4 single doses with 2 weeks between each treatment, n=12 healthy males. Part B: Repeated dose, balanced cross-over, double-blind, placebo- and amitriptyline-controls; citalopram 20 mg, 40 mg; 3 sequential regimens, 2 days + 7 nights, each separated by 2 weeks; n=12 healthy volunteers.
<b>Ongoing Studies</b>	
95220	Multiple dose, 4-way crossover in 12 healthy subjects, Day 1: theophylline 300 mg, Days 3-22: citalopram 40 mg, Day 23: theophylline 300 mg + 40 mg citalopram; Day 24: citalopram 40 mg.



**GROUP 3 STUDIES**

**Short-term ( $\leq$  8 weeks) placebo-controlled or placebo- and active-controlled in depressed patients**

8302	89423	8205	90A	84317					
------	-------	------	-----	-------	--	--	--	--	--

**Short-term, active-controlled in depressed patients**

93A	7902	90404	8005	94A	7901	7903	8003	8102	8207	8206	8212
8301	84327	90417	91304	95803	92413						

**Long-term ( $>8$  weeks) placebo-controlled or placebo- and active-controlled in depressed patients**

91403											
-------	--	--	--	--	--	--	--	--	--	--	--

**Long-term, active-controlled in depressed patients**

95809											
-------	--	--	--	--	--	--	--	--	--	--	--

**Dose form comparison studies in depressed patients**

8001	89418										
------	-------	--	--	--	--	--	--	--	--	--	--

**Uncontrolled, long-term studies in depressed patients**

7810	8210	88701	93429	92422	92414	89404	91410				
------	------	-------	-------	-------	-------	-------	-------	--	--	--	--

**Uncontrolled, short-term studies in depressed patients**

7601	7801	7802	7803	7806	7808	7809	7904	84315	90413	84-N-0084
8012	8104	8105	8203	8204	8307	84309	84310	89401	8101	95A 8202
89421	90406	90410	90411	90416	92421	92426	92427	92430	84315	8108 93405
93421	95812	92415	8304	92419	8106	91303	92420	94407	92432	95807 93420
7906	8010	8209	8303	89411	90413	91413	91901	92405	93408	92418 91408

APPENDIX 7.2.1.1

STUDY 85A: PRINCIPAL INVESTIGATORS	
Investigator (Center #)	Location
Joseph Mendels, M.D. (302)	Therapeutic Services, Inc. Philadelphia, PA
Ari Kiev, M.D. (202)	Social Psychiatry Research Institute, Inc. New York, NY
Louis Fabre, M.D., Ph.D. (102)	Research Testings, Inc. Houston, TX



APPENDIX 7.2.1.1.1

STUDY 85A: BASELINE DEMOGRAPHIC CHARACTERISTICS							
Treatment Groups	N	Age (Years)		Sex [N(%)]		Race [N(%)]	
		Mean	Range	Male	Female	White	Non-White
CIT	82	43.6		53 (65%)	29 (35%)	72 (88%)	10 (12%)
PLAC	87	42.9		58 (67%)	29 (33%)	78 (90%)	9 (10%)

STUDY 85A: COMPLETERS BY VISIT						
Treatment Groups	Randomized	ITT	Completers [N(%)]			
			Wk 1	Wk 2	Wk 3	Wk 4
CIT	89	82	82 (100%)	68 (83%)	54 (66%)	48 (59%)
PLAC	91	87	87 (100%)	79 (91%)	64 (74%)	51 (59%)

STUDY 85A: MEAN DOSE (mg/day) by VISIT				
Treatment Group	Wk 1	Wk 2	Wk 3	Wk 4
CIT	31.5	55.6	60.4	62.4

APPENDIX 7.2.1.1

STUDY 85A: LS MEAN CHANGE FROM BASELINE IN HAM-D TOTAL SCORE										
Treatment Group	Baseline		Week 1		Week 2		Week 3		Week 4	
	N*	Mean	N	Δ	N	Δ	N	Δ	N	Δ
LAST OBSERVATION CARRIED FORWARD ANALYSIS										
CIT	78	33.52	78	-6.42	78	-10.43	78	-12.04	78	-12.90
PLAC	82	33.72	82	-3.95	82	-6.66	82	-9.18	82	-9.58
2-sided p-values for pairwise comparisons										
C vs. P	0.7766	0.0116		0.0027		0.0565		0.0344		
OBSERVED CASES ANALYSIS										
CIT	78	33.52	75	-6.75	62	-12.42	48	-15.47	43	-18.29
PLAC	82	33.72	79	-4.13	69	-6.70	57	-11.25	42	-14.11
2-sided p-values for pairwise comparisons										
C vs. P	0.7766	0.0086		0.0001		0.0159		0.0250		

\* Four citalopram and five placebo patients were missing a HAM-D total score at baseline; they are excluded from this analysis.

APPENDIX 7.2.1.1.1

STUDY 85A: LS MEAN CHANGE FROM BASELINE IN HAM-D DEPRESSED MOOD ITEM										
Treatment Group	Baseline		Week 1		Week 2		Week 3		Week 4	
	N	Mean	N	Δ	N	Δ	N	Δ	N	Δ
LAST OBSERVATION CARRIED FORWARD ANALYSIS										
CIT	82	2.68	82	-0.68	82	-1.06	82	-1.19	82	-1.34
PLAC	87	2.71	87	-0.35	87	-0.64	87	-0.85	87	-0.85
2-sided p-values for pairwise comparisons										
C vs. P	0.7856		0.0044		0.0021		0.0234		0.0023	
OBSERVED CASES ANALYSIS										
CIT	82	2.68	80	-0.70	66	-1.17	53	-1.45	48	-1.84
PLAC	87	2.71	86	-0.35	75	-0.67	62	-1.06	50	-1.29
2-Sided p-values for pairwise comparisons										
C vs. P	0.7856		0.0026		0.0006		0.0240		0.0024	

APPENDIX 7.2.1.1.1

STUDY 85A: LS MEAN CHANGE FROM BASELINE IN CGI SEVERITY SCORE											
Treatment Group	Baseline		Week 1		Week 2		Week 3		Week 4		
	N*	Mean	N	Δ	N	Δ	N	Δ	N	Δ	
LAST OBSERVATION CARRIED FORWARD ANALYSIS											
CIT	81	3.61	81	-0.38	81	-0.74	81	-0.87	81	-0.94	
PLAC	87	3.61	87	-0.23	87	-0.40	87	-0.63	87	-0.68	
2-sided p-values for pairwise comparisons											
C vs. P	0.9841		0.0824		0.0024		0.0650		0.0508		
OBSERVED CASES ANALYSIS											
CIT	81	3.61	79	-0.39	63	-0.92	51	-1.09	47	-1.32	
PLAC	87	3.61	85	-0.23	75	-0.40	61	-0.81	51	-0.98	
2-Sided p-values for pairwise comparisons											
C vs. P	0.9841		0.0734		0.0001		0.0645		0.0373		

\* One citalopram patient was missing a CGI severity score at baseline and is excluded from this analysis.

APPENDIX 7.2.1.1.1

Study 85A: LS Mean Change from Baseline in HAM-D Retardation Factor							
	Baseline		Week 4 (LOCF)		Week 4 (OC)		
	N	Mean	N	Mean Δ	N	Mean Δ	p-value (vs. plac)
CIT	82	7.90	82	-3.30	48	-4.52	0.014
Placebo	86	7.80	86	-2.10	50	-3.32	-

Study 85A: LS Mean Change from Baseline in HAM-D Cognitive Disturbance Factor							
	Baseline		Week 4 (LOCF)		Week 4 (OC)		
	N	Mean	N	Mean Δ	N	Mean Δ	p-value (vs. plac)
CIT	82	5.75	82	-2.35	48	-3.19	0.014
Placebo	86	6.21	86	-1.73	50	-2.36	-

Study 85A: LS Mean Change from Baseline in HAM-D Sleep Disturbance Factor							
	Baseline		Week 4 (LOCF)		Week 4 (OC)		
	N	Mean	N	Mean Δ	N	Mean Δ	p-value (vs. plac)
CIT	82	3.82	82	-1.84	48	-2.64	0.028
Placebo	86	4.14	86	-1.25	50	-1.86	-

APPENDIX 7.2.1.2

STUDY 91206: PRINCIPAL INVESTIGATORS	
Investigator(s) (Center #)	Location
Jeffrey T. Apter, M.D. (1)	Princeton, N.J.
Richard L. Borison, M.D., Ph.D. (2)	Columbia, S.C.
William J. Burke, M.D. (3)	Omaha, NE
John S. Carman, M.D. (4)	Atlanta, GA
Lynn A. Cunningham, M.D. (5)	Springfield, IL
Louis Fabre, M.D. (6)	Houston, TX
John P. Feighner, M.D. (7)	San Diego, CA
Ronald R. Fieve, M.D. (8)	New York, NY
James Halikas, M.D. (9)	Minneapolis, MN
Carl A. Houck, M.D. (10)	Birmingham, AL
Peter B. Lucas, M.D. (11)	Northridge, CA
Ram K. Shrivastava, M.D. (12)	New York, NY

APPENDIX 7.2.1.1.2

STUDY 91206: BASELINE DEMOGRAPHIC CHARACTERISTICS							
Treatment Groups	N	Age (years)		Sex [N(%)]		Race [N(%)]	
		Mean	Range	Male	Female	White	Non-White
CIT 10mg	123	39.4		44 (36%)	79 (64%)	108 (88%)	15 (12%)
CIT 20mg	128	39.5		44 (34%)	84 (66%)	117 (91%)	11 (9%)
CIT 40mg	120	39.8		48 (40%)	72 (60%)	108 (90%)	12 (10%)
CIT 60mg	110	39.5		53 (48%)	57 (52%)	99 (90%)	11 (10%)
PLAC	124	38.4		54 (44%)	70 (56%)	104 (84%)	20 (16%)

STUDY 91206: COMPLETERS BY VISIT									
Treatment Groups	Randomized	ITT	Completers [N(%)]						
			Wk 1	Wk 2	Wk 3	Wk 4	Wk 5	Wk 6	
CIT 10mg	131	123	123 (100%)	120 (98%)	112 (91%)	103 (84%)	96 (78%)	95 (77%)	
CIT 20mg	130	128	128 (100%)	115 (90%)	109 (85%)	103 (80%)	95 (74%)	91 (71%)	
CIT 40mg	131	120	120 (100%)	108 (90%)	107 (89%)	102 (85%)	97 (81%)	92 (77%)	
CIT 60mg	129	110	110 (100%)	107 (97%)	97 (88%)	88 (80%)	82 (75%)	79 (72%)	
PLAC	129	124	124 (100%)	118 (95%)	116 (94%)	107 (86%)	98 (79%)	88 (71%)	

APPENDIX 7.2.1.2

STUDY 91206: LS MEAN CHANGE FROM BASELINE IN HAM-D TOTAL SCORE														
Treatment Group	Baseline		Wk 1		Week 2		Week 3		Week 4		Week 5		Week 6	
	N	Mean	N	Δ	N	Δ	N	Δ	N	Δ	N	Δ	N	Δ
LAST OBSERVATION CARRIED FORWARD ANALYSIS														
CIT 10mg	123	24.98	123	-4.41	123	-7.24	123	-8.66	123	-9.64	123	-10.42	123	-10.78
CIT 20mg	128	24.24	128	-4.11	128	-6.19	128	-8.08	128	-8.85	128	-9.60	128	-9.94
CIT 40mg	120	24.44	120	-4.27	120	-6.89	120	-9.34	120	-10.19	120	-11.34	120	-12.22
CIT 60mg	110	24.52	110	-4.22	110	-6.22	110	-8.76	110	-10.34	110	-11.15	110	-12.05
PLACEBO	124	24.62	124	-4.20	124	-6.44	124	-8.36	124	-8.65	124	-9.20	124	-9.31
2-sided p-values for pairwise comparisons														
10mg vs. P	0.3661		0.7181		0.2612		0.7117		0.2459		0.1875		0.1238	
20mg vs. P	0.3498		0.8904		0.7186		0.7333		0.8165		0.6631		0.5064	
40mg vs. P	0.6584		0.8962		0.5281		0.2309		0.0740		0.0223		0.0025	
60mg vs. P	0.8163		0.8866		0.7174		0.6345		0.0549		0.0415		0.0053	



APPENDIX 7.2.1.1.2

STUDY 91206: LS MEAN CHANGE FROM BASELINE IN HAM-D TOTAL SCORE														
Treatment Group	Baseline		Wk 1		Week 2		Week 3		Week 4		Week 5		Week 6	
	N	Mean	N	Δ	N	Δ	N	Δ	N	Δ	N	Δ	N	Δ
OBSERVED CASES ANALYSIS														
CIT 10mg	123	24.98	122	-4.42	116	-7.44	106	-9.51	101	-10.97	92	-12.86	89	-13.16
CIT 20mg	128	24.24	126	-4.14	113	-6.22	104	-8.48	104	-9.38	92	-10.76	87	-11.30
CIT 40mg	120	24.44	118	-4.33	108	-7.31	107	-9.87	100	-11.24	94	-12.79	86	-13.90
CIT 60mg	110	24.52	106	-4.22	100	-6.54	95	-9.21	90	-10.78	80	-12.15	76	-13.52
PLACEBO	124	24.62	119	-4.34	117	-6.54	112	-8.61	104	-9.38	92	-10.99	85	-11.91
2-sided p-values for pairwise comparisons														
10mg vs. P	0.3661		0.8979		0.2148		0.2837		0.0749		0.0564		0.2129	
20mg vs. P	0.3498		0.7323		0.6581		0.8849		0.9940		0.8169		0.5456	
40mg vs. P	0.6584		0.9821		0.2981		0.1325		0.0368		0.0658		0.0504	
60mg vs. P	0.8163		0.8376		0.9983		0.4875		0.1262		0.2552		0.1261	

APPENDIX 7.2.1.2

STUDY 91206: LS MEAN CHANGE FROM BASELINE IN HAM-D DEPRESSED MOOD ITEM														
Treatment Group	Baseline		Wk 1		Week 2		Week 3		Week 4		Week 5		Week 6	
	N	Mean	N	Δ	N	Δ	N	Δ	N	Δ	N	Δ	N	Δ
LAST OBSERVATION CARRIED FORWARD ANALYSIS														
CIT 10mg	123	2.93	123	-0.59	123	-0.99	123	-1.18	123	-1.31	123	-1.39	123	-1.46
CIT 20mg	128	2.86	128	-0.59	128	-0.97	128	-1.18	128	-1.27	128	-1.32	128	-1.38
CIT 40mg	120	2.86	120	-0.67	120	-0.96	120	-1.28	120	-1.40	120	-1.57	120	-1.61
CIT 60mg	110	2.88	110	-0.64	110	-1.04	110	-1.31	110	-1.54	110	-1.56	110	-1.71
PLACEBO	124	2.85	124	-0.43	124	-0.72	124	-0.95	124	-1.06	124	-1.04	124	-1.03
2-sided p-values for pairwise comparisons														
10mg vs. P	0.2205		0.1059		0.0239		0.0622		0.0660		0.0135		0.0031	
20mg vs. P	0.8987		0.0938		0.0345		0.0589		0.1029		0.0481		0.0155	
40mg vs. P	0.9940		0.0153		0.0417		0.0077		0.0116		0.0010		0.0010	
60mg vs. P	0.7346		0.0431		0.0091		0.0045		0.0010		0.0010		0.0010	

APPENDIX 7.2.1.1.2

STUDY 91206: LS MEAN CHANGE FROM BASELINE IN HAM-D DEPRESSED MOOD ITEM														
Treatment Group	Baseline		Wk 1		Week 2		Week 3		Week 4		Week 5		Week 6	
	N	Mean	N	Δ	N	Δ	N	Δ	N	Δ	N	Δ	N	Δ
OBSERVED CASES ANALYSIS														
CIT 10mg	123	2.93	121	-0.60	116	-1.05	109	-1.24	102	-1.48	94	-1.72	95	-1.81
CIT 20mg	128	2.86	126	-0.60	114	-0.96	106	-1.21	103	-1.29	92	-1.49	91	-1.55
CIT 40mg	120	2.86	114	-0.70	106	-1.03	106	-1.41	101	-1.57	93	-1.81	92	-1.84
CIT 60mg	110	2.88	108	-0.64	103	-1.06	92	-1.39	86	-1.65	79	-1.72	79	-1.93
PLACEBO	124	2.85	121	-0.44	115	-0.77	112	-1.02	102	-1.20	96	-1.31	88	-1.35
2-sided p-values for pairwise comparisons														
10mg vs. P	0.2205		0.1169		0.0175		0.0775		0.0467		0.0062		0.0025	
20mg vs. P	0.8987		0.1172		0.1022		0.1471		0.5132		0.2244		0.2024	
40mg vs. P	0.9940		0.0149		0.0297		0.0023		0.0108		0.0010		0.0017	
60mg vs. P	0.7346		0.0559		0.0171		0.0049		0.0029		0.0090		0.0010	

APPENDIX 7.2.1.1.2

STUDY 91206: LS MEAN CHANGE FROM BASELINE IN MADRS TOTAL SCORE															
Treatment Group	Baseline		Wk 1		Week 2		Week 3		Week 4		Week 5		Week 6		
	N	Mean	N	Δ	N	Δ	N	Δ	N	Δ	N	Δ	N	Δ	
LAST OBSERVATION CARRIED FORWARD ANALYSIS															
CIT 10mg	123	27.41	123	-4.33	123	-7.26	123	-8.85	123	-10.56	123	-11.20	123	-11.79	
CIT 20mg	127	26.78	127	-3.84	127	-5.72	127	-8.41	127	-9.74	127	-10.54	127	-11.02	
CIT 40mg	120	27.52	120	-4.34	120	-7.00	120	-9.95	120	-11.35	120	-13.09	120	-13.53	
CIT 60mg	110	27.21	110	-4.36	110	-7.20	110	-10.05	110	-11.66	110	-12.59	110	-13.74	
PLACEBO	124	26.94	124	-3.86	124	-6.38	124	-8.23	124	-9.10	124	-9.39	124	-9.36	
2-sided p-values for pairwise comparisons															
10mg vs. P	0.4643	0.5288	0.3349	0.5505	0.1919	0.1304	0.0525								
20mg vs. P	0.8002	0.9778	0.4633	0.8600	0.5637	0.3302	0.1798								
40mg vs. P	0.3709	0.5194	0.5015	0.1006	0.0452	0.0022	0.0010								
60mg vs. P	0.6825	0.5151	0.3832	0.0891	0.0260	0.0097	0.0010								

APPENDIX 7.2.1.1.2

STUDY 91206: LS MEAN CHANGE FROM BASELINE IN MADRS TOTAL SCORE														
Treatment Group	Baseline		Wk 1		Week 2		Week 3		Week 4		Week 5		Week 6	
	N	Mean	N	Δ	N	Δ	N	Δ	N	Δ	N	Δ	N	Δ
OBSERVED CASES ANALYSIS														
CIT 10mg	123	27.41	121	-4.38	116	-7.85	109	-9.77	102	-12.47	94	-14.23	95	-15.05
CIT 20mg	127	26.78	125	-3.87	113	-5.75	105	-8.72	101	-10.31	91	-12.06	90	-12.55
CIT 40mg	120	27.52	114	-4.57	106	-7.54	106	-10.77	101	-12.57	93	-15.13	92	-15.44
CIT 60mg	110	27.21	108	-4.39	103	-7.41	92	-10.91	85	-12.64	79	-13.75	79	-15.42
PLACEBO	124	26.94	121	-3.94	115	-6.80	112	-8.82	102	-10.10	96	-11.48	88	-12.41
2-sided p-values for pairwise comparisons														
10mg vs. P	0.4643		0.5546		0.2483		0.3734		0.0416		0.0252		0.0478	
20mg vs. P	0.8002		0.9278		0.2551		0.9268		0.8557		0.6428		0.9198	
40mg vs. P	0.3709		0.4094		0.4323		0.0701		0.0352		0.0032		0.0250	
60mg vs. P	0.6825		0.5597		0.5180		0.0616		0.0382		0.0772		0.0319	

APPENDIX 7.2.1.2

STUDY 91206: LS MEAN CHANGE FROM BASELINE IN CGI SEVERITY SCORE														
Treatment Group	Baseline		Wk 1		Week 2		Week 3		Week 4		Week 5		Week 6	
	N	Mean	N	Δ	N	Δ	N	Δ	N	Δ	N	Δ	N	Δ
LAST OBSERVATION CARRIED FORWARD ANALYSIS														
CIT 10mg	123	3.28	123	-0.29	123	-0.59	123	-0.67	123	-0.77	123	-0.82	123	-0.90
CIT 20mg	128	3.21	128	-0.26	128	-0.52	128	-0.73	128	-0.73	128	-0.83	128	-0.81
CIT 40mg	120	3.30	120	-0.28	120	-0.55	120	-0.75	120	-0.91	120	-0.99	120	-1.05
CIT 60mg	110	3.21	110	-0.31	110	-0.47	110	-0.72	110	-0.85	110	-0.90	110	-1.00
PLACEBO	124	3.27	124	-0.32	124	-0.52	124	-0.70	124	-0.75	124	-0.80	124	-0.84
2-sided p-values for pairwise comparisons														
10mg vs. P	0.8260		0.6937		0.3418		0.7579		0.8167		0.8391		0.6089	
20mg vs. P	0.1830		0.3635		0.9799		0.6989		0.8624		0.7596		0.7428	
40mg vs. P	0.5869		0.5568		0.6740		0.5612		0.0638		0.0557		0.0490	
60mg vs. P	0.2150		0.9047		0.4987		0.7483		0.2534		0.3471		0.1317	

APPENDIX 7.2.1.2

STUDY 91206: LS MEAN CHANGE FROM BASELINE IN CGI SEVERITY SCORE														
Treatment Group	Baseline		Wk 1		Week 2		Week 3		Week 4		Week 5		Week 6	
	N	Mean	N	Δ	N	Δ	N	Δ	N	Δ	N	Δ	N	Δ
OBSERVED CASES ANALYSIS														
CIT 10mg	123	3.28	121	-0.30	116	-0.64	109	-0.73	102	-0.90	94	-1.06	95	-1.17
CIT 20mg	128	3.21	126	-0.26	114	-0.53	106	-0.78	103	-0.78	92	-0.96	91	-0.91
CIT 40mg	120	3.30	114	-0.30	106	-0.58	106	-0.80	101	-1.00	93	-1.15	92	-1.19
CIT 60mg	110	3.21	108	-0.31	103	-0.47	92	-0.78	86	-0.90	79	-0.97	79	-1.13
PLACEBO	124	3.27	121	-0.33	115	-0.54	112	-0.74	102	-0.83	96	-0.98	88	-1.07
2-sided p-values for pairwise comparisons														
10mg vs. P	0.8260		0.6336		0.1941		0.9418		0.4557		0.4237		0.3755	
20mg vs. P	0.1830		0.3227		0.9351		0.6404		0.6298		0.8559		0.1672	
40mg vs. P	0.5896		0.6606		0.6182		0.4869		0.0672		0.1118		0.2896	
60mg vs. P	0.2150		0.8279		0.4078		0.6557		0.4781		0.9710		0.6093	

APPENDIX 7.2.1.2

STUDY 91206: LS MEAN CHANGE FROM BASELINE IN CGI IMPROVEMENT SCORE													
Treatment Group	Wk 1		Week 2		Week 3		Week 4		Week 5		Week 6		
	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean	
LAST OBSERVATION CARRIED FORWARD ANALYSIS													
CIT 10mg	122	3.33	123	2.98	123	2.79	123	2.59	123	2.54	123	2.48	
CIT 20mg	126	3.37	128	3.07	128	2.76	128	2.69	128	2.52	128	2.45	
CIT 40mg	117	3.33	120	2.95	120	2.60	120	2.41	120	2.26	120	2.14	
CIT 60mg	107	3.40	109	3.08	110	2.68	110	2.46	110	2.36	110	2.24	
PLACEBO	119	3.35	124	3.09	124	2.81	124	2.74	124	2.70	124	2.66	
2-sided p-values for pairwise comparisons													
10mg vs. P	0.9155		0.3767		0.8489		0.2942		0.2922		0.2179		
20mg vs. P	0.8325		0.8828		0.6880		0.7388		0.2330		0.1556		
40mg vs. P	0.8588		0.2450		0.1165		0.0228		0.0036		0.0010		
60mg vs. P	0.6270		0.9760		0.3380		0.0622		0.0270		0.0067		



APPENDIX 7.2.1.2

STUDY 91206: LS MEAN CHANGE FROM BASELINE IN CGI IMPROVEMENT SCORE													
Treatment Group	Wk 1		Week 2		Week 3		Week 4		Week 5		Week 6		
	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean	
OBSERVED CASES ANALYSIS													
CIT 10mg	122	3.33	116	2.93	107	2.62	101	2.36	92	2.16	89	2.11	
CIT 20mg	126	3.37	113	3.06	104	2.68	104	2.59	92	2.31	87	2.22	
CIT 40mg	117	3.33	108	2.88	106	2.49	100	2.24	94	2.01	88	1.87	
CIT 60mg	107	3.40	101	3.03	95	2.63	90	2.40	81	2.20	76	2.04	
PLACEBO	119	3.35	117	3.06	112	2.74	104	2.59	93	2.39	85	2.20	
2-sided p-values for pairwise comparisons													
10mg vs. P	0.9155		0.2916		0.3808		0.1128		0.1429		0.5546		
20mg vs. P	0.8325		0.9596		0.6898		0.9860		0.6283		0.8948		
40mg vs. P	0.8588		0.1552		0.0628		0.0167		0.0153		0.0394		
60mg vs. P	0.6270		0.8384		0.4302		0.2085		0.2473		0.3228		

APPENDIX 7.2.1.1.2

Study 91206: Summary of Efficacy Results Excluding Center #2			
	Mean Drug/Placebo $\Delta$	P-value for Drug/Placebo $\Delta$ (Parametric)	P-value for Drug/Placebo $\Delta$ (Non-parametric)
HAM-D Total Score (Week 6, LOCF)			
CIT 10mg	-1.624	0.072	0.051
CIT 20mg	-1.233	0.281	0.247
CIT 40mg	-3.312	0.001	0.001
CIT 60mg	-2.775	0.005	0.006
MADRS Total Score (Week 6, LOCF)			
CIT 10mg	-2.647	0.026	0.024
CIT 20mg	-2.409	0.053	0.086
CIT 40mg	-4.249	0.000	0.000
CIT 60mg	-3.934	0.001	0.002

APPENDIX 7.2.1.2

Study 91206: LS Mean Change from Baseline in HAM-D Retardation Factor									
	Baseline			Week 6 (LOCF)			Week 6 (OC)		
	N	Mean	N	Mean Δ	p-value (vs. plac)	N	Mean Δ	p-value (vs. plac)	
CIT 10mg	123	8.09	123	-3.62	0.025	89	-4.58	0.031	
CIT 20mg	128	7.95	128	-3.46	0.069	87	-3.97	0.556	
CIT 40mg	120	8.03	120	-4.12	0.001	86	-4.59	0.031	
CIT 60mg	110	8.02	110	-3.98	0.002	76	-4.58	0.037	
Placebo	124	8.02	124	-2.81	-	85	-3.74	-	

Study 91206: LS Mean Change from Baseline in HAM-D Cognitive Disturbance Factor									
	Baseline			Week 6 (LOCF)			Week 6 (OC)		
	N	Mean	N	Mean Δ	p-value (vs. plac)	N	Mean Δ	p-value (vs. plac)	
CIT 10mg	123	5.33	123	-2.62	0.316	89	-3.28	0.234	
CIT 20mg	128	5.38	128	-2.54	0.480	87	-2.87	0.770	
CIT 40mg	120	5.16	120	-3.25	0.001	86	-3.46	0.069	
CIT 60mg	110	5.50	110	-3.31	0.001	76	-3.58	0.0297	
Placebo	124	5.40	124	-2.36	-	85	-2.95	-	

**APPENDIX 7.2.1.3**

<b>STUDY 86141: PRINCIPAL INVESTIGATORS</b>	
<b>Investigator (Center #)</b>	<b>Location</b>
Jorgen Gylding-Sabroe, M.D. (1)	Charlottenlund, Denmark
Harald A. Nygaard, M.D. (2)	Fyllingsdalen, Norway
Hedvig-Elisabeth Refsum, M.D. (3)	Lier, Norway
Einer Ofsti, M.D. (4)	Brumunddal, Norway
C.G. Gottfries, M.D. (5)	Gothenburg, Sweden
Sture Eriksson, M.D. (6)	Umea, Sweden
Steinar Syversen, M.D. (7)	Jonkoping, Sweden

<b>STUDY 86141: BASELINE DEMOGRAPHIC CHARACTERISTICS</b>					
Treatment Groups	N	Age (years)		Sex [N(%)]	
		Mean	Range	Male	Female
CIT	98	76.8		30 (31%)	68 (69%)
PLAC	51	77.4		14 (27%)	37 (73%)

<b>STUDY 86141: COMPLETERS by VISIT</b>					
Treatment Groups	Randomized	ITT	Completers [N(%)]		
			Wk 2	Wk 4	Wk 6
CIT	98	97	97 (100%)	90 (93%)	64 (66%)
PLAC	51	50	50 (100%)	48 (96%)	38 (76%)

<b>STUDY 86141: MEAN DOSE (mg/day) by VISIT</b>			
Treatment Group	Wk 2	Wk 4	Wk 6
CIT	20	23	24

**APPENDIX 7.2.1.3**

<b>STUDY 86141: MEAN CHANGE FROM BASELINE IN HAM-D TOTAL SCORE</b>								
Treatment Group	Baseline		Week 2		Week 4		Week 6	
	N	Mean	N	Δ	N	Δ	N	Δ
<b>LAST OBSERVATION CARRIED FORWARD ANALYSIS</b>								
CIT	97	22.24	97	-2.41	97	-5.22	97	-6.32
PLAC	50	21.00	50	-3.16	50	-4.94	50	-4.94
<b>2-sided p-values for pairwise comparisons</b>								
C vs. P	0.277		0.374		0.815		0.316	
<b>OBSERVED CASES ANALYSIS</b>								
CIT	97	22.24	95	-2.46	89	-5.69	64	-9.61
PLAC	50	21.00	49	-3.22	46	-5.22	37	-6.19
<b>2-Sided p-values for pairwise comparisons</b>								
C vs. P	0.277		0.374		0.709		0.036	

<b>STUDY 86141: MEAN CHANGE FROM BASELINE IN HAM-D DEPRESSED MOOD ITEM</b>								
Treatment Group	Baseline		Week 2		Week 4		Week 6	
	N	Mean	N	Δ	N	Δ	N	Δ
<b>LAST OBSERVATION CARRIED FORWARD ANALYSIS</b>								
CIT	97	2.70	97	-0.44	97	-0.80	97	-0.91
PLAC	50	2.56	50	-0.42	50	-0.86	50	-0.70
<b>2-sided p-values for pairwise comparisons</b>								
C vs. P	0.261		0.865		0.764		0.323	
<b>OBSERVED CASES ANALYSIS</b>								
CIT	97	2.70	95	-0.45	89	-0.87	64	-1.38
PLAC	50	2.56	49	-0.43	46	-0.89	38	-0.84
<b>2-Sided p-values for pairwise comparisons</b>								
C vs. P	0.261		0.864		0.895		0.029	

**APPENDIX 7.2.1.3**

<b>STUDY 86141: MEAN CHANGE FROM BASELINE IN MADRS TOTAL SCORE</b>								
Treatment Group	Baseline		Week 2		Week 4		Week 6	
	N	Mean	N	Δ	N	Δ	N	Δ
<b>LAST OBSERVATION CARRIED FORWARD ANALYSIS</b>								
CIT	97	26.59	97	-3.98	97	-7.14	97	-8.57
PLAC	50	23.86	50	-3.80	50	-6.60	50	-6.54
<b>2-sided p-values for pairwise comparisons</b>								
C vs. P	0.111		0.885		0.756		0.313	
<b>OBSERVED CASES ANALYSIS</b>								
CIT	97	26.59	95	-4.06	89	-7.70	64	-12.94
PLAC	50	23.86	49	-3.88	46	-6.74	36	-8.56
<b>2-Sided p-values for pairwise comparisons</b>								
C vs. P	0.111		0.883		0.609		0.072	

<b>STUDY 86141: MEAN CHANGE FROM BASELINE IN CGI SEVERITY SCORE</b>								
Treatment Group	Baseline		Week 2		Week 4		Week 6	
	N	Mean	N	Δ	N	Δ	N	Δ
<b>LAST OBSERVATION CARRIED FORWARD ANALYSIS</b>								
CIT	97	3.23	97	-0.12	97	-0.40	97	-0.56
PLAC	50	3.12	50	-0.14	50	-0.34	50	-0.40
<b>2-sided p-values for pairwise comparisons</b>								
C vs. P	0.393		0.877		0.660		0.307	
<b>OBSERVED CASES ANALYSIS</b>								
CIT	97	3.23	95	-0.13	90	-0.44	64	-0.84
PLAC	50	3.12	50	-0.14	47	-0.36	38	-0.55
<b>2-Sided p-values for pairwise comparisons</b>								
C vs. P	0.393		0.897		0.577		0.124	

APPENDIX 7.2.1.4

STUDY 89303: PRINCIPAL INVESTIGATORS	
Investigator(s) (Center #)	Location
A. H. Mahmood, M.D. Al-Bachari, M.D. (1)	Merseyside, U.K.
Gilbert Andrews, M.D. (2)	Surrey, U.K.
Joseph M. A. Ansari, M.D. (3)	Merseyside, U.K.
R. K. Baruah, M.D. (4)	Nottingham, U.K.
G. S. Bhatt, M.D. (5)	Lancs, U.K.
John A. G. D'Souza, M.D. (6)	Blackpook, U.K.
Jasbir Singh, M.D. (7)	Chesterfield, U.K.
Kumar Mahadevan, M.D. (8)	General Hospital, U.K.
Rateek H. Mahmood, M.D. (9)	Merseyside, U.K.
Halley Mathew, M.D. (10)	Dewsbury W. York, U.K.
Yvonne I. Michael, M.D. (11)	Dettering, U.K.
Stuart Montgomery, M.D. (12)	London, England
Dennis H. Morgan, M.D. (13)	Gayton Road Kings-Lynn, U.K.
Achmau Perez, M.D. (15)	Northants, U.K.
Anees, M.D. (16)	Wolverhampton, U.K.
Sharma, M.D. (17)	Hartwood Shotts, U.K.
K. Sundararajan, M.D. (18)	Yorks, U.K.
A. G. Patel, M.D. (28)	Herts/Luton, U.K.

**APPENDIX 7.2.1.4**

<b>STUDY 89303: BASELINE DEMOGRAPHIC CHARACTERISTICS</b>					
Treatment Groups	N	Age (years)		Sex [N(%)]	
		Mean	Range	Male	Female
CIT 20mg	70	42.2	---	23 (33%)	47 (67%)
CIT 40mg	64	43.9		17 (27%)	47 (73%)
PLAC	66	43.7		21 (32%)	45 (68%)

<b>STUDY 89303: COMPLETERS by VISIT</b>						
Treatment Groups	Randomized	ITT	Completers [N(%)]			
			Wk 1	Wk 3	Wk 4	Wk 6
CIT 20mg	70	68	68 (100%)	59 (87%)	52 (76%)	51 (75%)
CIT 40mg	64	61	61 (100%)	56 (92%)	52 (85%)	49 (80%)
PLAC	66	64	64 (100%)	57 (89%)	53 (83%)	46 (72%)



APPENDIX 7.2.1.4

STUDY 89303: MEAN CHANGE FROM BASELINE IN HAM-D TOTAL SCORE												
Treatment Group	Baseline		Wk 1		Week 3		Week 4		Week 6		Δ	
	N	Mean	N	Δ	N	Δ	N	Δ	N	Δ		
<b>LAST OBSERVATION CARRIED FORWARD ANALYSIS</b>												
CIT 20mg	68	24.29	68	-4.25	68	-8.18	68	-10.26	68	-11.15		
CIT 40mg	61	22.98	61	-4.18	61	-10.26	61	-11.95	61	-13.31		
PLAC	64	23.72	64	-4.47	64	-6.98	64	-9.48	64	-10.56		
<b>2-sided p-values for pairwise comparisons</b>												
20mg vs. P	0.607		0.852		0.408		0.621		0.746			
40mg vs. P	0.502		0.814		0.026		0.115		0.120			
<b>OBSERVED CASES ANALYSIS</b>												
CIT 20mg	68	24.29	68	-4.25	58	-9.71	52	-13.48	51	-14.84		
CIT 40mg	61	22.98	61	-4.18	56	-10.89	52	-12.94	49	-15.04		
PLAC	64	23.72	64	-4.47	57	-7.61	52	-10.38	46	-12.91		
<b>2-Sided p-values for pairwise comparisons</b>												
20mg vs. P	0.607		0.852		0.161		0.055		0.327			
40mg vs. P	0.502		0.814		0.034		0.128		0.285			

APPENDIX 7.2.1.4

STUDY 89303: MEAN CHANGE FROM BASELINE IN HAM-D DEPRESSED MOOD ITEM												
Treatment Group	Baseline		Wk 1		Week 3		Week 4		Week 6		N	Δ
	N	Mean	N	Δ	N	Δ	N	Δ	N	Δ		
LAST OBSERVATION CARRIED FORWARD ANALYSIS												
CIT 20mg	68	2.79	68	-0.40	68	-0.94	68	-1.12	68	-1.22	68	-1.22
CIT 40mg	61	2.72	61	-0.49	61	-1.21	61	-1.48	61	-1.62	61	-1.62
PLAC	64	2.83	64	-0.45	64	-0.78	64	-1.11	64	-1.17	64	-1.17
2-sided p-values for pairwise comparisons												
20mg vs. P	0.778		0.725		0.382		0.966		0.824			
40mg vs. P	0.400		0.827		0.031		0.080		0.048			
OBSERVED CASES ANALYSIS												
CIT 20mg	68	2.79	68	-0.40	58	-1.07	52	-1.40	51	-1.57	51	-1.57
CIT 40mg	61	2.72	61	-0.49	56	-1.23	52	-1.52	49	-1.71	49	-1.71
PLAC	64	2.83	64	-0.45	57	-0.89	52	-1.21	46	-1.43	46	-1.43
2-Sided p-values for pairwise comparisons												
20mg vs. P	0.778		0.725		0.373		0.350		0.594			
40mg vs. P	0.400		0.827		0.100		0.161		0.279			

APPENDIX 7.2.1.4

STUDY 89303: MEAN CHANGE FROM BASELINE IN MADRS TOTAL SCORE												
Treatment Group	Baseline		Wk 1		Week 3		Week 4		Week 6		Δ	
	N	Mean	N	Δ	N	Δ	N	Δ	N	Δ		
LAST OBSERVATION CARRIED FORWARD ANALYSIS												
CIT 20mg	68	33.32	68	-5.74	68	-11.75	68	-14.54	68	-16.44		
CIT 40mg	61	32.26	61	-6.57	61	-14.41	61	-17.23	61	-19.15		
PLAC	64	33.20	64	-6.89	64	-10.13	64	-14.33	64	-16.22		
2-sided p-values for pairwise comparisons												
20mg vs. P	0.932		0.452		0.407		0.919		0.929			
40mg vs. P	0.489		0.846		0.030		0.174		0.224			
OBSERVED CASES ANALYSIS												
CIT 20mg	68	33.32	68	-5.74	58	-13.66	52	-18.63	51	-21.35		
CIT 40mg	61	32.26	61	-6.57	56	-15.16	52	-18.75	49	-21.94		
PLAC	64	33.20	64	-6.89	57	-11.33	52	-15.81	46	-19.85		
2-Sided p-values for pairwise comparisons												
20mg vs. P	0.932		0.452		0.254		0.200		0.582			
40mg vs. P	0.489		0.846		0.058		0.185		0.418			

APPENDIX 7.2.1.4

STUDY 89303: MEAN CHANGE FROM BASELINE IN CGI SEVERITY SCORE											
Treatment Group	Baseline		Wk 1		Week 3		Week 4		Week 6		
	N	Mean	N	Δ	N	Δ	N	Δ	N	Δ	
<b>LAST OBSERVATION CARRIED FORWARD ANALYSIS</b>											
CIT 20mg	68	3.38	68	-0.34	68	-0.72	68	-0.91	68	-0.99	
CIT 40mg	61	3.30	61	-0.33	61	-0.80	61	-0.85	61	-1.13	
PLAC	64	3.30	64	-0.25	64	-0.53	64	-0.70	64	-0.72	
<b>2-sided p-values for pairwise comparisons</b>											
20mg vs. P	0.362		0.447		0.140		0.136		0.098		
40mg vs. P	0.986		0.518		0.052		0.300		0.017		
<b>OBSERVED CASES ANALYSIS</b>											
CIT 20mg	68	3.38	68	-0.34	58	-0.81	52	-1.13	51	-1.24	
CIT 40mg	61	3.30	61	-0.33	56	-0.86	52	-0.94	49	-1.33	
PLAC	64	3.30	63	-0.25	57	-0.60	52	-0.77	46	-0.91	
<b>2-sided p-values for pairwise comparisons</b>											
20mg vs. P	0.362		0.470		0.120		0.018		0.085		
40mg vs. P	0.986		0.543		0.068		0.261		0.033		

APPENDIX 7.2.1.5

STUDY 89306: PRINCIPAL INVESTIGATORS	
Investigator(s) (Center #)	Location
A. H. Mahmood, M.D. Al-Bacari, M.D. (1)	Merseyside, U.K.
Gilbert Andrews, M.D. (2)	Surrey, U.K.
Joseph M. A. Ansari, M.D. (3)	Merseyside, U.K.
G. S. Bhatt, M.D. (5)	Lancs, U.K.
John A. G. D'Souza, M.D. (6)	Blackpook, U.K.
Jasbir Singh, M.D. (7)	Derbys, U.K.
Rateek H. Mahmood, M.D. (9)	Merseyside, U.K.
Rahman, M.D. (10)	Dewsbury W. York, U.K.
Achmau Perez, M.D. (15)	Northants, U.K.
K. Sundararajan, M.D. (18)	W. York, U.K.
Basic Paul Maragakis, M.D. (20)	Wigan, U.K.
Nas Choudry, M.D. (21)	Poole, U.K.
Michael Ford, M.D. (22)	Dorchester, U.K.
Kelly, M.D. (23)	Rotherham, U.K.
P. K. Brahma, M.D. (24)	London, U.K.
K. Bafasubramaniam, M.D. (25)	Bedford, U.K.
T. Venkateswarlu, M.D. (26)	St. Leonard-on-Sea, U.K.
B. S. Weerakoon, M.D. (27)	Ormskirk, U.K.
A. G. Patel, M.D. (28)	Herts, U.K.
Keith Bridges, M.D. (29)	Manchester, U.K.

**APPENDIX 7.2.1.5**

<b>STUDY 89306: BASELINE DEMOGRAPHIC CHARACTERISTICS</b>					
Treatment Groups	N	Age (years)		Sex [N(%)]	
		Mean	Range	Male	Female
CIT 20mg	88	44.1		30 (34%)	58 (66%)
CIT 40mg	97	42.6		42 (43%)	55 (57%)
PLAC	89	41.5		26 (29%)	63 (71%)

<b>STUDY 89306: COMPLETERS by VISIT</b>					
Treatment Groups	Randomized	ITT	Completers [N(%)]		
			Wk 1	Wk 3	Wk 6
CIT 20mg	88	88	82 (93%)	73 (83%)	65 (74%)
CIT 40mg	97	97	95 (98%)	86 (89%)	74 (76%)
PLAC	89	89	88 (99%)	76 (85%)	68 (76%)

**APPENDIX 7.2.1.5**

<b>STUDY 89306: MEAN CHANGE FROM BASELINE IN MADRS TOTAL SCORE</b>								
Treatment Group	Baseline		Wk 1		Week 3		Week 6	
	N	Mean	N	Δ	N	Δ	N	Δ
<b>LAST OBSERVATION CARRIED FORWARD ANALYSIS</b>								
CIT 20mg	88	32.70	88	-7.18	88	-13.00	88	-17.94
CIT 40mg	97	31.30	97	-7.48	97	-12.91	97	-16.04
PLAC	88	33.14	88	-7.53	88	-12.26	88	-15.95
<b>2-sided p-values for pairwise comparisons</b>								
20mg vs. P	0.689		0.804		0.659		0.308	
40mg vs. P	0.059		0.791		0.710		0.964	
<b>OBSERVED CASES ANALYSIS</b>								
CIT 20mg	88	32.70	82	-7.71	73	-14.95	65	-22.85
CIT 40mg	97	31.30	95	-7.64	86	-14.41	74	-19.95
PLAC	88	33.14	88	-7.53	76	-13.42	68	-18.79
<b>2-Sided p-values for pairwise comparisons</b>								
20mg vs. P	0.689		0.905		0.375		0.030	
40mg vs. P	0.059		0.937		0.582		0.552	

**APPENDIX 7.2.1.5**

<b>STUDY 89306: MEAN CHANGE FROM BASELINE IN CGI SEVERITY SCORE</b>								
Treatment Group	Baseline		Wk 1		Week 3		Week 6	
	N	Mean	N	Δ	N	Δ	N	Δ
<b>LAST OBSERVATION CARRIED FORWARD ANALYSIS</b>								
CIT 20mg	88	3.28	88	-0.35	88	-0.75	88	-1.03
CIT 40mg	97	3.22	97	-0.24	97	-0.58	97	-0.91
PLAC	89	3.30	89	-0.33	89	-0.61	89	-0.94
<b>2-sided p-values for pairwise comparisons</b>								
20mg vs. P	0.819		0.792		0.213		0.528	
40mg vs. P	0.290		0.364		0.814		0.807	
<b>OBSERVED CASES ANALYSIS</b>								
CIT 20mg	88	3.28	82	-0.38	73	-0.88	65	-1.32
CIT 40mg	97	3.22	95	-0.24	86	-0.69	74	-1.18
PLAC	89	3.30	88	-0.33	76	-0.70	68	-1.19
<b>2-Sided p-values for pairwise comparisons</b>								
20mg vs. P	0.819		0.641		0.155		0.373	
40mg vs. P	0.290		0.378		0.933		0.920	



APPENDIX 7.2.1.6

STUDY 89304: PRINCIPAL INVESTIGATORS	
Investigator(s) (Center #)	Location
Guy C. R. Robert, M.D. (1)	Rostrenen, France
Paul Houillon, M.D. (2)	Rostrenen, France
Jean-Michel Bouchard, M.D. (3)	Toulouse, France
Jean-Michel Luccioni, M.D. (4)	Marseille, France
Jean Francois Charbonnier, M.D. (5)	Clermont-Ferrand Cedex, France
Franck Peyre, M.D. (6)	Bordeaux, France
Henry Richou, M.D. (7)	Le Mesnil Saint-Denis, France
Jean Yves Metzger, M.D. (8)	Colmar, France
Jean Francois Mathey, M.D. (9)	Pessac, France
Jean DeLaunay, M.D. (11)	La Rochelle, France
Regis Pagot, M.D. (12)	Vannes, France
Bermard Aubin, M.D. (13)	Clermont-Ferrant, France
Henry Loo, M.D. (14)	Paris, France
Gerard Clerc, M.D. (16)	Pontorson, France
Philippe Robert, M.D. (17)	Nice, France
Vincent Mahe, M.D. (18)	Versailles, France
Ziad Hourri, M.D. (19)	Nantes, France
Philippe Coffinet, M.D. (20)	Faverney, France
Geneviere Lafon, M.D. (21)	Paris, France
Fabrice Lanvin, M.D. (24)	Lievin, France
Jacque Catteau, M.D. (26)	Arras, France
Jean-Paul Chabannes, M.D. (27)	Chambery, France
Michel Guibert, M.D. (28)	Saint-Lo, France
Michael Hanus, M.D. (29)	Paris, France
Jean-Pierre May, M.D. (30)	Hoerdt, France
Marie-France Patris, M.D. (31)	Brumath, France
Jean-George Rohmer, M.D. (32)	Strasbourg, France

**APPENDIX 7.2.1.6**

Patrice Van Amerongen, M.D. (34)	Saint-Germain-en-Laye, France
Jacqueline Verdeau-Paillis, M.D. (35)	Carcassonne, France
Christian Cyran, M.D. (36)	Lens, France
Philippe Dumont, M.D. (37)	Saint-Andre-Les-Lilles, France

<b>STUDY 89304: DEMOGRAPHIC CHARACTERISTICS AT RANDOMIZATION</b>					
Treatment Groups	N	Age (years)		Sex [N(%)]	
		Median	Range	Male	Female
CIT	152	49.5		41 (27%)	111 (73%)
PLAC	74	46.5		23 (31%)	51 (69%)

<b>STUDY 89304: COMPLETERS by VISIT</b>							
Treatment Groups	ITT	Completers [N(%)]					
		Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24
CIT	152	143 (94%)	130 (86%)	118 (78%)	110 (72%)	104 (68%)	96 (63%)
PLAC	74	68 (92%)	61 (82%)	53 (72%)	47 (64%)	44 (59%)	38 (51%)

**APPENDIX 7.2.1.6**

<b>STUDY 89304: MEAN DOSE (mg/day) by VISIT</b>						
	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24
CIT	36	36	36	35	35	35

<b>STUDY 89304: CUMULATIVE NUMBER(%) of PATIENTS WHO RELAPSED*</b>							
	ITT	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24
CIT	152	5 (3%)	10 (7%)	14 (9%)	16 (11%)	19 (13%)	21 (14%)
PLAC	74	3 (4%)	8 (11%)	10 (14%)	13 (18%)	15 (20%)	18 (24%)

\* Denominators = ITT.