

SUPPORTING INFORMATION

Table 1. Overview of the short-term studies

	Study	Treatment Arms	Dosing	No. of Patients^a	Normal Prolactin Range^b
<i>Schizophrenia</i>	RGH-MD-03 (NCT00404573)	Placebo Cariprazine 1.5–4.5 mg/d Cariprazine 6–12 mg/d	Flexible	129 127 133	Male: ≤17 ng/mL Female ≤25 ng/mL
	RGH-MD-04 ^c (NCT01104766)	Placebo Cariprazine 3 mg/d Cariprazine 6 mg/d Aripiprazole 10 mg/d	Fixed	153 155 157 152	Male: ≤20 ng/mL Female: ≤29 ng/mL
	RGH-MD-05 (NCT01104779)	Placebo Cariprazine 3–6 mg/d Cariprazine 6–9 mg/d	Fixed/Flexible	147 151 148	Male: ≤20 ng/mL Female: ≤29 ng/mL
	RGH-MD-16 ^c (NCT00694707)	Placebo Cariprazine 1.5 mg/d Cariprazine 3 mg/d Cariprazine 4.5 mg/d Risperidone 4 mg/d	Fixed	151 145 146 147 140	Male: ≤20 ng/mL Female: ≤29 ng/mL
	RGH-MD-31 (NCT00488618)	Placebo Cariprazine 3–12 mg/d	Flexible	118 118	Male: ≤20 ng/mL Female ≤29.1 ng/mL
	RGH-MD-32 (NCT01058096)	Placebo Cariprazine 3–12 mg/d	Flexible	154 158	Male: ≤20 ng/mL Female: ≤29 ng/mL
	RGH-MD-33 (NCT01058668)	Placebo Cariprazine 3–6 mg/d Cariprazine 6–12 mg/d	Fixed/Flexible	161 167 169	Male: ≤17 ng/mL Female ≤25 ng/mL
	RGH-MD-53 (NCT02670538)	Placebo Cariprazine 1.5 mg/d Cariprazine 3 mg/g	Fixed	165 167 158	Male: ≤24.4 ng/mL Female ≤23.3 ng/mL
	RGH-MD-54 (NCT02670551)	Placebo Cariprazine 1.5 mg/d Cariprazine 3 mg/d	Fixed	158 157 165	Male: ≤24.4 ng/mL Female ≤23.3 ng/mL
	RGH-MD-56 (NCT01396447)	Placebo Cariprazine 0.75 mg/d Cariprazine 1.5 mg/d Cariprazine 3 mg/d	Fixed	145 141 146 146	Male: ≤17 ng/mL Female ≤25 ng/mL

^aSafety population (patients who took ≥1 dose of double-blind study drug); ^bNormal ranges for prolactin were pre-defined for each study; ^cRisperidone and aripiprazole were included in RGH-MD-04 and MD-16, respectively, for assay sensitivity.

Table 2. Overview of the long-term studies

Study	From	No. of Patients^a	Treatment Duration
<i>Schizophrenia</i>			
RGH-MD-11 (NCT01104792)	Total	586	48 weeks
	MD-04	218	
	MD-05	133	
	New Patients	235	
RGH-MD-17 (NCT00839852)	Total/MD-16	93	48 weeks
RGH-MD-06 (NCT01412060)	OL phase	765	Up to 20 weeks
	DB phase	200	Up to 72 weeks
<i>Bipolar Mania</i>			
RGH-MD-36 (NCT01059539)	Total/New Patients	402	16 weeks

^aSafety population (patients who took ≥ 1 dose of double-blind study drug).

Table 3. Demographics (safety population)

Characteristic	Schizophrenia		Bipolar Mania		Bipolar Depression	
	Placebo (n=584)	Cariprazine 1.5–12 mg/d (n=1317)	Placebo (n=442)	Cariprazine 3–12 mg/d (n=623)	Placebo (n=468)	Cariprazine 1.5–3 mg/d (n=939)
Male, n (%)	415 (71.1)	945 (71.8)	268 (60.6)	365 (58.6)	190 (40.6)	357 (38.0)
Age, mean (SD), y	37.8 (11.0)	37.8 (10.4)	38.9 (11.6)	39.7 (11.7)	44.0 (12.0)	42.4 (11.7)
Race, n (%)						
White	237 (40.6)	574 (43.6)	203 (45.9)	316 (50.7)	345 (73.7)	708 (75.4)
Black	215 (36.8)	440 (33.4)	106 (24.0)	165 (26.5)	112 (23.9)	202 (21.5)
Other/Missing	132 (22.6)	303 (23.0)	133 (30.1)	142 (22.8)	11 (2.4)	29 (3.1)
Weight, mean (SD), kg	77.9 (19.8)	76.8 (18.6)	77.4 (19.1)	77.3 (18.9)	86.7 (17.2)	86.6 (18.2)
BMI, mean (SD), kg/m ²	26.4 (5.4)	26.1 (5.3)	26.9 (5.7)	26.9 (5.6)	31.3 (6.3)	31.2 (6.6)

BMI, body mass index; SD, standard deviation.

Table 4. Shifted categories of prolactin levels in patients with schizophrenia

Shift Category	Placebo	Cariprazine Modal Daily Dose			Risperidone	Aripiprazole
		1.5–3 mg/d	4.5–6 mg/d	9–12 mg/d	4 mg/d	10 mg/d
<i>Normal to 2X and 4X ULN</i>						
Male						
Normal at Baseline, n	271	219	261	105	62	64
2X ULN, ^a n (%)	0	1 (0.5)	1 (0.4)	0	12 (19.4)	0
4X ULN, ^a n (%)	0	0	0	0	0	0
Female						
Normal at Baseline, n	80	68	67	40	23	22
2X ULN, ^a n (%)	5 (6.3)	2 (2.9)	1 (1.5)	1 (2.5)	14 (60.9)	0
4X ULN, ^a n (%)	2 (2.5)	1 (1.5)	0	0	7 (30.4)	0
<i>>ULN to Normal</i>						
Male						
>ULN at Baseline, n	93	98	112	36	29	27
Normal, ^a n (%)	81 (87.1)	87 (88.8)	102 (91.1)	33 (91.7)	4 (13.8)	26 (96.3)
Female						
>ULN at Baseline, n	68	71	67	10	16	27
Normal, ^a n (%)	58 (85.3)	54 (76.1)	47 (70.2)	10 (100)	0	24 (88.9)

^aAt last available double-blind assessment.

ULN, upper limit of normal.

Table 5. Shifted categories of prolactin levels in patients with bipolar disorder

Shift Category	Bipolar Mania			Bipolar Depression		
	Placebo	Cariprazine Modal Daily Dose		Placebo	Cariprazine	
		3–6 mg/d	9–12 mg/d		1.5 mg/d	3 mg/d
<i>Normal to 2X and 4X ULN</i>						
Male						
Normal at Baseline, n	184	104	151	151	142	144
2X ULN, ^a n (%)	2 (1.1)	1 (1.0)	2 (1.3)	0	0	0
4X ULN, ^a n (%)	0	0	0	0	0	0
Female						
Normal at Baseline, n	108	75	96	220	240	220
2X ULN, ^a n (%)	1 (0.9)	2 (2.7)	0	0	2 (0.8)	2 (0.9)
4X ULN, ^a n (%)	0	1 (1.3)	0	0	2 (0.8)	0
<i>>ULN to Normal</i>						
Male						
>ULN at Baseline, n	53	23	45	22	9	17
Normal, ^a n (%)	34 (64.2)	18 (78.3)	44 (97.8)	10 (45.5)	7 (77.8)	9 (52.9)
Female						
>ULN at Baseline, n	46	27	35	30	37	33
Normal, ^a n (%)	35 (76.1)	14 (51.9)	23 (65.7)	17 (56.7)	18 (48.6)	19 (57.6)

^aAt last available double-blind assessment.
ULN, upper limit of normal.