

SUPPLEMENTARY MATERIALS

Supplementary Table 1. Change from baseline in the domains and total scores of the PSP scale at each assessment time point during the double blind (DB) phase

		Placebo			Risperidone ISM ^a		
		Day 29 vs BL (n=109)	Day 57 vs BL (n=94)	Day 85 vs BL (n=120)	Day 29 vs BL (n=232)	Day 57 vs BL (n=211)	Day 85 vs BL (n=254)
Personal and Social Relationships	Mean (95% CI)	-0.38 (-1; -0)	-0.46 (-1; -0)	-0.25 (-0; -0)	-0.57 (-1; -0)	-0.69 (-1; -1)	-0.68 (-1; -1)
	p value ^b	-	-	-	0.0341	0.0213	<.0001
Self-Care	Mean (95% CI)	-0.24 (-0; 0)	-0.29 (-0; -0)	-0.21 (-0; -0)	-0.32 (-0; -0)	-0.34 (-0; -0)	-0.36 (-0; -0)
	p value ^b	-	-	-	0.2927	0.5622	0.0970
Socially Useful	Mean (95% CI)	-0.21 (-0; -0)	-0.31 (-0; -0)	-0.25 (-0; -0)	-0.44 (-1; -0)	-0.60 (-1; -0)	-0.58 (-1; -0)
	p value ^b	-	-	-	0.0027	0.0029	0.0002
Disturbing and Aggressive Behaviors	Mean (95% CI)	-0.12 (-0; 0)	-0.17 (-0; -0)	-0.12 (-0; 0)	-0.36 (-0; -0)	-0.40 (-0; -0)	-0.31 (-0; -0)
	p value ^b	-	-	-	0.0026	0.0164	0.0391
Total score	Mean (95% CI)	5.19 (3; 7)	6.93 (5; 9)	4.76 (3; 7)	8.84 (7; 10)	11.03 (9; 13)	10.73 (9; 12)
	p value ^b	-	-	-	0.0020	0.0013	<.0001

Notes: Negative change from baseline scores on each of the 4 domains and positive change from baseline on total score indicate improvement in functioning. ^a Pooled data from Risperidone ISM 75 mg + Risperidone ISM 100 mg. ^b Comparison of Risperidone ISM versus placebo.

Abbreviations: DB, double blind; BL, baseline; CI, confidence interval; PSP, personal and social performance scale.

Supplementary Table 2. Change from baseline in the domains and total scores of the PSP scale at each assessment timepoint during the open label extension (OLE) phase, by subgroup of patients

		Unstable patients ^a			Stabilized patients ^b			Stable patients ^c		
		Week 12 vs BL (n=38)	Week 24 vs BL (n=35)	Week 52 vs BL (n=36)	Week 12 vs BL (n=50)	Week 24 vs BL (n=43)	Week 52 vs BL (n=51)	Week 12 vs BL (n=103)	Week 24 vs BL (n=97)	Week 52 vs BL (n=105)
Personal and social relationships	Mean (95% CI)	-0.62 (-1; -0)	-0.77 (-1; -1)	-0.75 (-1; -1)	-0.20 (-0; -0)	-0.20 (-0; -0)	-0.28 (-0; -0)	-0.16 (-0; 0)	0.06 (-0; 0)	0.03 (-0; 0)
	p value ^d	<.0001	<.0001	<.0001	0.0565	0.0295	0.0172	0.3880	0.6827	0.8914
Self-care	Mean (95% CI)	-0.40 (-1; -0)	-0.42 (-1; -0)	-0.41 (-1; -0)	-0.07 (-0; 0)	-0.06 (-0; 0)	-0.12 (-0; -0)	-0.08 (-0; 0)	-0.06 (-0; 0)	-0.09 (-0; 0)
	p value ^d	0.0048	0.0014	0.0055	0.6175	0.8176	0.1218	0.4347	0.6195	0.2070
Socially useful activities, including work and study	Mean (95% CI)	-0.42 (-1; -0)	-0.53 (-1; -0)	-0.57 (-1; -0)	-0.28 (-0; -0)	-0.39 (-1; -0)	-0.44 (-1; -0)	-0.03 (-0; 0)	0.06 (-0; 0)	0.14 (-0; 0)
	p value ^d	0.0165	0.0029	0.0045	0.0254	0.0012	0.0006	0.8632	0.5061	0.7117
Disturbing and aggressive behaviors	Mean (95% CI)	-0.36 (-1; -0)	-0.37 (-1; -0)	-0.39 (-1; -0)	-0.08 (-0; 0)	-0.13 (-0; -0)	-0.11 (-0; 0)	-0.03 (-0; 0)	0.09 (-0; 0)	0.09 (-0; 0)
	p value ^d	0.0002	<.0001	<.0001	0.3669	0.0459	0.1396	0.7490	0.2275	0.2484
Total score	Mean (95% CI)	6.84 (5; 9)	8.79 (6; 11)	8.94 (6; 11)	3.32 (2; 5)	4.13 (3; 6)	4.18 (3; 6)	1.22 (-0; 3)	-0.09 (-2; 2)	1.11 (-1; 3)
	p value ^d	0.0006	<.0001	<.0001	0.0292	0.0028	0.0073	0.6754	0.8540	0.4974

Notes: Negative change from baseline scores on each of the 4 domains and positive change from baseline on total score indicate improvement in functioning.

^a Unstable patients, placebo rollover patients from the previous DB phase who were randomly assigned to Risperidone ISM at dose of either 75 or 100 mg in the OLE phase; ^b Stabilized patients, patients treated with Risperidone ISM in the previous DB phase who continued to receive monthly Risperidone ISM in the OLE phase at the same dose (75 or 100 mg) as during the DB phase; ^c Stable patients, newly enrolled patients (de novo) who were on a previous stable

maintenance dose of oral risperidone; ^d Intra-group comparisons at each time point from OLE baseline. The three patient groups (unstable, stabilized and stable) contain pooled data from Risperidone ISM 75 mg + Risperidone ISM 100 mg.

Abbreviations: BL, baseline; CI, confidence interval; DB, double blind; OLE, open label extension; PSP, personal and social performance scale.

Supplementary Table 3. Change from baseline in the domains and total scores of the SWN-20 scale at each assessment time point during the double blind (DB) phase

		Placebo				Risperidone ISM ^b			
		BL (n=145)	Day 29 vs BL (n=109)	Day 57 vs BL (n=94)	Day 85 vs BL (n=120)	BL (n=286)	Day 29 vs BL (n=230)	Day 57 vs BL (n=210)	Day 85 vs BL (n=250)
Mental functioning	Mean (95% CI)	15.21 (14; 16)	0.97 (0; 2)	1.60 (1; 2)	0.81 (-0; 2)	15.10 (15; 16)	1.32 (1; 2)	2.02 (1; 3)	2.00 (1; 3)
	p value ^a	-	-	-	-	0.8136	0.4570	0.4066	0.0184
Self-control	Mean (95% CI)	16.81 (16; 17)	0.67 (0; 1)	1.40 (1; 2)	1.01 (0; 2)	17.16 (17; 18)	1.01 (1; 1)	1.31 (1; 2)	1.10 (1; 2)
	p value ^a	-	-	-	-	0.3296	0.4055	0.8452	0.8263
Emotional regulation	Mean (95% CI)	16.77 (16; 17)	0.71 (-0; 1)	1.49 (1; 2)	1.33 (1; 2)	17.07 (17; 18)	1.20 (1; 2)	1.45 (1; 2)	1.47 (1; 2)
	p value ^a	-	-	-	-	0.4394	0.2735	0.9315	0.7274
Physical functioning	Mean (95% CI)	17.05 (16; 18)	0.97 (0; 2)	1.21 (0; 2)	1.11 (0; 2)	17.37 (17; 18)	1.26 (1; 2)	1.34 (1; 2)	1.46 (1; 2)
	p value ^a	-	-	-	-	0.4666	0.5452	0.8153	0.4665
Social integration	Mean (95% CI)	14.45 (14; 15)	0.69 (-0; 1)	1.57 (1; 2)	1.45 (1; 2)	14.20 (14; 15)	2.10 (2; 3)	2.22 (2; 3)	2.46 (2; 3)
	p value ^a	-	-	-	-	0.5894	0.0060	0.2392	0.0357
SWN Total Score	Mean (95% CI)	80.28 (78; 83)	4.01 (1; 7)	7.28 (4; 10)	5.63 (3; 8)	80.86 (79; 83)	7.05 (5; 9)	8.49 (6; 11)	8.60 (7; 10)
	p value ^a	-	-	-	-	0.7197	0.0784	0.5072	0.0771

Notes: ^a Comparison of Risperidone ISM versus placebo. ^b Risperidone ISM group contains pooled data from Risperidone ISM 75 mg + Risperidone ISM 100 mg.

Abbreviations: BL, baseline; CI, confidence interval; DB, double blind; PSP, personal and social performance scale; SWN-20, 20-items scale Subjective Well-Being Under Neuroleptics Treatment.

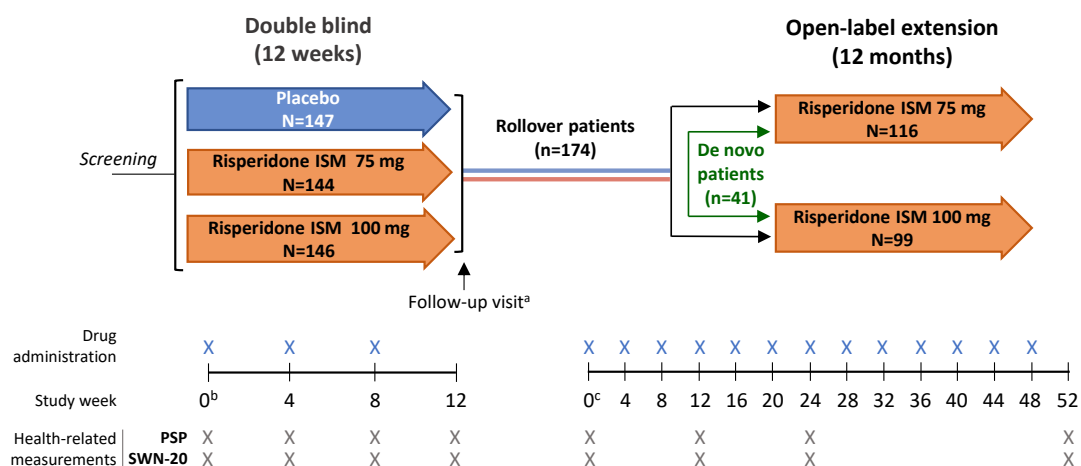
Supplementary table 4. Change from baseline in the domains and total scores of the SWN-20 scale at each assessment time point during the open label extension (OLE) phase, by subgroup of patients

		Unstable ^a			Stabilized ^b			Stable ^c		
		Week 12 vs BL (n=50)	Week 24 vs BL (n=43)	Week 52 vs BL (n=51)	Week 12 vs BL (n=103)	Week 24 vs BL (n=97)	Week 52 vs BL (n=105)	Week 12 vs BL (n=38)	Week 24 vs BL (n=35)	Week 52 vs BL (n=36)
Mental functioning	Mean (95% CI)	1.26 (0; 2)	1.74 (1; 3)	1.80 (1; 3)	0.57 (-0; 1)	0.45 (-0; 1)	0.68 (0; 1)	0.57 (-0; 1)	0.88 (-0; 2)	0.83 (-0; 2)
	p value ^d	0.0607	0.0104	0.0238	0.3487	0.5602	0.1740	0.4652	0.3004	0.2127
Self-control	Mean (95% CI)	1.26 (0; 2)	1.53 (1; 3)	1.16 (0; 2)	0.61 (0; 1)	0.39 (-0; 1)	0.67 (0; 1)	0.16 (-0; 1)	-0.06 (-1; 1)	0.51 (-0; 1)
	p value ^d	0.0255	0.0185	0.1172	0.2545	0.6213	0.1297	0.8890	0.6970	0.3896
Emotional regulation	Mean (95% CI)	0.70 (-0; 2)	1.35 (0; 3)	0.98 (-0; 2)	0.52 (-0; 1)	0.85 (0; 1)	0.74 (0; 1)	0.59 (-0; 1)	0.09 (-1; 1)	-0.34 (-1; 0)
	p value ^d	0.1852	0.0218	0.1828	0.4047	0.1765	0.0966	0.5056	0.8882	0.6776
Physical functioning	Mean (95% CI)	1.74 (1; 3)	2.05 (1; 3)	1.73 (1; 3)	0.45 (-0; 1)	0.86 (0; 1)	1.12 (1; 2)	0.70 (-0; 1)	-0.03 (-1; 1)	0.49 (-1; 2)
	p value ^d	0.0149	0.0140	0.0868	0.3898	0.0968	0.0183	0.3668	0.8691	0.4592
Social integration	Mean (95% CI)	1.68 (1; 3)	3.30 (2; 5)	2.41 (1; 4)	0.83 (0; 2)	0.89 (0; 2)	0.95 (0; 2)	0.70 (0; 1)	0.35 (-0; 1)	0.46 (-0; 1)
	p value ^d	0.0376	<.0001	0.0069	0.2127	0.2240	0.1042	0.3032	0.6461	0.6059
SWN Total score	Mean (95% CI)	6.64 (3; 11)	9.98 (5; 15)	8.08 (4; 12)	2.99 (1; 5)	3.43 (1; 6)	4.16 (2; 7)	2.73 (1; 5)	1.24 (-2; 4)	1.94 (-1; 5)
	p value ^d	0.0211	0.0017	0.0263	0.2296	0.1913	0.0400	0.4183	0.7662	0.4572

Notes: ^a Unstable patients, placebo rollover patients from the previous DB phase who were randomly assigned to Risperidone ISM at dose of either 75 or 100 mg in the OLE phase; ^b Stabilized patients, patients treated with Risperidone ISM in the previous DB phase who continued to receive monthly Risperidone ISM

in the OLE phase at the same dose (75 or 100 mg) as during the DB phase; ^c Stable patients, newly enrolled patients (de novo) who were on a previous stable maintenance dose of oral risperidone; ^d Intra-group comparisons at each time point from OLE baseline. Baseline of OLE for rollover subjects (unstable and stabilized) is equivalent to Visit 14 of DB phase. The three patient groups (unstable, stabilized and stable) contain pooled data from Risperidone ISM 75 mg + Risperidone ISM 100 mg.

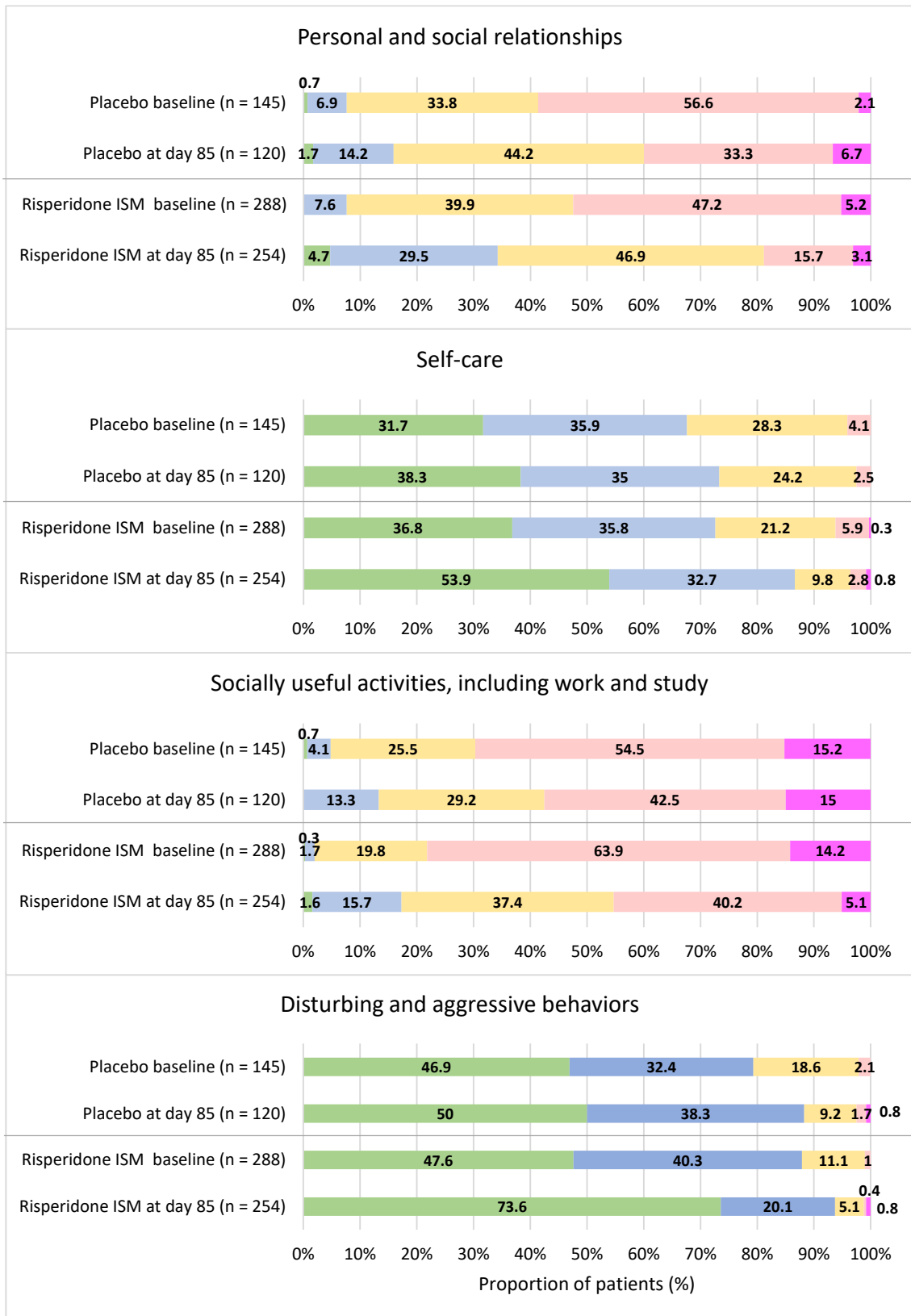
Abbreviations: BL, baseline; CI, confidence interval; DB, double blind; OLE, open label extension; SWN-20, 20-items scale Subjective Well-Being Under Neuroleptics Treatment.



Supplementary Figure 1. PRISMA-3 study diagram and PSP/SWN-20 assessments.

Notes: ^a If a patient did not enter the extension segment of the study, no additional doses of study drug were administered to that patient. ^b Baseline measurement, defined as day 1 of study in DB phase, was prior to the injection of study drug. ^c Baseline measurement for de novo patients (stable patients). Baseline data for rollover subjects (unstable and stabilized patients) in the OLE phase was those corresponding to Day 85 of the DB phase.

Abbreviations: DB, double blind; OLE, Open label extension; PSP, Personal and Social Performance scale; SWN-20, 20-items Subjective Well-Being Under Neuroleptics Treatment scale.



■ Absent
 ■ Mild
 ■ Manifest
 ■ Marked
 ■ Severe

Supplementary Figure 2. Frequency of Personal and Social Performance (PSP) scale domains in each response category at baseline and at Day 85 during the double blind (DB) phase.

Notes: No patients reported a “very severe” rating. Risperidone ISM group contains pooled data from Risperidone ISM 75 mg + Risperidone ISM 100 mg.

Abbreviations: DB, double blind; PSP, Personal and Social Performance scale.