SUPPLEMENTARY MATERIALS

FIGURE S1. Number of Days in the Study.

Data are shown for all 138 participants who were ongoing when the study was terminated by the sponsor due to commercial availability of valbenazine. Time in study ranged from 106 days (from March 1, 2017 to June 1, 2017) to 468 days (from March 18, 2016 to June 28, 2017).

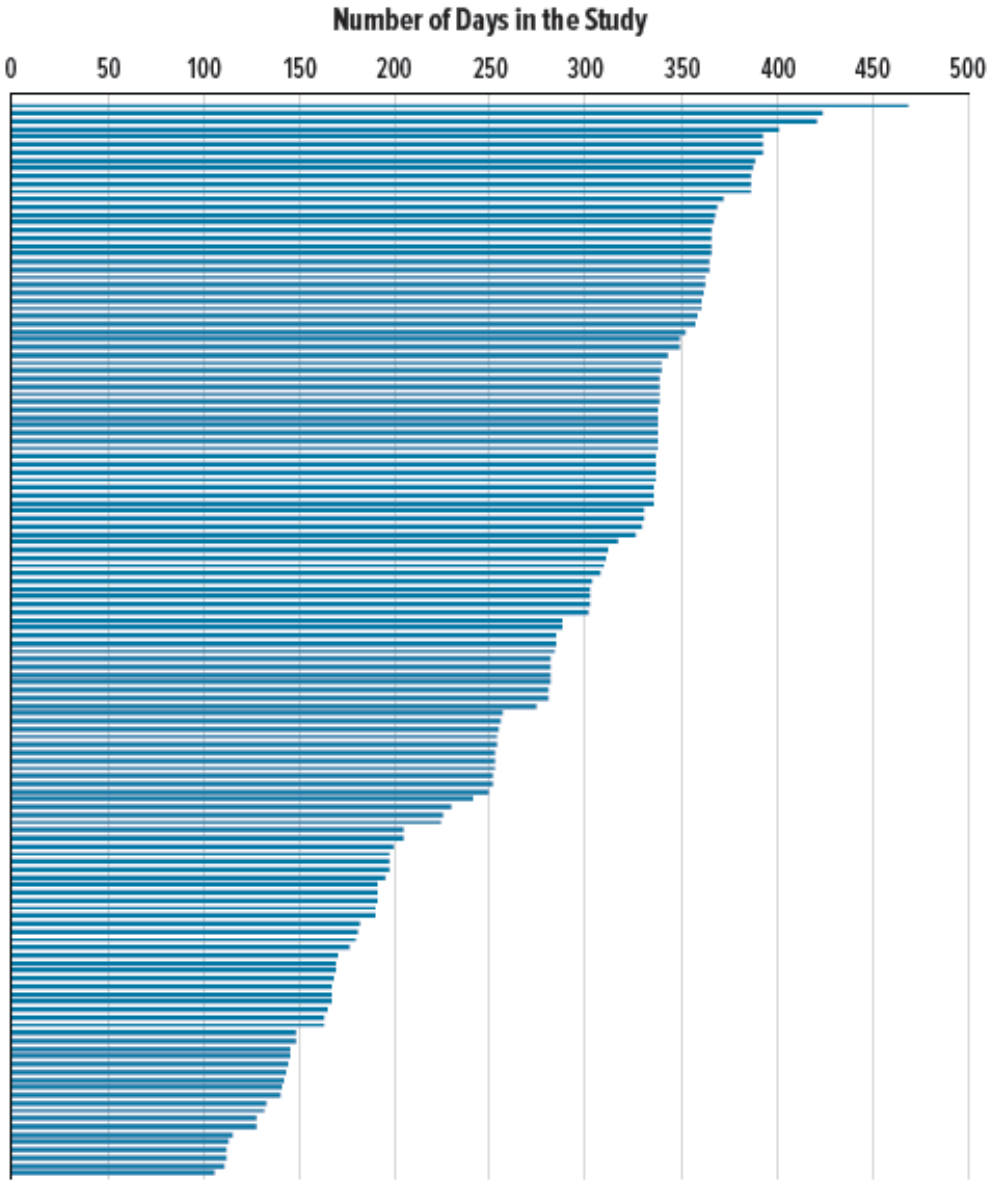

TABLE S1. Schedule of Assessments

	Week[a]																		
	BL	Open-Label Valbenazine Treatment Period																	
	Day 1	4	8	12	16	20	24	28	32	36	40	44	48	52	56	60	64	68	72/ET[b]
Outpatient clinic visit	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
AE monitoring	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Clinical laboratory tests	X			X			X			X			X			X			X
12-lead ECG	X	X		X			X			X			X			X			X
BPRS	X																		
C-SSRS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
CGIS-TD	X			X			X			X			X			X			X
PSQ	X			X			X			X			X			X			X

[a]The visits after Day 1 had a visit window of -7 to +2 days.

[b]Final visit for participants who completed the study (or early termination).

AE, adverse event; BL, baseline; BPRS, Brief Psychiatric Rating Scale; C-SSRS, Columbia-Suicide Severity Rating Scale; CGIS-TD, Clinical Global Impression of Severity-Tardive Dyskinesia; ECG, electrocardiogram; ET, early termination; PSQ, Patient Satisfaction Questionnaire.

TABLE S2. Medical History and Prior Medication Use

	40 mg/day (n=35)	80 mg/day (n=117)	80/40 mg/day (n=8)	Total (n=160)
Any medical history, n (%)[a]	35 (100.0)	116 (99.1)	8 (100.0)	159 (99.4)
Hypertension	21 (60.0)	64 (54.7)	5 (62.5)	90 (56.3)
Insomnia	12 (34.3)	61 (52.1)	2 (25.0)	75 (46.9)
Anxiety	10 (28.6)	57 (48.7)	2 (25.0)	69 (43.1)
Gastroesophageal reflux disease	9 (25.7)	53 (45.3)	3 (37.5)	65 (40.6)
Hypercholesterolemia	11 (31.4)	29 (24.8)	0	40 (25.0)
Depression	6 (17.1)	31 (26.5)	2 (25.0)	39 (24.4)
Chronic obstructive pulmonary disease	7 (20.0)	27 (23.1)	1 (12.5)	35 (21.9)
Hypothyroidism	9 (25.7)	19 (16.2)	1 (12.5)	29 (18.1)
Type 2 diabetes mellitus	6 (17.1)	22 (18.8)	1 (12.5)	29 (18.1)
Back pain	6 (17.1)	21 (17.9)	0	27 (16.9)
Hyperlipidemia	5 (14.3)	20 (17.1)	1 (12.5)	26 (16.3)
Osteoarthritis	3 (8.6)	22 (18.8)	1 (12.5)	26 (16.3)
Constipation	4 (11.4)	19 (16.2)	1 (12.5)	24 (15.0)
Any prior medication, n (%)[b]	35 (100.0)	116 (99.1)	8 (100.0)	159 (99.4)
Antipsychotics	28 (80.0)	96 (82.1)	7 (87.5)	131 (81.9)
Antidepressants	22 (62.9)	84 (71.8)	4 (50.0)	110 (68.8)
Lipid modifying agents, plain[c]	12 (34.3)	51 (43.6)	4 (50.0)	67 (41.9)
Antiepileptics	14 (40.0)	39 (33.3)	4 (50.0)	57 (35.6)
Drugs for peptic ulcer and GERD	7 (20.0)	46 (39.3)	2 (25.0)	55 (34.4)
Anxiolytics	10 (28.6)	42 (35.9)	2 (25.0)	54 (33.8)
Anticholinergics	12 (34.3)	29 (24.8)	2 (25.0)	43 (26.9)
ACE inhibitors, plain[c]	11 (31.4)	26 (22.2)	4 (50.0)	41 (25.6)
Antithrombotic agents	6 (17.1)	31 (26.5)	1 (12.5)	38 (23.8)
Blood glucose lowering drugs[d]	8 (22.9)	29 (24.8)	1 (12.5)	38 (23.8)
Hypnotics and sedatives	5 (14.3)	28 (23.9)	1 (12.5)	34 (21.3)
Anti-inflammatory and antirheumatic products, non-steroids	6 (17.1)	25 (21.4)	1 (12.5)	32 (20.0)
Adrenergics, inhalants	8 (22.9)	19 (16.2)	1 (12.5)	28 (17.5)
Thyroid preparations	8 (22.9)	19 (16.2)	1 (12.5)	28 (17.5)
Beta-blocking agents	6 (17.1)	20 (17.1)	1 (12.5)	27 (16.9)

[a]Table lists all MedDRA preferred terms reported in ≥15% of all participants.

[b]Defined as medications taken within 30 days prior to baseline. Table lists all World Health Organization drug ATC categories (level 3) reported in ≥15% of all participants; level 2 categories were used if no applicable level 3 category was available.

[c]Did not include combinations with other drug classes.

[d]Excluded insulins (categorized separately). Prior use of insulin or its analogues reported in 5.0% of all participants.

ACE, angiotensin-converting enzyme; ATC, Anatomical Therapeutic Chemical; GERD, gastroesophageal reflux disease; MedDRA, Medical Dictionary for Regulatory Activities.

TABLE S3. Serious TEAEs and TEAEs Leading to Study Discontinuation

	Baseline to Week 4 (n=160)	Week 4 to End of Study (n=157)
Any serious TEAE[a]	2 (1.3)	14 (8.9)
Aggression	0	1 (0.6)
Atrial fibrillation	0	1 (0.6)
Back pain	0	1 (0.6)
Chronic obstructive pulmonary disease	0	1 (0.6)
Coma	0	1 (0.6)
Depression	0	1 (0.6)
Diarrhea	0	1 (0.6)
Gangrene	0	1 (0.6)
Gout	0	1 (0.6)
Hemorrhagic stroke	0	1 (0.6)
Hip fracture	1 (0.6)	0
Hypertensive heart disease	0	1 (0.6)
Mental status changes	0	1 (0.6)
Non-cardiac chest pain	0	1 (0.6)
Paranoia	0	1 (0.6)
Pneumonia	0	1 (0.6)
Psychotic disorder	1 (0.6)	0
Renal failure	0	1 (0.6)
Rhabdomyolysis	0	1 (0.6)
Sepsis syndrome	0	1 (0.6)
Any TEAE leading to discontinuation[a]	2 (1.3)	7 (4.5)
Aggression	0	1 (0.6)
Chronic obstructive pulmonary disease	0	1 (0.6)
Coma	0	1 (0.6)
Dyskinesia	1 (0.6)	0
Hypertensive heart disease	0	1 (0.6)
Paranoia	0	1 (0.6)
Psychotic disorder	1 (0.6)	0
Sepsis syndrome	0	1 (0.6)
Schizophrenia	0	1 (0.6)

[a]All serious TEAEs and TEAEs leading to discontinuation are listed (MedDRA preferred terms)

MedDRA, Medical Dictionary for Regulatory Activities; TEAE, treatment-emergent adverse event.

Table S4. Mean Change from Baseline to Week 48 in Vital Sign, Electrocardiogram, and Laboratory Parameters[a]

	40 mg/day		80 mg/day		80/40 mg/day		Total	
	n	Mean Change (SD)	n	Mean Change (SD)	n	Mean Change (SD)	n	Mean Change (SD)
Vital sign parameter								
Supine SBP, mmHg	12	5.0 (13.5)	38	3.4 (17.8)	5	4.8 (17.2)	55	3.9 (16.6)
Supine DBP, mmHg	12	-6.5 (14.8)	38	0.9 (11.0)	5	-0.6 (7.1)	55	-0.9 (11.9)
Supine heart rate, bpm	12	7.8 (12.1)	38	2.1 (11.1)	5	11.8 (13.5)	55	4.2 (11.8)
Orthostatic SBP, mmHg	12	-5.0 (19.5)	38	-0.6 (14.8)	5	-3.8 (5.3)	55	-1.9 (15.5)
Orthostatic DBP, mmHg	12	3.8 (14.6)	38	2.0 (11.5)	5	2.8 (3.7)	55	2.4 (11.7)
Orthostatic heart rate, bpm	12	-1.1 (17.3)	38	-0.3 (11.4)	5	-0.6 (6.8)	55	-0.5 (12.4)
Weight, kg	12	-1.6 (5.0)	39	0.9 (3.9)	5	-1.3 (6.6)	56	0.1 (4.5)
Electrocardiogram parameter								
Heart rate, bpm	11	5.7 (12.0)	37	1.2 (13.2)	5	1.4 (4.6)	53	2.1 (12.4)
PR interval, ms	11	5.5 (14.1)	37	-0.3 (22.3)	5	6.8 (26.2)	53	1.6 (21.1)
QRS duration, ms	11	0.2 (6.1)	37	-0.2 (4.4)	5	-2.0 (7.4)	53	-0.3 (5.0)
QT interval, ms	11	-8.9 (25.8)	37	-3.7 (28.2)	5	-14.6 (29.3)	53	-5.8 (27.5)
QTcF interval, ms	11	1.1 (16.2)	37	-1.9 (15.7)	5	-11.8 (32.2)	53	-2.2 (17.7)
Laboratory value parameters								
Alkaline phosphatase, U/L	12	-2.6 (23.1)	39	-6.7 (14.7)	5	-8.8 (21.1)	56	-6.0 (17.1)
Alanine aminotransferase, U/L	12	-0.8 (4.8)	39	0.9 (9.1)	5	-2.6 (4.3)	56	0.2 (8.1)
Aspartate aminotransferase, U/L	12	0.9 (4.2)	39	-1.1 (7.4)	5	-2.2 (3.9)	56	-0.7 (6.6)
Total bilirubin, µmol/L	12	-0.7 (1.9)	39	0.4 (2.9)	5	0.0 (2.7)	56	0.1 (2.7)
Total cholesterol, mmol/L	12	-0.1 (0.4)	39	-0.1 (0.9)	5	-0.7 (0.9)	56	-0.2 (0.8)
Triglycerides, mmol/L	12	-0.1 (0.9)	39	-0.0 (1.8)	5	-0.1 (0.4)	56	-0.0 (1.6)
Glucose, mmol/L	12	-0.2 (3.8)	39	0.6 (1.8)	5	0.4 (1.8)	56	0.4 (2.4)
Creatine kinase, U/L	12	-0.3 (37.9)	39	0.6 (60.4)	5	-5.4 (51.1)	56	-0.2 (54.8)

[a]Data are shown to Week 48 given the small number of participants who completed the Week 60 visit (total n=4). Due to valbenazine becoming commercially available, the study was discontinued before any participant reached the final visit at Week 72.

DBP, diastolic blood pressure; SBP, systolic blood pressure; SD, standard deviation; QTcF, QT interval adjusted with Fridericia's correction.

Table S5. Prolactin Levels

	Median (Min, Max), µg/L					
	n	Level at Baseline	n	Level at Week 48[a]	n	Change from Baseline to Week 48[a]
In men[b]	81	6.7 (1.0, 55.7)	25	12.7 (0.8, 77.7)	25	5.7 (-14.6, 74.4)
In women[b]	75	7.6 (1.6, 141.2)	30	14.9 (2.9, 91.1)	30	3.7 (-96.1, 59.7)

[a]Data are shown to Week 48 given the small number of participants who completed the Week 60 visit (4 women, 0 men). Due to valbenazine becoming commercially available, the study was discontinued before any participant reached the final visit at Week 72.

[b]Normal range: men, 2-18 µg/mL; non-pregnant women, 2-29 µg/mL.

Table S6. Prior Long-Term Outcomes (Non-Rollover Patients vs Rollover Patients)[a]

Response in Participants who Completed Prior Long-Term Treatment, n (%)	Did Not Continue into the Rollover Study (N=63)	Continued into the Rollover Study (N=161)
AIMS ≥30% total score improvement from baseline	40 (63.5)	125 (77.6)*
AIMS ≥50% total score improvement from baseline	31 (49.2)	107 (66.5)*
CGI-TD score ≤3: “minimally improved” or better	58 (92.1)	156 (96.9)
CGI-TD score ≤2: “much” or “very much” improved	36 (57.1)	142 (88.2)*
PGIC score ≤3: “minimally improved” or better	54 (85.7)	155 (96.3)*
PGIC score ≤2: “much” or “very much” improved	41 (65.1)	139 (86.3)*

[a]Based on available Week 48 data from participants who completed KINECT 3 or KINECT 4.

*$P<0.05$ for participants who continued into the rollover study versus those who did not.

AIMS, Abnormal Involuntary Movement Scale; CGI-TD, Clinical Global Impression of Change-Tardive Dyskinesia; PGIC, Patient Global Impression of Change.