Supplemental Table 2: Detailed clinical case reports in select MS phenocopy carriers

Gene	DNA change	Protein	Inheritance	Disorder	Reported in Literature	Patient ID	Diagnosis	Study Phase	Sex	Age of onset	Family History	Clinical Symptoms	CSF	Brain imaging	Spinal cord imaging	Meets 2010 Criteria for PPMS	Treatment	Platform
REEP1	c.606+43G>T mRNA binding in 3'UTR	No change	AD	SPG31	Dominant variant for SPG31	65-0008	PPMS	WGS Discovery	F	50	No MS or other neurologic disorders	Spastic paraparesis, neurogenic bladder, mild ataxia, mild sensory deficits, left optic atrophy.	IgG index 1.1, > 5 OCBs	> 10 multifocal T2 hyperintensities in brain consistent with demyelination	Patchy T2 signal in cervical spinal cord	+	Tecfidera, failed Abagio due to hypertension. Copaxone, solumedrol.	CGI, OpenArray
						52-0139	PPMS	Replication Phase 1, UCSF cohort	F	26	Diabetes, hypertension, macular degeneration. No MS.	Foot drop at presentation. Severe spastic quadriplegia, preserved sensation, moderate to severe dysphagia	LP performed at NIH in 1977 was reported to be consistent with MS, results not available	21 punctate FLAIR hyperintense lesions in the supratentorial white matter and pons and pontomedullary junction.	Patchy T2 signal in the cervical spinal cord, cervical spinal cord atrophy at C3-C6	+	None	OpenArray
						52-1859	PPMS	Replication Phase 1, UCSF cohort	M	57	Cancer, hypertension. No MS	Lower extremity sensory changes, mild spastic paraparesis, bilateral intranuclear ophthalmoplegia neurogenic bladder, diminished reflexes at ankles suggestive of neuropathy	Not done	Multiple ovoid foci of increased T2 signal in corpus callosum, bilateral periventricular and subcortical white matter.	Not done	not enough data	Tecfidera, Betaseron	OpenArray
						21-0003	RMS	Replication Phase 2, UCSF cohort	F	41	No MS or other neurologic disorders	Unilateral optic neuritis, bladder abnormalities, cognitive impairment, sensory abnormalities. Latest MSSS 3.9 at age 46.	Not done	Multifocal lesions in the brain, some enhancing, consistent with demyelination.	Normal cervical spine imaging.	NA	Interferon	OpenArray
						MSGENE02-528	RMS	Replication Phase 2, Italian cohort	F	21	No MS or other neurologic disorders	A left sensory and motor hemisyndrome, clinical relapses. Latest EDSS 2.5 at age 28.	Positive OCBs	Multiple T2 lesions in the brain consistent with demyelination	3 lesions in the cervical spinal cord	NA	Interferon	OpenArray
KIF5A	c.1082C>T	p.A361V	AD	SPG10	Dominant variant for SPG10, reported age of onset is 35	02-0069	PPMS	WGS Discovery	F	37	No MS or other neurologic disorders	Spastic paraparesis, ataxia, vibratory sensory disturbance, bowel and bladder disturbance, cognitive disturbance, fatigue. 9 years to EDSS 6.0	Not done	4 T2 lesions on brain MRI consistent with demyelination	Abnormal T2 signal in the thoracic spinal cord	+	Copaxone, pulse dose solumedrol	CGI, OpenArray
						MSGENE02-539	RMS	Replication Phase 2, Italian cohort	M	18	No MS or other neurologic disorders	Vibratory sensory loss, saccadic eye movements. Latest EDSS 1.5 at age 26.	Positive unique OCBs	Multiple T2 lesions in the brain consistent with demyelination	Not done	NA	Interferon	OpenArray
MLC1	c.274C>T	p.P92S	AR	MLC	Heterozygote found in a carrier (father of patient with MLC)	04-1225	PPMS	WGS Discovery	F	51	F: Died of MI at 64. M: Lung CA	Progressive spastic paraparesis, urinary incontinence, intermittent vertigo.	4 unique OCBs, IgG index 1.04	T2 lesions in periventricular white matter, and cortical atrophy.	Cervical spondylosis, moderate stenosis of c-spine, no intrinsice cord abnormalities.	+	No progression on Rituximab x 3 yrs, some progression on IV solumedrol x 12 months.	CGI, OpenArray
						52-1463	RMS	Replication Phase 2, UCSF cohort	F	15	Mother with stroke, sister with epilepsy.	Minimal motor symptoms, few clinical attacks. Latest EDSS < 6.0 at age 55.	Not done	Mild burden of disease in the periventricular, pericallosal, and subcortical white matter.	Not done	NA	Betaseron	OpenArray
						60-0354	RMS	Replication Phase 2, UCSF cohort	F	37	Asthma, hay fever, ulcerative colitis, breast and prostate cancer.	Spastic paraparesis, bowel and bladder abnormalities, cognitive impairment, sensory abnormalities	Not done	Greater than 10 T2 hyperintense lesions in the brain, some enhancing.	Multiple T2 lesions in cervical and thoracic spinal cord consistent with demyelination	NA	Avonex	OpenArray
						60-0362	RMS	Replication Phase 2, UCSF cohort	F	35	Rheumatoid arthritis, migraines, cardiovascular disease.	Mild spastic paraparesis, neurogenic bladder	Not done	Moderate to severe burden of white matter abnormalities in supratentorial and infratentorial brain, some enhancing.	One lesion in the upper cervical spinal cord	NA	Copaxone, Rebif, Gilenya	OpenArray
						50-0032	RMS	Replication Phase 2, UCSF cohort	F	30	No MS or other neurologic disorders	not available for review	Not done	not available for review	not available for review	NA	unavailable	OpenArray
TSC2	c.223G>A	p.E75K	AD	Tuberous Sclerosis	p.E75G (not p.E75K) was found in a patient with TS	60-0385	PPMS	WGS Discovery	F	47	Mother with stroke and myeloproliferative disorder, father with cardiovascular	Mild spastic hemiparesis, mild sensory and cerebellar signs. EDSS 3 at age 62.	> 5 OCBs, IgG index 0.74	> 10 T2 lesions in the corpus callosum, juxtacortical, deep and periventricular white matter	One T2 lesion in cervical spinal cord	+	Gilenya. Discontinued therapy at age 60 due to clinical and radiographic stability	CGI, OpenArray
SPG7	c.1529C>T	p.A510V	AR, AD	SPG7	Reported dominant and recessive, most common mutation in SPG7	70-0019	PPMS	MS chip Discovery	F	61	No MS or other neurologic disorders	Mild asymmetric leg weakness and mild urinary urgency. Latest EDSS 2.0 at age 67.	> 5 OCBs, IgG index 0.9	Moderate burden (more than 10 lesions) of disease in the periventricular and subcortical white matter	Two lesions in the cervical spinal cord	+	None	MS chip
SPG7	c.1552+1G>T Splice site	-	AR, AD	SPG7	Recessive mutation for SPG7	65-0084	PPMS	MS chip Discovery	F	48	No history of MS or neurologic disease in the patient's parents and 5 siblings	Severe spastic paraparesis, moderate bladder symptoms, and moderate sensory deficits. Latest EDSS 6.5 at age 57.	3 OCBs	Multifocal white matter lesions in the brain white matter consistent with demyelination	Multiple T2 lesions in the cervical spinal cord	+	CellCept	MS chip