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Supplemental Table 1: S1P modulators currently in clinical trials

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Drug name	Target	Disease	Clinical Trial number	Phase	Status
ABC294640	SPHK2 antagonist	Advanced solid tumors	NCT01488513	1	Completed
ABC294640	SPHK2 antagonist	Refractory or relapsed multiple myeloma	NCT02757326	1b/2	Terminated*
AC-058B201 / Ponesimod	S1PR1 agonist	Relapsing-remitting multiple sclerosis	NCT01093326	2	Active
AC-058B201 / Ponesimod	S1PR1 agonist	Chronic GVHD	NCT02461134	2	Terminated**
AC-058B201 / Ponesimod	S1PR1 agonist	Psoriasis	NCT01208090	2	Completed
AC-058B201 / Ponesimod	S1PR1 agonist	Ponesimod vs teriflunomide in relapsing multiple sclerosis	NCT02425644/NCT03232072	3	Completed/Active
ACT-128800	S1PR1 agonist	Moderate to severe plaque psoriasis	NCT00852670 /NCT01208090	2	Completed
ACT-128800	S1PR1 agonist	Relapsing-remitting multiple sclerosis	NCT01006265	2	Completed
Amitriptyline	ASM	Cystic Fibrosis / Infection/ Pseudomonas Aeruginosa	NCT00515229	2	Completed
BAF312	S1PR1/R3 agonist	Renal impairment	NCT01904214	1	Completed
Ceralifimod (ONO-4641)	S1PR1/5 agonist	Relapsing-remitting multiple sclerosis	NCT01081782	2	Completed
Ceralifimod (ONO-4641)	S1PR1/5 agonist	Relapsing-remitting multiple sclerosis, Phase 2 extension	NCT01226745	2	Terminated***
CS-0777	S1PR1 agonist	Multiple sclerosis	NCT00616733	1	Completed
FTY720	S1PR1/3/4/5 agonist	Acute Stroke	NCT02002390	2	Completed
FTY720	S1PR1/3/4/5 agonist	Effect of FTY720 on pulmonary and cardiac function	NCT00416845	1	Completed
FTY720	S1PR1/3/4/5 agonist	Fingolimod Versus Dimethyl-fumarate in Multiple Sclerosis	NCT03345940	4	Terminated**
FTY720	S1PR1/3/4/5 agonist	Schizophrenia	NCT01779700	2	Completed****
FTY720	S1PR1/3/4/5 agonist	Ret's Syndrome	NCT02061137	2	Completed
FTY720	S1PR1/3/4/5 agonist	Primary progressive multiple sclerosis	NCT00731692	3	Terminated****
FTY720	S1PR1/3/4/5 agonist	PK study in patients with severe renal impairment	NCT00731523	1	Completed
FTY720	S1PR1/3/4/5 agonist	Moderate asthma	NCT00785083	2	Completed
FTY720	S1PR1/3/4/5 agonist	Kidney Transplantation	NG00099801	3	Completed
FTY720	S1PR1/3/4/5 agonist	Neurodegeneration	NCT02575365	4	Terminated**
FTY720	S1PR1/3/4/5 agonist	COVID-19	NCT04280558	2	Recruiting
GSK2018682	S1PR1 agonist	Healthy Volunteers	NCT01466322/ NCT01431937	1	Completed
KRP-203	S1P1	Subacute cutaneous lupus erythematosus	NCT01294774	2	Completed
KRP-203	S1P1	Stem cell transplant in hematological malignancies	NCT01830010	1	Completed
MT-1303	S1PR1 antagonist	Crohn's disease	NCT02148185/NCT02389790/ NCT02378688	2	Completed
MT-1303	S1PR1 antagonist	Relapsing-remitting multiple sclerosis	NCT02293967/NCT02310048/ NCT01890655/NCT01742052	1	Completed
MT-1303	S1PR1 antagonist	Plaque psoriasis	NCT01987843	2	Completed
MT-1303	S1PR1 antagonist	Inflammatory bowel disease	NCT01666327	1	Completed
MT-1303	S1PR1 antagonist	Systemic Lupus Erythematosus	NCT02307643	1	Completed
Opaganip	SPHK2 antagonist	COVID-19 Pneumonia	NCT04414618	2	Recruiting
Opaganip	SPHK2 antagonist	COVID-19 Pneumonia	NCT04467840	2/3	Recruiting
Ozanimod (RPC1063)	S1PR1/5 agonist	Multiple sclerosis	NCT02797015/NCT02047734/ NCT04140305/NCT02294058	1/3/3/3	Completed/Active/ Active/Completed
Ozanimod (RPC1063)	S1PR1/5 agonist	Crohn's disease	NCT02531113	2	Completed
Ozanimod (RPC1063)	S1PR1/5 agonist	Ulcerative colitis	NCT02531126	3	Active
Siponimod (BAF312)	S1PR1/5 agonist	Secondary progressive multiple sclerosis	NCT01665144/NCT02330965	3/3	Active/Completed
Siponimod (BAF312)	S1PR1/5 agonist	Relapsing-remitting multiple sclerosis	NCT00879658/NCT01185821	2	Completed
Siponimod (BAF312)	S1PR1/5 agonist	Intracerebral Hemorrhage	NCT03338998	2	Temporary Suspension
Siponimod (BAF312)	S1PR1/5 agonist	Polymyositis	NCT01801917	2	Terminated****
Siponimod (BAF312)	S1PR1/5 agonist	Active dermatomyositis	NCT02029274	2	Terminated*****
Siponimod (BAF312)	S1PR1/5 agonist	Active dermatomyositis/Polymyositis	NCT01148810	2	Terminated**
Siponimod (BAF312)	S1PR1/5 agonist	Hepatic impairment	NCT01565902	1	Completed
Siponimod (BAF312)	S1PR1/5 agonist	Renal impairment	NCT01904214	1	Completed
Sonepcizumab/LT1009	Human Anti-S1P recombinant antibody	Exudative Age-related Macular Degeneration	NCT01414153	2	Completed
Sonepcizumab/LT1009	Human Anti-S1P recombinant antibody	Renal Cell Carcinoma	NCT01762033	2	Terminated
Sonepcizumab/LT1009	Human Anti-S1P recombinant antibody	Neovascular Age-related Macular Degeneration	NCT00767949	1	Unknown
Sonepcizumab/LT1009	Human Anti-S1P recombinant antibody	Exudative Age-Related Macular Degeneration (AMD) or Polypoidal Choroidal Vasculopathy (PCV) (PED)	NCT01334255	1	Terminated*****
Sonepcizumab/LT1009	Human Anti-S1P recombinant antibody	Neovascular Age-related Macular Degeneration	NCT00767949	1A	Unknown
Sonepcizumab/LT1009	Human Anti-S1P recombinant antibody	Solid Tumors	NCT00661414	1	Completed
Sonepcizumab/LT1009	Human Anti-S1P recombinant antibody	Persistent Pigment Epithelial Detachment (PED)	NCT01334255	1	Terminated*****

* Expiration of NCI funding, ** low recruitment, *** Merck decided not to pursue Phase 3 development, **** Study results available, ***** no evidence of efficacy, ***** by sponsor decision