Developing DMTs

Phase III trials:

Drug	Indication	Rout	MOA	Adverse React.	Trials
Ozanimod *NIH, licensed to Receptos*	RRMS	Oral	Selective sphingosine-1 Rc agonist modulator **(similar to fingolimod but specific to S-1P1 & S-1p5 and spares S-1p3 so spares the heart)** Better selectivity, penetration and clearance than fingolimod	No serious side effects. No macular edema Mainly headache and pharyngitis	**RADIANCE**: reduced number of Gd enhancing lesions to compared with 11 in placebo after 24w. ARR 0.15 after 72w. Thorough QT/QTc: **doesn't prolong QT Shorter half life (19h) compared with fingolimod (1w).**
Siponimod *Novartis*	SPMS	Oral	Selective sphingosine-1-P receptor modulator **(similar to fingolimod but specific to S-1P1 & S-1p5 and spares S-1p3 so spares the heart)**		**BOLD**
Ponesimod	RRMS	Oral	Selective sphingosine-1-P receptor modulator		
Ocrelizumab *Roche/Biogen*	PPMS	IV	**CD20 blocker (similar to Rituximab)** Depletes B cells via antibody-dependent cell-mediated toxicity (ADCC) and complement-dependent cytotoxicity (CDC). **Compared to rituximab, induces more ADCC and less CDC, which could reduce infusion-related toxicity**	Serious infections Thrombotic microangiopathy	**ORATARIO**: compared with placebo, reduced the risk of disability progression by 24% **OPERA I, II:** compared with IFN B1a, ocrelizumab reduced the ARR by ~50% and slowed disease progression by 40% **Kappos et al:** 89% reduction in the number of gadolinium-enhancing lesions as compared to placebo
Mastinib *AB science*	PPMS - SPMS	Oral	Blocks KIT Rc (stem cell factor Rc), platlet derived growth factor, inhibits mast cell degranulation, slowed cognitive decline in Alzheimer.	Nausea, abdominal pain, diarrhea, neutropenia	**Mastinib in PPMS, SPMS**: still pending
Laquinimod *Teva*	RRMS	Oral	Suppresses gene expression related to antigen presentation and inflammation	abdominal pain, elevated LFT	ARPEGGIO – CONCERTO: pending ALLEGRO: compared with placebo 23% reduction in the ARR (0.30 versus 0.39) and a reduction in disease progression (11.1% versus 15.7%). Marked improvement in EDSS which raise concerns about being neuroprotective.
Idebenone	PPMS	Oral	Works on reactive oxygen species, increase ATP synthesis, electron transport in cells with	Fatigue, headache, diarrhea	IPPOMS: pending

(Roxane) *Takeda*			depressed mitochondrial functions → approved for Leber optic atrophy in EU.		
Dronabinol	SPMS for spasticity	Oral	Cannabinoid receptor agonist Decrease accumulation of cAMP, thought to be neuroprotective. Reduces signs of inflammation in animals.	Amnesia, ataxia, asthenia, euphoria, diarrhea, paranoid reactions	CUPID: not effective CAMS: didn't affect spasticity but increased patient's walking speed. Ungerleider et al: improved spasticity