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Blocking the LINGO-1 pathway as a novel therapeutic approach for CNS remyelination and repair: From discovery to clinical trials

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LINGO-1 is a leucine rich repeat, Ig domain containing, Nogo receptor interactive protein that is selectively expressed in CNS oligodendrocytes and neurons. Its expression is developmentally regulated, as well as up-regulated in CNS diseases and spinal cord injury. LINGO-1 negatively regulates oligodendrocyte differentiation and myelination, neuronal survival and axonal regeneration by activating RhoA and inhibiting ATK phosphorylation. Opicinumab (anti-LINGO-1) is the first anti-LINGO-1 antibody to enter clinical development for CNS repair. The Phase I study found anti-LINGO-1 to be safe and well tolerated up to the maximum planned dose of 100 mg/kg. In the Phase II Renew trial, compared with placebo, participants treated with opicinumab showed improved optic nerve conduction latency (measured by full-field visual evoked potential), and indicative of remyelination. In the phase 2b SYNERGY (active relapsing MS trial), an inverted U-shaped dose response was seen in SYNERGY suggesting a clinical effect of opicinumab.

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