

VSN16R – a novel treatment for spasticity in experimental multiple sclerosis

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Current symptomatic treatments for spasticity in multiple sclerosis often exhibit intolerable side-effects that limit their use. We synthesized a novel compound, VSN16R, which exhibited anti-spastic activity in experimental autoimmune encephalomyelitis (EAE) in mice and was as active as baclofen and cannabinoids but lacked their sedative side-effects. The drug was found to be a novel, potent BKCa calcium activated potassium channel modulator *in vitro*. VSN16R was orally active and remarkably well-tolerated, with over a thousand fold therapeutic window, and demonstrated no obvious adverse neurobehavioural effects in mice. It was also well tolerated in other larger animal species and importantly in humans, where phase 1 studies found VSN16R to produced high oral bioavailability and no serious adverse behavioural or physiological events at supra-therapeutic plasma concentrations. VSN16R has the potential to inhibit pathogenic spinal cord hyperreflexia and can drive neuronal potassium-induced hyperpolarisation to limit spasticity via BKCa opening. This study identifies a novel target for control of spasticity and suggests that VSN16R may be a useful novel therapeutic, which offers tolerability advantages over existing treatments. This may facilitate adoption of earlier treatment following to development of spasticity in MS. A phase II clinical trial (NCT02542787) is currently in progress.

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