

Remyelination: Promising Treatment Advances for Multiple Sclerosis

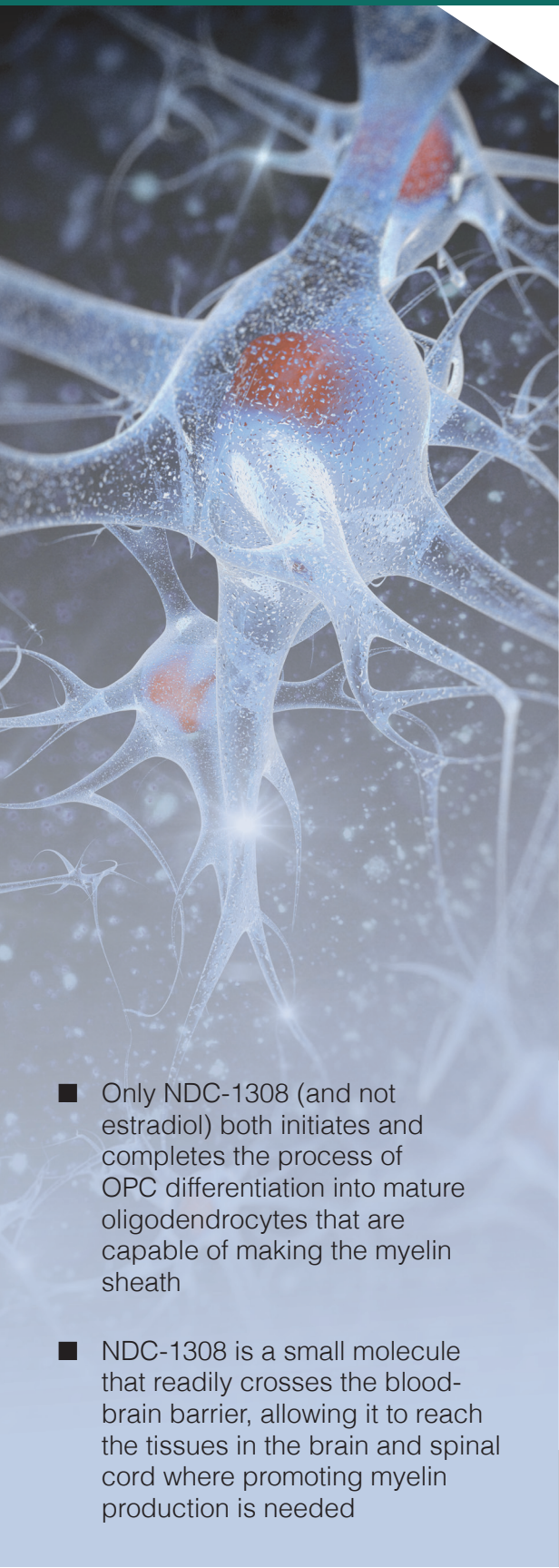
- Multiple sclerosis (MS) is an unpredictable, often disabling disease of the central nervous system that interrupts the flow of information within the brain, and between the brain and body
- In patients with MS, inflammation exposes nerves in the brain and spinal cord by destroying their protective, insulating cover, which is known as the myelin sheath

The destruction of the myelin sheath is a process called demyelination

- For decades, researchers have been trying to find ways to repair the myelin sheath, a process called remyelination, but advances have been elusive



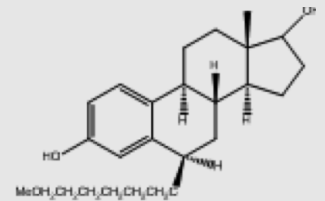
- Currently available therapies for MS are designed to impact inflammatory pathways in the immune system and primarily function to slow disease progression. By removing the inflammation, these therapies enable the body's natural processes to remyelinate damaged nerves
- However, as the disease progresses in patients with MS, the body's natural ability to remyelinate is reduced, creating a need for therapies to restart this remyelinating mechanism



Remyelination and the Potential of NDC-1308

- ENDECE Neural is leveraging decades of accumulated knowledge about how activation of nuclear receptors can regulate certain genes to control disease pathways
- Encouraging and reproducible results in animal models of demyelination suggest that ENDECE Neural's lead compound, NDC-1308, induces remyelination and offers hope to patients with MS

NDC-1308, a novel estradiol analog, derives its novel therapeutic potential from a patented modification to the chemical structure of estradiol: an alkoxyalkyl moiety that has been added to the C-6 position of the estradiol B-ring



- Only NDC-1308 (and not estradiol) both initiates and completes the process of OPC differentiation into mature oligodendrocytes that are capable of making the myelin sheath
- NDC-1308 is a small molecule that readily crosses the blood-brain barrier, allowing it to reach the tissues in the brain and spinal cord where promoting myelin production is needed

- Scientists at ENDECE Neural believe that NDC-1308 induces remyelination by activating estrogen receptors in a unique manner to upregulate the genes that promote the differentiation of oligodendrocyte progenitor cells (OPCs) - the precursors of oligodendrocytes, the cells that synthesize and maintain the myelin sheath - into mature oligodendrocytes

Unlike NDC-1308, estradiol does not induce OPCs to differentiate into mature oligodendrocyte cells