**Docket #:** S17-052

# Improved antibody therapy for multiple sclerosis and other autoimmune diseases

**Disease indication:**

- *Multiple sclerosis (MS)/autoimmune demyelinating disease*
- *Potential indications:* other autoimmune disorders (e.g. inflammatory bowel disease, type 1 diabetes, rheumatoid arthritis, psoriasis), cosmetic/tattoo removal

**Drug format** - Antibody

**Drug class** - First-in-class

**Research stage and Preliminary data** - In vivo results in a mouse model of multiple sclerosis (autoimmune encephalomyelitis, “EAE”) – mice treated with an anti-alpha5 integrin antibody had delayed onset of the disease with reduced severity (never reached paralytic stage)

**Target** - alpha5 integrin (also known as CD49e), a receptor in the integrin family whose primary ligand is fibronectin

**Background** - Multiple sclerosis (MS) is a neuroinflammatory disease that affects more than one million people worldwide, including 400,000 in the US. Current treatments are costly, limited in efficacy and have severe side effects. Patients treated with Natalizumab (an antibody against alpha 4 integrin) are at risk of developing a devastating opportunistic infection of the brain, progressive multifocal leukoencephalopathy (PML) because the drug blocks the entry of key T and B cells to the central nervous system, limiting the patient's lymphocyte immunity.

**Keywords** - Multiple sclerosis, therapeutic antibody, autoimmune disease, neuroinflammatory disease

**Mode of action** - Inventors used mass cytometry to identify alpha5 integrin on infiltrating myeloid cells (macrophages), but not in T cells (unlike alpha4 integrin which is expressed on all lymphocytes). They hypothesize that blocking alpha5 integrin will control autoimmune disease by suppressing macrophage function without impacting other immune cells. This mechanism of action is similar to Natalizumab, but is predicted to be safer because an anti-alpha5 antibody has a more specific target than an anti-alpha4 antibody.

**Competitive edge** - Predicted to be safer with fewer side effects than existing drugs. Because alpha5 integrin is not expressed on in T or B cells, the inventors hypothesize that patients treated with an anti alpha5 integrin agent would not be at increased risk of PML.

**Potential competitor** - The first line of approved therapies for MS in the US are Glatiramer Acetate (Copaxone), IFN-b1a (Avonex and Rebif), and IFN-b1b (Betaseron and Extavia) and the second line of approved therapies are mitoxantrone (Novantrone) and natalizumab (Tysabri). Recently, Gilenya, Aubagio, and Tecfidera, three new oral pills, have been separately approved by the US FDA as three new options of first line of therapy for the treatment of relapsing MS.

**Patent status** - Patent application filed

# Publications


- Ajami, B., Samusik, N., Wieghofer, P., Ho, P. P., Crotti, A., Bjornson, Z., ... & Steinman, L. (2018). Single-cell mass cytometry reveals distinct populations of brain myeloid cells in mouse neuroinflammation and neurodegeneration models. *Nature neuroscience*, 1.


# Patents

- Published Application: 20180346577
- Published Application: WO2018222670
- Published Application: 20230014308

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