one or more selected from the group consisting of an anti-gpNMB antibody or its fragment or a derivative thereof according to any one of claims 1 to 17, a nucleic acid molecule according to claim 18, a vector according to claim 19, and a recombinant cell according to claim 20.

[Aspect 25] The pharmaceutical composition according to claim 24, for use in decreasing the number of mal-functional microglia in a subject and/or removing amyloid β oligomers in a subject and/or increasing the number of synapses in a subject and/or treating or preventing neurodegenerative disease in a subject.

[Aspect 26] A pharmaceutical composition for use in removing amyloid β oligomers in a subject and/or increasing the number of synapses in a subject and/or treating or preventing neurodegenerative disease in a subject, comprising, as an active ingredient, an agent for decreasing the number of mal-functional microglia.

[Aspect 27] The pharmaceutical composition according to claim 25 or 26, wherein the neurodegenerative disease is Alzheimer's disease.

[Aspect 28] The pharmaceutical composition according to claim 27, further comprising a second active ingredient.

[Aspect 29] The pharmaceutical composition according to claim 28, wherein the second active ingredient is one or more selected from an anti-Tau antibody, anti-amyloid β antibody, anti-CD33 antibody, anti-semaphorin 4D antibody, anti-TNFα antibody, anti-sortilin antibody, anti-galactose-specific lectin (galectin) 3 antibody, and anti-TREM2 (triggering receptor expressed on myeloid cells 2) antibody.

[Aspect 30] The pharmaceutical composition according to claim 28, wherein the second active ingredient is a vaccine comprising a full-length or partial-length polypeptide of one or more proteins selected from Tau, amyloid β, CD33, semaphorin 4D, TNFα, sortilin, galactose-specific lectin (galectin) 3, and TREM2 (triggering receptor expressed on myeloid cells 2), or a nucleic acid encoding the polypeptide.

[0049a]

In another aspect, provided herein is use of the pharmaceutical composition as described herein in the manufacture of a medicament for decreasing the number of mal-functional microglia in a subject and/or removing amyloid β oligomers in a subject and/or increasing the number of synapses in a subject and/or treating or preventing neurodegenerative disease in a subject.

[0049b]

In another aspect, provided herein is use of a pharmaceutical composition in the manufacture of a medicament for removing amyloid β oligomers in a subject and/or increasing the number of synapses in a subject and/or treating or preventing neurodegenerative disease in a subject, wherein the pharmaceutical composition comprises an agent for decreasing the number of mal-functional microglia as an active ingredient.

[0049c]

In yet another aspect, provided herein is the pharmaceutical composition as

described herein for use in therapy.

[0050]

The term “pharmaceutical drug” used herein is to be interpreted as encompassing both the concepts of “therapeutic agent” and “prophylactic agent,” unless it is inconsistent with the context.

EFFECT OF THE INVENTION

[0051]

The anti-gpNMB antibodies of the present invention can exhibit extremely unexpected effects, e.g., the effects of decreasing the number of mal-functional microglia in a subject and/or removing amyloid β oligomers in a subject and/or increasing the number of synapses in a subject and/or restoring cognitive functions, by specifically binding to at least one site in a region from a PMEL-CAF-like domain to a PKD domain of