

CLAIMS

1. A chimeric antigen receptor (CAR) comprising a disialoganglioside (GD2)-binding domain which comprises:
 - (a) a heavy chain variable region (VH) having the sequence shown as SEQ ID NO: 10;
 - 5 and
 - (b) a light chain variable region (VL) having the sequence shown as SEQ ID NO: 12.
2. A CAR according to Claim 1, in which the GD2 binding domain comprises the sequence shown as SEQ ID NO: 8.
3. A CAR according to Claim 1 or 2, which comprises a transmembrane domain which

10 comprises the sequence shown as SEQ ID No. 13 or a variant thereof having at least 80% sequence identity.
4. A CAR according to Claim 1, 2 or 3, in which GD2-binding domain and the transmembrane domain are connected by a spacer.
5. A CAR according to Claim 4, in which the spacer comprises one of the following: a

15 human an IgG1 Fc domain; an IgG1 hinge; an IgG1 hinge-CD8 stalk; or a CD8 stalk.
6. A CAR according to Claim 5, in which the spacer comprises an IgG1 hinge-CD8 stalk or a CD8 stalk.
7. A CAR according to Claim 5, in which the spacer comprises an IgG1 Fc domain.
8. A CAR according to Claim 7, in which the spacer comprises an IgG1 Fc domain which

20 comprises the sequence shown as SEQ ID No. 23 or SEQ ID No. 24 or a variant thereof having at least 80% sequence identity.
9. A CAR according to any preceding claim which also comprises an intracellular T cell signalling domain.
10. A CAR according to Claim 9 in which the intracellular T cell signalling domain

25 comprises one or more of the following endodomains: CD28 endodomain; OX40 and CD3-Zeta endodomain.

11. A CAR according to Claim 10 in which the intracellular T cell signalling domain comprises all of the following endodomains: CD28 endodomain; OX40 and CD3-Zeta endodomain.
12. A CAR according to any preceding claim, which comprises the sequence shown as any
5 of SEQ ID No. 27 to 35 or a variant thereof which has at least 80% sequence identity but retains the capacity to (i) bind GD2 and (ii) induce T cell signalling.
13. A nucleic acid sequence which encodes a CAR according to any preceding claim.
14. A nucleic acid sequence according to Claim 13, which is codon-optimised.
15. A nucleic acid sequence according to Claim 13 or 14 which comprises the sequence
10 shown as SEQ ID No 25 or a variant thereof having at least 90% sequence identity.
16. A nucleic acid according to Claim 13, 14 or 15 which also encodes a suicide gene.
17. A vector which comprises a nucleic acid sequence according to any of Claims 13 to 16.
18. A T cell which expresses a CAR according to any of Claims 1 to 12.
19. A T cell which co-expresses a CAR according to any of Claims 1 to 12 and a suicide
15 gene.
20. A T cell according to Claim 19, in which the suicide gene is iCasp9 or RQR8.
21. A method for making a T cell according to Claim 18, 19 or 20, which comprises the step of introducing a nucleic acid according to any of Claims 13 to 16 into a T cell.
22. A pharmaceutical composition which comprises a T cell according to Claim 18, 19 or
20 20, together with a pharmaceutically acceptable carrier, diluent or excipient.
23. A T cell according to Claim 18, 19 or 20 for use in treating a cancer associated with elevated GD2-expression.
24. A T cell for use according to Claim 23, in which the cancer is neuroblastoma.
25. The use of a T cell according to Claim 18, 19 or 20 in the manufacture of a medicament
25 for treating cancer associated with elevated GD2 expression.
26. The use of a T cell according to Claim 25, in which the cancer is neuroblastoma.