

Finally, in a clinical trial evaluating CAR T cell monotherapy and combination therapy with CARVac in 3 dose levels, no dose limiting toxicities (DLTs) or serious adverse events (AEs) related to therapy have been observed. Efficacy data revealed participants showing partial responses and stable disease with shrinkage of target lesions. Most encouragingly, several partial responses have been achieved in testicular cancer patients that all relapsed on recent high-dose chemotherapy.

SUMMARY

In one aspect, the present disclosure provides a use of immune effector cells expressing a chimeric antigen receptor (CAR) molecule in the manufacture of a medicament for the treatment of a solid tumor in a human, wherein the human is to be administered immune effector cells expressing a CAR molecule, and wherein the CAR molecule comprises: i) a CLDN6 antigen binding domain; ii) a transmembrane domain; and iii) an intracellular domain that comprises a 4-1BB costimulatory domain, and a CD3-zeta signaling domain, optionally wherein the CAR molecule comprises: i) a CLDN6 antigen binding domain; ii) a CD8 α hinge domain; iii) a CD8 α transmembrane domain; and iv) an intracellular domain that comprises a 4-1BB costimulatory domain, and a CD3-zeta signaling domain, further optionally wherein the CAR molecule comprises the amino acid sequence of SEQ ID NO: 36 or a functional variant thereof. The present disclosure provides a method of treating a solid tumor in a human comprising administering to the human immune effector cells expressing a chimeric antigen receptor (CAR) molecule comprising:

- i) a CLDN6 antigen binding domain;
- ii) a transmembrane domain; and
- iii) an intracellular domain that comprises a 4-1BB costimulatory domain, and a CD3-zeta signaling domain.

In one example, the solid tumor is a CLDN6-positive solid tumor. In one example, the solid tumor is an advanced solid tumor. In one example, the solid tumor is a relapsed or refractory advanced solid tumor. In one example, the solid tumor is selected from the group consisting of liver cancer, lung cancer, ovarian cancer, gastric cancer, breast cancer, hepatic cancer, pancreatic cancer,

skin cancer, melanomas, head neck cancer, sarcomas, bile duct cancer, renal cell cancer, and urinary bladder cancer. In one example, the solid tumor is testicular cancer (including metastasis thereof; e.g., into lung and/or liver). In one example, treating a solid tumor in a human comprises inducing stable disease, inducing stable disease with shrinkage of target lesion, or inducing partial response.

In one example, the CLDN6 antigen binding domain comprises an antibody, an antibody fragment, an scFv, a Fv, a Fab, a (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain. In one example, the CLDN6 antigen binding domain comprises an scFv. In one example, the CLDN6 antigen binding domain comprises the amino acid sequence of SEQ ID NO: 35 or a functional variant thereof.

In one example, the 4-1BB costimulatory domain comprises the amino acid sequence of SEQ ID NO: 30 or a functional variant thereof. In one example, the CAR molecule of the disclosure does not comprise a further costimulatory domain.

- 5 In one example, the CD3-zeta signaling domain comprises the amino acid sequence of SEQ ID NO: 31 or a functional variant thereof.

In one example, the transmembrane domain comprises a transmembrane domain of a protein selected from the group consisting of the alpha, beta or zeta chain of the T cell receptor, CD28, 10 CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD154, KIRDS2, OX40, CD2, CD27, LFA-1 (CD11a, CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD40, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), CD160, CD19, IL2R beta, IL2R gamma, IL7Ra, ITGA1, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, 15 ITGB7, TNFR2, DNAMI (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, PAG/Cbp, NKp44, NKp30, NKp46, NKG2D, and NKG2C, or a functional variant thereof.

- 20 In one example, the transmembrane domain comprises a CD8 α transmembrane domain. In one example, the transmembrane domain comprises the amino acid sequence of SEQ ID NO: 28 or a functional variant thereof.

In one example, the antigen binding domain is connected to the transmembrane domain by a 25 hinge domain. In one example, the hinge domain is a CD8 α hinge domain. In one example, the hinge domain comprises the amino acid sequence of SEQ ID NO: 27 or a functional variant thereof.

In one example, the CAR molecule of the disclosure comprises:

- 30 i) a CLDN6 antigen binding domain;
ii) a CD8 α hinge domain;
iii) a CD8 α transmembrane domain; and

iv) an intracellular domain that comprises a 4-1BB costimulatory domain, and a CD3-zeta signaling domain.

In one example, the CAR molecule of the disclosure further comprises a leader sequence.

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In one example, the CAR molecule of the disclosure comprises the amino acid sequence of SEQ ID NO: 36 or a functional variant thereof.

10 In one example, the CAR molecule of the disclosure is encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 41 or a functional variant thereof. Accordingly, in one example, immune effector cells are transfected, e.g., stably transfected, with such nucleic acid.

15 The nucleic acid encoding a CAR molecule of the disclosure may be present in a vector. In one example, the vector is selected from the group consisting of a DNA vector, an RNA vector, a plasmid, a lentivirus vector, an adenoviral vector, and a retrovirus vector. In one example, the vector further comprises a promoter. In one example, the promoter is chosen from an EF-1 promoter, a CMV IE gene promoter, an EF-1 α promoter, an ubiquitin C promoter, or a phosphoglycerate kinase (PGK) promoter.

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In one example, the immune effector cells are genetically modified to express the CAR molecule. In one example, the immune effector cells are transfected with a nucleic acid or vector described herein. In one example, the immune effector cells are selected from the group consisting of T cells, Natural Killer (NK) cells, and cytotoxic T lymphocytes (CTL). In one
25 example, the immune effector cells are CD8⁺ T cells. In one example, the immune effector cells are human cells.

In one example, the immune effector cells lack expression or have low expression of a functional TCR or a functional HLA.

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The immune effector cells may be generated *ex vivo* and administered to the human or the immune effector cells may be generated in the human.

In one example, the immune effector cells are autologous or allogeneic to the human.

In one example, the method of the disclosure further comprises administering an agent that increases the efficacy of the immune effector cells. In one example, said agent is chosen from

5 one or more of:

a protein phosphatase inhibitor;

a kinase inhibitor;

a cytokine;

an inhibitor of an immune inhibitory molecule; or

10 an agent that decreases the level or activity of a TREG cell.

In one example, the method of the disclosure further comprises the step of contacting the immune effector cells, either *ex vivo* or in the human, with a cognate antigen molecule binding to the CLDN6 antigen binding domain. In one example, the cognate antigen molecule is
15 selected from the group consisting of CLDN6 or a fragment thereof, or a variant of CLDN6 or a CLDN6 fragment. In one example, the immune effector cells are contacted with the cognate antigen molecule under conditions such that expansion and/or activation of the immune effector cells occurs. In one example, the step of contacting the immune effector cells with the cognate antigen molecule takes place *in vivo* or *ex vivo*.

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In one example, the method of the disclosure comprises the step of administering the cognate antigen molecule or a nucleic acid coding therefor to the human. In one example, the nucleic acid encoding the cognate antigen molecule is expressed in cells of the human to provide the cognate antigen molecule. In one example, expression of the cognate antigen molecule is at
25 the cell surface. In one example, the nucleic acid encoding the cognate antigen molecule is transiently expressed in cells of the human. In one example, the nucleic acid encoding the cognate antigen molecule is RNA. In one example, the immune effector cells and/or the cognate antigen molecule or the nucleic acid coding therefor are administered systemically. In one example, after systemic administration of the nucleic acid encoding the cognate antigen
30 molecule, expression of the nucleic acid encoding the cognate antigen molecule in spleen occurs. In one example, after systemic administration

of the nucleic acid encoding the cognate antigen molecule, expression of the nucleic acid encoding the cognate antigen molecule in antigen presenting cells, preferably professional antigen presenting cells occurs. In one example, the antigen presenting cells are selected from the group consisting of dendritic cells, macrophages and B cells. In one example, after systemic administration of the nucleic acid encoding the cognate antigen molecule, no or essentially no expression of the nucleic acid encoding the cognate antigen molecule in lung and/or liver occurs. In one example, after systemic administration of the nucleic acid encoding the cognate antigen molecule, expression of the nucleic acid encoding the cognate antigen molecule in spleen is at least 5-fold the amount of expression in lung.

In one example, the nucleic acid encoding the cognate antigen molecule is formulated in a delivery vehicle. In one example, the delivery vehicle comprises particles. In one example, the delivery vehicle comprises at least one lipid. In one example, the at least one lipid comprises at least one cationic lipid. In one example, the lipid forms a complex with and/or encapsulates the nucleic acid encoding the cognate antigen molecule. In one example, the lipid is comprised in a vesicle encapsulating the nucleic acid encoding the cognate antigen molecule. In one example, the nucleic acid encoding the cognate antigen molecule is formulated in lipoplexes.

In one example, the method of the disclosure does not comprise administering the cognate antigen molecule or a nucleic acid coding therefor to the human. In one example, the method of the disclosure does not comprise administering an anti-cancer therapy other than the immune effector cells expressing a CAR molecule to the human.

In one example, the immune effector cells are administered in an amount of between about 10^6 to about 10^9 , about 5×10^6 to about 5×10^8 , or about 10^7 to about 10^8 . In one example, a single dose of the immune effector cells is administered.

In another aspect, the present disclosure provides a composition or medical preparation comprising between 10^6 to 10^9 immune effector cells expressing a chimeric antigen receptor (CAR) molecule, the CAR molecule comprising: i) a CLDN6 antigen binding domain; ii) a transmembrane domain; and iii) an intracellular domain that comprises a 4-1BB costimulatory domain, and a CD3-zeta signaling domain, optionally wherein the CAR molecule comprises:
5 i) a CLDN6 antigen binding domain; ii) a CD8 α hinge domain; iii) a CD8 α transmembrane domain; and iv) an intracellular domain that comprises a 4-1BB costimulatory domain, and a CD3-zeta signaling domain, further optionally wherein the CLDN6 antigen binding domain comprises an antibody, an antibody fragment, an scFv, a Fv, a Fab, a (Fab')₂, a single domain
10 antibody (SDAB), a VH or VL domain, or a camelid VHH domain, preferably wherein the CLDN6 antigen binding domain comprises an scFv. The present disclosure further provides a composition or medical preparation comprising between about 10^6 to about 10^9 , about 5×10^6 to about 5×10^8 , or about 10^7 to about 10^8 immune effector cells expressing a chimeric antigen receptor (CAR) molecule, the CAR molecule comprising:

i) a CLDN6 antigen binding domain;
ii) a transmembrane domain; and
iii) an intracellular domain that comprises a 4-1BB costimulatory domain, and a CD3-zeta signaling domain. Certain examples of the composition or medical preparation, in particular
5 of the immune effector cells, are as described above for the method of the disclosure.

In one example, the composition or medical preparation further comprises an agent that increases the efficacy of the immune effector cells and/or a cognate antigen molecule binding to the CLDN6 antigen binding domain or a nucleic acid coding therefor. Certain examples of
10 the composition or medical preparation, in particular of the agent that increases the efficacy of the immune effector cells and/or the cognate antigen molecule binding to the CLDN6 antigen binding domain or a nucleic acid coding therefor, are as described above for the method of the disclosure.

15 In another aspect, the present disclosure provides for the composition or medical preparation as described herein, which is a kit, optionally further comprising instructions for use of the kit in the use of the medicament for the treatment of a solid tumor as defined herein. In one example, the composition or medical preparation is a kit. In one example, the kit further comprises instructions for use of the kit in the methods of the disclosure.

20 In a further example, the disclosure provides the agents and compositions such as the immune effector cells or the cognate antigen molecule or a nucleic acid coding therefor described herein for use in the methods described herein. In yet another aspect, the present disclosure provides for the composition or medical preparation as described herein for use in treating a
25 solid tumor in a human, said use comprising administering to the human the composition or medical preparation. In yet another aspect, the present disclosure provides for a use of the immune effector cells as defined herein or the composition or medical preparation as defined herein in the manufacture of a medicament for the treatment of a solid tumor in a human.

30 Other features and advantages of the instant disclosure will be apparent from the following detailed description and claims.

CLAIMS

1. Use of immune effector cells expressing a chimeric antigen receptor (CAR) molecule in the manufacture of a medicament for the treatment of a solid tumor in a human, wherein the human is to be administered immune effector cells expressing a CAR molecule, and wherein the CAR molecule comprises:

- i) a CLDN6 antigen binding domain;
- ii) a transmembrane domain; and
- iii) an intracellular domain that comprises a 4-1BB costimulatory domain, and a CD3-zeta signaling domain,

optionally wherein the CAR molecule comprises:

- i) a CLDN6 antigen binding domain;
- ii) a CD8 α hinge domain;
- iii) a CD8 α transmembrane domain; and
- iv) an intracellular domain that comprises a 4-1BB costimulatory domain, and a CD3-zeta signaling domain,

further optionally wherein the CAR molecule comprises the amino acid sequence of SEQ ID NO: 36 or a functional variant thereof.

2. The use of claim 1, wherein the solid tumor is a CLDN6-positive solid tumor, and/or wherein the solid tumor is an advanced solid tumor, and/or wherein the solid tumor is a relapsed or refractory advanced solid tumor, and/or wherein the solid tumor is testicular cancer.

3. The use of claim 1 or 2, wherein the CLDN6 antigen binding domain comprises an antibody, an antibody fragment, an scFv, a Fv, a Fab, a (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain, and/or wherein the CLDN6 antigen binding domain comprises an scFv, and/or wherein the CLDN6 antigen binding domain comprises the amino acid sequence of SEQ ID NO: 35 or a functional variant thereof.

4. The use of any one of claims 1 to 3, wherein the 4-1BB costimulatory domain comprises the amino acid sequence of SEQ ID NO: 30 or a functional variant thereof.

5. The use of any one of claims 1 to 4, wherein the CAR molecule does not comprise a further costimulatory domain.

6. The use of any one of claims 1 to 5, wherein the CD3-zeta signaling domain comprises the amino acid sequence of SEQ ID NO: 31 or a functional variant thereof.

7. The use of any one of claims 1 to 6, wherein the transmembrane domain comprises a transmembrane domain of a protein selected from the group consisting of the alpha, beta or zeta chain of the T cell receptor, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD154, KIRDS2, OX40, CD2, CD27, LFA-1 (CD11a, CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD40, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), CD160, CD19, IL2R beta, IL2R gamma, IL7Ra, ITGA1, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, TNFR2, DNAMI (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGLI, CD100 (SEMA4D), SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, PAG/Cbp, NKp44, NKp30, NKp46, NKG2D, and NKG2C, or a functional variant thereof, and/or wherein the transmembrane domain comprises a CD8 α transmembrane domain, and/or wherein the transmembrane domain comprises the amino acid sequence of SEQ ID NO: 28 or a functional variant thereof.

8. The use of any one of claims 1 to 7, wherein the antigen binding domain is connected to the transmembrane domain by a hinge domain, optionally wherein the hinge domain is a CD8 α hinge domain, further optionally wherein the hinge domain comprises the amino acid sequence of SEQ ID NO: 27 or a functional variant thereof.

9. The use of any one of claims 1 to 8, wherein the CAR molecule further comprises a leader sequence.

10. The use of any one of claims 1 to 9, wherein the immune effector cells are genetically modified to express the CAR molecule.

11. The use of any one of claims 1 to 10, wherein the immune effector cells are selected from the group consisting of T cells, a Natural Killer (NK) cells, and cytotoxic T lymphocytes (CTL), and/or wherein the immune effector cells are CD8+ T cells, and/or wherein the immune effector cells are human cells, and/or wherein the immune effector cells lack expression or have low expression of a functional TCR or a functional HLA, and/or wherein the immune effector cells are autologous or allogeneic to the human.

12. The use of any one of claims 1 to 11, said method further comprising administering an agent that increases the efficacy of the immune effector cells, optionally wherein said agent is chosen from one or more of:

a protein phosphatase inhibitor;

a kinase inhibitor;

a cytokine;

an inhibitor of an immune inhibitory molecule; or

an agent that decreases the level or activity of a TREG cell.

13. The use of any one of claims 1 to 12, said use further comprising the step of contacting the immune effector cells with a cognate antigen molecule binding to the CLDN6 antigen binding domain, optionally wherein the cognate antigen molecule is selected from the group consisting of CLDN6 or a fragment thereof, or a variant of CLDN6 or a CLDN6 fragment, further optionally wherein the step of contacting the immune effector cells with the cognate antigen molecule takes place *in vivo* or *ex vivo*.

14. The use of claim 13, wherein the immune effector cells are contacted with the cognate antigen molecule under conditions such that expansion and/or activation of the immune effector cells occurs.

15. The use of claim 13 or 14, which further comprises the step wherein the cognate antigen molecule or a nucleic acid, preferably RNA, coding therefor is to be administered to the human, wherein the nucleic acid encoding the cognate antigen molecule is expressed in cells of the human to provide the cognate antigen molecule, optionally wherein expression of the

cognate antigen molecule is at the cell surface, further optionally wherein the nucleic acid encoding the cognate antigen molecule is transiently expressed in cells of the human.

16. The use of any one of claims 1 to 15, (i) wherein the immune effector cells and/or the cognate antigen molecule or the nucleic acid coding therefor are to be administered systemically, optionally wherein, after systemic administration of the nucleic acid encoding the cognate antigen molecule, expression of the nucleic acid encoding the cognate antigen molecule in spleen occurs, and/or (ii) wherein, after systemic administration of the nucleic acid encoding the cognate antigen molecule, expression of the nucleic acid encoding the cognate antigen molecule in antigen presenting cells, preferably professional antigen presenting cells occurs, optionally wherein the antigen presenting cells are selected from the group consisting of dendritic cells, macrophages and B cells, and/or (iii) wherein, after systemic administration of the nucleic acid encoding the cognate antigen molecule, no or essentially no expression of the nucleic acid encoding the cognate antigen molecule in lung and/or liver occurs, and/or (iv) wherein, after systemic administration of the nucleic acid encoding the cognate antigen molecule, expression of the nucleic acid encoding the cognate antigen molecule in spleen is at least 5-fold the amount of expression in lung.

17. The use of claim 15 or 16, wherein the nucleic acid encoding the cognate antigen molecule is formulated in a delivery vehicle, optionally wherein the delivery vehicle comprises particles.

18. The use of claim 17, wherein the delivery vehicle comprises at least one lipid, optionally wherein the at least one lipid comprises at least one cationic lipid, further optionally wherein the lipid forms a complex with and/or encapsulates the nucleic acid encoding the cognate antigen molecule and/or wherein the lipid is comprised in a vesicle encapsulating the nucleic acid encoding the cognate antigen molecule.

19. The use of any one of claims 15 to 18, wherein the nucleic acid encoding the cognate antigen molecule is formulated in lipoplexes.

20. The use of any one of claims 1 to 19, wherein the immune effector cells are to be administered in an amount of between 10^7 to 10^8 .

21. A composition or medical preparation comprising between 10^6 to 10^9 immune effector cells expressing a chimeric antigen receptor (CAR) molecule, the CAR molecule comprising:

- i) a CLDN6 antigen binding domain;
- ii) a transmembrane domain; and
- iii) an intracellular domain that comprises a 4-1BB costimulatory domain, and a CD3-zeta signaling domain,

optionally wherein the CAR molecule comprises:

- i) a CLDN6 antigen binding domain;
- ii) a CD8 α hinge domain;
- iii) a CD8 α transmembrane domain; and
- iv) an intracellular domain that comprises a 4-1BB costimulatory domain, and a CD3-zeta signaling domain, further optionally wherein the CLDN6 antigen binding domain comprises an antibody, an antibody fragment, an scFv, a Fv, a Fab, a (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain, preferably wherein the CLDN6 antigen binding domain comprises an scFv.

22. The composition or medical preparation of claim 21, wherein the CLDN6 antigen binding domain comprises the amino acid sequence of SEQ ID NO: 35 or a functional variant thereof, and/or wherein the 4-1BB costimulatory domain comprises the amino acid sequence of SEQ ID NO: 30 or a functional variant thereof, and/or wherein the CAR molecule does not comprise a further costimulatory domain, and/or wherein the CD3-zeta signaling domain comprises the amino acid sequence of SEQ ID NO: 31 or a functional variant thereof, and/or wherein the transmembrane domain comprises a transmembrane domain of a protein selected from the group consisting of the alpha, beta or zeta chain of the T cell receptor, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD154, KIRDS2, OX40, CD2, CD27, LFA-1 (CD11a, CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD40, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), CD160, CD19, IL2R beta, IL2R gamma, IL7Ra, ITGA1, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, TNFR2, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1,

CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, PAG/Cbp, NKp44, NKp30, NKp46, NKG2D, and NKG2C, or a functional variant thereof, optionally wherein the transmembrane domain comprises a CD8 α transmembrane domain, and/or wherein the transmembrane domain comprises the amino acid sequence of SEQ ID NO: 28 or a functional variant thereof.

23. The composition or medical preparation of claim 21 or 22 wherein the antigen binding domain is connected to the transmembrane domain by a hinge domain, optionally wherein the hinge domain is a CD8 α hinge domain, further optionally wherein the hinge domain comprises the amino acid sequence of SEQ ID NO: 27 or a functional variant thereof, and/or wherein the CAR molecule further comprises a leader sequence.

24. The composition or medical preparation of any one of claims 21 to 23, wherein the CAR molecule comprises the amino acid sequence of SEQ ID NO: 36 or a functional variant thereof.

25. The composition or medical preparation of any one of claims 21 to 24, wherein the immune effector cells are genetically modified to express the CAR molecule.

26. The composition or medical preparation of any one of claims 21 to 25, wherein the immune effector cells are selected from the group consisting of T cells, Natural Killer (NK) cells, and cytotoxic T lymphocytes (CTL), and/or wherein the immune effector cells are CD8 $^{+}$ T cells, and/or wherein the immune effector cells are human cells, and/or wherein the immune effector cells lack expression or have low expression of a functional TCR or a functional HLA.

27. The composition or medical preparation of any one of claims 21 to 26, further comprising an agent that increases the efficacy of the immune effector cells, optionally wherein said agent is chosen from one or more of:

a protein phosphatase inhibitor;

a kinase inhibitor;

a cytokine;

an inhibitor of an immune inhibitory molecule; or

an agent that decreases the level or activity of a TREG cell.

28. The composition or medical preparation of any one of claims 21 to 27, further comprising a cognate antigen molecule binding to the CLDN6 antigen binding domain or a nucleic acid, preferably RNA, coding therefor, optionally wherein the cognate antigen molecule is selected from the group consisting of CLDN6 or a fragment thereof, or a variant of CLDN6 or a CLDN6 fragment.

29. The composition or medical preparation of claim 28, wherein the nucleic acid encoding the cognate antigen molecule is formulated in a delivery vehicle, optionally wherein the delivery vehicle comprises particles and/or wherein the delivery vehicle comprises at least one lipid, optionally wherein the at least one lipid comprises at least one cationic lipid and/or wherein the lipid forms a complex with and/or encapsulates the nucleic acid encoding the cognate antigen molecule and/or wherein the lipid is comprised in a vesicle encapsulating the nucleic acid encoding the cognate antigen molecule.

30. The composition or medical preparation of claim 28 or 29, wherein the nucleic acid encoding the cognate antigen molecule is formulated in lipoplexes.

31. The composition or medical preparation of any one of claims 21 to 30, which is a kit, optionally further comprising instructions for use of the kit in the use of the medicament for the treatment of a solid tumor defined in any one of claims 1 to 20.

32. The composition or medical preparation of any one of claims 21 to 31 for use in treating a solid tumor in a human, said use comprising administering to the human the composition or medical preparation.

33. Use of the immune effector cells defined in any one of claims 1 to 20 or the composition or medical preparation defined in any one of claims 21 to 31 in the manufacture of a medicament for the treatment of a solid tumor in a human.