

cell expresses the at least one co-stimulatory ligand. In certain embodiments, the at least one co-stimulatory ligand is selected from the group consisting of 4-1BBL, CD80, CD86, CD70, OX40L, CD48, TNFRSF14, and combinations thereof. In certain embodiments, the isolated immunoresponsive cell is further transduced with at least one cytokine such that the immunoresponsive cell secretes the at least one cytokine. In certain embodiments, the at least cytokine is selected from the group consisting of IL-2, IL-3, IL-6, IL-7, IL-11, IL-12, IL-15, IL-17, IL-21, and combinations thereof. In some embodiments, the isolated immunoresponsive cell is selected from the group consisting of a T cell, a Natural Killer (NK) cell, a cytotoxic T lymphocyte (CTL), a regulatory T cell, a human embryonic stem cell, a lymphoid progenitor cell, a T cell-precursor cell, and a pluripotent stem cell from which lymphoid cells may be differentiated. In certain embodiments, the immunoresponsive cell is a T cell.

The presently disclosed subject matter further provides nucleic acid molecules encoding the presently disclosed CARs, vectors comprising the nucleic acid molecules, and host cells expressing such nucleic acid molecules. In certain embodiments, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:397. In certain embodiments, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:398. In certain embodiments, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:399. In certain embodiments, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:400. In certain embodiments, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:401. In certain embodiments, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:402. In certain embodiments, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:403. In certain embodiments, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:406. In certain embodiments, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:407. In certain embodiments, the nucleic acid molecule comprises nucleic acids having the sequence set forth in SEQ ID NO:408. In certain embodiments, the vector is a γ -retroviral vector. In certain embodiments, the host cell is a T cell.

The presently disclosed subject matter further provides use of an effective amount of the immunoresponsive cell as described herein, in manufacture of a medicament for reducing tumor burden in a subject.

- 5 The presently disclosed subject matter further provides use of an effective amount of the immunoresponsive cell as described herein, in the manufacture of a medicament for increasing or lengthening survival of a subject having neoplasia.

121. The vector of claim 120, wherein the vector is a γ -retroviral vector.
122. A host cell expressing the nucleic acid molecule of any one of claims 109-119.
123. The host cell of claim 122, wherein the host cell is a T cell.
124. Use of an effective amount of the immunoresponsive cell of any one of claims 100-108, in manufacture of a medicament for reducing tumor burden in a subject.
125. The use of claim 124, wherein the method reduces the number of tumor cells.
126. The use of claim 124, wherein the method reduces tumor size.
127. The use of claim 124, wherein the method eradicates the tumor in the subject.
128. The use of any one of claims 124-127, wherein the tumor is multiple myeloma or Waldenstrom's Macroglobulinemia.
129. The use of claim 128, wherein the tumor is multiple myeloma.
130. The use of any one of claims 124-129, wherein the subject is a human.
131. The use of any one of claims 124-130, wherein the immunoresponsive cell is a T cell.
132. Use of an effective amount of the immunoresponsive cell of any one of claims 100-108, in the manufacture of a medicament for increasing or lengthening survival of a subject having neoplasia.
133. The use of claim 132, wherein the neoplasia is multiple myeloma or Waldenstrom's Macroglobulinemia.
134. The use of claim 133, wherein the neoplasia is multiple myeloma.

135. The use of any one of claims 132-134, wherein the method reduces or eradicates tumor burden in the subject.
136. A method for producing an immunoresponsive cell that binds to a G-protein coupled receptor, comprising introducing into the immunoresponsive cell
a nucleic acid sequence that encodes a chimeric antigen receptor (CAR) comprising an extracellular antigen-binding domain, a transmembrane domain and an intracellular domain, wherein the extracellular antigen-binding domain that specifically binds to a G-protein coupled receptor.
137. The method of claim 136, wherein the G protein receptor is a G-protein coupled receptor family C group 5 member D (GPRC5D).
138. A pharmaceutical composition comprising an effective amount of the immunoresponsive cell of any one of claims 100-108 and a pharmaceutically acceptable excipient.
139. The pharmaceutical composition of claim 138, wherein the pharmaceutical composition is for treating a neoplasia.
140. The pharmaceutical composition of claim 139, wherein the neoplasia is multiple myeloma or Waldenstrom's Macroglobulinemia.
141. The pharmaceutical composition of claim 140, wherein the neoplasia is multiple myeloma.
142. A kit for treating multiple myeloma, comprising the immunoresponsive cell of any one of claims 100-108.
143. The kit of claim 142, wherein the kit further comprises written instructions for using the immunoresponsive cell for treating a subject having a neoplasia.
144. The kit of claim 142 or 143, wherein the neoplasia is multiple myeloma or Waldenstrom's Macroglobulinemia.
145. The kit of claim 144, wherein the neoplasia is multiple myeloma.