

CLAIMS

1. An interleukin 15 (IL15) fusion protein consisting of:
 - a) a first domain consisting of SEQ ID NO:2 (IL15 receptor alpha (IL15Ra));
 - b) a second domain consisting of SEQ ID NO:1 (IL15);
 - c) a third domain consisting of SEQ ID NO:3 (Interleukin-2 receptor beta (IL2Rb));
 - d) a fourth domain consisting of a first IgG1 Fc region; and
 - e) a fifth domain consisting of a second IgG1 Fc region;wherein
 - the first and second domains are linked via a first linker (L1),
 - the second and third domains are linked via a second linker comprising a protease-activatable moiety (L2),
 - the third and fourth domains are linked via a third linker (L3), and
 - the fourth and fifth domains are linked via a disulfide bond.
2. The IL15 fusion protein of claim 1, wherein the first and second IgG1 Fc regions are assembled, at least in part, through a knob into hole interaction.
3. The IL15 fusion protein of claim 1, comprising SEQ ID NO:77 (MK150) and SEQ ID NO:75 (MH8).
4. A pharmaceutical composition comprising the IL15 fusion protein of any one of claims 1 to 3 in combination with at least one additional IL15 construct.
5. Use of the IL15 fusion protein of any one of claims 1 to 3 in the manufacture of a medicament for the therapeutic treatment of cancer.
6. The use of claim 5, wherein the cancer is gastric cancer, colon cancer, pancreatic cancer, breast cancer, head and neck cancer, kidney cancer, liver cancer, small cell lung cancer, non-small cell lung cancer, ovarian cancer, skin cancer, mesothelioma, lymphoma, leukemia, myeloma and sarcoma.
7. Use of the IL15 fusion protein of any one of claims 1 to 3 in the manufacture of a medicament for the therapeutic treatment of cancer, wherein the medicament is to be administered in combination with another therapeutic agent.
8. The use of claim 7, wherein the therapeutic agent is an immune checkpoint agent.
9. The use of claim 8, wherein the immune checkpoint agent is a PD-1, PD-L1, PD-L2, TIM3, LAG-3, OX40 or TIGIT antibody.

10. The use of claim 7, wherein the cancer is gastric cancer, colon cancer, pancreatic cancer, breast cancer, head and neck cancer, kidney cancer, liver cancer, small cell lung cancer, non-small cell lung cancer, ovarian cancer, skin cancer, mesothelioma, lymphoma, leukemia, myeloma and sarcoma.