

CLAIMS

1. A bispecific antigen-binding molecule comprising:
 - (1) a cancer-specific antigen-binding Fab domain;
 - (2) CD137-binding Fab domain; and
 - (3) an FcRn-binding domain, wherein the FcRn-binding domain is an antibody Fc region having decreased Fc γ receptor-binding activity, wherein the antigen-binding molecule has an agonistic activity against CD137.
2. The antigen-binding molecule of claim 1, which is an antibody.
3. A pharmaceutical composition comprising as an active ingredient the antigen-binding molecule of claim 1 or 2.
4. The pharmaceutical composition of claim 3, which is a cytotoxicity-inducing composition.
5. A pharmaceutical composition comprising a combination of a first antigen-binding molecule of claim 1 or 2, and a second bispecific antigen-binding molecule that comprises:
 - (1) a cancer-specific antigen-binding domain; and
 - (2) CD3-binding domain.
6. The antigen-binding molecule of claim 1 or claim 2 or the composition of any one of claims 3 to 5 for use in the treatment of cancer.
7. Use of ~~an~~ a bispecific agonistic antigen-binding molecule comprising:
 - (1) a cancer-specific antigen-binding Fab domain;
 - (2) a CD137-binding Fab domain; and
 - (3) ~~n~~ FcRn-binding domain, wherein the FcRn-binding domain is an antibody Fc region having decreased Fc γ receptor-binding activity, wherein the antigen-binding molecule has agonistic activity against CD137, in the manufacture of a medicament for the treatment of cancer.
8. Use of a composition comprising a combination of:
 - a first bispecific agonistic antigen-binding molecule comprising:
 - (1) a cancer-specific antigen-binding Fab domain;
 - (2) a CD137-binding Fab domain; and
 - (3) an FcRn-binding domain, wherein the FcRn-binding domain is an antibody Fc region having decreased Fc γ receptor-binding activity, and
 - a second antigen-binding molecule comprising:

(1) a cancer-specific antigen-binding domain;
 (2) a ~~T-cell~~CD3 receptor complex-binding domain and
 (3) an FcRn-binding domain, wherein the FcRn-binding domain is an antibody Fc region having decreased Fcγ receptor-binding activity, wherein the first antigen-binding molecule has agonistic activity against CD137, in the manufacture of a medicament for the treatment of cancer.

~~9. The composition of claim 5 or the use of claim 8, wherein the T-cell receptor complex-binding domain is a T-cell receptor-binding domain.~~

~~10.9.~~ The composition of claim 5 or the use of claim 8, wherein the T cell receptor complex-binding domain is a CD3-binding domain.

~~11.10.~~ The composition of claim 5 or the use of claim 8, wherein the second antigen-binding molecule is an antibody.

~~12.11.~~ The composition of any one of claims 3 to 5 or the use of any one of claims ~~6~~ 7 to ~~11~~10, wherein the composition or medicament is cytotoxicity-inducing composition.

~~13.12.~~ A kit comprising:

- a) a pharmaceutical composition comprising as an active ingredient a first bispecific agonistic antigen-binding molecule that comprises:
 - (1) a cancer-specific antigen-binding Fab domain;
 - (2) a CD137-binding Fab domain; and
 - (3) an FcRn-binding domain, wherein the FcRn-binding domain is an antibody Fc region having decreased Fcγ receptor-binding activity; and
 - b) a second bispecific antigen-binding molecule that comprises:
 - (1) a cancer-specific antigen-binding domain;
 - (2) a ~~T-cell~~CD3 receptor complex-binding domain; and
 - (3) an FcRn-binding domain, wherein the FcRn-binding domain is an antibody Fc region having decreased Fcγ receptor-binding activity;
- wherein the first antigen-binding molecule has agonistic activity against CD137, and wherein the composition is for use concomitantly with the second antigen-binding molecule in the treatment of cancer.

~~14. Use of a kit comprising:~~

- ~~a) a pharmaceutical composition comprising as an active ingredient a first agonistic antigen-binding molecule that comprises:~~
 - ~~(1) a cancer specific antigen-binding Fab domain;~~
 - ~~(2) a CD137-binding Fab domain; and~~
 - ~~(3) an FcRn-binding domain, wherein the FcRn-binding domain is an antibody Fc region having decreased Fcγ receptor-binding activity;~~

~~in the manufacture of a medicament for the treatment of cancer; and~~

~~b) a second antigen-binding molecule that comprises:~~

~~(1) a cancer-specific antigen-binding domain;~~

~~(2) a T cell receptor complex-binding domain; and~~

~~(3) an FcRn-binding domain, wherein the FcRn-binding domain is an antibody Fc region having decreased Fcγ receptor-binding activity;~~

~~wherein the composition is to be used concomitantly with the second antigen-binding molecule.~~

~~15.13.~~ Use of a first **bispecific** agonistic antigen-binding molecule comprising:

(1) a cancer-specific antigen-binding Fab domain;

(2) a CD137-binding Fab domain; and

(3) an FcRn-binding domain, wherein the FcRn-binding domain is an antibody Fc region having decreased Fcγ receptor-binding activity,

wherein the first antigen-binding molecule has agonistic activity against CD137, in

the manufacture of a medicament for the treatment of cancer,

wherein the medicament is to be used concomitantly with a second antigen-binding molecule that comprises:

(1) a cancer-specific antigen-binding domain;

(2) a ~~T-cell~~**CD3** receptor complex-binding domain; and

(3) an FcRn-binding domain, wherein the FcRn-binding domain is an antibody Fc region having decreased Fcγ receptor-binding activity.

~~16.14.~~ The kit of claim ~~13-12~~ or the use of claim ~~14-13~~ or ~~claim 15~~, wherein the composition or medicament is cytotoxicity-inducing.

~~17.15.~~ The kit of claim ~~13-12~~ or the use of any one of claims ~~14-13~~ to ~~1614~~, wherein the T cell receptor complex-binding domain is a T cell receptor-binding domain.

~~18.16.~~ The kit of claim ~~13-12~~ or the use of any one of claims ~~14-13~~ to ~~1614~~, wherein the T cell receptor complex-binding domain is a CD3-binding domain.

~~19.17.~~ The kit of claim ~~13-12~~ or the use of any one of claims ~~14-13~~ to ~~1816~~, wherein the first antigen-binding molecule and/or the second antigen-binding molecule is an antibody.

~~20.18.~~ The kit of claim ~~13-12~~ or the use of any one of claims ~~14-13~~ to ~~1917~~, wherein the composition or medicament is to be administered either simultaneously with or separately from the second antigen-binding molecule.

~~21. Use of a kit comprising:~~

~~a) a pharmaceutical composition comprising as an active ingredient a second antigen-binding molecule that comprises:~~

~~(1) a cancer-specific antigen-binding domain;
 (2) a T cell receptor complex binding domain; and
 (3) an FcRn-binding domain, wherein the FcRn-binding domain is an antibody Fc region having decreased Fcγ receptor-binding activity;
 in the manufacture of a medicament for the treatment of cancer, and
 b) a first agonistic antigen-binding molecule that comprises:
 (1) a cancer-specific antigen-binding Fab domain;
 (2) a CD137-binding Fab domain; and
 (3) an FcRn-binding domain, wherein the FcRn-binding domain is an antibody Fc region having decreased Fcγ receptor-binding activity;
 wherein the composition is to be used concomitantly with the first agonistic antigen-binding molecule.~~

22.19. Use of a second bispecific antigen-binding molecule comprising:

- (1) a cancer-specific antigen-binding domain;
- (2) a T cellCD3 receptor complex-binding domain; and
- (3) an FcRn-binding domain, wherein the FcRn-binding domain is an antibody Fc region having decreased Fcγ receptor-binding activity, in the manufacture of a medicament for the treatment of cancer, wherein the medicament is to be used concomitantly with a first agonistic antigen-binding molecule that comprises:
 - (1) a cancer-specific antigen-binding Fab domain;
 - (2) a CD137-binding Fab domain; and
 - (3) an FcRn-binding domain, wherein the FcRn-binding domain is an antibody Fc region having decreased Fcγ receptor-binding activity
wherein the second antigen-binding molecule has agonistic activity against CD137.

23.20. The use of claim 22.19 ~~or claim 23~~, wherein the composition or medicament is cytotoxicity-inducing composition.

24.21. The use of any one of claims 22.19 to 24.21, wherein the T cell receptor complex-binding domain is a T cell receptor-binding domain.

25.22. The use of any one of claims 22.19 to 24.21, wherein the T cell receptor complex-binding domain is a CD3-binding domain.

26.23. The use of any one of claims 22.19 to 26.23, wherein the first agonistic antigen-binding molecule and/or the second antigen-binding molecule is an antibody.

27.24. The use of any one of claims 22.19 to 27.24, wherein the composition or medicament is to be administered either simultaneously with or separately from the first agonistic antigen-binding molecule.

