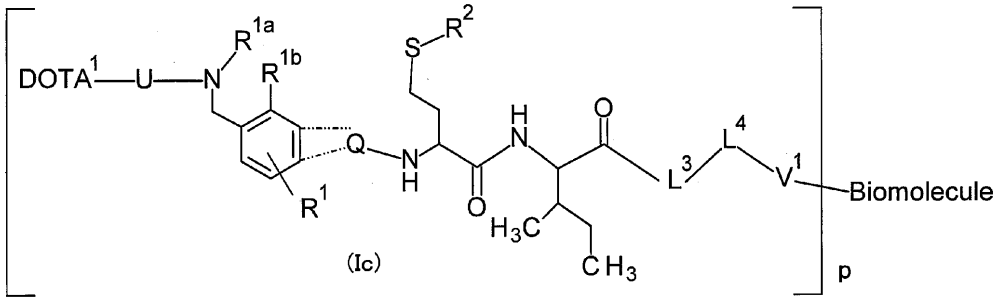
CLAIMS

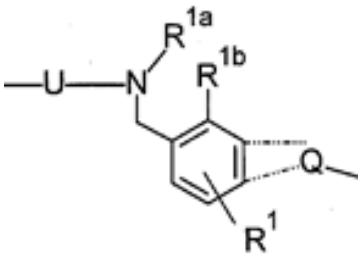
1. A conjugate represented by the following formula (Ic):



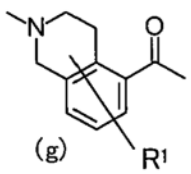
(Ic)

wherein

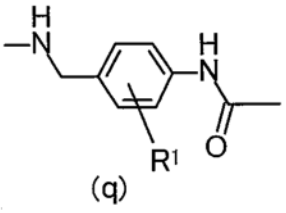
$DOTA^1$ is 3arm DOTA,



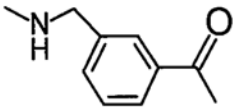
is



(g)



(q)



,

p is a natural number of 1 to 25 and is bonded to an adjacent carbon atom via p amino groups or thiol groups in Biomolecule;

R^1: H, a halogen, C_{1-6} alkyl, or halo C_{1-6} alkyl,

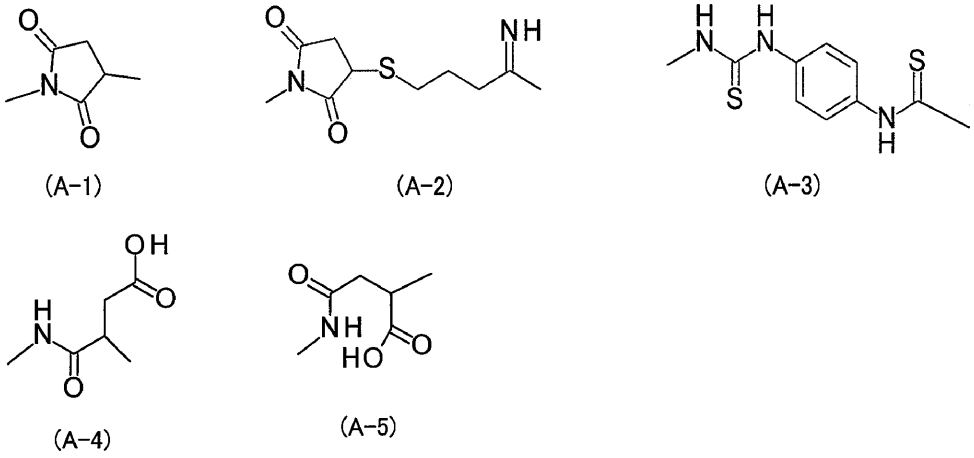
R^2: C_{1-6} alkyl or halo C_{1-6} alkyl,

L^3: a bond,

L^4: $-NH-(CH_2)_2-$, or $-NHCH(C(=O)OH)(CH_2)_4-$,

V^1: a group represented by any of the following formulas (A-1) to (A-5),

[Chemical Formula 127]

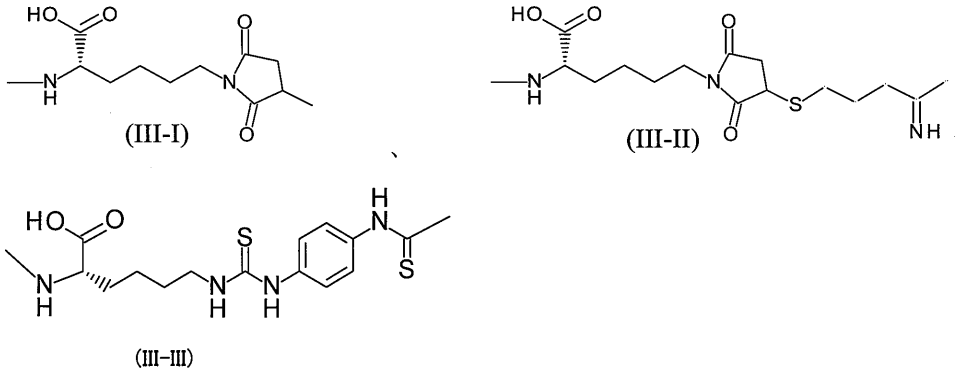


(A-1) (A-2) (A-3)

(A-4) (A-5)

or, formula -L^3-L^4-V^1- together forms the following formula

[Chemical Formula 128]



(III-I) (III-II)

(III-III)

Biomolecule is an anti-human MUC1 antibody Fab fragment selected from the group consisting of:

(a) an anti-human MUC1 antibody Fab fragment comprising a heavy chain fragment including a heavy chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 12 or SEQ ID NO: 14 and a light chain including a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 16,

and

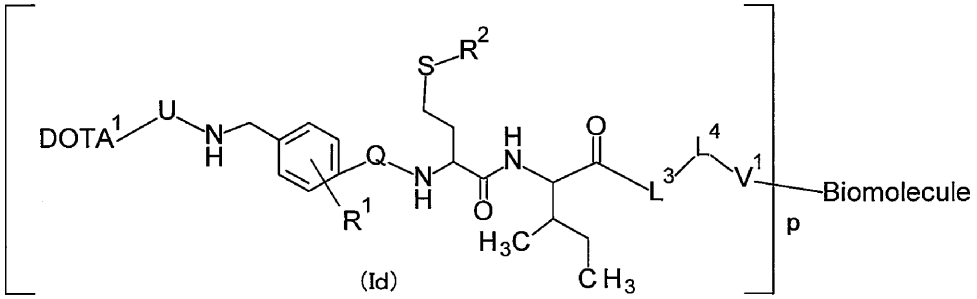
(b) an anti-human MUC1 antibody Fab fragment selected from the group consisting of an anti-human MUC1 antibody Fab fragment comprising a heavy chain fragment including a heavy chain variable region which consists of the amino acid sequence shown in SEQ ID NO: 12 or SEQ ID NO: 14 and in which glutamine of amino acid 1 of SEQ ID NO: 12 or SEQ ID NO: 14 is modified to pyroglutamic acid, and a light chain

including a light chain variable region consisting of the amino acid sequence shown in SEQ ID NO: 16,

and the fragment is bound to V^1 via p amino groups or thiol groups in the fragment.

2. The conjugate according to claim 1, wherein the conjugate is represented by the following formula (Id):

[Chemical Formula 135]

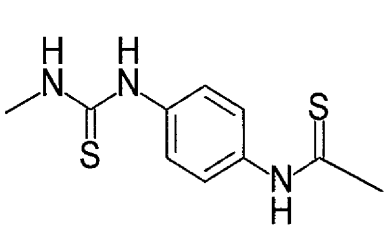


(Id)

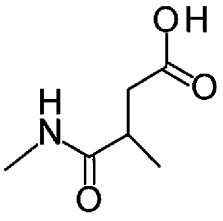
wherein U is bond, Q is -NH-C(O)-.

3. The conjugate according to any of claims 1 to 2, wherein V^1 is any of the following formulas (A-3) to (A-5):

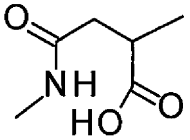
[Chemical Formula 136]



(A-3)

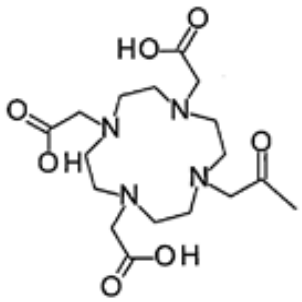


(A-4)



(A-5)

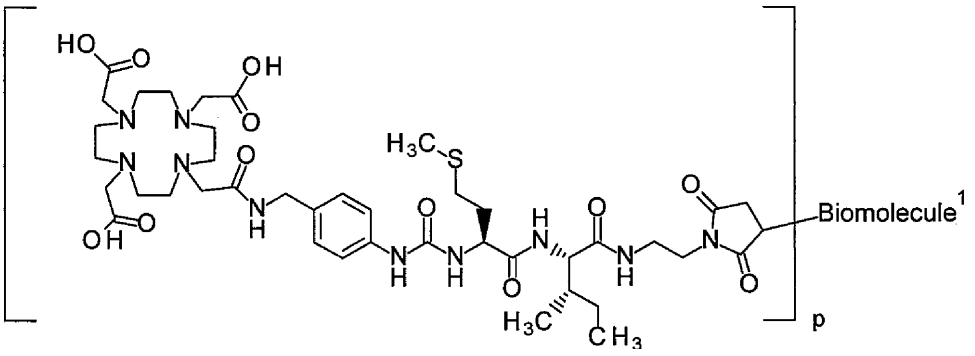
4. The conjugate according to any of claims 1 to 3, wherein $DOTA^1$ is



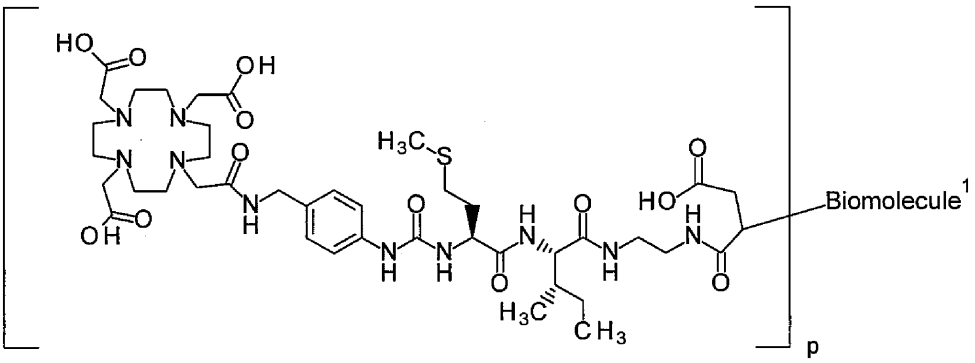
5. The conjugate according to any of claims 1 to 4, wherein R^2 is methyl.

6. The conjugate according to any of claims 1 to 5, wherein the conjugate is selected from the group consisting of the compounds represented by the following formulas:

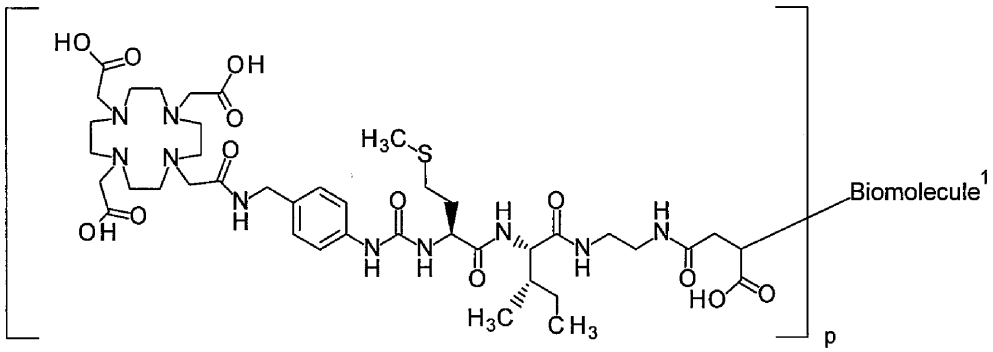
[Chemical Formula 137]



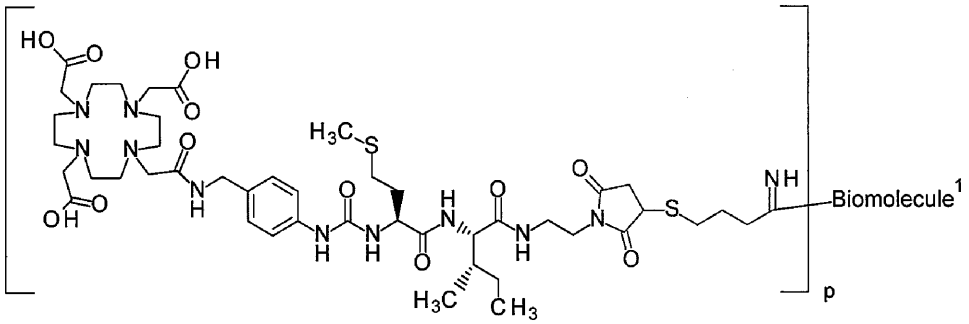
[Chemical Formula 138]



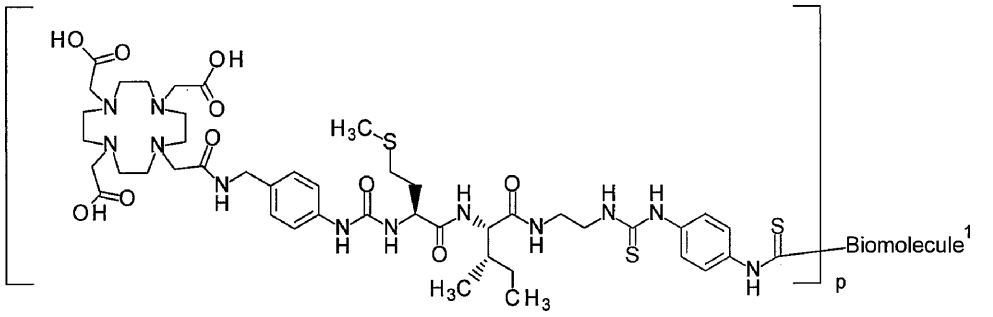
[Chemical Formula 139]



[Chemical Formula 140]



[Chemical Formula 141]



,

wherein Biomolecule[1] is the Biomolecule described in Claim 1.

7. The conjugate according to claim 1 to 6, wherein Biomolecule is an anti-human MUC1 antibody Fab fragment selected from the group consisting of:

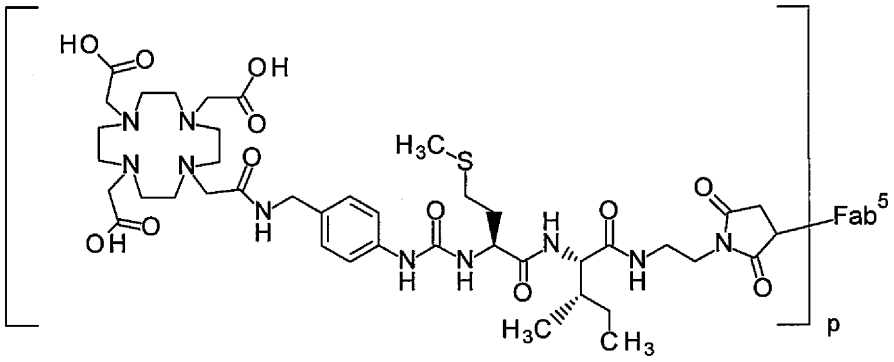
(a) an anti-human MUC1 antibody Fab fragment comprising a heavy chain fragment consisting of the amino acid sequence shown in SEQ ID NO: 8 and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 10; and

(b) an anti-human MUC1 antibody Fab fragment comprising a heavy chain fragment which consists of the amino acid sequence shown in SEQ ID NO: 8 and in which glutamine of amino acid 1 of SEQ ID NO: 8 is modified to pyroglutamic acid, and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 10.

8. The conjugate according to claim 7, wherein Biomolecule is an anti-human MUC1 antibody Fab fragment comprising a heavy chain fragment which consists of the amino acid sequence shown in SEQ ID NO: 8 and in which glutamine of amino acid 1 of SEQ ID NO: 8 is modified to pyroglutamic acid, and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 10.

9. A conjugate represented by the following formula:

[Chemical Formula 144]



wherein Fab^5 is the following antibody Fab fragment:

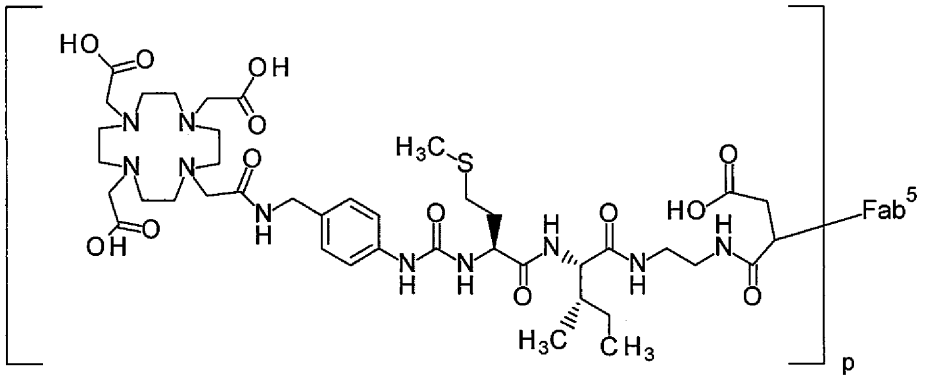
an anti-human MUC1 antibody Fab fragment comprising a heavy chain fragment which consists of the amino acid sequence shown in SEQ ID NO: 8 and in which glutamine of amino acid 1 of SEQ ID NO: 8 is modified to pyroglutamic acid, and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 10;

p is a natural number of 1 to 25; and

Fab^5 is bound to an adjacent carbon atom via p amino groups or thiol groups in the Fab^5.

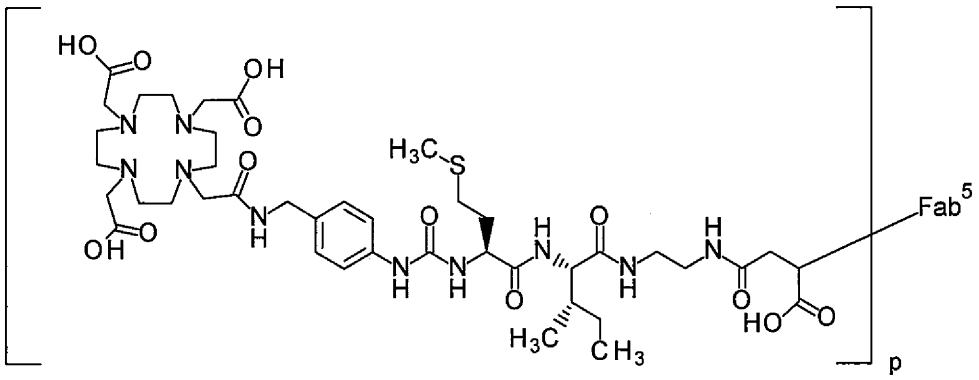
10. A conjugate represented by the following formula:

[Chemical Formula 145]



wherein Fab^5 is the following antibody Fab fragment:
an anti-human MUC1 antibody Fab fragment comprising a heavy chain fragment which consists of the amino acid sequence shown in SEQ ID NO: 8 and in which glutamine of amino acid 1 of SEQ ID NO: 8 is modified to pyroglutamic acid, and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 10;
p is a natural number of 1 to 25; and
Fab^5 is bound to an adjacent carbon atom via p amino groups or thiol groups in the Fab^5.

11. A conjugate represented by the following formula:
[Chemical Formula 146]

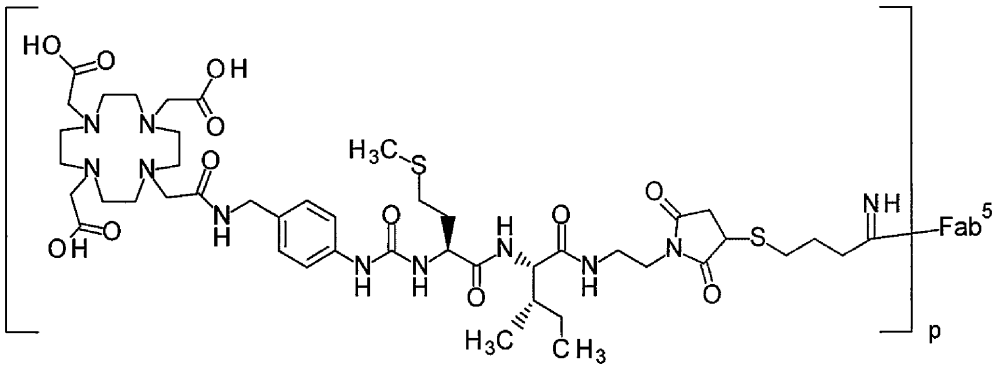


wherein Fab^5 is the following antibody Fab fragment:
an anti-human MUC1 antibody Fab fragment comprising a heavy chain fragment which consists of the amino acid sequence shown in SEQ ID NO: 8 and in which glutamine of amino acid 1 of SEQ ID NO: 8 is modified to pyroglutamic acid, and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 10;
p is a natural number of 1 to 25; and

Fab^5 is bound to an adjacent carbon atom via p amino groups or thiol groups in the Fab^5.

12. A conjugate represented by the following formula:

[Chemical Formula 147]



wherein Fab^5 is the following antibody Fab fragment:

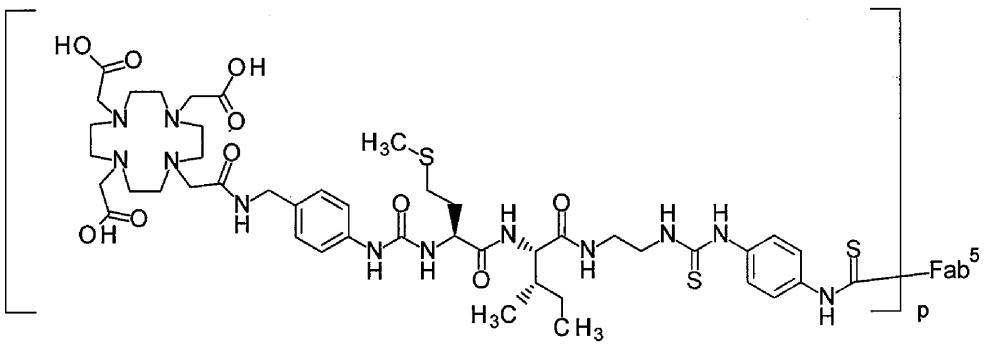
an anti-human MUC1 antibody Fab fragment comprising a heavy chain fragment which consists of the amino acid sequence shown in SEQ ID NO: 8 and in which glutamine of amino acid 1 of SEQ ID NO: 8 is modified to pyroglutamic acid, and a light chain consisting of the amino acid sequence shown in SEQ ID NO: 10;

p is a natural number of 1 to 25; and

Fab^5 is bound to an adjacent carbon atom via p amino groups or thiol groups in the Fab^5.

13. A conjugate represented by the following formula:

[Chemical Formula 148]



wherein Fab^5 is the following antibody Fab fragment:

an anti-human MUC1 antibody Fab fragment comprising a heavy chain fragment which consists of the amino acid sequence shown in SEQ ID NO: 8 and in which glutamine of amino acid 1 of SEQ ID NO: 8 is modified to pyroglutamic acid, and a light chain

consisting of the amino acid sequence shown in SEQ ID NO: 10;
p is a natural number of 1 to 25; and
Fab^5 is bound to an adjacent carbon atom via p amino groups or thiol groups in the Fab^5.

14. The conjugate according to any one of claims 1 to 13, wherein p is a natural number of 1 to 4.

15. The conjugate according to any one of claims 1 to 14, wherein a metal is coordinated to 3arm DOTA.

16. The conjugate according to claim 15, wherein the metal is a metal radioisotope.

17. The conjugate according to claim 16, wherein the metal is ^{89}Zr.

18. The conjugate according to claim 16, wherein the metal is a paramagnetic metal ion.

19. The conjugate according to claim 18, wherein the metal is Gd^{3+}.

20. The conjugate according to any one of claims 15 to 17, wherein the conjugate is a PET tracer.

21. A diagnostic composition comprising one or more conjugates according to any one of claims 15 to 20 and a pharmaceutically acceptable carrier.

22. A pharmaceutical composition comprising one or more conjugates according to any one of claims 15 to 19 and a pharmaceutically acceptable carrier.

23. The pharmaceutical composition according to claim 22, wherein the pharmaceutical composition is a pharmaceutical composition for treating a cancer expressing human MUC1.

24. The pharmaceutical composition according to claim 23, wherein the cancer is breast cancer, lung cancer, colorectal cancer, bladder cancer, skin cancer, thyroid cancer, gastric cancer, pancreatic cancer, kidney cancer, ovarian cancer, or cervical cancer.

25. Use of the conjugate according to any one of claims 15 to 19 for production of a diagnostic composition for a cancer and/or in the manufacture of a medicament in the form of a pharmaceutical composition for the treatment of cancer.