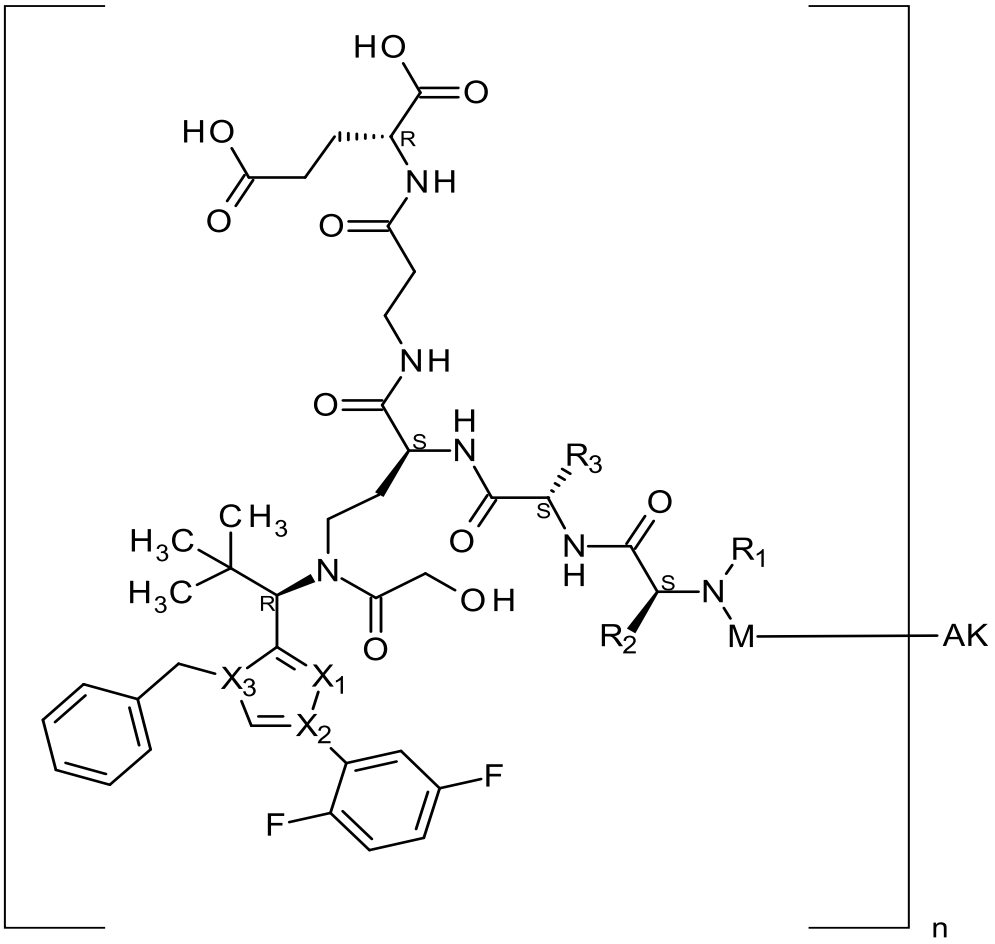
Claims

1. Binder-drug conjugates of the formula (I)



(I)

in which

X_1	represents CH,
X_2	represents C and
X_3	represents N;
R^1	represents hydrogen or methyl,
R^2	represents methyl, $-CH_2-CH(CH_3)_2$, $-CH_2-C(=O)OH$ or isopropyl,
R^3	represents methyl, $-CH_2-CH(CH_3)_2$ or $-CH_2-C(=O)-NH_2$,

M represents the group

#-C(=O)-CH(CH_3)-NH-C(=O)-CH_2-W,

#-C(=O)-CH_2-NH-C(=O)-CH_2-CH(##)-COOH,

#-C(=O)-CH_2-NH-C(=O)-CH(##)-CH_2-COOH,

#-C(=O)-CH_2-W,

#-C(=O)-CH(CH_3)-NH-C(=O)-$(CH_2)_3$-C(=O)-###,

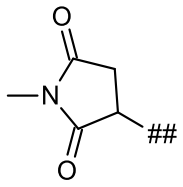
#-C(=O)- $(CH_2)_3$-C(=O)-###,

#-C(=O)-CH(CH_3)-NH-C(=O)-$(CH_2)_5$-W,

#-C(=O)-CH(CH_3)-NH-C(=O)-(CH_2)-## or

#-C(=O)-CH(CH_3)-NH-C(=O)-$(CH_2$-CH_2-$O)_4$-$(CH_2)_2$-NH-C(=O)-CH_2-##,

W represents the group



n represents a number from 1 to 50,

AK represents a binder or a derivative thereof, preferably an antibody or an antigen-binding antibody fragment,

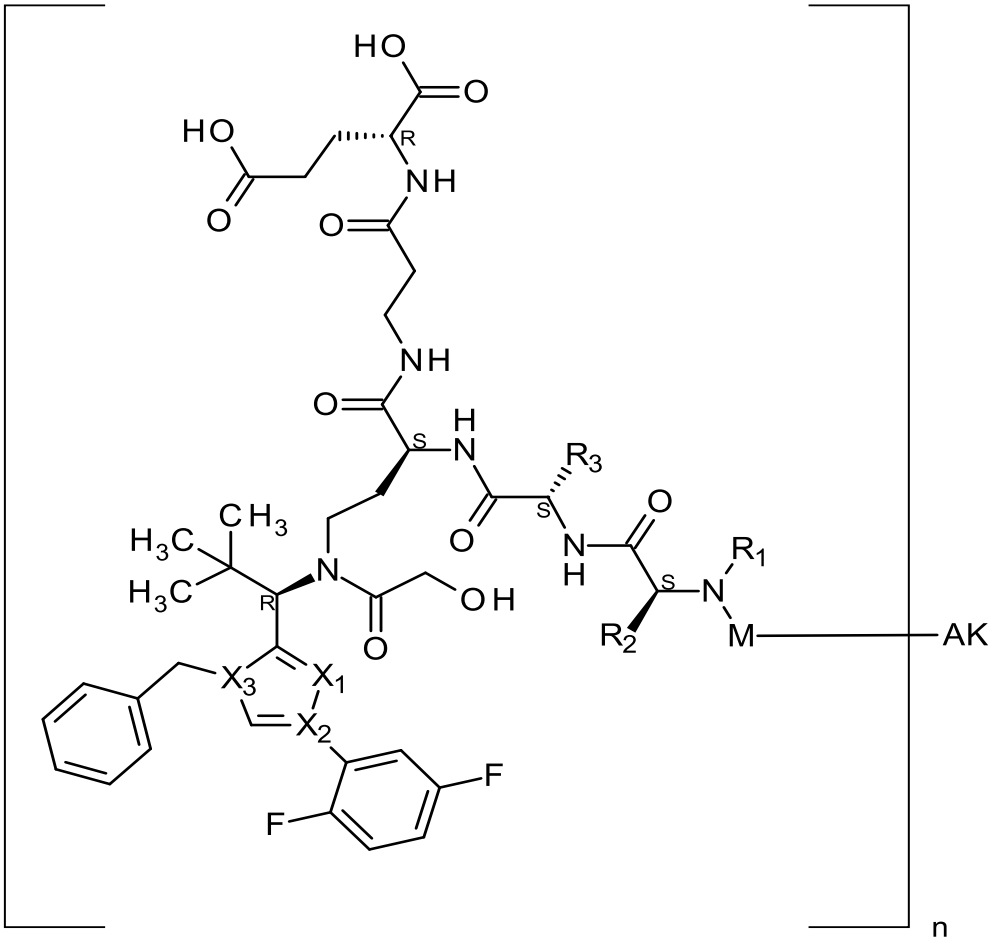
represents the bond to the compound,

represents the bond to a sulfur atom of a cysteine side-chain of the binder,

represents the bond to a nitrogen atom of a lysine side-chain of the binder,

and their salts, solvates and salts of these solvates.

2. Binder-drug conjugates of the formula (I)



(I)

in which

X_1 represents CH,

X_2 represents C,

X_3 represents N;

R^1 represents methyl,

R^2 represents methyl, $-CH_2-CH(CH_3)_2$, $-CH_2-C(=O)OH$ or isopropyl,

R^3 represents methyl, $-CH_2-CH(CH_3)_2$ or $-CH_2-C(=O)-NH_2$,

M represents the group

#-C(=O)-CH(CH_3)-NH-C(=O)-CH_2-NH-C(=O)-CH_2-CH(##)-COOH,

#-C(=O)-CH(CH_3)-NH-C(=O)-CH_2-NH-C(=O)-CH(##)-CH_2-COOH,

#-C(=O)-CH(CH_3)-NH-C(=O)-CH_2-W,

#-C(=O)-CH_2-NH-C(=O)-CH_2-CH(##)-COOH,

#-C(=O)-CH_2-NH-C(=O)-CH(##)-CH_2-COOH,

#-C(=O)-CH_2-W,

#-C(=O)-CH(CH_3)-NH-C(=O)-$(CH_2)_3$-C(=O)-###,

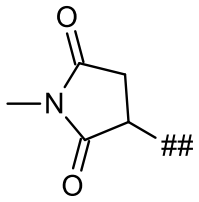
#-C(=O)- $(CH_2)_3$-C(=O)-###,

#-C(=O)-CH(CH_3)-NH-C(=O)-$(CH_2)_5$-W,

#-C(=O)-CH(CH_3)-NH-C(=O)-(CH_2)-## or

#-C(=O)-CH(CH_3)-NH-C(=O)-$(CH_2$-CH_2-O$)_4$-$(CH_2)_2$-NH-C(=O)-CH_2-##,

W represents the group



n represents a number from 1 to 50,

AK represents a binder or a derivative thereof, preferably an antibody or an antigen-binding antibody fragment,

represents the bond to the compound,

represents the bond to a sulfur atom of a cysteine side-chain of the binder,

represents the bond to a nitrogen atom of a lysine side-chain of the binder,

and their salts, solvates and salts of these solvates.

3. Binder-drug conjugates of the formula (I) according to Claims 1 and 2,

in which

R^1 represents methyl,

R^2 represents methyl or isopropyl,

R^3 represents methyl or $–CH_2$-C(=O)-NH_2,

M represents the group

#-C(=O)-CH(CH_3)-NH-C(=O)-$(CH_2)_3$-C(=O)-###,

n represents a number from 1 to 50,

AK represents a binder or a derivative thereof, preferably an antibody or an antigen-binding antibody fragment,

represents the bond to the compound,

represents the bond to a nitrogen atom of a lysine side-chain of the binder,

and their salts, solvates and salts of these solvates.

4. Binder-drug conjugates of the formula (I) according to Claims 1 to 3, in which

R^1 represents methyl,

R^2 represents methyl,

R^3 represents $–CH_2-C(=O)-NH_2$,

M represents the group

#-C(=O)-CH(CH_3)-NH-C(=O)-$(CH_2)_3$-C(=O)-###,

n represents a number from 1 to 50,

AK represents a binder or a derivative thereof, preferably an antibody or an antigen-binding antibody fragment,

represents the bond to the compound,

represents the bond to a nitrogen atom of a lysine side-chain of the binder,

and their salts, solvates and salts of these solvates.

5. Binder-drug conjugates of the formula (I) according to Claims 1 to 4, in which

R^1 represents methyl,

R^2 represents methyl,

R^3 represents $–CH_2-C(=O)-NH_2$,

M represents the group

#-C(=O)-CH(CH_3)-NH-C(=O)-$(CH_2)_3$-C(=O)-###,

n represents a number from 1 to 20,

AK represents a binder or a derivative thereof, preferably an antibody or an antigen-binding antibody fragment,

represents the bond to the compound,

represents the bond to a nitrogen atom of a lysine side-chain of the binder,

and their salts, solvates and salts of these solvates.

6. Binder-drug conjugates of the formula (I) according to Claims 1 to 5, in which

R^1 represents methyl,

R^2 represents methyl,

R^3 represents $–CH_2-C(=O)-NH_2$,

M represents the group

#-C(=O)-CH(CH_3)-NH-C(=O)-(CH_2)$_3$-C(=O)-###,

n represents a number from 1 to 20 and

AK represents an anti-CD123 antibody, an anti-CXCR5 antibody, an anti-B7H3 antibody, an anti-TWEAKR antibody, an anti-Her2 antibody or an anti-EGFR antibody or represents an antigen-binding antibody fragment of these,

represents the bond to the compound,

represents the bond to a nitrogen atom of a lysine side-chain of the antibody (AK) or of the antigen-binding antibody fragment thereof,

and their salts, solvates and salts of these solvates.

7. Binder-drug conjugates of the formula (I) according to Claims 1 to 6, in which

R^1 represents methyl,

R^2 represents methyl,

R^3 represents $–CH_2-C(=O)-NH_2$,

M represents the group

#-C(=O)-CH(CH_3)-NH-C(=O)-(CH_2)$_3$-C(=O)-###,

n represents a number from 1 to 20 and

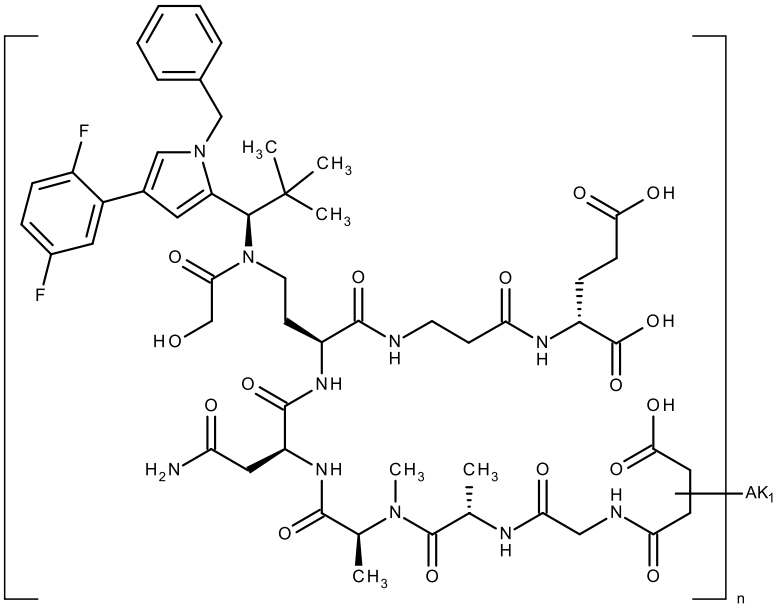
AK represents an anti-CD123 antibody selected from the group consisting of TPP-9476, TPP-8988, TPP-8987 and TPP-6013, represents an anti-CXCR5 antibody selected from the group consisting of TPP-9574 and TPP-9580, represents an anti-B7H3 antibody TPP-8382, represents an anti-TWEAKR antibody selected from the group consisting of TPP-7006 and TPP-7007, represents an anti-Her2 antibody TPP-1015 or represents an anti-EGFR antibody TPP- 981 or represents an antigen-binding antibody fragment of these,

represents the bond to the compound,

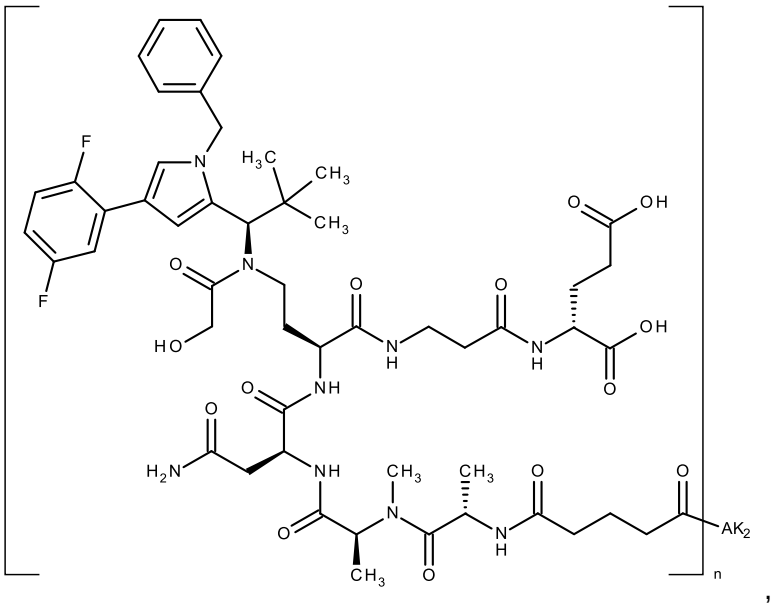
represents the bond to a nitrogen atom of a lysine side-chain of the antibody (AK) or of the antigen-binding antibody fragment thereof,

and their salts, solvates and salts of these solvates.

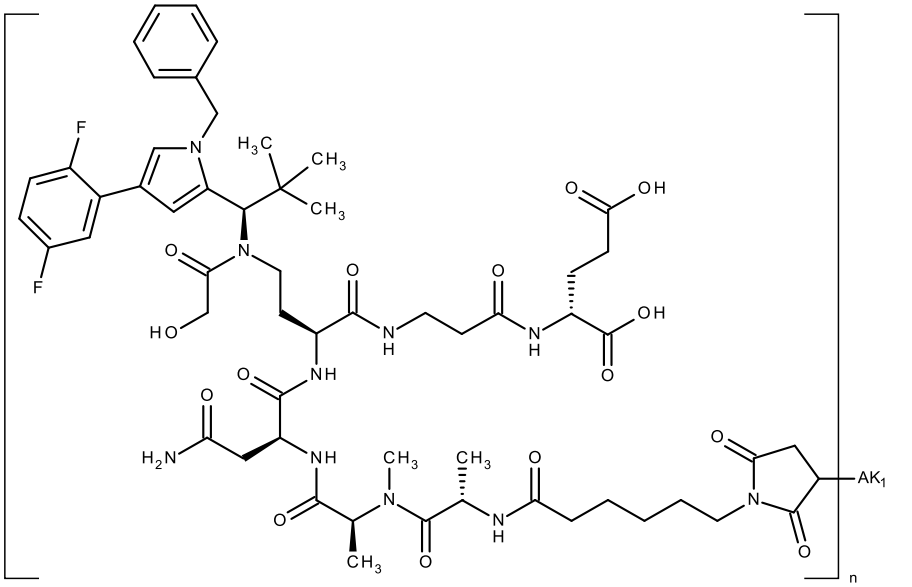
8. Binder-drug conjugates of the formula (I) according to Claims 2 to 7, of the structures



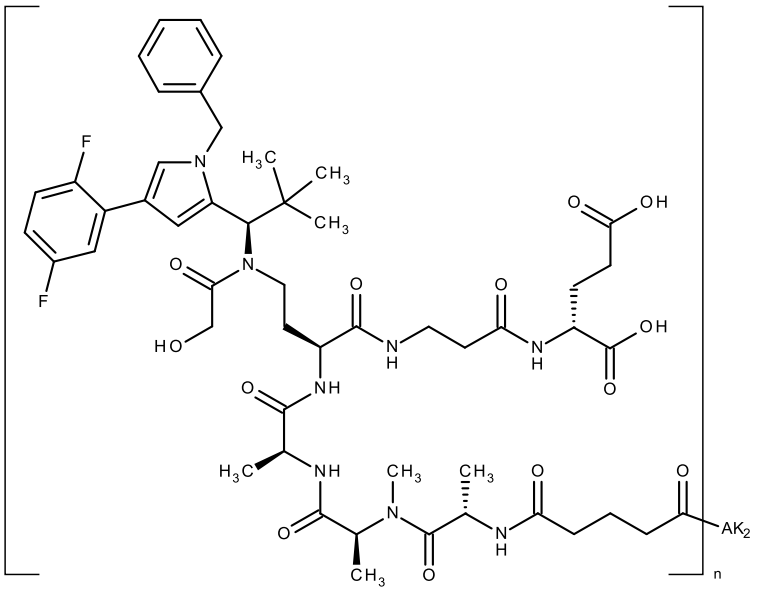
,



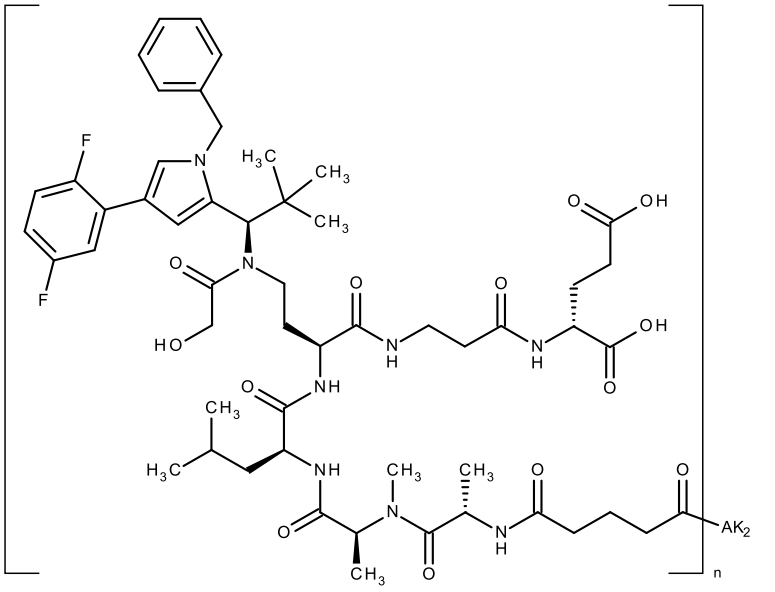
,



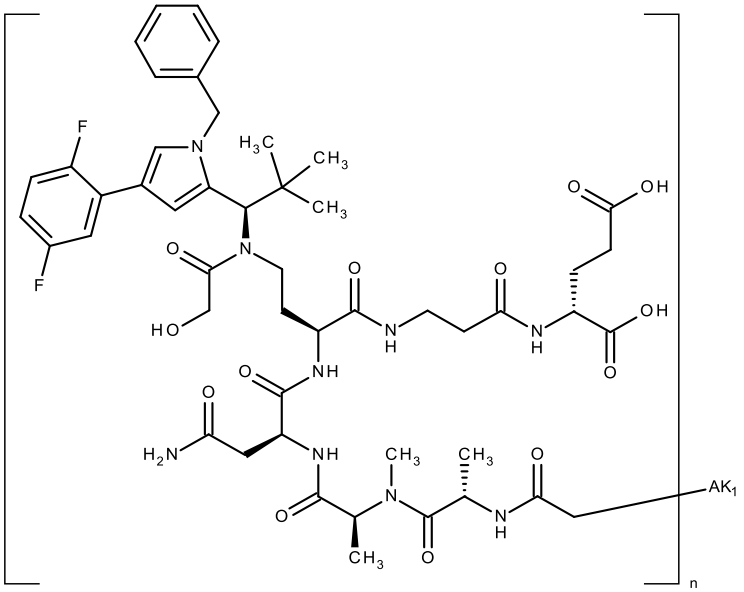
,



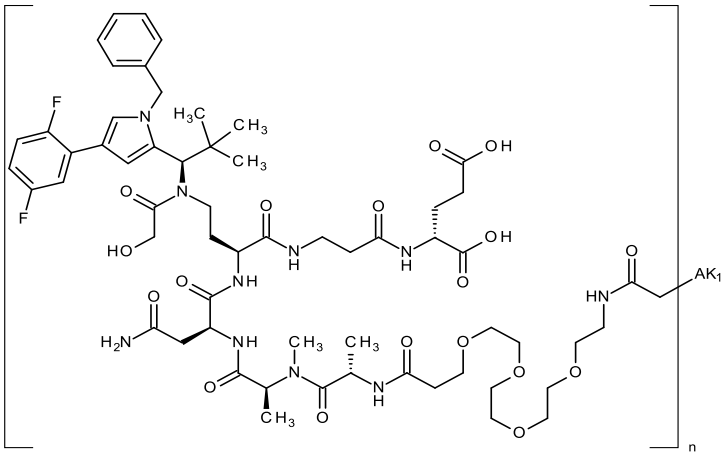
.



,



and



in which

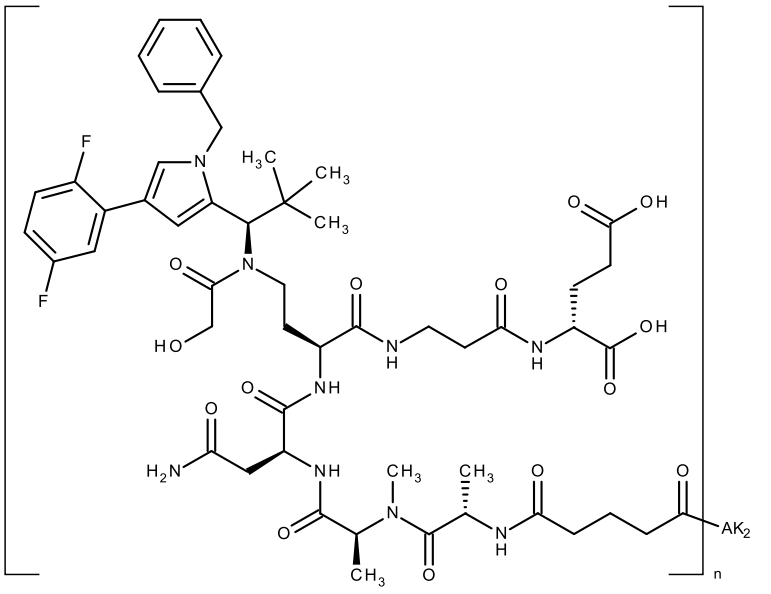
AK1 represents an antibody which is attached via a sulfur atom of a cysteine side-chain,

AK2 represents an antibody which is attached via a nitrogen atom of a lysine side-chain and

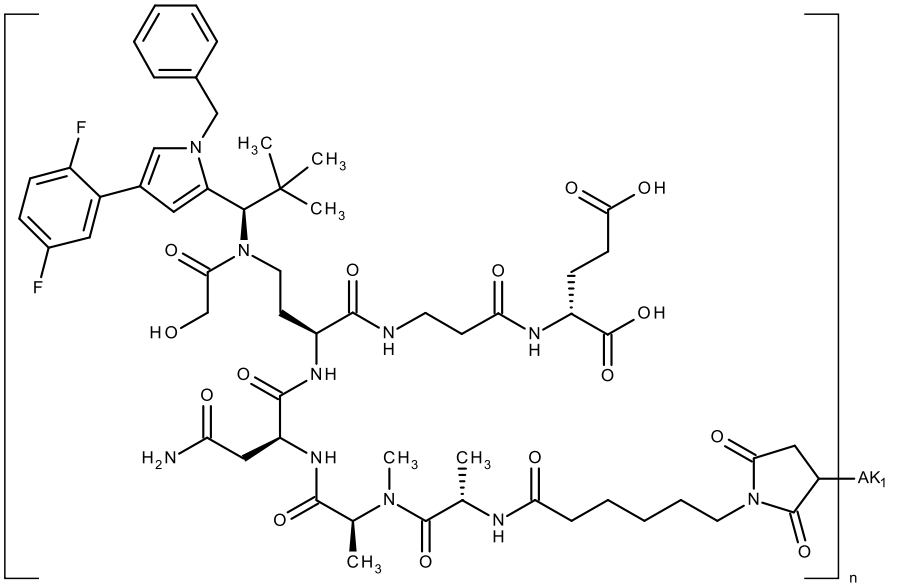
N represents 1 to 50,

and their salts, solvates and salts of these solvates.

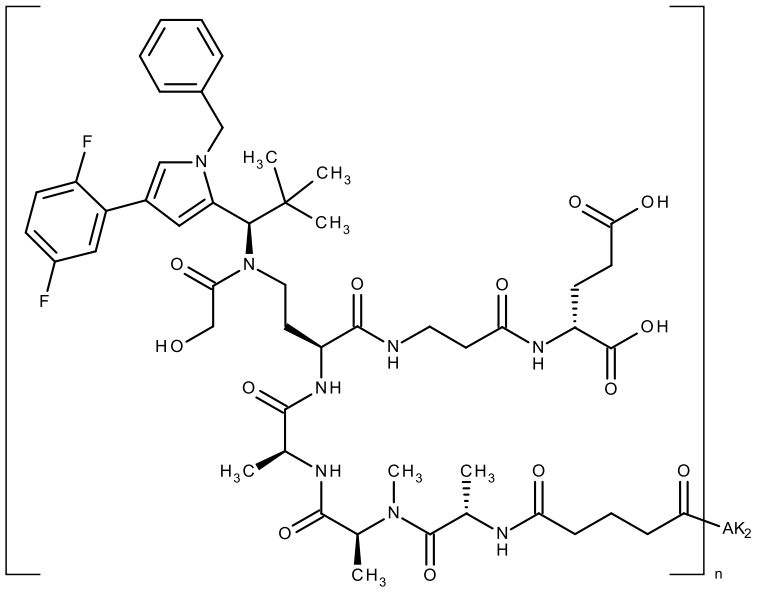
9. Binder-drug conjugates of the formula (I) according to Claim 1, of the structures



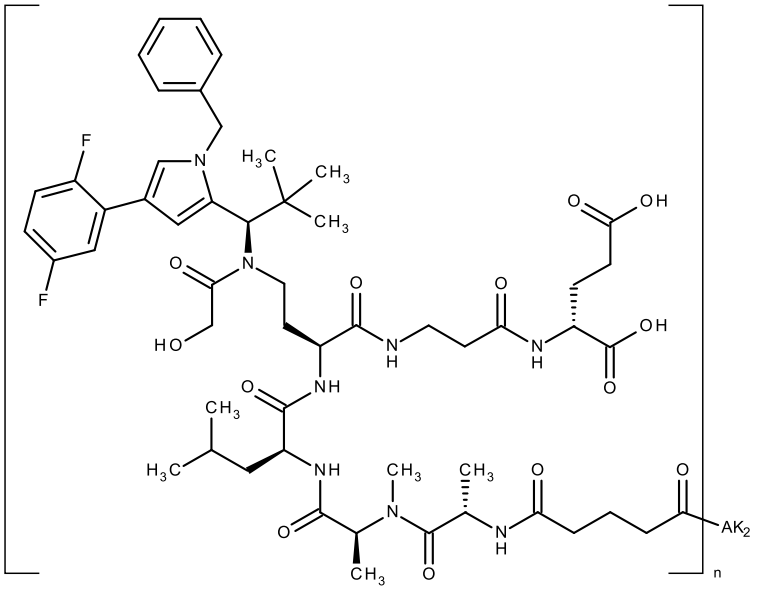
,


F
F
N
H3C
CH3
CH3
O
OH
O
N
O
O
HO
N
H
N
H
OH
O
O
NH
O
H2N
NH
CH3
CH3
O
O
N
N
O
AK1
CH3
O
N
H
O
CH3
O
n

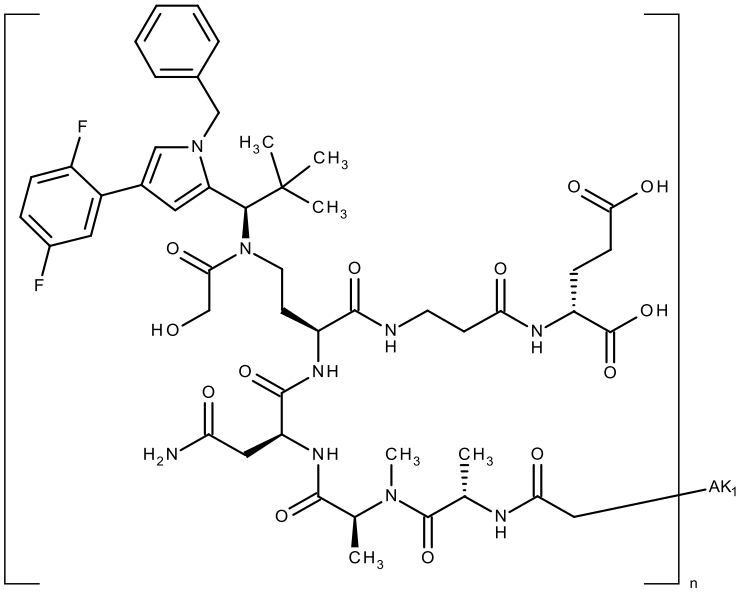
,


F
F
N
H3C
CH3
CH3
O
OH
O
N
O
O
HO
N
H
N
H
OH
O
O
NH
O
H3C
NH
CH3
CH3
O
O
N
N
O
AK2
CH3
O
N
H
O
CH3
O
n

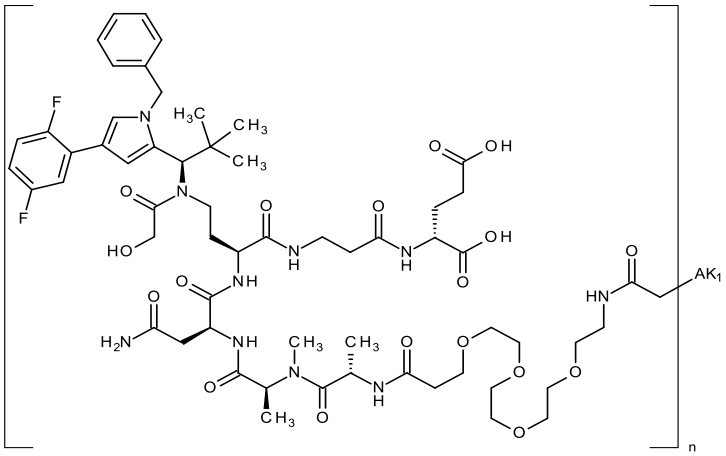
.



,



and



in which

AK1 represents an antibody which is attached via a sulfur atom of a cysteine side-chain,

AK2 represents an antibody which is attached via a nitrogen atom of a lysine side-chain and

N represents 1 to 50,

and their salts, solvates and salts of these solvates.

10. Binder-drug conjugates according to Claim 8 and 9, in which
n represents 1 to 20,
and their salts, solvates and salts of these solvates.

11. Binder-drug conjugates according to Claims 8 to 10, in which
n represents 1 to 8,
and their salts, solvates and salts of these solvates.

12. Binder-drug conjugates according to Claims 8 to 11, in which
n represents 4 to 8,
and their salts, solvates and salts of these solvates.

13. Binder-drug conjugates according to one or more of Claims 1 to 12, where

AK (AK1, AK2) represents an antibody selected from the group consisting of TPP-8382 (anti B7H3), TPP-6013 (anti-CD123), TPP-8987 (anti-CD123), TPP-8988 (anti-CD123), TPP 9476 (anti-CD123), TPP-9580 (anti-CXCR5) and TPP 9574 (anti-CXCR5), or an antigen-binding fragment of these.

14. Binder-drug conjugates according to one or more of Claims 1 to 13, where

AK (AK1, AK2) represents an anti-CD123 antibody TPP-6013,

represents an anti-CD123 antibody TPP-8987,

represents an anti-CD123 antibody TPP-8988 or

represents an anti-CD123 antibody TPP-9476,

or an antigen-binding fragment of these.

15. Binder-drug conjugates according to one or more of Claims 1 to 14, where AK (AK1, AK2)

(i) represents an anti-B7H3 antibody comprising a variable region of the heavy chain (VH) comprising the variable CDR1 sequence of the heavy chain (H-CDR1), as shown by SEQ ID NO: 52, the variable CDR2 sequence of the heavy chain (H-CDR2), as shown by SEQ ID NO: 53 and the variable CDR3 sequence of the heavy chain (H-CDR3), as shown by SEQ ID NO: 54, and a variable region of the light chain (VL) comprising the variable CDR1 sequence of the light chain (L-CDR1), as shown by SEQ ID NO: 56, the variable CDR2 sequence of the light chain (L-CDR2), as shown by SEQ ID NO: 57 and the variable CDR3 sequence of the light chain (L-CDR3), as shown by SEQ ID NO: 58,

(ii) represents an anti-CD123 antibody comprising a variable region of the heavy chain (VH) comprising the variable CDR1 sequence of the heavy chain (H-CDR1), as shown by SEQ ID NO: 22, the variable CDR2 sequence of the heavy chain (H-CDR2), as shown by SEQ ID NO: 23 and the variable CDR3 sequence of the

heavy chain (H-CDR3), as shown by SEQ ID NO: 24, and a variable region of the light chain (VL) comprising the variable CDR1 sequence of the light chain (L-CDR1), as shown by SEQ ID NO: 26, the variable CDR2 sequence of the light chain (L-CDR2), as shown by SEQ ID NO: 27 and the variable CDR3 sequence of the light chain (L-CDR3), as shown by SEQ ID NO: 28,

(iii) represents an anti-CD123 antibody comprising a variable region of the heavy chain (VH) comprising the variable CDR1 sequence of the heavy chain (H-CDR1), as shown by SEQ ID NO: 62, the variable CDR2 sequence of the heavy chain (H-CDR2), as shown by SEQ ID NO: 63 and the variable CDR3 sequence of the heavy chain (H-CDR3), as shown by SEQ ID NO: 64, and a variable region of the light chain (VL) comprising the variable CDR1 sequence of the light chain (L-CDR1), as shown by SEQ ID NO: 66, the variable CDR2 sequence of the light chain (L-CDR2), as shown by SEQ ID NO: 67 and the variable CDR3 sequence of the light chain (L-CDR3), as shown by SEQ ID NO: 68,

(iv) represents an anti-CD123 antibody comprising a variable region of the heavy chain (VH) comprising the variable CDR1 sequence of the heavy chain (H-CDR1), as shown by SEQ ID NO: 72, the variable CDR2 sequence of the heavy chain (H-CDR2), as shown by SEQ ID NO: 73 and the variable CDR3 sequence of the heavy chain (H-CDR3), as shown by SEQ ID NO: 74, and a variable region of the light chain (VL) comprising the variable CDR1 sequence of the light chain (L-CDR1), as shown by SEQ ID NO: 76, the variable CDR2 sequence of the light chain (L-CDR2), as shown by SEQ ID NO: 77 and the variable CDR3 sequence of the light chain (L-CDR3), as shown by SEQ ID NO: 78,

(v) represents an anti-CD123 antibody comprising a variable region of the heavy chain (VH) comprising the variable CDR1 sequence of the heavy chain (H-CDR1), as shown by SEQ ID NO: 82, the variable CDR2 sequence of the heavy chain (H-CDR2), as shown by SEQ ID NO: 83 and the variable CDR3 sequence of the heavy chain (H-CDR3), as shown by SEQ ID NO: 84, and a variable region of the light chain (VL) comprising the variable CDR1 sequence of the light chain (L-CDR1), as shown by SEQ ID NO: 86, the variable CDR2 sequence of the light chain (L-CDR2), as shown by SEQ ID NO: 87 and the variable CDR3 sequence of the light chain (L-CDR3), as shown by SEQ ID NO: 88,

(vi) represents an anti-CXCR5 antibody comprising a variable region of the heavy chain (VH) comprising the variable CDR1 sequence of the heavy chain (H-CDR1), as shown by SEQ ID NO: 92, the variable CDR2 sequence of the heavy chain (H-CDR2), as shown by SEQ ID NO: 93 and the variable CDR3 sequence of the heavy chain (H-CDR3), as shown by SEQ ID NO: 94, and a variable region of the light chain (VL) comprising the variable CDR1 sequence of the light chain (L-CDR1), as shown by SEQ ID NO: 96, the variable CDR2 sequence of the light chain (L-CDR2), as shown by SEQ ID NO: 97 and the variable CDR3 sequence of the light chain (L-CDR3), as shown by SEQ ID NO: 98, or

(vii) represents an anti-CXCR5 antibody comprising a variable region of the heavy chain (VH) comprising the variable CDR1 sequence of the heavy chain (H-CDR1), as shown by SEQ ID NO: 102, the variable CDR2 sequence of the heavy chain (H-CDR2), as shown by SEQ ID NO: 103 and the variable CDR3 sequence of the heavy chain (H-CDR3), as shown by SEQ ID NO: 104, and a variable region of the light chain (VL) comprising the variable CDR1 sequence of the light chain (L-CDR1), as shown by SEQ ID NO: 106, the variable CDR2 sequence of the light chain (L-CDR2), as shown by SEQ ID NO: 107 and the variable CDR3 sequence of the light chain (L-CDR3), as shown by SEQ ID NO: 108,

or represents an antigen-binding fragment of these antibodies.

16. Binder-drug conjugates according to one or more of Claims 1 to 15 where AK (AK1, AK2)

(I) represents an anti-B7H3 antibody comprising a variable region of the heavy chain (VH) as shown in SEQ ID NO: 51 and a variable region of the light chain (VL) as shown in SEQ ID NO: 55,

(ii) represents an anti-CD123 antibody comprising a variable region of the heavy chain (VH) as shown in SEQ ID NO: 21 and a variable region of the light chain (VL) as shown in SEQ ID NO: 25,

(iii) represents an anti-CD123 antibody comprising a variable region of the heavy chain (VH) as shown in SEQ ID NO: 61 and a variable region of the light chain (VL) as shown in SEQ ID NO: 65,

(iv) represents an anti-CD123 antibody comprising a variable region of the heavy chain (VH) as shown in SEQ ID NO: 71 and a variable region of the light chain (VL) as shown in SEQ ID NO: 75,

(v) represents an anti-CD123 antibody comprising a variable region of the heavy chain (VH) as shown in SEQ ID NO: 81 and a variable region of the light chain (VL) as shown in SEQ ID NO: 85,

(vi) represents an anti-CXCR5 antibody comprising a variable region of the heavy chain (VH) as shown in SEQ ID NO: 91 and a variable region of the light chain (VL) as shown in SEQ ID NO: 95,

(vii) represents an anti-CXCR5 antibody comprising a variable region of the heavy chain (VH) as shown in SEQ ID NO: 101 and a variable region of the light chain (VL) as shown in SEQ ID NO: 105,

or represents an antigen-binding fragment of these antibodies.

17. Binder-drug conjugates according to one or more of Claims 1 to 16, where AK (AK1, AK2)

(i) represents an anti-B7H3 antibody comprising a region of the heavy chain as shown in SEQ ID NO: 59 and a region of the light chain as shown in SEQ ID NO: 60,

(ii) represents an anti-CD123 antibody comprising a region of the heavy chain as shown in SEQ ID NO: 29 and a region of the light chain as shown in SEQ ID NO: 30,

(iii) represents an anti-CD123 antibody comprising a region of the heavy chain as shown in SEQ ID NO: 69 and a region of the light chain as shown in SEQ ID NO: 70,

(iv) represents an anti-CD123 antibody comprising a region of the heavy chain as shown in SEQ ID NO: 79 and a region of the light chain as shown in SEQ ID NO: 80,

(v) represents an anti-CD123 antibody comprising a region of the heavy chain as shown in SEQ ID NO: 89 and a region of the light chain as shown in SEQ ID NO: 90,

(vi) represents an anti-CXCR5 antibody comprising a region of the heavy chain as shown in SEQ ID NO: 99 and a region of the light chain as shown in SEQ ID NO: 100, or

(vii) represents an anti-CXCR5 antibody comprising a region of the heavy chain as shown in SEQ ID NO: 109 and a region of the light chain as shown in SEQ ID NO: 110,

or represents an antigen-binding fragment of these antibodies.

18. Binder-drug conjugates according to any of Claims 1 to 17, wherein the antibody or the antigen-binding antibody fragment binds to an extracellular target molecule.

19. Binder-drug conjugates according to any of Claims 1 to 18, wherein the antibody or the antigen-binding antibody fragment binds to an extracellular cancer target molecule.

20. Binder-drug conjugates according to any of Claims 1 to 19, wherein the antibody or the antigen-binding antibody fragment, after binding to its extracellular target molecule on the target cell, is internalized by the target cell through the binding.

21. Pharmaceutical composition comprising at least one binder-drug conjugate according to one or more of the preceding claims in combination with an inert, non-toxic, pharmaceutically suitable auxiliary.

22. Binder-drug conjugates according to one or more of the preceding claims for use in a method for the treatment and/or prophylaxis of diseases.

23. Binder-drug conjugates according to one or more of the preceding claims for use in a method for the treatment of hyperproliferative and/or angiogenic disorders.

24. Binder-drug conjugates according to one or more of the preceding claims for use in a method for the treatment of cancer and tumours.

25. Binder-drug conjugates according to one or more of the preceding claims for use in a method for the treatment of cancer and tumours in combination with one or more therapeutic approaches for cancer immunotherapy or with one or more active compounds directed against a molecular target of cancer immunotherapy.