

WHAT IS CLAIMED IS:

1. An antibody drug conjugate (ADC) comprising an anti-NaPi2b antibody (e.g., an antibody against NPT2B_HUMAN Sodium-dependent phosphate transport protein 2B, e.g., having UniProt Accession Number: O95436 or SEQ ID NO: 1 and/or an antibody against NPT2B_RAT Sodium-dependent phosphate transport protein 2B, e.g., having UniProt Accession Number: Q9JJ09 or SEQ ID NO: 2), wherein said NaPi2b antibody is capable of the following:
 - a) binding to human Napi2b (e.g., SEQ ID NO: 1) and/or rat Napi2b (e.g., SEQ ID NO: 2), preferably said binding to said human Napi2b and said rat Napi2b having about the same K_D , further preferably said binding to said human Napi2b and said rat Napi2b is the binding to endogenous Napi2b (e.g., located on cell surface), most preferably said antibody is selected from the group consisting of: AV-25, AV-15, AV-18, AV-21 and AV-29 antibody), further most preferably said about same K_D having up to 50% difference (e.g., up to 45%, 40%, 35%, 30%, 25%, 20%, 15%, 10%, 9%, 8%, 7%, 6%, 7%, 5%, 4%, 3%, 2% or 1% difference);
 - b) cross-reactivity with rat Napi2b (e.g., having UniProt Accession Number: Q9JJ09 or SEQ ID NO: 2), preferably by the means of the antigen-mediated antibody internalization; further preferably said internalization is improved (e.g., by at least 10%, e.g., 15%) compared to the corresponding internalization of the parental antibody (e.g., comprising SEQ ID NOs: 54 and 55, e.g., as shown in Figure 1);
 - c) cross-reactivity with cynomolgus monkey (e.g., *Macaca fascicularis*) Napi2b (e.g., having UniProtKB Accession Number: A0A2K5UHY1 or SEQ ID NO: 3;
 - d) internalization, preferably by the means of the antigen-mediated antibody internalization;
 - e) not having a dipeptide deamidation site in a heavy chain variable region's (V_H) CDR2, preferably said absent dipeptide deamidation site is NG (Asn-Gly) in V_H CDR2;

wherein said anti-NaPi2b antibody is conjugated to one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, preferably from 1 to 10, further preferably from 2 to 10, most preferably from 4 to 10, further most preferably from 6 to 10, further most preferably from 7 to 10, further most preferably 4 or 8, most preferably to 8) cytotoxic moieties (e.g., cytotoxic payloads, e.g., Tubulin disrupting agents, e.g.,

Topoisomerase-I inhibitor/s, e.g., Auristatins or camptothecin, e.g., MMAE (monomethyl auristatin E) or MMAF (monomethyl auristatin F), e.g., Exatecan), preferably via one or more linkers, further preferably via one or more phosphoramidate linkers.

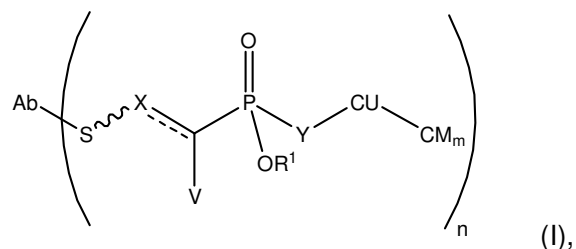
2. The antibody drug conjugate (ADC) according to claim 1, wherein said anti-NaPi2b antibody is an antibody comprising:

- a) a heavy chain variable region having an amino acid sequence with at least 80% (e.g., at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100%) identity to SEQ ID NO: 4 and a light chain variable region having an amino acid sequence with at least 80% (e.g., at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100%) identity to SEQ ID NO: 5; preferably said anti-NaPi2b antibody is the AV25 antibody comprising: a light chain comprising SEQ ID NO: 6 and a heavy chain comprising SEQ ID NO: 7;
- b) a heavy chain variable region having an amino acid sequence with at least 80% (e.g., at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100%) identity to SEQ ID NO: 8 and a light chain variable region having an amino acid sequence with at least 80% (e.g., at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100%) identity to SEQ ID NO: 9; preferably said anti-NaPi2b antibody is the AV-15 antibody comprising: a light chain comprising SEQ ID NO: 10 and a heavy chain comprising SEQ ID NO: 11;
- c) a heavy chain variable region having an amino acid sequence with at least 80% (e.g., at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100%) identity to SEQ ID NO: 12 and a light chain variable region having an amino acid sequence with at least 80% (e.g., at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%,

- at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100%) identity to SEQ ID NO: 13; preferably said anti-NaPi2b antibody is the AV-18 antibody comprising: a light chain comprising SEQ ID NO: 14 and a heavy chain comprising SEQ ID NO: 15;
- d) a heavy chain variable region having an amino acid sequence with at least 80% (e.g., at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100%) identity to SEQ ID NO: 16 and a light chain variable region having an amino acid sequence with at least 80% (e.g., at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100%) identity to SEQ ID NO: 17; preferably said anti-NaPi2b antibody is the AV-21 antibody comprising: a light chain comprising SEQ ID NO: 18 and a heavy chain comprising SEQ ID NO: 19;
- e) a heavy chain variable region having an amino acid sequence with at least 80% (e.g., at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100%) identity to SEQ ID NO: 20 and a light chain variable region having an amino acid sequence with at least 80% (e.g., at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100%) identity to SEQ ID NO: 21; preferably said anti-NaPi2b antibody is the AV-29 antibody comprising: a light chain comprising SEQ ID NO: 22 and a heavy chain comprising SEQ ID NO: 23.
3. The antibody drug conjugate (ADC) according to any one of the preceding claims, wherein said anti-NaPi2b antibody is:
- a) an antibody comprising a heavy chain variable region comprising heavy chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 24, heavy chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 25,

- and heavy chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 26 and a light chain variable region comprising light chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 27, light chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 28, and light chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 29;
- b) an antibody comprising a heavy chain variable region comprising heavy chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 30, heavy chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 31, and heavy chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 32 and a light chain variable region comprising light chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 33, light chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 34, and light chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 35;
- c) an antibody comprising a heavy chain variable region comprising heavy chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 36, heavy chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 37, and heavy chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 38 and a light chain variable region comprising light chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 39, light chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 40, and light chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 41;
- d) an antibody comprising a heavy chain variable region comprising heavy chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 42, heavy chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 43, and heavy chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 44 and a light chain variable region comprising light chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 45, light chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 46, and light chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 47;
- e) an antibody comprising a heavy chain variable region comprising heavy chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 48, heavy chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 49, and heavy chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 50 and a light chain variable region comprising light chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 51, light chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 52, and light chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 53.

4. The antibody drug conjugate (ADC) according to any one of claims 1 to 3, in particular of claim 1, having the formula (I):



or a pharmaceutically acceptable salt or solvate thereof;

wherein:

Ab is an anti-Na2Pi2b antibody as defined in any one of the preceding claims;

 is a double bond; or

 is a bond;

V is absent when  is a double bond; or

V is H or (C₁-C₈)alkyl when  is a bond;

X is R₃-C when  is a double bond; or

X is $\begin{matrix} R_4 \\ | \\ R_3-C \end{matrix}$ when  is a bond;

Y is NR⁵, S, O, or CR⁶R⁷;

R¹ is an optionally substituted aliphatic residue or an optionally substituted aromatic residue;

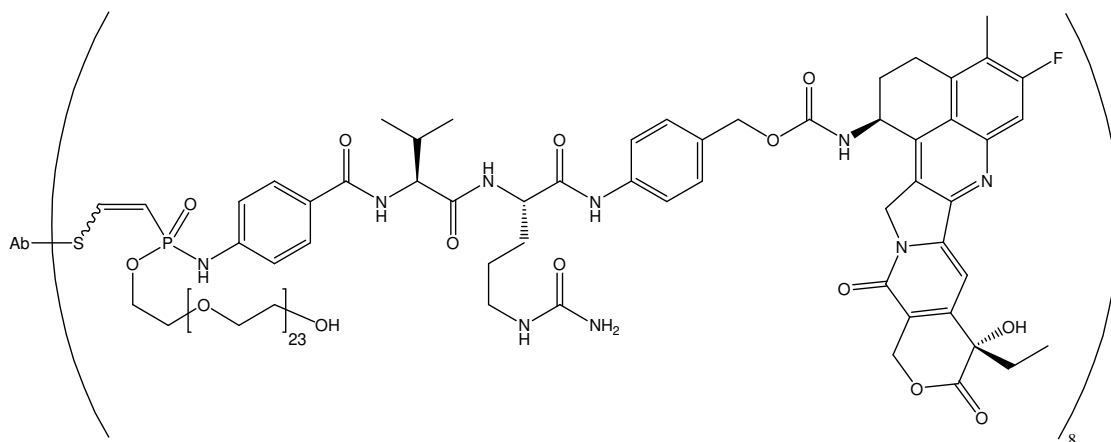
R³ is H; or an optionally substituted aliphatic residue or an optionally substituted aromatic residue;

R⁴ is H; or an optionally substituted aliphatic residue or an optionally substituted aromatic residue;

R⁵ is H; or an optionally substituted aliphatic residue or an optionally substituted aromatic residue;

- R⁶ is H; or an optionally substituted aliphatic residue or an optionally substituted aromatic residue;
 R⁷ is H; or an optionally substituted aliphatic residue or an optionally substituted aromatic residue;
 CU is a connector unit;
 CM is a cytotoxic moiety;
 m is an integer ranging from 1 to 10; and
 n is an integer ranging from 1 to 20.

5. The antibody drug conjugate (ADC) according to claim 4 having the following formula (Ia):



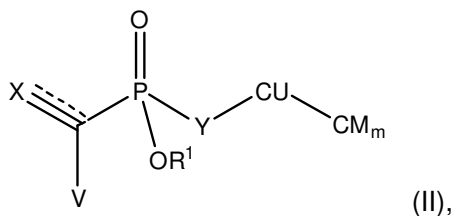
(Ia),

wherein Ab is an anti-NaPi2b antibody as defined in any one of the preceding claims.

6. A method of producing an antibody drug conjugate (ADC), said method comprising: conjugating the antibody according to any one of the preceding claims to one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, preferably from 1 to 10, further preferably from 2 to 10, most preferably from 4 to 10, further most preferably from 6 to 10, further most preferably from 7 to 10, further most preferably 4 or 8, most preferably to 8) cytotoxic moieties (e.g., cytotoxic payloads, e.g. Tubulin disrupting agents, e.g., Topoisomerase-I inhibitor/s, e.g., Auristatins or camptothecin, e.g., MMAE (monomethyl auristatin E) or MMAF (monomethyl auristatin F), e.g., Exatecan), preferably via one or more linkers, further preferably via one or more phosphoramidate linkers.

7. The method according to claim 6, said method comprising:

reacting a compound of formula (II)



or a pharmaceutically acceptable salt or solvate thereof;

wherein:

 is a triple bond; or

 is a double bond;

V is absent when  is a triple bond; or

V is H or (C₁-C₈)alkyl when  is a double bond;

X is R₃-C when  is a triple bond; or

X is $\text{R}_3-\overset{\text{R}_4}{\underset{|}{\text{C}}}$ when  is a double bond;

Y is NR⁵, S, O, or CR⁶R⁷;

R¹ is an optionally substituted aliphatic residue or an optionally substituted aromatic residue;

R³ is H; or an optionally substituted aliphatic residue or an optionally substituted aromatic residue;

R⁴ is H; or an optionally substituted aliphatic residue or an optionally substituted aromatic residue;

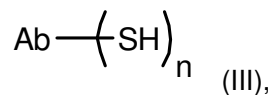
R⁵ is H; or an optionally substituted aliphatic residue or an optionally substituted aromatic residue;

R⁶ is H; or an optionally substituted aliphatic residue or an optionally substituted aromatic residue;

R⁷ is H; or an optionally substituted aliphatic residue or an optionally substituted aromatic residue;

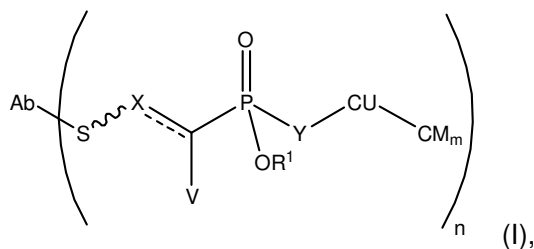
CU is a connector unit;
 CM is a cytotoxic moiety; and
 m is an integer ranging from 1 to 10;

with a thiol-containing molecule of formula (III)



wherein Ab is an anti-NaPi2b antibody as defined in any one of the preceding claims; and
 n is an integer ranging from 1 to 20;

resulting in an antibody drug conjugate (ADC) of formula (I)



or a pharmaceutically acceptable salt or solvate thereof;

wherein:

Ab is an anti-NaPi2b antibody as defined in any one of the preceding claims;

 is a double bond when  in a compound of formula (II) is a triple bond; or

 is a bond when  in a compound of formula (II) is a double bond;

V is absent when  is a double bond; or

V is H or (C₁-C₈)alkyl when  is a bond;

X is R₃-C when  is a double bond; or

X is $\text{R}_3-\overset{\text{R}_4}{\underset{|}{\text{C}}}$ when  is a bond;

Y is NR^5 , S, O, or CR^6R^7 ;

R^1 is an optionally substituted aliphatic residue or an optionally substituted aromatic residue;

R^3 is H; or an optionally substituted aliphatic residue or an optionally substituted aromatic residue;

R^4 is H; or an optionally substituted aliphatic residue or an optionally substituted aromatic residue;

R^5 is H; or an optionally substituted aliphatic residue or an optionally substituted aromatic residue;

R^6 is H; or an optionally substituted aliphatic residue or an optionally substituted aromatic residue;

R^7 is H; or an optionally substituted aliphatic residue or an optionally substituted aromatic residue;

CU is a connector unit;

CM is a cytotoxic moiety;

m is an integer ranging from 1 to 10; and

n is an integer ranging from 1 to 20.

8. An antibody drug conjugate (ADC) produced by the method according to any one of the preceding claims.
9. A composition or kit comprising an antibody drug conjugate (ADC) according to any one of the preceding claims.
10. The composition according to any one of the preceding claims, wherein said composition is a pharmaceutical and/or diagnostic composition.
11. A method for treatment, amelioration, prophylaxis and/or diagnostics of cancer, preferably said cancer is a solid and/or metastatic cancer, further preferably said cancer is selected from the group consisting of: lung cancer, ovarian cancer, thyroid cancer, nonsquamous non-small cell lung carcinoma, nonmucinous ovarian carcinoma, papillary thyroid carcinoma, renal cancer, endometrial cancer, uterus cancer, ureter cancer, bladder cancer and fallopian tube cancer, said method comprising: administering a therapeutically or prophylactically effective amount of the antibody drug conjugate (ADC), composition or kit according to any one of the preceding claims.

12. The antibody drug conjugate (ADC), composition or kit according to any one of the preceding claims, for use as a medicament and/or in therapy.
13. The antibody drug conjugate (ADC), composition or kit according to any one of the preceding claims, for use in one or more of the following methods:
 - (a) method for treatment, amelioration, prophylaxis and/or diagnostics of cancer, preferably said cancer is a solid and/or metastatic cancer, further preferably said cancer is selected from the group consisting of: lung cancer, ovarian cancer, thyroid cancer, nonsquamous non-small cell lung carcinoma, nonmucinous ovarian carcinoma, papillary thyroid carcinoma, renal cancer, endometrial cancer, uterus cancer, ureter cancer, bladder cancer and fallopian tube cancer;
 - (b) method for monitoring development of cancer and/or for assessing the efficacy of cancer therapy;
 - (c) method for screening a candidate compound for anti-cancer activity;
 - (d) method for altering resistance of cancer cells to chemotherapy;
 - (e) method for sensitizing cancer cells to chemotherapy;
 - (f) method for inhibiting the growth of cancer cell expressing NaPi2b;
 - (g) method for production or preparation of an antibody;
 - (h) method for immunizing a non-human animal;
 - (i) method for preparation of a hybridoma;
 - (j) method according to any one of the preceding claims;
 - (k) method according to any one of (a)-(j), wherein said method is an *in vivo*, *in vitro*, or *ex vivo* method.
14. Use of the antibody drug conjugate (ADC), composition or kit according to any one of the preceding claims, for one or more of the following:
 - (a) for treatment, amelioration, prophylaxis and/or diagnostics of cancer, preferably said cancer is a solid and/or metastatic cancer, further preferably said cancer is selected from the group consisting of: lung cancer, ovarian cancer, thyroid cancer, nonsquamous non-small cell lung carcinoma, nonmucinous ovarian carcinoma, papillary thyroid carcinoma, renal cancer, endometrial cancer, uterus cancer, ureter cancer, bladder cancer and fallopian tube cancer;
 - (b) for monitoring development of cancer and/or for assessing the efficacy of cancer therapy;
 - (c) for screening a candidate compound for anti-cancer activity;
 - (d) for altering resistance of cancer cells to chemotherapy;

- (e) for sensitizing cancer cells to chemotherapy;
- (f) for inhibiting the growth of cancer cell expressing NaPi2b;
- (g) for production or preparation of an antibody;
- (h) for immunizing a non-human animal;
- (i) for preparation of a hybridoma;
- (j) in a method according to any one of the preceding claims;
- (k) use according to any one of (a)-(j), wherein said use is an *in vivo*, *in vitro*, or *ex vivo* use.