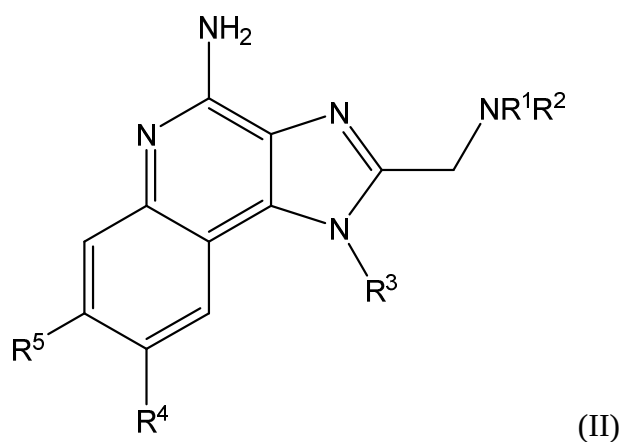


CLAIMS

1. A compound having formula (II),



or a pharmaceutically acceptable salt thereof, wherein:

R¹ is independently unsubstituted C₁₋₆ alkyl, or C(=O)R^a;

R² is independently H or unsubstituted C₁₋₆ alkyl;

R³ is:

(i) H;

(ii) unsubstituted C₁₋₂ alkyl;

(iii) **X-R⁸**, wherein **X** is an unbranched C₁₋₆ alkylene, and **R⁸** is -OH, C₁₋₄ alkoxy, -C₁₋₄ haloalkoxy, CO₂R^a, or -CONR^cR^d;

(iv) (C₁₋₃ alkylene)-(C₆-C₁₀ aryl), wherein the aryl is optionally substituted with from 1-3 substituents independently selected from C₁₋₆ alkyl, C₁₋₄ haloalkyl, C₁₋₄ alkoxy, and C₁₋₄ haloalkoxy; or

(v) (C₁₋₃ alkylene)heteroaryl including from 5 to 6 ring atoms, wherein from 1 to 4 ring atoms are each independently selected from N, N(**R^e**), O, and S, and wherein the heteroaryl is optionally substituted with from 1 to 3 substituents independently selected from C₁₋₆ alkyl, C₁₋₄ haloalkyl, C₁₋₄ alkoxy, and C₁₋₄ haloalkoxy;

R⁴ and **R⁵** are each independently selected from:

(i) H;

(ii) halo;

(iii) -(C₀₋₃ alkylene)-C₃₋₁₀ cycloalkyl, wherein the cycloalkyl is optionally substituted with from 1 to 4 independently selected **R^f**;

(iv) $-(C_{0-3} \text{ alkylene})\text{-heterocyclyl}$ including from 3 to 10 ring atoms, wherein from 1 to 3 ring atoms are each independently selected from: $N(R^e)$, O, and S, wherein the heterocyclyl is optionally substituted with from 1 to 4 R^f ;

(v) $-(C_{0-3} \text{ alkylene})\text{-(}C_6\text{-}C_{10} \text{ aryl)}$ optionally substituted with from 1 to 4 R^g ;

(vi) $-(C_{0-3} \text{ alkylene})\text{-heteroaryl}$ including from 5 to 10 ring atoms, wherein from 1 to 4 ring atoms are each independently selected from: N, NH, O, and S, wherein the heteroaryl is optionally substituted with from 1 to 3 R^g ;

(vii) C_{1-6} alkyl optionally substituted with from 1-2 independently selected R^h ;
and

(viii) $-(C_{0-3} \text{ alkylene})\text{-}C_{4-10} \text{ cycloalkenyl}$, wherein the cycloalkenyl is optionally substituted with from 1 to 2 R^f ;

R^a is:

(i) C_{1-6} alkyl optionally substituted with from 1 to 2 R^h ; or

(ii) $-(C_{0-3} \text{ alkylene})\text{-}C_{3-10} \text{ cycloalkyl}$, wherein the cycloalkyl is optionally substituted with from 1 to 2 R^f ;

(iii) $-(C_{1-3} \text{ alkylene})\text{-heterocyclyl}$ including from 3 to 10 ring atoms, wherein from 1 to 3 ring atoms are each independently selected from $N(R^e)$, O, and S, wherein the heterocyclyl is optionally substituted with from 1 to 4 independently selected R^f ;

(iv) $-(C_{0-3} \text{ alkylene})\text{-phenyl}$ optionally substituted with from 1 to 4 independently selected R^g ; or

(v) $-(C_{0-3} \text{ alkylene})\text{-heteroaryl}$ including from 5 to 10 ring atoms, wherein from 1 to 4 ring atoms are each independently selected from N, $N(R^e)$, O, and S, wherein the heteroaryl is optionally substituted with from 1 to 3 independently selected R^g ;

each occurrence of R^c and R^d is independently H or C_{1-4} alkyl;

each occurrence of R^e is independently H or C_{1-4} alkyl;

each occurrence of R^f is independently C_{1-6} alkyl, C_{1-4} haloalkyl, -OH, F, Cl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, cyano, or phenyl optionally substituted with from 1 to 4 R^g ;

each occurrence of R^g is independently halo, cyano, C_{1-6} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, or C_{1-4} haloalkoxy; and

each occurrence of **R^h** is independently -OH, F, C₁₋₄ alkoxy, C₁₋₄ haloalkoxy, or cyano.

2. The compound of claim 1, wherein:

R³ is H, unsubstituted C₁₋₂ alkyl, or **X-R⁸**, wherein **X** is an unbranched C₂₋₆ alkylene, and **R⁸** is CO₂R^a, or -CONR^cR^d;

R⁴ is independently H or halo;

R⁵ is independently selected from:

(i) H;

(ii) halo;

(iii) -(C₀₋₃ alkylene)-C₃₋₁₀ cycloalkyl, wherein the cycloalkyl is optionally substituted with from 1 to 4 independently selected **R^f**;

(iv) -(C₀₋₃ alkylene)-heterocyclyl including from 3 to 10 ring atoms, wherein from 1 to 3 ring atoms are each independently selected from: N(**R^e**), O, and S, wherein the heterocyclyl is optionally substituted with from 1 to 4 **R^f**;

(v) -(C₀₋₃ alkylene)-(C₆₋₁₀ aryl) optionally substituted with from 1 to 4 **R^g**;

(v) -(C₀₋₃ alkylene)-heteroaryl including from 5 to 10 ring atoms, wherein from 1 to 4 ring atoms are each independently selected from: N, NH, O, and S, wherein the heteroaryl is optionally substituted with from 1 to 3 **R^g**;

(vi) C₁₋₆ alkyl optionally substituted with from 1-2 independently selected **R^h**;
and

(vii) -(C₀₋₃ alkylene)-C₄₋₁₀ cycloalkenyl, wherein the cycloalkenyl is optionally substituted with from 1 to 2 **R^f**.

3. The compound of any one of claims 1-2, wherein:

R² is independently H or unsubstituted C₁₋₃ alkyl;

R³ is H, unsubstituted C₁₋₂ alkyl, or **X-R⁸**, wherein **X** is an unbranched C₂₋₄ alkylene, and **R⁸** is CO₂R^a, or -CONR^cR^d;

R⁵ is independently selected from:

(i) C₃₋₆ cycloalkyl optionally substituted with from 1 to 2 independently selected **R^f**;

(ii) phenyl optionally substituted with from 1 to 3 **R^g**;

(iii) heteroaryl including from 5 to 6 ring atoms, wherein from 1 to 3 ring atoms are each independently selected from: N, NH, O, and S, wherein the heteroaryl is optionally substituted with from 1 to 3 **R^g**;

(iv) C₁₋₆ alkyl optionally substituted with from 1 to 2 independently selected **R^h**; and

(v) C₅₋₆ cycloalkenyl optionally substituted with from 1 to 2 **R^f**;

R^a is H, C₁₋₄ alkyl optionally substituted with OH, C₃₋₆ cycloalkyl, phenyl, or heteroaryl including from 5 to 6 ring atoms, wherein from 1 to 4 ring atoms are each independently selected from N, N(**R^e**), O, and S; and

R^b is C₁₋₄ alkyl.

4. The compound of any one of claims 1-3, wherein:

R² is independently H, CH₃ or CH₂CH₃;

R³ is H, CH₃, or $-(CH_2)_3C(=O)OCH_3$;

R⁵ is independently CH₃, cyclopentyl, cyclopentenyl, phenyl, pyrazol-1-yl, or pyrazol-3-yl; and

R^a is H, CH₃, CH₂CH₃, CH(CH₃)₂, C(CH₃)₃, cyclopropyl, or thiazolyl.

5. The compound of any one of claims 1-4, wherein:

R² is independently H, CH₃ or CH₂CH₃;

R³ is H or CH₃;

R⁵ is independently CH₃, cyclopentyl, cyclopentenyl, phenyl, pyrazol-1-yl, or pyrazol-3-yl; and

R^a is CH₃, CH₂CH₃, CH(CH₃)₂, C(CH₃)₃, or cyclopropyl.

6. The compound of any one of claims 1-5, wherein:

R¹ is independently CH₃, CH₂CH₃, CH(CH₃)₂, C(CH₃)₃, or C(=O)**R^a**;

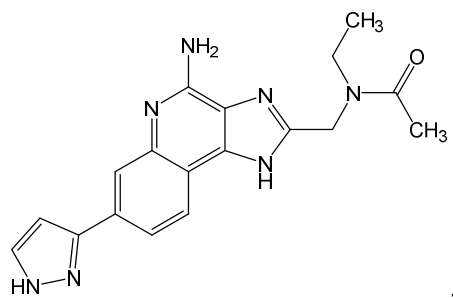
R² is independently H, CH₃ or CH₂CH₃;

R³ is H;

R⁵ is independently cyclopentyl, cyclopentenyl, phenyl, pyrazol-1-yl, or pyrazol-3-yl; and

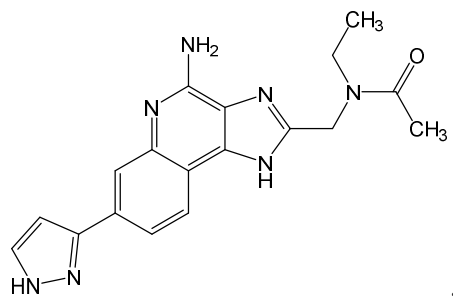
R^a is CH₃, CH₂CH₃, CH(CH₃)₂, C(CH₃)₃, or cyclopropyl.

7. The compound of claim 1, wherein the compound is

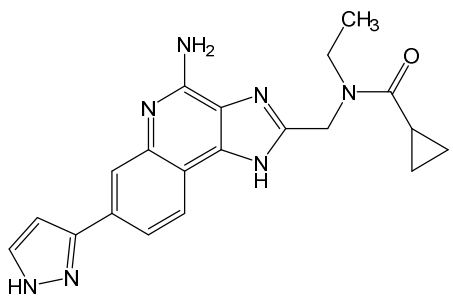


or a pharmaceutically acceptable salt thereof.

8. The compound of claim 1, wherein the compound is

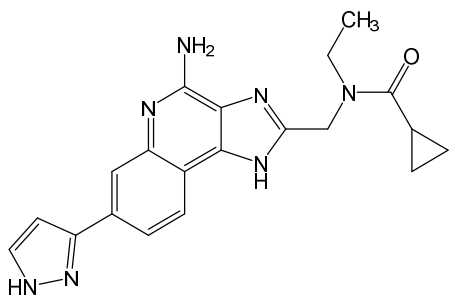


9. The compound of claim 1, wherein the compound is

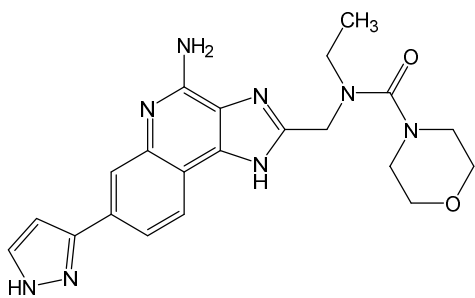


or a pharmaceutically acceptable salt thereof.

10. The compound of claim 1, wherein the compound is

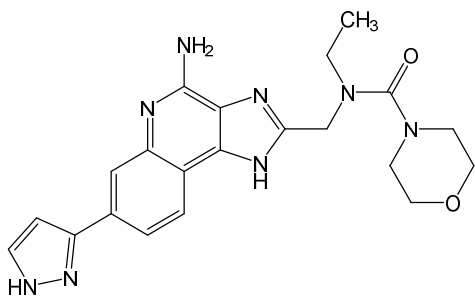


11. The compound of claim 1, wherein the compound is

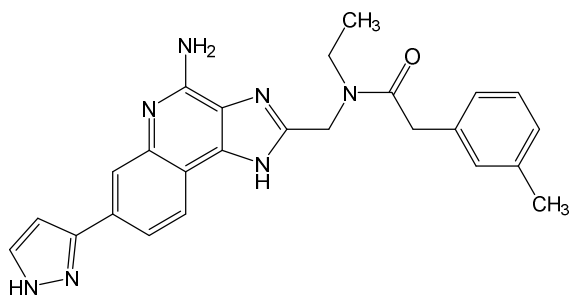


or a pharmaceutically acceptable salt thereof.

12. The compound of claim 1, wherein the compound is

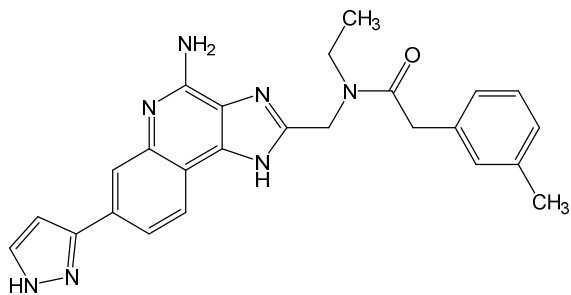


13. The compound of claim 1, wherein the compound is

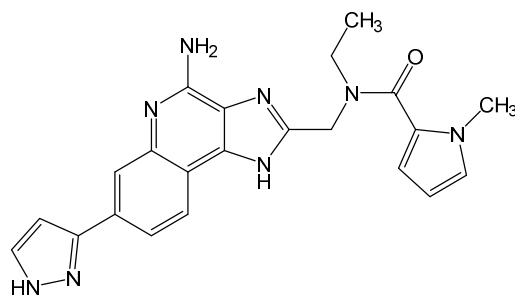


or a pharmaceutically acceptable salt thereof.

14. The compound of claim 1, wherein the compound is

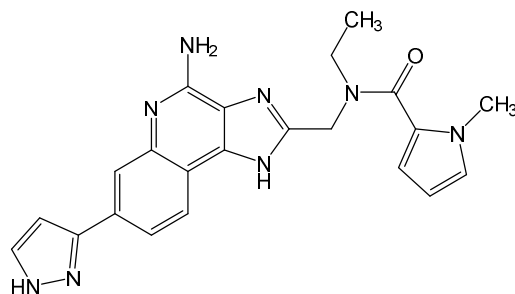


15. The compound of claim 1, wherein the compound is

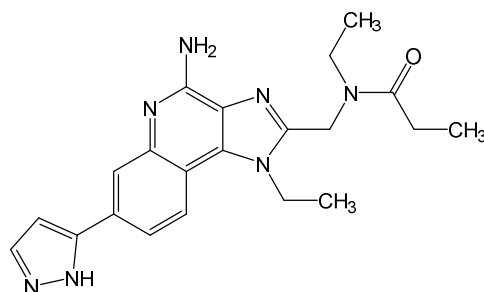


or a pharmaceutically acceptable salt thereof.

16. The compound of claim 1, wherein the compound is

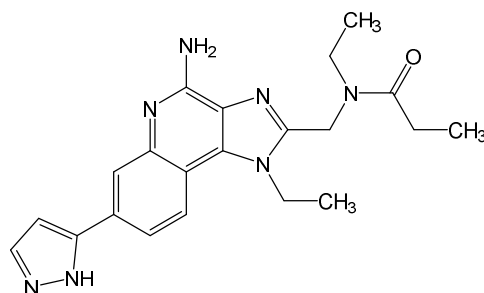


17. The compound of claim 1, wherein the compound is



or a pharmaceutically acceptable salt thereof.

18. The compound of claim 1, wherein the compound is



19. A pharmaceutical composition comprising a compound or a pharmaceutically acceptable salt thereof as claimed in any one of claims 1 to 18 and one or more pharmaceutically acceptable excipients.

20. A compound or a pharmaceutically acceptable salt thereof according to anyone of claims 1 to 18, or a pharmaceutical composition according to claim 19, for use as a medicament.

21. A compound or a pharmaceutically acceptable salt thereof according to anyone of claims 1 to 18, or a pharmaceutical composition according to claim 19, for use in the treatment of cancer in a subject.

22. The compound or composition for use of claim 21, wherein the cancer is selected from acute myeloid leukemia, adrenocortical carcinoma, Kaposi sarcoma, lymphoma, anal cancer, appendix cancer, teratoid/rhabdoid tumor, basal cell carcinoma, bile duct cancer, bladder cancer, bone cancer, brain cancer, breast cancer, bronchial tumor, carcinoid tumor, cardiac tumor, cervical cancer, chordoma, chronic lymphocytic leukemia, chronic myeloproliferative neoplasm, colon cancer, colorectal cancer, craniopharyngioma, bile duct cancer, endometrial cancer, ependymoma, esophageal cancer, esthesioneuroblastoma, Ewing sarcoma, eye cancer, fallopian tube cancer, gallbladder cancer, gastrointestinal carcinoid tumor, gastrointestinal stromal tumor, germ cell tumor, hairy cell leukemia, head and neck cancer, heart cancer, liver cancer, hypopharyngeal cancer, pancreatic cancer, kidney cancer, laryngeal cancer, chronic myelogenous leukemia, lip and oral cavity cancer, lung cancer, melanoma, Merkel cell carcinoma, mesothelioma, mouth cancer, oral cancer, osteosarcoma, ovarian cancer, penile cancer, pharyngeal cancer, prostate cancer, rectal cancer, salivary gland cancer, skin cancer, small intestine cancer, soft tissue sarcoma, testicular cancer, throat cancer, thyroid cancer, urethral cancer, uterine cancer, vaginal cancer, and vulvar cancer.

23. The compound or composition for use of claim 21 or claim 22, wherein the cancer is a refractory cancer.

24. The compound or composition for use of claim 21, wherein the cancer is selected from breast cancer, colon cancer, rectal cancer, colorectal cancer, pancreatic cancer, and prostate cancer.

25. The compound or composition for use of any one of claims 21 to 24, wherein the compound or composition is to be administered in combination with one or more additional cancer therapies.

26. The compound or composition for use of claim 25, wherein the one or more additional cancer therapies comprise surgery, radiotherapy, chemotherapy, toxin therapy, immunotherapy, cryotherapy or gene therapy, or a combination thereof.

27. The compound or composition for use of claim 25, wherein the additional cancer therapy comprises one or more agents selected from cisplatin, carboplatin, mechlorethamine, cyclophosphamide, chlorambucil, ifosfamide, oxaliplatin, azathioprine, mercaptopurine, vincristine, vinblastine, vinorelbine, vindesine, taxol, paclitaxel, docetaxel, irinotecan,, amsacrine, etoposide, etoposide phosphate, teniposide, actinomycin, anthracyclines, doxorubicin, daunorubicin, valrubicin, idarubicin, epirubicin, bleomycin, plicamycin, mitomycin, leuprolidine, goserelin, triptorelin, histrelin, bicalutamide, flutamide, nilutamide, abciximab, adalimumab, alemtuzumab, atlizumab, basiliximab, belimumab, bevacizumab, bretuximab vedotin, canakinumab, cetuximab, ceertolizumab pegol, daclizumab, denosumab, eculizumab, efalizumab, gemtuzumab, golimumab, golimumab, ibritumomab tiuxetan, infliximab, ipilimumab, muromonab-CD3, natalizumab, ofatumumab, omalizumab, palivizumab, panitumuab, ranibizumab, rituximab, tocilizumab, tositumomab, trastuzumab, interleukin-2, indoleamine 2,3-dioxygenase, IL-10, transforming growth factor- β , CD39, CD73 adenosine-CD39-CD73, and CXCR4-CXCL12.

28. The compound or composition for use of claim 25, wherein the additional cancer therapy comprises one or more agents selected from urelumab, PF-05082566, MEDI6469, TRX518, varlilumab, CP-870893, pembrolizumab, nivolumab, atezolizumab, MEDI4736, avelumab, PDR001, BMS-986016, MGA271, lirilumab, IPH2201, emactuzumab, INCB024360, galunisertib, ulocuplumab, BKT140, bavituximab, CC-90002, bevacizumab, and MNRP1685A.

29. The compound or composition for use of claim 25, wherein the additional cancer therapy comprises one or more agents selected from nivolumab, ipilimumab, pembrolizumab, atezolizumab, and avelumab.

30. The compound or composition for use of any one of claims 20 to 28, wherein the compound is to be administered intratumorally or systemically.