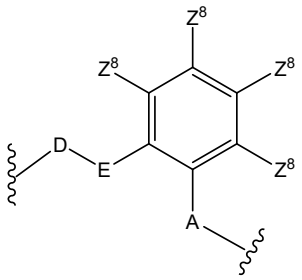


or



A is -(C_1-C_5)alkylene-O-C(O)-;

E is -O-, -O-C(O)N(H)-, -O-C(S)N(H)- or -S- or -S-C(O)N(H)-;

D is -(C_1-C_5)alkylene- or -(C_3-C_5)alkenylene-;

Y^1 is ~~C=C,~~ carbon or nitrogen, wherein if Y^1 is nitrogen, Z^1 is absent;

Each of Y^4 and ~~Y^5~~ Y^3 is independently carbon or nitrogen, wherein if Y^3 is nitrogen, Z^3 is absent and if Y^4 is nitrogen, Z^5 is absent;

Y^2 is C or N;

Y^5 is an oxygen, carbon, nitrogen or a sulfur atom, wherein Z^6 is absent when Y^5 is an oxygen, or a sulfur atom;

Each of Z^1, and Z^2, where present, are independently selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, alkyloxy, alkenyloxy, alkynyloxy, aryloxy, aralkyloxy, alkylthioxy, alkenylthioxy, alkynylthioxy, arylthioxy, aralkylthioxy, amino, hydroxy, thio, halo, carboxy, formyl, nitro and cyano, wherein each alkyl, alkenyl, alkynyl, alkoxy, and aryl moiety is independently optionally substituted with 1-3 halo;

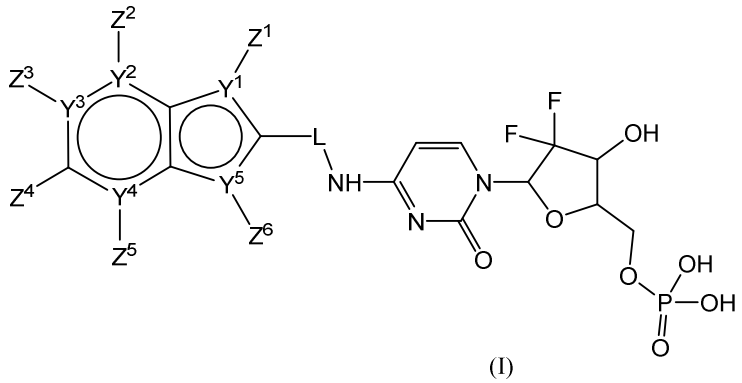
Z^3, Z^4, and Z^5 are each independently selected from hydrogen, alkyl, deuterated alkyl, $C_{1\text{-}6}$alkoxy, deuterated $C_{1\text{-}6}$alkoxy, alkenyl, alkynyl, aryl, aralkyl, alkyloxy, alkenyloxy, alkynyloxy, aryloxy, aralkyloxy, alkylthioxy, alkenylthioxy, alkynylthioxy, arylthioxy, aralkylthioxy, amino, hydroxy, thio, halo, carboxy, formyl, nitro and cyano, wherein each alkyl, alkenyl, alkynyl, alkoxy, and aryl moiety is independently optionally substituted with 1-3 halo;

provided that at least one of Z^1, Z^2 or Z^4 is H;

Z^6 is selected from hydrogen, alkyl, alkenyl, alkynyl, aryl and aralkyl, wherein each alkyl, alkenyl, alkynyl, alkoxy, and aryl moiety is independently optionally substituted with 1-3 halo;

What is claimed is:

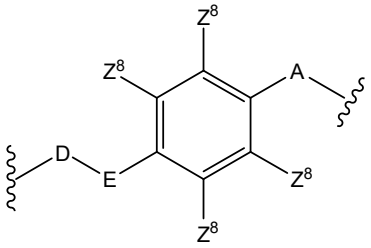
1. A compound of formula (I):



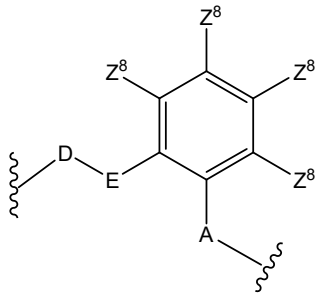
(I)

or a pharmaceutically acceptable salt, ester, solvate, or stereoisomer thereof, wherein:

-L- is defined as: -(C_1-C_5)alkylene-O-C(O)-, -(C_3-C_5)alkenylene-O-,



or



A is -(C_1-C_5)alkylene-O-C(O)-;

E is -O-, -O-C(O)N(H)-, -O-C(S)N(H)- or -S- or -S-C(O)N(H)-;

D is -(C_1-C_5)alkylene- or -(C_3-C_5)alkenylene-;

Y^1 is ~~C=C,~~ carbon or nitrogen, wherein if Y^1 is nitrogen, Z^1 is absent;

Each of Y^4 and ~~Y^5~~ Y^3 is independently carbon or nitrogen, wherein if Y^3 is nitrogen, Z^3 is absent and if Y^4 is nitrogen, Z^5 is absent;

Y^2 is C or N;

Y^5 is an oxygen, carbon, nitrogen or a sulfur atom, wherein Z^6 is absent when Y^5 is an oxygen, or a sulfur atom;

Each of Z^1, and Z^2, where present, are independently selected from hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, alkyloxy, alkenyloxy, alkynyloxy, aryloxy, aralkyloxy, alkylthioxy, alkenylthioxy, alkynylthioxy, arylthioxy, aralkylthioxy, amino, hydroxy, thio, halo, carboxy, formyl, nitro and cyano, wherein each alkyl, alkenyl, alkynyl, alkoxy, and aryl moiety is independently optionally substituted with 1-3 halo;

Z^3, Z^4, and Z^5 are each independently selected from hydrogen, alkyl, deuterated alkyl, C_{1-6}alkoxy, deuterated C_{1-6}alkoxy, alkenyl, alkynyl, aryl, aralkyl, alkyloxy, alkenyloxy, alkynyloxy, aryloxy, aralkyloxy, alkylthioxy, alkenylthioxy, alkynylthioxy, arylthioxy, aralkylthioxy, amino, hydroxy, thio, halo, carboxy, formyl, nitro and cyano, wherein each alkyl, alkenyl, alkynyl, alkoxy, and aryl moiety is independently optionally substituted with 1-3 halo;

provided that at least one of Z^1, Z^2 or Z^4 is H;

Z^6 is selected from hydrogen, alkyl, alkenyl, alkynyl, aryl and aralkyl, wherein each alkyl, alkenyl, alkynyl, alkoxy, and aryl moiety is independently optionally substituted with 1-3 halo;

Each Z^8 is independently hydrogen, unsubstituted C_1-C_6 alkyl, substituted C_1-C_6 alkyl, unsubstituted C_1-C_6 alkoxy, unsubstituted deuterated C_1-C_6 alkoxy, substituted C_1-C_6 alkoxy, and substituted deuterated C_1-C_6 alkoxy where the substituted alkyl, alkoxy and deuterated alkoxy are substituted with one or more groups selected from amino, mono- or di-substituted amino, cyclic C_1-C_5 alkylamino, imidazolyl, C_1-C_6 alkylpiperazinyl, morpholino, thiol, thioether, tetrazole, carboxylic acid, ester, amido, mono- or di-substituted amido, N-connected amide, N-connected sulfonamide, sulfoxy, sulfonate, sulfonyl, sulfoxy, sulfinate, sufinyl, phosphonooxy, phosphate or sulfonamide, wherein each alkyl, alkenyl, alkynyl, alkoxy, and aryl is optionally substituted with 1-3 halo.

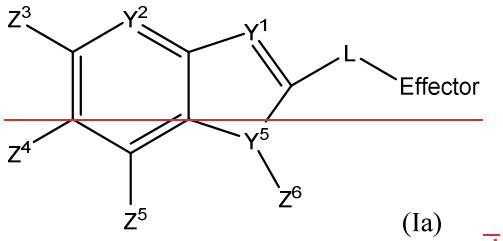
2. The compound, of claim 1, or a pharmaceutically acceptable salt, ester, amide, solvate, or stereoisomer thereof, wherein Y^3 and Y^4 are each carbon.

3. The compound according to any of the above claims, or a pharmaceutically acceptable salt, ester, amide, solvate, or stereoisomer thereof, wherein Z^3, Z^4 and Z^5 are each selected from halo, unsubstituted C_1-C_3 alkyl, substituted C_1-C_3 alkyl, unsubstituted C_1-C_3 alkoxy, substituted C_1-C_3 alkoxy, unsubstituted deuterated C_1-C_3 alkoxy, or substituted C_1-C_3 alkoxy, wherein each alkyl and alkoxy moiety can be independently substituted with 1-3 halo.

4. The compound according to any of the above claims, or a pharmaceutically acceptable salt, ester, amide, solvate, or stereoisomer thereof, wherein Z^3, Z^4 and Z^5 are each selected from

bromo, chloro, fluoro, methyl, deuterated methyl optionally substituted with 1-3 halo, methoxy optionally substituted with 1-3 halo, or deuterated methoxy.

5. The compound according to any of the above claims having formula (Ia):

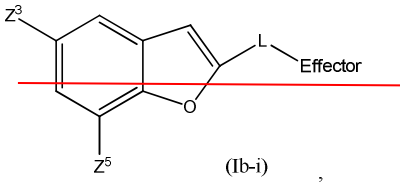


(Ia)

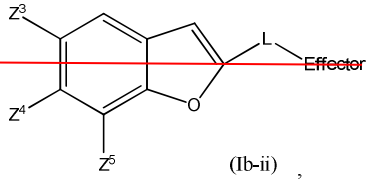
or a pharmaceutically acceptable salt, ester, amide, solvate, or stereoisomer thereof,

wherein L, Y^1, Y^2, Y^5, Z^3, Z^4, Z^5, and Z^6 are each as defined in any one of claims 1-4, and Effector is part of a (i) a phosphoric acid derivative of gemcitabine, or (ii) a salt form of a phosphoric acid derivative of gemcitabine.

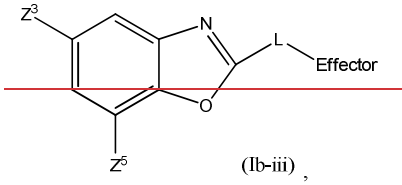
6. The compound according to any of the above claims having formulae (Ib-i), (Ib-ii), (Ib-iii), (Ib-iv), (Ib-v), (Ib-vi), (Ib-vii), (Ib-viii), (Ib-ix), (Ib-x), (Ib-xi), (Ib-xii), (Ib-xiii), (Ib-xiv), (Ib-xv), (Ib-xvi), (Ib-xvii), or (Ib-xviii):



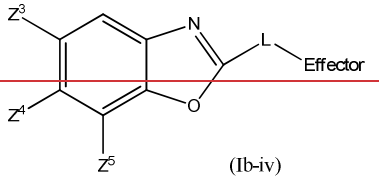
(Ib-i) ,



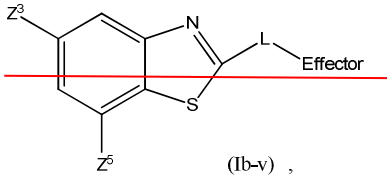
(Ib-ii) ,



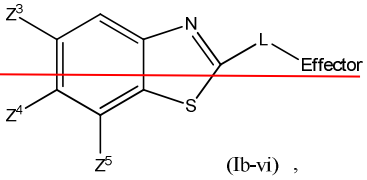
(Ib-iii) ,



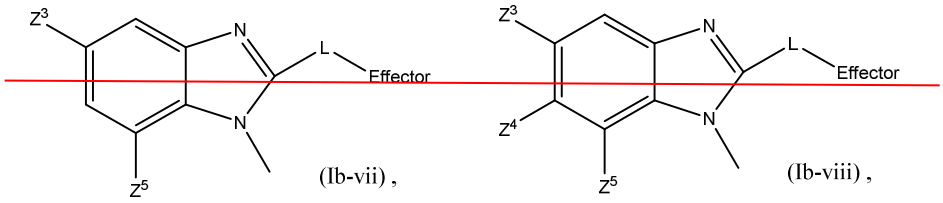
(Ib-iv) ,



(Ib-v) ,

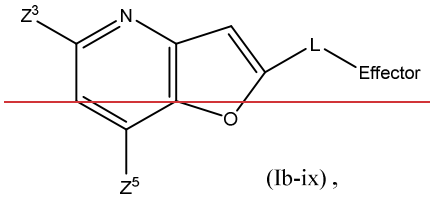


(Ib-vi) ,

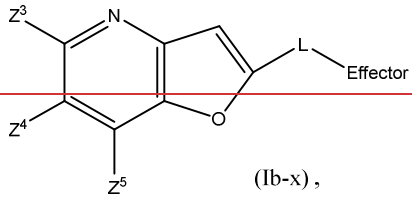


(Ib-vii) ,

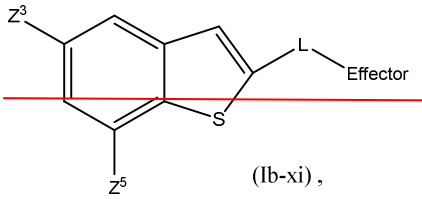
(Ib-viii) ,



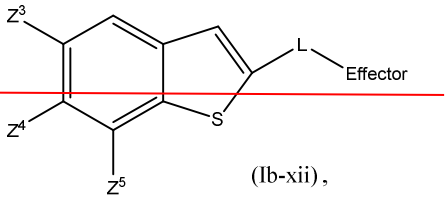
(Ib-ix) ,



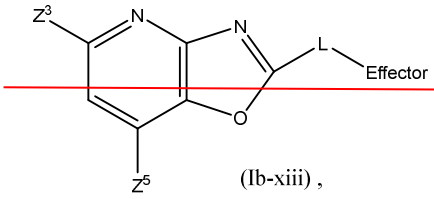
(Ib-x) ,



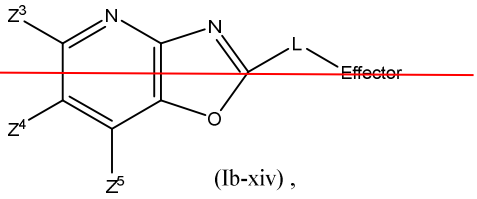
(Ib-xi) ,



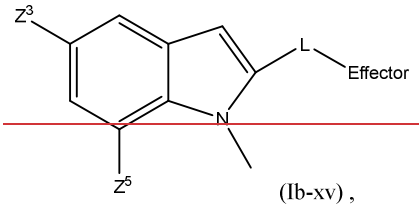
(Ib-xii) ,



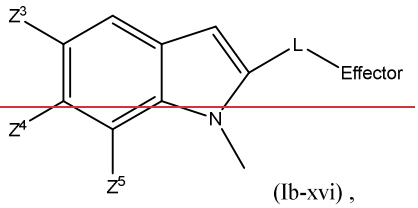
(Ib-xiii) ,



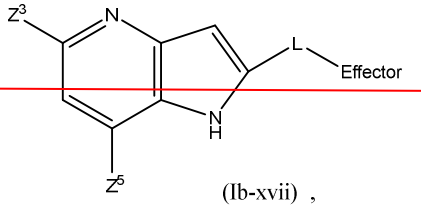
(Ib-xiv) ,



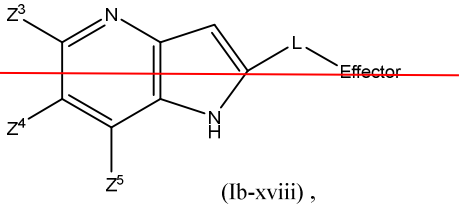
(Ib-xv) ,



(Ib-xvi) ,



(Ib-xvii) ,



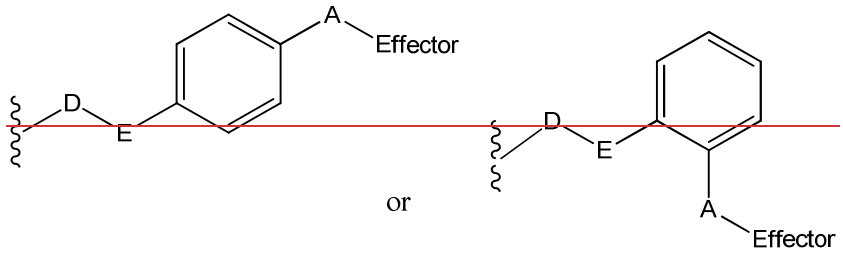
(Ib-xviii) ,

~~or a pharmaceutically acceptable salt, ester, amide, solvate, or stereoisomer of any of the above formulae, wherein:~~

~~Z^3 and Z^5 are each independently halo, methyl optionally substituted with 1-3 halo, methoxy optionally substituted with 1-3 halo or deuterated methoxy;~~

~~Z^4, when present, is halo, methyl optionally substituted with 1-3 halo, methoxy optionally substituted with 1-3 halo or deuterated methoxy;~~

~~-L-Effector is: -$(C_1$-$C_3)$alkylene-O-C(O)-Effector,~~



~~D is -$(C_1$-$C_3)$alkylene-;~~

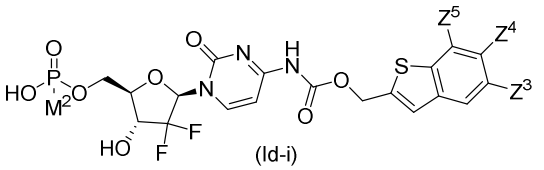
~~E is -O-, -O-C(O)N(H)-, -O-C(S)N(H)-, -S- or -S-C(O)N(H)-;~~

~~A is -$(C_1$-$C_3)$alkylene-O-C(O)-; and~~

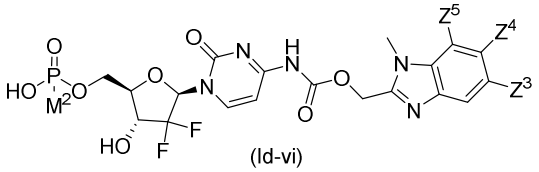
~~Effector is part of a (i) a phosphoric acid derivative of gemcitabine, or (ii) a salt form of a phosphoric acid derivative of gemcitabine.~~

~~7~~5. The compound according to ~~any of the above~~ claims 1-4, or a pharmaceutically acceptable salt, ester, amide, solvate, or stereoisomer thereof, wherein the linker region (L) is -$C(H)_2$-O-C(O)-.

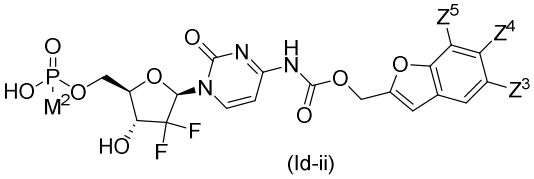
~~8~~6. The compound according to claim 1 having formulae (Id-i), (Id-ii), (Icd-iii), (Id-iv), (Id-v), (Id-vi), (Id-vii), (Id-viii), (Id-ix), (Id-x), (Id-xi), (Id-xii), (Id-xiii), (Id-xiv), (Id-xv), (Id-xvi), (Id-xvii), (Id-xviii), (Id-xix), or (Id-xx):



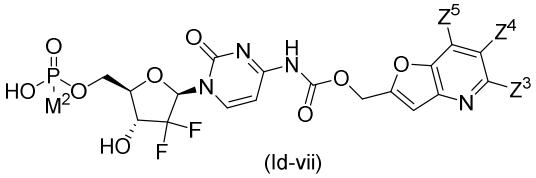
(Id-i),



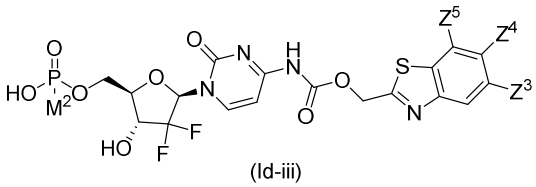
(Id-vi),



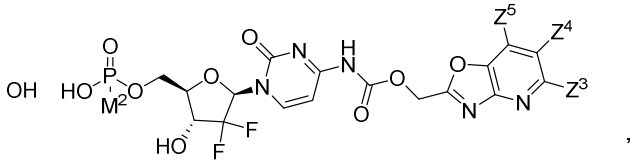
(Id-ii),



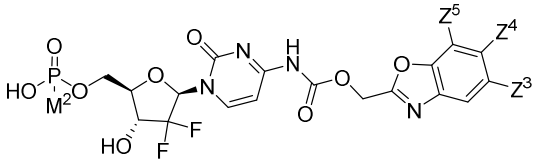
(Id-vii),



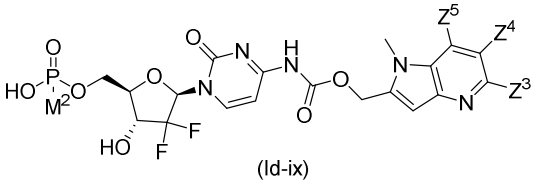
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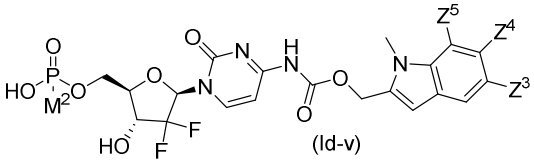
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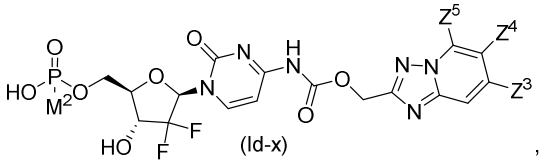
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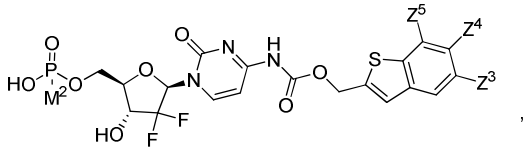
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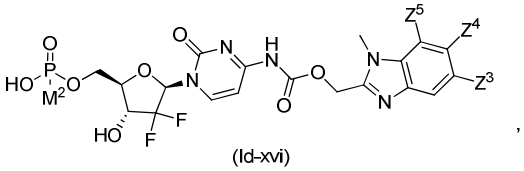
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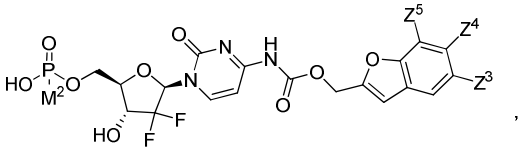
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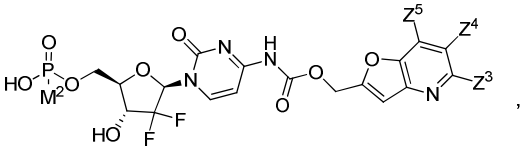
(Id-xi)



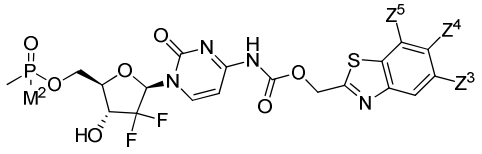
(Id-xvi)



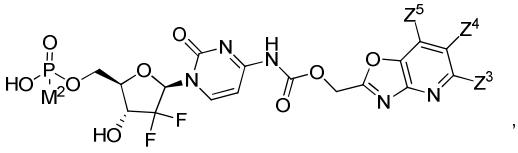
(Id-xii)



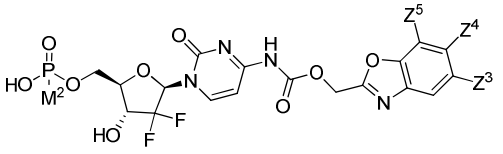
(Id-xvii)



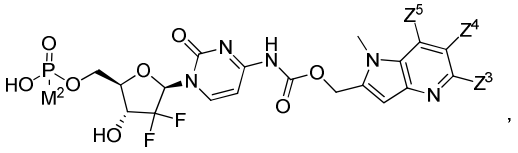
(Id-xiii)



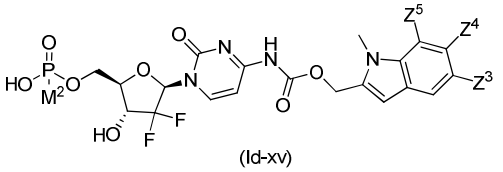
(Id-xviii)



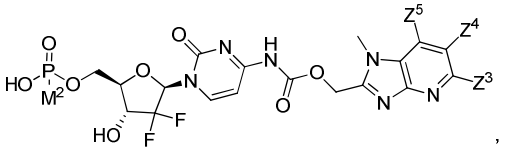
(Id-xiv)



(Id-xix)



(Id-xv)



(Id-xx)

or a pharmaceutically acceptable salt, ester, amide, solvate, or stereoisomer of anyof the above formulae, wherein:

Z^3, Z^4, and Z^5 are each independently methyl optionally substituted with 1-3 halo, halo, methoxy optionally substituted with 1-3 halo or deuterated methoxy; and

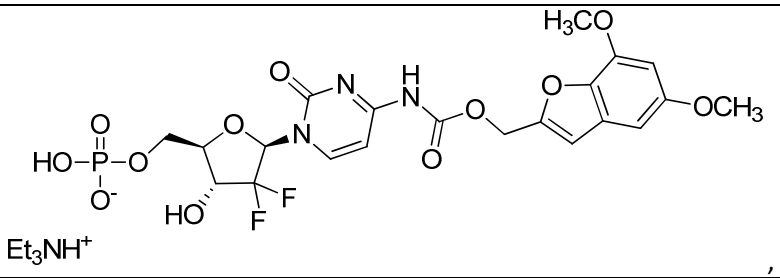
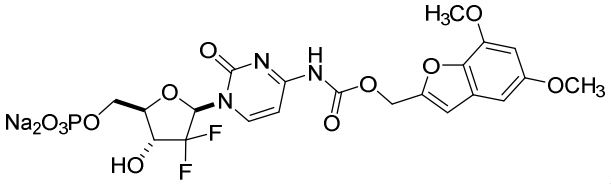
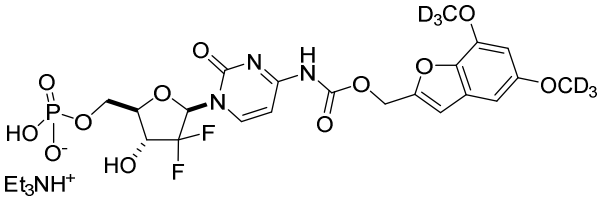
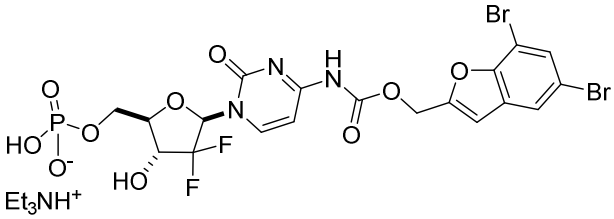
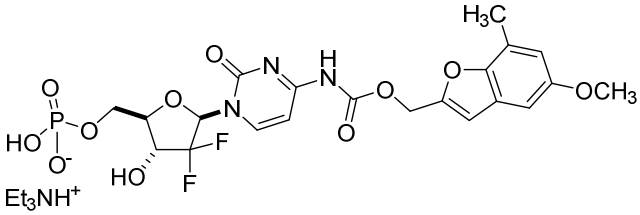
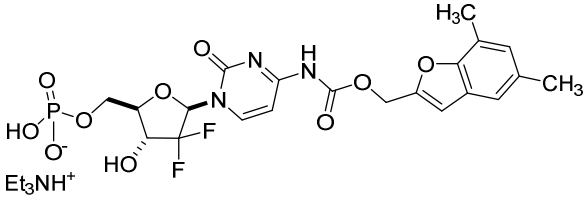
M^2 is $-O^-$ Na+, $-O^-$ Et_3NH^+, $-O^-$ K^+, $-O^-$ NH_4^+.

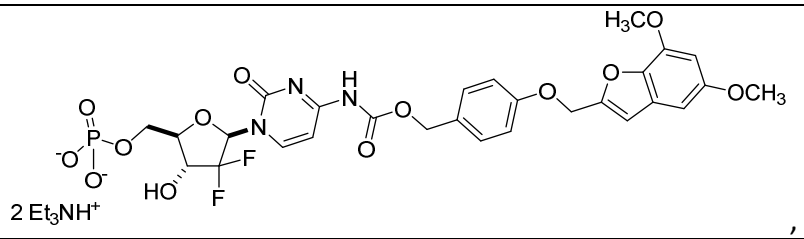
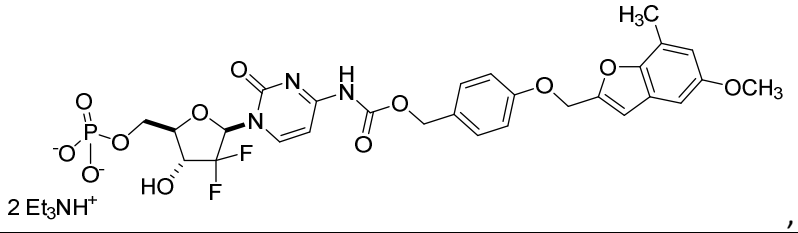
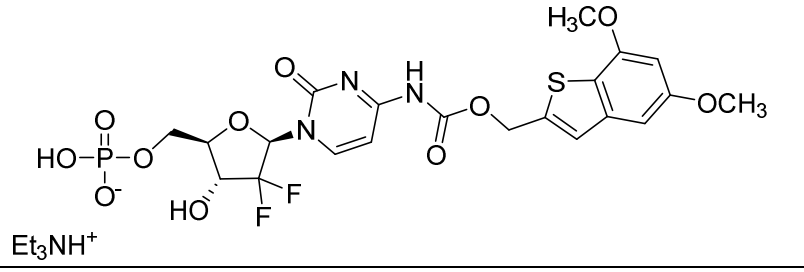
~~9~~7. The compound according to any of the above claims, or a pharmaceutically acceptable salt, ester, amide, solvate, or stereoisomer thereof, wherein Z^3, Z^5 and Z^4, when present, are each methoxy optionally substituted with 1-3 halo or deuterated methoxy.

~~10~~8. The compound according to any of the above claims, or a pharmaceutically acceptable salt, ester, amide, solvate, or stereoisomer thereof, wherein Z^3 and Z^5 are each independently bromo or fluoro, and Z^4, when present, is methoxy optionally substituted with 1-3 halo, or deuterated methoxy.

~~119~~. The compound according to any of the above claims, or a pharmaceutically acceptable salt, ester, amide, solvate, or stereoisomer thereof, wherein the compound is in a sodium phosphate or triethylammonium phosphate salt form thereof.

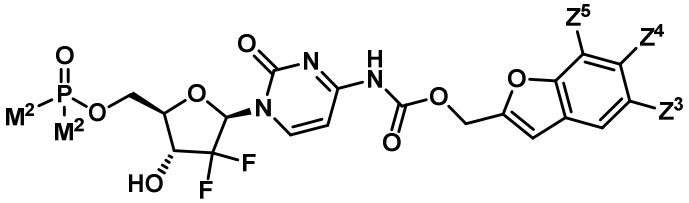
~~1210~~. The compound according to claim 1 having one of the following structures:

Compound #	Structure
1	 ,
2	 ,
3	 ,
4	 ,
5	 ,
6	 ,

7	
8	
9	

or a pharmaceutically acceptable salt, ester, amide, solvate, or stereoisomer of any one of compounds 1-9.

~~13~~11. The compound according to claim 1, having formula (Id-ii-1)



or a pharmaceutically acceptable salt, ester, amide, solvate, or stereoisomer thereof

wherein:

Z^3, Z^4, and Z^5 are each independently hydrogen, methyl optionally substituted with 1-3 halo, halo, methoxy optionally substituted with 1-3 halo or deuterated methoxy; and

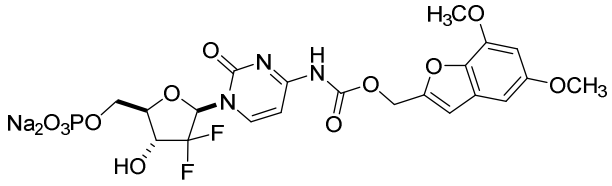
each M^2 is independently selected from the group consisting of OH and O^- (M^1), wherein (M^1) in each occurrence is independently a metal cation, ammonium, an alkyl ammonium cation, or an amino acid cation.

~~14~~12. The compound according to claim ~~13~~11, wherein (M^1) is selected from the group consisting of Na^+, Ca^{2+}, K^+, Mg^{2+}, Zn^{2+}, NH^{4+}, $(HNEt3)^+$, meglumine-H^+, Tromethamine-H^+, Diethanolamine-H^+, lysine-H^+, and arginine-H^+.

~~15~~13. The compound according to any one of claims ~~13~~11-~~14~~12, wherein each of Z^5 and Z^3 is independently methoxy.

~~16~~14. The compound according to any one of claims ~~13~~11-~~15~~13, wherein Z^4 is hydrogen.

~~17~~15. The compound according to any one of claims ~~13~~11-~~16~~14, wherein the compound is:



or a pharmaceutically acceptable salt, ester, amide, solvate, or stereoisomer thereof.

~~18~~16. A composition comprising a compound according to any of the above claims, together with a pharmaceutically acceptable carrier, or pharmaceutically acceptable salt, ester, amide or solvate of a compound according to any of the above claims, together with a pharmaceutically acceptable carrier thereof.

~~19~~17. A compound, or pharmaceutically acceptable salt, ester, amide or solvate, as defined in any one of claims 1 to ~~17~~15, for use in medicine.

~~20~~18. A compound, or pharmaceutically acceptable salt, ester, amide or solvate, as defined in any one of claims 1 to ~~17~~15, for use in treatment or prophylaxis of a proliferative condition.

~~21~~19. The compound, or pharmaceutically acceptable salt, ester, amide or solvate, for use in the treatment or prophylaxis of claim ~~20~~18, wherein the proliferative condition is a cancer selected from bladder, brain, breast, colon, head and neck, kidney, lung, liver, ovarian, pancreatic, prostate or skin cancer.

~~22~~20. Use of a compound, or pharmaceutically acceptable salt, ester, amide or solvate, as defined in any one of claims 1 to ~~21~~15, for the preparation of a medicament for treatment or prophylaxis of a proliferative condition.

~~23~~21. A method of diagnosis of a patient for the presence of tumor cells expressing the CYP1B1 enzyme comprising (a) determining the amount of corresponding hydroxylated metabolite which

is produced subsequent to administration of a specific compound according to any of claims 1-~~21~~ 15 to the patient; and, (b) correlating the amount with the presence or absence of the tumor cells in the patient.

~~24~~22. Use of a therapeutically or prophylactically useful amount of a compound according to any of claims 1-~~21~~15, or pharmaceutically acceptable salt, ester, amide or solvate thereof, for the preparation of a medicament for treating a patient, the use comprising (1) identifying the presence of a tumor in the patient; and (2) treating the patient, identified as needing the treatment.