R_2 and R_3 are each independently H, -CN, C_1-C_4alkyl, C_3-C_6cycloalkyl, or C_2-C_7heterocycloalkyl; or R_2 and R_3 are taken together to form a 5- or 6-membered heterocyclic ring;

R_4 is H, halogen, -CN, $-NO_2$, -OH, $-OCF_3$, $-OCH_2F$, $-OCF_2H$, $-SR_8$, $-N(R_8)S(=O)_2R_9$, $-S(=O)_2N(R_8)_2$, $-S(=O)R_9$, $-S(=O)_2R_9$, $-C(=O)R_9$, $-CO_2R_8$, $-N(R_8)_2$, $-C(=O)N(R_8)_2$, $-N(R_8)C(=O)R_9$, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6alkoxy, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_2-C_7heterocycloalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted C_6-C_{10}aryl, or substituted or unsubstituted C_2-C_7heteroaryl; or two R_1 are taken together to form a substituted or unsubstituted heterocyclic ring or a substituted or unsubstituted carbocyclic ring; wherein when n is 0, R_4 is not halogen;

R_5 is halogen, -CN, -OH, $-CF_3$, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6alkoxy, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_2-C_7heterocycloalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted C_6-C_{10}aryl, or substituted or unsubstituted C_2-C_7heteroaryl;

R_6 is $-(C(R_{14})(R_{15}))_mN(R_{11})(R_{12})$;

R_{11} and R_{12} are each independently H, or substituted or unsubstituted C_1-C_6alkyl; or R_{11} and R_{12} are taken together to form a 5-, 6-, 7-, or 8-membered heterocyclic ring;

R_{13} is H, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_2-C_7heterocycloalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted -C_1-C_4alkylC_6-C_{10}aryl, or substituted or unsubstituted -C_1-C_4alkylC_2-C_7heteroaryl;

each R_{14} and R_{15} are each independently H, or substituted or unsubstituted C_1-C_6alkyl; or R_{14} and R_{15} are taken together to form a 4-, 5-, 6-membered cycloalkyl ring;

each R_8 is independently H, or substituted or unsubstituted C_1-C_6alkyl;

R_9 is substituted or unsubstituted C_1-C_6alkyl;

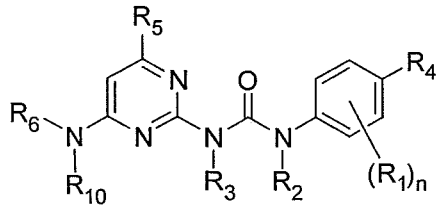
R_{10} is H, or C_1-C_4alkyl;

m is 2-6;

n is 0-4; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof.

[008a] In another aspect, described herein is compound having the structure of Formula (IIA):



Formula (IIA);

wherein:

each R_1 is independently halogen, -CN, $-NO_2$, -OH, $-OCF_3$, $-OCH_2F$, $-OCF_2H$, $-SR_8$, $-N(R_8)S(=O)_2R_9$, $-S(=O)_2N(R_8)_2$, $-S(=O)R_9$, $-S(=O)_2R_9$, $-C(=O)R_9$, $-CO_2R_8$, $-N(R_8)_2$, $-C(=O)N(R_8)_2$, $-N(R_8)C(=O)R_9$, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6alkoxy, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_2-C_7heterocycloalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted C_6-C_{10}aryl, or substituted or unsubstituted C_2-C_7heteroaryl; or two R_1 are taken together to form a substituted or unsubstituted heterocyclic ring or a substituted or unsubstituted carbocyclic ring;

R_2 and R_3 are each independently H, -CN, C_1-C_4alkyl, C_3-C_6cycloalkyl, or C_2-C_7heterocycloalkyl; or R_2 and R_3 are taken together to form a 5- or 6-membered heterocyclic ring;

R_4 is H, halogen, -CN, $-NO_2$, -OH, $-OCF_3$, $-OCH_2F$, $-OCF_2H$, $-SR_8$, $-N(R_8)S(=O)_2R_9$, $-S(=O)_2N(R_8)_2$, $-S(=O)R_9$, $-S(=O)_2R_9$, $-C(=O)R_9$, $-CO_2R_8$, $-N(R_8)_2$, $-C(=O)N(R_8)_2$, $-N(R_8)C(=O)R_9$, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6alkoxy, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_2-C_7heterocycloalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted C_6-C_{10}aryl, or substituted or unsubstituted C_2-C_7heteroaryl; or two R_1 are taken together to form a substituted or unsubstituted heterocyclic ring or a substituted or unsubstituted carbocyclic ring; wherein when n is 0, R_4 is not halogen;

R_5 is halogen, -CN, -OH, $-CF_3$, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6alkoxy, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_2-C_7heterocycloalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted C_6-C_{10}aryl, or substituted or unsubstituted C_2-C_7heteroaryl;

R_6 is $-(C(R_{14})(R_{15}))_mN(R_{11})(R_{12})$;

R_{11} and R_{12} are each independently H, or substituted or unsubstituted C_1-C_6alkyl; or R_{11} and R_{12} are taken together to form a 5-, 6-, 7-, or 8-membered heterocyclic ring;

R_{13} is H, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_2-C_7heterocycloalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted -C_1-C_4alkylC_6-C_{10}aryl, or substituted or unsubstituted -C_1-C_4alkylC_2-C_7heteroaryl;

each R_{14} and R_{15} are each independently H, or substituted or unsubstituted C_1-C_6alkyl; or R_{14} and R_{15} are taken together to form a 4-, 5-, 6-membered cycloalkyl ring;

each R_8 is independently H, or substituted or unsubstituted C_1-C_6alkyl;

R_9 is substituted or unsubstituted C_1-C_6alkyl;

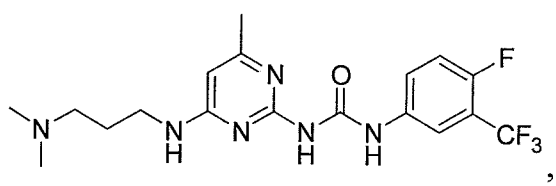
R_{10} is H, or C_1-C_4alkyl;

m is 2-6;

n is 0-4; or

a pharmaceutically acceptable salt, or solvate thereof.

[0009] In one embodiment is a compound of Formula (IIA) wherein R_2 and R_3 are each independently H, -CN, C_1-C_4alkyl, C_3-C_6cycloalkyl, or C_2-C_7heterocycloalkyl. In another embodiment is a compound of Formula (IIA) wherein R_2 and R_3 are each H. In another embodiment is a compound of Formula (IIA) wherein R_2 and R_3 are taken together to form a 5- or 6-membered heterocyclic ring. In another embodiment is a compound of Formula (IIA)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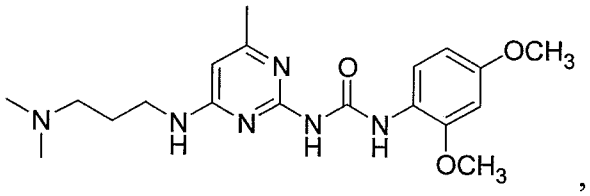
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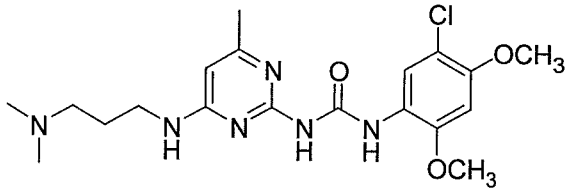
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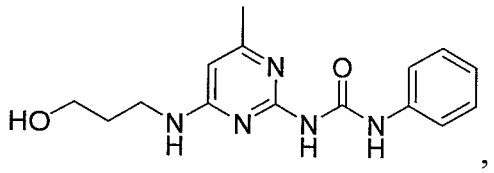
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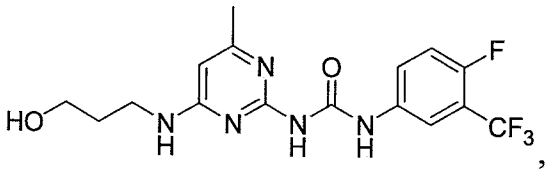
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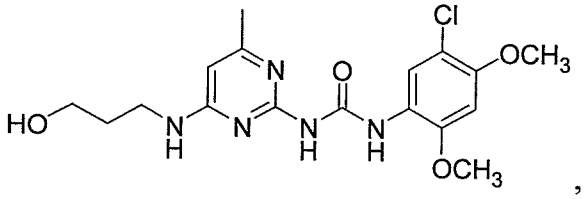
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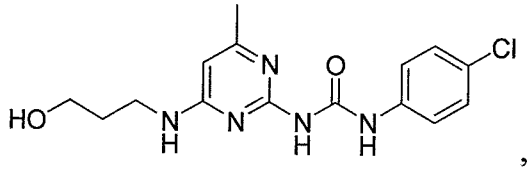
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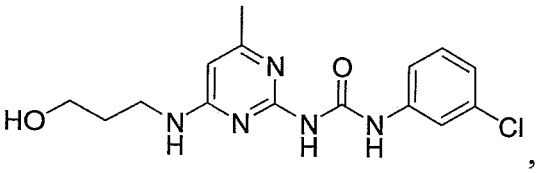
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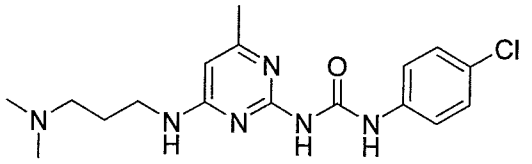
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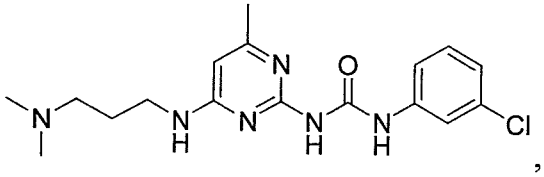
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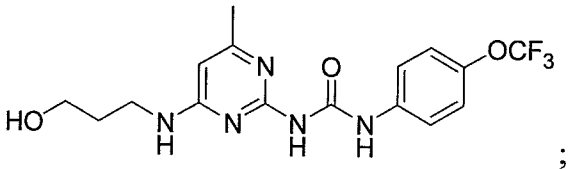

; or a pharmaceutically acceptable salt, solvate, or thereof.

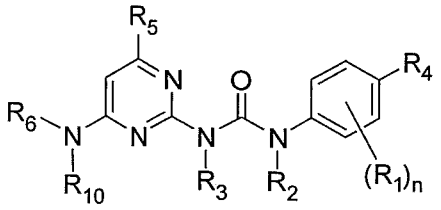
[0012] In another aspect is a pharmaceutical composition comprising a compound of Formula (I), (II), or (IIA) or a pharmaceutically acceptable salt, solvate, or prodrug thereof, and at least one pharmaceutically acceptable excipient. In another aspect is a pharmaceutical composition comprising a compound of Formula (I), (II), (IIA), or (VI) or a pharmaceutically acceptable salt or solvate thereof, and at least one pharmaceutically acceptable excipient.

[0012a] In another aspect is a pharmaceutical composition comprising a compound of Formula (I), (II), or (IIA) or a pharmaceutically acceptable salt or solvate thereof, and at least one pharmaceutically acceptable excipient. In another aspect is a pharmaceutical composition comprising a compound of Formula (I), (II), (IIA), or (VI) or a pharmaceutically acceptable salt or solvate thereof, and at least one pharmaceutically acceptable excipient.

[0012b] In another aspect, there is provided use of a composition comprising a compound as described herein, or a pharmaceutically acceptable salt, solvate thereof; in the manufacture of a medicament for treating a disease in a subject wherein the disease is cancer or Down's Syndrome.

WHAT IS CLAIMED IS:

1. A compound having the structure of Formula (IIA):



Formula (IIA);

wherein:

each R_1 is independently halogen, -CN, -NO_2, -OH, -OCF_3, -OCH_2F, -OCF_2H, -SR_8, -$N(R_8)S(=O)_2R_9$, -$S(=O)_2N(R_8)_2$, -$S(=O)R_9$, -$S(=O)_2R_9$, -$C(=O)R_9$, -CO_2R_8, -$N(R_8)_2$, -$C(=O)N(R_8)_2$, -$N(R_8)C(=O)R_9$, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6alkoxy, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_2-C_7heterocycloalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted C_6-C_{10}aryl, or substituted or unsubstituted C_2-C_7heteroaryl; or two R_1 are taken together to form a substituted or unsubstituted heterocyclic ring or a substituted or unsubstituted carbocyclic ring;

R_2 and R_3 are each independently H, -CN, C_1-C_4alkyl, C_3-C_6cycloalkyl, or C_2-C_7heterocycloalkyl; or R_2 and R_3 are taken together to form a 5- or 6-membered heterocyclic ring;

R_4 is H, halogen, -CN, -NO_2, -OH, -OCF_3, -OCH_2F, -OCF_2H, -SR_8, -$N(R_8)S(=O)_2R_9$, -$S(=O)_2N(R_8)_2$, -$S(=O)R_9$, -$S(=O)_2R_9$, -$C(=O)R_9$, -CO_2R_8, -$N(R_8)_2$, -$C(=O)N(R_8)_2$, -$N(R_8)C(=O)R_9$, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6alkoxy, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_2-C_7heterocycloalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted C_6-C_{10}aryl, or substituted or unsubstituted C_2-C_7heteroaryl; or two R_1 are taken together to form a substituted or unsubstituted heterocyclic ring or a substituted or unsubstituted carbocyclic ring; wherein when n is 0, R_4 is not halogen;

R_5 is halogen, -CN, -OH, -CF_3, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6alkoxy, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_2-C_7heterocycloalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted C_6-C_{10}aryl, or substituted or unsubstituted C_2-C_7heteroaryl;

R_6 is -$(C(R_{14})(R_{15}))_mN(R_{11})(R_{12})$;

R_{11} and R_{12} are each independently H, or substituted or unsubstituted C_1-C_6alkyl; or R_{11} and R_{12} are taken together to form a 5-, 6-, 7-, or 8-membered heterocyclic ring;

R_{13} is H, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_2-C_7heterocycloalkyl, substituted or unsubstituted C_3-C_8cycloalkyl,

substituted or unsubstituted -C_1-C_4alkylC_6-C_{10}aryl, or substituted or unsubstituted -C_1-C_4alkylC_2-C_7heteroaryl;
each R_{14} and R_{15} are each independently H, or substituted or unsubstituted C_1-C_6alkyl; or R_{14} and R_{15} are taken together to form a 4-, 5-, 6-membered cycloalkyl ring;
each R_8 is independently H, or substituted or unsubstituted C_1-C_6alkyl;
R_9 is substituted or unsubstituted C_1-C_6alkyl;
R_{10} is H, or C_1-C_4alkyl;
m is 2-6;
n is 0-4; or
a pharmaceutically acceptable salt, or solvate thereof.

2. The compound of claim 1, wherein R_2 and R_3 are each independently H, -CN, C_1-C_4alkyl, C_3-C_6cycloalkyl, or C_2-C_7heterocycloalkyl.

3. The compound of claim 2, wherein R_2 and R_3 are each H.

4. The compound of any one of claims 1-3, wherein R_6 is -$(C(R_{14})(R_{15}))_mN(R_{11})(R_{12})$ and R_{14} and R_{15} are each H.

5. The compound of claim 4, wherein R_{11} and R_{12} are each independently H, or substituted or unsubstituted C_1-C_6alkyl.

6. The compound of claim 5, wherein R_{11} and R_{12} are each independently unsubstituted C_1-C_6alkyl.

7. The compound of claim 6, wherein R_{11} and R_{12} are each -CH_3.

8. The compound of any one of claims 1-7, wherein m is 2.

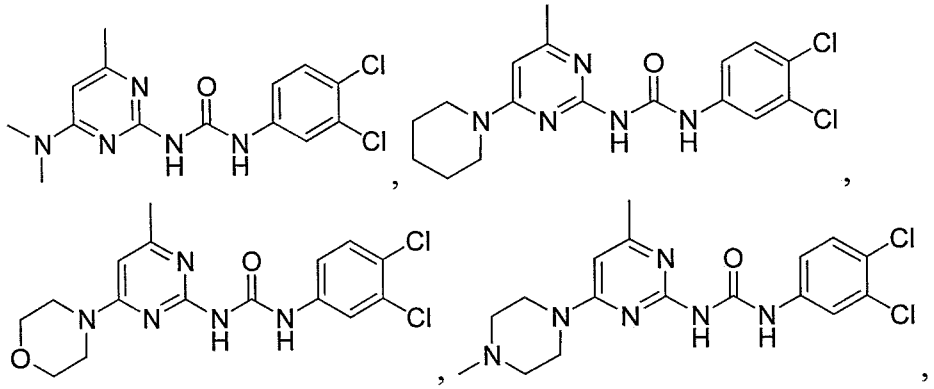
9. The compound of any one of claims 1-7, wherein m is 3.

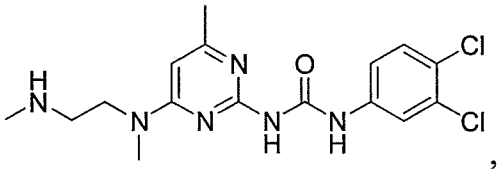
10. The compound of any one of claims 1-9, wherein R_{10} is H or CH_3.

11. The compound of any one of claims 1-10, wherein n is 0.

12. The compound of any one of claims 1-10, wherein n is 1.

13. A compound having a structure selected from:

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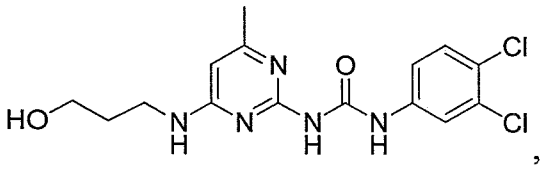
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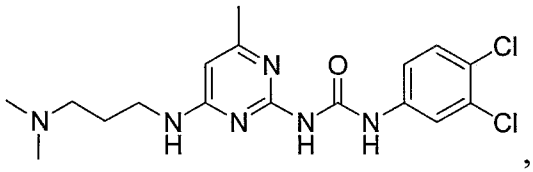
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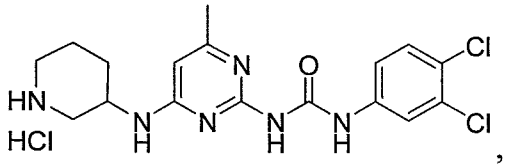
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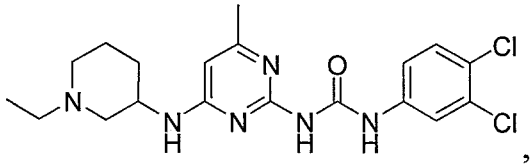
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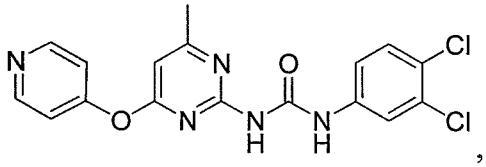
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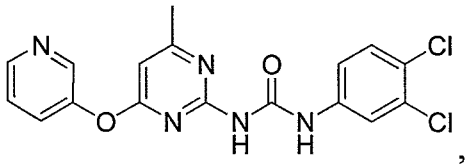
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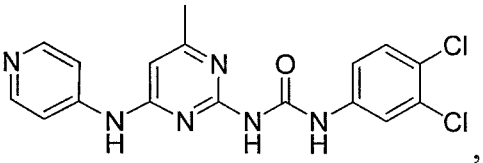
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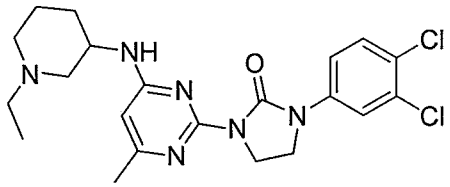
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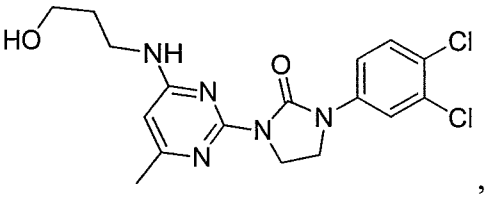
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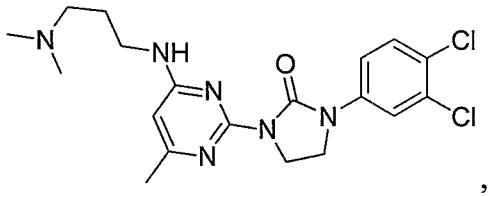
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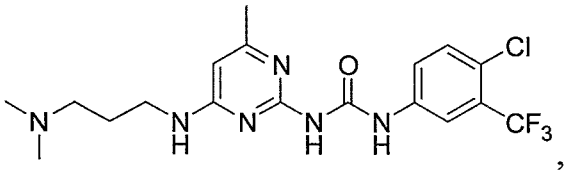
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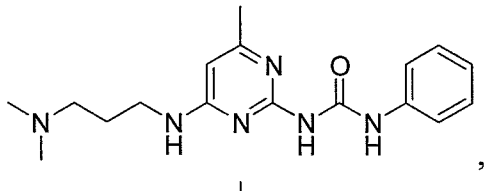
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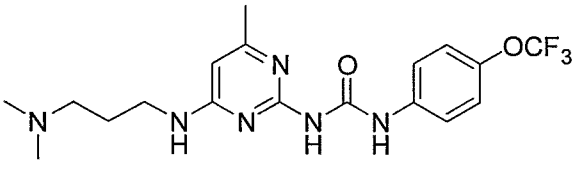
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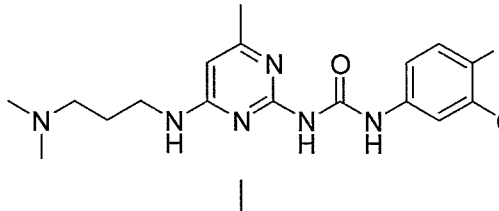
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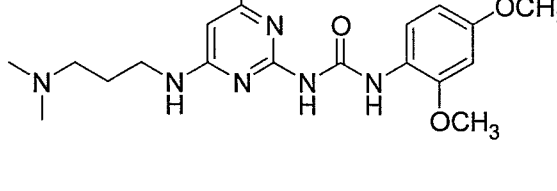
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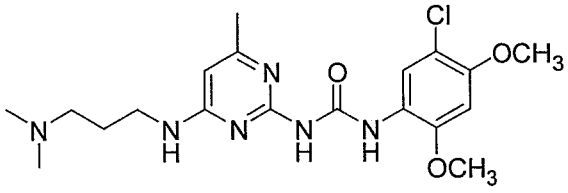
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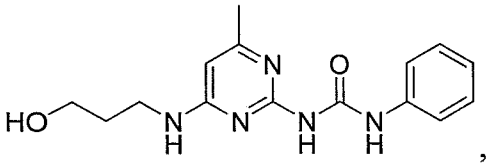
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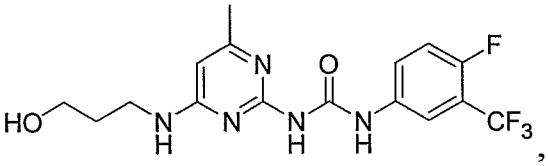
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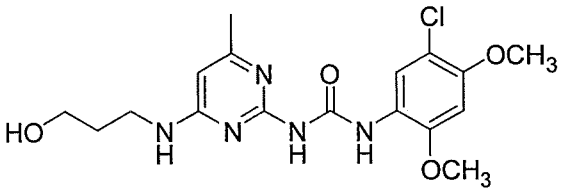
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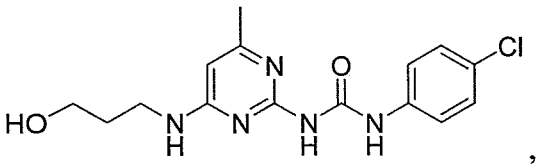
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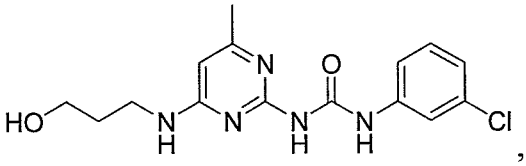
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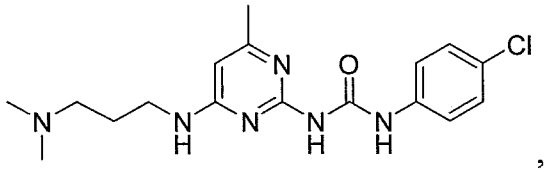
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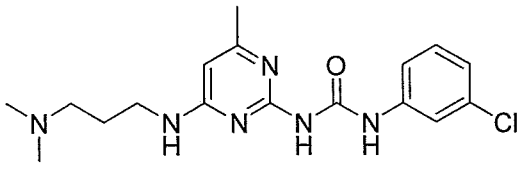
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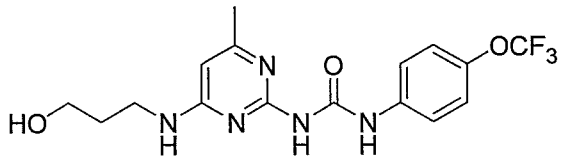
; or a pharmaceutically acceptable salt, or solvate thereof.

14. A pharmaceutical composition comprising a compound of any one of claims 1-13, or a pharmaceutically acceptable salt, or solvate thereof, and at least one pharmaceutically acceptable excipient.

15. Use of a composition comprising a compound of any one of claims 1-13, or a pharmaceutically acceptable salt, or solvate thereof; in the manufacture of a medicament for treating a disease in a subject wherein the disease is cancer or Down's Syndrome.

16. The use of claim 15, wherein the disease is cancer.

17. The use of claim 16, wherein the cancer is brain cancer, glioblastoma multiforme, medulloblastoma, astrocytomas, brain stem gliomas, meningiomas, oligodendrogliomas, melanoma, lung cancer, breast cancer, or leukemia.

18. The use of claim 15, wherein the disease is Down's Syndrome.