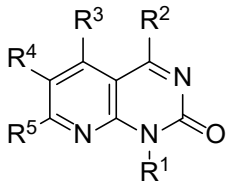
CLAIMS:

1. A compound of formula (IIId):



(IIId),

or a pharmaceutically accepetable salt thereof, wherein

R^3 is hydrogen;

R^5 is C_{1-6} haloalkyl;

R^4 is hydrogen;

R^1 is R^7 wherein R^7 is phenyl or 5- to 6-membered heteroaryl, wherein phenyl or heteroaryl is unsubstituted or substituted with R^d, R^e, and/or R^f;

R^2 is $-NR^9R^{10}$;

R^9 is hydrogen;

R^{10} is hydrogen, C_{1-6} alkyl, or C_{3-6} cycloalkyl, wherein C_{3-6} cycloalkyl is unsubstituted or substituted with halo;

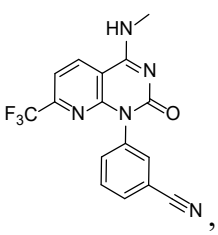
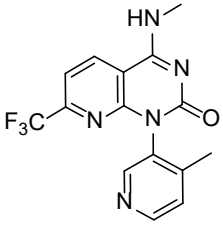
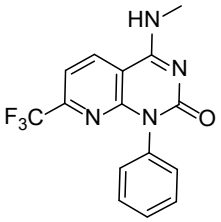
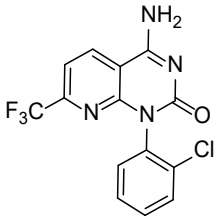
R^d and R^e are independently selected from the group consisting of C_{1-6} alkyl, halo, C_{1-6} alkoxy, and cyano; and

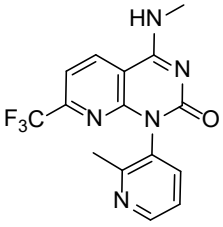
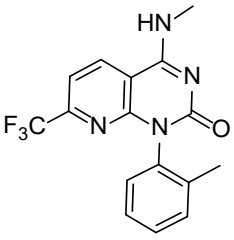
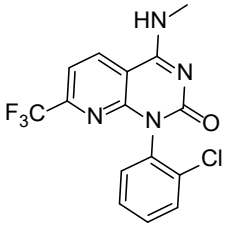
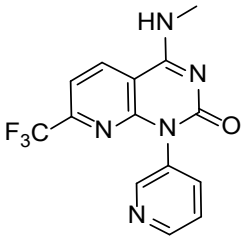
R^f is selected from the group consisting of C_{1-6} alkyl, halo, C_{1-6} alkoxy, and cyano.

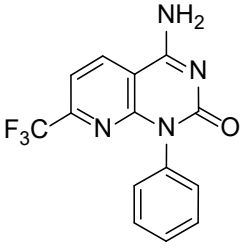
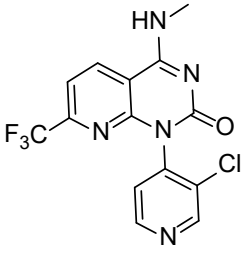
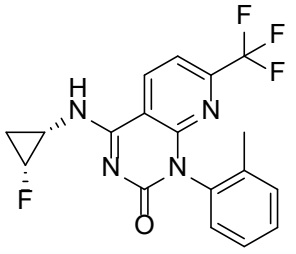
2. The compound of claim 1 or a pharmaceutically acceptable salt thereof wherein R^7 is phenyl which is unsubstituted or substituted with R^d, R^e, and/or R^f, wherein R^d and R^e are independently selected from the group consisting of C_{1-6} alkyl, halo, and cyano; and R^f is selected from the group consisting of C_{1-6} alkyl, halo, and cyano.

3. The compound of claim 1 or a pharmaceutically acceptable salt thereof wherein R^7 is pyridinyl which is unsubstituted or substituted with R^d, R^e, and/or R^f where R^d and R^e are independently selected from the group consisting of C_{1-6} alkyl and halo; and R^f is selected from the group consisting of C_{1-6} alkyl and halo.

4. A compound that is selected from the group consisting of:

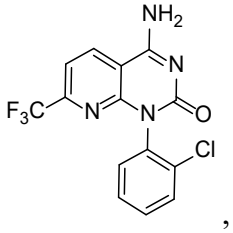
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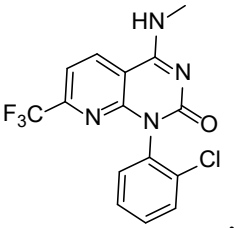
or a pharmaceutically acceptable salt thereof.

5. A compound having the formula:

,

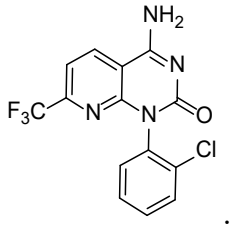
or a pharmaceutically acceptable salt thereof.

6. A compound having the formula:

,

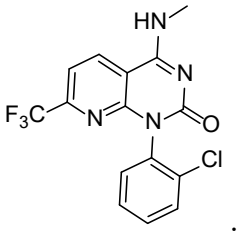
or a pharmaceutically acceptable salt thereof.

7. A compound having the formula:



.

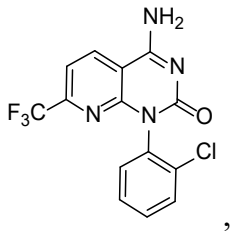
8. A compound having the formula:



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9. A pharmaceutical composition comprising a compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

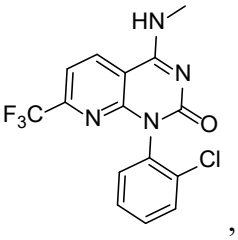
10. A pharmaceutical composition comprising a compound having the formula:



,

or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

11. A pharmaceutical composition comprising a compound having the formula:



,

or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

12. A compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, for use in the treatment of a disease mediated by MAT2A in a patient.

13. A compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, for use in the treatment of:

(a) a MTAP null cancer in a patient, or

(b) a cancer characterized by a reduction or absence of MTAP gene expression, the absence of the MTAP gene, or reduced function of MTAP protein.

14. Use of a compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease mediated by MAT2A.

15. Use of a compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating:

(a) a MTAP null cancer, or

(b) a cancer characterized by a reduction or absence of MTAP gene expression, the absence of the MTAP gene, or reduced function of MTAP protein.

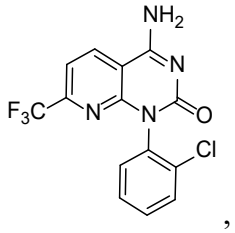
16. The compound for use of claim 12, or the use of claim 14, wherein the disease is cancer.

17. The compound for use of claim 13 or 16, or the use of claim 15 or 16, wherein the cancer is leukemia, glioma, melanoma, pancreatic, non-small cell lung cancer, bladder cancer, astrocytoma, osteosarcoma, head and neck cancer, myxoid chondrosarcoma, ovarian cancer, endometrial cancer, breast cancer, soft tissue sarcoma, gallbladder carcinoma, non-Hodgkin lymphoma, esophageal cancer, or mesothelioma,

optionally wherein the cancer is non-small cell lung cancer, gastric cancer, or bladder cancer.

18. The compound for use of any one of claims 12, 13, 16, or 17, or the use of any one of claims 14 to 17, wherein the medicament is for use in combination with at least one additional therapeutic agent.

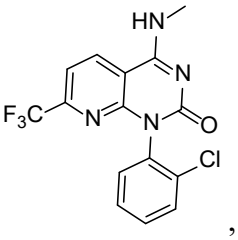
19. The compound for use of any one of claims 12, 13, or 16 to 18, or the use of any one of claims 14 to 18, wherein the compound has the formula:



,

or a pharmaceutically acceptable salt thereof.

20. The compound for use of any one of claims 12, 13, or 16 to 18, or the use of any one of claims 14 to 18, wherein the compound has the formula:



,

or a pharmaceutically acceptable salt thereof.