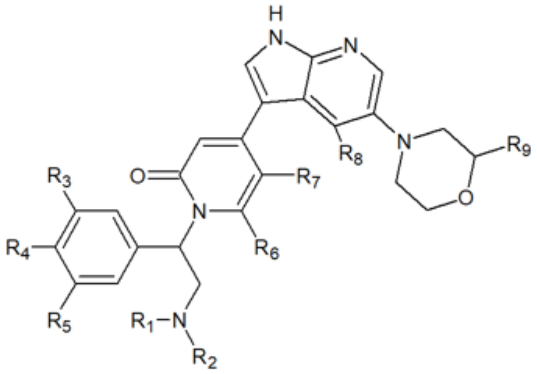
Another subject concerns processes for preparing the compounds of general formula (I).

Another subject concerns the compounds of general formula (I) for their use especially in medicaments or in pharmaceutical compositions.

A further subject concerns the compounds according to the invention for use as inhibitors of the ERK kinases activity, particularly for use as inhibitors of the ERK1 and/or ERK2 kinases activity.

SUMMARY

In one aspect, the present disclosure refers to a compound of formula (I):



(I)

wherein:

- R_1 represents a $(C_1\text{-}C_6)$alkyl group;

- R_2 represents a $(C_1\text{-}C_6)$alkyl group, a $(C_3\text{-}C_6)$cycloalkyl group, or a $(C_1\text{-}C_6)$alkyl group substituted by one or more radicals selected from halogen atoms, cyano group, $(C_1\text{-}C_6)$alkoxy group and $(C_3\text{-}C_6)$cycloalkyl group;

or R_1 and R_2 form together with the nitrogen atom a 3- to 6-membered heterocyclic group;

- R_3, R_4, R_5, R_6, R_7, R_8 and R_9 represent, independently of each other, a hydrogen atom, a halogen atom, a $(C_1\text{-}C_6)$alkyl group, a trifluoromethyl group or a cyano group, wherein said $(C_1\text{-}C_6)$alkyl is itself optionally substituted with a $(C_1\text{-}C_6)$alkoxy group;

or one of its pharmaceutically acceptable salts.

In another aspect, there present disclosure refers to a compound as defined above, for us in preventing and/or inhibiting and/or treating a disease or a condition mediated by ERK kinases activity, in particular by ERK2 kinase activity.

In another aspect, there is provided the use of a compound as defined above, in the manufacture of a medicament for preventing and/or inhibiting and/or treating a disease or a condition mediated by ERK kinases activity, in particular by ERK2 kinase activity.

In another aspect, there is provided the use of a compound as defined above, in the manufacture of a medicament for preventing and/or inhibiting and/or treating the Human Immunodeficiency Virus (HIV).

In another aspect, the present disclosure refers to a medicament comprising at least one compound as defined above, or a pharmaceutically acceptable salt thereof.

In another aspect, the present disclosure refers to a pharmaceutical comprising at least one compound as defined above, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

ABBREVIATIONS AND DEFINITIONS

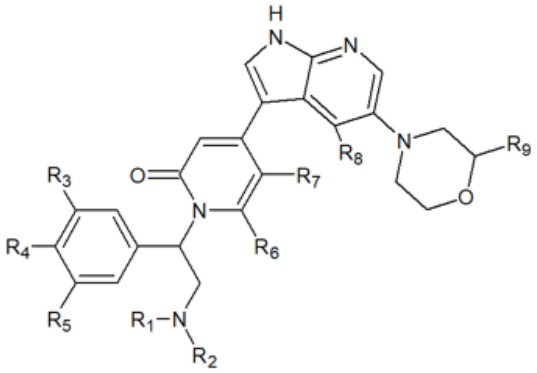
In the context of the present invention, the following abbreviations and empirical formulae are used:

ATP	adenosine 5'-triphosphate
Brij-35	Polyoxyethyleneglycol dodecyl ether
Boc	tert-butyloxycarbonyl
Bs	Brosyl
C18 column	Reversed-phase C18 column
CMC	Carboxymethylcellulose
Cs_2CO_3	Cesium carbonate
DABCO	1,4-Diazabicyclo[2.2.2]octane
DIEA	*N*,*N*-Diisopropylethylamine
DMF	Dimethylformamide
DMEM	Dulbecco's Modified Eagle Medium
DMSO	Dimethylsulfoxide
°C	Degree Celsius
DCM	Dichloromethane
ee	Enantiomeric excess
EGTA	Egtazic acid
Eq	Equivalent

Et_3N	Triethylamine
Et_2O	Diethyl ether
EtOAc	Ethyl acetate
EtOH	Ethanol

CLAIMS

1. Compound of formula (I):



(I)

wherein:

- R_1 represents a (C_1-C_6)alkyl group;

- R_2 represents a (C_1-C_6)alkyl group, a (C_3-C_6)cycloalkyl group, or a (C_1-C_6)alkyl group substituted by one or more radicals selected from halogen atoms, cyano group, (C_1-C_6)alkoxy group and (C_3-C_6)cycloalkyl group;

or R_1 and R_2 form together with the nitrogen atom a 3- to 6-membered heterocyclic group;

- R_3, R_4, R_5, R_6, R_7, R_8 and R_9 represent, independently of each other, a hydrogen atom, a halogen atom, a (C_1-C_6)alkyl group, a trifluoromethyl group or a cyano group, wherein said (C_1-C_6)alkyl is itself optionally substituted with a (C_1-C_6)alkoxy group;

or one of its pharmaceutically acceptable salts.

2. Compound according to claim 1, wherein R_1 represents a methyl group.

3. Compound according to anyone of the preceding claims, wherein R_2 represents a (C_1-C_6)alkyl group, and preferably R_2 represents a methyl group.

4. Compound according to anyone of the preceding claims, wherein both R_1 and R_2 represent a methyl group.

5. Compound according to anyone of the preceding claims, wherein the asymmetric carbon bearing the group $-CH_2NR_1R_2$ is of S configuration.

6. Compound according to anyone of the preceding claims, wherein R_3 represents a halogen atom, a (C_1-C_6)alkyl group, a trifluoromethyl group or a cyano group, wherein said (C_1-C_6)alkyl is itself optionally substituted with a (C_1-C_6)alkoxy group.

7. Compound according to anyone of the preceding claims, wherein R_3 represents a halogen atom, in particular a chlorine atom, a fluorine atom, a bromine atom, or

an iodine atom, more particularly R_3 represents a chlorine atom or a fluorine atom, and preferably R_3 represents a chlorine atom.

8. Compound according to anyone of the preceding claims, wherein R_4 represents a hydrogen atom or a halogen atom, in particular a chlorine atom, a fluorine atom, a bromine atom, or an iodine atom, more particularly R_4 represents a hydrogen atom, a chlorine atom, or a fluorine atom, and preferably R_4 represents a hydrogen atom or a chlorine atom.

9. Compound according to anyone of the preceding claims, wherein R_5 represents a hydrogen atom or a halogen atom, in particular a chlorine atom, a fluorine atom, a bromine atom, or an iodine atom, more particularly R_5 represents a hydrogen atom, a chlorine atom, or a fluorine atom, and preferably R_5 represents a hydrogen atom.

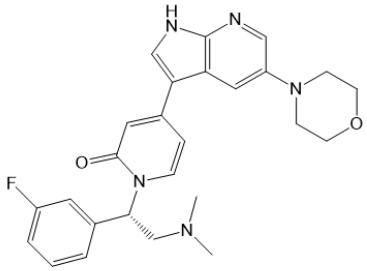
10. Compound according to anyone of the preceding claims, wherein R_6 represents a hydrogen atom or a $(C_1\text{-}C_6)$alkyl group, more particularly R_6 represents a hydrogen atom or a methyl group, and preferably R_6 represents a hydrogen atom.

11. Compound according to anyone of the preceding claims, wherein R_7 represents a hydrogen atom or a halogen atom, in particular a chlorine atom, a fluorine atom, a bromine atom, or an iodine atom, more particularly R_7 represents a hydrogen atom, a chlorine atom, or a fluorine atom, and preferably R_7 represents a hydrogen atom.

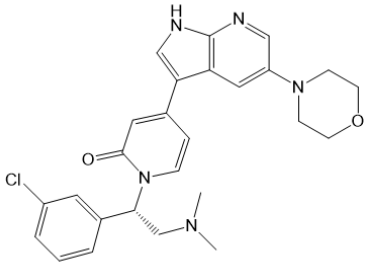
12. Compound according to anyone of the preceding claims, wherein R_8 represents a hydrogen atom or a halogen atom, in particular a chlorine atom, a fluorine atom, a bromine atom, or an iodine atom, more particularly R_8 represents a hydrogen atom, a chlorine atom, or a fluorine atom, and preferably R_8 represents a hydrogen atom.

13. Compound according to anyone of the preceding claims, wherein R_9 represents a hydrogen atom, a halogen atom or a trifluoromethyl group, more particularly R_9 represents a hydrogen atom or a trifluoromethyl group, and preferably R_9 represents a hydrogen atom.

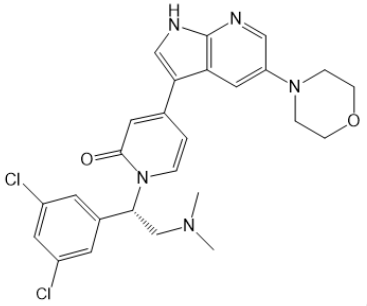
14. Compound according to claim 1, chosen among:



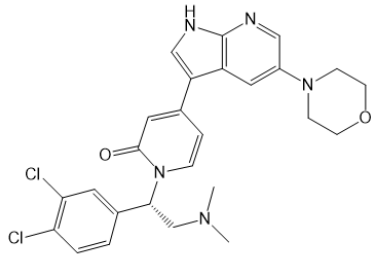
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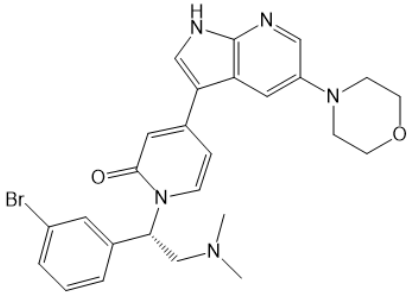
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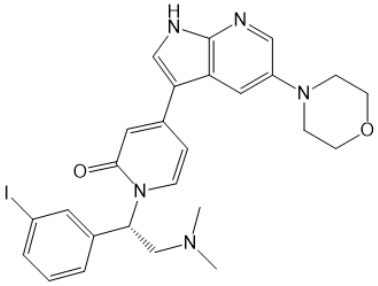
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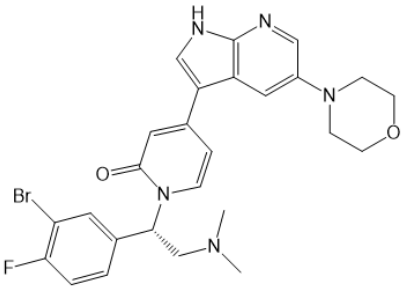
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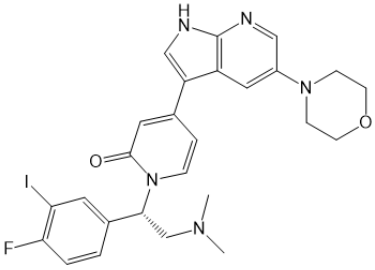
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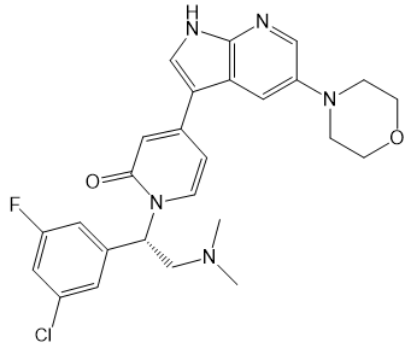
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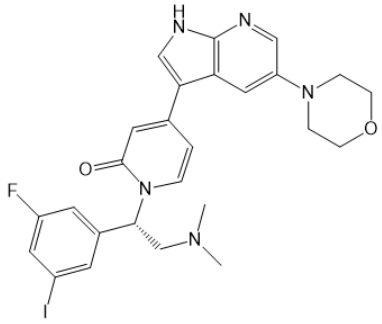
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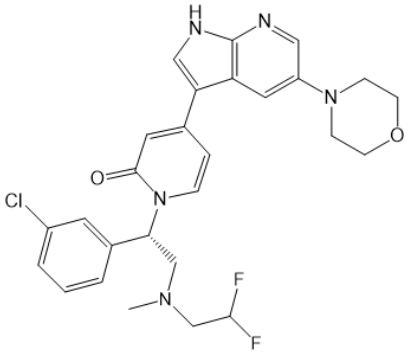
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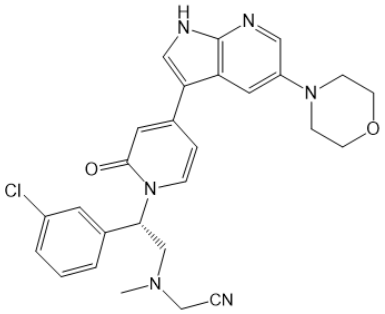
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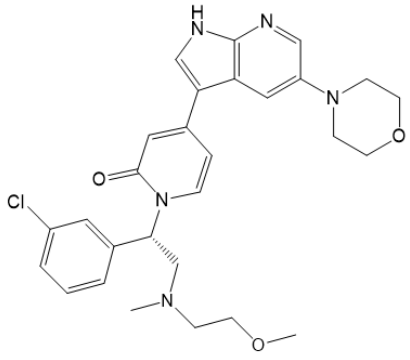
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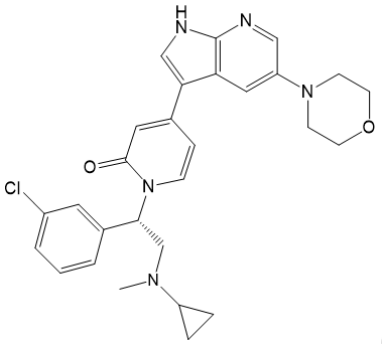
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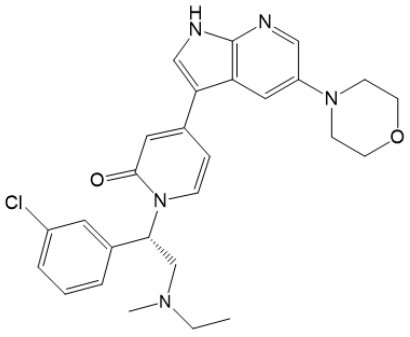
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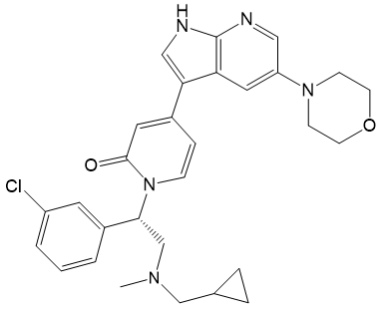
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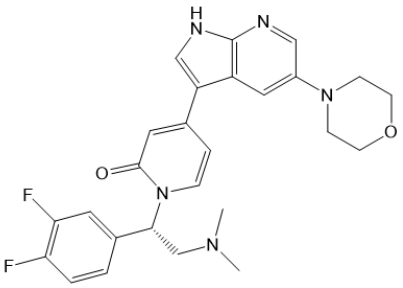
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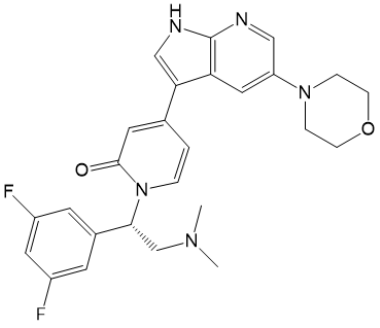
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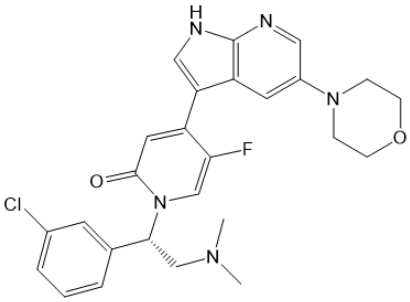
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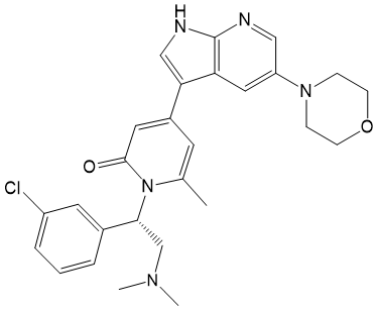
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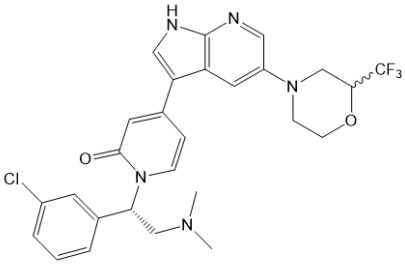
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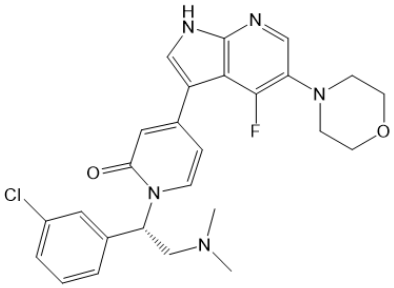
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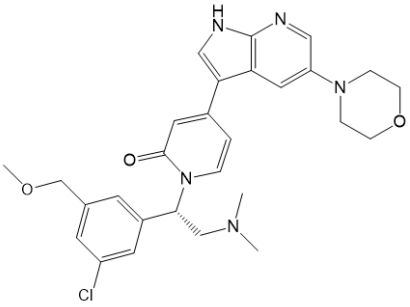
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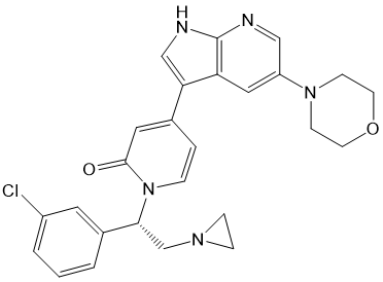
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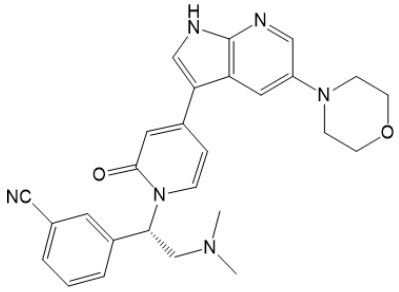
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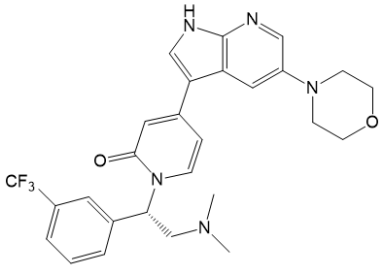
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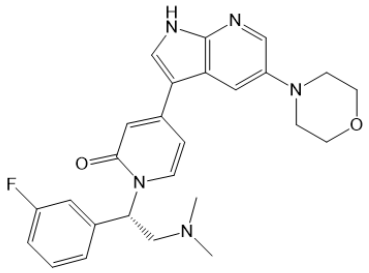
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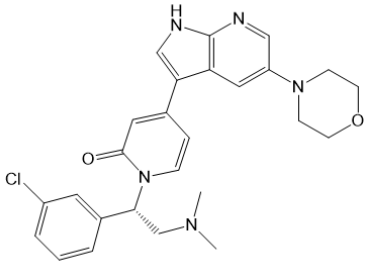
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or one of their pharmaceutically acceptable salts.

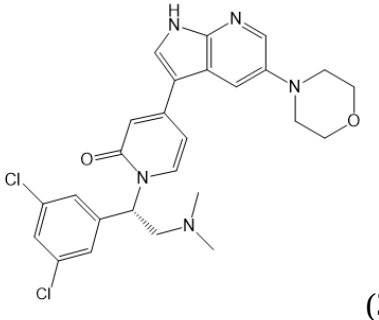
15. Compound according to claim 1, chosen among:



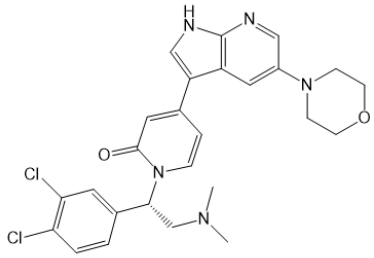
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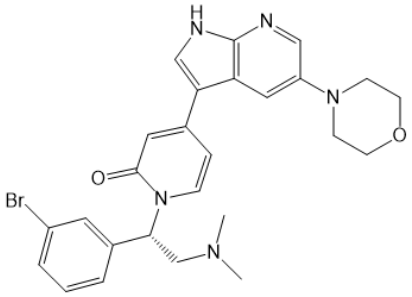
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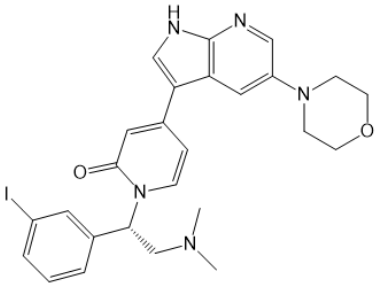
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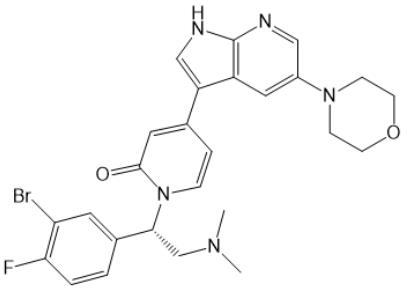
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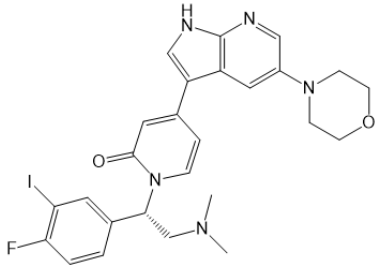
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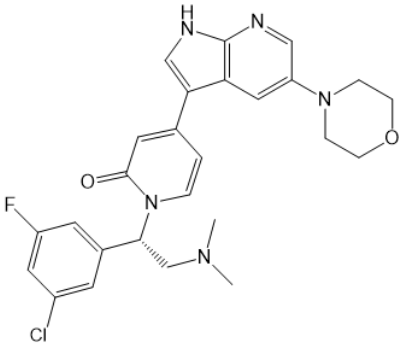
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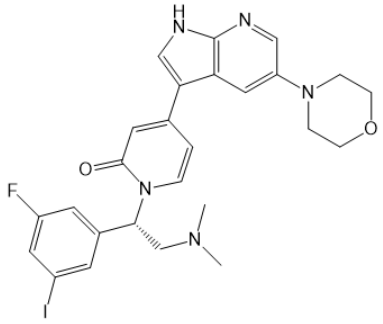
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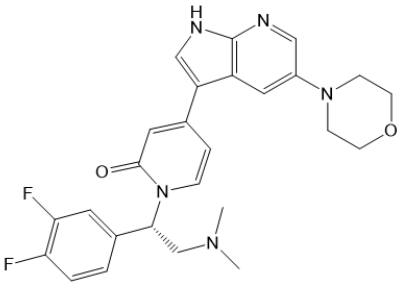
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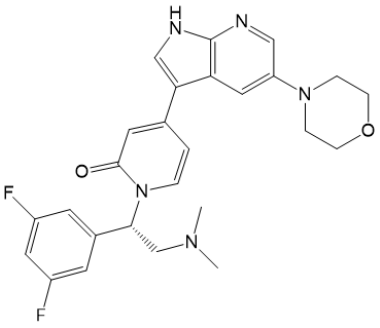
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(10)



(17)



(18)

or one of their pharmaceutically acceptable salts.

16. Compound according to anyone of the preceding claims, for use in preventing and/or inhibiting and/or treating a disease or a condition mediated by ERK kinases activity, in particular by ERK2 kinase activity.

17. Use of a compound according to any one of claims 1 to 16, in the manufacture of a medicament for preventing and/or inhibiting and/or treating a disease or a condition mediated by ERK kinases activity, in particular by ERK2 kinase activity.

18. The use according to claim 17, wherein the disease or the condition is chosen among cancers and metastases.

19. The use according to claim 17 or 18, wherein the disease or the condition is chosen among glioblastomas, multiple myelomas, carcinomas, leukemia, in particular myeloid (AML), lymphocytic, myelocytic, myelogenous (CML) or lymphoblastic leukemias, myelodysplastic syndromes, Kaposi's sarcomas, cutaneous angiosarcomas, solid tumours, lymphomas, in particular non-hodgkin's lymphomas, melanomas, in particular malignant melanomas, bladder cancers, breast cancers, gastric cancers, colon cancers, colorectal cancers, endometrial cancers, lung cancers, including non-small-cell cancers, pancreatic cancers, prostate cancers, rectal cancers, kidney cancers, head and neck cancers, liver cancers, ovarian cancers, in particular serous ovarian cancers, seminoma cancers,

cancers of the respiratory tract and chest, thyroid cancers, in particular papillary or follicular thyroid cancers, and other tumours expressing ERK.

20. The use according to claim 17, wherein the disease or the condition is chosen among a neoplastic disorder, an allergy disorder, an inflammatory disorder, an autoimmune disorder, a Plasmodium related disease, a mast cell associated disease, a graft- versus -host disease, a metabolic syndrome, a CNS related disorder, a neurodegenerative disorder, a pain condition, a substance abuse disorder, a prion disease, a heart disease, a fibrotic disease, idiopathic arterial hypertension (IPAH), and primary pulmonary hypertension (PPH).

21. Use of a compound according to any one of claims 1 to 16, in the manufacture of a medicament for preventing and/or inhibiting and/or treating the Human Immunodeficiency Virus (HIV).

22. Medicament comprising at least one compound according to anyone of claims 1 to 15, or a pharmaceutically acceptable salt thereof.

23. A pharmaceutical composition comprising at least one compound according to anyone of claims 1 to 15, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.