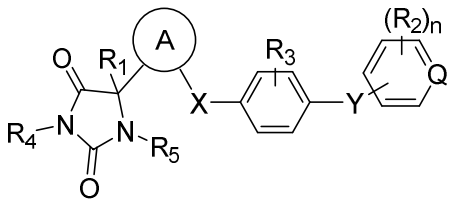
CLAIMS

~~We claim:~~

1. A compound of formula (I):



(I),

or a tautomer, stereoisomer, pharmaceutically acceptable salt, or hydrate thereof, wherein:

ring A is an optionally substituted heteroaryl;

Q is CR_2 or N;

R_1 is hydrogen or alkyl;

each R_2 is independently hydrogen, alkyl, halo, hydroxyl, haloalkyl, alkoxy, alkylthio, amino, amido, alkylamino, aminoalkyl, cyano, hydroxyalkyl, $-(CH_2)_pC(O)OR_6$, or $-(CH_2)_pOC(O)R_6$;

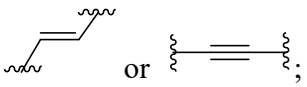
R_3 is hydrogen, halo, or alkyl;

each R_4 and R_5 is independently hydrogen or alkyl;

each R_6 is independently hydrogen or alkyl, wherein the alkyl is unsubstituted or substituted with one or more groups independently selected from amino, hydroxyl, halo, and alkoxy;

X is S or O;

Y is:

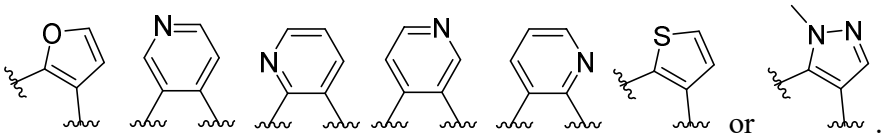


n is 1, 2, 3 or 4; and

p is 0, 1, 2, 3, 4, or 5.

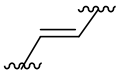
2. The compound of claim 1, wherein ring A is a 5- to 6-membered monocyclic heteroaryl having 1 to 3 heteroatoms independently selected from O, S and N, wherein the 5- to 6-membered monocyclic heteroaryl is optionally substituted with alkyl.

3. The compound of claim 1, wherein ring A is pyridinyl, furanyl, thienyl, or N-methyl pyrazolyl.
4. The compound of claim 1, wherein ring A is:

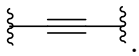


or .

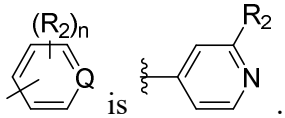
5. The compound of any one of claims 1-4, wherein R_1 is hydrogen or C_{1-4} alkyl.
6. The compound of any one of claims 1-5, wherein n is 1 and R_2 is $-CH_3$.
7. The compound of any one of claims 1-6, wherein R_3 is hydrogen.
8. The compound of any one of claims 1-7, wherein each of R_4 and R_5 is hydrogen.
9. The compound of any one of claims 1-8, wherein X is S.
10. The compound of any one of claims 1-8, wherein X is O.
11. The compound of any one of claims 1-10, wherein Q is N.
12. The compound of any one of claims 1-11, wherein Y is:


.

13. The compound of any one of claims 1-11, wherein Y is:


.

14. The compound of any one of claims 1-13, wherein:



is .

15. The compound of claim 1, wherein:

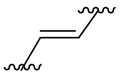
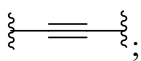
ring A is pyridinyl, furanyl, thienyl, or N-methyl pyrazolyl;

R_1 is hydrogen, $-CH_3$ or $-CH_2CH_3$;

R_2 is $-CH_3$, $-C(O)NH_2$, $-CH_2OH$, $-OCH_3$, or -OH;

each of R_3, R_4, and R_5 is hydrogen;

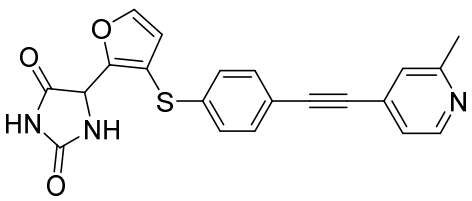
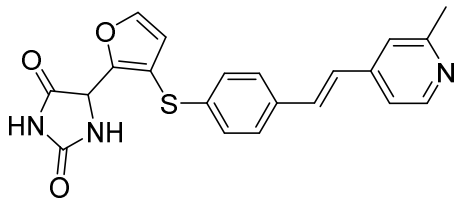
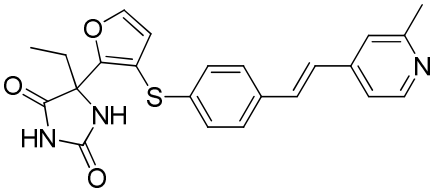
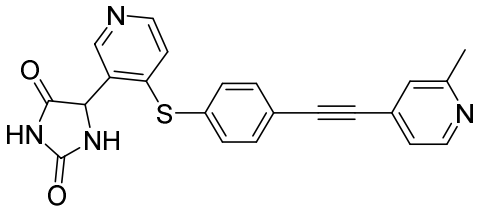
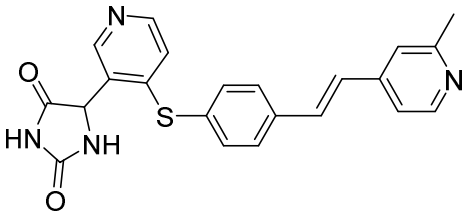
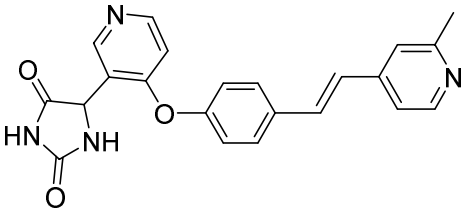
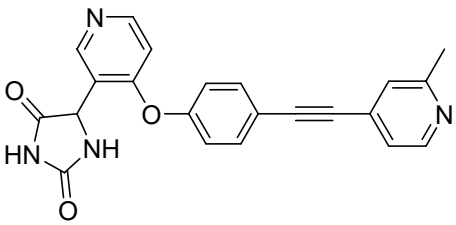
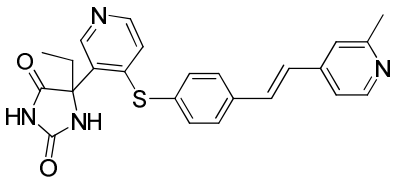
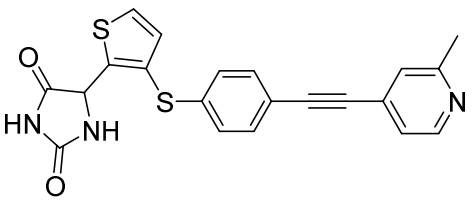
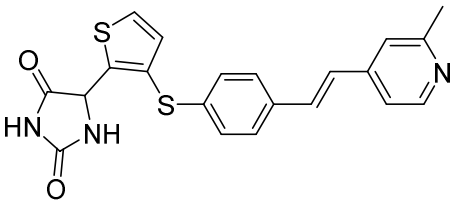
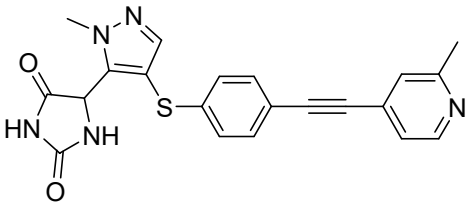
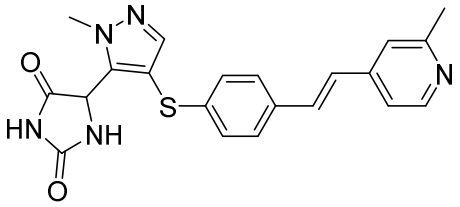
X is S or O;

Y is  or ;

Q is CH or N; and

n is 1.

16. A compound selected from the group consisting of:












and ,

or a tautomer, stereoisomer, pharmaceutically acceptable salt, or hydrate thereof.

17. The compound of claim 16, or a pharmaceutically acceptable salt thereof.

18. A pharmaceutical composition comprising the compound of any one of claims 1-17, and at least one pharmaceutically acceptable carrier.

~~19. A method of inhibiting macrophage elastase (MMP-12) in a subject in need thereof, the method comprising administering to the subject the pharmaceutical composition of claim 18.~~

~~20.~~19. ~~A method of treating a disease mediated by macrophage elastase (MMP-12) in a subject in need thereof, the method comprising administering to the subject~~ Use of the compound of any one of claims 1-17 or the pharmaceutical composition of claim 18 in the manufacture of a medicament for the treatment of a disease mediated by macrophage elastase (MMP-12) in a subject in need thereof, wherein the compound or the pharmaceutical composition is to be administered to the subject, and wherein the disease is selected from the group consisting of asthma, chronic obstructive pulmonary disease (COPD), a emphysema, acute lung injury, idiopathic pulmonary fibrosis (IPF), sarcoidosis, systemic sclerosis, liver fibrosis, nonalcoholic steatohepatitis (NASH), arthritis, cancer, heart disease, inflammatory bowel disease (IBD), acute kidney injury (AKI), chronic kidney disease (CKD), Alport syndrome, and nephritis.

~~21.~~20. The compound of any one of claims 1-17 or the pharmaceutical composition of claim 18 for use in therapy.~~inhibiting macrophage elastase (MMP-12) or treating a disease mediated by MMP-12 in a subject in need thereof, preferably, the subject is in need of a treatment of a disease selected from the group consisting of asthma, chronic obstructive pulmonary disease (COPD), a emphysema, acute lung injury, idiopathic pulmonary fibrosis (IPF), sarcoidosis, systemic sclerosis, liver fibrosis, nonalcoholic steatohepatitis (NASH), arthritis, cancer, heart disease, inflammatory bowel disease (IBD), acute kidney injury (AKI), chronic kidney disease (CKD), Alport syndrome, and nephritis.~~