

As most available EGFR tyrosine kinase inhibitors target the ATP-site of the kinase, there is a need for new therapeutic agents that work differently, for example through targeting drug-resistant EGFR mutants.

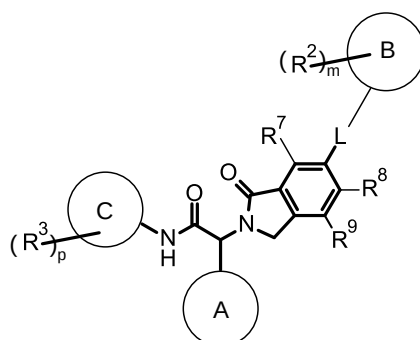
Recent studies suggest that purposefully targeting allosteric sites might lead to mutant-selective inhibitors (Jia *et al*⁹.)

There is just a need in the generation of selective molecules that specifically inhibit T790M/L858R, T790M/L858R/C797S, L858R, L858R/C797S containing EGFR mutants useful for the therapeutic and/or prophylactic treatment of cancer, in particular T790M and C797S containing EGFR mutants.

WO2009158369¹⁰ describes certain heterocyclic antibacterial agents. WO2016183534¹¹ describes certain heterocyclic compounds suitable as EBNA1 inhibitors. WO2011128279 describes certain heterocyclic compounds suitable as mGluR5 modulators.

Summary

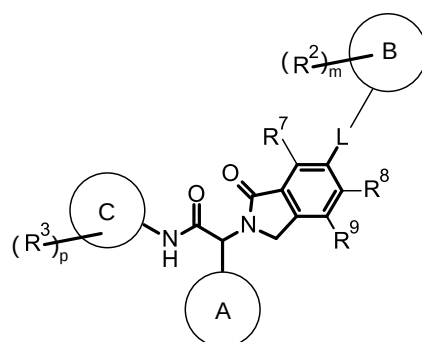
The present disclosure provides compounds of formula I, or a pharmaceutically acceptable salt thereof,



I

wherein the substituents and variables are as described below and in the claims, or a pharmaceutically acceptable salt thereof.

In one aspect, the present disclosure provides a compound of formula I,

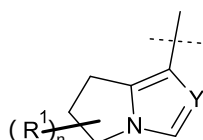


I

wherein

L is absent or $-(C\equiv C)-$,

5 A is



B is aryl or heteroaryl,

C is heteroaryl,

Y is N, C(OH) or CH,

10 R^1 is each independently selected from the group consisting of

- i) amino,
- ii) C_{1-6} -alkyl,
- iii) C_{1-6} -alkoxy,
- iv) cyano,
- 15 v) halogen,
- vi) halogen- C_{1-6} -alkyl,
- vii) halogen- C_{1-6} -alkoxy, and
- viii) hydroxy;

R^2 is each independently selected from the group consisting of

- 20 i) $-(CH_2)_k-N(R^4, R^5)$,
- ii) $-(C=O)-N(R^4, R^5)$,
- iii) halogen,
- iv) halogen- C_{1-6} -alkyl,
- v) $-NH-(C=O)-C_{1-6}$ -alkyl, and
- 25 vi) C_{1-6} -alkyl, optionally substituted by OH;

R^3 is each independently selected from the group consisting of

- i) amino,

- ii) C₁₋₆-alkyl,
- iii) C₁₋₆-alkoxy,
- iv) cyano,
- v) halogen,
- vi) halogen-C₁₋₆-alkyl,
- vii) halogen-C₁₋₆-alkoxy, and
- viii) hydroxy;

R⁴ is each independently selected from the group consisting of

- i) H, and
- ii) C₁₋₆-alkyl;

R⁵ is each independently selected from the group consisting of

- i) H,
- ii) C₁₋₆-alkyl, and
- iii) -(C=O)-C₁₋₆-alkyl;

or R⁴ and R⁵ form together with the N they are attached to a heterocyclyl, which heterocyclyl is optionally substituted by one to three R⁶.

R⁶ is each independently selected from the group consisting of

- i) -OH,
- ii) halogen,
- iii) C₃₋₈-cycloalkyl,
- iv) halogen-C₁₋₆-alkyl,
- v) C₁₋₆-alkoxy-C₁₋₆-alkyl,
- vi) cyano-C₁₋₆-alkyl,
- vii) C₁₋₆-alkyl, and
- viii) -(C=O)-C₁₋₆-alkyl;

R⁷ is each independently selected from the group consisting of

- i) H,
- ii) halogen,
- iii) halogen-C₁₋₆-alkoxy,
- iv) C₁₋₆-alkoxy, and
- v) C₁₋₆-alkyl;

R⁸ is each independently selected from the group consisting of

- i) H,
- ii) halogen,
- iii) C₁₋₆-alkoxy, and
- iv) C₁₋₆-alkyl;

R⁹ is each independently selected from the group consisting of

- i) H,
- ii) halogen,
- iii) halogen-C₁₋₆-alkoxy,

iv) C₁₋₆-alkoxy, and

v) C₁₋₆-alkyl;

k is 0, 1 or 2,

n is 0, 1, 2, 3 or 4;

5 m is 0, 1 or 2;

p is 0 or 1;

or a pharmaceutically acceptable salt thereof.

The present compounds are useful for the therapeutic and/or prophylactic treatment of cancer.

10 In another aspect, the present disclosure provides the compound of formula I, or a pharmaceutically acceptable salt thereof, according to the disclosure, for use as therapeutically active substance.

In another aspect, the present disclosure provides the compound of formula I, or a pharmaceutically acceptable salt thereof, according to the disclosure, for the use in the therapeutic
15 and/or prophylactic treatment of cancer.

In another aspect, the present disclosure provides a use of the compound of formula I, or a pharmaceutically acceptable salt thereof, according to the disclosure, in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of cancer.

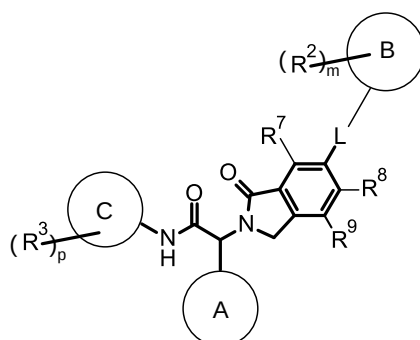
In another aspect, the present disclosure provides a pharmaceutical composition comprising
20 the compound of formula I, or a pharmaceutically acceptable salt thereof, according to the disclosure and a pharmaceutically acceptable auxiliary substance.

Detailed Description of the Invention

The present invention provides a compound of formula I and their pharmaceutically acceptable salts thereof, the preparation of the above-mentioned compounds, medicaments
25 containing them and their manufacture as well as the use of the above-mentioned compounds in the therapeutic and/or prophylactic treatment of cancer, in particular non-small-cell lung cancer.

Claims

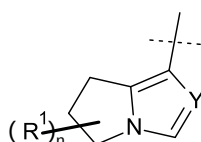
1. A compound of formula I,



I

wherein

- 5 L is absent or $-(C\equiv C)-$,
A is



,

- B is aryl or heteroaryl,
C is heteroaryl,
10 Y is N, C(OH) or CH,
R¹ is each independently selected from the group consisting of
i) amino,
ii) C₁₋₆-alkyl,
iii) C₁₋₆-alkoxy,
15 iv) cyano,
v) halogen,
vi) halogen-C₁₋₆-alkyl,
vii) halogen-C₁₋₆-alkoxy, and
viii) hydroxy;
20 R² is each independently selected from the group consisting of
i) $-(CH_2)_k-N(R^4, R^5)$,
ii) $-(C=O)-N(R^4, R^5)$,
iii) halogen,
iv) halogen-C₁₋₆-alkyl,
25 v) $-NH-(C=O)-C_{1-6}-alkyl, and
vi) C₁₋₆-alkyl, optionally substituted by OH;$

R³ is each independently selected from the group consisting of

- i) amino,
- ii) C₁₋₆-alkyl,
- iii) C₁₋₆-alkoxy,
- iv) cyano,
- v) halogen,
- vi) halogen-C₁₋₆-alkyl,
- vii) halogen-C₁₋₆-alkoxy, and
- viii) hydroxy;

5

10 R⁴ is each independently selected from the group consisting of

- i) H, and
- ii) C₁₋₆-alkyl;

R⁵ is each independently selected from the group consisting of

- i) H,
- ii) C₁₋₆-alkyl, and
- iii) -(C=O)-C₁₋₆-alkyl;

15

or R⁴ and R⁵ form together with the N they are attached to a heterocyclcyl, which heterocyclcyl is optionally be substituted by one to three R⁶.

R⁶ is each independently selected from the group consisting of

- i) -OH,
- ii) halogen,
- iii) C₃₋₈-cycloalkyl,
- iv) halogen-C₁₋₆-alkyl,
- v) C₁₋₆-alkoxy-C₁₋₆-alkyl,
- vi) cyano-C₁₋₆-alkyl,
- vii) C₁₋₆-alkyl, and
- viii) -(C=O)-C₁₋₆-alkyl;

20

25

R⁷ is each independently selected from the group consisting of

- i) H,
- ii) halogen,
- iii) halogen-C₁₋₆-alkoxy,
- iv) C₁₋₆-alkoxy, and
- v) C₁₋₆-alkyl;

30

R⁸ is each independently selected from the group consisting of

- i) H,
- ii) halogen,
- iii) C₁₋₆-alkoxy, and
- iv) C₁₋₆-alkyl;

35

R⁹ is each independently selected from the group consisting of

- i) H,

40

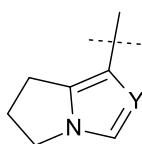
- ii) halogen,
- iii) halogen-C₁₋₆-alkoxy,
- iv) C₁₋₆-alkoxy, and
- v) C₁₋₆-alkyl;

- 5 k is 0, 1 or 2,
 n is 0, 1, 2, 3 or 4;
 m is 0, 1 or 2;
 p is 0 or 1;

or a pharmaceutically acceptable salt thereof.

- 10 2. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to claim 1, wherein

- L is absent or $-(C\equiv C)-$,
 A is



- 15 B is aryl or heteroaryl,
 C is heteroaryl,
 Y is N or CH,
 R² is each independently selected from the group consisting of
- i) $-(CH_2)_k-N(R^4, R^5)$,
 - 20 ii) halogen-C₁₋₆-alkyl, and
 - iii) C₁₋₆-alkyl, optionally substituted by OH;

R⁴ and R⁵ form together with the N they are attached to a heterocyclyl, which heterocyclyl is optionally be substituted by one to three R⁶.

R⁶ is each independently selected from the group consisting of

- 25 i) $-OH$,
 ii) halogen,
 iii) C₃₋₈-cycloalkyl,
 iv) halogen-C₁₋₆-alkyl,
 v) C₁₋₆-alkoxy-C₁₋₆-alkyl,
 30 vi) cyano-C₁₋₆-alkyl, and
 vii) C₁₋₆-alkyl;

R⁷ is H or halogen;

R⁸ is H;

R⁹ is halogen;

- k is 0 or 1;
n is 0;
m is 1;
p is 0.

- 5 3. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-2, wherein A is



, in particular

wherein

Y is N or CH, and

- 10 R^a, R^b, R^c or R^d is each independently selected from the group consisting of

- i) H,
- ii) amino,
- iii) C₁₋₆-alkyl,
- iv) C₁₋₆-alkoxy,
- 15 v) cyano,
- vi) halogen,
- vii) halogen-C₁₋₆-alkyl,
- viii) halogen-C₁₋₆-alkoxy, and
- ix) hydroxyl.

- 20 4. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to claim 3, wherein A is 6,7-Dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl or 6,7-Dihydro-5H-pyrrolizin-1-yl.

5. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-4, wherein B is aryl.

- 25 6. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to claim 5, wherein B is phenyl.

7. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-5, wherein B is heteroaryl.

- 30 8. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to claim 7, wherein B is pyridinyl.

9. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-8, wherein C is heteroaryl.
10. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to claim 9, wherein C is thiazolyl.
- 5 11. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-10, wherein n is 0.
12. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-11, wherein m is 1.
- 10 13. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-12, wherein p is 0.
14. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-12, wherein R^2 is $-(CH_2)_k-N(R^4, R^5)$, k is 0 or 1 and R^4 and R^5 form together with the N they are attached to a heterocyclyl, which heterocyclyl is optionally substituted by R^6 .
- 15 15. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-12, wherein R^2 is $-(CH_2)_k-N(R^4, R^5)$, k is 0 or 1 and R^4 and R^5 form together with the N they are attached to piperazinyl, piperidinyl or morpholino, which piperazinyl, piperidinyl or morpholino are optionally substituted by R^6 .
- 20 16. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-13, that is selected from the group consisting of
- (2RS)-2-(6,7-Dihydro-5H-pyrrolizin-1-yl)-2-[4-fluoro-6-[2-[4-[(4-hydroxy-1-piperidyl)methyl]phenyl]ethynyl]-1-oxo-isoindolin-2-yl]-N-thiazol-2-yl-acetamide,
- (2RS)-2-(6,7-Dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-2-[4-fluoro-6-[2-[4-[(4-methylpiperazin-1-yl)methyl]phenyl]ethynyl]-1-oxo-isoindolin-2-yl]-N-thiazol-2-yl-
- 25 acetamide,
- (2RS)-2-(6,7-Dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-2-[4-fluoro-6-[2-[4-[(4-hydroxy-1-piperidyl)methyl]phenyl]ethynyl]-1-oxo-isoindolin-2-yl]-N-thiazol-2-yl-acetamide,
- (2RS)-2-(6,7-Dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-2-[4-fluoro-1-oxo-6-(4-piperazin-1-ylphenyl)isoindolin-2-yl]-N-thiazol-2-yl-acetamide,
- 30 (2RS)-2-(6,7-Dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-2-[4-fluoro-6-[4-(4-hydroxy-1-piperidyl)phenyl]-1-oxo-isoindolin-2-yl]-N-thiazol-2-yl-acetamide,
- (2RS)-2-(6,7-Dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-2-[4-fluoro-6-[2-[4-(hydroxymethyl)phenyl]ethynyl]-1-oxo-isoindolin-2-yl]-N-thiazol-2-yl-acetamide,

(2*RS*)-2-(6,7-Dihydro-5H-pyrrolo[1,2-*c*]imidazol-1-yl)-2-[4-fluoro-1-oxo-6-[2-[4-(1-piperidylmethyl)phenyl]ethynyl]isoindolin-2-yl]-N-thiazol-2-yl-acetamide,
(2*RS*)-2-(6,7-Dihydro-5H-pyrrolo[1,2-*c*]imidazol-1-yl)-2-[6-[4-(4-ethylpiperazin-1-yl)phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-N-thiazol-2-yl-acetamide,
5 (2*RS*)-2-(6,7-Dihydro-5H-pyrrolo[1,2-*c*]imidazol-1-yl)-2-[6-[6-(4-ethylpiperazin-1-yl)-3-pyridyl]-4-fluoro-1-oxo-isoindolin-2-yl]-N-thiazol-2-yl-acetamide,
(2*RS*)-2-[4-Chloro-6-[2-[4-[(4-hydroxy-1-piperidyl)methyl]phenyl]ethynyl]-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-*c*]imidazol-1-yl)-N-thiazol-2-yl-acetamide,
(2*RS*)-2-[4-Chloro-6-[4-(4-ethylpiperazin-1-yl)phenyl]-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-10 5H-pyrrolo[1,2-*c*]imidazol-1-yl)-N-thiazol-2-yl-acetamide,
(2*RS*)-2-[4-Chloro-6-[4-(4-hydroxy-1-piperidyl)phenyl]-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-*c*]imidazol-1-yl)-N-thiazol-2-yl-acetamide,
(2*RS*)-2-[4-Chloro-6-[6-(4-hydroxy-1-piperidyl)-3-pyridyl]-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-*c*]imidazol-1-yl)-N-thiazol-2-yl-acetamide, and
15 (2*RS*)-2-[7-chloro-4-fluoro-6-[2-[4-[(4-hydroxy-1-piperidyl)methyl]phenyl]ethynyl]-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-*c*]imidazol-1-yl)-N-thiazol-2-yl-acetamide.

17. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-13, that is selected from the group consisting of

20 2-[4-chloro-1-oxo-6-[2-[4-(1-piperidylmethyl)phenyl]ethynyl]isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-*c*]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

2-(6,7-dihydro-5H-pyrrolo[1,2-*c*]imidazol-1-yl)-2-[6-[4-(1-ethyl-4-piperidyl)phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-N-thiazol-2-yl-acetamide;

2-[4-fluoro-6-[2-[4-[(4-hydroxy-1-piperidyl)methyl]phenyl]ethynyl]-1-oxo-isoindolin-2-yl]-2-[rac-(6*R*)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-*c*]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

25 2-[6-[3-chloro-4-(4-ethylpiperazin-1-yl)phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-*c*]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

2-[6-[3-chloro-4-[rac-(3*R*)-3-methylpiperazin-1-yl]phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-*c*]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

30 2-[6-[3-chloro-4-[rac-(3*R*)-4-ethyl-3-methyl-piperazin-1-yl]phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-*c*]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

2-[4-chloro-6-[4-[(1-ethyl-4-piperidyl)oxy]phenyl]-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-*c*]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

2-[6-(3-chloro-4-morpholino-phenyl)-4-fluoro-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-*c*]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

2-[6-[3-chloro-4-(4-ethylpiperazin-1-yl)phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

2-[6-(3-chloro-4-morpholino-phenyl)-4-fluoro-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

5 2-[6-[3-chloro-4-[rac-(3R)-4-ethyl-3-methyl-piperazin-1-yl]phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

2-[6-[4-(1-ethyl-4-piperidyl)-3-fluoro-phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

10 2-[6-[4-(1-cyclopropyl-4-piperidyl)phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

2-[4-chloro-6-[4-(1-cyclopropyl-4-piperidyl)phenyl]-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

15 2-[4-chloro-6-[4-(1-ethyl-4-piperidyl)phenyl]-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

2-[6-[3-chloro-4-(1-ethyl-4-piperidyl)phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

2-[6-[4-(1-ethyl-4-piperidyl)phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

20 2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-2-[4-fluoro-1-oxo-6-[4-[rac-(3R,4R)-1-ethyl-3-fluoro-4-piperidyl]phenyl]isoindolin-2-yl]-N-thiazol-2-yl-acetamide;

2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-2-[6-[4-(1-ethyl-4-piperidyl)-3-fluoro-phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-N-thiazol-2-yl-acetamide;

25 2-[6-[4-[1-(2,2-difluoroethyl)-4-piperidyl]phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-2-[4-fluoro-6-[4-[1-(2-methoxyethyl)-4-piperidyl]phenyl]-1-oxo-isoindolin-2-yl]-N-thiazol-2-yl-acetamide;

2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-2-[4-fluoro-6-[4-[1-(2-fluoroethyl)-4-piperidyl]phenyl]-1-oxo-isoindolin-2-yl]-N-thiazol-2-yl-acetamide;

2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-2-[6-[3-ethyl-4-(1-ethyl-4-piperidyl)phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-N-thiazol-2-yl-acetamide;

2-[6-[4-(4-cyclopropylpiperazin-1-yl)-3-fluoro-phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

5 2-[6-[3-chloro-4-(4-cyclopropylpiperazin-1-yl)phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

2-[4-chloro-6-[4-(4-cyclopropylpiperazin-1-yl)-3-fluoro-phenyl]-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

10 2-[6-[3-chloro-4-[4-(2,2-difluoroethyl)piperazin-1-yl]phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

2-[6-[4-(4-cyclopropylpiperazin-1-yl)-3-fluoro-phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

2-[6-[2-(2-chlorophenyl)ethynyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

15 2-[6-[2-[4-[(4,4-difluoro-1-piperidyl)methyl]phenyl]ethynyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

2-(6,7-dihydro-5H-pyrrolizin-1-yl)-2-[4-fluoro-6-(3-fluoro-4-morpholino-phenyl)-1-oxo-isoindolin-2-yl]-N-thiazol-2-yl-acetamide;

20 2-[6-[3-chloro-4-(4-cyclopropylpiperazin-1-yl)phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-2-[4-fluoro-1-oxo-6-[2-[4-(trifluoromethyl)phenyl]ethynyl]isoindolin-2-yl]-N-thiazol-2-yl-acetamide;

2-(6,7-dihydro-5H-pyrrolizin-1-yl)-2-[6-[4-(1-ethyl-4-piperidyl)phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-N-thiazol-2-yl-acetamide;

25 2-[6-[3-chloro-4-[4-(2-fluoroethyl)piperazin-1-yl]phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

2-[6-[3-ethyl-4-(1-ethyl-4-piperidyl)phenyl]-4-fluoro-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

30 2-[7-chloro-4-fluoro-6-(4-morpholinophenyl)-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

2-[4-chloro-6-[3-ethyl-4-(1-ethyl-4-piperidyl)phenyl]-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

2-[4-chloro-6-[4-(1-ethyl-4-piperidyl)phenyl]-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

5 2-[4-chloro-6-[4-(1-cyclopropyl-4-piperidyl)phenyl]-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

2-[4-chloro-6-[4-[1-(2-fluoroethyl)-4-piperidyl]phenyl]-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

10 2-[4-chloro-6-[4-[1-(2-cyanoethyl)-4-piperidyl]phenyl]-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

2-[4-chloro-6-[3-ethyl-4-[1-(2-fluoroethyl)-4-piperidyl]phenyl]-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

2-[4-chloro-6-[4-[1-(2-fluoroethyl)-4-piperidyl]phenyl]-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

15 2-[4-chloro-6-[4-[1-(2,2-difluoroethyl)-4-piperidyl]phenyl]-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

2-[4,7-dichloro-6-[4-(1-ethyl-4-piperidyl)phenyl]-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

20 2-[4,7-dichloro-6-[4-(1-ethyl-4-piperidyl)phenyl]-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

2-[4,7-dichloro-6-[4-[1-(2-fluoroethyl)-4-piperidyl]phenyl]-1-oxo-isoindolin-2-yl]-2-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl)-N-thiazol-2-yl-acetamide;

2-[4,7-dichloro-6-[4-[1-(2-fluoroethyl)-4-piperidyl]phenyl]-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

25 2-[4,7-dichloro-6-(4-morpholinophenyl)-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

2-[4-chloro-1-oxo-6-[4-[rac-(3R,4R)-1-ethyl-3-fluoro-4-piperidyl]phenyl]isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

2-[4-fluoro-6-[2-[4-[[4-(hydroxymethyl)-1-piperidyl]methyl]phenyl]ethynyl]-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

5 2-[4-chloro-6-[4-(1-ethyl-3,3-difluoro-4-piperidyl)phenyl]-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

2-[4-chloro-6-[4-[1-(2-hydroxyethyl)-4-piperidyl]phenyl]-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide.

18. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-13, that is selected from the group consisting of

10 2-[4-chloro-6-[3-ethyl-4-[1-(2-fluoroethyl)-4-piperidyl]phenyl]-1-oxo-isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide;

2-[4-chloro-1-oxo-6-[4-[rac-(3R,4R)-1-ethyl-3-fluoro-4-piperidyl]phenyl]isoindolin-2-yl]-2-[rac-(6R)-6-fluoro-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-1-yl]-N-thiazol-2-yl-acetamide.

15 19. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-15, for use as therapeutically active substance.

20. The compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-15, for the use in the therapeutic and/or prophylactic treatment of cancer.

20 21. The compound of formula I, or a pharmaceutically acceptable salt thereof, for use according to claim 20, wherein the cancer is non-small-cell lung cancer.

22. Use of the compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-15, in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of cancer.

23. The use according to claim 22, wherein the cancer is non-small-cell lung cancer.

25 24. A pharmaceutical composition comprising the compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-15 and a pharmaceutically acceptable auxiliary substance.