wherein:

R^1 is selected from ~~H and~~ halogen;

R^2 is selected from

- aryl that optionally may be substituted with C_{1-6}-alkyl, OR^4, and halogen,
- aryl that is fused with C_{3-7}-cycloalkyl, and
- heteroaryl that optionally may be substituted with C_{1-6}-alkyl;

R^3 is selected from

- C_{1-6}-alkyl that optionally may be substituted with OR^4 and aryl,
- C_{3-7}-cycloalkyl,
- heterocyclyl, and
- aryl;

R^4 is selected from H and C_{1-6}-alkyl;

n is 1 or 2;

m is 0 or 1; and

q is 0, 1 or 2;

or a pharmaceutically acceptable salt of the foregoing compound,

wherein "heteroaryl" refers to a substituted or unsubstituted aromatic heterocyclic ring system containing up to two rings, at least one ring of which includes 1, 2, or 3 heteroatoms, the remaining ring atoms being carbon, and

"heterocyclyl" refers to a substituted or unsubstituted monovalent saturated or partly unsaturated mono- or bicyclic ring, non-aromatic hydrocarbon system of 3 to 9 ring atoms, comprising 1, 2, or 3 ring heteroatoms selected from N, O and S, the remaining ring atoms being carbon.

In a second aspect, the present disclosure provides for a compound selected from the group comprising:

(S)-N-(2,6-difluorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide hydrochloride;

(S)-N-(2,6-dichlorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido) butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((S)-3,3-dimethyl-2-((S)-2-(methylamino)propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((2S,3R)-3-methoxy-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido) butanoyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide

(S)-2-[(S)-2-Cyclohexyl-2-((S)-2-methylamino-propionylamino)-acetyl]-1,2,3,4-tetrahydro-isoquinoline-1-carboxylic acid (2,6-difluoro-phenyl)-amide hydrochloride;

(S)-2-((S)-2-cyclopentyl-2-((S)-2-(methylamino)propanamido)acetyl)-N-(2,6-difluorophenyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((S)-2-((S)-2-(methylamino)propanamido)-2-phenylacetyl)isoindoline-1-carboxamide hydrochloride;

(S)-2-[(S)-3-Methyl-2-((S)-2-methylamino-propionylamino)-butyryl]-2,3-dihydro-1H-isoindole-1-carboxylic acid (2,6-difluoro-phenyl)-amide hydrochloride;

((S)-2-[(S)-2-Cyclohexyl-2-((S)-2-methylamino-propionylamino)-acetyl]-2,3-dihydro-1H-isoindole-1-carboxylic acid (2,6-difluoro-phenyl)-amide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-2-[(S)-3-Methyl-2-((S)-2-methylamino-propionylamino)-butyryl]-1,2,3,4-tetrahydro-isoquinoline-1-carboxylic acid (2-chloro-6-fluoro-phenyl)-amide hydrochloride;

6-Chloro-2-[(S)-3-methyl-2-((S)-2-methylamino-propionylamino)-butyryl]-1,2,3,4-tetrahydro-isoquinoline-1-carboxylic acid (2,6-difluoro-phenyl)-amide;

6-Fluoro-2-[(S)-3-methyl-2-((S)-2-methylamino-propionylamino)-butyryl]-1,2,3,4-tetrahydro-isoquinoline-1-carboxylic acid (2,6-difluoro-phenyl)-amide;

(S)-N-(2,6-dichlorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido) butanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(2-chloro-6-fluorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(benzo[b]thiophen-4-yl)-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((2S,3S)-3-methyl-2-((S)-2-(methylamino) propanamido)pentanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((S)-3,3-dimethyl-2-((S)-2-(methylamino) propanamido)butanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((S)-2-((S)-2-(methylamino)propanamido)-2-(tetrahydro-2H-pyran-4-yl)acetyl)isoindoline-1-carboxamide hydrochloride;

(S)-2-((S)-2-cyclopentyl-2-((S)-2-(methylamino)propanamido)acetyl)-N-(2,6-difluorophenyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((S)-2-((S)-2-(methylamino)propanamido)-2-(tetrahydro-2H-pyran-4-yl)acetyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((2S,3S)-3-methyl-2-((S)-2-(methylamino) propanamido)pentanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide hydrochloride; and

N-(2,6-difluorophenyl)-7-fluoro-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide;

or a pharmaceutically acceptable salt of each of the foregoing compounds.

The present disclosure also relates to pharmaceutical compositions comprising one or more compounds of the invention, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient.

In a third aspect, the present disclosure provides for a pharmaceutical composition comprising any of the compounds as disclosed herein, or a pharmaceutically acceptable salt thereof, as an active ingredient together with a pharmaceutically acceptable carrier or excipient.In a fourth aspect, the present disclosure provides for compounds as defined herein for use as a therapeutically active substance.

In a fifth aspect, the present disclosure provides for use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the therapeutic and/or prophylactic treatment of cancer.

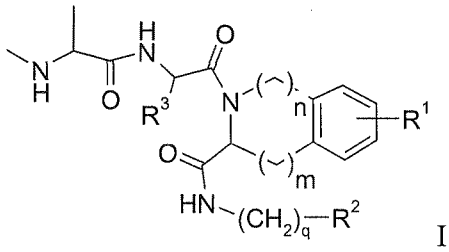
In a sixth aspect, the present disclosure provides for a compound as defined herein, or a pharmaceutically acceptable salt thereof, for use in the therapeutic and/or prophylactic treatment of cancer.

The present disclosure further relates to a method of ameliorating, controlling or treating cancer, including specifically solid tumors, for example lung, pancreatic, colon, breast, bone and prostate cancers in a mammal, specifically a human, comprising administering to said mammal a therapeutically effective amount of a compound according to the invention or a pharmaceutically acceptable salt thereof.

Detailed Description of the Invention

Claims

1. A compound of Formula I:



I

wherein:

R^1 is ~~selected from H and~~ halogen;

R^2 is selected from

- aryl that optionally may be substituted with C_{1-6}-alkyl, OR^4, and halogen,
- aryl that is fused with C_{3-7}-cycloalkyl, and
- heteroaryl that optionally may be substituted with C_{1-6}-alkyl;

R^3 is selected from

- C_{1-6}-alkyl that optionally may be substituted with OR^4 and aryl,
- C_{3-7}-cycloalkyl,
- heterocyclyl, and
- aryl;

R^4 is selected from H and C_{1-6}-alkyl;

n is 1 or 2;

m is 0 or 1; and

q is 0, 1 or 2;

or a pharmaceutically acceptable salt of the foregoing compound,

wherein "heteroaryl" refers to a substituted or unsubstituted aromatic heterocyclic ring system containing up to two rings, at least one ring of which includes 1, 2, or 3 heteroatoms, the remaining ring atoms being carbon, and

"heterocyclyl" refers to a substituted or unsubstituted monovalent saturated or partly unsaturated mono- or bicyclic ring, non-aromatic hydrocarbon system of 3 to 9 ring atoms, comprising 1, 2, or 3 ring heteroatoms selected from N, O and S, the remaining ring atoms being carbon.

~~2. The compound of claim 1 wherein R^1 is halogen, or a pharmaceutically acceptable salt thereof.~~

~~3. The compound of claim 1 wherein R^1 is H.~~

~~4.~~3. The compound according to claims ~~1–3~~ wherein R^2 is aryl that optionally may be substituted with OR^4, halogen and C_{1-6}-alkyl, or a pharmaceutically acceptable salt thereof.

~~5.~~4. The compound of claim 24 wherein R^2 is phenyl or naphthalenyl, or a pharmaceutically acceptable salt thereof.

~~6.~~5. The compound according to claims ~~1–3~~ wherein R^2 is heteroaryl that optionally may be substituted with C_{1-6}-alkyl, or a pharmaceutically acceptable salt thereof.

~~7.~~6. The compound of claim ~~4~~6 wherein R^2 is selected from selected from quinolinyl, benzo[b]thiophenyl or indolyl.

~~8.~~7. The compound according to claims 1-~~7~~5 wherein R^3 is C_{1-6}-alkyl that optionally may be substituted with OR^4 and aryl, or a pharmaceutically acceptable salt thereof.

~~9.~~8. The compound of claim ~~6~~8 wherein R^3 is C_{1-6}-alkyl substituted with phenyl, or a pharmaceutically acceptable salt thereof.

~~10.~~9. The compound of claim ~~8~~6 wherein R^3 is OR^4 and R^4 is H, or a pharmaceutically acceptable salt thereof.

~~11.~~10. The compound according to claims 1-~~7~~5 wherein R^3 is C_{3-7}-cycloalkyl, or a pharmaceutically acceptable salt thereof.

~~12.~~11. The compound of claim ~~11~~9 wherein R^3 is cyclohexyl or cyclopentyl, or a pharmaceutically acceptable salt thereof.

~~13.~~12. The compound according to claims 1-~~7~~5 wherein R^3 is aryl, or a pharmaceutically acceptable salt thereof.

~~14.~~13. The compound of claim ~~13~~11 wherein R^3 is phenyl.

~~15.~~14. The compound according to claims 1-~~7~~5 wherein R^3 is heterocyclyl, or a pharmaceutically acceptable salt thereof.

~~16.~~15. The compound of claim ~~15~~13 wherein R^3 is tetrahydropyran.

~~17.~~16. The compound according to claims 1-~~16~~14 wherein m is 0, n is 1, and q is 0, or a pharmaceutically acceptable salt thereof.

~~18. The compound of claim 1 wherein R^1 is H, R^2 is aryl, R^3 is C_{1-6}-alkyl, n is 1 and m and q are 0.~~

~~19. The compound of claim 1 wherein R^3 is C_{1-6}-alkyl, n is 1 and m is 0, said compound being selected from the group comprising:~~

~~(S)-2-[(S)-3-Methyl-2-((S)-2-methylamino-propionylamino)-butyryl]-2,3-dihydro-1H-isoindole-1-carboxylic acid (2,6-difluoro-phenyl)-amide hydrochloride;~~

~~((S)-N-(2,6-dichlorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido) butanoyl)isoindoline-1-carboxamide hydrochloride;~~

~~(S)-N-(2-chloro-6-fluorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)isoindoline-1-carboxamide hydrochloride;~~

~~(S)-N-(benzo[b]thiophen-4-yl)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido) butanoyl)isoindoline-1-carboxamide hydrochloride ;~~

~~(S)-N-(2,6-difluorophenyl)-2-((2S,3S)-3-methyl-2-((S)-2-(methylamino) propanamido)pentanoyl)isoindoline-1-carboxamide hydrochloride;~~

~~(S)-N-(2,6-difluorophenyl)-2-((S)-3,3-dimethyl-2-((S)-2-(methylamino)propanamido) butanoyl)isoindoline-1-carboxamide hydrochloride;~~

~~2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido)butanoyl)-N-phenylisoindoline-1-carboxamide hydrochloride;~~

~~N-(2-methoxyphenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido) butanoyl)isoindoline-1-carboxamide hydrochloride;~~

~~N-(2-methoxyphenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido) butanoyl)isoindoline-1-carboxamide hydrochloride;~~

~~N-benzyl-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido)butanoyl)isoindoline-1-carboxamide hydrochloride;~~

2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido)butanoyl)-N-phenethylisoindoline-1-carboxamide hydrochloride;

(S)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido)butanoyl)-N-(naphthalen-1-yl)isoindoline-1-carboxamide hydrochloride;

(R)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido)butanoyl)-N-(naphthalen-1-yl)isoindoline-1-carboxamide hydrochloride;

(S)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido)butanoyl)-N-(naphthalen-2-yl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(2-fluorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido) butanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(2-chlorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido) butanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido)butanoyl)-N-(5,6,7,8-tetrahydronaphthalen-1-yl)isoindoline-1-carboxamide hydrochloride;

(S)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido)butanoyl)-N-(quinolin-8-yl)isoindoline-1-carboxamide hydrochloride;

N-(isoquinolin-1-yl)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido) butanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(1-methyl-1H-indol-4-yl)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido) butanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((2S,3S)-3-methoxy-2-((S)-2-(methylamino) propanamido)butanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((2S,3R)-3-hydroxy-2-((S)-2-(methylamino) propanamido)butanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((S)-4-methyl-2-((S)-2-(methylamino)propanamido) pentanoyl)isoindoline-1-carboxamide hydrochloride;

~~(S)-N-(2,6-difluorophenyl)-2-((2S,3S)-2-((S)-2-(methylamino)propanamido)-3-phenylbutanoyl)isoindoline-1-carboxamide hydrochloride; and~~

~~(S)-N-(2-fluoro-6-methylphenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)isoindoline-1-carboxamide hydrochloride;~~

~~or a pharmaceutically acceptable salt of any of the foregoing compounds.~~

17. The compound of claim 1, said compound being selected from the group consisting of:

6-Chloro-2-[(S)-3-methyl-2-((S)-2-methylamino-propionylamino)-butyryl]-1,2,3,4-tetrahydro-isoquinoline-1-carboxylic acid (2,6-difluoro-phenyl)-amide;

6-Fluoro-2-[(S)-3-methyl-2-((S)-2-methylamino-propionylamino)-butyryl]-1,2,3,4-tetrahydro-isoquinoline-1-carboxylic acid (2,6-difluoro-phenyl)-amide;

N-(2,6-difluorophenyl)-7-fluoro-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide;

N-(2,6-difluorophenyl)-7-fluoro-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide;

N-(2,6-difluorophenyl)-6-fluoro-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide;

7-chloro-N-(2,6-difluorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide;

7-chloro-N-(2,6-difluorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide; and

6-chloro-N-(2,6-difluorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide;

or a pharmaceutically acceptable salt of any of the foregoing compounds.

~~20.~~18. ~~The~~ A compound ~~of claim 1 wherein R^3 is C_{1-6} alkyl, n is 2 and m is 0, said compound being~~ selected from the group comprising:

~~(S)-2-[(S)-3-Methyl-2-((S)-2-methylamino-propionylamino)-butyryl]-1,2,3,4-tetrahydro-isoquinoline-1-carboxylic acid (2-chloro-6-fluoro-phenyl)-amide hydrochloride;~~

~~6-Chloro-2-[(S)-3-methyl-2-((S)-2-methylamino-propionylamino)-butyryl]-1,2,3,4-tetrahydro-isoquinoline-1-carboxylic acid (2,6-difluoro-phenyl)-amide;~~

~~6-Fluoro-2-[(S)-3-methyl-2-((S)-2-methylamino-propionylamino)-butyryl]-1,2,3,4-tetrahydro-isoquinoline-1-carboxylic acid (2,6-difluoro-phenyl)-amide;~~

~~(S)-N-(2,6-difluorophenyl)-2-((2S,3S)-3-methyl-2-((S)-2-(methylamino) propanamido)pentanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide hydrochloride;~~

(S)-N-(2,6-difluorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide hydrochloride;

(S)-N-(2,6-dichlorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido) butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((S)-3,3-dimethyl-2-((S)-2-(methylamino)propanamido) butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((2S,3R)-3-methoxy-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide hydrochloride;

~~N-(2,6-difluorophenyl)-7-fluoro-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide;~~

~~N-(2,6-difluorophenyl)-7-fluoro-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide;~~

~~N-(2,6-difluorophenyl)-6-fluoro-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide;~~

~~7-chloro-N-(2,6-difluorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide;~~

~~7-chloro-N-(2,6-difluorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide; and~~

~~6-chloro-N-(2,6-difluorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide;~~

~~or a pharmaceutically acceptable salt of any of the foregoing compounds.~~

~~21. The compound of claim 1 wherein R^3 is C_{1-6}-alkyl, n is 1 and m is 1, said compound being~~

(S)-N-(2,6-difluorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido) butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide~~;~~

~~or a pharmaceutically acceptable salt thereof.~~

~~22. The compound of claim 1 wherein R^3 is C_{3-7}-cycloalkyl and n is 1, said compound being selected from the group comprising:~~

~~(S)-2-[(S)-2-Cyclohexyl-2-((S)-2-methylamino-propionylamino)-acetyl]-2,3-dihydro-1H-isoindole-1-carboxylic acid (2,6-difluoro-phenyl)-amide hydrochloride; and~~

~~(S)-2-((S)-2-cyclopentyl-2-((S)-2-(methylamino)propanamido)acetyl)-N-(2,6-difluorophenyl)isoindoline-1-carboxamide hydrochloride;~~

~~or a pharmaceutically acceptable salt of either of the foregoing compounds.~~

~~23. The compound of claim 1 wherein R^3 is C_{3-7}-cycloalkyl and n is 2, said compound being selected from the group comprising:~~

(S)-2-[(S)-2-Cyclohexyl-2-((S)-2-methylamino-propionylamino)-acetyl]-1,2,3,4-tetrahydro-isoquinoline-1-carboxylic acid (2,6-difluoro-phenyl)-amide hydrochloride; ~~and~~

(S)-2-((S)-2-cyclopentyl-2-((S)-2-(methylamino)propanamido)acetyl)-N-(2,6-difluorophenyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide hydrochloride;

~~or a pharmaceutically acceptable salt of either of the foregoing compounds.~~

~~24. The compound of claim 1 wherein R^3 is heterocyclyl, said compound being selected from the group comprising:~~

~~(S)-N-(2,6-difluorophenyl)-2-((S)-2-((S)-2-(methylamino)propanamido)-2-(tetrahydro-2H-pyran-4-yl)acetyl)isoindoline-1-carboxamide hydrochloride; and~~

~~(S)-N-(2,6-difluorophenyl)-2-((S)-2-((S)-2-(methylamino)propanamido)-2-(tetrahydro-2H-pyran-4-yl)acetyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide hydrochloride;~~

~~or a pharmaceutically acceptable salt of either of the foregoing compounds.~~

~~25. The compound of claim 1 wherein R^3 is aryl, said compound being~~

(S)-N-(2,6-difluorophenyl)-2-((S)-2-((S)-2-(methylamino)propanamido)-2-phenylacetyl)isoindoline-1-carboxamide hydrochloride;

~~or a pharmaceutically acceptable salt of the foregoing compound.~~

~~26. A compound selected from the group comprising:~~

(S)-2-[(S)-3-Methyl-2-((S)-2-methylamino-propionylamino)-butyryl]-2,3-dihydro-1H-isoindole-1-carboxylic acid (2,6-difluoro-phenyl)-amide hydrochloride;

((S)-2-[(S)-2-Cyclohexyl-2-((S)-2-methylamino-propionylamino)-acetyl]-2,3-dihydro-1H-isoindole-1-carboxylic acid (2,6-difluoro-phenyl)-amide hydrochloride ;

(S)-N-(2,6-difluorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-2-[(S)-3-Methyl-2-((S)-2-methylamino-propionylamino)-butyryl]-1,2,3,4-tetrahydro-isoquinoline-1-carboxylic acid (2-chloro-6-fluoro-phenyl)-amide hydrochloride;

~~6-Chloro-2-[(S)-3-methyl-2-((S)-2-methylamino-propionylamino)-butyryl]-1,2,3,4-tetrahydro-isoquinoline-1-carboxylic acid (2,6-difluoro-phenyl)-amide;~~

~~6-Fluoro-2-[(S)-3-methyl-2-((S)-2-methylamino-propionylamino)-butyryl]-1,2,3,4-tetrahydro-isoquinoline-1-carboxylic acid (2,6-difluoro-phenyl)-amide;~~

(S)-N-(2,6-dichlorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino)propanamido) butanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(2-chloro-6-fluorophenyl)-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(benzo[b]thiophen-4-yl)-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((2S,3S)-3-methyl-2-((S)-2-(methylamino) propanamido)pentanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((S)-3,3-dimethyl-2-((S)-2-(methylamino) propanamido)butanoyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((S)-2-((S)-2-(methylamino)propanamido)-2-(tetrahydro-2H-pyran-4-yl)acetyl)isoindoline-1-carboxamide hydrochloride;

(S)-2-((S)-2-cyclopentyl-2-((S)-2-(methylamino)propanamido)acetyl)-N-(2,6-difluorophenyl)isoindoline-1-carboxamide hydrochloride;

(S)-N-(2,6-difluorophenyl)-2-((S)-2-((S)-2-(methylamino)propanamido)-2-(tetrahydro-2H-pyran-4-yl)acetyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide hydrochloride; and

(S)-N-(2,6-difluorophenyl)-2-((2S,3S)-3-methyl-2-((S)-2-(methylamino) propanamido)pentanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide hydrochloride; ~~and~~

~~N-(2,6-difluorophenyl)-7-fluoro-2-((S)-3-methyl-2-((S)-2-(methylamino) propanamido)butanoyl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamide;~~

or a pharmaceutically acceptable salt of each of the foregoing compounds.

~~27.~~19. A pharmaceutical composition comprising any of the compounds according to claims 1-~~26~~17, or a pharmaceutically acceptable salt thereof, as an active ingredient together with a pharmaceutically acceptable carrier or excipient.

~~28.~~20. Compounds according to any of claims 1-~~26~~17 for use as a therapeutically active substance.

~~29.~~21. Use of a compound according to any of claims 1-~~26~~17, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the therapeutic and/or prophylactic treatment of cancer.

~~30.~~22. A compound according to any of claims 1-~~26~~17, or a pharmaceutically acceptable salt thereof, for use in the therapeutic and/or prophylactic treatment of cancer.