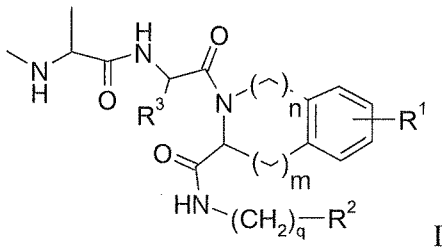
domain, in contrast, binds to and inhibits caspases 3 and 7. The proapoptotic protein Smac (also known as DIABLO) can block the BIR2 and BIR3 domains of IAPs competing with activated caspases resulting in release of the activated caspases from the IAPs and completion of the apoptotic program. See, e.g., S. Wang, "Design of Small-Molecule Smac Mimetics as IAP Antagonists," Current Topics in Microbiology and Immunology 348, DOI 10.1007/82_2010_111, pp. 89-113.

Peptides and small molecules have been reported to bind to the BIR3 region of XIAP and cIAP, mimicking the action of Smac protein and releasing activated caspases. See, e.g., Dean, supra; and M. Gyrd-Hanse et al., "IAPs: From caspase inhibitors to modulators of NF-κB, inflammation and cancer," Nature Review/Cancer, August 2010, Vol 10:561-574.

Summary ~~of the Invention~~

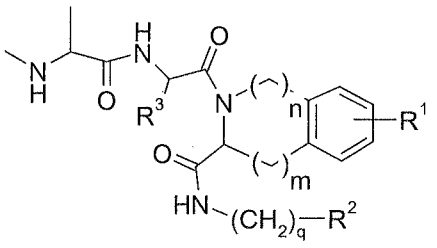
~~One aspect of t~~The present ~~invention~~ disclosure relates to ~~is~~ a compound of Formula I



I

or pharmaceutically acceptable salts thereof, wherein R^1, R^2, R^3, m, n and q are described in this application.

Hence, in a first aspect, the present disclosure provides for 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.

In a second aspect, the present disclosure provides for 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;

(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 ~~invention~~ 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 ~~invention~~ 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

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

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

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

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

~~31. A method of treating or ameliorating cancer comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound according to any of claims 1-26.~~