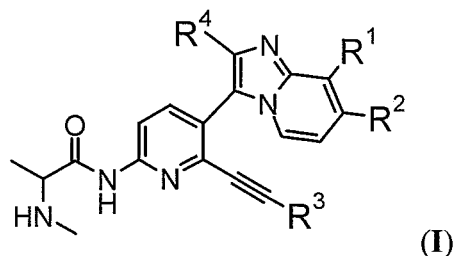


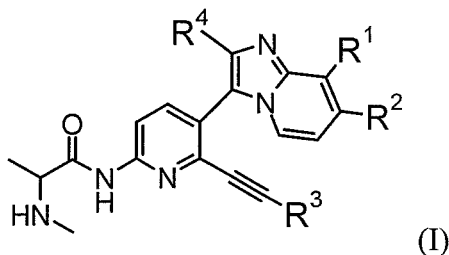
Detailed description

The present disclosure relates to compounds of formula (I)



wherein **R¹** to **R⁴** are as defined in the description and in the claims. The compounds
5 according to formula (I) act as SMAC mimetics. Thus, the compounds of the disclosure
may be used for example for the treatment of diseases which are characterized by an
increased apoptosis threshold due to overexpression of IAP protein. Preferably, the
compounds of the disclosure can be used in the treatment of cancer.

In one aspect, the present disclosure therefore relates to compounds of general formula (I)



10

Wherein

R¹ is selected from hydrogen, -C₁₋₃alkyl and halogen;

R² is selected from hydrogen, -C₁₋₃alkyl and halogen;

R³ is selected from phenyl or a 9- to 14-membered heteroaryl wherein each of these
15 groups is optionally substituted with **R⁵** or

R³ is a phenyl moiety fused with a 5-6 membered heterocycloalkyl, wherein each of
these groups is optionally and independently substituted with one or more **R⁶**;

R⁴ is a 5- or 6-membered heteroaryl substituted with -C₁₋₃alkyl or -O-C₁₋₃alkyl;

R⁵ is -C₁₋₃alkyl;

R⁶ is =O or -C₁₋₃alkyl;

and wherein the compounds of formula (I) may optionally be present in the form of salts.

5

In a preferred embodiment the disclosure relates to compounds of formula (I), wherein R¹ is selected from hydrogen, -CH₃, -Cl.

In a preferred embodiment the disclosure relates to compounds of formula (I), wherein R² is selected from -H, -CH₃, -Cl.

10 In a preferred embodiment the disclosure relates to compounds of formula (I), wherein R¹ is hydrogen and R² is selected from hydrogen, -CH₃ and Cl.

In a preferred embodiment the disclosure relates to compounds of formula (I), wherein R⁴ is a 6-membered heteroaryl substituted with -C₁₋₃alkyl or -O-C₁₋₃alkyl.

15

In a preferred embodiment the disclosure relates to compounds of formula (I), wherein R⁴ is a 6-membered heteroaryl substituted with -CH₃ or -O-CH₃.

20 In a preferred embodiment the disclosure relates to compounds of formula (I), wherein R⁴ is selected from pyridyl, pyrimidinyl, pyrazolyl, imidazolyl, each of which is independently substituted with -C₁₋₃alkyl or -O-C₁₋₃alkyl.

25 In a preferred embodiment the disclosure relates to compounds of formula (I), wherein R⁴ is selected from pyridyl, pyrimidinyl, pyrazolyl, imidazolyl, each of which is independently substituted with -CH₃ or -O-CH₃.

In a preferred embodiment the disclosure relates to compounds of formula (I), wherein R⁴ is pyridyl substituted with -CH₃.

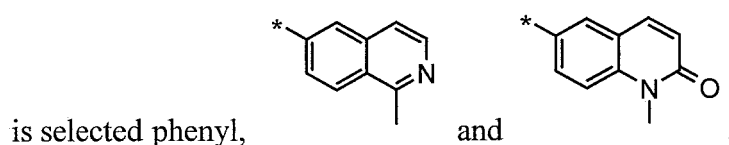
In a preferred embodiment the disclosure relates to compounds of formula (I), wherein R⁴ is pyridyl substituted with -O-CH₃.

In a preferred embodiment the disclosure relates to compounds of formula (I), wherein R⁴ is pyrimidinyl substituted with -CH₃.

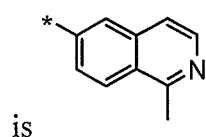
In a preferred embodiment the disclosure relates to compounds of formula (I), wherein R⁴ is pyrazolyl substituted with -CH₃.

In a preferred embodiment the disclosure relates to compounds of formula (I), wherein R⁴ is imidazolyl substituted with -CH₃.

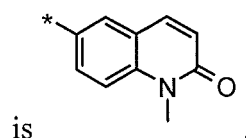
In a preferred embodiment the disclosure relates to compounds of formula (I), wherein R³



In a preferred embodiment the disclosure relates to compounds of formula (I), wherein R³



In a preferred embodiment the disclosure relates to compounds of formula (I), wherein R³



The disclosure relates to compounds of general formula (I) or of anyone of the embodiments as disclosed above for use in the treatment of cancer.

In another aspect the disclosure relates to compounds of general formula **(I)** or of anyone of the embodiments as disclosed above – or the pharmaceutically acceptable salts thereof – for use as medicaments.

5 In another aspect the disclosure relates to compounds of general formula **(I)** or of anyone of the embodiments as disclosed above – or the pharmaceutically acceptable salts thereof – for use in the treatment and/or prevention of cancer, infections, inflammations and autoimmune diseases.

10 The disclosure relates to compounds of general formula **(I)** or of anyone of the embodiments as disclosed above – or the pharmaceutically acceptable salts thereof – for use in the treatment and/or prevention of cancer, preferably of carcinomas of the breast, in particular triple negative breast cancer (TNBC), prostate, brain or ovary, non-small-cell lung carcinomas (NSCLC), melanomas, acute myeloid leukaemia (AML) and chronic lymphatic leukaemias (CLL).

15 In another aspect the disclosure relates to compounds of general formula **(I)** or of anyone of the embodiments as disclosed above – or the pharmaceutically acceptable salts thereof – for use in the treatment and/or prevention of carcinomas of the breast, in particular triple negative breast cancer (TNBC), prostate, brain or ovary, non-small-cell lung carcinomas (NSCLC), melanomas, acute myeloid leukaemia (AML) and chronic lymphatic leukaemias (CLL).

20 The disclosure relates to a method for the treatment and/or prevention of cancer comprising administering a therapeutically effective amount of a compound of general formula **(I)** or of anyone of the embodiments as disclosed above – or one of the pharmaceutically acceptable salts thereof – to a human being.

25 The disclosure relates to a method for the treatment and/or prevention of carcinoma of the breast, in particular triple negative breast cancer (TNBC), prostate, brain or ovary, non-small-cell lung carcinomas (NSCLC), melanomas acute myeloid leukaemia (AML) and chronic lymphatic leukemias (CLL) comprising administering a therapeutically effective amount of a compound of general formula **(I)** or of anyone of the embodiments as

disclosed above – or one of the pharmaceutically acceptable salts thereof – to a human being.

In another aspect the disclosure relates to a pharmaceutical preparation containing as active substance one or more compounds of general formula **(I)** or of anyone of the embodiments
5 as disclosed above – or the pharmaceutically acceptable salts thereof – optionally in combination with conventional excipients and/or carriers.

The disclosure relates to a pharmaceutical preparation comprising a compound of general formula **(I)** or of anyone of the embodiments as disclosed above – or one of the pharmaceutically acceptable salts thereof – and at least one other cytostatic or cytotoxic
10 active substance, different from formula **(I)**.

Definitions

Terms that are not specifically defined here have the meanings that are apparent to the skilled man in the light of the overall disclosure and the context as a whole.

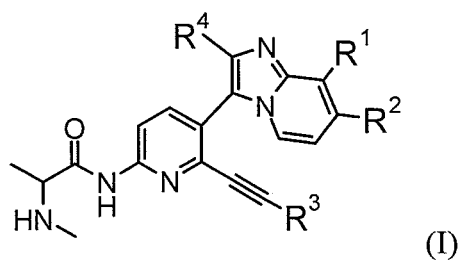
15 As used herein, the following definitions apply, unless stated otherwise:

In the groups, radicals, or moieties defined below, the number of carbon atoms is often specified preceding the group, for example, -C₁₋₅alkyl means an alkyl group or radical having 1 to 5 carbon atoms. In general, for groups comprising two or more subgroups, the first named sub-group is the radical attachment point, for example the substituent
20 -C₁₋₅alkyl-C₃₋₁₀cylcoalkyl, means a C₃₋₁₀cylcoalkyl group which is bound to a C₁₋₅alkyl, the latter of which is bound to the core structure or to the group to which the substituent is attached.

The indication of the number of members in groups that contain one or more heteroatom(s) (heteroalkyl, heteroaryl, heteroarylalkyl, heterocyclyl, heterocyclalkyl) relates to the total
25 atomic number of all the ring members or chain members or the total of all the ring and chain members.

Claims

1. A compound of formula I



wherein

R¹ is selected from hydrogen, -C₁₋₃alkyl and halogen;

R² is selected from hydrogen, -C₁₋₃alkyl and halogen;

R³ is selected from phenyl or a 9- to 14-membered heteroaryl wherein each of these groups is optionally substituted with R⁵ or

R³ is a phenyl moiety fused with a 5-6 membered heterocycloalkyl, wherein each of these groups is optionally and independently substituted with one or more R⁶;

R⁴ is a 5- or 6-membered heteroaryl substituted with -C₁₋₃alkyl or -O-C₁₋₃alkyl;

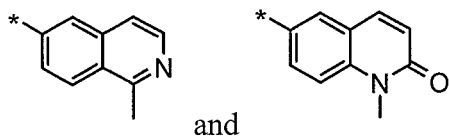
R⁵ is -C₁₋₃alkyl;

R⁶ is =O or -C₁₋₃alkyl;

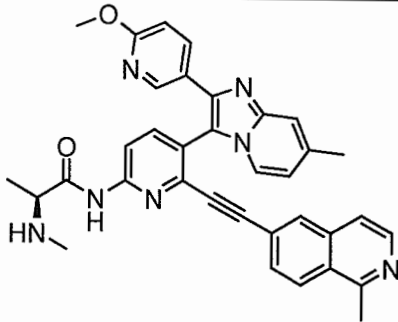
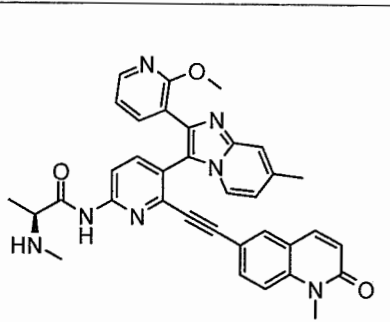
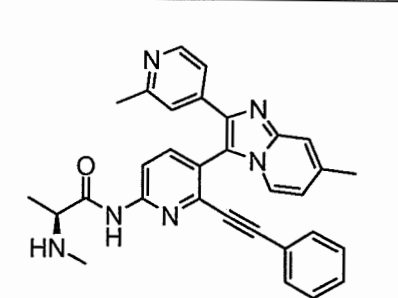
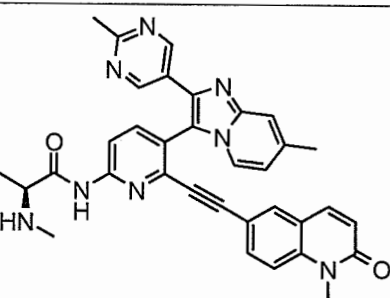
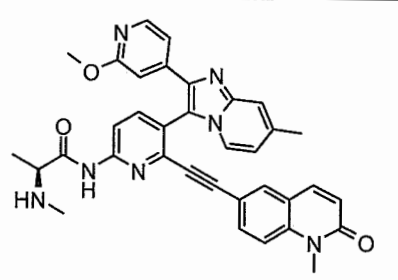
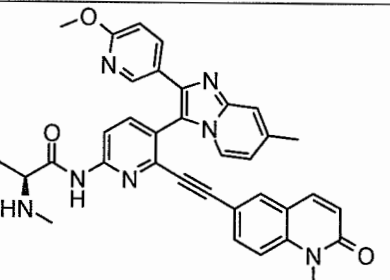
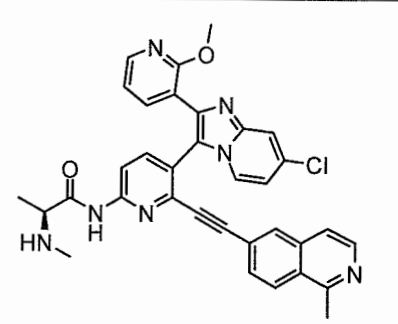
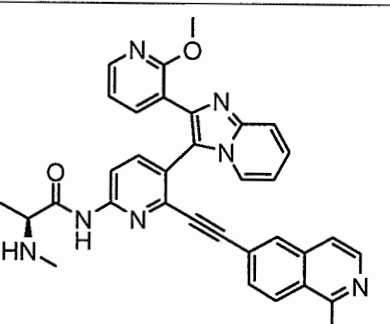
or salts thereof.

2. The compound or salts of claim 1, wherein R¹ is selected from hydrogen, -CH₃ and Cl.
3. The compound or salts of claim 1 or 2, wherein R² is selected from hydrogen, -CH₃ and Cl.
4. The compound or salts of anyone of claims 1 to 3, wherein R¹ is hydrogen and R² is selected from hydrogen, -CH₃ and Cl.

5. The compound or salts of anyone of claims 1 to 4, wherein R⁴ is a 6-membered heteroaryl substituted with -C₁₋₃alkyl or -O-C₁₋₃alkyl.
6. The compound or salts of anyone of claims 1 to 4, wherein R⁴ is selected from pyridyl, pyrimidinyl, pyrazolyl, imidazolyl, each of which is independently substituted with -C₁₋₃alkyl or -O-C₁₋₃alkyl.
7. The compound or salts of anyone of claims 1 to 4, wherein R⁴ is selected from pyridyl, pyrimidinyl, pyrazolyl, imidazolyl, each of which is independently substituted with -CH₃ or -O-CH₃.
8. The compound or salts of anyone of claims 1 to 7, wherein R³ is selected from phenyl,

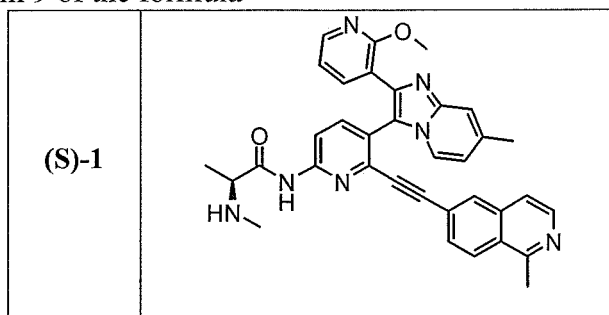


9. The compound of claim 1 selected from

(S)-9		(S)-10	
(S)-11		(S)-12	
(S)-13		(S)-14	
(S)-15		(S)-16	

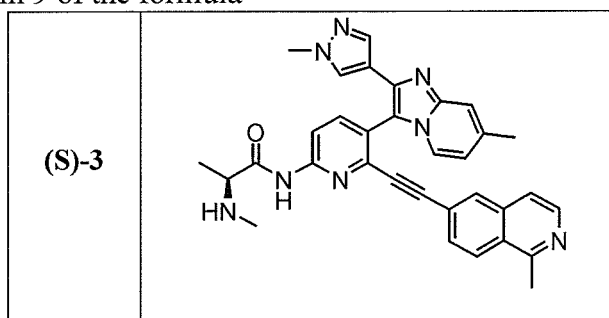
or salts thereof.

10. A compound of claim 9 of the formula



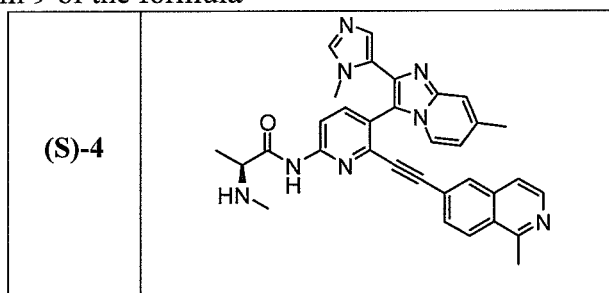
or salts thereof.

11. A compound of claim 9 of the formula



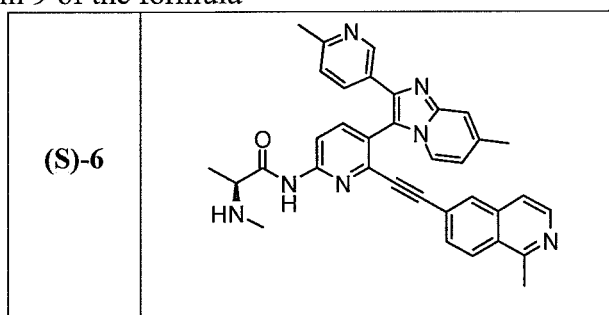
or salts thereof.

12. A compound of claim 9 of the formula



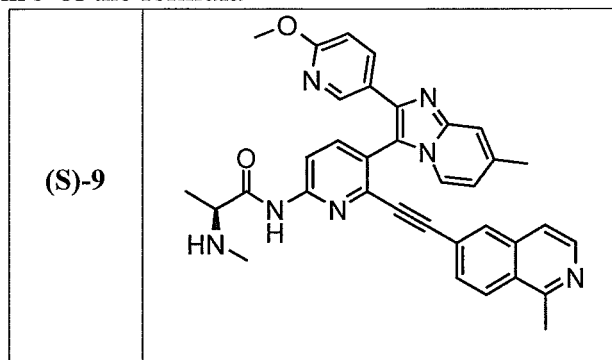
or salts thereof.

13. A compound of claim 9 of the formula



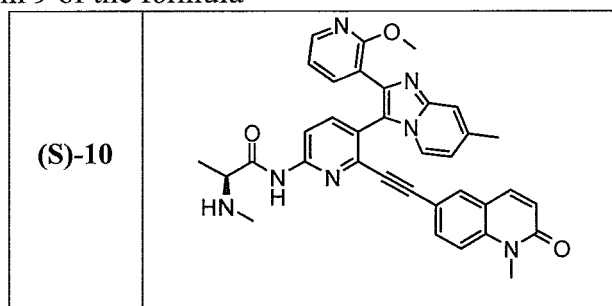
or salts thereof.

14. A compound of claim 9 of the formula



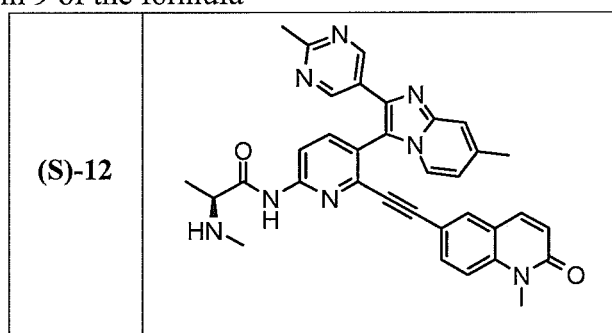
or salts thereof.

15. A compound of claim 9 of the formula



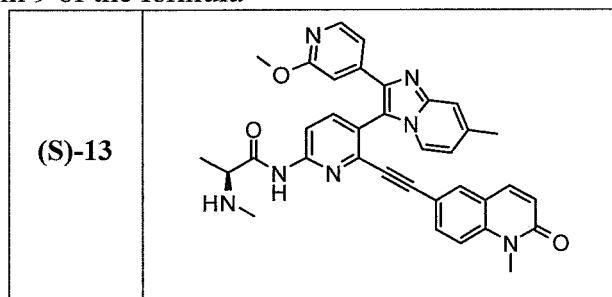
or salts thereof.

16. A compound of claim 9 of the formula



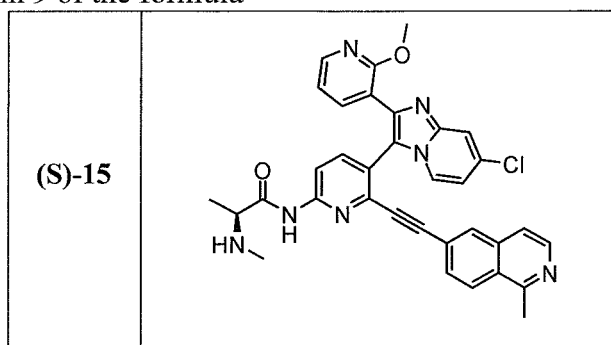
or salts thereof.

17. A compound of claim 9 of the formula



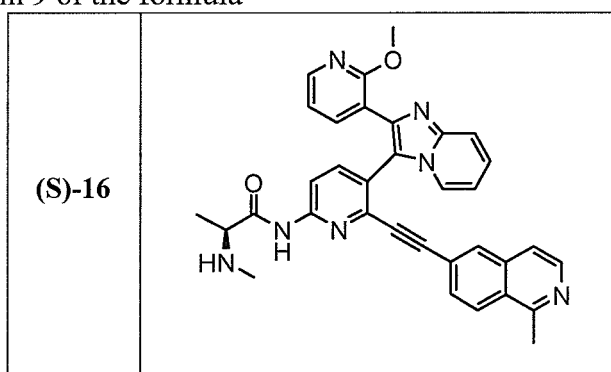
or salts thereof.

18. A compound of claim 9 of the formula



or salts thereof.

19. A compound of claim 9 of the formula



or salts thereof.

20. A compound of anyone of claims 1 to 19 – or the pharmaceutically acceptable salts thereof – for use as medicaments.
21. A compound of anyone of claims 1 to 19 – or the pharmaceutically acceptable salts thereof – for use in the treatment and/or prevention of cancer.
22. A pharmaceutical preparation containing as active substance one or more compounds of anyone of claims 1 to 19 – or the pharmaceutically acceptable salts thereof – optionally in combination with conventional excipients and/or carriers.
23. A compound of anyone of claims 1 to 19 – or the pharmaceutically acceptable salts thereof – for use in the treatment and/or prevention of carcinomas of the breast, in particular triple negative breast cancer (TNBC), prostate, brain or ovary, non-small-cell lung carcinomas (NSCLC), melanomas, acute myeloid leukaemia (AML) and chronic lymphatic leukaemias (CLL).