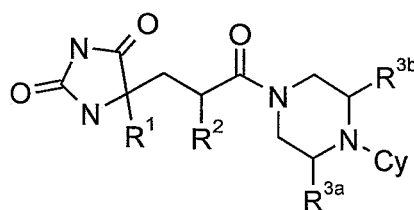


SUMMARY OF THE INVENTION

[0021] The present invention is based on the identification of novel hydantoin compounds that may be useful for the prophylaxis and/or treatment of inflammatory conditions, and/or diseases involving degradation of cartilage and/or disruption of cartilage homeostasis. In a particular aspect, the compounds of the invention are inhibitors of ADAMTS-5. The present invention also provides methods for the production of these compounds, pharmaceutical compositions comprising these compounds and methods for treating inflammatory conditions, and/or diseases involving degradation of cartilage and/or disruption of cartilage homeostasis by administering the compounds of the invention.

[0021a] Accordingly, in a first aspect of the invention, the present invention provides a compound according to Formula I:



I

wherein

R¹ is:

- H,
- C₁₋₄ alkyl optionally substituted with one or more independently selected R⁴ groups,
- C₃₋₇ monocyclic cycloalkyl optionally substituted with one or more independently selected R⁴ groups,
- 4-7 membered monocyclic heterocycloalkyl comprising 1 to 2 heteroatoms independently selected from N, O, and S, optionally substituted with one or more independently selected C₁₋₄ alkyl, –C(=O)C₁₋₄ alkyl, or –C(=O)OC₁₋₄ alkyl,
- phenyl optionally substituted with one or more independently selected R⁵ groups,
- phenyl fused to a 5-6 membered monocyclic heterocycloalkyl comprising 1, 2 or 3 heteroatoms independently selected from N, O, and S, which heterocycloalkyl is optionally substituted with one or more =O,
- 5-6 membered monocyclic heteroaryl comprising 1 or 2 heteroatoms independently selected from N, O, and S, optionally substituted with one or more independently selected R⁵ groups;

R² is independently selected from:

- H,
- OH,
- C₁₋₄ alkoxy, and
- C₁₋₄ alkyl optionally substituted with one
 - OH,

4a

- -CN,
- C₁₋₄ alkoxy optionally substituted with one phenyl, and
- 5-6 membered monocyclic heteroaryl comprising 1 or 2 heteroatoms independently selected from N, O, and S, optionally substituted with one or more independently selected C₁₋₄ alkyl;

each R^{3a}, and R^{3b} is independently selected from:

- H, and
- C₁₋₄ alkyl;

Cy is

- 6-10 membered monocyclic or fused bicyclic aryl optionally substituted with one or more independently selected R⁶ groups,
- 5-10 membered monocyclic or fused bicyclic heteroaryl comprising 1, 2 or 3 heteroatoms independently selected from N, O, and S, optionally substituted with one or more independently selected R⁶ groups;

R⁴ is

- halo,
- OH,
- -CN,
- C₁₋₄ alkyl,
- C₁₋₄ alkoxy optionally substituted with C₁₋₄ alkoxy, or phenyl,
- C₁₋₄ thioalkoxy,
- 4-7-membered monocyclic heterocycloalkyl comprising one or more heteroatoms independently selected from N, S, and O, optionally substituted with one or more halo, or -C(=O)OC₁₋₄ alkyl,
- phenyl,
- -S(=O)₂C₁₋₄ alkyl
- -C(=O)OR^{7a}
- -C(=O)NR^{7b}R^{7c}
- -NHC(=O)OR^{7d}
- -NHC(=O)R^{7e}
- -NR^{8a}R^{8b};

each R⁵ is

- halo,
- OH,
- -CN,

4b

- C₁₋₄ alkyl optionally substituted with one or more independently selected halo, -NR^{9a}R^{9b}, or -C(=O)NR^{9c}R^{9d},
- C₁₋₄ alkoxy optionally substituted with -NR^{9e}R^{9f}, or
- -S(=O)₂C₁₋₄ alkyl;

each R⁶ is

- halo,
- -CN,
- -NO₂,
- -CH₃,
- 5-10 membered monocyclic or fused bicyclic heteroaryl comprising 1, 2 or 3 heteroatoms independently selected from N, O, and S, optionally substituted with one or more independently selected halo, C₁₋₄ alkyl, or C₁₋₄ alkoxy, or
- -NR^{9g}R^{9h};

each R^{7a}, R^{7b}, R^{7c}, R^{7d}, or R^{7e}, is

- H, or
- C₁₋₄ alkyl optionally substituted with OH, or C₁₋₄ alkoxy;

each R^{8a}, or R^{8b} is independently selected from

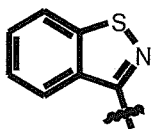
- H, and
- C₁₋₄ alkyl optionally substituted with OH, C₁₋₄ alkoxy, or phenyl;

each R^{9a}, R^{9b}, R^{9c}, R^{9d}, R^{9e}, R^{9f}, R^{9g}, and R^{9h} is independently selected from H, and C₁₋₄ alkyl;

or a pharmaceutically acceptable salt, or a solvate, or a pharmaceutically acceptable salt of a solvate thereof;

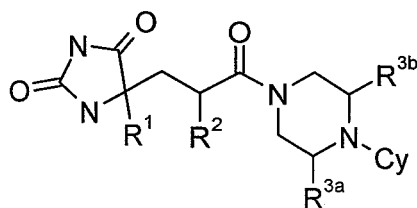
provided that:

- R¹ and R² are not simultaneously H, and
- when R¹ is Me, and R² is H, then Cy is not



or a pharmaceutically acceptable salt, or a solvate, or the salt of the solvate thereof.

[0022] Disclosed is a compound according to Formula (I):



I

wherein

R¹ is:

- H,
- C₁₋₄ alkyl optionally substituted with one or more independently selected R⁴ groups,
- C₃₋₇ monocyclic cycloalkyl optionally substituted with one or more independently selected R⁴ groups,
- 4-7 membered monocyclic heterocycloalkyl comprising 1 to 2 heteroatoms independently selected from N, O, and S, optionally substituted with one or more independently selected C₁₋₄ alkyl, –C(=O)C₁₋₄ alkyl, or –C(=O)OC₁₋₄ alkyl,
- phenyl optionally substituted with one or more independently selected R⁵ groups,
- phenyl fused to a 5-6 membered monocyclic heterocycloalkyl comprising 1, 2 or 3 heteroatoms independently selected from N, O, and S, which heterocycloalkyl is optionally substituted with one or more =O, or
- 5-6 membered monocyclic heteroaryl comprising 1 or 2 heteroatoms independently selected from N, O, and S, optionally substituted with one or more independently selected R⁵ groups;

R² is independently selected from:

- H,
- OH,
- C₁₋₄ alkoxy, and

- 5-10 membered monocyclic or fused bicyclic heteroaryl comprising 1, 2 or 3 heteroatoms independently selected from N, O, and S, optionally substituted with one or more independently selected halo, C₁₋₄ alkyl, or C₁₋₄ alkoxy, or

– -NR^{9g}R^{9h};

each R^{7a}, R^{7b}, R^{7c}, R^{7d}, or R^{7e}, is

- H, or
- C₁₋₄ alkyl optionally substituted with OH, or C₁₋₄ alkoxy;

each R^{8a}, or R^{8b} is independently selected from

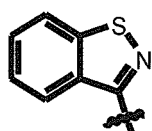
- H, and
- C₁₋₄ alkyl optionally substituted with OH, C₁₋₄ alkoxy, or phenyl;

each R^{9a}, R^{9b}, R^{9c}, R^{9d}, R^{9e}, R^{9f}, R^{9g}, and R^{9h} is independently selected from H, and C₁₋₄ alkyl;

or a pharmaceutically acceptable salt, or a solvate, or a pharmaceutically acceptable salt of a solvate thereof;

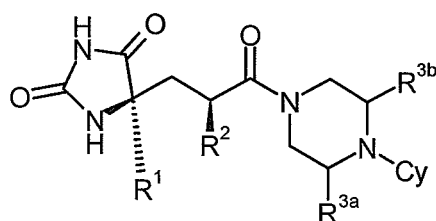
provided that:

- R¹ and R² are not simultaneously H, and
- When R¹ is Me, and R² is H, then Cy is not



or a pharmaceutically acceptable salt, or a solvate, or the salt of the solvate thereof.

- 2) A compound or pharmaceutically acceptable salt thereof, according to claim 1, wherein the compound is according to Formula II:



II

wherein R¹, R², R^{3a}, R^{3b}, and Cy are as defined above.

- 3) A compound or pharmaceutically acceptable salt thereof, according to claim 1 or 2, wherein R¹ is H.
- 4) A compound or pharmaceutically acceptable salt thereof, according to claim 1 or 2, wherein R¹ is C₁₋₄ alkyl.
- 5) A compound or pharmaceutically acceptable salt thereof, according to claim 1 or 2, wherein R¹ is C₃₋₇ monocyclic cycloalkyl.