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(54) Title: TRP-P8 ACTIVE COMPOUNDS AND THERAPEUTIC TREATMENT METHODS

(57) Abstract: Compounds of the disclosure provide compositions, which are effective for prophylaxis and treatment of diseases or disorders, such as cell-proliferation, angiogenesis, or apoptosis mediated diseases. The disclosure encompasses compounds, analogs, prodrugs, metabolites, and pharmaceutically acceptable salts thereof, pharmaceutical compositions, and methods for prophylaxis and treatment of diseases and other maladies or conditions involving cancer, tumors, and like conditions. The disclosure also provides therapeutic methods including the administration of an effective amount of a compound of the disclosure.



national Application No PCT/US2004/021509

Relevant to claim No.

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K31/513 A61K31/16 A61K31/66 A61K31/175 A61P35/00 A61K31/00 C07C233/58 C07C233/59 C07C233/60 C07D295/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data

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"A" docume consid "E" earlier of filling of which citatio "O" docume other other docume other docume."	ent defining the general state of the art which is not lered to be of particular relevance document but published on or after the international late ent which may throw doubts on priority claim(s) or is cited to establish the publication date of another n or other special reason (as specified) ent referring to an oral disclosure, use, exhibition or means ent published prior to the international filling date but nan the priority date claimed	 "T" later document published after the interest or priority date and not in conflict with cited to understand the principle or the invention "X" document of particular relevance; the cannot be considered novel or cannot involve an inventive step when the document of particular relevance; the cannot be considered to involve an indocument is combined with one or moments, such combination being obvious in the art. "&" document member of the same patent 	eary underlying the standard invention be considered to cument is taken alone claimed invention wentive step when the ore other such docuus to a person skilled
Date of the	actual completion of the international search	Date of mailing of the international sea	rch report
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Name and	mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Greif, G	

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nternational application No. PCT/US2004/021509

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. X No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-19 (all partially)
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-19 (all partially)

A method of treating cancer comprising contacting cancerous cells with a compound of the formula I, or a method of inhibiting or killing cancerous cells comprising administering to the cells a therapeutically effective amount of compound of the formula I, or a method of causing apoptosis in cancerous cells comprising contacting the cells with an effective amount of a compound of formula I, or a method for treating a disease or condition in a mammal wherein a Trp-p-8 receptor is implicated, comprising an effective amount of compound of formula I, or a method for treating or preventing a Trp-p-8 receptor related condition comprising administering a compound of formula I. or a pharmmaceutical composition comprising a compound of formula I, or the use of compound of formula I to prepare a medicament useful for treating or preventing a disease or Trp-p-8 related condition, or a compound of formula I in combination with at least one additional chemotherapeutic agent for use in treating or preventing a disease or Trp-p-8 receptor related condition.

2. claims: 1-19 (all partially), 20

A method of treating cancer comprising contacting cancerous cells with a compound of the formula II, or a method of inhibiting or killing cancerous cells comprising administering to the cells a therapeutically effective amount of compound of the formula II, or a method of causing apoptosis in cancerous cells comprising contacting the cells with an effective amount of a compound of formula II, or a method for treating a disease or condition in a mammal wherein a Trp-p-8 receptor is implicated, comprising an effective amount of compound of formula II, or a method for treating or preventing a Trp-p-8 receptor related condition comprising administering a compound of formula II, or a pharmmaceutical composition comprising a compound of formula II, or the use of compound of formula I to prepare a medicament useful for treating or preventing a disease or Trp-p-8 related condition, or a compound of formula II in combination with at least one additional chemotherapeutic agent for use in treating or preventing a disease or Trp-p-8 receptor related condition, or a compound of formula IIa.

A method of treating cancer comprising contacting cancerous cells with a compound of the formula III, or a method of inhibiting or killing cancerous cells comprising administering to the cells a therapeutically effective amount of compound of the formula III, or a method of causing apoptosis in cancerous cells comprising contacting the cells with an effective amount of a compound of formula III, or a method for treating a disease or condition in a mammal wherein a Trp-p-8 receptor is implicated, comprising an effective amount of compound of formula III, or a method for treating or preventing a Trp-p-8 receptor related condition comprising administering a compound of formula III, or a pharmmaceutical composition comprising a compound of formula III, or the use of compound of formula III to prepare a medicament useful for treating or preventing a disease or Trp-p-8 related condition, or a compound of formula III in combination with at least one additional chemotherapeutic agent for use in treating or preventing a disease or Trp-p-8 receptor related condition.

4. claims: 1-19 (all partially)

A method of treating cancer comprising contacting cancerous cells with a compound of the formula IV, or a method of inhibiting or killing cancerous cells comprising administering to the cells a therapeutically effective amount of compound of the formula IV, or a method of causing apoptosis in cancerous cells comprising contacting the cells with an effective amount of a compound of formula IV, or a method for treating a disease or condition in a mammal wherein a Trp-p-8 receptor is implicated, comprising an effective amount of compound of formula IV, or a method for treating or preventing a Trp-p-8 receptor related condition comprising administering a compound of formula IV, or a pharmmaceutical composition comprising a compound of formula I, or the use of compound of formula IV to prepare a medicament useful for treating or preventing a disease or Trp-p-8 related condition, or a compound of formula IV in combination with at least one additional chemotherapeutic agent for use in treating or preventing a disease or Trp-p-8 receptor related condition.

A method of treating cancer comprising contacting cancerous cells with a compound of the formula V, or a method of inhibiting or killing cancerous cells comprising administering to the cells a therapeutically effective amount of compound of the formula V, or a method of causing apoptosis in cancerous cells comprising contacting the cells with an effective amount of a compound of formula V, or a method for treating a disease or condition in a mammal wherein a Trp-p-8 receptor is implicated, comprising an effective amount of compound of formula V, or a method for treating or preventing a Trp-p-8 receptor related condition comprising administering a compound of formula V, or a pharmmaceutical composition comprising a compound of formula V, or the use of compound of formula V to prepare a medicament useful for treating or preventing a disease or Trp-p-8 related condition, or a compound of formula V in combination with at least one additional chemotherapeutic agent for use in treating or preventing a disease or Trp-p-8 receptor related condition.

6. claims: 1-19 (all partially)

A method of treating cancer comprising contacting cancerous cells with a compound of the formula VI, or a method of inhibiting or killing cancerous cells comprising administering to the cells a therapeutically effective amount of compound of the formula VI, or a method of causing apoptosis in cancerous cells comprising contacting the cells with an effective amount of a compound of formula VI, or a method for treating a disease or condition in a mammal wherein a Trp-p-8 receptor is implicated, comprising an effective amount of compound of formula VI, or a method for treating or preventing a Trp-p-8 receptor related condition comprising administering a compound of formula VI, or a pharmmaceutical composition comprising a compound of formula VI, or the use of compound of formula VI to prepare a medicament useful for treating or preventing a disease or Trp-p-8 related condition, or a compound of formula VI in combination with at least one additional chemotherapeutic agent for use in treating or preventing a disease or Trp-p-8 receptor related condition.

A method of treating cancer comprising contacting cancerous cells with a compound of the formula VII, or a method of inhibiting or killing cancerous cells comprising administering to the cells a therapeutically effective amount of compound of the formula VII, or a method of causing apoptosis in cancerous cells comprising contacting the cells with an effective amount of a compound of formula VII, or a method for treating a disease or condition in a mammal wherein a Trp-p-8 receptor is implicated, comprising an effective amount of compound of formula VII, or a method for treating or preventing a Trp-p-8 receptor related condition comprising administering a compound of formula VII, or a pharmmaceutical composition comprising a compound of formula VII, or the use of compound of formula I to prepare a medicament useful for treating or preventing a disease or Trp-p-8 related condition, or a compound of formula VII in combination with at least one additional chemotherapeutic agent for use in treating or preventing a disease or Trp-p-8 receptor related condition.

8. claims: 1-19 (all partially)

A method of treating cancer comprising contacting cancerous cells with a compound of the formula VIII, or a method of inhibiting or killing cancerous cells comprising administering to the cells a therapeutically effective amount of compound of the formula VIII, or a method of causing apoptosis in cancerous cells comprising contacting the cells with an effective amount of a compound of formula VIII, or a method for treating a disease or condition in a mammal wherein a Trp-p-8 receptor is implicated, comprising an effective amount of compound of formula VIII, or a method for treating or preventing a Trp-p-8 receptor related condition comprising administering a compound of formula VIII, or a pharmmaceutical composition comprising a compound of formula I, or the use of compound of formula VIII to prepare a medicament useful for treating or preventing a disease or Trp-p-8 related condition, or a compound of formula VIII in combination with at least one additional chemotherapeutic agent for use in treating or preventing a disease or Trp-p-8 receptor related condition.

A method of treating cancer comprising contacting cancerous cells with a compound of the formula IX or a method of inhibiting or killing cancerous cells comprising administering to the cells a therapeutically effective amount of compound of the formula IX, or a method of causing apoptosis in cancerous cells comprising contacting the cells with an effective amount of a compound of formula IX, or a method for treating a disease or condition in a mammal wherein a Trp-p-8 receptor is implicated, comprising an effective amount of compound of formula IX or a method for treating or preventing a Trp-p-8 receptor related condition comprising administering a compound of formula IX, or a pharmmaceutical composition comprising a compound of formula IX, or the use of compound of formula IX to prepare a medicament useful for treating or preventing a disease or Trp-p-8 related condition, or a compound of formula IX in combination with at least one additional chemotherapeutic agent for use in treating or preventing a disease or Trp-p-8 receptor related condition.

10. claims: 1-19 (all partially)

A method of treating cancer comprising contacting cancerous cells with a compound of the formula X, or a method of inhibiting or killing cancerous cells comprising administering to the cells a therapeutically effective amount of compound of the formula X, or a method of causing apoptosis in cancerous cells comprising contacting the cells with an effective amount of a compound of formula X, or a method for treating a disease or condition in a mammal wherein a Trp-p-8 receptor is implicated, comprising an effective amount of compound of formula X, or a method for treating or preventing a Trp-p-8 receptor related condition comprising administering a compound of formula X, or a pharmmaceutical composition comprising a compound of formula X, or the use of compound of formula X to prepare a medicament useful for treating or preventing a disease or Trp-p-8 related condition, or a compound of formula X in combination with at least one additional chemotherapeutic agent for use in treating or preventing a disease or Trp-p-8 receptor related condition.

A method of treating cancer comprising contacting cancerous cells with a compound of the formula XI, or a method of inhibiting or killing cancerous cells comprising administering to the cells a therapeutically effective amount of compound of the formula XI, or a method of causing apoptosis in cancerous cells comprising contacting the cells with an effective amount of a compound of formula XI, or a method for treating a disease or condition in a mammal wherein a Trp-p-8 receptor is implicated, comprising an effective amount of compound of formula XI, or a method for treating or preventing a Trp-p-8 receptor related condition comprising administering a compound of formula xI, or a pharmmaceutical composition comprising a compound of formula XI, or the use of compound of formula XI to prepare a medicament useful for treating or preventing a disease or Trp-p-8 related condition, or a compound of formula XI in combination with at least one additional chemotherapeutic agent for use in treating or preventing a disease or Trp-p-8 receptor related condition.

12. claims: 1-19 (all partially)

A method of treating cancer comprising contacting cancerous cells with a compound of the formula XII, or a method of inhibiting or killing cancerous cells comprising administering to the cells a therapeutically effective amount of compound of the formula XII, or a method of causing apoptosis in cancerous cells comprising contacting the cells with an effective amount of a compound of formula XII, or a method for treating a disease or condition in a mammal wherein a Trp-p-8 receptor is implicated, comprising an effective amount of compound of formula XII, or a method for treating or preventing a Trp-p-8 receptor related condition comprising administering a compound of formula XII, or a pharmmaceutical composition comprising a compound of formula I, or the use of compound of formula XII to prepare a medicament useful for treating or preventing a disease or Trp-p-8 related condition, or a compound of formula XII in combination with at least one additional chemotherapeutic agent for use in treating or preventing a disease or Trp-p-8 receptor related condition.

A method of treating cancer comprising contacting cancerous cells with a compound of the formula XIII, or a method of inhibiting or killing cancerous cells comprising administering to the cells a therapeutically effective amount of compound of the formula XIII, or a method of causing apoptosis in cancerous cells comprising contacting the cells with an effective amount of a compound of formula XIII, or a method for treating a disease or condition in a mammal wherein a Trp-p-8 receptor is implicated, comprising an effective amount of compound of formula XIII, or a method for treating or preventing a Trp-p-8 receptor related condition comprising administering a compound of formula XIII, or a pharmmaceutical composition comprising a compound of formula XIII, or the use of compound of formula I to prepare a medicament useful for treating or preventing a disease or Trp-p-8 related condition, or a compound of formula XIII in combination with at least one additional chemotherapeutic agent for use in treating or preventing a disease or Trp-p-8 receptor related condition.

Information on patent family members

PCT/US2004/021509

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