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Title: INHIBITORS OF BRUTON'S TYROSINE KINASE

Abstract: Disclosed herein are compounds that form covalent bonds with Bruton’s tyrosine kinase (Btk). Also described are irreversible inhibitors of Btk. Methods for the preparation of the compounds are disclosed. Also disclosed are pharmaceutical compositions that include the compounds. Methods of using the Btk inhibitors are disclosed, alone or in combination with other therapeutic agents, for the treatment of autoimmune diseases or conditions, heteroimmune diseases or conditions, cancer, including lymphoma, and inflammatory diseases or conditions.
INTERNATIONAL SEARCH REPORT

A CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A01N 43/90, A61K 31/519 (2008.01)
USPC - 514/262.1

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)
USPC 514/262 1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC 514/49, 259 3, 256, 269, 274, 406 (see search terms below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WEST, PUBMED, Google Scholar (bruton$4 and (bruton$4 near 5 kinase or btk)) and inhibit$4 and pharmaceut$6 and cysteine and covalent

C DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category*</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No</th>
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Further documents are listed in the continuation of Box C

* Special categories of cited documents
  "A" document defining the general state of the art which is not considered to be of particular relevance
  "B" earlier application or patent but published on or after the international filing date
  "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
  "O" document referring to an oral disclosure, use, exhibition or other means
  "P" document published prior to the international filing date but later than the priority date claimed
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  "X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
  "Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
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13 March 2008 (13 03 2008)

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Form PCT/ISA/210 (second sheet) (April 2007)
This application contains the following inventions or groups of inventions, which have certain common technical feature, which do not constitute a contribution over the prior art.

Group I claims 1-9 and 12-13 are drawn to a compound having formula D and a pharmaceutical composition comprising the compound of formula D and a method of treating an autoimmune disease comprising administering a composition containing therapeutically effective amount of that compound.

Group II claims 10-11 are drawn to an inhibited tyrosine kinase comprising Bruton's tyrosine kinase or its homolog bound to an inhibitor of formula D.

Group III claims 14-15 are drawn to a method for treating a heteroimmune condition comprising administering a composition containing a pharmaceutically effective amount of a compound of formula D.

Group IV claims 16-17 are drawn to a method for treating an inflammatory disease comprising administering a composition containing a therapeutically effective amount of a compound of formula D.

Group V claims 18-21 are drawn to a method for treating cancer comprising administering a composition containing a therapeutically effective amount of a compound of formula D.

The inventions are linked by a compound having the common structural element of links the inventions: 3-phenyl-4-amino-1H-pyrazolo [3,4-d] pyrimidin-1-yl.

However, this common structural element is not a technical feature which is 'special' as it does not constitute an advancement over the art [HIRST et al WO2002/080926 A1, 17 OCT 2002, see claim 55]. Thus, the inventions listed as groups I-V do not contain a special technical feature, and therefore lack unity of invention.

Further more, each group involves method steps or starting materials not required by the other.

Group I is drawn to the compound represented by formula D, and the pharmaceutical composition comprising the same compound.

Group II is drawn to an inhibited tyrosine kinase comprising Bruton's tyrosine kinase bound to compound of group I.

Group III involves a first method using the compound of group V and I requiring different patient population from group IV.

Group IV a second method using the compound of group I requiring different patient population from groups III and V.

Group V a third method using the compound of group I requiring different patient population from group III and IV.