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(54) **CRYSTALLINE FORMS OF A BRUTON'S TYROSINE KINASE INHIBITOR**

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(58) **Field of Classification Search**

USPC 544/256; 546/184

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,824,982	A	4/1989	Vahlensieck et al.
5,033,252	A	7/1991	Carter
5,052,558	A	10/1991	Carter
5,145,684	A	9/1992	Liversidge et al.
5,323,907	A	6/1994	Kalvelage
5,397,787	A	3/1995	Buzzetti et al.
5,593,997	A	1/1997	Dow et al.
6,160,010	A	12/2000	Uckun et al.
6,221,900	B1	4/2001	Uckun et al.
6,303,652	B1	10/2001	Uckun et al.
6,306,897	B1	10/2001	Uckun et al.
6,326,469	B1	12/2001	Ullrich et al.
6,410,054	B1	6/2002	Thosar et al.
6,506,769	B2	1/2003	Snow et al.
6,660,744	B1	12/2003	Hirst et al.
6,753,348	B2	6/2004	Uckun et al.
6,770,639	B2	8/2004	Snow et al.
6,921,763	B2	7/2005	Hirst et al.
7,138,420	B2	11/2006	Bentzien et al.
7,332,497	B2	2/2008	Hirst et al.
7,514,444	B2	4/2009	Honigberg et al.
7,718,662	B1	5/2010	Chen et al.
7,732,454	B2	6/2010	Verner
7,741,330	B1	6/2010	Chen et al.
7,825,118	B2	11/2010	Honigberg et al.
7,960,396	B2	6/2011	Honigberg et al.

(Continued)

FOREIGN PATENT DOCUMENTS

CN	101610676	A	12/2009
CN	103121999	A	5/2013

(Continued)

OTHER PUBLICATIONS

ACS 2015 (http://www.cancer.org/cancer/non-hodgkinlymphoma/detailedguide/non-hodgkin-lymphoma-types-of-non-hodgkinlymphoma).

(Continued)

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(57) **ABSTRACT**

Described herein is the Bruton's tyrosine kinase (Btk) inhibitor 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one, including crystalline forms, solvates and pharmaceutically acceptable salts thereof. Also disclosed are pharmaceutical compositions that include the Btk inhibitor, as well as methods of using the Btk inhibitor, 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.

30 Claims, 16 Drawing Sheets