US009409908B2

(12) **United States Patent**
Yang et al.

(10) **Patent No.: US 9,409,908 B2**
(45) **Date of Patent: Aug. 9, 2016**

(54) **DIHYDROPYRIDONE P1 AS FACTOR XIA INHIBITORS**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **14/419,002**

(22) PCT Filed: **Aug. 2, 2013**

(86) PCT No.: **PCT/US2013/053416**

§ 371 (c)(1),
(2) Date: **Feb. 2, 2015**

(87) PCT Pub. No.: **WO2014/022767**

PCT Pub. Date: **Feb. 6, 2014**

(65) **Prior Publication Data**

US 2015/0203492 A1 Jul. 23, 2015

Related U.S. Application Data

(60) Provisional application No. 61/679,197, filed on Aug. 3, 2012, provisional application No. 61/787,081, filed on Mar. 15, 2013.

(51) **Int. Cl.**

C07D 401/04	(2006.01)
C07D 471/08	(2006.01)
C07D 487/08	(2006.01)
C07D 487/18	(2006.01)
C07D 471/18	(2006.01)
C07H 17/02	(2006.01)

(52) **U.S. Cl.**
CPC ***C07D 471/08*** (2013.01); ***C07D 401/04*** (2013.01); ***C07D 471/18*** (2013.01); ***C07D 487/08*** (2013.01); ***C07D 487/18*** (2013.01); ***C07H 17/02*** (2013.01)

(58) **Field of Classification Search**
CPC .. C07D 401/04; C07D 471/08; C07D 487/08; C07D 487/18
See application file for complete search history.

(56) **References Cited**

FOREIGN PATENT DOCUMENTS

WO	WO 2004/080971	9/2004
WO	WO 2004/094372	11/2004
WO	WO 2005/099709	10/2005
WO	WO 2005/123050	12/2005
WO	WO 2005/123680	12/2005
WO	WO 2006/076575	7/2006
WO	WO 2006/089005	8/2006
WO	WO 2007/070816	6/2007
WO	WO 2007/070818	6/2007
WO	WO 2007/070826	6/2007
WO	WO 2008/076805	6/2008
WO	WO 2008/157162	12/2008
WO	WO 2009/114677	9/2009
WO	WO 2011/100401	8/2011
WO	WO 2011/100402	8/2011
WO	WO 2013/022814	2/2013
WO	WO 2013/022818	2/2013
WO	WO 2013/055984	4/2013
WO	WO 2013/056034	4/2013
WO	WO 2013/056060	4/2013
WO	WO 2013/093484	6/2013
WO	WO 2013/118805	8/2013
WO	WO 2013/174937	11/2013

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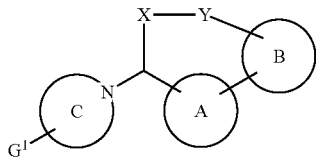
(57) **ABSTRACT**

The present invention provides compounds of Formula (X): (Formula (X), or stereoisomers, tautomers, or pharmaceutically acceptable salts thereof, wherein all the variables are as defined herein. These compounds are selective factor XIa inhibitors or dual inhibitors of FXIa and plasma kallikrein. This invention also relates to pharmaceutical compositions comprising these compounds and methods of treating thromboembolic and/or inflammatory disorders using the same.

(X)



14 Claims, No Drawings