US009408829B2

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

(10) **Patent No.: US 9,408,829 B2**
(45) **Date of Patent: Aug. 9, 2016**

(54) **INHIBITORS OF CD40-TRAF6 INTERACTION**

(71) Applicants: **Ludwig-Maximilians-Universitaet Muenchen**, Munich (DE); **Maastricht University**, Maastricht (NL); **Academisch Ziekenhuis Maastricht**, Maastricht (NL)

(72) Inventors: **Esther Lutgens**, Munich (DE); **Christian Weber**, Munich (DE); **Gerry Nicolaes**, Sint Geertruid (NL)

(73) Assignees: **LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN**, München (DE); **MAASTRICHT UNIVERSITY**, Maastricht (NL); **ACADEMISCH ZIEKENHUIS MAASTRICHT**, Maastricht (NL)

( * ) 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.: **14/417,708**

(22) PCT Filed: **Aug. 27, 2013**

(86) PCT No.: **PCT/EP2013/067714**

§ 371 (c)(1),
(2) Date: **Jan. 27, 2015**

(87) PCT Pub. No.: **WO2014/033122**

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

(65) **Prior Publication Data**

US 2015/0190370 A1 Jul. 9, 2015

(30) **Foreign Application Priority Data**

Aug. 27, 2012 (EP) ..... 12181862

(51) **Int. Cl.**

| | |
|---|---|
| ***A01N 43/06*** | (2006.01) |
| ***A01N 43/08*** | (2006.01) |
| ***A61K 31/135*** | (2006.01) |
| ***A61K 31/381*** | (2006.01) |
| ***C07D 333/22*** | (2006.01) |
| ***C07C 251/24*** | (2006.01) |
| ***C07C 251/26*** | (2006.01) |
| ***C07D 307/52*** | (2006.01) |
| ***A61K 31/137*** | (2006.01) |
| ***A61K 31/341*** | (2006.01) |

(52) **U.S. Cl.**

CPC ..... ***A61K 31/381*** (2013.01); ***A61K 31/137*** (2013.01); ***A61K 31/341*** (2013.01); ***C07C 251/24*** (2013.01); ***C07C 251/26*** (2013.01); ***C07D 307/52*** (2013.01); ***C07D 333/22*** (2013.01)

(58) **Field of Classification Search**

CPC ..... C07C 251/24
USPC ..... 514/448, 417, 649
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2009/0163545 A1* 6/2009 Goldfarb ..... 514/312

FOREIGN PATENT DOCUMENTS

WO WO 2009/143141 A1 11/2009

OTHER PUBLICATIONS

Zarzycka et al. J. Chem. Inf. Model. 2015, 55, 294-307.*
Almazroa, Sarah et al., "Studies with Enaminones: The reaction of enaminones with Aminoheterocycles. A route to Azolopyrimidines, Azolopyridines and Quinolines," *Journal of Heterocyclic Chemisty*, 2004, 41(2):267-272.
El Turk, Farah et al., "An integrative in silico methodology for the identification of modulators of macrophage migration inhibitory factor (MIF) tautomerase activity," *Bioorganic & Medicinal Chemistry*, 2010, 18:5425-5440.
Kurbatov, V.P. et al., "Cobalt (II) Internal Complexes of Some 2-Aminovinyl Ketones," *Journal of General Chemistry USSR*, 1968, 38(10):2194-2197.

* cited by examiner

*Primary Examiner* — Nizal Chandrakumar
(74) *Attorney, Agent, or Firm* — Saliwanchik, Lloyd & Eisenschenk

(57) **ABSTRACT**

The present invention relates to compounds acting as selective inhibitors of CD40-TRAF6 interaction, their use as medicaments and their use in the treatment of (chronic) inflammatory diseases. The present invention also relates to pharmaceutical compositions comprising these compounds.

**1 Claim, 23 Drawing Sheets**