US009636391B2

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

(10) **Patent No.: US 9,636,391 B2**
(45) **Date of Patent: May 2, 2017**

(54) **TUBERCULOSIS VACCINE AND METHOD OF USING SAME**

(71) Applicant: **Mico Bio, Inc.**, New York, NY (US)

(72) Inventors: **Jason Fisher**, New York, NY (US); **Jennifer Lighter**, New York, NY (US)

(73) Assignee: **Mico Bio, Inc.**, New York, NY (US)

(*) 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.: **14/561,774**

(22) Filed: **Dec. 5, 2014**

(65) **Prior Publication Data**

US 2015/0258187 A1 Sep. 17, 2015

Related U.S. Application Data

(63) Continuation of application No. 13/764,241, filed on Feb. 11, 2013, now Pat. No. 8,932,608, which is a continuation of application No. 12/595,006, filed as application No. PCT/US2008/060065 on Apr. 11, 2008, now Pat. No. 8,394,389.

(60) Provisional application No. 60/923,301, filed on Apr. 12, 2007.

(51) **Int. Cl.**

A61K 39/04	(2006.01)
A61K 39/085	(2006.01)
A61K 49/00	(2006.01)
A61K 9/00	(2006.01)
A61K 39/00	(2006.01)

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

CPC ***A61K 39/04*** (2013.01); ***A61K 9/0073*** (2013.01); *A61K 2039/521* (2013.01)

(58) **Field of Classification Search**

USPC 424/9.1, 9.2, 243.1, 248.1; 435/243, 435/252.1, 253.1

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,724,114	A	2/1988	McFarland et al.
8,394,389	B2	3/2013	Lighter et al.
8,932,608	B2	1/2015	Fisher et al.

FOREIGN PATENT DOCUMENTS

WO	WO-00/47225	A2	8/2000
WO	WO-00/47225	A3	8/2000
WO	WO-03/051288	A2	6/2003
WO	WO-03/051288	A3	6/2003
WO	WO-03/075824	A2	9/2003
WO	WO-03/075824	A3	9/2003
WO	WO-2006/136162	A2	12/2006
WO	WO-2006/136162	A3	12/2006
WO	WO-2008/128065	A2	10/2008
WO	WO-2008/128065	A3	10/2008

OTHER PUBLICATIONS

Attiyah et al. "A Model for the Investigation of Factors Influencing Haemorrhagic Necrosis Mediated by Tumour Necrosis Factor in Tissue Sltes Primed With Mycobacterial Antigen Preparations." *Clin. Exp. Immunol.* 88(1992):537-542.

Bahr et al. "Improved Immunotherapy for Pulmonary Tuberculosis With *Mycobacterium caccae*." *Tubercle*. 71(1990):259-266.

Bahr et al. "Two Potential Improvements to BCG and Their Effect on Skin Test Reactivity in the Lebanon." *Tubercle*. 67(1986):205-218.

Bothamley et al. "The Koch Phenomenon and Delayed Hypersensitivity: 1891-1991." *Tubercle*. 72(1991):7-11.

Brennan et al. "Tuberculosis Vaccine Development: Research, Regulatory and Clinical Strategies." *Exp. Opin. Biol. Ther.* 4.9(2004):1493-1504.

Cardona et al. "Immunotherapy With Fragmented *Mycobacterium tuberculosis* Cells Increases the Effectiveness of Chemotherapy Against a Chronical Infection in a Murine Model of Tuberculosis." *Vaccine*. 23(2005):1393-1398.

Cardona et al. "Origina and Development of RUTI, a New Therapeutic Vaccine Against *Mycobacterium tuberculosis* Infection." *Arch. Bronconeumol.* 42.1(2006):25-32.

Cardona et al. "Towards a 'Human-Like' Model of Tuberculosis: Intranasal Inoculation of LPS Induces Intragranulomatous Lung Necrosis in Mice Infected Aerogenically With *Mycobacterium tuberculosis*." *Scand. J. Immunol.* 53(2001):65-71.

Cardona. "RUTI: A New Chance to Shorten the Treatment of Latent Tuberculosis Infection." *Tuberculosis*. 86(2006):273-289.

Carpenter et al. "Preliminary Report on Vaccines Prepared from Gamma-Irradiated *Mycobacterium tuberculosis* and *Brucella suis*." *Am. Rev. Tuberculosis*. 79.3(1959):374-377.

Chen et al. "Single Intranasal Mucosal *Mycobacterium bovis* BCG Vaccination Confers IMproved Protection Compared to Subcutaneous Vaccination Against Pulmonary Tuberculosis." *Infect. Immun.* 72.1(2004) :238-246.

De La Barrera et al. "IL-10 Down-Regulates Costimulatory Molecules on *Mycobacterium tuberculosis*-Pulsed Macrophages and Impairs the Lytic Activity of CD4 and CD8 CTL in Tuberculosis Patients." *Clin. Exp. Immunol.* 138(2004):128-138.

Domingo et al. "Effectiveness and Safety of a Treatment Regimen Based on Isoniazid Plus Vaccination With *Mycobacterium tuberculosis* Cells' Fragments: Field-Study With Naturally *Mycobacterium caprae*-Infected Goats." *Scand. J. Immunol.* 69.6(2009):500-507.

Dubos et al. "Antituberculosis Immunity in Mice Vaccinated With Killed Tubercle Bacilli." *J. Exp. Med.* 97(1953):221-231.

(Continued)

Primary Examiner — Rodney P Swartz

(74) *Attorney, Agent, or Firm* — Mintz Levin Cohn Ferris Glovsky and Popeo, P.C.; Muriel Liberto, Esq.

(57) **ABSTRACT**

Provided is a pharmaceutical composition that includes one or more inactivated *Mycobacterium* spp., which are preferably inactivated using gamma irradiation, and which is then formulated for mucosal or pulmonary delivery to a subject. The pharmaceutical compositions are useful for preventing or treating *mycobacterium*-associated infections in a subject, including a human subject.

13 Claims, No Drawings