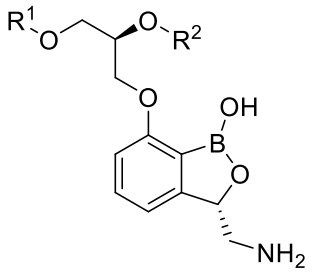
prodrugs described herein exhibit enhanced oral bioavailability and improved systemic exposure critical for the pathogen eradication. Certain compounds described herein exhibit important advantageous dual therapeutic properties: potency against mycobacteria and oral bioavailability. This represent a significant advancement over the majority of antibiotics, such as cephalosporins, that can only be given via intravenous administration in a hospital setting.

Provided herein is a method of treating a nontuberculous mycobacterial infection comprising the administration of a therapeutically effective amount of a compound of Formula (I):



I

or pharmaceutically acceptable salts thereof to a mammal in the need of therapy;

wherein:

R^1 is selected from H, C_{1-24}alkyl-C(=O)-, C_{1-24}alkoxy-C(=O)-, C_{3-7}cycloalkyl-C(=O)-, heteroalkyl-C(=O)-, aryl-C(=O)-, heteroaryl-C(=O)-, and (5-methyl-1,3-dioxol-2-one-4-yl)methyl; and

R^2 is selected from C_{1-24}alkyl-C(=O)-, C_{1-24}alkoxy-C(=O)-, C_{3-7}cycloalkyl-C(=O)-, heteroalkyl-C(=O)-, aryl-C(=O)-, heteroaryl-C(=O)-, and (5-methyl-1,3-dioxol-2-one-4-yl)methyl; or

R^1 and R^2 taken together form a heterocyclic group selected from 1,3-dioxane, 2-C_{1-6}-alkyl-1,3-dioxane, 2,2-di(C_{1-6}-alkyl)-1,3-dioxane, 2-methyl-1,3-dioxane, 2-aryl-1,3-dioxane, 2-(2-carboxyphenyl)-1,3-dioxane, 2-(4-carboxyphenyl)-1,3-dioxane, and 2-C_{1-6}-alkylOC(=O)-1,3-dioxane; each of which is optionally substituted with one to four R^3;

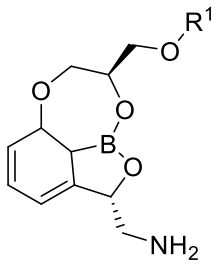
R^3 at each occurrence is independently selected from the group consisting of halo, hydroxy, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, aryl, and heteroaryl; or

two R^3 groups when attached to adjacent carbons are taken together with the carbons to which they are attached to form a fused C_3-C_6 cycloalkyl; or

two R^3 groups when attached to the same carbon are taken together with the carbon to which they are attached to form a spiro C_3-C_6 cycloalkyl;

wherein each R^3 is optionally independently substituted with one to three halo, hydroxy, or C_1-C_3 alkyl; or

the hydrogen in the –OH attached to the boron atom is not present and R^2 in the compound of Formula I, together with the oxygen attached to the boron atom, form a compound of Formula II. Therefore, also provided herein is a method of treating a nontuberculous mycobacterial infection comprising the administration of a therapeutically effective amount of a compound of Formula II:



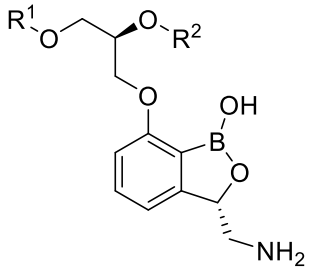
II

or a pharmaceutically acceptable salt thereof to a mammal in the need of therapy;

wherein:

R^1 is selected from H, C_{1-24}alkyl-C(=O)-, C_{1-24}alkoxy-C(=O)-, C_{3-7}cycloalkyl-C(=O)-, heteroalkyl-C(=O)-, aryl-C(=O)-, heteroaryl-C(=O)-, and (5-methyl-1,3-dioxol-2-one-4-yl)methyl.

An aspect of the present disclosure provides a use of a compound of Formula I:



I

or a pharmaceutically acceptable salt or a pharmaceutical composition thereof, in the manufacture of a medicament for treating a nontuberculous mycobacterial infection;

wherein:

R^1 is selected from H, C_{1-24}alkyl-C(=O)-, C_{1-24}alkoxy-C(=O)-, C_{3-7}cycloalkyl-C(=O)-, heteroalkyl-C(=O)-, aryl-C(=O)-, heteroaryl-C(=O)-, and (5-methyl-1,3-dioxol-2-one-4-yl)methyl; and

R^2 is selected from C_{1-24}alkyl-C(=O)-, C_{1-24}alkoxy-C(=O)-, C_{3-7}cycloalkyl-C(=O)-, heteroalkyl-C(=O)-, aryl-C(=O)-, heteroaryl-C(=O)-, and (5-methyl-1,3-dioxol-2-one-4-yl)methyl; or

R^1 and R^2 taken together form a heterocyclic group selected from 1,3-dioxane, 2-C_{1-6}-alkyl-1,3-dioxane, 2,2-di(C_{1-6}alkyl)-1,3-dioxane, 2-methyl-1,3-dioxane, 2-aryl-1,3-dioxane, 2-(2-carboxyphenyl)-1,3-dioxane, 2-(4-carboxyphenyl)-1,3-dioxane, and 2-C_{1-6}alkylOC(=O)-1,3-dioxane; each of which is optionally substituted with one to four R^3;

R^3 at each occurrence is independently selected from the group consisting of halo, hydroxy, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, aryl, and heteroaryl; or

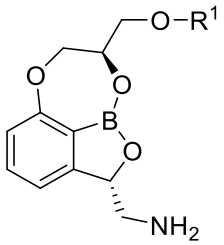
two R^3 groups when attached to adjacent carbons are taken together with the carbons to which they are attached to form a fused C_3-C_6 cycloalkyl; or

two R^3 groups when attached to the same carbon are taken together with the carbon to which they are attached to form a spiro C_3-C_6 cycloalkyl;

wherein each R^3 is optionally independently substituted with one to three halo, hydroxy, or C_1-C_3 alkyl;

and wherein the nontuberculous mycobacteria is selected from *Mycobacterium scrofulaceum, Mycobacterium gordonae, Mycobacterium avium, Mycobacterium abscessus, Mycobacterium intercelleulare, Mycobacterium fortuitum, Mycobacterium peregrinum, Mycobacterium smegmatis,* and *Mycobacterium massiliense.*

Another aspect of the present disclosure provides a use of a compound of Formula II:



II

or a pharmaceutically acceptable salt or a pharmaceutical composition thereof, in the manufacture of a medicament for treating a nontuberculous mycobacterial infection;

wherein:

R^1 is selected from H, C_{1-24}alkyl-C(=O)-, C_{1-24}alkoxy-C(=O)-, C_{3-7}cycloalkyl-C(=O)-, heteroalkyl-C(=O)-, aryl-C(=O)-, heteroaryl-C(=O)-, and (5-methyl-1,3-dioxol-2-one-4-yl)methyl;

and wherein the nontuberculous mycobacteria is selected from *Mycobacterium scrofulaceum, Mycobacterium gordonae, Mycobacterium avium, Mycobacterium abscessus,*

Mycobacterium intercelleulare, Mycobacterium fortuitum, Mycobacterium peregrinum, Mycobacterium smegmatis, and *Mycobacterium massiliense*.

In another example, provided herein is a use of the compounds of Formula I or Formula II or a pharmaceutically acceptable salt thereof in the manufacturing of a medicament for treating nontuberculous mycobacterial infections.

In yet another example, provided herein is a pharmaceutical composition comprising a compound of Formula I or Formula II, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier, for the treatment of nontuberculous mycobacterial infections.

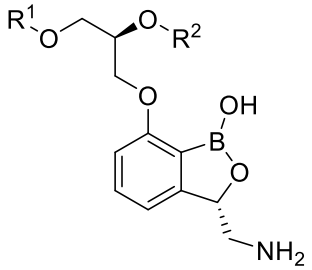
Nontuberculous mycobacteria include, but not limited to, *Mycobacterium scrofulaceum, Mycobacterium gordonae, Mycobacterium avium, Mycobacterium abscessus, Mycobacterium intercelleulare, Mycobacterium fortuitum, Mycobacterium peregrinum, Mycobacterium smegmatis*, and *Mycobacterium massiliense.*

BRIEF DESCRIPTION OF FIGURES

FIG. 1 is a graph for the count of the colony-forming units (CFU) in the lungs of mice 14 days following administration of the compound of Example 4 (10 mg/kg subcutaneously,

WHAT IS CLAIMED IS:

1. Use of a compound of Formula I:



I

or a pharmaceutically acceptable salt or a pharmaceutical composition thereof, in the manufacture of a medicament for treating a nontuberculous mycobacterial infection;

wherein:

R^1 is selected from H, C_{1-24}alkyl-C(=O)-, C_{1-24}alkoxy-C(=O)-, C_{3-7}cycloalkyl-C(=O)-, heteroalkyl-C(=O)-, aryl-C(=O)-, heteroaryl-C(=O)-, and (5-methyl-1,3-dioxol-2-one-4-yl)methyl; and

R^2 is selected from C_{1-24}alkyl-C(=O)-, C_{1-24}alkoxy-C(=O)-, C_{3-7}cycloalkyl-C(=O)-, heteroalkyl-C(=O)-, aryl-C(=O)-, heteroaryl-C(=O)-, and (5-methyl-1,3-dioxol-2-one-4-yl)methyl; or

R^1 and R^2 taken together form a heterocyclic group selected from 1,3-dioxane, 2-C_{1-6}alkyl-1,3-dioxane, 2,2-di(C_{1-6}alkyl)-1,3-dioxane, 2-methyl-1,3-dioxane, 2-aryl-1,3-dioxane, 2-(2-carboxyphenyl)-1,3-dioxane, 2-(4-carboxyphenyl)-1,3-dioxane, and 2-C_{1-6}alkylOC(=O)-1,3-dioxane; each of which is optionally substituted with one to four R^3;

R^3 at each occurrence is independently selected from the group consisting of halo, hydroxy, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, aryl, and heteroaryl; or

two R^3 groups when attached to adjacent carbons are taken together with the carbons to which they are attached to form a fused C_3-C_6 cycloalkyl; or

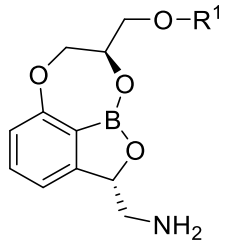
two R^3 groups when attached to the same carbon are taken together with the carbon to which they are attached to form a spiro C_3-C_6 cycloalkyl;

wherein each R^3 is optionally independently substituted with one to three halo, hydroxy, or C_1-C_3 alkyl;

and wherein the nontuberculous mycobacteria is selected from *Mycobacterium scrofulaceum*, *Mycobacterium gordonae*, *Mycobacterium avium*, *Mycobacterium abscessus*,

Mycobacterium intercelleulare, Mycobacterium fortuitum, Mycobacterium peregrinum, Mycobacterium smegmatis, and *Mycobacterium massiliense.*

2. Use of a compound of Formula II:



II

or a pharmaceutically acceptable salt or a pharmaceutical composition thereof, in the manufacture of a medicament for treating a nontuberculous mycobacterial infection;

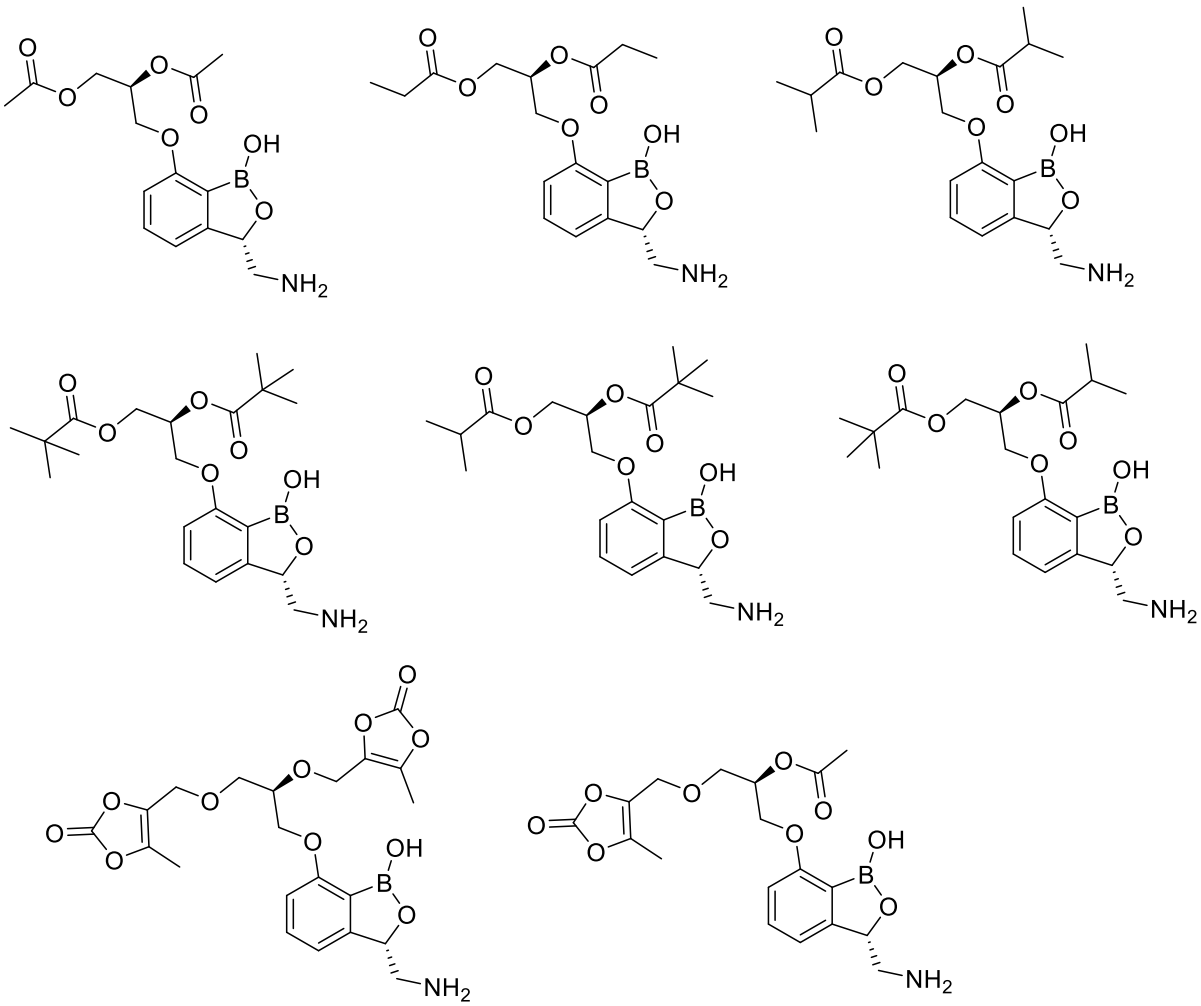
wherein:

R^1 is selected from H, C_{1-24}alkyl-C(=O)-, C_{1-24}alkoxy-C(=O)-, C_{3-7}cycloalkyl-C(=O)-, heteroalkyl-C(=O)-, aryl-C(=O)-, heteroaryl-C(=O)-, and (5-methyl-1,3-dioxol-2-one-4-yl)methyl;

and wherein the nontuberculous mycobacteria is selected from *Mycobacterium scrofulaceum, Mycobacterium gordonae, Mycobacterium avium, Mycobacterium abscessus, Mycobacterium intercelleulare, Mycobacterium fortuitum, Mycobacterium peregrinum, Mycobacterium smegmatis,* and *Mycobacterium massiliense*.

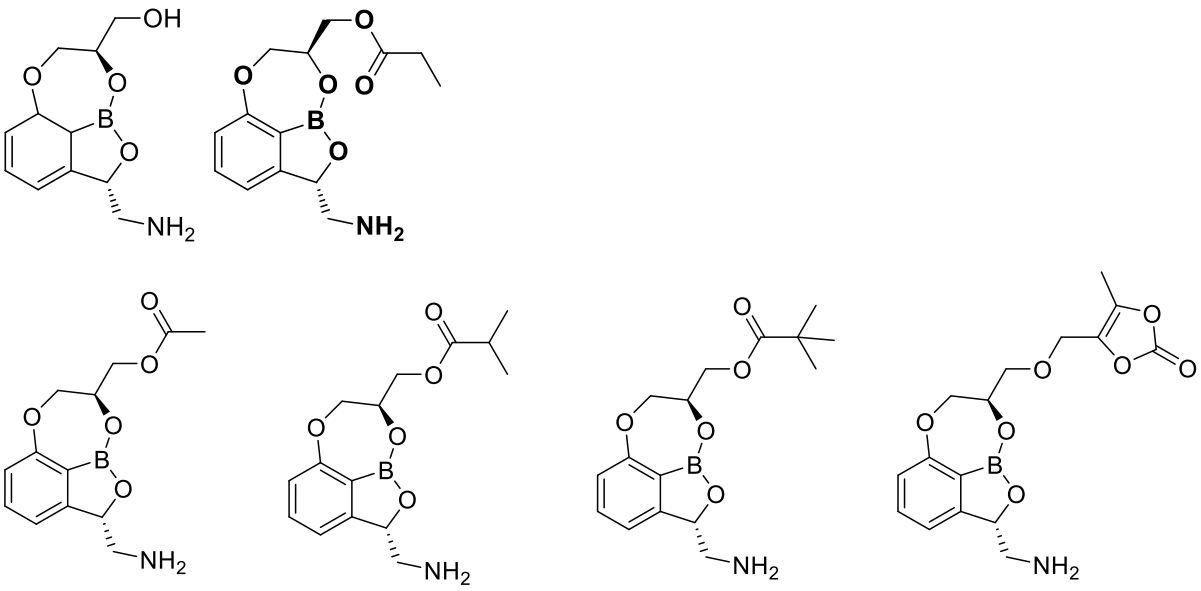
3. The use according to claim 1, wherein R^1 is C_{1-4}alkyl-C(=O)- and R^2 is C_{1-4}alkyl-C(=O)-.

4. The use according to claim 1, wherein the compound is selected:



or a pharmaceutically acceptable salt or a pharmaceutical composition thereof.

5. The use according to claim 2, wherein the compound is selected from:



or a pharmaceutically acceptable salt or a pharmaceutical composition thereof.

6. The use according to any one of claims 1-5, wherein the pharmaceutically acceptable salt is a hydrochloride salt.

7. The use according to any one of claims 1-5, wherein the compound or pharmaceutically acceptable salt thereof is to be administered orally, parenterally, intraperitoneally, intravenously, intraarterially, transdermally, sublingually, intramuscularly, rectally, transbuccally, intranasally, via inhalation, vaginally, intraoccularly, via local administration, subcutaneously, intraadiposally, intraarticularly, intraperitoneally or intrathecally.

8. The use according to any one of claims 1-5, wherein the compound or pharmaceutically acceptable salt thereof is to be administered as a single dosage in a range of 10-1000 mg.

9. The use according to any one of claims 1-5, wherein the compound or pharmaceutically acceptable salt thereof is to be administered as a single dosage in a range of 100-400 mg.

10. The use according to any one of claims 1-5, wherein the compound or pharmaceutically acceptable salt thereof is to be administered once or twice per day in the form of a single dosage.

11. The use according to any one of claims 1-5, wherein the compound or pharmaceutically acceptable salt thereof is to be administered twice per day in a single dosage suitable for an oral solid formulation.

12. The use according to any one of claims 1-5, wherein the infection is a skin, soft tissue, respiratory, blood, intra-abdominal, urinary, bone, or eye infection.

13. The use according to any one of claims 1-5, wherein the compound or pharmaceutical composition is to be administrated for 4-12 months.

14. The use according to any one of claims 1-5 wherein the compound or pharmaceutically acceptable salt thereof or pharmaceutical composition thereof, is to be administered in a dosage form suitable for oral administration.

15. The use according to any one of claims 1-5 wherein the compound, or pharmaceutically acceptable salt thereof or pharmaceutical composition thereof, is to be administered in a dosage form suitable for oral administration, and the compound exhibits an oral bioavailability from about 50% to about 100%.