HUMAN EFFICACIOUS DOSE AND DOSAGE SCHEDULE OF SPR720

CROSS REFERENCE TO RELATED APPLICATION

[0001] This application claims priority to U.S. Provisional Appl. No. 63/272,052, filed October 26, 2021, which is hereby incorporated by reference in its entirety.

BACKGROUND

[0002] Nontuberculous mycobacteria pulmonary disease (NTM-PD) is a chronic, progressive disease that occurs through inhalation of mycobacteria from environmental sources. Among numerous NTM species worldwide, NTM-PD is primarily caused by Mycobacterium avium complex (MAC) which includes *M. avium*, *M. intracellulare*, *M. chimaera* and several subspecies; *M. abscessus* and *M. kansasii*. No systemic oral antimicrobial agents are approved for the treatment of pulmonary nontuberculous mycobacteria infections. Increasing rates of resistance to current standard of care agents, along with tolerability issues, and high rates of clinical relapse, highlight the urgent need for new antimicrobials to treat NTM-PD and also pulmonary tuberculosis. SPR720, the phosphate pro-drug of SPR719, is a novel aminobenzimidazole bacterial DNA gyrase (GyrB) inhibitor. SPR719 has broad-spectrum activity against clinically relevant mycobacteria in vitro and in vivo, in hollow fiber (HF) infection models. Antibacterial agents amendable to safe and efficacious dosing with a single daily dosage are particularly desirable.

SUMMARY

[0003] The present disclose provides methods of treating NTM-PD and other bacterial infections, including pulmonary tuberculous. Clinical studies have established the safety of SPR720 up to daily oral dosages of 2000 mg and that once daily oral dosing is sufficient to provide efficacious plasma levels of the active agent, SPR719. Clinical studies have also shown that there is no significant food effect for SPR720 and that the drug may be given in to a patient in the fed or fasted state. Clinical studies have also established that SPR720 can be administered safely to elderly patients. The present disclosure provides a method of treating a bacterial infection in a patient comprising administering a daily oral dose of SPR720, or a pharmaceutically acceptable salt thereof, the oral dose comprising 100 mg SPR720 to 1500 mg SPR720. In an embodiment the patient is an adult human patient. In an embodiment the daily oral SPR720 comprises 500 mg SPR 720 to 1000 mg SPR720, or 500

mg SPR720, or 1000 mg SPR720. SPR720 can be administered to a patient in the fed or fasted state. The disclosure provides methods of treating tuberculosis infections and nontuberculous mycobacteria infections. The nontuberculous mycobacteria infection can be nontuberculous mycobacteria pulmonary disease (NTM-PD) or treatment refractory NTM-PD. The nontuberculous mycobacteria infection can be due to Mycobacterium avium complex (MAC) infection. SPR720 or a pharmaceutically acceptable salt thereof can be administered to a patient for a period of 7 days to 28 days. In an embodiment, a daily dose of 500 mg or 1000 mg SPR720 is administered to the patient for this period of time as a single oral daily dose. SPR720 or pharmaceutically acceptable salt thereof can be administered alone or in combination with an additional antibacterial agent. The additional antibacterial agent can be, for example, clarithromycin, ethambutol hydrochloride, azithromycin, rifampin, and rifabutin.

[0004] The disclosure provides a method of treating a condition in a patient caused or exacerbated by a nontuberculous mycobacteria infection comprising administering a once daily oral dosage comprising SPR720 or a pharmaceutically acceptable salt thereof to the patient, wherein the patient is an adult human patient, the oral dosage contains 500 mg SPR720 or 1000 mg SPR720, and the once daily oral dosage is administered for 7 days to 28 days.

BRIEF DESCRIPTION OF THE DRAWINGS

[0005] FIGURE 1. Study design for Single Ascending Dose (SAD) and Multiple Ascending Dose (MAD) studies.

[0006] FIGURE 2. Geometric mean plasma SPR719 concentration-time curves Following SPR720 administration. FIG. 2A. Single-ascending doses (SAD) of SPR720 administered in the fed and fasted state and FIG. 2B. SPR720 1000 mg dose administered in the fed and fasting states.

[0007] FIGURE 3. Geometric mean plasma SPR719 concentration-time curves following multiple ascending dose administration of SPR720 over 7 and 14 days. FIG. 3A. Day 1, FIG. 3B, Day 7, and FIG. 3C, Day 14.

DETAILED DESCRIPTION

TERMINOLOGY

[0008] Prior to describing the disclosure in detail, the following terms may be helpful. Unless otherwise specified all terms care their ordinary meaning, accepted in the art of pharmaceutical formulations or methods of treating bacterial infections in patients.

[0009] Recitation of ranges of values are merely intended to serve as a shorthand method of referring individually to each separate value falling within the range, unless otherwise indicated herein, and each separate value is incorporated into the specification as if it were individually recited herein. The endpoints of all ranges are included within the range and independently combinable. All methods described herein can be performed in a suitable order unless otherwise indicated herein or otherwise clearly contradicted by context. The use of any and all examples, or language indicating an example (*e.g.*, "such as"), is intended merely for illustration and does not pose a limitation on the scope of the invention unless otherwise claimed. No language in the specification should be construed as indicating any non-claimed element as essential to the practice of the invention.

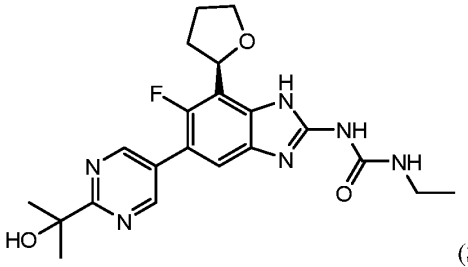
[0010] The terms "a" and "an" do not denote a limitation of quantity, but rather denote the presence of at least one of the referenced items.

[0011] The term "about" is used synonymously with the term "approximately." As one of ordinary skill in the art would understand, the exact boundary of "about" will depend on the component of the composition. Illustratively, the use of the term "about" indicates that values slightly outside the cited values, *i.e.*, plus or minus 0.1% to 10%, which are also effective and safe are included in the value. Thus, compositions slightly outside the cited ranges are also encompassed by the scope of the present claims.

[0012] The terms "comprising," "including," and "containing" are non-limiting. Other non-recited elements may be present in embodiments claimed by these transitional phrases. Where "comprising," "containing," or "including" are used as transitional phrases other elements may be included and still form an embodiment within the scope of the claim. The open-ended transitional phrase "comprising" encompasses the intermediate transitional phrase "consisting essentially of" and the close-ended phrase "consisting of."

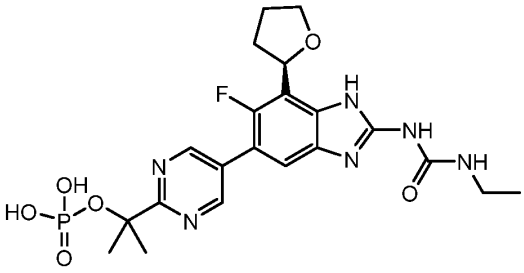
[0013] When a weight of SPR720 that may be in a salt form is given the value refers to the amount of SPR720 rather than the weight of SPR720 salt. Unless clearly contraindicated by the context, "SPR720" includes SPR720 in free phosphate form or as a pharmaceutically acceptable salt or hydrate and can be in an amorphous solid or crystalline form.

[0014] SPR719 (also known as VXc-486, CAS Reg. No. 1384984-18-2) is a potent antibacterial agent, with gyrase B/ Par E inhibitory activity, having the following structure:



(SPR 719)

[0015] SPR720 (CAS Reg. No. 1384984-31-9), generic name fobrepodacin, is an orally active phosphate prodrug of SPR719 having the structure:



(SPR 720)

PHARMACEUTICAL COMPOSITIONS

[0016] "Pharmaceutical compositions" are compositions comprising at least one active agent, such as a SPR720, and at least one other substance, such as a carrier. Pharmaceutical compositions meet the U.S. FDA's GMP (good manufacturing practice) standards for human or non-human drugs. The term "carrier" applied to pharmaceutical compositions/combinations of the disclosure refers to a diluent, excipient, or vehicle with which an active compound is provided.

[0017] Pharmaceutical compositions of the disclosure include any pharmaceutically acceptable formulations capable of delivering systemic SPR719 to the patient. Examples include oral, nasal, transdermal, sublingual, rectal, intravenous (both bolus and infusion), inhalable, and injection (intraperitoneal, subcutaneous, intramuscular, or parenteral) formulations. Oral formulations are particularly contemplated. Oral formulation may be in a dosage unit such as a tablet, pill, capsule, powder, granule, liquid, syrup, emulsion, or droplet.

[0018] The dosage form containing the SPR720 contains an amount sufficient to provide a therapeutic effect by the chosen route of administration. The composition may contain from about 2,000 mg to about 50 mg (preferably, from about 1,000 mg to about 100 mg) of SPR720 or salt form thereof (weight is given for the free base form) and may be

constituted into any form suitable for the selected mode of administration. The dosage form may be formulated for immediate release or controlled release, including delayed release or sustained release. An SPR720 dosage form can include SPR719 as the only active agent or can be formulated in combination with one or more additional active agents, such as another antibacterial agent. Suitable additional active agents include standard of care agents for treating mycobacterial infections, such as clarithromycin (e.g. 500 mg to 1000 mg daily dose) ethambutol hydrochloride (e.g., approximately 15 mg/ kg daily dose), azithromycin (e.g.,250 mg to 500 mg daily dose), streptomycin (no more than 2 grams daily, oral or IM), rifampin (e.g., 100 mg to 1000 mg daily dose or 600 mg daily dose), rifabutin (e.g., 100 mg to 500 mg daily dose or 300 mg daily dose), isoniazid (100 mg to 1000 mg daily dose, or 200 mg, 300 mg, 400 mg, or 500 mg daily dose), or pyrazinamide (100 mg to 1000 mg daily dose, or 200 mg, 300 mg, 400 mg, 500 mg, 600 mg, or 700 mg daily dose), ethionamide (100 mg to 500 mg daily dose, or 200 mg, 250 mg, 300 mg, or 350 mg daily dose), clofazimine, inhaled amikacin, or bedaquiline.

METHODS OF TREATMENT

[0019] The disclosure includes methods of treating bacterial infections, such as tuberculosis and non-tubercular mycobacterial infections. Non-tubercular mycobacterial infections that may be treated with SPR720/SPR719 include infections due to *Mycobacterium avium* complex (MAC), which includes *M. avium*, *M. intracellulare*, *M. chimaera* and several subspecies. Other non-tubercular mycobacterial infections that may be treated with SPR720/ SPR719 include photochromogens such as *M. kansasii*, *M. simiae,* and *M. marinum*; scotochromogens such as *M. scrofulaceum*, *M. parascrofulaceum* and *M. szulgai*; nonchromogens, a group that includes MAC, as well as *M. ulcerans, M. xenopi, M. malmoense, M. terrae, M. haeomphilium*, and *M. genavense*; and rapid growing nonchromogenic species such as *M. chelonae*, *M. chelonae-abscessus, M. fortuitum*, and *M. peregrinum*; and other non-tubercular mycobacterial organisms, such as *M. smegmatis*, *M. paratuberculosis, M. marinum, M. simiae,* and *M. flavescens.*

[0020] NTMs are responsible for a number of conditions. This disclosure includes a method of treating a condition caused by NTM infection comprising administering a SPR720 or salt thereof, where SPR720 the only active agent or is administered in combination with another active agent, to a patient having such a condition. This disclosure also includes a method of treating a condition exacerbated by NTM infection. Conditions than can be due to NTM infection or exacerbated by NTM infection include respiratory

infection, lung infections, Johne's disease (in ruminants), Crohn's disease, osteomyelitis, peritonitis, pyelonephritis, cervical lymphadenitis, disseminated infection in immunocompromised patients, pulmonary disease, disseminated NTM infection, extrapulmonary NTM, and refractory NTM infection.

[0021] A "therapeutically effective amount of a pharmaceutical composition" is an amount effective, when administered to a subject, to provide a therapeutic benefit, such as to decrease the morbidity and mortality associated with bacterial infection and/ or effect a cure. In certain circumstances a subject suffering from a bacterial infection may not present symptoms of being infected. Thus, a therapeutically effective amount of a compound is also an amount sufficient to significantly reduce the detectable level of microorganism in the subject's blood, serum, sputum, or other bodily fluids, or tissues. A therapeutically effective amount of SPR720 can also be an amount sufficient to reduce the clinical symptoms of a bacterial infection or mycobacteria infection.

[0022] Individuals with NTM infections have considerable variability in their clinical presentation. Diagnosis can be made from clinical symptoms or via culture of respiratory fluid, sputum, or mucous. The symptoms of mycobacteria infection include chronic cough, fatigue, frequent throat clearing, shortness of breath (dyspnea), excessive mucus (sputum) production, fever, night sweats, loss of appetite, unintended weight loss, wheezing, and chest pain. The disclosure also includes, in certain embodiments, using compounds of the disclosure in prophylactic treatment and therapeutic treatment. A therapeutically effective amount of SPR720 includes an oral dosage sufficient to relieve or reduce one or more clinical symptoms of NTM infection.

[0023] In the context of prophylactic or preventative treatment, a "therapeutically effective amount" is an amount sufficient to significantly decrease the incidence of or morbidity and mortality associated with bacterial infection. For example, prophylactic treatment may be administered when a subject is known to be at enhanced risk of bacterial infection, such as a cystic fibrosis or ventilator patient. A significant reduction is any detectable negative change that is statistically significant in a standard parametric test of statistical significance such as Student's T-test, where $p < 0.05$.

[0024] Additional indicators of infective treatment include fewer colony forming units (CFU)/ mL in sputum relative after treatment to the number of CFU/ mL in sputum from a patient prior to SPR720 treatment.

[0025] A "patient" is any individual that can benefit from treatment with SPR720. Patients include adult human patients and pediatric and infant patients. Patients include

human and non-human patients. For examples a patient can be a livestock animal such as a cow, pig, sheep, horse, or goat or a companion animal such as a dog or cat. Dosages of SPR720 are given for adult human patients unless otherwise indicated.

[0026] SPR720 may be administered on any dosage schedule that provides a therapeutically effective amount of SPR720 to the patient. For example, SPR720 can be administered 1, 2, 3, or 4 times per day. An embodiment includes once daily oral administration for a period of one or more days. For example, SPR720 can be administered one or two times daily, or once daily, for 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 days. SPR720 can be orally administered for one or two times daily, or one time daily for a period of 1 month, 2 month, or 3 months. In an embodiment, SPR720 is administered once daily for a period of 7 days, 14 days, or 28 days, 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, or up to 12 months.

[0027] SPR720 can be administered via any acceptable route for capable of providing therapeutically effective plasma levels of SPR719 in the patient. Examples include oral, nasal, transdermal, sublingual, rectal, intravenous (both bolus and infusion), inhalable, and injection (intraperitoneal, subcutaneous, intramuscular, or parenteral) administration. Oral administration is particularly contemplated. Oral administration of SPR720 can be effected by any pharmaceutically acceptable oral dosage form, such as a tablet, pill, capsule, powder, granule, liquid, syrup, emulsion, or droplet.

[0028] SPR720 can be administered in any amount capable of providing a safe and therapeutically effective amount of SPR719 to the patient. For example, a daily dose of from about 2,000 mg to about 50 mg (preferably, from about 1,000 mg to about 100 mg) of SPR720 or salt form thereof (weight is given for the free base form) can be administered to an adult human patient. For example 100 mg, 200 mg, 250 mg, 300 mg, 400 mg, 500 mg, 600 mg, 700 mg, 750 mg, 800 mg, 900 mg, 1000, 1100 mg, 1200 mg, or 1250 mg SPR720 can be administered daily.

[0029] SPR720 or a pharmaceutically acceptable salt thereof can be administered alone to provide SPR719 as the only active agent or SPR720 can be administered in combination with one or more additional active agents, such as an additional antibacterial agent. For an adult human patient, a method of treatment in which an oral dose of 500 mg or 1000 mg SPR720 is administered for a period of 7 to 28 days in included as an embodiment of this disclosure. Pediatric patients can also be treated with SPR720. The pediatric dose can be reduced relative to the adult dose to account for the lower weight of the pediatric patient.

[0030] There is only one approved method for treating NTM infection, amikacin liposome inhalation suspension. SPR720 can be administered in combination with amikacin liposome inhalation suspension. SPR720 can be administered to a patient who has been treated with amikacin liposome inhalation suspension for a period of 1 or more months, for example 6 weeks, 6 months, or 12 months, without improvement or whose symptoms have not been adequately addressed. Methods of treatment include administering SPR720 in combination with 1 or 2 additional active agents for a period of up to 18 months. Suitable additional active agents include standard of care agents for treating mycobacterial infections, such as clarithromycin (e.g. 500 mg to 1000 mg daily dose) ethambutol hydrochloride (e.g., approximately 15 mg/ kg daily dose), azithromycin (e.g.,250 mg to 500 mg daily dose), streptomycin (no more than 2 grams daily, oral or IM), rifampin (e.g., 100 mg to 1000 mg daily dose or 600 mg daily dose), rifabutin (e.g., 100 mg to 500 mg daily dose or 300 mg daily dose), isoniazid (100 mg to 1000 mg daily dose, or 200 mg, 300 mg, 400 mg, or 500 mg daily dose), or pyrazinamide (100 mg to 1000 mg daily dose, or 200 mg, 300 mg, 400 mg, 500 mg, 600 mg, or 700 mg daily dose), ethionamide (100 mg to 500 mg daily dose, or 200 mg, 250 mg, 300 mg, or 350 mg daily dose), clofazimine, inhaled amikacin, or bedaquiline.

[0031] It is recommended that SPR720 not be administered in combination with a strong inhibitor or inducer of CYP3A. Methods of treatment include advising the patient that SPR720 should not be administered in combination with a strong CYP3A inhibitor or inducer, and if the patient is currently taking a strong CYP3A inducer or inhibitor switching the patient to a different medication prior to administering SPR720, temporarily discontinuing the strong CYP3A inhibitor or inducer, or administering the strong CYP3A inhibitor or inducer medication in combination with SPR720 and monitoring the patient's SPR719 plasma levels weekly and reducing or increasing the dose of SPR720 so that the patient's SPR719 plasma levels remain between 100 ng/nl and 10000 ng/nl.

EXAMPLES

EXAMPLE 1. Pharmacokinetics of SPR720/SPR719 Administered in the Fed and Fasted States in Single Ascending Dose Study

[0032] The following study was conducted in healthy volunteers to evaluate the safety, tolerability, and pharmacokinetics of SPR720/SPR719. The study included 7 SAD cohorts, of which one was a food effect cohort. SPR720 or placebo (n=8/ cohort, 3:1 randomization) were administered to subjects at doses of 100 to 2000 mg in the fasted or fed

state. The cohorts administered SPR720 in the fed state were administered 1000 mg or 500 mg (healthy elderly cohort) SPR720. A schematic of the study design appears in FIG. 1.

[0033] Across SAD cohorts, a dose proportional and greater-than dose proportional increase in plasma SPR719 C_{max} and AUC_{0-24}, was observed. Following administration of a high fat meal, a small decrease in plasma exposure relative to plasma exposure in the fasted state. This decrease was considerer non-clinically significant. The median T_{max} for SPR719 ranged from 2.75 hours to 8 hours across cohorts and the mean elimination half-life ($t_{1/2}$) ranged from 2.92 to 4.5 hrs. Urinary excretion of SPR719 (0-24 hrs.) was low (0.5%). Mean plasma concentration/ time curves for fasted and elderly fed cohorts are provided in FIG. 1A and for fed and fasted cohorts each administered 1000 mg SPR720 are provided in FIG. 1B. Treatment adverse events for all SAD cohorts are listed in Table. 1.

Table 1. Incidence of treatment-emergent adverse events in single-ascending dose cohorts

SAD	Number (%) of Subjects				
Event	Placebo Overall (n=14)	Cohort 1 100 mg (N=6)	Cohort 2 250 mg (N=6)	Cohort 3 500 mg (N=6)	Cohort 4 1000 mg Fasted (N=6)
Nausea	0	0	0	0	0
Headache	1 (7.1)	0	0	0	1 (16.7)
Vomiting	0	0	0	0	0
Diarrhea	0	0	0	1 (16.7)	0
Event	Cohort 4 1000 mg Fed (N=6)	Cohort 5 1500 mg (N=6)	Cohort 6 2000 mg (N=6)	500 mg Elderly (N=6)	Overall SPR720 (n=42)
Nausea	0	4 (66.7)	5 (83.3)	0	9 (21.4)
Headache	0	3 (50.0)	3 (50.0)	0	7 (16.7)
Vomiting	0	3 (50.0)	5 (83.3)	0	8 (19.0)
Diarrhea	0	0	2 (33.3)	0	3 (7.1)

Of 42 subjects, 18 (42.9%) reported a total of 35 TEAEs; all were mild or moderate. More subjects reported TEAEs in the 1500 mg and 2000 mg cohorts (66.7% and 100%, respectively)

EXAMPLE 2. Pharmacokinetics of SPR720/SPR719 Administered in the Fed and Fasted States in Multiple Ascending Dose Study

[0034] The multiple ascending dose study utilized 5 cohorts of 8 subject. Three cohorts were administered a total daily dose of 500 mg to 1500 mg in the fasted state for 7 days. Two cohorts were administered a total daily dose of 500 mg or 1000 mg in the fed state for 14 days. Safety was also monitored throughout the study. Across MAD cohorts, SPR719 both plasma C_{max} and AUC increased in a greater than dose proportional manner with increasing oral doses of SPR720. Repeated oral dosing of SPR720 in healthy human subject resulted in a decrease (~40%) in plasm exposure of SPR719 at day 7 relative to day 1, suggesting induction of elimination pathways for APR719. Plasma AUC_{0-24} was similar at Days 7 and 14 indicating that induction of elimination had stabilized by Days 7-14. This conclusion was further supported by stable SPR719 trough concentrations by Day 7 (data not shown). Mean plasma concentration/ time curves are shown for the MAD cohorts at days 1 (FIG. 3A), 7 (FIG. 3B), and 14 (FIG. 3C). Treatment adverse events for all SAD cohorts are listed in Table. 2.

Table 2. Incidence of treatment-emergent adverse events in multiple-ascending dose cohorts

MAD	Number (%) of Subjects						
Event	Placebo Overall (N=10)	Cohort 1 500 mg 7 days (N=6)	Cohort 2 1000 mg 7 days (N=6)	Cohort 3 750 mg q12h 7days (N=6)	Cohort 4 500 mg 14 days (N=6)	Cohort 5 1000 mg 14 days (N=6)	Overall MAD SPR720 (N=30)
Diarrhea	1 (10.0)	2 (33.3)	4 (66.7)	4 (66.7)	0	3 (50.0)	13 (42.3)
Headache	0	2 (33.3)	3 (50.0)	2 (33.3)	1 (16.7)	0	8 (26.7)
Nausea	0	2 (33.3)	1 (16.7)	3 (50.0)	0	1 (16.7)	7 (23.3)
Vomiting	0	1 (16.7)	2 (33.3)	1 (16.7)	0	0	4 (13.3)
Diarrhea	0	0	2 (33.3)	1 (16.7)	0	0	3 (10.0)
Abdominal Pain	0	0	1 (16.7)	0	0	1 (16.7)	2 (6.7)

[0035] No serious adverse events were reported in either the SAD or MAD study.

Of 30 subjects who received SPR720, 18 (60.0%) reported a total of 101 TEAEs; all were mild or moderate severity. More subjects reported TEAEs in the 1000 mg or 1500 mg (750 mg q12h) cohorts (50.0% and 66.7%, respectively). One subject in MAD cohort 3 (750 mg q12h) discontinued study drug due to increased pancreatic enzymes; this was asymptomatic and resolved without interventional treatment. This could be attributed to persistently high trough plasma concentrations of SPR719 >1000 ng/mL throughout the

dosing period. Slight elevations in ALT (<3xULN) were observed over 14 days of dosing, which were asymptomatic and reversible; there were no cases of Hy's Law. SPR720 was well-tolerated at repeat daily oral doses up to 1000 mg over the maximum duration of 14 days. In SAD cohorts, C_{max} and AUC increased in a dose-proportional and greater than dose-proportional manner, respectively. In MAD cohorts, exposure declined between Days 1 and 7, but was similar at Days 7 and 14; urinary excretion of SPR719 was minimal. Together with HF pharmacodynamic data, the human safety and PK data for SPR720 suggest that predicted therapeutic exposures can be attained with a well-tolerated once-daily dose.

CLAIMS

1. A method of treating a bacterial infection in a human patient comprising administering one or two times daily an oral dosage comprising 100 mg SPR720 to 1500 mg SPR720 to the patient.

2. The method of claim 1, the patient is an adult human patient.

3. The method of claim 1 or 2, wherein the bacterial infection is a mycobacterial infection and an oral dosage comprising SPR720 or a pharmaceutically acceptable excipient is administered once daily to the patient, wherein the oral dosage contains 500 mg SPR720 or 1000 mg SPR720.

4. The method of any one of claims 1 to 3, wherein the bacterial infection is a tuberculosis infection.

5. The method of any one of claims 1 to 3, wherein the bacterial infection is a nontuberculous mycobacteria infection.

6. The method of claim 5, wherein the nontuberculous mycobacteria infection is an end-stage nontuberculous mycobacteria pulmonary disease (NTM-PD) or treatment refractory NTM-PD.

7. The method of claim 5 wherein the nontuberculous mycobacteria infection is a Mycobacterium avium complex (MAC) infection.

8. The method of any one of claims 1 to 6 wherein SPR720 or a pharmaceutically acceptable salt thereof is orally administered once day for a period of 7 to 28 days.

9. The method of any one of claims 1 to 8, wherein the SPR720 or pharmaceutically acceptable salt thereof is a first antibacterial agent and is administered in combination with one or more additional antibacterial agents selected from clarithromycin, ethambutol hydrochloride, azithromycin, rifampin, and rifabutin.

10. The method of claim 9, wherein the daily dose of the additional agent is 500 mg to 1000 mg clarithromycin, 10 mg/kg to 20 mg/ kg ethambutol hydrochloride, 250 mg to 500 mg, 100 mg to 1000m rifampin, or 100 mg to 500 mg rifabutin.

11. A method of treating a condition in a patient caused or exacerbated by a nontuberculous mycobacteria infection comprising administering a once daily oral dosage comprising SPR720 or a pharmaceutically acceptable salt to the patient, wherein the patient is an adult human patient, the oral dosage contains 500 mg SPR720 or 1000 mg SPR720, and the once daily oral dosage is administered for 7 days to 28 days.

12. A method of treating an NTM infection in a patient comprising administering

(i) a once daily oral dosage of SPR720 or a pharmaceutically acceptable salt thereof, the oral dosage of SPR720 comprising 500 mg to 1000 mg SPR720;

(ii) a once daily oral dosage of clarithromycin or a pharmaceutically acceptable salt thereof, the oral dosage of clarithromycin comprising 500 mg to 1000 g clarithromycin; and

(iii) a once daily oral dosage of ethambutol HCl comprising about 15 mg/ kg ethambutol.