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(54) Title: SECNIDAZOLE FOR USE IN THE TREATMENT OF BACTERIAL VAGINOSIS

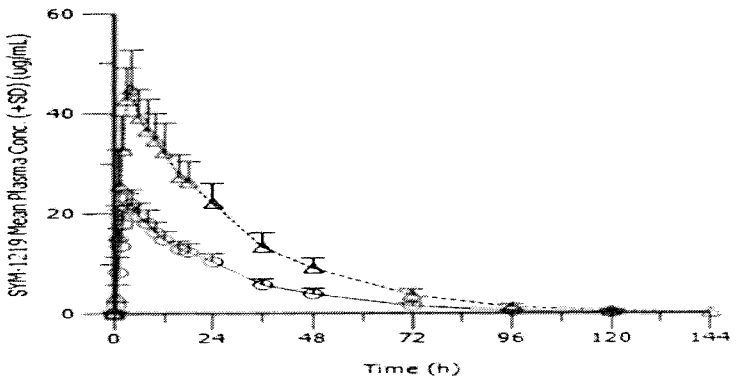

Figure 1

(57) Abstract: Embodiments are directed to a secnidazole formulations and the use of a secnidazole formulation for the treatment of bacterial vaginosis (BV). Embodiments described herein are directed to a method of treating bacterial vaginosis in a subject in need thereof comprising administering to the subject a therapeutically effective amount of secnidazole in a microgranule formulation. In some embodiments, the secnidazole in a microgranule formulation is administered orally. In some embodiments, the secnidazole in a microgranule formulation comprises a plurality of microgranules.

WO 2016/037131 A1

A. Title: Secnidazole For Use In The Treatment Of Bacterial Vaginosis

B. Cross-Reference to Related Applications

[0001] This application claims the benefit of priority to U.S. provisional patent application Serial No. 62/046,731 entitled "Secnidazole for use in the treatment of bacterial vaginosis" filed on September 5, 2014 and U.S. provisional patent application Serial No. 62/101,636 entitled "Secnidazole for use in the treatment of bacterial vaginosis" filed on January 9, 2015, each of which is hereby incorporated by reference in its entirety.

C. Brief Summary of the Invention

[0002] Embodiments described herein are directed to a method of treating bacterial vaginosis in a subject in need thereof comprising administering to the subject a therapeutically effective amount of secnidazole in a microgranule formulation. In some embodiments, the secnidazole in a microgranule formulation is administered orally. In some embodiments, the secnidazole in a microgranule formulation comprises a plurality of microgranules. In some embodiments, the plurality of microgranules each have a particle size range of about 400 to about 841 microns. In some embodiments, the microgranule formulation further comprises at least one of sugar spheres, povidone, polyethylene glycol 4000, Eudragit NE30D, talc, colloidal silicon dioxide or a combination thereof. In some embodiments, the microgranule formulation further comprises at least one of sugar spheres, povidone, polyethylene glycol 4000, Eudragit NE30D, talc, or a combination thereof. In some embodiments, the secnidazole in a microgranule formulation may be mixed, stirred, or otherwise integrated into a food substance. In some embodiments, the food substance includes, but is not limited to applesauce, yogurt, and pudding.

[0003] In some embodiments, the subject is a female. In some embodiments, the subject is an otherwise healthy female. In some embodiments, the subject is a pregnant female. In some embodiments, the subject is an otherwise healthy pregnant female. In some embodiments, the subject is a female having had 3 or fewer bacterial vaginosis infections/episodes in the past 12 months. In some embodiments, the subject is a female having had 4 or more bacterial vaginosis infections/episodes in the past 12 months. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, an odor, or a combination thereof. In some embodiments, the subject is a female presenting with abnormal vaginal discharge, a positive KOH Whiff test, vaginal fluid pH greater than or equal to 4.7, and the presence of "clue cells" greater than

20% of total epithelial cells or any combination thereof. In some embodiments, the subject is a female with confirmed bacterial vaginosis. In some embodiments, the female with confirmed bacterial vaginosis presents with an off-white (milky or gray), thin, homogeneous vaginal discharge, an odor, or a combination thereof. In some embodiments, the subject is a female presenting with abnormal vaginal discharge, a positive KOH Whiff test, vaginal fluid pH greater than or equal to 4.7, and the presence of "clue cells" greater than 20% of total epithelial cells or any combination thereof. In some embodiments, the female with confirmed bacterial vaginosis presents with four Amsel criteria parameters and a gram stain slide Nugent score equal to, or higher than four on bacterial analysis of vaginal samples. In some embodiments, the four Amsel criteria parameters are abnormal vaginal discharge, a positive KOH Whiff test, vaginal fluid pH greater than or equal to 4.7, and the presence of clue cells greater than 20% of total epithelial cells. In some embodiments, the subject is a female with suspected bacterial vaginosis. In some embodiments, the female with suspected bacterial vaginosis presents with an off-white (milky or gray), thin, homogeneous vaginal discharge, an odor, or a combination thereof. In some embodiments, the subject is a female presenting with abnormal vaginal discharge, a positive KOH Whiff test, vaginal fluid pH greater than or equal to 4.7, and the presence of "clue cells" greater than 20% of total epithelial cells or any combination thereof. In some embodiments, the female with suspected bacterial vaginosis presents with four Amsel criteria parameters. In some embodiments, the four Amsel criteria parameters are abnormal vaginal discharge, a positive KOH Whiff test, vaginal fluid pH greater than or equal to 4.7, and the presence of clue cells greater than 20% of total epithelial cells.

[0004] In some embodiments, the therapeutically effective amount of secnidazole in a microgranule formulation is administered as a single dose. In some embodiments, the therapeutically effective amount of secnidazole in a microgranule formulation administered as a single dose is the only dose required to be administered to the subject to achieve a post treatment clinical outcome, resolution of one or more symptoms of bacterial vaginosis, or a combination thereof. In some embodiments, the therapeutically effective amount of secnidazole in a microgranule formulation is 2 grams. In some embodiments, the therapeutically effective amount of secnidazole in a microgranule formulation is an amount of secnidazole in a microgranule formulation that exhibits a plasma Cmax of between about 34.5 μg/ml and about 58.3 μg/ml in the subject. In some embodiments, the therapeutically effective amount of secnidazole in a microgranule formulation is an amount of secnidazole in

a microgranule formulation that exhibits a plasma Cmax of between about 17.4 μg/ml and about 26.5 μg/ml in the subject. In some embodiments, the therapeutically effective amount of secnidazole in a microgranule formulation is an amount of secnidazole that exhibits a tmax of about 3 hours to about 4.05 hours. In some embodiments, the therapeutically effective amount of secnidazole in a microgranule formulation is an amount of secnidazole that exhibits a tmax of about 2 hours to about 6 hours. In some embodiments, the therapeutically effective amount of secnidazole in a microgranule formulation is co-administered with an additional compound selected from ethinyl estradiol (EE2), norethindrone (NET), and a combination thereof.

[0005] Some embodiments further comprise determining a post-treatment clinical outcome. In some embodiments, a post-treatment clinical outcome is indicative of a clinical outcome responder. Some embodiments further comprise determining a post-treatment clinical outcome. In some embodiments, a post-treatment clinical outcome of clinical cure is defined as a clinical outcome responder. In some embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, and clue cells less than 20% of total epithelial cells, post-treatment. In some embodiments, a clinical outcome responder is a subject with a gram stain slide Nugent score of less than four, post-treatment. In some embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, clue cells less than 20% of total epithelial cells), and a gram stain slide Nugent score of less than four, post-treatment. In some embodiments, administering to the subject a therapeutically effective amount of secnidazole in a microgranule formulation results in better than expected effectiveness than FDA-approved drugs used in the treatment of bacterial vaginosis. In some embodiments, administering to the subject a therapeutically effective amount of secnidazole in a microgranule formulation results in superior effectiveness than FDA-approved drugs used in the treatment of bacterial vaginosis. In some embodiments, administering to the subject a therapeutically effective amount of secnidazole in a microgranule formulation results in a higher rate of clinical cure than FDA-approved drugs used in the treatment of bacterial vaginosis. In some embodiments, administering to the subject a therapeutically effective amount of secnidazole in a microgranule formulation results in a better than expected safety profile than FDA-approved drugs used in the treatment of bacterial vaginosis. In some embodiments, administering to the subject a therapeutically effective amount of secnidazole in a microgranule formulation results in a more favorable safety profile than FDA-approved drugs

used in the treatment of bacterial vaginosis. In some embodiments, the therapeutically effective amount of secnidazole in a microgranule formulation is mixed into a food substance. In some embodiments, the food substance includes, but is not limited to applesauce, yogurt, and pudding.

[0006] Some embodiments further comprise administering an additional compound selected from ethinyl estradiol (EE2), norethindrone (NET), or a combination thereof. In some embodiments, the additional compound is administered on the same day as the secnidazole microgranule formulation. In some embodiments, the additional compound is administered on a different day than the secnidazole microgranule formulation. In some embodiments, the secnidazole microgranule formulation does not affect the contraceptive efficacy of the additional compound. In some embodiments, the subject has a resolution of one or more symptoms of bacterial vaginosis within up to about seven days after administration. In some embodiments, the subject has an alleviation of one or more symptoms of bacterial vaginosis within up to about three days after administration.

[0007] Embodiments herein are directed to a microgranule formulation comprising secnidazole, or pharmaceutically acceptable salts thereof. In some embodiments, the microgranule formulation comprises a therapeutically effective amount of secnidazole, or pharmaceutically acceptable salts thereof. In some embodiments, the microgranule formulation is a delayed release formulation. In some embodiments, the delayed release formulation, when administered to a subject provides a secnidazole concentration profile characterized by a change in secnidazole concentration as function of time that is less than that of an immediate release secnidazole microgranule formulation. In some embodiments, the delayed release formulation, when administered to a subject provides a secnidazole concentration profile characterized by a T_{max} that is greater than that of an immediate release secnidazole microgranule formulation. In some embodiments, the delayed release formulation, when administered to a subject provides a secnidazole concentration profile characterized by a C_{max} that is greater than that of an immediate release secnidazole microgranule formulation. In some embodiments, the delayed release formulation, when administered to a subject provides a secnidazole concentration profile characterized by a AUC that is greater than that of an immediate release secnidazole microgranule formulation. In some embodiments, the microgranule formulation comprises about 1 g to about 2 g of secnidazole or pharmaceutically acceptable salts thereof. In some embodiments, the

microgranule formulation comprises about 2 g of secnidazole or pharmaceutically acceptable salts thereof. In some embodiments, the microgranule formulation is suitable for oral administration. Some embodiments further comprise sugar spheres, povidone, polyethylene glycol 4000, Eudragit NE30D, talc, colloidal silicon dioxide or any combination thereof. In some embodiments, the microgranule formulation further comprises at least one of sugar spheres, povidone, polyethylene glycol 4000, Eudragit NE30D, talc, colloidal silicon dioxide or a combination thereof. Some embodiments further comprise polyethylene glycol 4000 and Eudragit NE30D. In some embodiments, the microgranule formulation comprises a plurality of microgranules. In some embodiments, the plurality of microgranules each have a particle size range of about 400 to about 841 microns.

H. Brief Description of the Figures

[0008] Figure 1 illustrates the mean (±SD) SYM-1219 plasma concentration (μg/mL) for the 1 g dose (circle markers) and the 2 g dose (triangle markers) over time.

[0009] Figure 2 illustrates the mean (±SD) EE2 plasma concentrations (pg/mL) for Group B1 over time where (1) EE2 was administered alone (circle markers) on Day 1 of Period 1; and (2) EE2 was administered in conjunction with 2 gram microgranule formulation SYM-1219 on Day 1 of Period 2 (triangle markers).

[0010] Figure 3 illustrates the mean (±SD) EE2 plasma concentrations (pg/mL) for Group B2 over time where (1) EE2 was administered alone (circle markers) on Day 1 of Period 1; and (2) 2 gram microgranule formulation SYM-1219 was administered on Day 1 of Period 2 and EE2 was administered on Day 2 of Period 2 (triangle markers).

[0011] Figure 4 illustrates the mean (±SD) NET plasma levels (ng/mL) for Group B1 over time where (1) NET alone was administered on Day 1 of Period 1 (circle markers), and (2) NET followed by 2 gram microgranule formulation of SYM-1219 was administered on Day 1 of Period 2 (triangle markers).

[0012] Figure 5 illustrates the mean (±SD) NET plasma levels (ng/mL) for Group B2 over time where (1) NET alone was administered on Day 1 of Period 1 (circle markers), and (2) 2 gram microgranule formulation of SYM-1219 was administered on Day 1 of Period 2 and NET was administered on Day 2 of Period 2 (triangle markers).

I. Detailed Description

[0013] Before the present formulations and methods are described, it is to be understood that this invention is not limited to the particular processes, compounds, or methodologies described, as these may vary. It is also to be understood that the terminology used in the description is for the purpose of describing the particular versions or embodiments only, and is not intended to limit the scope of the present invention. Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of embodiments of the present invention, the preferred methods, devices, and materials are now described. All publications mentioned herein are incorporated by reference in their entirety.

[0014] Secnidazole [1-(2-hydroxypropyl)-2-methyl-5-nitromidazole and pharmaceutically acceptable salts thereof; SYM-1219] is a 5-nitroimidazole compound. Embodiments described in this document are directed to secnidazole formulations and the use of a secnidazole formulation for the treatment of bacterial vaginosis.

[0015] In some embodiments, the secnidazole formulation comprises a secnidazole microgranule formulation. In some embodiments, the secnidazole microgranule formulation is a delayed release formulation. In some embodiments, a delayed release formulation, when administered to a subject that provides a secnidazole concentration profile characterized by a change in secnidazole concentration as function of time that is less than that of an immediate release secnidazole microgranule formulation. In some embodiments, the secnidazole microgranule formulation comprises about 1 g to about 2 g of secnidazole or pharmaceutically acceptable salts thereof. In some embodiments, the secnidazole microgranule formulation comprises about 2 g of secnidazole or pharmaceutically acceptable salts thereof. In some embodiments, the secnidazole microgranule formulation may be suitable for oral administration. In some embodiments, the microgranule formulation may further comprise one or more of the following ingredients selected from sugar spheres, povidone, polyethylene glycol 4000, Eudragit NE30D, talc, and colloidal silicon dioxide. In some embodiments, the microgranule formulation may further comprise one or more of the following ingredients selected from sugar spheres, povidone, polyethylene glycol 4000, Eudragit NE30D, and talc. In some embodiments, the secnidazole microgranule formulation

comprises a plurality of microgranules. In some embodiments, the plurality of microgranules are white to off-white in color. In some embodiments, the plurality of microgranules each have a particle size range of about 400 to about 841 microns. In some embodiments, the microgranules are packaged as unit doses. In some embodiments, the microgranules are packaged as single unit doses. In some embodiments, the microgranules are packaged in such a way as to provide a barrier to oxygen and moisture. In some embodiments, the microgranules are packaged in a foil pouch or sachet. In some embodiments, the foil pouch or sachet is made of a polyester-faced laminated or polyethylene-metallocene-lined aluminum foil pouching material that provides a barrier to oxygen and moisture. In some embodiments, the pouch or sachet is made from a material such as, but not limited to, Fasson® Rapid-Roll® White Cosmetic Web 350 HB.

[0016] In some embodiments, a method of making the secnidazole microgranule formulation comprises coating sugar spheres. In some embodiments, the coating is a process, such as a four-step process. In some embodiments, the process comprises layering the secnidazole on the spheres, seal coating with polyethylene glycol 4000, coating with Eudragit NE30D, and curing. In some embodiments, coating with Eudragit provides a delayed release formulation. In some embodiments, a method of making the secnidazole microgranule formulation comprises blending with talc. In some embodiments, blending with talc increases the flowability of the secnidazole microgranule formulation.

[0017] In some embodiments, a method of making the secnidazole microgranule formulation comprises coating sugar spheres. In some embodiments, the coating is a process, such as a three-step process. In some embodiments, the process comprises layering the secnidazole on the spheres, coating with Eudragit NE30D, and curing. In some embodiments, coating with Eudragit provides a delayed release formulation. In some embodiments, a method of making the secnidazole microgranule formulation comprises blending with talc. In some embodiments, blending with talc increases the flowability of the secnidazole microgranule formulation.

[0018] In some embodiments, a method of treating bacterial vaginosis in a subject in need thereof comprises administering to the subject a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof. In some embodiments, a method of treating bacterial vaginosis in a subject in need thereof comprises administering to the subject a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof

in a microgranule formulation. In some embodiments, the secnidazole microgranule formulation may be suitable for oral administration. In some embodiments, the secnidazole microgranule formulation comprises a plurality of microgranules. In some embodiments, the plurality of microgranules are white to off-white in color. In some embodiments, the plurality of microgranules each have a particle size range of about 400 to about 841 microns. In some embodiments, the secnidazole microgranule formulation may be mixed, stirred, or otherwise integrated into a food substance. In some embodiments, the food substance may be a semisolid or soft food. In some embodiments, the food substance may include, but is not limited to applesauce, pudding, yogurt or the like. In some embodiments, integration of the secnidazole microgranule formulation into a food substance has a taste masking function.

[0019] In some embodiments, the subject is a human. In yet other embodiments, the subject is a human female. In some embodiments, the human female is of an age ranging from a postmenarachal adolescent to a premenopausal woman. In some embodiments, the subject is a pregnant human female.

[0020] In some embodiments, the subject is a female. In some embodiments, the subject is an otherwise healthy female. In some embodiments, the subject is a pregnant female. In some embodiments, the subject is an otherwise healthy pregnant female. In some embodiments, the subject is a female having had 3 or fewer bacterial vaginosis infections in the past 12 months. In some embodiments, the subject is a female having had 4 or more bacterial vaginosis infections in the past twelve months. In some embodiments, the subject is a female with recurring bacterial vaginosis. In some embodiments, a subject with recurring bacterial vaginosis is a subject with 4 or more bacterial vaginosis infections within a twelve-month period. In some embodiments, the subject is a female with frequent bacterial vaginosis infections. In some embodiments, a female with frequent bacterial vaginosis infections is a female with 4 or more bacterial vaginosis infections within a twelve-month period. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, a positive 10% KOH Whiff test or a combination thereof. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on

microscopic examination of a vaginal saline wet mount, and a positive 10% KOH Whiff test. In some embodiments, the subject is a female with confirmed bacterial vaginosis. In some embodiments, bacterial vaginosis is confirmed by the presence of four (4) Amsel criteria parameters selected from an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, a positive 10% KOH Whiff test and a gram stain slide Nugent score equal to, or higher than four (4) on bacterial analysis of vaginal samples. In some embodiments, the subject is a female with suspected bacterial vaginosis. In some embodiments, suspected bacterial vaginosis is indicated by the presence of four (4) Amsel criteria parameters selected from an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, and a positive 10% KOH Whiff test. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, odor, or a combination thereof.

[0021] In some embodiments, a method of treating bacterial vaginosis in a subject comprises administering to the subject a single dose of a therapeutically effective amount of secnidazole in a microgranule formulation, wherein the secnidazole comprises about 1g to about 2 g of the microgranule formulation. In some embodiments, the secnidazole microgranule formulation is co-administered with an additional compound selected from ethinyl estradiol (EE2), norethindrone (NET), or a combination thereof. In some embodiments, the secnidazole microgranule formulation is mixed into a semisolid or soft food substance, such as but not limited to applesauce yogurt and pudding. In some embodiments, the amount of the food substance is about 4-6 ounces.

[0022] In some embodiments, a method of treating bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a plasma Cmax of between about 34.5 μg/ml and about 58.3 μg/ml. In some embodiments, a method of treating bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a plasma Cmax of between about 17.4 μg/ml and about 26.5 μg/ml.

[0023] In some embodiments, a method of treating bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule

formulation that exhibits a tmax of about 3 hours to about 4.05 hours. In some embodiments, a method of treating bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a tmax of about 2 hours to about 6 hours.

[0024] In some embodiments, a method of treating bacterial vaginosis in a subject comprises co-administering to the subject a single dose of a therapeutically effective amount of secnidazole in a microgranule formulation and an additional compound selected from ethinyl estradiol (EE2), norethindrone (NET), or a combination thereof, wherein the secnidazole comprises about 1 g to about 2 g of the microgranule formulation. In some embodiments, the additional compound is co-administered on the same day as the secnidazole microgranule formulation. In some embodiments, the additional compound is administered on a different day than the secnidazole microgranule formulation. In some embodiments, the secnidazole microgranule formulation does not affect the contraceptive efficacy of the additional compound.

[0025] In some embodiments, a method of treating bacterial vaginosis in a subject further comprises determining a post treatment clinical outcome. In some embodiments, a post treatment clinical outcome is indicative of a clinical outcome responder. Some embodiments further comprise determining a post-treatment clinical outcome. In some embodiments, a post-treatment clinical outcome of clinical cure is defined as a clinical outcome responder. In some embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, and clue cells less than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount after treatment with a microgranule formulation comprising about 1 to about 2 grams of secnidazole. In some embodiments, a clinical outcome responder has a gram stain slide Nugent score of less than four (4) after treatment with a single dose of secnidazole. In yet other embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, clue cells less than 20% of total epithelial cells, and a gram stain slide Nugent score of less than four (4) after treatment with a single dose of secnidazole. In some embodiments, a clinical outcome responder has a gram stain slide Nugent score of less than four (4) after treatment with a 2 gram single dose of secnidazole. In yet other embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, clue cells less than 20% of total epithelial cells, and a gram stain

slide Nugent score of less than four (4) after treatment with a 2 gram single dose of secnidazole. In some embodiments, a post-treatment clinical outcome is observable after about 24 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 48 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 72 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 96 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 120 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 168 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 7 to about 10 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 11 to about 20 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 21 to about 30 days after administration.

[0026] In some embodiments, a method of treating bacterial vaginosis further comprises an alleviation of one or more symptoms of bacterial vaginosis within up to about three days after administration to the subject. In some embodiments, a method of treating bacterial vaginosis further comprises an alleviation of one or more symptoms of bacterial vaginosis within up to about three days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, abnormal vaginal odor, abnormal vaginal discharge or a combination thereof. In some embodiments, alleviation refers to a lessening of the severity of one or more symptoms. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 24 hours after administration. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 48 hours after administration. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 72 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 96 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 120 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 168 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about

11 to about 20 days after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 21 to about 30 days after administration to the subject.

[0027] In some embodiments, a method of treating bacterial vaginosis further comprises a resolution of one or more symptoms of bacterial vaginosis within up to about seven days after administration to the subject. In some embodiments, a method of treating bacterial vaginosis further comprises a resolution of one or more symptoms of bacterial vaginosis within up to about seven days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, abnormal vaginal odor, abnormal vaginal discharge or a combination thereof. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 24 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 48 hours after administration. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 72 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 96 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 120 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 168 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 11 to about 20 days after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 21 to about 30 days after administration to the subject.

[0028] In some embodiments, treatment of bacterial vaginosis with a single, 2 gram dose of secnidazole in a microgranule formulation results in better than expected efficacy compared with FDA approved drugs used in the treatment of bacterial vaginosis. In some embodiments, treatment of bacterial vaginosis with a single, 2 gram dose of secnidazole in a microgranule formulation results in superior effectiveness compared with other FDA-approved drugs used in the treatment of bacterial vaginosis. In some embodiments, treatment of bacterial vaginosis with a single, 2 gram dose of secnidazole in a microgranule formulation

results in a higher rate of clinical cure than FDA-approved drugs used in the treatment of bacterial vaginosis. In some embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, and clue cells less than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount after treatment In some embodiments, a single dose of 2 grams of secnidazole results in a better than expected efficacy compared with FDA approved drugs currently used in the treatment of bacterial vaginosis. In some embodiments, treatment of bacterial vaginosis with a single, 2 gram dose of secnidazole results in superior efficacy compared with FDA approved drugs used in the treatment of bacterial vaginosis. In some embodiments, a single dose of 2 grams of secnidazole results in superior efficacy compared with FDA drugs used in the treatment of bacterial vaginosis requiring multiple doses during treatment. For example, Secnidazole has been shown to have a higher rate of clinical cure after 21-30 days of treatment (67.7% clinical cure after a single, 2g oral dose) compared with other FDA approved drugs for the treatment of bacterial vaginosis (Nuvessa – 37% after vaginal single application; Tindamax – 35.6% after 3 day oral regimen and 51.3% after 5 day oral regimen; Clindesse – 41.0-53.45 clinical cure after vaginal single application; Flagyl ER – 61.1 – 62.2% clinical cure after 7 day oral regimen; and Metrogel-Vaginal – 53.0% after 5 day vaginal regimen (all clinical cure rates are 21-30 days after treatment)).

[0029] In some embodiments, treatment of bacterial vaginosis with a single, 2 gram dose of secnidazole results in a better than expected safety profile compared with FDA approved drugs used in the treatment of bacterial vaginosis. In some embodiments, a single dose of 2 grams of secnidazole results in a better than expected safety profile compared with FDA approved drugs used in the treatment of bacterial vaginosis requiring multiple doses during treatment. In some embodiments, treatment of bacterial vaginosis with a single, 2 gram dose of secnidazole results in a superior safety profile compared with FDA approved drugs used in the treatment of bacterial vaginosis. In some embodiments, a single dose of 2 grams of secnidazole results in a superior safety profile compared with FDA approved drugs used in the treatment of bacterial vaginosis requiring multiple doses during treatment. In some embodiments, treatment of bacterial vaginosis with a single, 2 gram dose of secnidazole in a microgranule formulation results in a better than expected safety profile compared with FDA approved drugs used in the treatment of bacterial vaginosis. In some embodiments, a single dose of 2 grams of secnidazole in a microgranule formulation results in a better than expected safety profile compared with FDA approved drugs used in the treatment of bacterial

vaginosis requiring multiple doses during treatment. In some embodiments, treatment of bacterial vaginosis with a single, 2 gram dose of secnidazole in a microgranule formulation results in a superior safety profile compared with FDA approved drugs used in the treatment of bacterial vaginosis. In some embodiments, a single dose of 2 grams of secnidazole in a microgranule formulation results in a superior safety profile compared with FDA approved drugs used in the treatment of bacterial vaginosis requiring multiple doses during treatment. In some embodiments, multiple doses may be given at pre-determined intervals such as but not limited to once a week, bi-weekly, monthly, bimonthly for the duration of treatment. In some embodiment, the duration of treatment may be at least one week. In some embodiment, the duration of treatment may be at least one month. In some embodiments, the duration of treatment is about six months. For example, as can be seen in Table 1, secnidazole has superior safety profile compared with other FDA approved drugs for the treatment of bacterial vaginosis.

[0030] Table 1 – Comparison of key adverse events

Adverse Event	Secnidazole 2 grams (n=72)	Flagyl ER (N=267)	Clindesse (n=368)	Metrogel-Vaginal (n=505)
Headache	1%	18%	3%	5%
Nausea	1%	10%	1%	4%
Abdominal pain	0%	4%	1%	Not reported
Diarrhea	0%	4%	1%	1%
Metallic/Unusual Taste	1%	9%	Not reported	2%
Fungal Infection	3%	Not reported	14%	10%
Vulva/Vaginal Irritation	1%	Not reported	3%	9%

[0031] In some embodiments, treatment of bacterial vaginosis with a single, 2 gram dose of secnidazole results in better than expected efficacy compared with FDA approved drugs used in the treatment of bacterial vaginosis in subjects with frequent bacterial vaginosis infections. In some embodiments, a single dose of 2 grams of secnidazole results in a better than expected efficacy compared with FDA approved drugs used in the treatment of bacterial vaginosis requiring multiple doses during treatment in subjects with frequent bacterial vaginosis infections. In some embodiments, treatment of bacterial vaginosis with a single, 2 gram dose of secnidazole results in superior efficacy compared with FDA approved drugs used in the treatment of bacterial vaginosis in subjects with frequent bacterial vaginosis infections. In some embodiments, a single dose of 2 grams of secnidazole results in superior efficacy compared with FDA approved drugs used in the treatment of bacterial vaginosis requiring multiple doses during treatment in subjects with frequent bacterial vaginosis infections. In some embodiments, subjects with frequent bacterial vaginosis infections are subjects with 4 or more bacterial vaginosis infections within a twelve month period.

[0032] In some embodiments, treatment of bacterial vaginosis with a single, 2 gram dose of secnidazole results in better than expected safety profile compared with FDA approved drugs used in the treatment of bacterial vaginosis with frequent bacterial vaginosis infections. In some embodiments, a single dose of 2 grams of secnidazole results in a better than expected safety profile compared with FDA approved drugs used in the treatment of bacterial vaginosis requiring multiple doses during treatment in subjects with frequent bacterial vaginosis infections. In some embodiments, treatment of bacterial vaginosis with a single, 2 gram dose of secnidazole results in a superior safety profile compared with FDA approved drugs used in the treatment of bacterial vaginosis in subjects with frequent bacterial vaginosis infections. In some embodiments, a single dose of 2 grams of secnidazole results in a superior safety profile compared with FDA approved drugs used in the treatment of bacterial vaginosis requiring multiple doses during treatment in subjects with frequent bacterial vaginosis infections. In some embodiments, subjects with frequent bacterial vaginosis infections are those with 4 or more bacterial vaginosis infections within a twelve month period.

[0033] In some embodiments, a method of treating bacterial vaginosis in a subject in need thereof further comprises administering to at least one of the subjects' sexual partners, a therapeutically effective amount of secnidazole or pharmaceutically acceptable

salts thereof. In some embodiments, a method of treating bacterial vaginosis in a subject in need thereof further comprises administering to at least one of the subjects' sexual partners, a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof in a microgranule formulation. In some embodiments, the secnidazole microgranule formulation may be suitable for oral administration. In some embodiments, the secnidazole microgranule formulation comprises a plurality of microgranules. In some embodiments, the plurality of microgranules are white to off-white in color. In some embodiments, the plurality of microgranules each have a particle size range of about 400 to about 841 microns. In some embodiments, the secnidazole microgranule formulation may be mixed, stirred, or otherwise integrated into a food substance. In some embodiments, the food substance may be a semisolid or soft food. In some embodiments, the food substance may include, but is not limited to applesauce, pudding, yogurt or the like. In some embodiments, integration of the secnidazole microgranule formulation into a food substance has a taste masking function. In some embodiments, the at least one sexual partner of the subject may be a male or a female. In some embodiments, a single dose of a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof may be administered. In some embodiments, a single dose of a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof in a microgranule formulation may be administered. In some embodiments, multiple doses may be given at pre-determined intervals such as but not limited to once a week, bi-weekly, monthly, bimonthly for the duration of treatment. In some embodiment, the duration of treatment may be at least one week. In some embodiment, the duration of treatment may be at least one month. In some embodiments, the duration of treatment is about six months.

[0034] Some embodiments are directed to a method of reducing the incidence and/or risk of a preterm birth. Bacterial vaginosis infections may increase the risk of a preterm birth in a subject. In some embodiments, a method of reducing the incidence and/or risk of a preterm birth in a subject comprises administering to the subject a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof. In some embodiments, a method of reducing the incidence and/or risk of a preterm birth in a subject comprises administering to the subject a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof in a microgranule formulation. In some embodiments, the secnidazole microgranule formulation may be suitable for oral administration. In some embodiments, the secnidazole microgranule formulation comprises a

plurality of microgranules. In some embodiments, the plurality of microgranules are white to off-white in color. In some embodiments, the plurality of microgranules each have a particle size range of about 400 to about 841 microns. In some embodiments, the secnidazole microgranule formulation may be mixed, stirred, or otherwise integrated into a food substance. In some embodiments, the food substance may be a semisolid or soft food. In some embodiments, the food substance may include, but is not limited to applesauce, pudding, yogurt or the like. In some embodiments, integration of the secnidazole microgranule formulation into a food substance has a taste masking function. In some embodiments, the subject is a human. In yet other embodiments, the subject is a pregnant human female.

[0035] In some embodiments, the subject is a female. In some embodiments, the subject is an otherwise healthy female. In some embodiments, the subject is a pregnant female. In some embodiments, the subject is an otherwise healthy pregnant female. In some embodiments, the subject is a female having had 3 or fewer bacterial vaginosis infections in the past 12 months. In some embodiments, the subject is a female having had 4 or more bacterial vaginosis infections in the past twelve months. In some embodiments, the subject is a female with recurring bacterial vaginosis. In some embodiments, a subject with recurring bacterial vaginosis is a subject with 4 or more bacterial vaginosis infections within a twelve-month period. In some embodiments, the subject is a female with frequent bacterial vaginosis infections. In some embodiments, a female with frequent bacterial vaginosis infections is a female with 4 or more bacterial vaginosis infections within a twelve-month period. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, a positive 10% KOH Whiff test or a combination thereof. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, and a positive 10% KOH Whiff test. In some embodiments, the subject is a female with confirmed bacterial vaginosis. In some embodiments, bacterial vaginosis is confirmed by the presence of four (4) Amsel criteria parameters selected from an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to

20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, a positive 10% KOH Whiff test and a gram stain slide Nugent score equal to, or higher than four (4) on bacterial analysis of vaginal samples. In some embodiments, the subject is a female with suspected bacterial vaginosis. In some embodiments, suspected bacterial vaginosis is indicated by the presence of four (4) Amsel criteria parameters selected from an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, and a positive 10% KOH Whiff test. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, odor, or a combination thereof.

[0036] In some embodiments, a method of reducing the incidence and/or risk of a preterm birth in a subject comprises administering to the subject a single dose of a therapeutically effective amount of secnidazole in a microgranule formulation, wherein the secnidazole comprises about 1g to about 2 g of the microgranule formulation. In some embodiments, the secnidazole microgranule formulation is co-administered with an additional compound selected from ethinyl estradiol (EE2), norethindrone (NET), or a combination thereof. In some embodiments, the secnidazole microgranule formulation is mixed into a semisolid or soft food substance, such as but not limited to applesauce yogurt and pudding. In some embodiments, the amount of the food substance is about 4-6 ounces.

[0037] In some embodiments, a method of reducing the incidence and/or risk of a preterm birth in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a plasma Cmax of between about 34.5 μg/ml and about 58.3 μg/ml. In some embodiments, a method of treating bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a plasma Cmax of between about 17.4 μg/ml and about 26.5 μg/ml.

[0038] In some embodiments, a method of reducing the incidence and/or risk of a preterm birth in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a tmax of about 3 hours to about 4.05 hours. In some embodiments, a method of treating bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a tmax of about 2 hours to about 6 hours.

[0039] In some embodiments, a method of reducing the incidence and/or risk of a preterm birth in a subject further comprises a term birth. In some embodiments, a method of reducing the incidence and/or risk of a preterm birth in a subject further comprises determining a post treatment clinical outcome. In some embodiments, a post treatment clinical outcome is indicative of a clinical outcome responder. Some embodiments further comprise determining a post-treatment clinical outcome. In some embodiments, a post-treatment clinical outcome of clinical cure is defined as a clinical outcome responder. In some embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, and clue cells less than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount after treatment with a microgranule formulation comprising about 1 to about 2 grams of secnidazole. In some embodiments, a clinical outcome responder has a gram stain slide Nugent score of less than four (4) after treatment with a single dose of secnidazole. In yet other embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, clue cells less than 20% of total epithelial cells, and a gram stain slide Nugent score of less than four (4) after treatment with a single dose of secnidazole. In some embodiments, a clinical outcome responder has a gram stain slide Nugent score of less than four (4) after treatment with a 2 gram single dose of secnidazole. In yet other embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, clue cells less than 20% of total epithelial cells, and a gram stain slide Nugent score of less than four (4) after treatment with a 2 gram single dose of secnidazole. In some embodiments, a post-treatment clinical outcome is observable after about 24 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 48 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 72 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 96 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 120 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 168 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 7 to about 10 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 11 to about 20 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 21 to about 30 days after administration.

[0040] In some embodiments, a method of reducing the incidence and/or risk of a preterm birth in a subject further comprises an alleviation of one or more symptoms of bacterial vaginosis within up to about three days after administration to the subject. In some embodiments, a method of treating bacterial vaginosis further comprises an alleviation of one or more symptoms of bacterial vaginosis within up to about three days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, abnormal vaginal odor, abnormal vaginal discharge or a combination thereof. In some embodiments, alleviation refers to a lessening of the severity of one or more symptoms. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 24 hours after administration. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 48 hours after administration. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 72 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 96 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 120 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 168 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 11 to about 20 days after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 21 to about 30 days after administration to the subject.

[0041] In some embodiments, a method of reducing the incidence and/or risk of a preterm birth in a subject further comprises a resolution of one or more symptoms of bacterial vaginosis within up to about seven days after administration to the subject. In some embodiments, a method of treating bacterial vaginosis further comprises a resolution of one or more symptoms of bacterial vaginosis within up to about seven days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, abnormal vaginal odor, abnormal vaginal discharge or a combination thereof. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 24 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 48 hours after administration. In some

embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 72 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 96 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 120 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 168 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 11 to about 20 days after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 21 to about 30 days after administration to the subject.

[0042] Some embodiments are directed to a method of reducing the incidence and/or risk of a subject transmitting human immunodeficiency virus (HIV) to a sexual partner. Bacterial vaginosis infections may increase the risk of a HIV transmission to sexual partner. In some embodiments, a method of reducing the incidence and/or risk of the subject transmitting HIV to a sexual partner in a subject comprises administering to the subject a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof. In some embodiments, a method of reducing the incidence and/or risk of a preterm birth in a subject comprises administering to the subject a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof in a microgranule formulation. In some embodiments, the secnidazole microgranule formulation may be suitable for oral administration. In some embodiments, the secnidazole microgranule formulation comprises a plurality of microgranules. In some embodiments, the plurality of microgranules are white to off-white in color. In some embodiments, the plurality of microgranules each have a particle size range of about 400 to about 841 microns. In some embodiments, the secnidazole microgranule formulation may be mixed, stirred, or otherwise integrated into a food substance. In some embodiments, the food substance may be a semisolid or soft food. In some embodiments, the food substance may include, but is not limited to applesauce, pudding, yogurt or the like. In some embodiments, integration of the secnidazole microgranule formulation into a food substance has a taste masking function.

[0043] In some embodiments, the subject is a human female.In some embodiments, the subject is a female. In some embodiments, the subject is an otherwise healthy female. In some embodiments, the subject is a female with HIV. In some embodiments, the subject is an otherwise healthy pregnant female. In some embodiments, the subject is a female having had 3 or fewer bacterial vaginosis infections in the past 12 months. In some embodiments, the subject is a female having had 4 or more bacterial vaginosis infections in the past twelve months. In some embodiments, the subject is a female with recurring bacterial vaginosis. In some embodiments, a subject with recurring bacterial vaginosis is a subject with 4 or more bacterial vaginosis infections within a twelve-month period. In some embodiments, the subject is a female with frequent bacterial vaginosis infections. In some embodiments, a female with frequent bacterial vaginosis infections is a female with 4 or more bacterial vaginosis infections within a twelve-month period. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, a positive 10% KOH Whiff test or a combination thereof. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, and a positive 10% KOH Whiff test. In some embodiments, the subject is a female with confirmed bacterial vaginosis. In some embodiments, bacterial vaginosis is confirmed by the presence of four (4) Amsel criteria parameters selected from an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, a positive 10% KOH Whiff test and a gram stain slide Nugent score equal to, or higher than four (4) on bacterial analysis of vaginal samples. In some embodiments, the subject is a female with suspected bacterial vaginosis. In some embodiments, suspected bacterial vaginosis is indicated by the presence of four (4) Amsel criteria parameters selected from an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, and a positive 10% KOH Whiff test. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, odor, or a combination thereof.

[0044] In some embodiments, a method of reducing the incidence and/or risk of a subject transmitting HIV to a sexual partner in a subject comprises administering to the subject a single dose of a therapeutically effective amount of secnidazole in a microgranule formulation, wherein the secnidazole comprises about 1g to about 2 g of the microgranule formulation. In some embodiments, the secnidazole microgranule formulation is co-administered with an additional compound selected from ethinyl estradiol (EE2), norethindrone (NET), or a combination thereof. In some embodiments, the secnidazole microgranule formulation is mixed into a semisolid or soft food substance, such as but not limited to applesauce yogurt and pudding. In some embodiments, the amount of the food substance is about 4-6 ounces.

[0045] In some embodiments, a method of reducing the incidence and/or risk of a subject transmitting HIV to a sexual partner in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a plasma Cmax of between about 34.5 μg/ml and about 58.3 μg/ml. In some embodiments, a method of treating bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a plasma Cmax of between about 17.4 μg/ml and about 26.5 μg/ml.

[0046] In some embodiments, a method of reducing the incidence and/or risk of a subject transmitting HIV to a sexual partner in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a tmax of about 3 hours to about 4.05 hours. In some embodiments, a method of treating bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a tmax of about 2 hours to about 6 hours.

[0047] In some embodiments, a method of reducing the incidence and/or risk of a subject transmitting HIV to a sexual partner in a subject further comprises the absence of HIV transmission. In some embodiments, a method of reducing the incidence and/or risk of a subject transmitting human immunodeficiency virus (HIV) to a sexual partner in a subject further comprises determining a post treatment clinical outcome. In some embodiments, a post treatment clinical outcome is indicative of a clinical outcome responder. Some embodiments further comprise determining a post-treatment clinical outcome. In some embodiments, a post-treatment clinical outcome of clinical cure is defined as a clinical outcome responder. In some embodiments, a clinical outcome responder is a subject with

normal vaginal discharge, a negative KOH Whiff test, and clue cells less than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount after treatment with a microgranule formulation comprising about 1 to about 2 grams of secnidazole. In some embodiments, a clinical outcome responder has a gram stain slide Nugent score of less than four (4) after treatment with a single dose of secnidazole. In yet other embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, clue cells less than 20% of total epithelial cells, and a gram stain slide Nugent score of less than four (4) after treatment with a single dose of secnidazole. In some embodiments, a clinical outcome responder has a gram stain slide Nugent score of less than four (4) after treatment with a 2 gram single dose of secnidazole. In yet other embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, clue cells less than 20% of total epithelial cells, and a gram stain slide Nugent score of less than four (4) after treatment with a 2 gram single dose of secnidazole. In some embodiments, a post-treatment clinical outcome is observable after about 24 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 48 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 72 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 96 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 120 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 168 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 7 to about 10 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 11 to about 20 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 21 to about 30 days after administration.

[0048] In some embodiments, a method of reducing the incidence and/or risk of a subject transmitting HIV to a sexual partner in a subject further comprises an alleviation of one or more symptoms of bacterial vaginosis within up to about three days after administration to the subject. In some embodiments, a method of treating bacterial vaginosis further comprises an alleviation of one or more symptoms of bacterial vaginosis within up to about three days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, abnormal vaginal odor, abnormal vaginal discharge or a combination thereof. In some embodiments, alleviation refers to a lessening of the

severity of one or more symptoms. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 24 hours after administration. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 48 hours after administration. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 72 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 96 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 120 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 168 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 11 to about 20 days after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 21 to about 30 days after administration to the subject.

[0049] In some embodiments, a method of reducing the incidence and/or risk of a subject transmitting HIV to a sexual partner a subject further comprises a resolution of one or more symptoms of bacterial vaginosis within up to about seven days after administration to the subject. In some embodiments, a method of treating bacterial vaginosis further comprises a resolution of one or more symptoms of bacterial vaginosis within up to about seven days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, abnormal vaginal odor, abnormal vaginal discharge or a combination thereof. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 24 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 48 hours after administration. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 72 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 96 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 120 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 168 hours after administration to the subject. In some embodiments,

resolution of one or more symptoms of bacterial vaginosis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 11 to about 20 days after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 21 to about 30 days after administration to the subject.

[0050] Some embodiments are directed to a method of reducing the incidence and/or risk of a subject acquiring HIV from a sexual partner. Bacterial vaginosis infections may increase the risk of a HIV transmission to sexual partner as well as the risk of acquiring HIV from a sexual partner. In some embodiments, a method of reducing the incidence and/or risk of the subject transmitting HIV to a sexual partner comprises administering to the subject a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof. In some embodiments, a method of reducing the incidence and/or risk of a preterm birth in a subject comprises administering to the subject a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof in a microgranule formulation. In some embodiments, the secnidazole microgranule formulation may be suitable for oral administration. In some embodiments, the secnidazole microgranule formulation comprises a plurality of microgranules. In some embodiments, the plurality of microgranules are white to off-white in color. In some embodiments, the plurality of microgranules each have a particle size range of about 400 to about 841 microns. In some embodiments, the secnidazole microgranule formulation may be mixed, stirred, or otherwise integrated into a food substance. In some embodiments, the food substance may be a semisolid or soft food. In some embodiments, the food substance may include, but is not limited to applesauce, pudding, yogurt or the like. In some embodiments, integration of the secnidazole microgranule formulation into a food substance has a taste masking function.

[0051] In some embodiments, the subject is a human. In yet other embodiments, the subject is a pregnant human female. In some embodiments, the subject is an otherwise healthy female. In some embodiments, the subject is a female without HIV. In some embodiments, the subject has a sexual partner that is HIV positive. In some embodiments, the subject is an otherwise healthy pregnant female. In some embodiments, the subject is a female having had 3 or fewer bacterial vaginosis infections in the past 12 months. In some embodiments, the subject is a female having had 4 or more bacterial vaginosis infections in the past twelve months. In some embodiments, the subject is a female with recurring

bacterial vaginosis. In some embodiments, a subject with recurring bacterial vaginosis is a subject with 4 or more bacterial vaginosis infections within a twelve-month period. In some embodiments, the subject is a female with frequent bacterial vaginosis infections. In some embodiments, a female with frequent bacterial vaginosis infections is a female with 4 or more bacterial vaginosis infections within a twelve-month period. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, a positive 10% KOH Whiff test or a combination thereof. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, and a positive 10% KOH Whiff test. In some embodiments, the subject is a female with confirmed bacterial vaginosis. In some embodiments, bacterial vaginosis is confirmed by the presence of four (4) Amsel criteria parameters selected from an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, a positive 10% KOH Whiff test and a gram stain slide Nugent score equal to, or higher than four (4) on bacterial analysis of vaginal samples. In some embodiments, the subject is a female with suspected bacterial vaginosis. In some embodiments, suspected bacterial vaginosis is indicated by the presence of four (4) Amsel criteria parameters selected from an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, and a positive 10% KOH Whiff test. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, odor, or a combination thereof.

[0052] In some embodiments, a method of reducing the incidence and/or risk of a subject acquiring HIV from a sexual partner comprises administering to the subject a single dose of a therapeutically effective amount of secnidazole in a microgranule formulation, wherein the secnidazole comprises about 1g to about 2 g of the microgranule formulation. In some embodiments, the secnidazole microgranule formulation is co-administered with an additional compound selected from ethinyl estradiol (EE2), norethindrone (NET), or a

combination thereof. In some embodiments, the secnidazole microgranule formulation is mixed into a semisolid or soft food substance, such as but not limited to applesauce yogurt and pudding. In some embodiments, the amount of the food substance is about 4-6 ounces.

[0053] In some embodiments, a method of reducing the incidence and/or risk of a subject acquiring HIV from a sexual partner comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a plasma Cmax of between about 34.5 μg/ml and about 58.3 μg/ml. In some embodiments, a method of treating bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a plasma Cmax of between about 17.4 μg/ml and about 26.5 μg/ml.

[0054] In some embodiments, a method of reducing the incidence and/or risk of a subject acquiring HIV from a sexual partner comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a tmax of about 3 hours to about 4.05 hours. In some embodiments, a method of treating bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a tmax of about 2 hours to about 6 hours.

[0055] In some embodiments, a method of reducing the incidence and/or risk of a subject acquiring HIV from a sexual partner in a subject further comprises the absence of HIV transmission. In some embodiments, a method of reducing the incidence and/or risk of a subject transmitting human immunodeficiency virus (HIV) to a sexual partner in a subject further comprises determining a post treatment clinical outcome. In some embodiments, a post treatment clinical outcome is indicative of a clinical outcome responder. Some embodiments further comprise determining a post-treatment clinical outcome. In some embodiments, a post-treatment clinical outcome of clinical cure is defined as a clinical outcome responder. In some embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, and clue cells less than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount after treatment with a microgranule formulation comprising about 1 to about 2 grams of secnidazole. In some embodiments, a clinical outcome responder has a gram stain slide Nugent score of less than four (4) after treatment with a single dose of secnidazole. In yet other embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, clue cells less than 20% of total epithelial cells, and a gram stain

slide Nugent score of less than four (4) after treatment with a single dose of secnidazole. In some embodiments, a clinical outcome responder has a gram stain slide Nugent score of less than four (4) after treatment with a 2 gram single dose of secnidazole. In yet other embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, clue cells less than 20% of total epithelial cells, and a gram stain slide Nugent score of less than four (4) after treatment with a 2 gram single dose of secnidazole. In some embodiments, a post-treatment clinical outcome is observable after about 24 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 48 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 72 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 96 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 120 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 168 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 7 to about 10 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 11 to about 20 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 21 to about 30 days after administration.

[0056] In some embodiments, a method of reducing the incidence and/or risk of a subject acquiring HIV from a sexual partner further comprises an alleviation of one or more symptoms of bacterial vaginosis within up to about three days after administration to the subject. In some embodiments, a method of treating bacterial vaginosis further comprises an alleviation of one or more symptoms of bacterial vaginosis within up to about three days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, abnormal vaginal odor, abnormal vaginal discharge or a combination thereof. In some embodiments, alleviation refers to a lessening of the severity of one or more symptoms. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 24 hours after administration. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 48 hours after administration. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 72 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 96 hours after administration to the subject. In some embodiments, alleviation of one or

more symptoms of bacterial vaginosis occurs within about 120 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 168 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 11 to about 20 days after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 21 to about 30 days after administration to the subject.

[0057] In some embodiments, a method of reducing the incidence and/or risk of a subject acquiring HIV from a sexual partner further comprises a resolution of one or more symptoms of bacterial vaginosis within up to about seven days after administration to the subject. In some embodiments, a method of treating bacterial vaginosis further comprises a resolution of one or more symptoms of bacterial vaginosis within up to about seven days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, abnormal vaginal odor, abnormal vaginal discharge or a combination thereof. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 24 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 48 hours after administration. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 72 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 96 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 120 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 168 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 11 to about 20 days after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 21 to about 30 days after administration to the subject.

[0058] Some embodiments are directed to a method of reducing the incidence and/or risk of a subject acquiring a sexually transmitted infection (STI) from a sexual partner. Bacterial vaginosis infections may increase the risk of acquiring an STI from a sexual partner. In some embodiments, STI's include, but are not limited to chlamydia, gonorrhea, trichomoniasis, HSV-2, and HPV. In some embodiments, a method of reducing the incidence and/or risk of the subject transmitting HIV to a sexual partner in a subject comprises administering to the subject a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof. In some embodiments, a method of reducing the incidence and/or risk of a preterm birth in a subject comprises administering to the subject a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof in a microgranule formulation. In some embodiments, the secnidazole microgranule formulation may be suitable for oral administration. In some embodiments, the secnidazole microgranule formulation comprises a plurality of microgranules. In some embodiments, the plurality of microgranules are white to off-white in color. In some embodiments, the plurality of microgranules each have a particle size range of about 400 to about 841 microns. In some embodiments, the secnidazole microgranule formulation may be mixed, stirred, or otherwise integrated into a food substance. In some embodiments, the food substance may be a semisolid or soft food. In some embodiments, the food substance may include, but is not limited to applesauce, pudding, yogurt or the like. In some embodiments, integration of the secnidazole microgranule formulation into a food substance has a taste masking function.

[0059] In some embodiments, the subject is a human. In yet other embodiments, the subject is a pregnant human female. In some embodiments, the subject is an otherwise healthy female. In some embodiments, the subject is a female with an STI. In some embodiments, the subject is a female having had 3 or fewer bacterial vaginosis infections in the past 12 months. In some embodiments, the subject is a female having had 4 or more bacterial vaginosis infections in the past twelve months. In some embodiments, the subject is a female with recurring bacterial vaginosis. In some embodiments, a subject with recurring bacterial vaginosis is a subject with 4 or more bacterial vaginosis infections within a twelve-month period. In some embodiments, the subject is a female with frequent bacterial vaginosis infections. In some embodiments, a female with frequent bacterial vaginosis infections is a female with 4 or more bacterial vaginosis infections within a twelve-month period. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, presence

of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, a positive 10% KOH Whiff test or a combination thereof. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, and a positive 10% KOH Whiff test. In some embodiments, the subject is a female with confirmed bacterial vaginosis. In some embodiments, bacterial vaginosis is confirmed by the presence of four (4) Amsel criteria parameters selected from an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, a positive 10% KOH Whiff test and a gram stain slide Nugent score equal to, or higher than four (4) on bacterial analysis of vaginal samples. In some embodiments, the subject is a female with suspected bacterial vaginosis. In some embodiments, suspected bacterial vaginosis is indicated by the presence of four (4) Amsel criteria parameters selected from an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, and a positive 10% KOH Whiff test. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, odor, or a combination thereof.

[0060] In some embodiments, a method of reducing the incidence and/or risk of a subject acquiring an STI from a sexual partner comprises administering to the subject a single dose of a therapeutically effective amount of secnidazole in a microgranule formulation, wherein the secnidazole comprises about 1g to about 2 g of the microgranule formulation. In some embodiments, the secnidazole microgranule formulation is co-administered with an additional compound selected from ethinyl estradiol (EE2), norethindrone (NET), or a combination thereof. In some embodiments, the secnidazole microgranule formulation is mixed into a semisolid or soft food substance, such as but not limited to applesauce yogurt and pudding. In some embodiments, the amount of the food substance is about 4-6 ounces.

[0061] In some embodiments, a method of reducing the incidence and/or risk of a subject acquiring an STI from a sexual partner comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a plasma Cmax of between

about 34.5 μg/ml and about 58.3 μg/ml. In some embodiments, a method of treating bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a plasma Cmax of between about 17.4 μg/ml and about 26.5 μg/ml.

[0062] In some embodiments, a method of reducing the incidence and/or risk of a subject acquiring an STI from a sexual partner comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a tmax of about 3 hours to about 4.05 hours. In some embodiments, a method of treating bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a tmax of about 2 hours to about 6 hours.

[0063] In some embodiments, a method of reducing the incidence and/or risk of a subject acquiring an STI from a sexual partner further comprises the absence of an STI transmission or acquisition of an STI by the subject. In some embodiments, a method of reducing the incidence and/or risk of a subject acquiring an STI from a sexual partner further comprises determining a post treatment clinical outcome. In some embodiments, a post treatment clinical outcome is indicative of a clinical outcome responder. Some embodiments further comprise determining a post-treatment clinical outcome. In some embodiments, a post-treatment clinical outcome of clinical cure is defined as a clinical outcome responder. In some embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, and clue cells less than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount after treatment with a microgranule formulation comprising about 1 to about 2 grams of secnidazole. In some embodiments, a clinical outcome responder has a gram stain slide Nugent score of less than four (4) after treatment with a single dose of secnidazole. In yet other embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, clue cells less than 20% of total epithelial cells, and a gram stain slide Nugent score of less than four (4) after treatment with a single dose of secnidazole. In some embodiments, a clinical outcome responder has a gram stain slide Nugent score of less than four (4) after treatment with a 2 gram single dose of secnidazole. In yet other embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, clue cells less than 20% of total epithelial cells, and a gram stain slide Nugent score of less than four (4) after treatment with a 2 gram single dose of secnidazole. In some

embodiments, a post-treatment clinical outcome is observable after about 24 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 48 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 72 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 96 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 120 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 168 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 7 to about 10 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 11 to about 20 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 21 to about 30 days after administration.

[0064] In some embodiments, a method of reducing the incidence and/or risk of a subject acquiring an STI from a sexual partner further comprises an alleviation of one or more symptoms of bacterial vaginosis within up to about three days after administration to the subject. In some embodiments, a method of treating bacterial vaginosis further comprises an alleviation of one or more symptoms of bacterial vaginosis within up to about three days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, abnormal vaginal odor, abnormal vaginal discharge or a combination thereof. In some embodiments, alleviation refers to a lessening of the severity of one or more symptoms. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 24 hours after administration. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 48 hours after administration. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 72 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 96 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 120 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 168 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 11 to about 20 days after

administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 21 to about 30 days after administration to the subject.

[0065] In some embodiments, a method of reducing the incidence and/or risk of a subject acquiring an STI from a sexual partner further comprises a resolution of one or more symptoms of bacterial vaginosis within up to about seven days after administration to the subject. In some embodiments, a method of treating bacterial vaginosis further comprises a resolution of one or more symptoms of bacterial vaginosis within up to about seven days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, abnormal vaginal odor, abnormal vaginal discharge or a combination thereof. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 24 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 48 hours after administration. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 72 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 96 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 120 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 168 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 11 to about 20 days after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 21 to about 30 days after administration to the subject.

[0066] Some embodiments are directed to a method of preventing recurrence of bacterial vaginosis. In some embodiments, the method of preventing recurrence of bacterial vaginosis comprises administering a microgranule formulation comprising about 1 to about 2 grams secnidazole to a subject in need thereof. In some embodiments, the recurrence of bacterial vaginosis is decreased after administration of a single, 2 gram dose of secnidazole. In some embodiments, the recurrence of bacterial vaginosis is decreased after administration of a multiple, 2 gram doses of secnidazole. In some embodiments, multiple doses may be

given at pre-determined intervals such as but not limited to once a week, bi-weekly, monthly, bimonthly for the duration of treatment. In some embodiment, the duration of treatment may be at least one week. In some embodiment, the duration of treatment may be at least one month. In some embodiments, the duration of treatment is about six months. Some embodiments are directed to a method of preventing recurrence of bacterial vaginosis comprising administering a microgranule formulation comprising about 2 grams secnidazole, to a subject in need thereof. In some embodiments, the microgranule formulation comprising about 2 grams secnidazole is administered as a single dose. In some embodiments, the single dose of secnidazole is the only dose need to prevent recurrence of bacterial vaginosis. In some embodiments, the microgranule formulation comprising about 2 grams secnidazole is administered in multiple doses. In some embodiments, multiple doses may be given at pre-determined intervals such as but not limited to once a week, bi-weekly, monthly, bimonthly for the duration of treatment. In some embodiment, the duration of treatment may be at least one week. In some embodiment, the duration of treatment may be at least one month. In some embodiments, the duration of treatment is about six months.

[0067] In some embodiments, the method of preventing recurrence of bacterial vaginosis in a subject in need thereof comprises administering to the subject a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof in a microgranule formulation. In some embodiments, the secnidazole microgranule formulation may be suitable for oral administration. In some embodiments, the secnidazole microgranule formulation comprises a plurality of microgranules. In some embodiments, the plurality of microgranules are white to off-white in color. In some embodiments, the plurality of microgranules each have a particle size range of about 400 to about 841 microns. In some embodiments, the secnidazole microgranule formulation may be mixed, stirred, or otherwise integrated into a food substance. In some embodiments, the food substance may be a semisolid or soft food. In some embodiments, the food substance may include, but is not limited to applesauce, pudding, yogurt or the like. In some embodiments, integration of the secnidazole microgranule formulation into a food substance has a taste masking function.

[0068] In some embodiments, the subject is a female. In some embodiments, the subject is an otherwise healthy female. In some embodiments, the subject is a pregnant female. In some embodiments, the subject is an otherwise healthy pregnant female. In some embodiments, the subject is a female having had 3 or fewer bacterial vaginosis infections in

the past 12 months. In some embodiments, the subject is a female having had 3 or more bacterial vaginosis infections in the past 12 months. In some embodiments, the subject is a female having had 4 or more bacterial vaginosis infections in the past twelve months. In some embodiments, the subject is a female with recurring bacterial vaginosis. In some embodiments, a subject with recurring bacterial vaginosis is a subject with 3 or more bacterial vaginosis infections within a twelve-month period. In some embodiments, a subject with recurring bacterial vaginosis is a subject with 4 or more bacterial vaginosis infections within a twelve-month period. In some embodiments, the subject is a female with frequent bacterial vaginosis infections. In some embodiments, a female with frequent bacterial vaginosis infections is a female with 4 or more bacterial vaginosis infections within a twelve-month period. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, a positive 10% KOH Whiff test or a combination thereof. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, and a positive 10% KOH Whiff test. In some embodiments, the subject is a female with confirmed bacterial vaginosis. In some embodiments, bacterial vaginosis is confirmed by the presence of four (4) Amsel criteria parameters selected from an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, a positive 10% KOH Whiff test and a gram stain slide Nugent score equal to, or higher than four (4) on bacterial analysis of vaginal samples. In some embodiments, the subject is a female with suspected bacterial vaginosis. In some embodiments, suspected bacterial vaginosis is indicated by the presence of four (4) Amsel criteria parameters selected from an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, and a positive 10% KOH Whiff test. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, odor, or a combination thereof.

[0069] In some embodiments, a method of preventing recurrence of bacterial vaginosis in a subject comprises administering to the subject a single dose of a therapeutically effective amount of secnidazole in a microgranule formulation, wherein the secnidazole comprises about 1g to about 2 g of the microgranule formulation. In some embodiments, a method of preventing recurrence of bacterial vaginosis in a subject comprises administering to the subject multiple doses of a therapeutically effective amount of secnidazole in a microgranule formulation, wherein the secnidazole comprises about 1g to about 2 g of the microgranule formulation. In some embodiments, multiple doses may be given at pre-determined intervals such as but not limited to once a week, bi-weekly, monthly, bimonthly for the duration of treatment. In some embodiment, the duration of treatment may be at least one week. In some embodiment, the duration of treatment may be at least one month. In some embodiments, the duration of treatment is about six months. In some embodiments, the secnidazole microgranule formulation is mixed into a semisolid or soft food substance, such as but not limited to applesauce yogurt and pudding. In some embodiments, the amount of the food substance is about 4-6 ounces.

[0070] In some embodiments, a method of preventing recurrence of bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a plasma Cmax of between about 34.5 μg/ml and about 58.3 μg/ml. In some embodiments, a method of preventing recurrence of bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a plasma Cmax of between about 17.4 μg/ml and about 26.5 μg/ml. In some embodiments, a method of preventing recurrence of bacterial vaginosis in a subject comprises administering to the subject multiple doses of a secnidazole microgranule formulation wherein each dose exhibits a plasma Cmax of between about 34.5 μg/ml and about 58.3 μg/ml. In some embodiments, multiple doses may be given at pre-determined intervals such as but not limited to once a week, bi-weekly, monthly, bimonthly for the duration of treatment. In some embodiment, the duration of treatment may be at least one week. In some embodiment, the duration of treatment may be at least one month. In some embodiments, the duration of treatment is about six months. In some embodiments, a method of preventing recurrence of bacterial vaginosis in a subject comprises administering to the subject multiple doses of a secnidazole microgranule formulation wherein each dose exhibits a plasma Cmax of between about 17.4 μg/ml and about 26.5 μg/ml. In some embodiments, multiple doses may be given at pre-determined intervals such as but not

limited to once a week, bi-weekly, monthly, bimonthly for the duration of treatment. In some embodiment, the duration of treatment may be at least one week. In some embodiment, the duration of treatment may be at least one month. In some embodiments, the duration of treatment is about six months.

[0071] In some embodiments, a method of preventing recurrence of bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a tmax of about 3 hours to about 4.05 hours. In some embodiments, a method of preventing recurrence of bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a tmax of about 2 hours to about 6 hours. In some embodiments, a method of preventing recurrence of bacterial vaginosis in a subject comprises administering to the subject multiple doses of a secnidazole microgranule formulation wherein a single dose exhibits a tmax of about 3 hours to about 4.05 hours. In some embodiments, a method of preventing recurrence of bacterial vaginosis in a subject comprises administering to the subject multiple doses of a secnidazole microgranule formulation wherein each dose exhibits a tmax of about 2 hours to about 6 hours. In some embodiments, multiple doses may be given at pre-determined intervals such as but not limited to once a week, bi-weekly, monthly, bimonthly for the duration of treatment. In some embodiment, the duration of treatment may be at least one week. In some embodiment, the duration of treatment may be at least one month. In some embodiments, the duration of treatment is about six months.

[0072] In some embodiments, a method of preventing recurrence of bacterial vaginosis in a subject further comprises determining a post treatment clinical outcome. In some embodiments, a post treatment clinical outcome is indicative of a clinical outcome responder. Some embodiments further comprise determining a post-treatment clinical outcome. In some embodiments, a post-treatment clinical outcome of clinical cure is defined as a clinical outcome responder. In some embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, and clue cells less than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount after treatment with an oral microgranule formulation comprising about 1 to about 2 grams of secnidazole. In some embodiments, a clinical outcome responder has a gram stain slide Nugent score of less than four (4) after treatment with a single dose of secnidazole. In yet other embodiments, a clinical outcome responder is a subject with normal vaginal

discharge, a negative KOH Whiff test, clue cells less than 20% of total epithelial cells, and a gram stain slide Nugent score of less than four (4) after treatment with a single dose of secnidazole. In some embodiments, a clinical outcome responder has a gram stain slide Nugent score of less than four (4) after treatment with a 2 gram single dose of secnidazole. In yet other embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, clue cells less than 20% of total epithelial cells, and a gram stain slide Nugent score of less than four (4) after treatment with a 2 gram single dose of secnidazole. In some embodiments, a post-treatment clinical outcome is observable after about 24 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 48 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 72 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 96 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 120 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 168 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 7 to about 10 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 11 to about 20 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 21 to about 30 days after administration.

[0073] In some embodiments, a method of preventing recurrence of bacterial vaginosis further comprises an alleviation of one or more symptoms of bacterial vaginosis within up to about three days after administration to the subject. In some embodiments, a method of preventing recurrence of bacterial vaginosis further comprises an alleviation of one or more symptoms of bacterial vaginosis within up to about three days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, abnormal vaginal odor, abnormal vaginal discharge or a combination thereof. In some embodiments, alleviation refers to a lessening of the severity of one or more symptoms. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 24 hours after administration. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 48 hours after administration. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 72 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 96 hours after administration to

the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 120 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 168 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 11 to about 20 days after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 21 to about 30 days after administration to the subject.

[0074] In some embodiments, a method of preventing recurrence of bacterial vaginosis further comprises a resolution of one or more symptoms of bacterial vaginosis within up to about seven days after administration to the subject. In some embodiments, a method of preventing recurrence of bacterial vaginosis further comprises a resolution of one or more symptoms of bacterial vaginosis within up to about seven days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, abnormal vaginal odor, abnormal vaginal discharge or a combination thereof. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 24 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 48 hours after administration. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 72 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 96 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 120 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 168 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 11 to about 20 days after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 21 to about 30 days after administration to the subject.

[0075] In some embodiments, a method of treating bacterial vaginosis in a subject in need thereof further comprises administering to at least one of the subjects sexual partners, a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof. In some embodiments, a method of treating bacterial vaginosis in a subject in need thereof further comprises administering to at least one of the subjects sexual partners, a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof in a microgranule formulation. In some embodiments, the secnidazole microgranule formulation may be suitable for oral administration. In some embodiments, the secnidazole microgranule formulation comprises a plurality of microgranules. In some embodiments, the plurality of microgranules are white to off-white in color. In some embodiments, the plurality of microgranules each have a particle size range of about 400 to about 841 microns. In some embodiments, the secnidazole microgranule formulation may be mixed, stirred, or otherwise integrated into a food substance. In some embodiments, the food substance may be a semisolid or soft food. In some embodiments, the food substance may include, but is not limited to applesauce, pudding, yogurt or the like. In some embodiments, integration of the secnidazole microgranule formulation into a food substance has a taste masking function. In some embodiments, the at least one sexual partner of the subject may be a male or a female. In some embodiments, a single dose of a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof may be administered. In some embodiments, a single dose of a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof in a microgranule formulation may be administered. In some embodiments, multiple doses may be given at pre-determined intervals such as but not limited to once a week, bi-weekly, monthly, bimonthly for the duration of treatment. In some embodiment, the duration of treatment may be at least one week. In some embodiment, the duration of treatment may be at least one month. In some embodiments, the duration of treatment is about six months.

[0076] Some embodiments are directed to methods of treating vaginitis. In some embodiments, the vaginitis is trichomoniasis. Trichomoniasis is a genitourinary infection with the protozoan Trichomonas vaginalis. It is the most common non-viral sexually transmitted disease (STD) worldwide. Women are affected more often than men. Trichomoniasis is one of the three major causes of vaginal complaints among reproductive aged women, along with bacterial vaginosis and candida vulvovaginitis, and a cause of urethritis in men; however, the infection is often asymptomatic. In some embodiments, a

method of treating trichomoniasis in a subject in need thereof comprises administering to the subject a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof in a microgranule formulation. In some embodiments, the secnidazole microgranule formulation may be suitable for oral administration. In some embodiments, the secnidazole microgranule formulation comprises a plurality of microgranules. In some embodiments, the plurality of microgranules are white to off-white in color. In some embodiments, the plurality of microgranules each have a particle size range of about 400 to about 841 microns. In some embodiments, the secnidazole microgranule formulation may be mixed, stirred, or otherwise integrated into a food substance. In some embodiments, the food substance may be a semisolid or soft food. In some embodiments, the food substance may include, but is not limited to applesauce, pudding, yogurt or the like. In some embodiments, integration of the secnidazole microgranule formulation into a food substance has a taste masking function.

[0077] In some embodiments, the subject is a human. In yet other embodiments, the subject is a human female. In some embodiments, the human female is of an age ranging from a postmenarachal adolescent to a premenopausal woman. In some embodiments, the subject is a pregnant human female.

[0078] In some embodiments, the subject is a female. In some embodiments, the subject is an otherwise healthy female. In some embodiments, the subject is a pregnant female. In some embodiments, the subject is an otherwise healthy pregnant female. In some embodiments, the subject is a female presenting with purulent malodorous discharge (associated with burning, pruritus, dysuria, frequency, lower abdominal pain), dyspareunia, burning postcoital bleeding, dyspareunia, dysuria, a thin green-yellow frothy discharge, vulvovaginal erythema (erythema of the vulva and vaginal mucosa), punctate hemorrhages, urethritis, cystitis, purulent vaginitis, sequamative inflammatory vaginitis, atrophic vaginitis, erosive lichen planus, an elevated vaginal pH (about 5.0 to about 6.0), and any combination thereof. In some embodiments, the subject is asymptomatic. In some embodiments, the subject is a female with confirmed trichomoniasis. In some embodiments, the diagnosis of Trichomonas vaginalis is confirmed by laboratory testing (including, but not limited to motile trichomonads on wet mount, positive culture, increase in polymorphonuclear leukocytes, positive nucleic acid amplification test, or positive rapid antigen, nucleic acid probe test cervical cytology or any combination thereof). Microscopy (such as, but not limited to culture on Diamond's medium) is a key step in the evaluation of vaginal discharge, and is often the

first step in the diagnostic evaluation for trichomoniasis. Microscopy is convenient and low cost. In some embodiments, nucleic acid amplification tests (NAAT) can then be done for subjects with non-diagnostic (or negative) wet mounts. In some embodiments, if NAAT is not available, rapid diagnostic kits or culture are then performed. Additional laboratory tests include but are not limited to the APTIMA Trichomonas vaginalis assay, the APTIMA TV assay the Amplicor assay (PCR assay for detection of N. gonorrhoeae and C. trachomatis that has been modified to detect T. vaginalis in vaginal/endocervical swabs or urine); NuSwab VGor any combination thereof. positive rapid antigen, nucleic acid probe test include but are not limited to the Affirm VP III Microbial Identification System, and the OSOM Trichomonas Rapid Test. In some embodiments, the subject is a female with suspected trichomoniasis. In some embodiments, suspected trichomoniasis is indicated by the presence of purulent malodorous discharge (associated with burning, pruritus, dysuria, frequency, lower abdominal pain), or dyspareunia, burning postcoital bleeding, dyspareunia, dysuria, a thin green-yellow frothy discharge, vulvovaginal erythema (erythema of the vulva and vaginal mucosa), punctate hemorrhages, urethritis, cystitis, purulent vaginitis, sequamative inflammatory vaginitis, atrophic vaginitis, erosive lichen planus, elevated vaginal pH (about 5.0 to about 6.0), and any combination thereof.

[0079] In some embodiments, a method of treating trichomoniasis in a subject comprises administering to the subject a single dose of a therapeutically effective amount of secnidazole in a microgranule formulation, wherein the secnidazole comprises about 1g to about 2 g of the microgranule formulation. In some embodiments, the secnidazole microgranule formulation is co-administered with an additional compound selected from ethinyl estradiol (EE2), norethindrone (NET), or a combination thereof. In some embodiments, the secnidazole microgranule formulation is mixed into a semisolid or soft food substance, such as but not limited to applesauce, yogurt, and pudding. In some embodiments, the amount of the food substance is about 4-6 ounces.

[0080] In some embodiments, a method of treating trichomoniasis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a plasma Cmax of between about 34.5 μg/ml and about 58.3 μg/ml. In some embodiments, a method of treating bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a plasma Cmax of between about 17.4 μg/ml and about 26.5 μg/ml.

[0081] In some embodiments, a method of treating trichomoniasis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a tmax of about 3 hours to about 4.05 hours. In some embodiments, a method of treating trichomoniasis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a tmax of about 2 hours to about 6 hours.

[0082] In some embodiments, a method of treating trichomoniasis in a subject comprises co-administering to the subject a single dose of a therapeutically effective amount of secnidazole in a microgranule formulation and an additional compound selected from ethinyl estradiol (EE2), norethindrone (NET), or a combination thereof, wherein the secnidazole comprises about 1 g to about 2 g of the microgranule formulation. In some embodiments, the additional compound is co-administered on the same day as the secnidazole microgranule formulation. In some embodiments, the additional compound is administered on a different day than the secnidazole microgranule formulation. In some embodiments, the secnidazole microgranule formulation does not affect the contraceptive efficacy of the additional compound.

[0083] In some embodiments, a method of treating trichomoniasis in a subject further comprises determining a post treatment clinical outcome. In some embodiments, a post treatment clinical outcome is indicative of a clinical outcome responder. In some embodiments, a clinical outcome responder is a subject that is asymptomatic. In some embodiments, a clinical outcome responder is a subject with normal vaginal discharge, normal vaginal pH, normal laboratory testing results (including, but not limited to the absence of motile trichomonads on wet mount, negative culture, normal polymorphonuclear leukocytes, negative nucleic acid amplification test, negative rapid antigen, negative nucleic acid probe test, negative rapid diagnostic kits or culture, negative cervical cytology, or any combination thereof) after treatment with an oral microgranule formulation comprising about 1 to about 2 grams of secnidazole. In some embodiments, a clinical outcome responder is a subject with without purulent malodorous discharge (associated with burning, pruritus, dysuria, frequency, lower abdominal pain), or dyspareunia, burning postcoital bleeding, dyspareunia, dysuria, a thin green-yellow frothy discharge, vulvovaginal erythema (erythema of the vulva and vaginal mucosa), punctate hemorrhages, urethritis, cystitis, purulent vaginitis, sequamative inflammatory vaginitis, atrophic vaginitis, erosive lichen planus,

elevated vaginal pH (about 5.0 to about 6.0), and any combination thereof. In some embodiments, a post-treatment clinical outcome is observable after about 24 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 48 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 72 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 96 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 120 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 168 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 7 to about 10 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 11 to about 20 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 21 to about 30 days after administration.

[0084] In some embodiments, a method of treating trichomoniasis further comprises an alleviation of one or more symptoms of trichomoniasis within up to about three days after administration to the subject. In some embodiments, a method of treating trichomoniasis further comprises an alleviation of one or more symptoms of trichomoniasis within up to about three days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, purulent malodorous discharge (associated with burning, pruritus, dysuria, frequency, lower abdominal pain), or dyspareunia, burning postcoital bleeding, dyspareunia, dysuria, a thin green-yellow frothy discharge, vulvovaginal erythema (erythema of the vulva and vaginal mucosa), punctate hemorrhages, urethritis, cystitis, purulent vaginitis, sequamative inflammatory vaginitis, atrophic vaginitis, erosive lichen planus, elevated vaginal pH (about 5.0 to about 6.0), and any combination thereof. In some embodiments, alleviation refers to a lessening of the severity of one or more symptoms. In some embodiments, alleviation of one or more symptoms of trichomoniasis occurs within about 24 hours after administration. In some embodiments, alleviation of one or more symptoms of trichomoniasis occurs within about 48 hours after administration. In some embodiments, alleviation of one or more symptoms of trichomoniasis occurs within about 72 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of trichomoniasis occurs within about 96 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of trichomoniasis occurs within about 120 hours after administration to the subject. In some embodiments,

alleviation of one or more symptoms of trichomoniasis occurs within about 168 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of trichomoniasis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, alleviation of one or more symptoms of trichomoniasis occurs within about 11 to about 20 days after administration to the subject. In some embodiments, alleviation of one or more symptoms of trichomoniasis occurs within about 21 to about 30 days after administration to the subject.

[0085] In some embodiments, a method of treating trichomoniasis further comprises a resolution of one or more symptoms of trichomoniasis within up to about seven days after administration to the subject. In some embodiments, a method of treating trichomoniasis further comprises a resolution of one or more symptoms of trichomoniasis within up to about seven days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, purulent malodorous discharge (associated with burning, pruritus, dysuria, frequency, lower abdominal pain), or dyspareunia, burning postcoital bleeding, dyspareunia, dysuria, a thin green-yellow frothy discharge, vulvovaginal erythema (erythema of the vulva and vaginal mucosa), punctate hemorrhages, urethritis, cystitis, purulent vaginitis, sequamative inflammatory vaginitis, atrophic vaginitis, erosive lichen planus, elevated vaginal pH (about 5.0 to about 6.0), and any combination thereof. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 24 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 48 hours after administration. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 72 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 96 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 120 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 168 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 11 to about 20 days after administration to the subject. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 21 to about 30 days after administration to the subject.

[0086] In some embodiments, treatment of trichomoniasis with a single, 2 gram dose of secnidazole in a microgranule formulation results in better than expected efficacy compared with FDA approved drugs used in the treatment of trichomoniasis. In some embodiments, a single dose of 2 grams of secnidazole results in a better than expected efficacy compared with FDA approved drugs currently used in the treatment of trichomoniasis. In some embodiments, treatment of trichomoniasis with a single, 2 gram dose of secnidazole results in superior efficacy compared with FDA approved drugs used in the treatment of trichomoniasis. In some embodiments, a single dose of 2 grams of secnidazole results in superior efficacy compared with FDA drugs used in the treatment of trichomoniasis requiring a single dose during treatment.

[0087] In some embodiments, treatment of trichomoniasis with a single, 2 gram dose of secnidazole results in a better than expected safety profile compared with FDA approved drugs used in the treatment of trichomoniasis. In some embodiments, a single dose of 2 grams of secnidazole results in a better than expected safety profile compared with FDA approved drugs used in the treatment of trichomoniasis requiring multiple doses during treatment. In some embodiments, treatment of trichomoniasis with a single, 2 gram dose of secnidazole results in a superior safety profile compared with FDA approved drugs used in the treatment of trichomoniasis. In some embodiments, a single dose of 2 grams of secnidazole results in a superior safety profile compared with FDA approved drugs used in the treatment of trichomoniasis requiring a single dose during treatment.

[0088] In some embodiments, a method of treating trichomoniasis in a subject in need thereof further comprises administering to at least one of the subjects sexual partners, a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof in a microgranule formulation. In some embodiments, the secnidazole microgranule formulation may be suitable for oral administration. In some embodiments, the secnidazole microgranule formulation comprises a plurality of microgranules. In some embodiments, the plurality of microgranules are white to off-white in color. In some embodiments, the plurality of microgranules each have a particle size range of about 400 to about 841 microns. In some embodiments, the secnidazole microgranule formulation may be mixed, stirred, or otherwise integrated into a food substance. In some embodiments, the food substance may be a semisolid or soft food. In some embodiments, the food substance may include, but is not

limited to applesauce, pudding, yogurt or the like. In some embodiments, integration of the secnidazole microgranule formulation into a food substance has a taste masking function.

[0089] In some embodiments, the subject is a human. In yet other embodiments, the subject is a human female. In some embodiments, the human female is of an age ranging from a postmenarachal adolescent to a premenopausal woman. In some embodiments, the subject is a pregnant human female. In some embodiments, the at least one sexual partner of the subject may be a male or a female.

[0090] In some embodiments, a method of treating bacterial vaginosis and/or trichmoniasis in a subject in need thereof comprises administering to the subject a therapeutically effective amount of secnidazole or pharmaceutically acceptable salts thereof in a microgranule formulation. In some embodiments, the secnidazole microgranule formulation may be suitable for oral administration. In some embodiments, the secnidazole microgranule formulation comprises a plurality of microgranules. In some embodiments, the plurality of microgranules are white to off-white in color. In some embodiments, the plurality of microgranules each have a particle size range of about 400 to about 841 microns. In some embodiments, the secnidazole microgranule formulation may be mixed, stirred, or otherwise integrated into a food substance. In some embodiments, the food substance may be a semisolid or soft food. In some embodiments, the food substance may include, but is not limited to applesauce, pudding, yogurt or the like. In some embodiments, integration of the secnidazole microgranule formulation into a food substance has a taste masking function.

[0091] In some embodiments, the subject is a human. In yet other embodiments, the subject is a human female. In some embodiments, the human female is of an age ranging from a postmenarachal adolescent to a premenopausal woman. In some embodiments, the subject is a pregnant human female.

[0092] In some embodiments, the subject is a female. In some embodiments, the subject is an otherwise healthy female. In some embodiments, the subject is a pregnant female. In some embodiments, the subject is an otherwise healthy pregnant female. In some embodiments, the subject is a female having had 3 or fewer bacterial vaginosis infections in the past 12 months. In some embodiments, the subject is a female having had 4 or more bacterial vaginosis infections in the past twelve months. In some embodiments, the subject is a female with recurring bacterial vaginosis. In some embodiments, a subject with recurring

bacterial vaginosis is a subject with 4 or more bacterial vaginosis infections within a twelve-month period. In some embodiments, the subject is a female with frequent bacterial vaginosis infections. In some embodiments, a female with frequent bacterial vaginosis infections is a female with 4 or more bacterial vaginosis infections within a twelve-month period. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, a positive 10% KOH Whiff test or a combination thereof. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, and a positive 10% KOH Whiff test. In some embodiments, the subject is a female with confirmed bacterial vaginosis. In some embodiments, bacterial vaginosis is confirmed by the presence of four (4) Amsel criteria parameters selected from an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, a positive 10% KOH Whiff test and a gram stain slide Nugent score equal to, or higher than four (4) on bacterial analysis of vaginal samples. In some embodiments, the subject is a female with suspected bacterial vaginosis. In some embodiments, suspected bacterial vaginosis is indicated by the presence of four (4) Amsel criteria parameters selected from an off-white (milky or gray), thin, homogeneous vaginal discharge, vaginal pH greater than or equal to 4.7, the presence of clue cells of greater than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount, and a positive 10% KOH Whiff test. In some embodiments, the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, odor, or a combination thereof. In some embodiments, the subject is a female presenting with purulent malodorous discharge (associated with burning, pruritus, dysuria, frequency, lower abdominal pain), dyspareunia, burning postcoital bleeding, dyspareunia, dysuria, a thin green-yellow frothy discharge, vulvovaginal erythema (erythema of the vulva and vaginal mucosa), punctate hemorrhages, urethritis, cystitis, purulent vaginitis, sequamative inflammatory vaginitis, atrophic vaginitis, erosive lichen planus, an elevated vaginal pH (about 5.0 to about 6.0), and any combination thereof. In some embodiments, the subject is asymptomatic. In some embodiments, the subject is a female with confirmed trichomoniasis. In some embodiments, the diagnosis of

Trichomonas vaginalis is confirmed by laboratory testing (including, but not limited to motile trichomonads on wet mount, positive culture, increase in polymorphonuclear leukocytes, positive nucleic acid amplification test, or positive rapid antigen, nucleic acid probe test cervical cytology or any combination thereof). Microscopy (such as, but not limited to culture on Diamond's medium) is a key step in the evaluation of vaginal discharge, and is often the first step in the diagnostic evaluation for trichomoniasis. Microscopy is convenient and low cost. In some embodiments, nucleic acid amplification tests (NAAT) can then be done for subjects with non-diagnostic (or negative) wet mounts. In some embodiments, if NAAT is not available, rapid diagnostic kits or culture are then performed. Additional laboratory tests include but are not limited to the APTIMA Trichomonas vaginalis assay, the APTIMA TV assay the Amplicor assay (PCR assay for detection of N. gonorrhoeae and C. trachomatis that has been modified to detect T. vaginalis in vaginal/endocervical swabs or urine); NuSwab VGor any combination thereof. positive rapid antigen, nucleic acid probe test include but are not limited to the Affirm VP III Microbial Identification System, and the OSOM Trichomonas Rapid Test. In some embodiments, the subject is a female with suspected trichomoniasis. In some embodiments, suspected trichomoniasis is indicated by presence of purulent malodorous discharge (associated with burning, pruritus, dysuria, frequency, lower abdominal pain), or dyspareunia, burning postcoital bleeding, dyspareunia, dysuria, a thin green-yellow frothy discharge, vulvovaginal erythema (erythema of the vulva and vaginal mucosa), punctate hemorrhages, urethritis, cystitis, purulent vaginitis, sequamative inflammatory vaginitis, atrophic vaginitis, erosive lichen planus, elevated vaginal pH (about 5.0 to about 6.0), and any combination thereof. In some embodiments, the subject is suspected of having both bacterial vaginosis and/or trichmoniasis. In some embodiments, a diagnosis of bacterial vaginosis and/or trichmoniasis is not confirmed.

[0093] In some embodiments, a method of treating bacterial vaginosis and/or trichmoniasis in a subject comprises administering to the subject a single dose of a therapeutically effective amount of secnidazole in a microgranule formulation, wherein the secnidazole comprises about 1g to about 2 g of the microgranule formulation. In some embodiments, the secnidazole microgranule formulation is mixed into a semisolid or soft food substance, such as but not limited to applesauce yogurt and pudding. In some embodiments, the amount of the food substance is about 4-6 ounces.

[0094] In some embodiments, a method of treating bacterial vaginosis and/or trichmoniasis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a plasma Cmax of between about 34.5 μg/ml and about 58.3 μg/ml. In some embodiments, a method of treating bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a plasma Cmax of between about 17.4 μg/ml and about 26.5 μg/ml.

[0095] In some embodiments, a method of treating bacterial vaginosis and/or trichmoniasis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a tmax of about 3 hours to about 4.05 hours. In some embodiments, a method of treating bacterial vaginosis in a subject comprises administering to the subject a single dose of a secnidazole microgranule formulation that exhibits a tmax of about 2 hours to about 6 hours.

[0096] In some embodiments, a method of treating bacterial vaginosis and/or trichmoniasis in a subject comprises co-administering to the subject a single dose of a therapeutically effective amount of secnidazole in a microgranule formulation and an additional compound selected from ethinyl estradiol (EE2), norethindrone (NET), or a combination thereof, wherein the secnidazole comprises about 1 g to about 2 g of the microgranule formulation. In some embodiments, the additional compound is co-administered on the same day as the secnidazole microgranule formulation. In some embodiments, the additional compound is administered on a different day than the secnidazole microgranule formulation. In some embodiments, the secnidazole microgranule formulation does not affect the contraceptive efficacy of the additional compound.

[0097] In some embodiments, a method of treating bacterial vaginosis and/or trichmoniasis in a subject further comprises determining a post treatment clinical outcome. In some embodiments, a post treatment clinical outcome is indicative of a clinical outcome responder. Some embodiments further comprise determining a post-treatment clinical outcome. In some embodiments, a post-treatment clinical outcome of clinical cure is defined as a clinical outcome responder. In some embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, and clue cells less than or equal to 20% of the total epithelial cells on microscopic examination of a vaginal saline wet mount after treatment with a microgranule formulation comprising about 1 to about 2 grams

of secnidazole. In some embodiments, a clinical outcome responder has a gram stain slide Nugent score of less than four (4) after treatment with a single dose of secnidazole. In yet other embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, clue cells less than 20% of total epithelial cells, and a gram stain slide Nugent score of less than four (4) after treatment with a single dose of secnidazole. In some embodiments, a clinical outcome responder has a gram stain slide Nugent score of less than four (4) after treatment with a 2 gram single dose of secnidazole. In yet other embodiments, a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, clue cells less than 20% of total epithelial cells, and a gram stain slide Nugent score of less than four (4) after treatment with a 2 gram single dose of secnidazole. In some embodiments, a post-treatment clinical outcome is observable after about 24 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 48 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 72 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 96 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 120 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 168 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 7 to about 10 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 11 to about 20 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 21 to about 30 days after administration. In some embodiments, a method of treating trichomoniasis in a subject further comprises determining a post treatment clinical outcome. In some embodiments, a post treatment clinical outcome is indicative of a clinical outcome responder. In some embodiments, a clinical outcome responder is a subject that is asymptomatic. In some embodiments, a clinical outcome responder is a subject with normal vaginal discharge, normal vaginal pH, normal laboratory testing results (including, but not limited to the absence of motile trichomonads on wet mount, negative culture, normal polymorphonuclear leukocytes, negative nucleic acid amplification test, negative rapid antigen, negative nucleic acid probe test, negative rapid diagnostic kits or culture, negative cervical cytology, or any combination thereof) after treatment with an oral microgranule formulation comprising about 1 to about 2 grams of secnidazole. In some embodiments, a clinical outcome responder is a subject with without purulent malodorous discharge (associated with burning, pruritus, dysuria, frequency, lower

abdominal pain), or dyspareunia, burning postcoital bleeding, dyspareunia, dysuria, a thin green-yellow frothy discharge, vulvovaginal erythema (erythema of the vulva and vaginal mucosa), punctate hemorrhages, urethritis, cystitis, purulent vaginitis, sequamative inflammatory vaginitis, atrophic vaginitis, erosive lichen planus, elevated vaginal pH (about 5.0 to about 6.0), and any combination thereof. In some embodiments, a post-treatment clinical outcome is observable after about 24 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 48 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 72 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 96 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 120 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 168 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 7 to about 10 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 11 to about 20 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 21 to about 30 days after administration.

[0098] In some embodiments, a method of treating bacterial vaginosis and/or trichmoniasis further comprises an alleviation of one or more symptoms of bacterial vaginosis within up to about three days after administration to the subject. In some embodiments, a method of treating bacterial vaginosis further comprises an alleviation of one or more symptoms of bacterial vaginosis within up to about three days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, abnormal vaginal odor, abnormal vaginal discharge or a combination thereof. In some embodiments, alleviation refers to a lessening of the severity of one or more symptoms. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 24 hours after administration. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 48 hours after administration. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 72 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 96 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 120 hours after administration to the subject. In some

embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 168 hours after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 11 to about 20 days after administration to the subject. In some embodiments, alleviation of one or more symptoms of bacterial vaginosis occurs within about 21 to about 30 days after administration to the subject. In some embodiments, a method of treating trichomoniasis in a subject further comprises determining a post treatment clinical outcome. In some embodiments, a post treatment clinical outcome is indicative of a clinical outcome responder. In some embodiments, a clinical outcome responder is a subject that is asymptomatic. In some embodiments, a clinical outcome responder is a subject with normal vaginal discharge, normal vaginal pH, normal laboratory testing results (including, but not limited to the absence of motile trichomonads on wet mount, negative culture, normal polymorphonuclear leukocytes, negative nucleic acid amplification test, negative rapid antigen, negative nucleic acid probe test, negative rapid diagnostic kits or culture, negative cervical cytology, or any combination thereof) after treatment with an oral microgranule formulation comprising about 1 to about 2 grams of secnidazole. In some embodiments, a clinical outcome responder is a subject with without purulent malodorous discharge (associated with burning, pruritus, dysuria, frequency, lower abdominal pain), or dyspareunia, burning postcoital bleeding, dyspareunia, dysuria, a thin green-yellow frothy discharge, vulvovaginal erythema (erythema of the vulva and vaginal mucosa), punctate hemorrhages, urethritis, cystitis, purulent vaginitis, sequamative inflammatory vaginitis, atrophic vaginitis, erosive lichen planus, elevated vaginal pH (about 5.0 to about 6.0), and any combination thereof. In some embodiments, a post-treatment clinical outcome is observable after about 24 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 48 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 72 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 96 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 120 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 168 hours after administration. In some embodiments, a post-treatment clinical outcome is observable after about 7 to about 10 days after administration. In some embodiments, a post-treatment clinical outcome is observable after about 11 to about 20 davs after administration. In some

embodiments, a post-treatment clinical outcome is observable after about 21 to about 30 days after administration.

[0099] In some embodiments, a method of treating bacterial vaginosis and/or trichmoniasis further comprises a resolution of one or more symptoms of bacterial vaginosis within up to about seven days after administration to the subject. In some embodiments, a method of treating bacterial vaginosis further comprises a resolution of one or more symptoms of bacterial vaginosis within up to about seven days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, abnormal vaginal odor, abnormal vaginal discharge or a combination thereof. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 24 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 48 hours after administration. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 72 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 96 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 120 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 168 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 11 to about 20 days after administration to the subject. In some embodiments, resolution of one or more symptoms of bacterial vaginosis occurs within about 21 to about 30 days after administration to the subject. In some embodiments, a method of treating trichomoniasis further comprises a resolution of one or more symptoms of trichomoniasis within up to about seven days after administration to the subject. In some embodiments, a method of treating trichomoniasis further comprises a resolution of one or more symptoms of trichomoniasis within up to about seven days after administration to the subject. In some embodiments, the one or more symptoms include, but are not limited to, purulent malodorous discharge (associated with burning, pruritus, dysuria, frequency, lower abdominal pain), or dyspareunia, burning postcoital bleeding, dyspareunia, dysuria, a thin green-yellow frothy discharge, vulvovaginal erythema (erythema of the vulva and vaginal mucosa), punctate hemorrhages, urethritis, cystitis, purulent vaginitis, sequamative

inflammatory vaginitis, atrophic vaginitis, erosive lichen planus, elevated vaginal pH (about 5.0 to about 6.0), and any combination thereof. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 24 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 48 hours after administration. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 72 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 96 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 120 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 168 hours after administration to the subject. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 7 to about 10 days after administration to the subject. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 11 to about 20 days after administration to the subject. In some embodiments, resolution of one or more symptoms of trichomoniasis occurs within about 21 to about 30 days after administration to the subject.

[0100] This invention and embodiments illustrating the method and materials used may be further understood by reference to the following non-limiting examples.

J. Examples

Example 1

[0101] This study evaluated the safety and pharmacokinetics (PK) of a 1 g or 2 g dose of a new microgranule formulation (formulation shown in Table 2) for SYM-1219, a 5-nitroimidazole being developed for the treatment of women with bacterial vaginosis (BV).

Table 2: Composition of SYM-1219 Drug Product

Component	Function	Quality Standard	Quantity, mg/1g Dose	Quantity, mg/2g Dose
Secnidazole	Active Ingredient	Manufacturer's specifications	1000.00	2000.00
Sugar Spheres (size 35-40 mesh)	Inert core	NF	940.00	1880.00
Povidone (Plasdone K-29/32)	Dispersion and binding	USP	100.82	201.63
Polyethylene Glycol 4000	Seal coating	NF	41.50	83.00

Eudragit NE30D (Ethyl Acrylate, Methyl Methacrylate Copolymer	Delayed release coating	NF	138.30	273.60
Talc	Anti-tacking agent	USP	138.30	273.60
Total			**2365.00**	**4730.00**

[0102] Methods: 28 healthy female subjects (14/group) ages 18-65 years were randomized to receive a single oral dose of either 1 or 2 grams of SYM-1219, mixed into 4 oz. of applesauce. Serial blood samples were collected over 168 hours to determine SYM-1219 plasma concentrations. A non-compartmental analysis was performed and the PK parameters for each treatment group are reported. Safety was evaluated by recording adverse events, vital signs, ECGs and laboratory tests.

[0103] Results: All subjects (N=28) completed the study and were evaluable for PK and safety. Table 2 below discloses the plasma pharmacokinetics of SYM-1219 (1 g or 2 g) administered according to methods described in this Example to fasted healthy female subjects. Table 4 below discloses the urine pharmacokinetics of SYM-1219 (1 g or 2 g) administered according to methods described in this Example to fasted healthy female subjects. Figure 1 illustrates the mean (+SD) SYM-1219 plasma concentration (ug/mL) for the 1 g dose (circle markers) and the 2 g dose (triangle markers) over time.

[0104] The PK of SYM-1219 was consistent between individuals, as demonstrated by low %CV estimates. Mean maximum concentrations were 22.6 mcg/mL for the 1 g dose and 45.4 mcg/mL for the 2 g dose and were achieved by approximately 4 hrs. in both dose groups. Exposure estimates (AUCinf) were 619 mcg*hr./mL for the 1 g dose and 1331 mcg*hr./mL for the 2 g dose. The pharmacokinetics of SYM-1219 was dose proportional when comparing the 1 and 2 g doses. The intersubject variability was low (<20% CV) for C_{max} and AUC. Urinary excretion of unchanged SYM-1219 accounted for 13.6% (1 g dose) and 15.3% (2 g dose) of the administered dose. The amount excreted into the urine increased in proportion to dose. Renal clearance was similar after 1 g and 2 g doses and the renal clearance is only a small percentage (ie, <5%) of the glomerular filtration rate typically found in healthy subjects with normal renal function.

[0105] SYM-1219 was safe and well-tolerated. The most common adverse events were headache and nausea. All adverse events were mild and resolved without sequelae. There were no significant changes in vital signs, ECG or laboratory parameters.

Table 3: Plasma Pharmacokinetics of SYM-1219 After a Single Oral Dose Administered to Fasted Healthy Female Subjects (Part A)

Pharmacokinetic Population

Parameter	SYM-1219 1 gram (N=14)	SYM-1219 2 grams (N=14)
C_{max} (µg/mL)		
n	14	14
Mean (SD)	22.62 (2.871)	45.43 (7.642)
%CV	12.69	16.82
Geometric Mean (SD)	22.45 (2.938)	44.84 (7.467)
Median	22.75	45.05
Min, Max	17.4, 26.5	34.5, 58.3
T_{max} (h)		
n	14	14
Median	3.060	4.000
Min, Max	2.00, 6.00	3.00, 4.05
AUC_{0-t} (h*µg/mL)		
n	14	14
Mean (SD)	609.66 (96.685)	1322.40 (230.256)
%CV	15.86	17.41
Geometric Mean (SD)	602.94 (92.067)	1305.35 (214.383)
Median	587.42	1290.41
Min, Max	487.6, 832.5	1048.5, 1899.5
$AUC_{0-\infty}$ (h*µg/mL)		
n	14	14
Mean (SD)	618.89 (98.093)	1331.63 (230.159)
%CV	15.85	17.28
Geometric Mean (SD)	612.09 (93.248)	1314.74 (214.081)
Median	595.25	1299.10
Min, Max	498.5, 847.0	1055.1, 1911.9
$t_{1/2}$ (h)		
n	14	14
Mean (SD)	17.05 (1.611)	16.86 (2.649)
Median	16.79	17.13
Min, Max	14.7, 20.4	11.3, 20.4
λz (1/h)		
n	14	14
Mean (SD)	0.04099 (0.003757)	0.04220 (0.007544)
Median	0.04129	0.04047
Min, Max	0.0339, 0.0471	0.0340, 0.0613
Source: Table 14.1.2.4, Listing 16.2.1.11.2		

Table 4: Urine Pharmacokinetics of SYM-1219 After a Single Oral Dose Administered to Fasted Healthy Female Subjects (Part A)

Pharmacokinetic Population

Parameter	SYM-1219 1 gram (N=14)	SYM-1219 2 grams (N=14)
Ae_{0-168} (g)		
n	14	14
Mean (SD)	0.136 (0.0238)	0.306 (0.0711)
%CV	17.478	23.234
Geometric Mean (SD)	0.134 (0.0241)	0.300 (0.0602)
Median	0.140	0.299
Min, Max	0.10, 0.18	0.22, 0.52
CLr (mL/min)		
n	14	14
Mean (SD)	3.742 (0.8255)	3.935 (1.0568)
%CV	22.060	26.859
Geometric Mean (SD)	3.650 (0.8701)	3.801 (1.0532)
Median	3.965	3.962
Min, Max	2.37, 4.89	2.23, 6.19
%FE		
n	14	14
Mean (SD)	13.602 (2.3773)	15.300 (3.5549)
%CV	17.478	23.234
Geometric Mean (SD)	13.403 (2.4100)	14.991 (3.0081)
Median	13.981	14.943
Min, Max	10.19, 17.56	11.03, 26.20
Source: Table 14.1.2.5, Listing 16.2.1.12.1		

[0106] Conclusions: This study characterized the single dose PK of a 1 g and 2 g dose of a new microgranule formulation of a 5-nitroimidazole, SYM-1219. SYM-1219 was safe and well-tolerated. The consistent PK and resulting exposure, with low variability between subjects, makes this a promising new therapeutic option. Ongoing studies will further evaluate the safety and efficacy of SYM-1219 for the treatment of women with BV.

Example 2

[0107] Background: This study evaluated the effect of a single 2 g dose of SYM-1219, a new microgranule formulation of a 5-nitroimidazole in development to treat women with bacterial vaginosis, on the pharmacokinetics (PK) of ethinyl estradiol (EE2) and norethindrone (NET).

[0108] Methods: Fifty-four (54) healthy female subjects, ages 18-65, received EE2/NET alone and in combination, where SYM-1219+ EE2/NET were co-administered on Day 1 (Group B1; N=27) or SYM-1219 on Day 1 and EE2/NET on Day 2 (Group B2; N=27). Serial blood samples were drawn to measure plasma concentrations of EE2/NET. A non-compartmental analysis was performed and the PK parameters for each treatment group

are reported. Safety was evaluated by recording of adverse events, vital signs, ECGs and standard laboratory tests.

[0109] Results: Fifty-one (N=26 for B1 and N=25 for B2) subjects completed the study. Figure 2 illustrates the mean (+SD) EE2 plasma concentrations (pg/mL) over time when EE2 was administered alone (circle markers) on Day 1 of Period 1 and when EE2 was administered in conjunction with 2 gram microgranule formulation SYM-1219 on Day 1 of Period 2 (triangle markers) (Group B1). Figure 3 illustrates the mean (+SD) EE2 plasma concentrations (pg/mL) over time when (1) EE2 was administered alone (circle markers) on Day 1 of Period 1; and (2) when 2 gram microgranule formulation SYM-1219 was administered on Day 1 of Period 2 and EE2 was administered on Day 2 of Period 2 (triangle markers) (Group B2). Figure 4 illustrates the mean (+SD) net plasma levels (ng/mL) over time when (1) NET alone was administered on Day 1 of Period 1 (circle markers), and (2) NET followed by 2 gram microgranule formulation of SYM-1219 was administered on Day 1 of Period 2 (triangle markers) (Group B1). Figure 5 illustrates the mean (+SD) net plasma levels (ng/mL) over time when (1) NET alone was administered on Day 1 of Period 1 (circle markers), and (2) 2 gram microgranule formulation of SYM-1219 was administered on Day 1 of Period 2 and NET was administered on Day 2 of Period 2 (triangle markers) (Group B2). Table 4 below is a summary of the NET plasma pharmacokinetic parameters for Group B1 where (1) EE2/NET was administered on Day 1 of Period 1, and (2) EE2/NET was administered followed by SYM-1219 on Day 1 of Period 2; and Group B2 where (1) EE2/NET were administered on Day 1 of Period 1, and (2) 2 g microgranule formulation of SYM-1219 was administered followed by on Day 1 of Period 2 and EE2/NET was administered on Day 2 of Period 2. Table 5 below is a summary of the percent of relative bioavailability for EE2 plasma pharmacokinetic parameters C_{max}, AUC_{0-t}, and $AUC_{0-\infty}$ for Group B1 where (1) EE2/NET was administered on Day 1 of Period 1, and (2) EE2/NET followed by SYM-1219 2 grams were administered on Day 1 of Period 2; and Group B2 where (1) EE2/NET was administered on Day 1 of Period 1, and (2) 2 grams microgranule formulation of SYM-1219 was administered on Day 1 and EE2/NET was administered on Day 2 of Period 2. Table 6 is a summary of the percent of relative bioavailability for NET plasma pharmacokinetic parameters C_{max}, AUC_{0-t}, and $AUC_{0-\infty}$ for Group B1 where (1) EE2/NET was administered on Day 1 of Period 1, and (2) EE2/NET followed by SYM-1219 2 grams were administered on Day 1 of Period 2; and Group B2 where (1) EE2/NET was

administered on Day 1 of Period 1, and (2) 2 grams microgranule formulation of SYM-1219 was administered on Day 1 and EE2/NET was administered on Day 2 of Period 2.

Table 5: Summary of NET Plasma Pharmacokinetic Parameters by Period and Treatment - Pharmacokinetic Population (Part B)

	Group B1[a] (N=26)		Group B2[a] (N=25)	
Parameter	**Period 1**	**Period 2**	**Period 1**	**Period 2**
C_{max} (ng/mL)				
n	26	26	25	25
Mean (SD)	9.18 (5.148)	10.07 (4.394)	9.63 (5.419)	10.69 (5.169)
%CV	56.07	43.62	56.25	48.34
Median	8.00	9.45	8.16	9.39
Min, Max	2.7, 23.0	4.3, 20.7	3.6, 22.7	4.8, 28.6
T_{max} (h)				
n	26	26	25	25
Median	1.000	1.000	1.000	1.000
Min, Max	1.00, 4.00	0.50, 4.00	0.50, 2.08	0.25, 2.00
AUC_{0-t} (h*ng/mL)				
n	26	26	25	25
Mean (SD)	49.37 (34.588)	53.45 (24.132)	61.35 (56.872)	61.16 (40.799)
%CV	70.06	45.15	92.70	66.70
Median	38.67	48.94	41.66	44.53
Min, Max	16.7, 151.0	17.6, 117.6	17.4, 261.5	22.9, 185.9
$AUC_{0-\infty}$ (h*ng/mL)				
n	26	26	25	25
Mean (SD)	57.79 (43.184)	62.39 (29.937)	74.98 (81.529)	71.53 (51.804)
%CV	74.72	47.98	108.73	72.42
Median	45.33	54.33	47.35	51.59
Min, Max	18.0, 196.9	20.2, 144.5	20.3, 397.1	26.2, 224.6
$t_{1/2}$ (h)				
n	26	26	25	25
Mean (SD)	9.60 (2.826)	9.60 (2.922)	10.04 (2.829)	9.51 (2.430)
Median	8.71	9.12	9.29	9.19
Min, Max	6.2, 17.8	5.1, 16.4	6.8, 17.3	6.1, 16.6
λz (1/h)				
n	26	26	25	25
Mean (SD)	0.07709 (0.018293)	0.07886 (0.023816)	0.07369 (0.017781)	0.07685 (0.016908)
Median	0.07966	0.07642	0.07458	0.07539
Min, Max	0.0389, 0.1125	0.0422, 0.1366	0.0401, 0.1022	0.0418, 0.1146

a: Group B1 = EE2/NET on Day 1 of Period 1, then EE2/NET followed by SYM-1219 2 grams on Day 1 of Period 2.
Group B2 = EE2/NET on Day 1 of Period 1, then SYM-1219 2 grams on Day 1 and EE2/NET on Day 2 of Period 2.
Source: Table 14.2.2.13; Listings 16.2.2.12.4 – 16.2.2.12.6

Table 6: Summary of the Percent of Relative Bioavailability for EE2 Plasma Pharmacokinetic Parameters C_{max}, AUC_{0-t}, and $AUC_{0-\infty}$ by Treatment (Part B)

Parameter Treatment	Period	n	Mean (%CV)	Geometric LSMeans (SE)[b]	% Ratio: 100*Test/Reference[c]	
					Geometric LSMean % Ratio (SE)[b]	90% C.I.[b]
C_{max} (pg/mL)						
Group B1[a]	Period 2	26	59.88 (42.19)	55.38 (2.728)	71.07 (4.951)	(63.09, 80.05)
	Period 1	26	80.63 (26.84)	77.92 (3.839)		
Group B2[a]	Period 2	25	92.60 (34.77)	87.16 (2.369)	104.96 (4.034)	(98.28, 112.09)
	Period 1	25	89.12 (36.36)	83.04 (2.257)		
AUC_{0-t} (h*pg/mL)						
Group B1[a]	Period 2	26	615.55 (31.20)	590.74 (11.892)	94.26 (2.683)	(89.78, 98.95)
	Period 1	26	643.67 (23.85)	626.75 (12.617)		
Group B2[a]	Period 2	25	668.63 (26.22)	643.74 (10.529)	99.04 (2.291)	(95.20, 103.04)
	Period 1	25	680.48 (28.91)	649.96 (10.631)		
$AUC_{0-\infty}$ (h*pg/mL)						
Group B1[a]	Period 2	25	954.35 (28.75)	924.75 (28.869)	105.37 (4.565)	(97.84, 113.48)
	Period 1	26	911.11 (29.39)	877.60 (26.363)		
Group B2[a]	Period 2	25	937.42 (33.60)	882.24 (23.866)	93.32 (3.570)	(87.41, 99.63)
	Period 1	25	994.55 (28.91)	945.39 (25.575)		

a: Group B1 = EE2/NET on Day 1 of Period 1, then EE2/NET followed by SYM-1219 2 grams on Day 1 of Period 2.
Group B2 = EE2/NET on Day 1 of Period 1, then SYM-1219 2 grams on Day 1 and EE2/NET on Day 2 of Period 2.
b: From an ANOVA model for the log-transformed results with effects treatment (Period 1: EE2/NET alone, Period 2: EE2/NET in combination with SYM-1219) and subject.
c: Test is Period 2 [EE2/NET followed by SYM-1219 2 grams on Day 1 (Group B2) or SYM-1219 2 grams on Day 1 and EE2/NET on Day 2 (Group B2)]; Reference is
Period 1 (EE2/NET Alone)
Source: Table 14.2.2.15

Table 7: Summary of the Percent of Relative Bioavailability for NET Plasma Pharmacokinetic Parameters C_{max}, AUC_{0-t}, and $AUC_{0-\infty}$ by Treatment (Part B)

Parameter Treatment	Period	n	Mean (%CV)	Geometric LSMeans (SE)[b]	% Ratio: 100*Test/Reference[c]	
					Geometric LSMean % Ratio (SE)[b]	90% C.I.[b]
C_{max} (ng/mL)						
Group B1[a]	Period 2	26	10.07 (43.62)	9.16 (0.455)	113.18 (7.958)	(100.37, 127.63)
	Period 1	26	9.18 (56.07)	8.09 (0.402)		
Group B2[a]	Period 2	25	10.69 (48.34)	9.74 (0.483)	116.46 (8.178)	(103.27, 131.32)
	Period 1	25	9.63 (56.25)	8.36 (0.415)		
AUC_{0-t} (h*ng/mL)						
Group B1[a]	Period 2	26	53.45 (45.15)	48.72 (1.738)	115.52 (5.828)	(105.99, 125.92)
	Period 1	26	49.37 (70.06)	42.17 (1.504)		
Group B2[a]	Period 2	25	61.16 (66.70)	51.94 (1.361)	110.78 (4.104)	(103.97, 118.03)
	Period 1	25	61.35 (92.70)	46.88 (1.228)		
$AUC_{0-\infty}$ (h*ng/mL)						
Group B1[a]	Period 2	26	62.39 (47.98)	56.42 (2.070)	116.27 (6.032)	(106.41, 127.04)
	Period 1	26	57.79 (74.72)	48.53 (1.780)		
Group B2[a]	Period 2	25	71.53 (72.42)	59.95 (1.640)	108.75 (4.207)	(101.78, 116.19)
	Period 1	25	74.98 (108.73)	55.13 (1.508)		

a: Group B1 = EE2/NET on Day 1 of Period 1, then EE2/NET followed by SYM-1219 2 grams on Day 1 of Period 2.
Group B2 = EE2/NET on Day 1 of Period 1, then SYM-1219 2 grams on Day 1 and EE2/NET on Day 2 of Period 2.
b: From an ANOVA model for the log-transformed results with effects treatment (Period 1: EE2/NET alone, Period 2: EE2/NET in combination with SYM-1219) and subject.
c: Test is Period 2 [EE2/NET followed by SYM-1219 2 grams on Day 1 (Group B2) or SYM-1219 2 grams on Day 1 and EE2/NET on Day 2 (Group B2)]; Reference is
Period 1 (EE2/NET Alone)
Source: Table 14.2.2.16

[0110] EE2 C_{max} was reduced by 29% (90% CI 63.09, 80.05) for Group B1; no change in EE2 AUC was seen. EE2 PK was not altered for Group B2. NET C_{max} and AUC increased (13%) slightly for Group B1. NET C_{max} increased by 16% for Group B2; no change was seen for NET AUC. There was no effect (90% CIs within 80-125%) on AUC_{0-t} or $AUC_{0-\infty}$ when SYM-1219 was administered immediately after EE2/NET administration. When EE2/NET was administered 1 day after SYM-1219 administration, there was no effect (90% CIs within 80-125%) from SYM-1219 on EE2 C_{max}, AUC_{0-t} or $AUC_{0-\infty}$.

[0111] Simultaneous co-administration of EE2/NET and SYM-1219 appears to decrease the rate but not the extent of EE2 absorption. Administration of EE2/NET one day after SYM-1219 appears to have no effect on EE2 absorption.

[0112] NET C_{max}, AUC_{0-t} or $AUC_{0-\infty}$ were increased by 13-16% and the upper value of 90% CIs were just above 125% when SYM-1219 was administered immediately after EE2/NET administration. When EE2/NET was administered 1 day after SYM-1219 administration the NET C_{max}, AUC_{0-t} or $AUC_{0-\infty}$ were increased by 9-16%. The NET upper value of the 90% CI for C_{max} was 131% and there was no effect (90% CIs within 80-125%) from SYM-1219 on AUC_{0-t} or $AUC_{0-\infty}$.

[0113] Simultaneous co-administration of EE2/NET and SYM-1219 may result in small (13-16%) increases in the rate and the extent of NET absorption. Administration of EE2/NET one day after SYM-1219 may result in a small (16%) increase in the rate but not the extent of NET absorption.

[0114] SYM-1219 was safe and well-tolerated when taken alone or in combination with EE2/NET. The most common adverse events were headache and nausea. All adverse events were mild and resolved without sequelae. There were no significant changes in vital signs, ECG or laboratory parameters. Concomitant administration of SYM-1219 with EE2/NET is not expected to have an effect on contraceptive efficacy.

[0115] Conclusions: This study characterized the PK of EE2/NET with SYM-1219 co-administration. Minor, clinically insignificant, reductions in EE2 exposure were seen when SYM-1219 and EE2/NET were co-administered on the same day. No change in EE2 exposure was seen when the SYM-1219 and EE2/NET doses were staggered by one day. No reductions in drug exposure were evident for NET for either treatment group. These in vivo data indicate that contraceptive efficacy for EE2/NET will not be altered by SYM-1219 administration. This was surprising in light of in vitro metabolism data indicating that concentrations of EE2 and NET may be lowered and contraceptive efficacy may be adversely affected by co-administration of SYM-1219.

Example 3

[0116] This study was a Phase 2, multicenter, prospective, double-blind, placebo-controlled study to evaluate the effectiveness and safety of SYM-1219 for the treatment of women with bacterial vaginosis. The study was designed in accordance with FDA guidance for

pivotal bacterial vaginosis trials with a primary end point clinical cure in the Modified Intent-to-Treat (mITT) population at day 21 to 30 versus placebo (two-sided test at alpha = 0.05). Subjects were recruited to the study they presented with the following Amsel criteria: presence of typical discharge. a positive KOH Whiff test vaginal fluid pH greater than or equal to 4.7, and the presence of "clue cells" (epithelial cells with adhering bacteria) on microscopic examination. Table 8 shows that a 2 gram single-dose of SYM-1219 is effective for bacterial vaginosis compared with placebo.

Table 8: Summary of Clinical Outcome Responder Rates by Treatment Modified Intent-to-Treat Population (mITT)

	SYM-1219 2 grams (N=62) n (%)	**Placebo (N=62) n (%)**
Clinical Outcome Responder[a]	42 (67.7)	11 (17.7)
Non-Responder	20 (32.3)	51 (82.3)
P-value[b]	<0.001	
95% Exact Binomial C.I. for Responder Rate	54.7, 79.1	9.2, 29.5
a: Clinical Outcome Responder is defined as a subject who had all three of the following at TOC/EOS: normal vaginal discharge, negative KOH Whiff test, and clue cells <20%. b: P-value versus placebo from CMH test adjusted for BV strata (≤3 or >3 episodes in the past 12 months)		

[0117] As can be seen in Table 9, a single dose of 2 grams of SM-1219 was surprisingly well tolerated.

Table 9: Summary of treatment-emergent adverse events by treatment safety population

System Organ Class Preferred Term		**SYM-1219 2 grams (N=72)**	**Placebo (N=72)**
Any Adverse Event			
Overall	Subjects[a], [n (%)]	14(19.4)	7 (9.7)
	Events, [n]	19	7
Infections and infestations			
Overall	Subjects[a], [n (%)]	5 (6.9)	6 (8.3)
	Events, [n]	7	6
Vulvovaginal mycotic infection	Subjects[a], [n (%)]	2 (2.8)	1 (1.4)
	Events, [n]	2	1
Candida infection	Subjects[a], [n (%)]	0	0

	Events, [n]	0	1
Chlamydial infection	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Fungal infection	Subjects[a], [n (%)]	0	1 (1.4)
	Events, [n]	0	1
Gonorrhoea	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Tooth abscess	Subjects[a], [n (%)]	1 (1.4)	1 (1.4)
	Events, [n]	1	1
Tooth infection	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Urinary tract infection	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Upper respiratory tract infection	Subjects[a], [n (%)]	0	2 (2.8)
	Events, [n]	0	2
Acute sinusitis	Subjects[a], [n (%)]	0	1 (1.4)
	Events, [n]	0	1
Nervous system disorders			
Overall	Subjects[a], [n (%)]	3 (4.2)	0
	Events, [n]	3	0
Headache	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Dizziness	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Dysgeusia	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Reproductive system and breast disorders			
Overall	Subjects[a], [n (%)]	2 (2.8)	0
	Events, [n]	3	0
Vaginal discharge	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Vaginal odor	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Vulvovaginal pruritus	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Investigations			
Overall	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	2	0
Alanine aminotransferase increased	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Aspartate aminotransferase increased	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Renal and urinary disorders			
Overall	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Chromaturia	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0

Gastrointestinal disorders			
Overall	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Nausea	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Injury, poisoning and procedural complications			
Overall	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Thermal burn	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Respiratory, thoracic and mediastinal disorders			
Overall	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Oropharyngeal pain	Subjects[a], [n (%)]	1 (1.4)	0
	Events, [n]	1	0
Surgical and medical procedures			
Overall	Subjects[a], [n (%)]	0	1 (1.4)
	Events, [n]	0	1
Tooth extraction	Subjects[a], [n (%)]	0	1 (1.4)
	Events, [n]	0	1
a: Subjects experiencing multiple adverse events are only counted once within a given cell.			

Table 10: Summary of clinical outcome responder rates by bacterial vaginosis strata and treatment modified intent-to-treat population.

	SYM-1219 2 grams (N=62) n (%)	**Placebo (N=62) n (%)**
3 or fewer episodes in the past 12 months		
Clinical Outcome Responder[a]	30 (73.2)	10 (23.3)
Non-Responder	11 (26.8)	33 (76.7)
P-value[b]	<0.001	
95% Exact Binomial C.I. for Responder Rate	57.1, 85.8	11.8, 38.6
4 or more episodes in the past 12 months		
Clinical Outcome Responder[a]	12 (57.1)	1 (5.3)
Non-Responder	9 (42.9)	18 (94.7)
P-value[b]	<0.001	
95% Exact Binomial C.I. for Responder Rate	34.0, 78.2	0.1, 26.0
a: Clinical Outcome Responder is defined as a subject who had all three of the following at TOC/EOS: normal vaginal discharge, negative KOH Whiff test, and clue cells <20%. b: P-value versus placebo from CMH test Source: Listing 16.2.1.6		

[0118] A 2 gram single dose of SYM-219 was found to be effective in treating bacterial vaginosis in subjects having had 3 or fewer bacterial vaginosis infections/episodes in the past 12 months, as well as in subjects having had 4 or more bacterial vaginosis infections/episodes in the past twelve months (See Table 10).

Example 3:

[0119] In the mITT population, using a time stamped telephone diary questionnaire, on a five point scale composed of (1) Normal/Not an Issue, (2) Mildly Abnormal, (3) Moderately Abnormal, (4) Severely Abnormal and (5) Very Severely Abnormal, the proportion of women on a 2g dose reporting 3-5 for vaginal discharge declined from 59% on day 1, to 30 % on day 3 (~48 hours), and to 14% on day 7 as can be seen in Table 11. The proportion of women on a 2g dose reporting 4-5 for vaginal discharge declined from 36% on day 1, to 11 % on day 3 (~48 hours), and to 0% on day 7 as can be seen in Table 11. The proportion of women on a 2g dose reporting 3-5 for vaginal odor declined from 66% on day 1, to 20 % on day 3 (~48 hours), and to 9% on day 7 as can be seen in Table 11. The proportion of women on a 2g dose reporting 4-5 for vaginal odor declined from 38% on day 1, to 9 % on day 3 (~48 hours), and to 0% on day 7 as can be seen in Table 11

[0120] Table 11 – Results of telephone diary questionnaire

		Day															
mITT	**Points**	**1**		**2**		**3**		**4**		**5**		**6**		**7**		**EOS**	
2g - Discharge	1	6	10%	9	17%	13	24%	19	35%	21	43%	22	47%	24	55%	36	68%
	2	18	31%	20	38%	25	46%	22	40%	17	35%	15	32%	14	32%	9	17%
	3	13	22%	15	29%	10	19%	8	15%	4	8%	7	15%	6	14%	4	8%
	4	17	29%	3	6%	3	6%	5	9%	6	12%	2	4%	0	0%	3	6%
	5	4	7%	5	10%	3	6%	1	2%	1	2%	1	2%	0	0%	1	2%
	Total	58		52		54		55		49		47		44		53	
2g - Odor	1	8	14%	10	19%	20	37%	27	49%	28	58%	29	62%	33	75%	36	69%
	2	12	21%	23	44%	23	43%	18	33%	12	25%	12	26%	7	16%	7	13%
	3	16	28%	10	19%	6	11%	6	11%	5	10%	5	11%	4	9%	9	17%
	4	17	29%	8	15%	4	7%	4	7%	3	6%	1	2%	0	0%	0	0%
	5	5	9%	1	2%	1	2%	0	0%	0	0%	0	0%	0	0%	0	0%
	Total	58		52		54		55		48		47		44		52	

[0121] While the illustrative embodiments of the invention have been described with particularity, it will be understood that various other modifications will be apparent to and can be readily made by those skilled in the art without departing from the spirit and scope of the

invention. Accordingly, it is not intended that the scope of the embodiments above be limited to the examples and descriptions set forth hereinabove but rather that the invention be construed as encompassing all the features of patentable novelty which reside in embodiments described herein, including all features which would be treated as equivalents thereof by those skilled in the relevant art.

K. Claims

What is claimed:

1. A method of treating bacterial vaginosis in a subject in need thereof comprising administering to the subject a therapeutically effective amount of secnidazole in a microgranule formulation.

2. The method of claim 1, wherein the secnidazole in a microgranule formulation is administered orally.

3. The method of claim 1, wherein the secnidazole in a microgranule formulation comprises a plurality of microgranules.

4. The method of claim 3, wherein the plurality of microgranules each have a particle size range of about 400 to about 841 microns.

5. The method of claim 1, wherein the microgranule formulation further comprises at least one of sugar spheres, povidone, polyethylene glycol 4000, Eudragit NE30D, talc, or a combination thereof.

6. The method of claim 1, wherein the secnidazole in a microgranule formulation may be mixed, stirred, or otherwise integrated into a food substance.

7. The method of claim 1, wherein the subject is a female.

8. The method of claim 1, wherein the subject is a pregnant female.

9. The method of claim 1, wherein the subject is a female having had 3 or more bacterial vaginosis infections/episodes in the past 12 months.

10. The method of claim 1, wherein the subject is a female having had 4 or more bacterial vaginosis infections/episodes in the past 12 months.

11. The method of claim 1, wherein the subject is a female presenting with an off-white (milky or gray), thin, homogeneous vaginal discharge, an odor, or a combination thereof.

12. The method of claim 1, wherein the subject is a female presenting with abnormal vaginal discharge, a positive KOH Whiff test, vaginal fluid pH greater than or equal to 4.7, and the presence of "clue cells" greater than 20% of total epithelial cells.

13. The method of claim 1, wherein the subject is a female with confirmed bacterial vaginosis.

14. The method of claim 13, wherein the female with confirmed bacterial vaginosis presents with four Amsel criteria parameters and a gram stain slide Nugent score equal to, or higher than four on bacterial analysis of vaginal samples.

15. The method of claim 14, wherein the four Amsel criteria parameters are abnormal vaginal discharge, a positive KOH Whiff test, vaginal fluid pH greater than or equal to 4.7, and the presence of clue cells greater than 20% of total epithelial cells.

16. The method of claim 1, wherein the subject is a female with suspected bacterial vaginosis.

17. The method of claim 16, wherein the female with suspected bacterial vaginosis presents with four Amsel criteria parameters.

18. The method of claim 17, wherein the four Amsel criteria parameters are abnormal vaginal discharge, a positive KOH Whiff test, vaginal fluid pH greater than or equal to 4.7, and the presence of clue cells greater than 20% of total epithelial cells.

19. The method of claim 1, wherein the therapeutically effective amount of secnidazole in a microgranule formulation is administered as a single dose.

20. The method of claim 19, wherein the therapeutically effective amount of secnidazole in a microgranule formulation administered as a single dose is the only dose required

to be administered to the subject to achieve a post treatment clinical outcome, resolution of one or more symptoms of bacterial vaginosis, or a combination thereof.

21. The method of claim 1, wherein the therapeutically effective amount of secnidazole in a microgranule formulation is 2 grams.

22. The method of claim 1, wherein the therapeutically effective amount of secnidazole in a microgranule formulation is an amount of secnidazole in a microgranule formulation that exhibits a plasma Cmax of between about 8 ng/ml and about 11 ng/ml in the subject.

23. The method of claim 1, wherein the therapeutically effective amount of secnidazole in a microgranule formulation is an amount of secnidazole that exhibits a plasma Cmax of between about 34.5 μg/ml and about 58.3 μg/ml.

24. The method of claim 1, wherein the therapeutically effective amount of secnidazole in a microgranule formulation is an amount of secnidazole that exhibits a plasma Cmax of between about 17.4 μg/ml and about 26.5 μg/ml.

25. The method of claim 1, wherein the therapeutically effective amount of secnidazole in a microgranule formulation is an amount of secnidazole that exhibits a tmax of about 3 hours to about 4.055 hours.

26. The method of claim 1, wherein the therapeutically effective amount of secnidazole in a microgranule formulation is an amount of secnidazole that exhibits a tmax of about 2 hours to about 6 hours.

27. The method of claim 1, wherein the therapeutically effective amount of secnidazole in a microgranule formulation is co-administered with an additional compound selected from ethinyl estradiol (EE2), norethindrone (NET), and a combination thereof.

28. The method of claim 1 further comprising determining a post-treatment clinical outcome.

29. The method of claim 28, wherein a post-treatment clinical outcome is indicative of a clinical outcome responder.

30. The method of claim 29, wherein a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, and clue cells less than 20% of total epithelial cells, post-treatment.

31. The method of claim 29, wherein a clinical outcome responder is a subject with a gram stain slide Nugent score of less than four, post-treatment.

32. The method of claim 29, wherein a clinical outcome responder is a subject with normal vaginal discharge, a negative KOH Whiff test, clue cells less than 20% of total epithelial cells, and a gram stain slide Nugent score of less than four, post-treatment.

33. The method of claim 1, wherein administering to the subject a therapeutically effective amount of secnidazole in a microgranule formulation results in better than expected effectiveness than FDA-approved drugs used in the treatment of bacterial vaginosis.

34. The method of claim 1, wherein administering to the subject a therapeutically effective amount of secnidazole in a microgranule formulation results in a better than expected safety profile than FDA-approved drugs used in the treatment of bacterial vaginosis.

35. The method of claim 1, wherein the therapeutically effective amount of secnidazole in a microgranule formulation is mixed into a food substance.

36. The method of claim 1 further comprising administering an additional compound selected from ethinyl estradiol (EE2), norethindrone (NET), or a combination thereof.

37. The method of claim 36, wherein the additional compound is administered on the same day as the secnidazole microgranule formulation.

38. The method of claim 36, wherein the additional compound is administered on a different day than the secnidazole microgranule formulation.

39. The method of claim 36, wherein the secnidazole microgranule formulation does not affect the contraceptive efficacy of the additional compound.

40. The method of claim 1, wherein the subject has a resolution of one or more symptoms of bacterial vaginosis within up to about seven days after administration.

41. The method of claim 1, wherein the subject has an alleviation of one or more symptoms of bacterial vaginosis within up to about three days after administration.

42. A microgranule formulation comprising secnidazole, or pharmaceutically acceptable salts thereof.

43. The microgranule formulation of claim 42, comprising a therapeutically effective amount of secnidazole, or pharmaceutically acceptable salts thereof.

44. The microgranule formulation of claim 42, wherein the microgranule formulation is a delayed release formulation.

45. The microgranule formulation of claim 44, wherein the delayed release formulation, when administered to a subject that provides a secnidazole concentration profile characterized by a change in secnidazole concentration as function of time that is less than that of an immediate release secnidazole microgranule formulation.

46. The microgranule formulation of claim 42, wherein the microgranule formulation comprises about 1 g to about 2 g of secnidazole or pharmaceutically acceptable salts thereof.

47. The microgranule formulation of claim 42, wherein the microgranule formulation comprises about 2 g of secnidazole or pharmaceutically acceptable salts thereof.

48. The microgranule formulation of claim 42, wherein the microgranule formulation is suitable for oral administration.

49. The microgranule formulation of claim 42, further comprising sugar spheres, povidone, polyethylene glycol 4000, Eudragit NE30D, talc, or any combination thereof.

50. The microgranule formulation of claim 42, further comprising. polyethylene glycol 4000 and Eudragit NE30D.

51. The microgranule formulation of claim 42, wherein the microgranule formulation comprises a plurality of microgranules.

52. The method of claim 51, wherein the plurality of microgranules each have a particle size range of about 350 to about 600 microns.

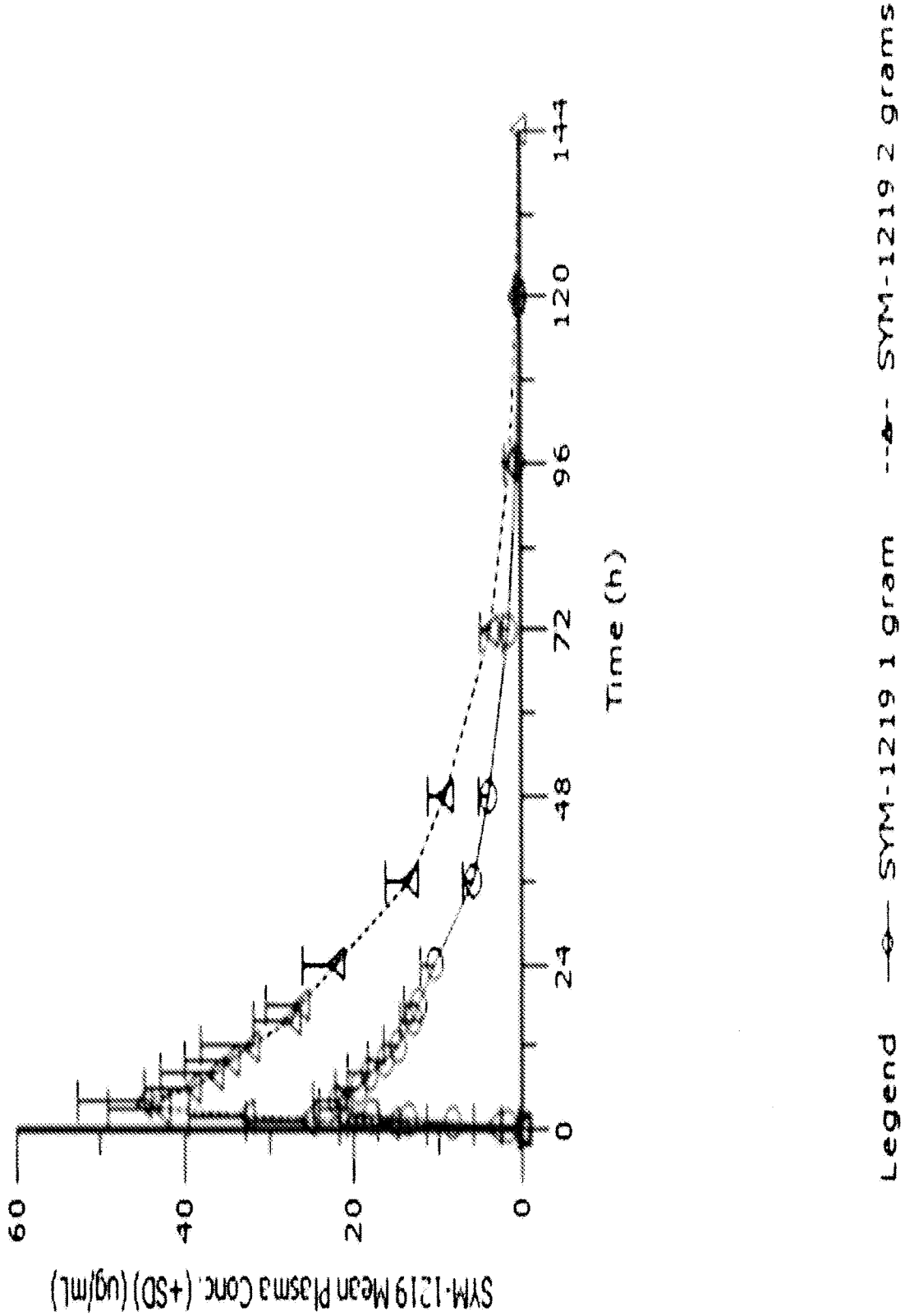
SYM-1219 Mean Plasma Conc. (+SD) (ug/mL)
60
40
20
0
0
24
48
72
96
120
144
Time (h)
Legend
SYM-1219 1 gram
SYM-1219 2 grams

Figure 1

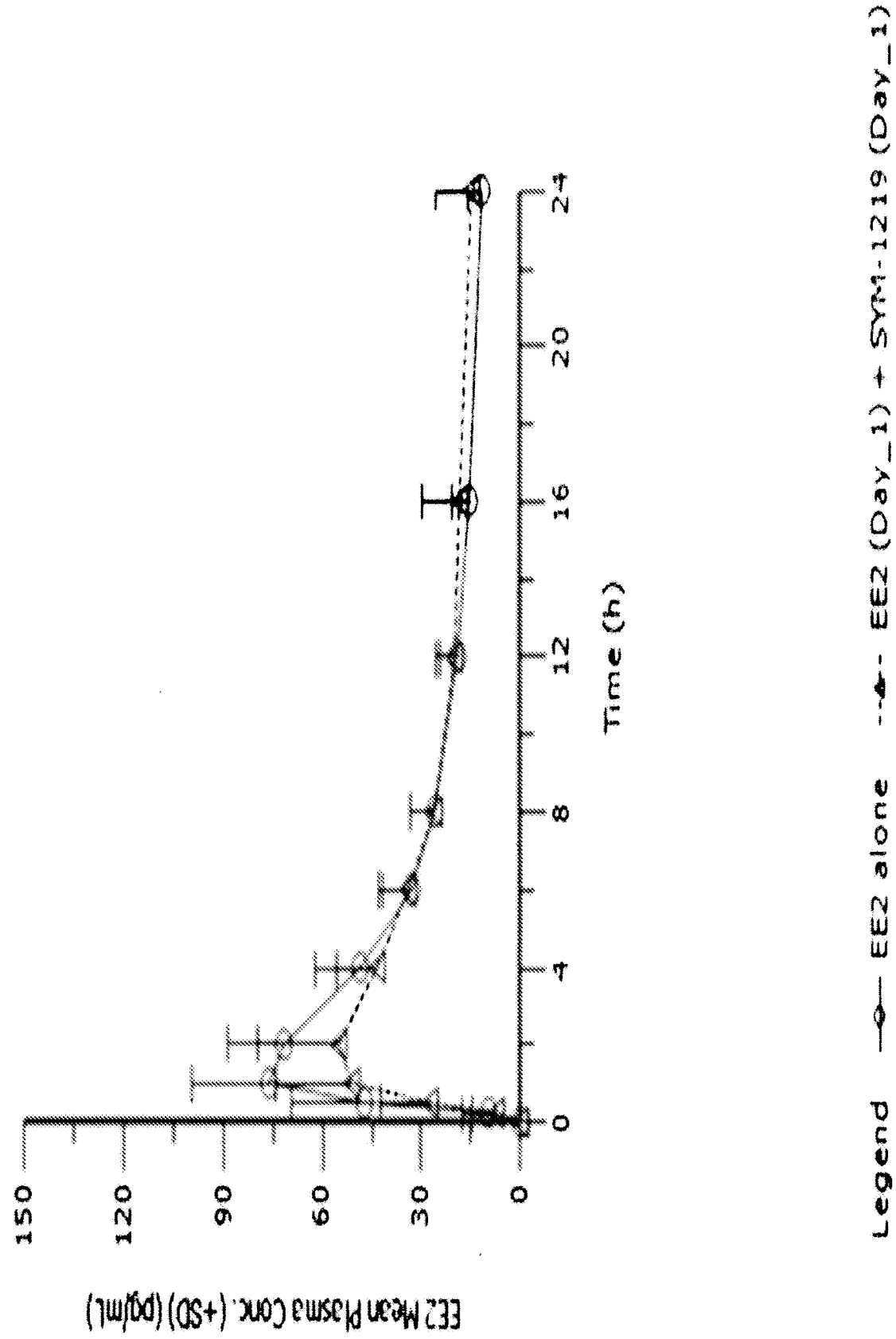
EE2 Mean Plasma Conc. (+SD) (pg/mL)
150
120
90
60
30
0
0
4
8
12
16
20
24
Time (h)
Legend
EE2 alone
EE2 (Day_1) + SYM-1219 (Day_1)

Figure 2

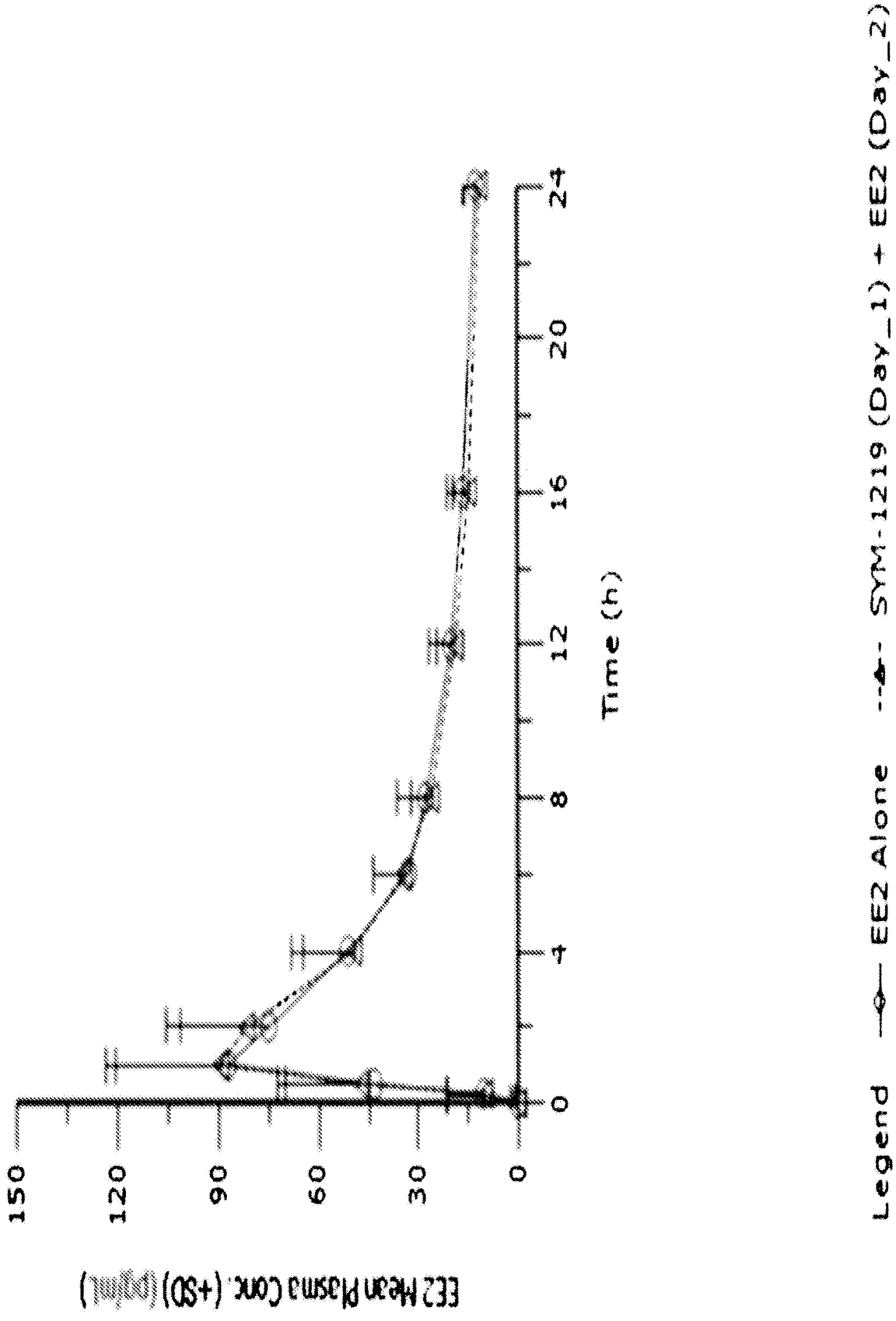
EE2 Mean Plasma Conc. (+SD) (pg/mL)
150
120
90
60
30
0
0
4
8
12
16
20
24
Time (h)
Legend
EE2 Alone
SYM-1219 (Day_1) + EE2 (Day_2)

Figure 3

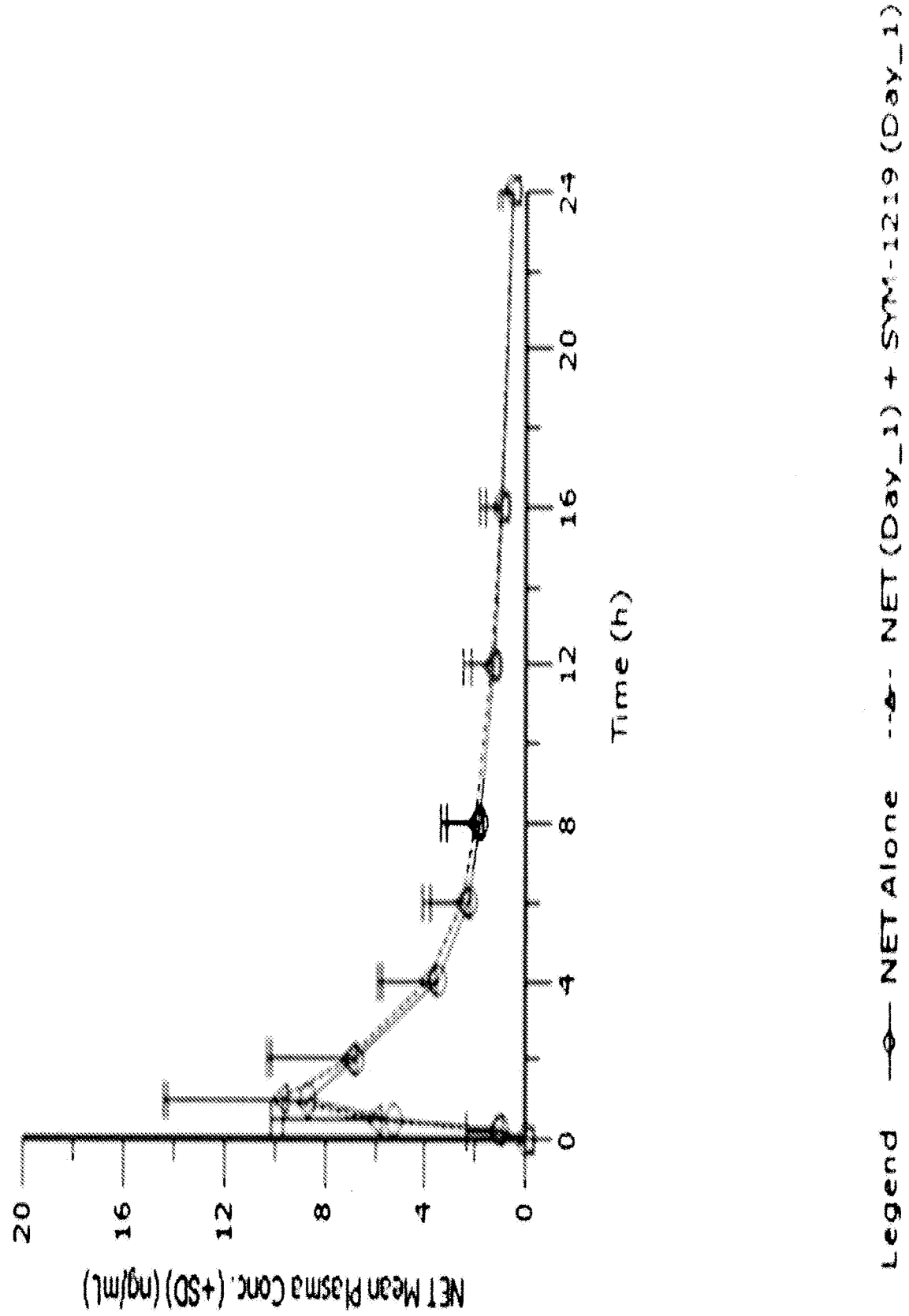
NET Mean Plasma Conc. (+SD) (ng/mL)
20
16
12
8
4
0
0
4
8
12
16
20
24
Time (h)
Legend
NET Alone
NET (Day_1) + SYM-1219 (Day_1)

Figure 4

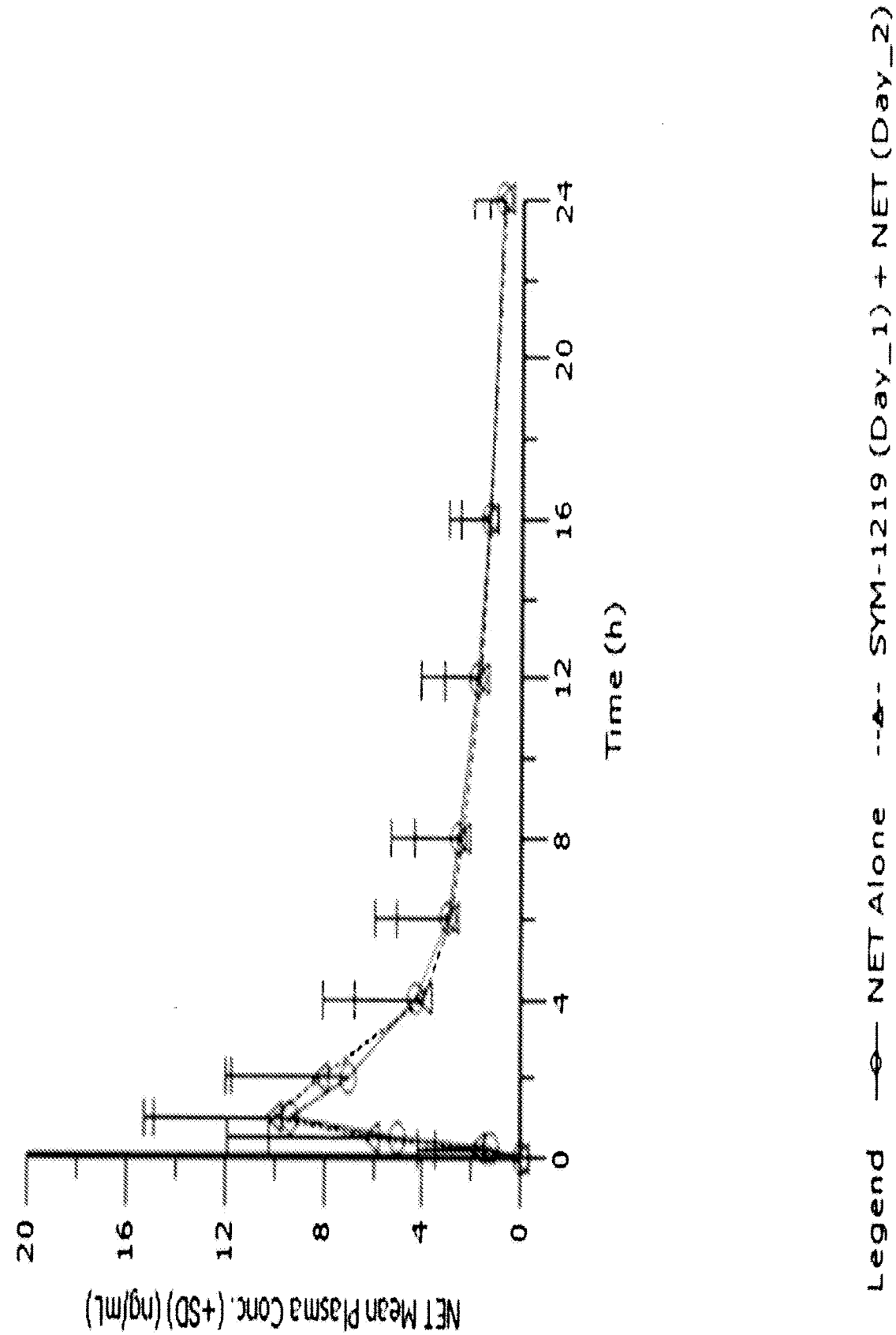
NET Mean Plasma Conc. (+SD) (ng/mL)
20
16
12
8
4
0
0
4
8
12
16
20
24
Time (h)
Legend
NET Alone
SYM-1219 (Day_1) + NET (Day_2)

Figure 5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2015/048681

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 31/4164 (2015.01)
CPC - A61K 31/4164 (2015.10)
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - A61K 31/4164; A61P 15/02 (2015.01)
CPC - A61K 31/4164 (2015.10)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
IPC(8) - A61K 31/4164; A61P 15/02 (2015.01); CPC - A61K 31/4164 (2015.10) (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatBase, Google Patents, Google Scholar
Search terms used: bacterial vaginosis secnidazole Flagentyl Sindose Secnil microgranule microsphere microparticle microencapsule microcapsule pellet particulate oral po size diameter food cmax tmax pharmacokinetic PK povidone polyethylene PEG Eudragit NE30D

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CN 1973838 A (HUBEI KEYI PHARMACEUTICAL INDUSTRY CO) 06 June 2007 (06.06.2007) see machine translation	1-5, 7, 42, 43, 48, 49, 51, 52
---		---
Y		6, 8-21, 27-32, 35-37, 44-47, 50
X	CN 1546020 A (ZHEJIANG JUDU GROUP CO LTD) 17 November 2004 (17.11.2004) see machine translation	1, 40, 41
Y	WO 2014/121298 A2 (SERES HEALTH INC) 07 August 2014 (07.08.2014) entire document	6, 35
Y	US 2007/0154516 A1 (BORTZ et al) 05 July 2007 (05.07.2007) entire document	8, 10
Y	US 2012/0295839 A1 (PAULL et al) 22 November 2012 (22.11.2012) entire document	9, 11-18, 28-32
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