METHODS AND PRODUCTS FOR TREATMENT OF GASTROINTESTINAL DISORDERS

PRIORITY

[0001] This application claims the benefit of, and priority to, U.S. Provisional Application No. 62/876,350, filed July 19, 2019, and U.S. Provisional Application No. 63/001,888, filed March 30, 2020, the contents of each of which are hereby incorporated by reference in their entirety.

FIELD OF THE INVENTION

[0002] The present invention relates to, in part, compositions and methods for the delivery of bacterial isolates and/or cocktails of bacterial isolates useful for the treatment of disorders related to intestinal dysbiosis.

DESCRIPTION OF THE TEXT FILE SUBMITTED ELECTRONICALLY

[0003] This application contains a sequence listing. It has been submitted electronically *via* EFS-Web as an ASCII text file entitled "FIN-019PC_ST25". The sequence listing is 65,811 bytes in size, and was prepared on July 16, 2020. The sequence listing is hereby incorporated by reference in its entirety.

BACKGROUND

[0004] The human GI tract harbors a diverse microbial community of over one thousand distinct bacterial species and an estimated excess of 1×10^{14} microorganisms. This microbial community, also referred to as the microbiota (and the genetic component being the microbiome), has proven to be critical for human health. For example, a healthy microbiome provides the human host with multiple benefits, including resistance to pathogen infection, nutrient biosynthesis and absorption, and immune stimulation. A dysbiosis or disruption of the microbiome results in increased susceptibility to pathogens, altered metabolic profiles, and systemic inflammation or autoimmunity. Indeed, dysbiosis of the microbiome (i.e., intestinal dysbiosis) can predispose the human host to a variety of pathological conditions including gastrointestinal disorders such as inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS) as well as infections by pathogens including *Clostridium difficile* (*C. diff., e.g. Clostridium difficile* infection (CDI)).

[0005] IBD affects over 1.6 million Americans with as many as 70,000 new cases being diagnosed in the United States each year. IBD is characterized by chronic inflammation in the

GI tract. The two most common forms of IBD include ulcerative colitis (UC) and Crohn's Disease (CD). UC occurs in the colon while CD may be present in the entire GI tract. The clinical symptoms are diarrhea, abdominal pain, occasional rectal bleeding, weight loss, tiredness and sometimes fever. For most patients, IBD is a chronic condition with symptoms lasting for months to years. Currently, there are no medical cures for IBD. Instead, current therapies are directed to controlling the GI symptoms by reducing inflammation. In severe cases, surgical procedures including colectomy, proctocolectomy, and ileostomy may be used.

[0006] Researchers have attempted to restore a healthy microbiome in such patients to alleviate or eliminate these diseases. For instance, one approach involves transplantation of a fecal microbiota derived from stool of a healthy human donor, to repopulate the gut (so-called Fecal Microbiota Transplant (FMT)). However, this treatment is not ideal and particularly unpalatable. Accordingly, a more recent approach is to develop a rationally selected, defined mix of bacteria, which could be taken by patients and replace fecal transplants. This "bugs as drugs" concept looks to convert the therapeutic benefits of FMT to a more standardized and drugable system. Unfortunately, but not surprisingly, this approach has been met with early stumbles. For example, a recent clinical trial with SER-109, a mix of bacterial spores designed to treat patients with CDI, failed to meet its main goal in a Phase 2 trial. This drug failed to reduce the relative risk of CDI recurrence, compared to a placebo, up to eight weeks after treatment.

[0007] Accordingly, there remains a need for effective therapeutics that can restore a healthy intestinal microbiota thereby providing effective treatments for a variety of disorders related to intestinal dysbiosis, e.g., gastrointestinal disorders.

SUMMARY

[0008] In various aspects, the present invention provides compositions and methods that are useful treating or preventing inflammatory bowel disease (IBD) in a subject in need thereof. For instance, the present invention, in part, relates to a plurality of bacterial isolates, wherein at least two of the plurality of bacterial isolates are isolated from a stool of different human donors.

[0009] An aspect of the present invention is a method of treating or preventing inflammatory bowel disease (IBD) in a subject in need thereof, the method comprising administering to the subject a plurality of bacterial isolates, wherein the plurality of bacterial isolates comprises *Bacteroides stercoris*, and at least two of *Bacteroides cellulosilyticus, Bacteroides uniformis,*

Suboligranulum variabile, Anaerostipes hadrus, Odoribacter splanchnicus, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*, wherein at least two of the plurality of bacterial isolates are isolated from a stool of different human donors.

[0010] An aspect of the present invention is a pharmaceutical composition comprising a plurality of bacterial isolates, wherein the plurality of bacterial isolates comprise *Bacteroides stercoris*, and at least two of *Bacteroides cellulosilyticus, Bacteroides uniformis, Suboligranulum variabile, Anaerostipes hadrus, Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*, wherein at least two of the plurality of bacterial isolates are isolated from a stool of different human donors.

[0011] In embodiments, the plurality of bacterial isolates comprises at least two, or at least three, or at least four, or at least five, or at least six, or at least seven, or at least eight, or at least nine, or each of *Bacteroides cellulosilyticus, Bacteroides uniformis, Odoribacter splanchnicus*, *Roseburia faecis*, *Anaerostipes hadrus, Faecalibacterium prausnitzii*, *Suboligranulum variabile, Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

[0012] In embodiments, the plurality of bacterial isolates comprises at least three of *Bacteroides cellulosilyticus, Bacteroides uniformis, Suboligranulum variabile, Anaerostipes hadrus, Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least four of *Bacteroides cellulosilyticus, Bacteroides uniformis, Suboligranulum variabile, Anaerostipes hadrus, Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least five of *Bacteroides cellulosilyticus, Bacteroides uniformis, Suboligranulum variabile, Anaerostipes hadrus, Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least five of *Bacteroides cellulosilyticus, Bacteroides uniformis, Suboligranulum variabile, Anaerostipes hadrus, Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least six of *Bacteroides cellulosilyticus, Bacteroides uniformis, Suboligranulum variabile, Anaerostipes hadrus, Odoribacter splanchnicus*, *Roseburia faecis*,

Faecalibacterium prausnitzii, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least seven of *Bacteroides cellulosilyticus*, *Bacteroides uniformis*, *Suboligranulum variabile*, *Anaerostipes hadrus*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least eight of *Bacteroides cellulosilyticus*, *Bacteroides uniformis*, *Suboligranulum variabile*, *Anaerostipes hadrus*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

[0013] In embodiments, the composition comprises a 16S rRNA sequence that is at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity with nucleotide sequences selected from SEQ ID NOs: 1, 2, 3, 7, 8, 11, 14, 18, 19, 20, 22 and 23. In embodiments, the pharmaceutical composition comprises at least two bacterial isolates comprising *Faecalibacterium prausnitzii*, wherein the at least two bacterial isolates comprise different 16S rRNA sequences. In embodiments, the pharmaceutical composition comprises 16S rRNA sequences that are at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% identity sequence identity with nucleotide sequences of SEQ ID NOs: 1 and 7.

[0014] In embodiments, the *Bacteroides stercoris* comprises a 16S ribosomal ribonucleic acid (rRNA) sequence that has at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity with the nucleotide sequence of SEQ ID NO: 13. In embodiments, the plurality of bacterial isolates comprises at least three of *Bacteroides cellulosilyticus*, *Bacteroides uniformis*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Anaerostipes hadrus*, *Faecalibacterium prausnitzii*, *Suboligranulum variabile*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least three, or at least four, or at least five, or at least six, or at least seven, or at least eight, or at least nine, or each of *Bacteroides cellulosilyticus*, *Bacteroides uniformis*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Anaerostipes hadrus*, *Faecalibacterium prausnitzii*, *Suboligranulum variabile*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

[0015] In embodiments, the plurality of bacterial isolates comprises a 16S rRNA sequence that has at least about 95%, or at least about 97%, or at least about 98%, or at least about 99%

sequence identity with nucleotide sequences selected from SEQ ID NOs: 1, 2, 3, 7, 8, 11, 14, 18, 19, 20, 22 and 23.

[0016] In embodiments, the plurality of bacterial isolates comprises at least two bacterial isolates comprising *Faecalibacterium prausnitzii*, wherein the at least two bacterial isolates comprise different 16S rRNA sequences. In embodiments, the at least two bacterial isolates comprising *Faecalibacterium prausnitzii* comprise 16S rRNA sequences that are at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% identity sequence identity with nucleotide sequences of SEQ ID NOs: 1 and/or 7. In embodiments, the at least two bacterial isolates comprising *Faecalibacterim prausnitzii* are isolated from a stool of different human donors.

[0017] Described herein are compositions and methods for protecting the GI microbiome of a subject. In various embodiments, provided herein is a pharmaceutical composition comprising an isolated or purified bacterial isolate and/or a cocktail of isolated or purified bacterial isolates (*e.g.* from a human, *e.g.* from stool of a healthy human).

[0018] Disclosed herein is a pharmaceutical composition comprising a cocktail of bacterial isolates, wherein at least one of the bacterial isolates comprises a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1. In embodiments, at least two of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1. In embodiments, at least three of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1. In embodiments, at least four of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1. In embodiments, at least five of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1. In embodiments, at least six of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1. In embodiments, at least seven of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1. In embodiments, at least eight of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1. In embodiments, at least nine of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1. In

embodiments, at least ten of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1.

[0019] Disclosed herein is a pharmaceutical composition comprising a plurality of bacterial isolates, wherein the plurality of bacterial isolates comprises at least two bacterial isolates selected from the group consisting of *Eubacterium rectale*, *Odoribacter splanchnicus* and *Subdoligranulum variabile*. In embodiments, the *Subdoligranulum variabile* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 22 or SEQ ID NO: 23. In embodiments, the *Odoribacter* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 2. In embodiments, the *Eubacterium rectale* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 8. In embodiments, the at least two bacterial isolates do not include *Eubacterium rectale*. In embodiments, the at least two bacterial isolates do not include *Odoribacter splanchnicus*. In embodiments, the at least two bacterial isolates do not include *Subdoligranulum variabile*.

[0020] In embodiments, the at least two bacterial isolates comprise *Odoribacter splanchnicus* and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises *Odoribacter splanchnicus* and *Eubacterium* rectale, and further comprises at least one of *Bacteroides cellulosilyticus*, *Faecalibacterium prausnitzii*, *Alistipes shahii*, and *Blautia obeum*. In embodiments, the plurality of bacterial isolates comprises *Odoribacter splanchnicus* and *Eubacterium rectale*, and further comprises each of *Bacteroides cellulosilyticus*, *Faecalibacterium prausnitzii*, *Alistipes shahii*, and *Blautia obeum*. In embodiments, the *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 14. In embodiments, the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7. In embodiments, the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 18. In embodiments, the *Blautia obeum* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 9.

[0021] In embodiments, the plurality of bacterial isolates comprises *Odoribacter splanchnicus* and *Eubacterium rectale*, and further comprises at least one of *Bacteroides cellulosilyticus*, *Bacteroides stercoris*, *Faecalibacterium prausnitzii*, *Alistipes shahii*, *Anaerostipes hadrus*, *Roseburia faecis*, and *Blautia obeum*. In embodiments, the plurality of bacterial isolates does not comprise at least one of *Blautia obeum* and *Anaerostipes hadrus*. In embodiments, the plurality of bacterial isolates comprises *Odoribacter splanchnicus* and *Eubacterium rectale*, and further comprises each of *Bacteroides cellulosilyticus*, *Bacteroides*

stercoris, *Faecalibacterium prausnitzii*, *Alistipes shahii*, *Anaerostipes hadrus*, and *Roseburia faecis* In embodiments, the *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 14. In embodiments, the *Bacteroides stercoris* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 13. In embodiments, the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7. In embodiments, the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 18. In embodiments, the *Anaerostipes hadrus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 3. In embodiments, the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19.

[0022] In embodiments, the plurality of bacterial isolates comprises *Odoribacter splanchnicus* and *Eubacterium rectale*, and further comprises each of *Bacteroides cellulosilyticus*, *Bacteroides stercoris*, *Faecalibacterium prausnitzii*, *Alistipes shahii*, *Blautia obeum*, and *Roseburia faecis*. In embodiments, the *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 14. In embodiments, the *Bacteroides stercoris* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 13. In embodiments, the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7. In embodiments, the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 18. In embodiments, the *Blautia obeum* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 9. In embodiments, the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19.

[0023] In embodiments, the plurality of bacterial isolates comprises *Odoribacter splanchnicus* and *Eubacterium rectale*, and further comprises at least one of *Bacteroides cellulosilyticus*, *Bacteroides stercoris*, *Alistipes shahii*, and *Roseburia faecis*. In embodiments, the plurality of bacterial isolates comprises *Odoribacter splanchnicus* and *Eubacterium rectale*, and further comprises each of *Bacteroides cellulosilyticus*, *Bacteroides stercoris*, *Alistipes shahii*, and *Roseburia faecis*. In embodiments, the *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 14. In embodiments, the *Bacteroides stercoris* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 13. In embodiments, the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19. In embodiments, the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 18.

[0024] In embodiments, the plurality of bacterial isolates comprises *Odoribacter splanchnicus* and *Eubacterium rectale*, and further comprises at least one of *Faecalibacterium prausnitzii*, *Bacteroides stercoris*, *Roseburia faecis*, and *Anaerostipes hadrus*. In embodiments, the plurality of bacterial isolates comprises *Odoribacter splanchnicus* and *Eubacterium rectale*, and further comprises each of *Faecalibacterium prausnitzii*, *Bacteroides stercoris*, *Roseburia faecis*, and *Anaerostipes hadrus*. In embodiments, the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7. In embodiments, the *Bacteroides stercoris* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 13. In embodiments, the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19. In embodiments, the *Anaerostipes hadrus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 3.

[0025] In embodiments, the plurality of bacterial isolates comprises *Odoribacter splanchnicus* and *Eubacterium rectale*, and further comprises at least one of *Bacteroides cellulosilyticus*, *Bacteroides stercoris*, *Blautia obeum*, and *Alistipes shahii*. In embodiments, the plurality of bacterial isolates comprises *Odoribacter splanchnicus* and *Eubacterium rectale*, and further comprises each of *Bacteroides cellulosilyticus*, *Bacteroides stercoris*, *Blautia obeum*, and *Alistipes shahii*. In embodiments, the *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 14. In embodiments, the *Bacteroides stercoris* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 13. In embodiments, the *Blautia obeum* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 9. In embodiments, the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 18.

[0026] In embodiments, the plurality of bacterial isolates comprises *Odoribacter splanchnicus* and *Eubacterium rectale*, and further comprises at least one of *Faecalibacterium prausnitzii*, *Bacteroides stercoris*, *Alistipes shahii*, and *Roseburia faecis*. In embodiments, the plurality of bacterial isolates comprises *Odoribacter splanchnicus* and *Eubacterium rectale*, and further comprises each of *Faecalibacterium prausnitzii*, *Bacteroides stercoris*, *Alistipes shahii*, and *Roseburia faecis*. In embodiments, the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7. In embodiments, the *Bacteroides stercoris* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 13. In embodiments, the *Alistipes shahii* comprises a 16S

rRNA sequence that is at least 95% identical to SEQ ID NO: 18. In embodiments, the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19.

[0027] In embodiments, the plurality of bacterial isolates comprises *Odoribacter splanchnicus* and *Eubacterium rectale*, and further comprises at least one of *Faecalibacterium prausnitzii*, *Bacteroides stercoris*, *Blautia obeum*, and *Roseburia faecis*. In embodiments, the plurality of bacterial isolates comprises *Odoribacter splanchnicus* and *Eubacterium rectale*, and further comprises each of *Faecalibacterium prausnitzii*, *Bacteroides stercoris*, *Blautia obeum*, and *Roseburia faecis*. In embodiments, the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7. In embodiments, the *Bacteroides stercoris* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 13. In embodiments, the *Blautia obeum* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 9. In embodiments, the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19.

[0028] In embodiments, the plurality of bacterial isolates comprises at least one of *Bacteroides stercoris* and *Clostridium aldenense*. In embodiments, the plurality of bacterial isolates produces an aryl hydrocarbon for binding to an aryl hydrocarbon receptor. In embodiments, the aryl hydrocarbon receptor is expressed by a cell of a subject administered the composition. In embodiments, the cell is an intestinal cell or an immune cell. In embodiments, the aryl hydrocarbon is selected from the group consisting of indole, indole-3-acetic acid (IAA), indole-3-aldehyde (IAId), indole-3-lactic acid, indole-3-carbinol (I3C), indole-3-acetonitrile (I3ACN), 3,3'-diindolylmethane (DIM), 2-(indol-3-ylmethyl)-3,3'-diindolylmethane (Ltr-1), indolo[3,2-*b*]carbazole (ICZ), 2-(1'H-indole-3'carbonyl)-thiazole-4-carboxylic acid methyl ester (ITE), 3-methyl-indole (skatole), tryptamine, kynurenine, kynurenate, indigo, indirubin, indoxyl-3-sulfate (I3S), xanthurenic acid, cinnabarinic acid, and any combination thereof. In embodiments, the aryl hydrocarbon is IAA. In embodiments, the IAA is secreted at a concentration of at least 1 μM. In embodiments, the IAA is secreted at a concentration of at least 10 μM. In embodiments, the IAA is secreted at a concentration of at least 20 μM. In embodiments, the IAA is secreted at a concentration of at least 40 μM. In embodiments, the IAA is secreted at a concentration of at least 50 μM. In embodiments, the IAA is secreted at a concentration of at least 75 μM. In embodiments, the IAA is secreted at a concentration of at least 100 μM.

[0029] In embodiments, the at least two bacterial isolates comprise *Eubacterium rectale* and *Subdoligranulum variabile*. In embodiments, the plurality of bacterial isolates comprises

Eubacterium rectale and *Subdoligranulum variabile*, and further comprises at least one of *Faecalibacterium prausnitzii*, *Coprococcus comes*, *Anaerostipes hadrus*, and *Roseburia faecis*. In embodiments, the plurality of bacterial isolates comprises *Eubacterium rectale* and *Subdoligranulum variabile*, and further comprises each of *Faecalibacterium prausnitzii*, *Coprococcus comes*, *Anaerostipes hadrus*, and *Roseburia faecis*. In embodiments, the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7. In embodiments, the *Anaerostipes hadrus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 3. In embodiments, the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19. In embodiments, the *Coprococcus comes* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 17.

[0030] In embodiments, the plurality of bacterial strains does not include at least one of *Faecalibacterium prausnitzii*, *Roseburia faecis*, *Bacteroides cellulosilyticus*, *Alistipes shahii*, or *Blautia obeum*.

[0031] An aspect of the present invention is a pharmaceutical composition comprising a plurality of bacterial isolates, wherein the plurality of bacterial isolates comprise *Bacteroides stercoris*, and at least two of *Bacteroides cellulosilyticus, Bacteroides uniformis, Suboligranulum variabile, Anaerostipes hadrus, Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*, wherein at least two of the plurality of bacterial isolates are isolated from a stool of different human donors.

[0032] Disclosed herein is a pharmaceutical composition comprising a plurality of bacterial isolates, wherein the plurality of bacterial isolates comprises *Roseburia faecis* and *Bacteroides cellulosilyticus*, and at least one of *Faecalibacterium prausnitzii* and *Alistipes shahii*. In embodiments, the plurality of bacterial isolates further comprises at least one of *Eubacterium rectale*, *Anaerostipes hadrus*, and *Blautia obeum*. In embodiments, the plurality of bacterial isolates does not comprise at least one of *Anaerostipes hadrus* and *Blautia obeum*. In embodiments, the plurality of bacterial isolates comprises each of *Roseburia faecis*, *Bacteroides cellulosilyticus*, *Faecalibacterium prausnitzii*, *Alistipes shahii*, *Eubacterium rectale*, and *Anaerostipes hadrus*. In embodiments, the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19. In embodiments, the *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 14. In embodiments, the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is

at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7. In embodiments, the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 18. In embodiments, the *Eubacterium rectale* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 8. In embodiments, the *Anaerostipes hadrus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 3.

[0033] In embodiments, the plurality of bacterial isolates comprises each of *Roseburia faecis*, *Bacteroides cellulosilyticus*, *Faecalibacterium prausnitzii*, *Alistipes shahii*, *Eubacterium rectale*, and *Blautia obeum*. In embodiments, the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19. In embodiments, the *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 14. In embodiments, the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7. In embodiments, the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 18. In embodiments, the *Eubacterium rectale* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 8. In embodiments, the *Blautia obeum* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 9.

[0034] In embodiments, one or more of the plurality of bacterial isolates in the above pharmaceutical compositions secretes a short-chain fatty acid (SCFA) in an intestine of a subject administered the composition. In embodiments, the SCFA is selected from the group consisting of acetic acid, butyric acid, caproic acid, formic acid, heptanoic acid, isobutyric acid, isocaproic acid, isovaleric acid, propionic acid, valeric acid, and a combination thereof. In embodiments, the SCFA is butyric acid. In embodiments, a level of the butyric acid produced by the one or more bacterial isolates over a period of 24 hours is at least 5 mM. In embodiments, a level of the butyric acid produced by the one or more bacterial isolates over a period of 24 hours is at least 10 mM. In embodiments, a level of the butyric acid produced by the one or more bacterial isolates over a period of 24 hours is at least 15 mM. In embodiments, a level of the butyric acid produced by the one or more bacterial isolates over a period of 24 hours is at least 20 mM. In embodiments, a level of the butyric acid produced by the one or more bacterial isolates over a period of 24 hours is at least 25 mM. In embodiments, a level of the butyric acid produced by the one or more bacterial isolates over a period of 24 hours is at least 30 mM. In embodiments, a level of the butyric acid produced by the one or more bacterial isolates over a period of 24 hours is at least 35 mM. In embodiments, a level of the butyric acid produced by the one or more bacterial isolates over a period of 24 hours is at least 40 mM. In embodiments,

the one or more bacterial isolates producing at least one SCFA comprises a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 2.

[0035] Disclosed herein is a pharmaceutical composition comprising a plurality of bacterial isolates, wherein the plurality of bacterial isolates comprises a bacterial isolate comprising *Parabacteroides merdae* and at least one of *Alistipes finegoldii* and *Alistipes onderdonkii*. In embodiments, the plurality of bacterial isolates comprises both *Alistipes finegoldii* and *Alistipes onderdonkii*. In embodiments, the plurality of bacterial isolates does not include one of *Alistipes finegoldii* and *Alistipes onderdonkii*. In embodiments, the plurality of bacterial isolates further comprises at least one of *Akkermansia muciniphila*, *Dorea longicatena*, *Blautia obeum*, *Blautia* sp., *Bacteroides uniformis* or *Bacteroides vulgatus*. In embodiments, the plurality of bacterial isolates comprises *Parabacteroides merdae* and each of *Akkermansia muciniphila*, *Alistipes finegoldii*, *Dorea longicatena*, *Alistipes onderdonkii*, *Blautia* sp., *Bacteroides uniformis* and *Bacteroides vulgatus*. In embodiments, the *Parabacteroides merdae* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 5. In embodiments, the *Akkermansia muciniphila* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 20. In embodiments, the *Alistipes finegoldii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 15. In embodiments, the *Dorea longicatena* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 6. In embodiments, the *Alistipes onderdonkii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 4. In embodiments, the *Blautia* sp. comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 34. In embodiments, the *Bacteroides uniformis* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 11 and SEQ ID NO: 16. In embodiments, the *Bacteroides vulgatus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 12.

[0036] In embodiments, the plurality of bacterial isolates comprises *Parabacteroides merdae* and each of *Akkermansia muciniphila*, *Alistipes finegoldii*, *Dorea longicatena*, *Blautia obeum*, *Blautia* sp., *Bacteroides uniformis* and *Bacteroides vulgatus*. In embodiments, the *Parabacteroides merdae* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 5. In embodiments, the *Akkermansia muciniphila* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 20. In embodiments, the *Alistipes finegoldii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 15. In embodiments, the *Dorea longicatena* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID

NO: 6. In embodiments, the *Blautia obeum* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 9. In embodiments, the *Blautia* sp. comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 34. In embodiments, the *Bacteroides uniformis* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 11 and SEQ ID NO: 16. In embodiments, the *Bacteroides vulgatus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 12.

[0037] Disclosed herein is a pharmaceutical composition comprising a plurality of bacterial isolates, wherein the plurality of bacteria isolates comprises *Alistipes finegoldii* and at least one of *Bacteroides uniformis* and *Dorea longicatena*. In embodiments, the plurality of bacterial isolates does not comprise one of *Bacteroides uniformis* or *Dorea longicatena*. In embodiments, the plurality of bacterial isolates further comprises at least one of *Akkermansia muciniphila*, *Bacteroides vulgatus*, and *Blautia* sp. In embodiments, the plurality of bacterial isolates comprises each of *Alistipes finegoldii*, *Bacteroides uniformis*, *Dorea longicatena*, *Akkermansia muciniphila*, *Bacteroides vulgatus*, and *Blautia* sp. In embodiments, the *Alistipes finegoldii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 15. In embodiments, the *Bacteroides uniformis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 11. In embodiments, the *Dorea longicatena* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 6. In embodiments, the *Akkermansia muciniphila* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 20. In embodiments, the *Bacteroides vulgatus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 12. In embodiments, the *Blautia* sp. comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 34.

[0038] In embodiments, the plurality of bacterial isolates of any of the above pharmaceutical compositions comprises at least one bacterial isolate provided in Table 3. In embodiments, the at least one bacterial isolate modulates cytokine production or release by a eukaryotic cell. In embodiments, the at least one bacterial isolate decreases production or release of a pro-inflammatory cytokine by the eukaryotic cell. In embodiments, the pro-inflammatory cytokine is selected from the group consisting of: IFNγ, IL-12p70, IL-1 (e.g., IL-1α, IL-1β), IL-6, IL-8, IL-12, IL-17, IL-18, IL-23, MCP1, MIP1α, MIP1β, TNFα, TNF-γ, and a combination thereof. In embodiments, the at least one bacterial isolate increases production or release of an anti-inflammatory cytokine by the eukaryotic cell. In embodiments, the anti-inflammatory cytokine is selected from the group consisting of: IL-10, IL-13, IL-4, IL-5, TGF-β, and a combination thereof. In embodiments, the anti-inflammatory cytokine is IL-10. In embodiments, the at least

one bacterial isolate induces the eukaryotic cell to produce or release at least 500 pg/ml of IL-10. In embodiments, the at least one bacterial isolate induces the eukaryotic cell to produce or release at least 1000 pg/ml of IL-10. In embodiments, the at least one bacterial isolate induces the eukaryotic cell to produce or release at least 1500 pg/ml of IL-10. In embodiments, the at least one bacterial isolate induces the eukaryotic cell to produce or release at least 2000 pg/ml of IL-10. In embodiments, the at least one bacterial isolate induces the eukaryotic cell to produce or release at least 2500 pg/ml of IL-10. In embodiments, the at least one bacterial isolate induces the eukaryotic cell to produce or release at least 3000 pg/ml of IL-10. In embodiments, the eukaryotic cell is a cultured cell. In embodiments, the eukaryotic cell is a cultured peripheral blood mononuclear cell (PBMC). In embodiments, the eukaryotic cell is a cell of a subject administered the composition. In embodiments, the cell of the subject is selected from the group consisting of: an epithelial cell, an intestinal lamina propria cell, an endothelial cell, a fibroblast, a stromal cell, a macrophage, a B lymphocyte, a T lymphocyte, a mast cell, and a peripheral blood mononuclear cell (PBMC). In embodiments, the cell of the subject is an epithelial cell and the epithelial cell is an intestinal epithelial cell.

[0039] In embodiments, the pharmaceutical composition is formulated as a capsule for oral administration. In embodiments, the capsule comprises a delayed-release coating. In embodiments, the capsule comprises a hydrophobic coating. In embodiments, the pharmaceutical composition is formulated for delivery of the microbial cocktail to the intestine. In embodiments, the pharmaceutical composition is formulated for delivery of the microbial cocktail to the small intestine. In embodiments, the composition is formulated for delivery of the microbial cocktail to the large intestine. In embodiments, the microbial cocktail is lyophilized. In embodiments, the pharmaceutical composition further comprises at least one of a pharmaceutically acceptable antioxidant, cryoprotectant, lyoprotectant, binder, disintegrant, excipient, filler, preservative, acid suppressant, antacid, H2 antagonist, and/or proton pump inhibitor.

[0040] In embodiments, the pharmaceutical composition is for administration to a subject having a disorder related to an intestinal dysbiosis. In embodiments, the disorder is selected from the group consisting of inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), *C. difficile* infection (CDI), *C. difficile*-associated disease (CDAD), an antibiotic-induced adverse effect, and a combination thereof.

[0041] Disclosed herein is a method of treating or preventing inflammatory bowel disease in a subject in need thereof, comprising administering to the subject a bacterial isolate comprising

Bacteroides cellulosilyticus. In embodiments, the *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 26. In embodiments, the method further comprises administering to the subject a bacterial isolate comprising *Odoribacter splanchnicus* and/or a bacterial isolate comprising *Subdoligranulum* sp.

[0042] Disclosed herein is a method of manufacturing a pharmaceutical composition containing a cocktail of bacterial isolates, the method comprising selecting a first bacterial isolate based on a level of a short-chain fatty acid (SCFA) produced by the first bacterial isolate; selecting a second bacterial isolate based on a relative abundance of a corresponding bacterial strain in a healthy human subject versus a subject having inflammatory bowel disease, wherein the second bacterial isolate comprises a 16S rRNA sequence at least 97% identical to a 16S rRNA sequence of the corresponding bacterial strain; and combining the first and second bacterial isolates to produce the cocktail of bacterial isolates. In embodiments, the first bacterial isolate comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 2. In embodiments, the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 4. In embodiments, the method further comprises selecting a third bacterial isolate based on a modulation of a cytokine's level induced by the bacterial isolate. In embodiments, the third bacterial isolate comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 3. In embodiments, the method further comprises selecting a fourth bacterial isolate based on a level of an aryl hydrocarbon produced by the third bacterial isolate. In embodiments, the fourth bacterial isolate comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 6.

[0043] Disclosed herein is a pharmaceutical composition, comprising: a first human-derived bacterial isolate which induces at least one of an IL-10:IL-12 ratio of at least 50 or an IL-10:TNF-alpha ratio of at least 1 when incubated with a population of eukaryotic cells in a first functional assay; and a second human-derived bacterial isolate which produces a short chain fatty acid (SCFA) at a concentration of at least 10 mM as measured by a second functional assay; wherein the first and second bacterial isolates are capable of engrafting into the intestine of a subject following administration of the pharmaceutical composition to the subject.

[0044] In an aspect, the IL-10:IL-12 ratio is at least 100. In an aspect, the IL-10:IL-12 ratio is at least 500. In an aspect, the IL-10:IL-12 ratio is at least 1000. In an aspect, the IL-10:IL-12 ratio is at least 2000. In an aspect, the IL-10:TNF-alpha ratio is at least 2. In an aspect, the IL-

10:TNF-alpha ratio is at least 5. In an aspect, the IL-10:TNF-alpha ratio is at least 10. In an aspect, the IL-10:TNF-alpha ratio is at least 20. In an aspect, the population of eukaryotic cells comprises a population of PBMCs. In an aspect, the first human-derived bacterial isolate is incubated with the population of eukaryotic cells for about 24 hours. In an aspect, the SCFA is butyrate. In an aspect, the SCFA is produced at a concentration of at least 20 mM. In an aspect, the SCFA is produced at a concentration of at least 25 mM. In an aspect, the SCFA is produced at a concentration of at least 30 mM. In an aspect, the SCFA is produced at a concentration of at least 35 mM. In an aspect, the SCFA is butyrate.

[0045] In an aspect, the second functional assay comprises incubating the second bacterial isolate with a substrate. In an aspect, the substrate comprises at least one of an oligosaccharide, sunfiber, or barley malt. In an aspect, the oligosaccharide comprises at least one of a fructooligosaccharide (FOS) and an xylooligosaccharide (XOS). In an aspect, the substrate comprises both of a fructooligosaccharide (FOS) and an xylooligosaccharide (XOS). In an aspect, the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 2. In an aspect, the second bacterial isolate comprises *Anaerostipes* sp. In an aspect, the *Anaerostipes* sp. is *Anaerostipes hadrus*. In an aspect, the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the sequence corresponding to SEQ ID NO: 3. In an aspect, the second bacterial isolate comprises *Roseburia* sp. In an aspect, the *Roseburia* sp. is *Roseburia faecis*. In an aspect, the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the sequence corresponding to SEQ ID NO: 19. In an aspect, the second bacterial isolate comprises *Eubacterium* sp. In an aspect, the *Eubacterium* sp. is *Eubacterium rectale*. In an aspect, the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the sequence corresponding to SEQ ID NO: 8. In an aspect, the second bacterial isolate comprises *Coprococcus* sp. In an aspect, the *Coprococcus* sp. is *Coprococcus comes*. In an aspect, the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the sequence corresponding to SEQ ID NO: 17. In an aspect, the first bacterial isolate comprises a 16S sequence at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 3.

[0046] A pharmaceutical composition, comprising: a first human-derived bacterial isolate which produces a short chain fatty acid (SCFA) at a concentration of at least 10 mM as measured by a first functional assay; and a second human-derived bacterial isolate which, as measured by a second functional assay, produces at least one of: (i) indole at a level at least 5x greater than a level of indole produced by a control bacterial strain; (ii) tryptamine at a level at

least 1.4x greater than a level of tryptamine produced by a control bacterial strain; (iii) kynurenate at a level at least 1.4x greater than a level of kynurenate produced by a control bacterial strain; (iv) kynurenine at a level at least 2.5x greater than a level of kynurenine produced by a control bacterial strain; and (v) indole-3-acetic acid at a level at least 2x greater than a level of indole-3-acetic acid produced by a control bacterial strain; wherein the control bacterial strain is selected from at least one of *Peptostreptococcus russellii* and *Peptostreptococcus anaerobius*; wherein the first and second bacterial isolates are capable of engrafting into the intestine of a subject following administration of the pharmaceutical composition to the subject.

[0047] In an aspect, the second functional assay comprises separately incubating the second bacterial isolate and the control strain with tryptophan. In an aspect, the second bacterial isolate produces indole at a level at least 50x greater than the level of indole produced by the control bacterial strain. In an aspect, the second bacterial isolate produces indole at a level at least 100x greater than the level of indole produced by the control bacterial strain. In an aspect, the second bacterial isolate produces indole at a level at least 150x greater than the level of indole produced by the control bacterial strain. In an aspect, the second bacterial isolate comprises *Clostridium aldenense*. In an aspect, the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to SEQ ID NO: 10.

[0048] In an aspect, the second bacterial isolate produces tryptamine at a level at least 1.5x greater than the level of tryptamine produced by the control bacterial strain. In an aspect, the second bacterial isolate comprises *Odoribacter splanchnicus*. In an aspect, the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to SEQ ID NO: 2.

[0049] In an aspect, the second bacterial isolate produces kynurenate at a level at least 1.5x greater than the level of kynurenate produced by the control bacterial strain. In an aspect, the second bacterial isolate comprises *Odoribacter splanchnicus*. In an aspect, the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to SEQ ID NO: 2. In an aspect, the second bacterial isolate produces kynurenine at a level at least 3x greater than the level of tryptamine produced by the control bacterial strain. In an aspect, the second bacterial isolate comprises *Odoribacter splanchnicus* or *Bacteroides stercoris*. In an aspect, the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to SEQ ID NO: 2 or SEQ ID NO: 13. In an aspect, the control bacterial strain comprises *Peptostreptococcus anaerobius*.

[0050] In an aspect, the second bacterial isolate produces indole-3-acetic acid at a level at least 3x greater than the level of indole-3-acetic acid produced by the control bacterial strain. In an aspect, the second bacterial isolate produces indole-3-acetic acid at a level at least 8x greater

than the level of indole-3-acetic acid produced by the control bacterial strain. In an aspect, the second bacterial isolate comprises *Odoribacter splanchnicus* or *Clostridium aldenense*. In an aspect, the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to SEQ ID NO: 2 or SEQ ID NO: 10.

[0051] In an aspect, the SCFA is butyrate. In an aspect, the SCFA is produced at a concentration of at least 20 mM. In an aspect, the SCFA is produced at a concentration of at least 25 mM. In an aspect, the SCFA is produced at a concentration of at least 30 mM. In an aspect, the SCFA is produced at a concentration of at least 35 mM. In an aspect, the second functional assay comprises incubating the second bacterial isolate with a substrate. In an aspect, the substrate comprises at least one of an oligosaccharide, sunfiber, or barley malt. In an aspect, the oligosaccharide comprises at least one of a fructooligosaccharide (FOS) and an xylooligosaccharide (XOS). In an aspect, the substrate comprises both of a fructooligosaccharide (FOS) and an xylooligosaccharide (XOS). In an aspect, the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 2.

[0052] Disclosed herein is a method of treating inflammatory bowel disease comprising administering the pharmaceutical composition comprising the first and second human-derived bacterial isolates to a subject in need thereof. In an aspect, the dosage of at least one of the first and second bacterial isolates is less than 10^{10} cells/ml.

[0053] In an aspect, there is provded a pharmaceutical composition comprising a plurality of bacterial isolates, wherein the plurality of bacterial isolates comprises *Bacteroides cellulosilyticus* and at least one of *Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, *Subdoligranulum variabile*, and *Eubacterium rectale*, wherein at least two of the plurality of bacterial isolates are isolated from stool samples of different donors.

[0054] In embodiments, the plurality of bacterial isolates comprises *Odoribacter splanchnicus*. In embodiments, the plurality of bacterial isolates comprises *Faecalibacterium prausnitzii*. In embodiments, the plurality of bacterial isolates comprises two different bacterial isolates that are each members of the species *Faecalibacterium prausnitzii*. In embodiments, the plurality of bacterial isolates comprises *Subdoligranulum variabile*. In embodiments, the plurality of bacterial isolates comprises *Roseburia faecis, Akkermansia muciniphila, Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises *Roseburia faecis, Akkermansia muciniphila, Alistipes shahii*, and *Eubacterium rectale*.

[0055] In an aspect, there is provded a pharmaceutical composition comprising a plurality of bacterial isolates, wherein the plurality of bacterial isolates comprises two different bacterial isolates that are each members of the species *Faecalibacterium prausnitzii*.

[0056] In embodiments, the two different bacterial isolates are isolated from stool samples of different human donors. In embodiments, the plurality of bacterial isolates further comprises at least one of *Bacteroides cellulosilyticus*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates further comprises each of *Bacteroides cellulosilyticus*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

[0057] In an aspect, there is provded a method of treating or preventing irritable bowel syndrome in a subject in need thereof, comprising administering to the subject a plurality of bacterial isolates, wherein one of the bacterial isolates comprises *Bacteroides cellulosilyticus*, and wherein at least two of the plurality of bacterial isolates are administered to the subject in different pharmaceutical compositions.

[0058] In embodiments, the plurality of bacterial isolates further comprises at least one of *Faecalibacterium prausnitzii*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Akkermansia muciniphila*, *Alistipes shahii*, *Subdoligranulum variabile* and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates further comprises each of *Faecalibacterium prausnitzii*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Akkermansia muciniphila*, *Alistipes shahii*, *Subdoligranulum variabile* and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates further comprises each of *Odoribacter splanchnicus*, *Roseburia faecis*, *Akkermansia muciniphila*, *Alistipes shahii*, *Eubacterium rectale*, and two different bacterial isolates that are each members of the species *Faecalibacterium prausnitzii*.

[0059] In an aspect, there is provded a method of manufacture, the method comprising culturing *Bacteroides cellulosilyticus* as a pure culture; and lyophilizing bacteria from the pure culture of *B. cellulosilyticus* to produce a *B. cellulosilyticus* lyophilate.

[0060] In embodiments, the method further comprises combining the *B. cellulosilyticus* lyophilate with a second lyophilate, wherein the second lyophilate is produced by lyophilizing bacteria from a pure culture of at least one of *Faecalibacterium prausnitzii*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Akkermansia muciniphila*, *Alistipes shahii*, *Subdoligranulum variabile* and *Eubacterium rectale*.

[0061] In an aspect, there is provded a pharmaceutical composition comprising a plurality of bacterial isolates, wherein an amount of cells of a first bacterial isolate of the plurality of bacterial isolates is at least 1% greater than an amount of cells of a second bacterial isolate of the plurality of bacterial isolates, wherein the plurality of bacterial isolates are selected from the group consisting of: *Bacteroides cellulosilyticus*, *Faecalibacterium prausnitzii*, *Subdogranulum variabile*, *Eubacterium rectale*, *Odoribacter splanchnicus*, *Alistipes shahii*, and *Akkermansia muciniphila*.

[0062] In embodiments, the amount of cells of the first bacterial isolate is at least 10% greater than the amount of cells of the second bacterial isolate. In embodiments, the first bacterial isolate comprises one of *Eubacterium rectale* and *Faecalibacterium prausnitzii*. In embodiments, the second bacterial isolate comprises one of *Alistipes shahii*, and *Akkermansia muciniphila*. In embodiments, the first and second bacterial isolates comprises *Faecalibacterium prausnitzii*. In embodiments, the first bacterial isolate comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 7. In embodiments, the second bacterial isolate comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 1.

[0063] In an aspect, there is provded a pharmaceutical composition comprising a plurality of bacterial isolates, wherein an amount of cells of a first bacterial isolate of the plurality of bacterial isolates is at least 1% greater than an amount of cells of a second bacterial isolate of the plurality of bacterial isolates, wherein each of the first and second bacterial isolates comprises *Faecalibacterium prausnitzii*.

[0064] In embodiments, the amount of cells of the first bacterial isolate is at least 10% greater than the amount of cells of the second bacterial isolate. In embodiments, the first bacterial isolate comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 7. In embodiments, the second bacterial isolate comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 1.

[0065] In an aspect, there is provded a pharmaceutical composition comprising a bacterial isolate, wherein the bacterial isolate comprises a 16S rRNA sequence that is at least 97% identical to a 16S rRNA sequence of a bacterial strain that is either (i) enriched in a group of healthy subjects over a group of patients with ulcerative colitis (UC) and/or (ii) correlated with clinical remission of one or more UC symptoms in a group of patients following treatment of each patient of the group of patients with a fecal microbiota transplant, wherein a cross-sectional combined p-value of the bacterial strain is less than $1x10^{-10}$.

[0066] In embodiments, the bacterial isolate comprises a 16S rRNA sequence that is at least 99% identical to a 16S rRNA sequence of the bacterial strain. In embodiments, the bacterial isolate comprises at least one of *Odoribacter splanchnicus*, *Eubacterium rectale*, *Bacteroides cellulosilyticus* and *Alistipes shahii*. In embodiments, the cross-sectional combined p-value of the bacterial strain is less than $1x10^{-14}$. In embodiments, the bacterial isolate comprises at least one of *Odoribacter splanchnicus* and *Alistipes shahii*. In embodiments, the cross-sectional combined p-value of the bacterial strain is less than $1x10^{-20}$. In embodiments, the bacterial isolate comprises *Alistipes shahii*. In embodiments, the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 97% identical to SEQ ID NO: 18.

[0067] In embodiments, the plurality of bacterial isolates comprises lyophilized bacteria. In embodiments, the plurality of bacterial isolates does not include *Escherichia coli*. In embodiments, the pharmaceutical composition of any of the embodiments disclosed herein is not a stoll sample or a minimally processed version thereof.

[0068] In embodiments, there is provided a pharmaceutical composition comprising (a) a bacterial isolate and (b) a pharmaceutically acceptable antioxidant, cryoprotectant, lyoprotectant, binder, disintegrant, excipient, filler, preservative, acid suppressant, antacid, H2 antagonist, and/or proton pump inhibitor; the bacterial isolate comprising one, or two, or three, or four, or five, or six, or seven, or eight, or nine, or ten (in the case of Tables 42 or 43) of the bacterial isolates of any one of Tables 36-43. In embodiments, there is provided a pharmaceutical composition comprising (a) a bacterial isolate and (b) a pharmaceutically acceptable antioxidant, cryoprotectant, lyoprotectant, binder, disintegrant, excipient, filler, preservative, acid suppressant, antacid, H2 antagonist, and/or proton pump inhibitor; the bacterial isolate comprising nine of the bacterial isolates of any one of Tables 36-43. In embodiments, there is provided a pharmaceutical composition comprising (a) a bacterial isolate and (b) a pharmaceutically acceptable antioxidant, cryoprotectant, lyoprotectant, binder, disintegrant, excipient, filler, preservative, acid suppressant, antacid, H2 antagonist, and/or proton pump inhibitor; the bacterial isolate consisting of nine of the bacterial isolates of any one of Tables 36-43.

[0069] In aspects, there is provided a method of treating inflammatory bowel disease comprising administering the pharmaceutical composition described herein to a subject in need thereof.

[0070] In aspects, there is provided a method of treating inflammatory bowel disease comprising administering a bacterial isolate comprising one, or two, or three, or four, or five, or six, or seven, or eight, or nine, or ten (in the case of Tables 42 or 43) of the bacterial isolates of any one of Tables 36-43. In embodiments, the bacterial isolate(s) are co-formulated and/or co-administered. In embodiments, there is provided a method of treating inflammatory bowel disease comprising administering a pharmaceutical composition comprising (a) a bacterial isolate and (b) a pharmaceutically acceptable antioxidant, cryoprotectant, lyoprotectant, binder, disintegrant, excipient, filler, preservative, acid suppressant, antacid, H2 antagonist, and/or proton pump inhibitor; the bacterial isolate comprising one, or two, or three, or four, or five, or six, or seven, or eight, or nine, or ten (in the case of Tables 42 or 43) of the bacterial isolates of any one of Tables 36-43. In embodiments, there is provided a method of treating inflammatory bowel disease comprising administering a pharmaceutical composition comprising (a) a bacterial isolate and (b) a pharmaceutically acceptable antioxidant, cryoprotectant, lyoprotectant, binder, disintegrant, excipient, filler, preservative, acid suppressant, antacid, H2 antagonist, and/or proton pump inhibitor; the bacterial isolate comprising nine of the bacterial isolates of any one of Tables 36-43. In embodiments, there is provided a method of treating inflammatory bowel disease comprising administering a pharmaceutical composition comprising (a) a bacterial isolate and (b) a pharmaceutically acceptable antioxidant, cryoprotectant, lyoprotectant, binder, disintegrant, excipient, filler, preservative, acid suppressant, antacid, H2 antagonist, and/or proton pump inhibitor; the bacterial isolate consisting of nine of the bacterial isolates of any one of Tables 36-43.

[0071] Any aspect or embodiment described herein can be combined with any other aspect or embodiment as disclosed herein.

BRIEF DESCRIPTION OF THE FIGURES

[0072] **FIG. 1A** is a graph showing the results of a short-chain fatty acid (SCFA) quantification assay measuring butyrate concentration (in mM) secreted by various bacterial isolates after a twenty-four incubation in substrate buffer. **FIG. 1B** shows the percentage of converted butyrate normalized to carbon count.

[0073] **FIG. 2A** to **FIG. 2E** show production by bacterial isolates of aryl hydrocarbons, namely indole (**FIG. 2A**), tryptamine (**FIG. 2B**), kynurenic acid (**FIG. 2C**), kynurenine (**FIG. 2D**), and indole-3-acetic acid (**FIG. 2E**).

[0074] **FIG. 3** shows the relationship between the dosage of various bacterial strains corresponding by 16S rRNA sequence to bacterial isolates and engraftment of the strains following the administration to a subject of uncultured fecal bacteria containing the strains.

[0075] **FIG. 4A-E** shows the anti-inflammatory effects of an 8-strain bacterial cocktail when incubated with PBMCs treated with inflammation-inducing *E. coli* on IL-23 (FIG. 4A), TNF-α (FIG. 4B), IL-10 (FIG. 4C), IFN-γ (FIG. 4D) and IL-12p70 (FIG. 4E).

[0076] **FIG. 5A-E** shows the anti-inflammatory effects of a 7-strain bacterial cocktail when incubated with PBMCs treated with inflammation-inducing *E. coli* on IL-23 (FIG. 5A), TNF-α (FIG. 5B), IL-10 (FIG. 5C), IFN-γ (FIG. 5D) and IL-12p70 (FIG. 5E).

[0077] **FIG. 6** shows the engraftment of four bacterial isolates following administration to germ free mice of a pharmaceutical composition comprising the isolates.

DETAILED DESCRIPTION

[0078] Described herein are bacterial isolates and cocktails of bacterial isolates that can be utilized for the effective prevention and/or treatment of various disorders related to an intestinal dysbiosis.

[0079] Unless defined otherwise herein, terms are to be understood according to conventional usage by those of ordinary skill in the relevant art.

[0080] As used in the description of the disclosure and the appended claims, the singular forms "a," "an" and "the" are intended to include the plural forms as well, unless the context clearly indicates otherwise.

[0081] As used herein, "and/or" refers to and encompasses any and all possible combinations of one or more of the associated listed items, as well as the lack of combinations when interpreted in the alternative ("or").

[0082] The terms "about" and "approximately" as used herein when referring to a measurable value such as a percentage, density, volume and the like, is meant to encompass variations of 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 11% 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.5%, or even 0.1% of the specified amount.

[0083] As used herein, the term "substantially", when used to modify a quality, generally allows certain degree of variation without that quality being lost. For example, in certain aspects such degree of variation can be less than 0.1%, about 0.1%, about 0.2%, about 0.3%,

about 0.4%, about 0.5%, about 0.6%, about 0.7%, about 0.8%, about 0.9%, about 1%, between 1-2%, between 2-3%, between 3-4%, between 4-5%, or greater than 5%.

[0084] As used herein, the term "treating" refers to (i) completely or partially inhibiting a disease, disorder or condition, for example, arresting its development; (ii) completely or partially relieving a disease, disorder or condition, for example, causing regression of the disease, disorder and/or condition; or (iii) completely or partially preventing a disease, disorder or condition from occurring in a patient that may be predisposed to the disease, disorder and/or condition, but has not yet been diagnosed as having it. Similarly, "treatment" refers to both therapeutic treatment and prophylactic or preventative measures.

[0085] As used herein, "therapeutically effective amount" or "pharmaceutically active dose" refers to an amount of a composition which is effective in treating the named disease, disorder or condition.

[0086] As used herein, "microbiota," and "flora" refer to a community of microbes that live in or on a subject's body, both sustainably and transiently, including eukaryotes, archaea, bacteria, and viruses (including bacterial viruses (*i.e.*, phage)). A non-selected fecal microbiota refers to a community or mixture of fecal microbes derived from a donor's fecal sample without selection and substantially resembling microbial constituents and population structure found in such fecal sample.

[0087] As used herein, a "sterile fecal filtrate" or a "non-cellular fecal filtrate" refers to a liquid component of a fecal material, where the liquid component is free or substantially free of cell-based living organisms (*e.g.*, bacteria, fungi, or their spores), but retains bacteriophages and non-cellular biological materials. In embodiments, a non-cellular or sterile fecal filtrate is also free of viruses for eukaryotic host cells.

[0088] As used herein, "eukaryotic" refers to belonging to a cell that contains a nucleus and membrane-bound organelles.

[0089] As used herein, "bacteria," "bacterium," and "archaea" refer to single-celled prokaryotes that lack membrane bound nuclei and organelles.

[0090] As used herein, "colony forming units" (cfu) refers to an estimate of the number of viable microorganism cells in a given sample.

[0091] As used herein, "viable" means possessing the ability to multiply. In one embodiment, a bacterial spore is viable. In another embodiment, a vegetative bacterial cell is viable.

[0092] As used herein, "fecal bacteria" refers to bacteria that can be found in fecal matter.

[0093] As used herein, "isolated" or "purified" refers to a bacterium or other entity or substance that has been (1) separated from at least some of the components with which it was associated when initially produced (whether in nature or in an experimental setting), and/or (2) produced, prepared, purified, and/or manufactured by the hand of man. Isolated or purified bacteria can be separated from at least about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, or more of the other components with which they were initially associated.

[0094] As used herein, "cytotoxic" activity or bacterium includes the ability to kill a bacterial cell, such as a pathogenic bacterial cell. A "cytostatic" activity or bacterium includes the ability to inhibit, partially or fully, growth, metabolism, and/or proliferation of a bacterial cell, such as a pathogenic bacterial cell.

[0095] As used herein, the terms "pathogen" and "pathogenic" in reference to a bacterium or any other organism or entity includes any such organism or entity that is capable of causing or affecting a disease, disorder or condition of a host organism containing the organism or entity.

[0096] As used herein, "spore" or a population of "spores" includes bacteria (or other single-celled organisms) that are generally viable, more resistant to environmental influences such as heat and bacteriocidal agents than vegetative forms of the same bacteria, and typically capable of germination and out-growth. "Spore-formers" or bacteria "capable of forming spores" are those bacteria containing the genes and other necessary abilities to produce spores under suitable environmental conditions.

[0097] As used herein, a "combination" of two or more bacteria includes the physical co-existence of the two bacteria, either in the same material or product or in physically connected products, as well as the temporal co-administration or co-localization of the two bacteria.

[0098] As used herein, a "bacterial isolate" refers to a population of substantially genetically identical bacterial cells generated by proliferation via binary fission from a single predecessor bacterial cell (e.g., by culturing the bacteria). Typically, a bacterial isolate is originally isolated as a genetically pure cell or population of cells, for example, as a single colony on solid culture media or via serial dilutions in liquid culture, and thereafter archived (e.g. as a frozen stock) to provide a consistent and stable source for the isolate. Once isolated, in some embodiments, bacterial isolate can be grown as a pure population of cells; in other embodiments, multiple isolates of bacteria can be grown simultaneously in the same vessel as a mixed culture. The

term "substantially genetically identical" refers to the very high (>99%) genetic identity shared by different cells in uncontaminated mixtures, owing to their proliferation from a common predecessor, but accounts for minor genetic dissimilarity within the population due to accumulations of relatively rare mutations. Generally, a bacterial isolate is synonymous with a cultured population of cells. Typically, a bacterial isolate consists of non-pathogenic bacteria.

[0099] As used herein, the term "microbial cocktail", sometimes called a "microbial consortium" or "synthetic bacterial mixture" or "bacterial mixture", refers to an engineered composition (e.g. pharmaceutical composition) comprising a defined consortium of multiple bacterial isolates. The term "defined consortium of multiple bacterial isolates" means that the microbial cocktail contains two or more bacterial isolates, and that the number and identity of each bacterial isolate in the cocktail is known, and thus the cocktail can be consistently produced (e.g. by combining isolated bacterial strains) as a pharmaceutical composition having stable properties across separate batches. Herein "identity" of a bacterial isolate can refer to any characteristic of the isolate that uniquely identifies the isolate as different from one or more other isolates or bacterial strains. Examples of identifying characteristics include DNA sequences such as 16S rRNA sequence, the sequence of one or more coding or non-coding regions and entire genome sequences, levels of gene expression, physiological or metabolic traits, or anatomical traits such as staining pattern or cell wall characteristics.

[00100] A microbial cocktail or consortium described herein (e.g. derived from bacterial strains of fecal origin) can be distinguished from a composition (e.g. pharmaceutical composition) comprising an "uncultured fecal microbiota", which refers to a mixture of multiple bacterial strains that have been at least partially extracted or purified from a stool sample without culturing the strains in culture medium. Steps taken to extract a microbiota or fecal bacteria from a stool sample can include, for example, homogenization and filtering of the stool sample to separate the fecal bacterial strains from non-cellular stool material such as fiber and rough particulate matter, as well as, for example, eukaryotic host cells and viruses. Preparation of a pharmaceutical composition comprising an uncultured fecal microbiota can in some embodiments involve removal of certain types (e.g. species) of bacteria from the microbiota and/or addition of one or more bacterial strains to the microbiota. In certain embodiments, a pharmaceutical composition can comprise one or more cultured bacterial strains (e.g. bacterial isolates) combined with an uncultured fecal microbiota.

[00101] Herein "uncultured fecal bacteria" or a "preparation of uncultured fecal bacteria" refer to a preparation comprising multiple non-pathogenic viable bacterial strains that have

been harvested, extracted or purified from one or more stool samples, without culturing the strains (e.g. in culturing medium). Such a preparation of uncultured fecal bacteria can also be referred to as a collection of uncultured fecal bacteria or a population of uncultured fecal bacteria. In certain embodiments, an uncultured fecal microbiota comprises a preparation of uncultured fecal bacteria.

[00102] The present disclosure contemplates compositions (e.g. pharmaceutical compositions) that comprise both a bacterial isolate (e.g., single microbial isolate or microbial cocktail) and an uncultured fecal microbiota or preparation of uncultured fecal bacteria. For example, in certain embodiments, a composition can comprise a substantially complete fecal microbiota or a preparation of uncultured fecal bacteria extracted or purified from a stool sample of a healthy individual supplemented or "spiked" with one or more bacterial isolates.

[00103] Herein the terms "microbial mixture" and "microbial therapeutic" are meant to broadly encompass any composition or treatment that incorporates a bacterial isolate, microbial cocktail, preparation of uncultured fecal bacteria and/or uncultured fecal microbiota.

[00104] Herein "at least 95% identical", when used with reference to a 16S rRNA sequence, refers to a subject DNA sequence that shares identity to a reference DNA sequence of at least 95%, at least 95.5%, at least 96%, at least 96.5%, at least 97%, at least 97.5%, at least 98%, at least 98.5%, at least 99%, at least 99.5% or 100%.

[00105] As used herein, a "subject" refers to any animal subject including humans, laboratory animals (e.g., primates, rats, mice), livestock (e.g., cows, sheep, goats, pigs, turkeys, chickens), and household pets (e.g., dogs, cats, rodents, etc.). In some embodiments, the subject and/or animal is a mammal, *e.g.*, a human, mouse, rat, guinea pig, dog, cat, horse, cow, pig, rabbit, sheep, or non-human primate, such as a monkey, chimpanzee, or baboon. In other embodiments, the subject and/or animal is a non-mammal, such, for example, a zebrafish. Preferred subjects are human subjects. The human subject may be a pediatric, adult or a geriatric subject. In some embodiments, the terms "patient" and "subject" are used interchangeably.

[00106] As used herein, "Shannon Diversity Index" refers to a diversity index that accounts for abundance and evenness of species present in a given community using the formula

$$H = -\sum_{i=1}^{R} p_i \ln p_i$$

where H is Shannon Diversity Index, R is the total number of species in the community, and p_i is the proportion of R made up of the *i*th species. Higher values indicate diverse and equally

distributed communities, and a value of 0 indicates only one species is present in a given community. For further reference, *see* Shannon and Weaver, (1949) *The mathematical theory of communication*. The University of Illinois Press, Urbana. 117pp.

[00107] As used herein, "antibiotic" refers to a substance that is used to treat and/or prevent bacterial infection by killing bacteria, inhibiting the growth of bacteria, or reducing the viability of bacteria.

[00108] As used herein, an "intermittent dosing schedule" refers to a dosing schedule where a pharmaceutical composition is administered for a period of time (initial treatment period) which is then followed by a second period of time where treatment with such pharmaceutical composition is withheld (a rest period). The rest period can optionally be followed by a third period wherein the treatment is again administered (either at the same or different dosage as in the initial treatment period), which can be followed by further rest and treatment periods as needed. Intermittent dosing regimens can be expressed as treatment period in days or weeks/rest period in days or weeks. For example, a 4/1 intermittent dosing schedule refers to an intermittent dosing schedule where the treatment period is four weeks/days and the rest period is one week/day, as the case may be.

[00109] As used herein, a "continuous dosing schedule" refers to a dosing schedule where a pharmaceutical composition is administered during a treatment period without a rest period. Throughout the treatment period of a continuous dosing schedule, a pharmaceutical composition can be administered, for example, daily, or every other day, or every third day. On a day when a pharmaceutical composition is administered, it can be administered in a single dose, or in multiple doses throughout the day.

[00110] As used herein, "dosing frequency" refers to the frequency of administering doses of a pharmaceutical composition in a given time. Dosing frequency can be indicated as the number of doses per a given time, for example, once per day, once a week, or once in two weeks.

[00111] As used herein, "dosing interval" refers to the amount of time that elapses between consecutive doses of a pharmaceutical composition being administered to a subject.

[00112] As used herein, "a disorder related to an intestinal dysbiosis" or "a disorder related to an GI dysbiosis" or "dysbiosis" refers to a disorder or disease caused by an atypical or unhealthy microbiome, e.g., which comprises certain undesirable bacterial strains and/or lacks certain desirable bacterial strains. Examples include but are not limited to inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), *C. difficile* infection (CDI), *C. difficile*-

associated disease (CDAD), and antibiotic-induced adverse effect. Examples of IBD include ulcerative colitis (UC), Crohn's disease (CD), and pouchitis.

[00113] In one aspect, the subject has been diagnosed with a disorder related to an intestinal dysbiosis. In another aspect, a subject being treated is at risk for or is predisposed to having a disorder related to an intestinal dysbiosis is to be prevented. In aspects, a subject being treated is a subject in which a disorder related to an intestinal dysbiosis is to be prevented.

Bacterial Isolates and microbial cocktails

[00114] Described herein are pharmaceutical compositions, formulations, methods of manufacture, and uses of bacterial isolates and microbial cocktails of bacterial isolates in the treatment of various disorders related to an intestinal dysbiosis, e.g., gastrointestinal disorders.

[00115] An aspect of the present invention is a pharmaceutical composition comprising a plurality of bacterial isolates, wherein the plurality of bacterial isolates comprise *Bacteroides stercoris*, and at least two of *Bacteroides cellulosilyticus*, *Bacteroides uniformis*, *Suboligranulum variabile*, *Anaerostipes hadrus*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*, wherein at least two of the plurality of bacterial isolates are isolated from a stool of different human donors.

[00116] In embodiments, the plurality of bacterial isolates comprises at least three of *Bacteroides cellulosilyticus*, *Bacteroides uniformis*, *Suboligranulum variabile*, *Anaerostipes hadrus*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least four of *Bacteroides cellulosilyticus*, *Bacteroides uniformis*, *Suboligranulum variabile*, *Anaerostipes hadrus*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least five of *Bacteroides cellulosilyticus*, *Bacteroides uniformis*, *Suboligranulum variabile*, *Anaerostipes hadrus*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least five of *Bacteroides cellulosilyticus*, *Bacteroides uniformis*, *Suboligranulum variabile*, *Anaerostipes hadrus*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of

bacterial isolates comprises at least six of *Bacteroides cellulosilyticus*, *Bacteroides uniformis*, *Suboligranulum variabile*, *Anaerostipes hadrus*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least seven of *Bacteroides cellulosilyticus*, *Bacteroides uniformis*, *Suboligranulum variabile*, *Anaerostipes hadrus*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least eight of *Bacteroides cellulosilyticus*, *Bacteroides uniformis*, *Suboligranulum variabile*, *Anaerostipes hadrus*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

[00117] In embodiments, the composition comprises a 16S rRNA sequence that is at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity with nucleotide sequences selected from SEQ ID NOs: 1, 2, 3, 7, 8, 11, 14, 18, 19, 20, 22 and 23. In embodiments, the pharmaceutical composition comprises at least two bacterial isolates comprising *Faecalibacterium prausnitzii*, wherein the at least two bacterial isolates comprise different 16S rRNA sequences. In embodiments, the pharmaceutical composition comprises 16S rRNA sequences that are at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% identity sequence identity with nucleotide sequences of SEQ ID NOs: 1 and 7.

[00118] In aspects, a pharmaceutical composition comprises one or more bacterial isolates that comprised a 16S rRNA sequence at least 95% identical (e.g., at least 95% identical, at least 95.5% identical, at least 96% identical, at least 96.5% identical, at least 97% identical, at least 97.5% identical, at least 98% identical, at least 98.5% identical, at least 99% identical, at least 99.5% identical, or 100% identical) to the 16S rRNA sequence of one of the bacterial isolates provided in Table 1. In embodiments, the composition comprises a single bacterial isolate. In embodiments, the composition is a microbial cocktail that comprises at least two bacterial isolates, at least three bacterial isolates, at least four bacterial isolates, at least five bacterial isolates, at least six bacterial isolates, at least seven bacterial isolates, at least eight bacterial isolates, at least nine bacterial isolates, at least ten bacterial isolates, or a greater number of bacterial isolates, e.g., fifteen, twenty, twenty-five, thirty, or more bacterial isolates. In embodiments, each of the, for example, three, four, five, six, seven, eight, nine, or ten bacterial

isolates comprises a 16S rRNA sequence that is at least 95% identical to the 16S rRNA sequence of one of the bacterial isolates provided in Table 1.

[00119] In one aspect, a pharmaceutical composition administered herein comprises fecal bacteria. In one aspect, a pharmaceutical composition administered herein comprises one or more bacterial isolates extracted, isolated and/or cultured from a stool sample of a healthy human donor. In one aspect, a pharmaceutical composition administered herein comprises one or more, two or more, three or more, four or more, or five or more isolated, purified, or cultured microorganisms selected from the group consisting of *Akkermansia*, *Alistipes*, *Anaerostipes*, *Bacillus*, *Bacteroides, Blautia*, *Clostridium, Collinsella, Coprococcus*, *Dorea*, *Eubacterium, Faecalibacterium*, *Fusobacterium*, *Odoribacter*, *Parabacteroides*, *Phascolarctobacterium*, *Propionibacterium, Roseburia*, *Subdoligranulum*, *Lactobacillus, Ruminococcus, Escherichia, Gemmiger, Desulfomonas, Peptostreptococcus,* and a combination thereof.

[00120] In one aspect, a pharmaceutical composition administered herein comprises at least one, at least two, at least three, at least four, at least five, at least six, or at least seven, at least eight, at least nine, at least ten, at least eleven, or at least twelve fecal microorganisms (e.g., bacterial isolates) selected from the group consisting of a *Faecalibacterium prausnitzii, Odoribacter splanchnicus*, *Anaerostipes hadrus, Alistipes onderdonkii, Alistipes putredinis*, *Parabacteroides merdae, Dorea longicatena, Eubacterium rectale, Blautia obeum, Blautia* sp., *Clostridium aldenense, Bacteroides uniformis, Bacteroides vulgatus, Bacteroides stercoris, Bacteroides cellulosilyticus, Alistipes finegoldii, Coprococcus comes, Alistipes shahii, Roseburia faecis, Akkermansia muciniphila, Phascolarctobacterium faecium, Subdoligranulum variabile*, and a combination thereof. In embodiments, a bacterial isolate comprises *Odoribacter* sp. In an embodiment, *Odoribacter* sp. comprises *Odoribacter splanchnicus*. In embodiments, a bacterial isolate comprising *Odoribacter* sp. comprises *Odoribacter laneus*. In embodiments, a bacterial isolate comprising *Blautia* sp. comprises *Blautia obeum*. In embodiments, a bacterial isolate comprising *Blautia* sp. comprises *Blautia massiliensis*. In embodiments, a bacterial isolate comprising *Blautia* sp. comprises *Blautia coccoides*. In embodiments, a bacterial isolate comprising *Blautia* sp. comprises *Blautia producta*. In embodiments, a bacterial isolate comprising *Blautia* sp. comprises *Blautia schinkii*. In embodiments, a bacterial isolate comprising *Blautia* sp. comprises *Blautia hydrogenotrophica*. In embodiments, a bacterial isolate comprising *Blautia* sp. comprises *Blautia luti*. In embodiments, a bacterial isolate comprising *Blautia* sp. comprises *Blautia hansenii*. In embodiments, a bacterial isolate comprising *Blautia* sp. comprises *Blautia faecis*.

In embodiments, a bacterial isolate comprising *Blautia* sp. comprises *Blautia stercoris*. In embodiments, a bacterial isolate comprising *Blautia* sp. comprises *Blautia wexlerae*.

[00121] In one aspect, a pharmaceutical composition administered herein comprises no viable *Bacteroides, Fusobacterium, Propionibacterium, Lactobacillus, Ruminococcus, Escherichia coli, Gemmiger, Desulfomonas, Peptostreptococcus, Bifidobacterium, Monilia,* or any combination thereof. In another aspect, a pharmaceutical composition administered herein comprises no viable *Bacteroides fragilis* sp. *vulgatus*, *Collinsella aerofaciens, Bacteroides fragilis* sp. *thetaiotaomicron*, *Peptostreptococcus productus* II, *Parabacteroides distasonis, Fusobacterium prausnitzii, Coprococcus eutactus, Collinsella aerofaciens* III, *Peptostreptococcus productus* I, *Ruminococcus bromii, Bifidobacterium adolescentis, Gemmiger formicilis*, *Bifidobacterium longum*, *Eubacterium siraeum, Ruminococcus torques, Eubacterium rectale*, *Eubacterium eligens*, *Bacteroides eggerthii, Clostridium leptum, Bacteroides fragilis* sp. A, *Eubacterium biforme, Bifidobacterium infantis, Eubacterium rectale* III-F, *Coprococcus comes*, *Pseudoflavonifractor capillosus*, *Ruminococcus albus*, *Dorea formicigenerans*, *Eubacterium hallii*, *Eubacterium ventriosum* I, *Fusobacterium russi*, *Ruminococcus obeum*, *Eubacterium rectale*, *Clostridium ramosum*, *Lactobacillus leichmannii*, *Ruminococcus callidus*, *Butyrivibrio crossotus*, *Acidaminococcus fermentans*, *Eubacterium ventriosum*, *Bacteroides fragilis* sp. *fragilis*, *Bacteroides* AR, *Coprococcus catus*, *Aerostipes hadrus*, *Eubacterium cylindroides*, *Eubacterium ruminantium*, *Eubacterium* CH-1, *Staphylococcus epidermidis*, *Peptostreptococcus* BL, *Eubacterium limosum*, *Tissirella praeacuta*, *Bacteroides* L, *Fusobacterium mortiferum* I, *Fusobacterium naviforme*, *Clostridium innocuum*, *Clostridium ramosum*, *Propionibacterium acnes*, *Ruminococcus flavefaciens*, *Ruminococcus* AT, *Peptococcus* AU-1, *Bacteroides fragilis* sp. *ovatus*, -sp. d, -sp. f; *Bacteroides* L-1, L-5; *Fusobacterium nucleatum*, *Fusobacterium mortiferum*, *Escherichia coli*, *Gemella morbillorum*, *Finegoldia magnus*, *Peptococcus* G, -AU-2; *Streptococcus intermedius*, *Ruminococcus lactaris*, *Ruminococcus* CO *Gemmiger* X, *Coprococcus* BH, -CC; *Eubacterium tenue*, *Eubacterium ramulus*, *Bacteroides clostridiiformis* sp. *clostridliformis*, *Bacteroides coagulans, Prevotella oralis, Prevotella ruminicola, Odoribacter* sp. *(e.g. Odoribacter splanchnicus and/or Odoriacter laneus*), *Desuifomonas pigra*, *Lactobacillus* G, *Succinivibrio* A, or a combination thereof.

[00122] In various embodiments, the bacterial isolates described herein comprise bacteria isolated or purified from a human. In various embodiments, all or a subset of bacterial isolates incorporated into a microbial cocktail described herein are isolated or purified from a human.

For instance, one or more bacterial isolates can be purified or isolated from a stool sample of one or more healthy human donors pre-screened for infectious agents. In other examples, a bacterial isolate can be isolated or purified from aspirates of the fluid in the GI tract or mucosal biopsies from a site in the GI tract.

[00123] In embodiments, a pharmaceutical composition or microbial cocktail comprises a plurality of bacterial isolates isolated or purified from stool samples of multiple human donors. In embodiments, a pharmaceutical composition or microbial cocktail comprises a plurality of bacterial isolates isolated or purified from a stool sample or stool samples of only a single human donor.

[00124] In some embodiments, a bacterial isolate incorporated into a pharmaceutical composition described herein comprises live, vegetative cells. In some embodiments, the bacterial isolate comprises bacteria capable of forming spores. In some embodiments, the bacterial isolate comprises bacteria in the form of spores, *e.g.* viable spores. In some embodiments, the bacterial isolate comprises bacteria in the form of live, vegetative cells and spores. In some embodiments, a bacterial isolate is substantially free of live, vegetative cells. In some embodiments, an entire microbial cocktail is substantially free of live vegetative cells. In some embodiments, a bacterial isolate is substantially free of spores. In some embodiments, an entire microbial cocktail is substantially free of spores.

[00125] In aspects, a pharmaceutical composition comprises at least one bacterial isolate provided in Table 1, or a bacterial isolate comprising a 16S rRNA sequence that is at least 95% identical to the 16S rRNA sequence of one or more of the bacterial isolates provided in Table 1. In certain embodiments, a pharmaceutical composition comprises a microbial cocktail comprising at least two bacterial isolates provided in Table 1, or at least two bacterial isolates comprising a 16S rRNA sequence that is at least 95% identical to the 16S rRNA sequence of one or more of the bacterial isolates provided in Table 1. Each bacterial isolate in Table 1 is identified by Latin name, an Identification Number (ID number), and the Sequence Identifier (SEQ ID NO) for its 16S rRNA sequence.

Table 1

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence
Faecalibacterium prausnitzii	PI00000329	1
Odoribacter splanchnicus	PI00000072	2
Anaerostipes hadrus	PI00000094	3

Alistipes onderdonkii	IS00004389	4
Parabacteroides merdae	IS00006167	5
Dorea longicatena	IS00006618	6
Faecalibacterium prausnitzii	IS00006632	7
Eubacterium rectale	IS00006864	8
Blautia obeum	PI00000053	9
Clostridium aldenense	PI00000097	10
Bacteroides uniformis	PI00000137	11
Bacteroides vulgatus	PI00000138	12
Bacteroides stercoris	PI00000146	13
Bacteroides cellulosilyticus	PI00000316	14
Alistipes finegoldii	PI00000340	15
Bacteroides uniformis	PI00000352	16
Coprococcus comes	PI00000370	17
Alistipes shahii	PI00000395	18
Roseburia faecis	PI00000404	19
Akkermansia muciniphila	IS00007180	20
Phascolarctobacterium faecium	PI00000289	21
Subdoligranulum variabile	IS00007359	22
Subdoligranulum variabile	IS00007357	23
Blautia sp.	IS00002788	34
Alistipes putredinis	IS00008139	35
Alistipes putredinis	IS00008142	36
Alistipes putredinis	IS00008177	37

[00126] In embodiments, the pharmaceutical composition comprises a microbial cocktail comprising about 2 to about 50 bacterial isolates, about 3 to about 50 bacterial isolates, about 3 to about 45 bacterial isolates, about 3 to about 40 bacterial isolates, about 3 to about 35 bacterial isolates, about 3 to about 30 bacterial isolates, about 3 to about 20 bacterial isolates, about 3 to about 15 bacterial isolates, about 3 to about 10 bacterial isolates, and about 3 to about 9 bacterial isolates. In embodiments, the pharmaceutical composition comprises a microbial cocktail comprising about 30 bacterial isolates, or about 29 bacterial isolates, or about 28 bacterial isolates, or about 27 bacterial isolates, or about 26 bacterial isolates, or about 25 bacterial isolates, or about 24 bacterial isolates, or about 23 bacterial isolates, or about 22 bacterial isolates, or about 21 bacterial isolates, or about 19 bacterial isolates, or about 18 bacterial isolates, or about 17 bacterial isolates, or about 16 bacterial isolates, or about 15 bacterial isolates, or about 14 bacterial isolates, or about 13 bacterial isolates, or about 12 bacterial isolates, or about 11 bacterial isolates. In embodiments, the pharmaceutical composition comprises a microbial cocktail comprising 10 bacterial isolates. In embodiments,

the pharmaceutical composition comprises a microbial cocktail comprising 9 bacterial isolates. In embodiments, the pharmaceutical composition comprises a microbial cocktail comprising 8 bacterial isolates. In embodiments, the pharmaceutical composition comprises a microbial cocktail comprising 7 bacterial isolates. In embodiments, the pharmaceutical composition comprises a microbial cocktail comprising 6 bacterial isolates. In embodiments, the pharmaceutical composition comprises a microbial cocktail comprising 5 bacterial isolates. In embodiments, the pharmaceutical composition comprises a microbial cocktail comprising 4 bacterial isolates. In embodiments, the pharmaceutical composition comprises a microbial cocktail comprising 3 bacterial isolates. In embodiments, the pharmaceutical composition comprises a microbial cocktail comprising 2 bacterial isolates.

[00127] In embodiments, the microbial cocktail comprises at least two bacterial isolates, at least three bacterial isolates, at least four bacterial isolates, at least five bacterial isolates, at least six bacterial isolates, at least seven bacterial isolates, at least eight bacterial isolates, at least nine bacterial isolates, at least ten bacterial isolates, or a greater number of bacterial isolates, e.g., fifteen, twenty, twenty-five, thirty, or more bacterial isolates. In embodiments, each of the three, four, five, six, seven, eight, nine, or ten bacterial isolates comprises a 16S rRNA sequence that is at least 95% identical to the 16S rRNA sequence of at least one of the bacterial isolates provided in Table 1.

[00128] In embodiments, the pharmaceutical composition comprises a microbial cocktail comprising about 6 to about 20 bacterial isolates provided in Table 1, or having a 16S rRNA sequence that is at least 95% identical to the 16S rRNA sequence of at least one of the bacterial isolates provided in Table 1, or e.g., about 6 to about 15 bacterial isolates, about 6 to about 10 bacterial isolates, about 6 to about 9 bacterial isolates. In embodiments, the pharmaceutical composition comprises a microbial cocktail comprising 30 bacterial isolates, or 29 bacterial isolates, or 28 bacterial isolates, or 27 bacterial isolates, or 26 bacterial isolates, or 25 bacterial isolates, or 24 bacterial isolates, or 23 bacterial isolates, or 22 bacterial isolates, or 21 bacterial isolates, or 20 bacterial isolates, or 19 bacterial isolates, or 18 bacterial isolates, or 17 bacterial isolates, or 16 bacterial isolates, or 15 bacterial isolates, or 14 bacterial isolates, or 13 bacterial isolates, or 12 bacterial isolates, or 11 bacterial isolates, or 10 bacterial isolates, or 9 bacterial isolates, or 8 bacterial isolates, or 7 bacterial isolates, or 6 bacterial isolates, or 5 bacterial isolates, or 4 bacterial isolates, or 3 bacterial isolates, or 2 bacterial isolates, or 1 bacterial isolate provided in Table 1, or having a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 1. In embodiments, the

pharmaceutical composition comprises a microbial cocktail comprising 8 bacterial isolates provided in Table 1, or having a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 1. In embodiments, the pharmaceutical composition comprises a microbial cocktail comprising 7 bacterial isolates provided in Table 1, or having a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 1. In embodiments, the pharmaceutical composition comprises a microbial cocktail comprising 6 bacterial isolates provided in Table 1, or having a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 1. In embodiments, the pharmaceutical composition comprises one bacterial isolate provided in Table 1, or having a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 1.

[00129] In embodiments, a bacterial isolate incorporated into a pharmaceutical composition described herein is capable of improving the health of a subject administered the composition. In embodiments, the bacterial isolate impacts the health of a subject by inducing or influencing one or more biological mechanisms that act in the subject to impact the health of the subject. Exemplary mechanisms include the production of SCFA by the bacterial isolate in the gut of the subject or the modulation by the bacterial isolate of cytokine production and/or release by a cell of the subject (e.g., intestinal cell). Another exemplary mechanism is the production by the bacterial isolate of an aryl hydrocarbon capable of binding to and activating an aryl hydrocarbon receptor (AhR) of a cell of the subject. In another example, a bacterial isolate is more abundant in the gut or fecal microbiota of a healthy human subject relative to a patient with an intestinal dysbiosis, or a more abundant in a human subject in remission from an intestinal dysbiosis relative to a patient having the intestinal dysbiosis. The increased abundance of the bacterial isolate in the intestine of a healthy subject can be indicative of a positive impact of the bacterial isolate on the health of the subject, even though the precise mechanism of action by which the bacterial isolate produces its effect may not be understood (i.e., the bacterial isolate has an impact on the health of the subject that is mechanism agnostic).

[00130] In embodiments, a pharmaceutical composition comprises one or more bacterial isolates having the ability to produce one or more SCFAs, or to enhance SCFA production by one or more bacterial strains. As used herein, an 'SCFA' refers to fatty acids with an aliphatic tail of one to six carbon atoms. SCFAs can be produced by bacteria during bacterial metabolism, such as during fermentation of, for example, carbohydrates, proteins, peptides and glycoprotein

precursors. Illustrative SCFAs include, but are not limited to, acetic acid, butyric acid, caproic acid, formic acid, heptanoic acid, isobutyric acid, isocaproic acid, isovaleric acid, propionic acid, and valeric acid. Without wishing to be bound by theory, SCFAs are thought to play an essential role in maintaining the health of colonic mucosa, and the presence of gut SCFA-producing bacteria are associated with sustained clinical remission of certain gut dysbioses, such as UC. Accordingly, in some embodiments, a bacterial isolate incorporated into a pharmaceutical composition described herein can produce one or more SCFAs. For example, a bacterial isolate can produce one or more SCFAs in an intestine of a subject after the composition (e.g., comprising a microbial cocktail) is administered to the subject (e.g., a subject having UC). In another example, a bacterial isolate can produce one or more SCFAs in an *in vitro* assay capable of detecting and/or measuring SCFA production by bacteria.

[00131] In embodiments, a bacterial isolate described herein produces an SCFA selected from the group consisting of: acetic acid, butyric acid, caproic acid, formic acid, heptanoic acid, isobutyric acid, isocaproic acid, isovaleric acid, propionic acid, valeric acid, and a combination thereof.

[00132] In embodiments, a pharmaceutical composition comprises one or more bacterial isolates that produce an SCFA (e.g., butyrate) at a concentration of at least 5 mM, at least 10 mM, at least 15 mM, at least 20 mM, at least 25 mM, at least 30 mM, at least 35 mM, at least 40 mM, at least 45 mM at least 50 mM, at least 60 mM, at least 70 mM, at least 80 mM, at least 90 mM, at least 100 mM, at least 110 mM, at least 120 mM, at least 130 mM, at least 140 mM, at least 150 mM, or greater than 150 mM during a period of 24 hours. In an embodiment, the SCFA is measured in a functional assay (i.e., an assay conducted *ex vivo* and designed to measure the concentration or amount of an SCFA produced by a bacterial isolate, microbial cocktail, a preparation of uncultured fecal bacteria, or an uncultured fecal microbiota during a period of time (e.g., 24 hours)). For example, a functional assay can comprise incubating one or more bacterial isolates with a substrate (e.g., for 24 hours); and measuring the level of SCFA (e.g., butyrate) produced by the one or more bacterial isolates after metabolism of the substrate. In embodiments, the substrate can comprise at least one of an oligosaccharide (e.g., a fructooligosaccharide (FOS) or an xylooligosaccharide (XOS)), sunfiber/partially hydrolyzed guar gum (PHGG), or barley malt.

[00133] In an embodiment, the SCFA is produced in the intestine of a subject administered a composition described herein.

[00134] In an embodiment, a pharmaceutical composition comprises *Odoribacter splanchnicus*, wherein the *Odoribacter splanchnicus* produces an SCFA (e.g., butyrate) at a concentration of at least 20 mM, at least 21 mM, at least 22 mM, at least 23 mM, at least 24 mM, at least 25 mM, at least 26 mM, at least 27 mM, at least 28 mM, at least 29 mM, at least 30 mM, at least 31 mM, at least 32 mM, at least 33 mM, at least 34 mM, at least 35 mM, at least 36 mM, at least 37 mM, at least 38 mM, at least 39 mM, at least 40 mM, at least 41 mM, at least 42 mM, at least 43 mM, at least 44 mM, at least 45 mM, at least 46 mM, at least 47 mM, at least 48 mM, at least 49 mM, at least 50 mM, or greater than 50 mM over a period of 24 hours. In an embodiment, the *Odoribacter splanchnicus* comprises a 16S rRNA sequence having at least 95% sequence identity to SEQ ID NO: 2.

[00135] In an embodiment, a pharmaceutical composition comprises *Roseburia* sp. (e.g., *Roseburia faecis*), wherein the *Roseburia* sp. produces an SCFA (e.g., butyrate) at a concentration of at least 20 mM, at least 21 mM, at least 22 mM, at least 23 mM, at least 24 mM, at least 25 mM, at least 26 mM, at least 27 mM, at least 28 mM, at least 29 mM, at least 30 mM, at least 31 mM, at least 32 mM, at least 33 mM, at least 34 mM, at least 35 mM, at least 36 mM, at least 37 mM, at least 38 mM, at least 39 mM, at least 40 mM, at least 41 mM, at least 42 mM, at least 43 mM, at least 44 mM, at least 45 mM, at least 46 mM, at least 47 mM, at least 48 mM, at least 49 mM, at least 50 mM, or greater than 50 mM over a period of 24 hours. In an embodiment, the *Roseburia* sp. comprises a 16S rRNA sequence having at least 95% sequence identity to SEQ ID NO: 19.

[00136] In an embodiment, a pharmaceutical composition comprises *Eubacteria* sp. (e.g., *Eubacteria rectale*), wherein the *Eubacteria* sp. produces an SCFA (e.g., butyrate) at a concentration of at least 20 mM, at least 21 mM, at least 22 mM, at least 23 mM, at least 24 mM, at least 25 mM, at least 26 mM, at least 27 mM, at least 28 mM, at least 29 mM, at least 30 mM, at least 31 mM, at least 32 mM, at least 33 mM, at least 34 mM, at least 35 mM, at least 36 mM, at least 37 mM, at least 38 mM, at least 39 mM, at least 40 mM, at least 41 mM, at least 42 mM, at least 43 mM, at least 44 mM, at least 45 mM, at least 46 mM, at least 47 mM, at least 48 mM, at least 49 mM, at least 50 mM, or greater than 50 mM over a period of 24 hours. In an embodiment, the *Eubacteria* sp. comprises a 16S rRNA sequence having at least 95% sequence identity to SEQ ID NO: 8.

[00137] In an embodiment, a pharmaceutical composition comprises *Coprococcus* sp. (e.g., *Coprococcus comes*), wherein the *Coprococcus* sp. produces an SCFA (e.g., butyrate) at a concentration of at least 20 mM, at least 21 mM, at least 22 mM, at least 23 mM, at least 24

mM, at least 25 mM, at least 26 mM, at least 27 mM, at least 28 mM, at least 29 mM, at least 30 mM, at least 31 mM, at least 32 mM, at least 33 mM, at least 34 mM, at least 35 mM, at least 36 mM, at least 37 mM, at least 38 mM, at least 39 mM, at least 40 mM, at least 41 mM, at least 42 mM, at least 43 mM, at least 44 mM, at least 45 mM, at least 46 mM, at least 47 mM, at least 48 mM, at least 49 mM, at least 50 mM, or greater than 50 mM over a period of 24 hours. In an embodiment, the *Coprococcus* sp. comprises a 16S rRNA sequence having at least 95% sequence identity to SEQ ID NO: 17.

[00138] In an embodiment, a pharmaceutical composition comprises a microbial cocktail comprising two or more bacterial isolates comprising *Odoribacter splanchnicus*, *Roseburia* sp. (e.g., *Roseburia faecis*), *Eubacteria* sp. (e.g., *Eubacteria rectale*), or *Coprococcus* sp. (e.g., *Coprococcus comes*), wherein the microbial cocktail produces an SCFA (e.g., butyrate) at a concentration of at least 20 mM, at least 21 mM, at least 22 mM, at least 23 mM, at least 24 mM, at least 25 mM, at least 26 mM, at least 27 mM, at least 28 mM, at least 29 mM, at least 30 mM, at least 31 mM, at least 32 mM, at least 33 mM, at least 34 mM, at least 35 mM, at least 36 mM, at least 37 mM, at least 38 mM, at least 39 mM, at least 40 mM, at least 41 mM, at least 42 mM, at least 43 mM, at least 44 mM, at least 45 mM, at least 46 mM, at least 47 mM, at least 48 mM, at least 49 mM, at least 50 mM, at least 60 mM, at least 65 mM, at least 70 mM, at least 75 mM, at least 80 mM, at least 85 mM, at least 90 mM, at least 95 mM, at least 100 mM, at least 105 mM, at least 110 mM, at least 115 mM, at least 120 mM, at least 125 mM, at least 130 mM, at least 135 mM, at least 140 mM, at least 145 mM, at least 150 mM, or greater than 150 mM over a period of 24 hours. In an embodiment, the *Odoribacter splanchnicus* comprises a 16S rRNA sequence having at least 95% sequence identity to SEQ ID NO: 2. In an embodiment, the *Roseburia* sp. comprises a 16S rRNA sequence having at least 95% sequence identity to SEQ ID NO: 19. In an embodiment, the *Eubacteria* sp. comprises a 16S rRNA sequence having at least 95% sequence identity to SEQ ID NO: 8. In an embodiment, the *Coprococcus* sp. comprises a 16S rRNA sequence having at least 95% sequence identity to SEQ ID NO: 17.

[00139] Additionally, in some embodiments, one or more bacterial isolates administered in a composition described herein can produce levels of SCFAs comparable to that of a healthy individual in a subject previously having a functionally deficient microbial community (*e.g.*, the microbial community of an IBD patient) who exhibited SCFA production levels lower than that of the healthy individual.

[00140] In certain embodiments, a bacterial isolate described herein can induce one or more bacterial strains to produce one or more SCFAs when the bacterial isolate and the bacterial strain(s) are present together in a common microbiota. For example, a bacterial isolate, upon administration to a subject in a composition described herein, can induce one or more bacterial strains endogenous to a gut microbiota of the subject (i.e., present in the gut of the subject prior to administration of the microbial cocktail) to produce one or more SCFAs. In another example, a bacterial isolate administered to a subject in a composition described herein can induce a second bacterial isolate administered to the subject (either in the same or a different composition) to produce one or more SCFAs. Without wishing to be bound by theory, induction of SCFA production by a second bacterial isolate can involve, for example, the production and release (e.g., by secretion) by the first bacterial isolate of one or more compounds that can be utilized by the second bacterial isolate to generate an SCFA. In one example, the compound produced and released by the first bacterial isolate to be used by the second bacterial strain to generate an SCFA is succinate, lactic acid or a lactic acid derivative. In one embodiment, the SCFA produced by the second bacterial isolate in response to exposure to the compound (e.g., lactic acid or lactic acid derivative) produced by the first bacterial isolate is butyric acid. Non-limiting examples of lactic acid derivatives include sodium isostearoyl lactate, sodium lactate, calcium lactate, aluminum lactate, ammonium lactate, potassium lactate, cetyl lactate, myristyl lactate, sodium stearoyl lactate, lactide, butyl lactate, and ethyl lactate.

[00141] In embodiments, a lactic acid-producing bacterial isolate (i.e., first bacterial isolate) included in a pharmaceutical composition described herein belongs to the *Bifidobacterium* genus. For example, the lactic acid-producing bacterial isolate can belong to *Bifidobacterium longum* or *Bifidobacterium adolescentis*. In embodiments, a second bacterial isolate (e.g., included with a first bacterial isolate in a microbial cocktail described herein or in a separate composition) is capable of using lactic acid produced by the *Bifidobacterium* to generate one or more SCFAs. In certain examples, the second bacterial isolate comprises a 16S rRNA sequence that is at least 95% identical to the 16S rRNA sequence of one of the bacterial isolates provided in Table 2.

[00142] In embodiments, a bacterial isolate incorporated into a pharmaceutical composition is capable of using lactic acid produced by the gut microbiota following administration of the cocktail to generate one or more SCFAs. In certain examples, the bacterial isolate comprises a 16S rRNA sequence that is at least 95% identical to the 16S rRNA sequence of one of the bacterial isolates provided in Table 2.

[00143] In embodiments, upon administration of a first and a second bacterial isolate to a subject (e.g., in the form of a microbial cocktail or in separate compositions), the first bacterial isolate produces and secretes lactic acid, and the second bacterial isolate utilizes the lactic acid to generate one or more SCFAs (e.g., butyrate). Thus, multiple bacterial isolates administered to a subject can interact synergistically within the gut of the subject to produce therapeutic effects (e.g., generation of one or more SCFAs) for treatment of an intestinal dysbiosis (e.g., IBD or ulcerative colitis) of the subject.

[00144] In embodiments, one or more bacterial isolates described herein can be administered with a probiotic that includes one or more bacterial strains that when administered to a subject produce and release a compound that can be used by the bacterial isolate to produce one or more SCFAs. For example, the probiotic can include one or more bacterial strains belonging to the genus *Bifidobacterium* (e.g., *Bifidobacterium adolescentis* or *Bifidobacterium longum*). In embodiments, the probiotic can be administered to a subject at the same time as a bacterial isolate, before administration of the bacterial isolate, or after administration of the bacterial isolate. In embodiments, a pharmaceutical composition comprises the probiotic and the bacterial isolate. In other embodiments, the probiotic and the bacterial isolate are in separate compositions. In some embodiments, the composition comprises a microbial cocktail of bacterial isolates.

[00145] In embodiments, one or more bacterial isolates described herein can be administered together with a prebiotic (e.g., comprising lactic acid and/or high fiber) that provides a nutrient that when utilized (e.g., metabolized) by the bacterial isolate facilitates a therapeutic effect in the subject (e.g., production of an SCFA). In embodiments, the prebiotic can be administered to a subject at the same time as a bacterial isolate, before administration of the bacterial isolate, or after administration of the bacterial isolate. In embodiments, a pharmaceutical composition comprises the prebiotic and the bacterial isolate. In other embodiments, the prebiotic and the bacterial isolate are in separate compositions. In some embodiments, the composition comprises a microbial cocktail of bacterial isolates. In some embodiments, the prebiotic is selected from the group consisting of an amino acid, lactic acid, ammonium nitrate, amylose, barley mulch, biotin, carbonate, cellulose, chitin, choline, fructooligosaccharides (FOSs), fructose, galactooligosaccharides (GOSs), glucose, glycerol, heteropolysaccharide, histidine, homopolysaccharide, hydroxyapatite, inulin, isomaltulose, lactose, lactulose, maltodextrins, maltose, mannooligosaccharides, nitrogen, oligodextrose, oligofructoses, oligofructose-enriched inulin, an oligosaccharide, pectin, phosphate salts, phosphorus, a polydextrose, a

polyol, potash, potassium, sodium nitrate, starch, sucrose, sulfur, sun fiber, tagatose, thiamine, trans-galactooligosaccharides, trehalose, a vitamin, a water-soluble carbohydrate, a xylooligosaccharide (XOS), and a combination thereof.

[00146] In embodiments, a bacterial isolate having the ability to produce one or more SCFAs (e.g., bacterial isolates listed in Table 2) refers to a bacterial isolate actually demonstrated (e.g., by a laboratory assay) to produce one or more SCFAs. Any method can be used to detect an SCFA produced by a bacterial strain, including chromatography (e.g., liquid or gas) and/or mass spectrometry. In other embodiments, a bacterial isolate having the ability to produce one or more SCFAs refers to a bacterial isolate predicted to produce butyrate. A prediction that a bacterial isolate can produce an SCFA can be based, for example, on the isolate's taxonomy (e.g., genus and/or species) and/or a sequence of a gene or polypeptide of the bacterial isolate known to mediate SCFA production. For example, an example of a gene known to mediate butyrate production is butyrate kinase. In an embodiment, a bacterial isolate is predicted to produce butyrate based on the identification of a butyrate kinase gene in the genome of the bacterial isolate. In an embodiment, the butyrate kinase gene when translated into a protein is predicted to generate a functional (i.e., enzymatically active) butyrate kinase enzyme.

[00147] Examples of bacterial isolates having the ability to produce SCFA are provided in Table 2. Each bacterial isolate is identified by Latin name, an Identification Number (ID number), and the Sequence Identifier (SEQ ID NO) for its 16S rRNA sequence. In aspects, a pharmaceutical composition (e.g., a microbial cocktail) comprises at least one bacterial isolate provided in Table 2, or at least one bacterial isolate comprising a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence of one or more of the bacterial isolates provided in Table 2. In embodiments, the pharmaceutical composition comprises at least two bacterial isolates, at least three bacterial isolates, at least four bacterial isolates, at least five bacterial isolates, at least six bacterial isolates, at least seven bacterial isolates, at least eight bacterial isolates, or at least nine bacterial isolates that each comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of at least one of the bacterial isolates provided in Table 2.

Table 2

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence
Faecalibacterium prausnitzii	PI00000329	1
Odoribacter splanchnicus	PI00000072	2
Anaerostipes hadrus	PI00000094	3
Faecalibacterium prausnitzii	IS00006632	7

Eubacterium rectale	IS00006864	8
Coprococcus comes	PI00000370	17
Roseburia faecis	PI00000404	19
Subdoligranulum variabile	IS00007359	22
Subdoligranulum variabile	IS00007357	23

[00148] In embodiments, a pharmaceutical composition (e.g., comprising a microbial cocktail) comprises one or more bacterial isolates having the ability to modulate production of a cytokine (e.g., IL-10, GM-CSF, IFN-gamma, TNF-alpha, IL-23, and IL-12) by a eukaryotic cell. Herein "eukaryotic cell" refers to both a cell (e.g. intestinal cell) positioned '*in situ*' within a body of a subject administered a composition described herein, as well as a cell grown or growing "*ex vivo*" outside of an organism, for example, in culture medium.

[00149] In one example, one or more bacterial isolates in a pharmaceutical composition described herein, once administered to a subject, can modulate production of a cytokine in a cell of the subject (referred to herein as a "host cell"). In embodiments, one or more bacterial isolates modulate production and/or secretion of a cytokine from a host cell of the subject, wherein the cytokine tends to exert anti-inflammatory effects on a tissue of the subject (e.g., intestinal tissue). Examples of such anti-inflammatory cytokines that can be produced and/or secreted from a host cell in response to the presence of a bacterial isolate administered in a composition described herein include IL-10, IL-13, IL-4, IL-5, TGF-β, and a combination thereof. In other embodiments, one or more bacterial isolates administered in a composition described herein inhibit production and/or secretion of a cytokine from a host cell of a subject, wherein the cytokine tends to exert pro-inflammatory effects on a tissue of the subject (e.g., intestinal tissue). Examples of such pro-inflammatory cytokines include IFNγ, IL-12p70, IL-1 (e.g., IL-1α, IL-1β), IL-6, IL-8, IL-12, IL-17, IL-18, IL-23, MCP1, MIP1α, MIP1β, TNFα, TNF-γ, and a combination thereof. By providing a composition containing one or more bacterial isolates that can induce a host cell to produce or secrete an anti-inflammatory cytokine and/or inhibit production and/or secretion by the host cell of a pro-inflammatory cytokine, the compositions (e.g., microbial cocktails) described herein can treat, alleviate, inhibit, and/or prevent inflammation associated with an intestinal dysbiosis of a subject, for example, Inflammatory Bowel Disease. Herein a bacterial isolate capable of modulating cytokine production and/or secretion by a host cell is referred to as an "immunomodulatory" bacterial isolate.

[00150] In embodiments, a bacterial isolate can directly and/or indirectly modulate production and/or release of a cytokine from a cell of a subject administered a pharmaceutical composition. In one embodiment an immunomodulatory bacterial isolate can act directly on a host cell of a subject via, for example, microbe-associated molecular patterns (MAMPS) secreted by the bacterial isolate or displayed on the surface of the bacterial isolate. Such MAMPS play a major role in host immune responses to particular bacterial species. MAMPS are sensed by pattern recognition receptors (PRRs) expressed on most host cell types that are in contact with bacteria. Examples of MAMPS of a bacterial isolate described herein include unmethylated 2′-deoxyribo(cytidine-phosphate-guanine) (CpG) dinucleotides, bacterial peptidogylcans, bacterial lipopolysaccharides (LPS, which interacts with co-receptors MD-2, CD14, and LPB to facilitate high affinity binding to TLR-4 and subsequent host cell activation), bacterial lipoproteins (LPs), lipoteichoic acid, flagellin, membrane vesicles, and exopolysaccharides. Examples of PRRs expressed by host cells in the gut and resident intestinal immune cells that can mediate modulation of cytokine production via interaction with MAMPS include Toll-like receptors (TLRs), nucleotide-binding oligomerization domains (Nods), NOD like receptors and C-type lectins. The interaction of intestinal cell PRRs and microbial ligands trigger signaling pathways associated with the innate and adaptive immune systems that are required to maintain immune tolerance and intestinal health.

[00151] In another embodiment, an immunomodulatory bacterial isolate can act indirectly on a cell (e.g., immune cell) of a subject administered a pharmaceutical composition by, for example, secreting a metabolite that modulates the activity of the host cell of the subject, for example, by inducing the cell to express a cytokine.

[00152] Examples of host cells whose production and/or release of cytokines can be modulated by a bacterial isolate described herein include an intestinal cell, an epithelial cell, an intestinal mucosal cell, an intestinal epithelial cell, an intestinal lamina propria cell, an endothelial cell, fibroblast, a stromal cell, a macrophage, a B lymphocyte, a T lymphocyte, a mast cell, and a peripheral blood mononuclear cell (PBMC).

[00153] In another embodiment, a bacterial isolate described herein can modulate cytokine production and/or release (e.g., increase cytokine production) by a eukaryotic cell (e.g., PBMC) situated or growing in culture medium, when the bacterial isolate is co-cultured with the eukaryotic cell.

[00154] In certain embodiments, a bacterial isolate described herein can induce production and/or release of a cytokine (e.g., IL-10) by a eukaryotic cell at a level of at least 500 pg/ml, at least 1000 pg/ml, at least 1500 pg/ml, at least 2000 pg/ml, at least 2500 pg/ml, or at least 3000 pg/ml. In an embodiment, the cytokine is measured in a functional assay (i.e., an assay conducted *ex vivo* and designed to measure the concentration or amount of a cytokine produced by a eukaryotic cell (e.g., PBMC) in contact with a bacterial isolate, microbial cocktail, a preparation of uncultured fecal bacteria, or an uncultured fecal microbiota during a period of time (e.g., 24 hours)). In an embodiment, the cytokine is produced in the intestine of a subject administered a composition described herein.

[00155] In certain embodiments, a bacterial isolate described herein can induce an anti-inflammatory cytokine profile. In an embodiment, a bacterial isolate exhibits an anti-inflammatory cytokine profile when it produces a level of IL-10 that is increased relative to that of a control strain. In an embodiment, a bacterial isolate exhibits an anti-inflammatory cytokine profile when it produces a level of IL-12 that is decreased relative to that of a control strain. In an embodiment, a bacterial isolate exhibits an anti-inflammatory cytokine profile when it produces a level of GM-CSF that is decreased relative to that of a control strain. In an embodiment, a bacterial isolate exhibits an anti-inflammatory cytokine profile when it produces a level of IFN-gamma that is decreased relative to that of a control strain. In an embodiment, a bacterial isolate exhibits an anti-inflammatory cytokine profile when it produces a level of TNF-alpha that is decreased relative to that of a control strain. In an embodiment, a bacterial isolate exhibits an anti-inflammatory cytokine profile when it produces a level of IL-23 that is decreased relative to that of a control strain. In an embodiment, a bacterial isolate exhibits an anti-inflammatory cytokine profile when it produces a level of IL-12 that is decreased relative to that of a control strain. In an embodiment, a bacterial isolate exhibits an anti-inflammatory cytokine profile when it produces a ration of IL-10:IL-12 that is increased relative to that of a control strain. In an embodiment, a bacterial isolate exhibits an anti-inflammatory cytokine profile when it produces a ration of IL-10:TNF-alpha that is increased relative to that of a control strain.

[00156] In embodiments, a pharmaceutical composition comprises one or more bacterial isolates which, when in contact with a eukaryotic cell (e.g., population of PBMCs) during a period of time (e.g., 24 hours), induce production of IL-10 at a concentration of at least 1000 pg/ml, at least 1500 pg/ml, at least 2000 pg/ml, at least 2500 pg/ml, at least 3000 pg/ml, at least 3500 pg/ml, at least 4000 pg/ml, at least 5000 pg/ml, at least 6000 pg/ml, at least 7000 pg/ml,

at least 8000 pg/ml, at least 9000 pg/ml, at least 10,000 pg/ml, or greater than 10,000 pg/ml. In an embodiment, the bacterial isolate is provided in Table 3, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 3.

[00157] In embodiments, a pharmaceutical composition comprises one or more bacterial isolates which, when in contact with a eukaryotic cell (e.g., population of PBMCs) during a period of time (e.g., 24 hours), limit production of GM-CSF to a concentration of no more than 5 pg/ml, 10 pg/ml, 15 pg/ml, 20 pg/ml, 25 pg/ml, 30 pg/ml, 35 pg/ml, 40 pg/ml, 45 pg/ml, 50 pg/ml, 55 pg/ml, 60 pg/ml, 65 pg/ml, 70 pg/ml, 75 pg/ml, 80 pg/ml, 85 pg/ml, 90 pg/ml, 95 pg/ml, 100 pg/ml, 105 pg/ml, 110 pg/ml, 115 pg/ml, 120 pg/ml, 125 pg/ml, 130 pg/ml, 135 pg/ml, 140 pg/ml, 145 pg/ml, 150 pg/ml, 155 pg/ml, 160 pg/ml, 165 pg/ml, 170 pg/ml, 175 pg/ml, 180 pg/ml, 185 pg/ml, 190 pg/ml, 195 pg/ml, or 200 pg/ml. In an embodiment, the bacterial isolate is provided in Table 3, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 3.

[00158] In embodiments, a pharmaceutical composition comprises one or more bacterial isolates which, when in contact with a eukaryotic cell (e.g., population of PBMCs) during a period of time (e.g., 24 hours), limit production of IL-12 (e.g., IL-12p70) to a concentration of no more than 5 pg/ml, 10 pg/ml, 15 pg/ml, 20 pg/ml, 25 pg/ml, 30 pg/ml, 35 pg/ml, 40 pg/ml, 45 pg/ml, 50 pg/ml, 55 pg/ml, 60 pg/ml, 65 pg/ml, 70 pg/ml, 75 pg/ml, 80 pg/ml, 85 pg/ml, 90 pg/ml, 95 pg/ml, 100 pg/ml, 105 pg/ml, 110 pg/ml, 115 pg/ml, 120 pg/ml, 125 pg/ml, 130 pg/ml, 135 pg/ml, 140 pg/ml, 145 pg/ml, 150 pg/ml, 155 pg/ml, 160 pg/ml, 165 pg/ml, 170 pg/ml, 175 pg/ml, 180 pg/ml, 185 pg/ml, 190 pg/ml, 195 pg/ml, or 200 pg/ml. In an embodiment, the bacterial isolate is provided in Table 3, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 3.

[00159] In embodiments, a pharmaceutical composition comprises one or more bacterial isolates which, when in contact with a eukaryotic cell (e.g., population of PBMCs) during a period of time (e.g., 24 hours), limit production of IFN-gamma to a concentration of no more than 5 pg/ml, 10 pg/ml, 15 pg/ml, 20 pg/ml, 25 pg/ml, 30 pg/ml, 35 pg/ml, 40 pg/ml, 45 pg/ml, 50 pg/ml, 55 pg/ml, 60 pg/ml, 65 pg/ml, 70 pg/ml, 75 pg/ml, 80 pg/ml, 85 pg/ml, 90 pg/ml, 95 pg/ml, 100 pg/ml, 105 pg/ml, 110 pg/ml, 115 pg/ml, 120 pg/ml, 125 pg/ml, 130 pg/ml, 135 pg/ml, 140 pg/ml, 145 pg/ml, 150 pg/ml, 155 pg/ml, 160 pg/ml, 165 pg/ml, 170 pg/ml, 175

pg/ml, 180 pg/ml, 185 pg/ml, 190 pg/ml, 195 pg/ml, or 200 pg/ml. In an embodiment, the bacterial isolate is provided in Table 3, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 3.

[00160] In embodiments, a pharmaceutical composition comprises one or more bacterial isolates which, when in contact with a eukaryotic cell (e.g., population of PBMCs) during a period of time (e.g., 24 hours), limit production of TNF-alpha to a concentration of no more than 20 pg/ml, 30 pg/ml, 40 pg/ml, 50 pg/ml, 75 pg/ml, 100 pg/ml, 150 pg/ml, 200 pg/ml, 250 pg/ml, 300 pg/ml, 350 pg/ml, 400 pg/ml, 450 pg/ml, 500 pg/ml, 550 pg/ml, 600 pg/ml, 650 pg/ml, 700 pg/ml, 750 pg/ml, 800 pg/ml, 850 pg/ml, 900 pg/ml, 950 pg/ml, 1000 pg/ml, 1100 pg/ml, 1200 pg/ml, 1300 pg/ml, 1400 pg/ml, 1500 pg/ml, 1600 pg/ml, 1700 pg/ml, 1800 pg/ml, 1900 pg/ml, 2000 pg/ml, 2100 pg/ml, 2200 pg/ml, 2300 pg/ml, 2400 pg/ml, or 2500 pg/ml. In an embodiment, the bacterial isolate is provided in Table 3, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 3.

[00161] In embodiments, a pharmaceutical composition comprises one or more bacterial isolates which, when in contact with a eukaryotic cell (e.g., population of PBMCs) during a period of time (e.g., 24 hours), limit production of IL-23 to a concentration of no more than 5 pg/ml, 10 pg/ml, 15 pg/ml, 20 pg/ml, 25 pg/ml, 30 pg/ml, 35 pg/ml, 40 pg/ml, 45 pg/ml, 50 pg/ml, 55 pg/ml, 60 pg/ml, 65 pg/ml, 70 pg/ml, 75 pg/ml, 80 pg/ml, 85 pg/ml, 90 pg/ml, 95 pg/ml, 100 pg/ml, 105 pg/ml, 110 pg/ml, 115 pg/ml, 120 pg/ml, 125 pg/ml, 130 pg/ml, 135 pg/ml, 140 pg/ml, 145 pg/ml, 150 pg/ml, 155 pg/ml, 160 pg/ml, 165 pg/ml, 170 pg/ml, 175 pg/ml, 180 pg/ml, 185 pg/ml, 190 pg/ml, 195 pg/ml, 200 pg/ml, 250 pg/ml, or 300 pg/ml. In an embodiment, the bacterial isolate is provided in Table 3, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 3.

[00162] In embodiments, a pharmaceutical composition comprises one or more bacterial isolates which, when in contact with a eukaryotic cell (e.g., population of PBMCs) during a period of time (e.g., 24 hours), induce a ratio of IL-10:IL-12 of at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50, at least 55, at least 60, at least 65, at least 70, at least 75, at least 80, at least 85, at least 90, at least 95, at least 100, at least 110, at least 120, at least 130, at least 140, at least 150, at least 160, at least 170, at least 180, at least 190, at least 200, at least 210, at least 220, at least 230, at least 240, at least 250, at least 260, at least 270,

at least 280, at least 290, at least 300, at least 325, at least 350, at least 375, at least 400, at least 425, at least 450, at least 475, at least 500, at least 550, at least 600, at least 650, at least 700, at least 750, at least 800, at least 850, at least 900, at least 950, at least 1000, at least 1100, at least 1200, at least 1300, at least 1400, at least 1500, at least 1600, at least 1700, at least 1800, at least 1900, at least 2000, at least 2200, at least 2400, at least 2600, at least 2800, at least 3000, at least 3200, at least 3400, at least 3600, at least 3800, at least 4000, or greater than 4000. In an embodiment, the bacterial isolate is provided in Table 3, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 3.

[00163] In embodiments, a pharmaceutical composition comprises one or more bacterial isolates which, when in contact with a eukaryotic cell (e.g., population of PBMCs) during a period of time (e.g., 24 hours), induce a ratio of IL-10:TNF-alpha of at least 0.5, at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, at least 26, at least 27, at least 28, at least 29, at least 30, at least 31, at least 32, at least 33, at least 34, at least 35, at least 36, at least 37, at least 38, at least 39, at least 40, at least 45, at least 50, at least 55, at least 60, at least 65, at least 70, at least 75, at least 80, at least 85, at least 90, at least 95, or at least 100. In an embodiment, the bacterial isolate is provided in Table 3, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 3.

[00164] Examples of bacterial isolates having the ability to modulate cytokine production by a host cell are provided in Table 3. Each isolate is identified by Latin name, an Identification Number (ID number), and the Sequence Identifier (SEQ ID NO) for its 16S rRNA sequence. In aspects, a pharmaceutical composition (e.g., comprising a microbial cocktail) comprises at least one bacterial isolate provided in Table 3, or at least one bacterial isolate that comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence of one or more of the bacterial isolates provided in Table 3. In embodiments, the pharmaceutical composition comprises at least two bacterial isolates, at least three bacterial isolates, at least four bacterial isolates, at least five bacterial isolates, at least six bacterial isolates, at least seven bacterial isolates, at least eight bacterial isolates, at least nine bacterial isolates, at least ten bacterial isolates, at least eleven bacterial isolates, at least twelve bacterial isolates, at least thirteen bacterial isolates, or at least fourteen bacterial isolates that each comprise a 16S rRNA sequence

at least 95% identical to a 16S rRNA sequence of at least one of the bacterial isolates provided in Table 3.

Table 3

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence
Faecalibacterium prausnitzii	PI00000329	1
Odoribacter splanchnicus	PI00000072	2
Anaerostipes hadrus	PI00000094	3
Faecalibacterium prausnitzii	IS00006632	7
Clostridium aldenense	PI00000097	10
Bacteroides uniformis	PI00000137	11
Bacteroides vulgatus	PI00000138	12
Bacteroides stercoris	PI00000146	13
Bacteroides uniformis	PI00000352	16
Coprococcus comes	PI00000370	17
Alistipes shahii	PI00000395	18
Akkermansia muciniphila	IS00007180	20
Subdoligranulum variabile	IS00007359	22
Subdoligranulum variabile	IS00007357	23

[00165] In embodiments, a pharmaceutical composition comprises at least one bacterial isolate corresponding to a bacterial strain having a greater relative abundance in a healthy human subject relative to a patient with an intestinal dysbiosis (e.g., an IBD such as UC), or a greater relative abundance in a human subject in remission from an intestinal dysbiosis relative to a patient having the intestinal dysbiosis. Herein the term "greater relative abundance" refers to a higher number of viable cells of the bacterial strain (i.e., corresponding to the bacterial isolate) in a healthy human subject (compared to a patient with an intestinal dysbiosis) or in a human subject in remission from an intestinal dysbiosis (compared to a patient having the dysbiosis). In some embodiments, the term "higher number of viable cells" refers to the absolute number of viable cells of the bacterial strain in an intestinal microbiota or portion thereof (e.g., in a stool sample), while in other embodiments, the term refers to the proportional number of viable cells of the bacterial strain relative to the approximate entire number of viable cells in the intestinal microbiota or portion thereof (e.g., in a stool sample). In certain examples, a bacterial strain corresponding to a bacterial isolate included in a pharmaceutical composition can have a greater relative abundance across multiple tested human subjects (e.g., healthy individuals, or individuals in remission from an intestinal dysbiosis), for example, at least 5 human subjects, at least 10 human subjects, at least 20 human subjects, at least 30 human

subjects, at least 40 human subjects, at least 50 human subjects, at least 75 human subjects, at least 100 human subjects, at least 200 human subjects, at least 300 human subjects, at least 400 human subjects, at least 500 human subjects, at least 750 human subjects, at least 1000 human subjects, or greater than 1000 human subjects. In addition or alternatively, a bacterial strain corresponding to a bacterial isolate can have a greater relative abundance in a proportion of tested human subjects (e.g., healthy individuals, or individuals in remission from an intestinal dysbiosis), for example, at least 50% of tested individuals, at least 55% of tested individuals, at least 60% of tested individuals, at least 65% of tested individuals, at least 70% of tested individuals, at least 75% of tested individuals, at least 80% of tested individuals, at least 80% of tested individuals, at least 85% of tested individuals, at least 90% of tested individuals, at least 95% of tested individuals, or 100% of tested individuals. Herein a bacterial strain "corresponding to a bacterial isolate" refers to a bacterial strain in a gut microbiota of a subject, wherein the bacterial strain has a 16S rRNA sequence that typically shares at least 97% identity (e.g., at least 97.5% identity, at least 98% identity, at least 98.5% identity, at least 99% identity, at least 99.5% identity, or greater than 99.5% identity) to a 16S rRNA sequence of the bacterial isolate. Likewise, a bacterial isolate "corresponding to a bacterial strain" refers to a bacterial isolate that typically shares at least 97% identity (e.g., at least 97.5% identity, at least 98% identity, at least 98.5% identity, at least 99% identity, at least 99.5% identity, or greater than 99.5% identity) to a 16S rRNA sequence of a bacterial strain in a gut microbiota of a subject.

[00166] In embodiments, a bacterial isolate can correspond to a bacterial strain having a greater relative abundance in a human subject in remission from an intestinal dysbiosis relative to a patient having the intestinal dysbiosis. The increased abundance of the bacterial strain in the subject in remission identifies the bacterial isolate corresponding to the bacterial strain as potentially advantageous for the treatment of a disorder related to an intestinal dysbiosis, such as UC. The remission of the intestinal dysbiosis in the human subject can be related to or caused by an intervention administered to the subject while the dysbiosis is active. For example, the remission can arise following treatment of the subject with a microbial therapeutic. Examples of a microbial therapeutic include compositions comprising a preparation of uncultured fecal bacteria, an uncultured fecal microbiota, a cultured fecal microbiota, and/or a bacterial isolate. In embodiments, the microbial therapeutic which induces remission from an intestinal dysbiosis is a substantially complete uncultured fecal microbiota. For example, a subject can be administered a fecal microbiota transplant (FMT) to induce remission of the intestinal

dysbiosis. In certain embodiments, the intestinal dysbiosis of the subject is due to ulcerative colitis (UC).

[00167] In an embodiment, this mechanism agnostic approach to identifying a bacterial isolate reduces the dysbiosis associated with Ulcerative Colitis (UC). In an embodiment, 16S ribosomal DNA (rDNA) and shotgun metagenomic sequences can be incorporated from for example interventional (FMT), cross-sectional and time series datasets to develop predictive features associated with either a healthy status or clinical response to FMT. These features can be used to rank and select bacterial phylogenetic clades for (i) enrichment in healthy subjects over patients diagnosed with UC; and/or (ii) association/correlation with clinical remission or response of UC symptoms in UC patients following FMT treatment. Clades can be ranked based on a "cross-sectional combined p-value" which compares the presence and abundances of bacterial strains in fecal material between healthy subjects and patients with UC. The lower the p-value, the more likely the organisms in the clade are having an effect on the treatment, inhibition or prevention of UC based on: (i) depletion of the strain in UC patients and/or (ii) high abundance of the strain in healthy subjects. Isolated bacterial strains can then be selected from donor stool samples by 16S rDNA similarity to the ranked phylogenetic clades or by ranking their 16S rDNA directly according to the aforementioned criteria.

[00168] In an embodiment, a value of a cross-sectional combined p-value is less than 0.1, less than 0.01, less than $1x10^{-3}$, less than $1x10^{-4}$, less than $1x10^{-5}$, less than $1x10^{-6}$, less than $1x10^{-7}$, less than $1x10^{-8}$, less than $1x10^{-9}$, less than $1x10^{-10}$, less than $1x10^{-11}$, less than $1x10^{-12}$, less than $1x10^{-13}$, less than $1x10^{-14}$, less than $1x10^{-15}$, less than $1x10^{-16}$, less than $1x10^{-17}$, less than $1x10^{-18}$, less than $1x10^{-19}$, less than $1x10^{-20}$, less than $1x10^{-21}$, less than $1x10^{-22}$, less than $1x10^{-23}$, or less than $1x10^{-24}$.

[00169] Table 4 lists examples of bacterial isolates which can be included in a pharmaceutical composition (e.g., comprising a microbial cocktail) that have corresponding bacterial strains present and/or more highly abundant in a healthy subject relative to a patient with UC. Each isolate is identified by Latin name, an Identification Number (ID number), and the Sequence Identifier (SEQ ID NO) for its 16S rRNA sequence. In aspects, a pharmaceutical composition comprises at least one bacterial isolate provided in Table 4, or at least one bacterial isolate that comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence of one or more of the bacterial isolates provided in Table 4. In embodiments, the pharmaceutical composition comprises at least two bacterial isolates, at least three bacterial isolates, at least four bacterial isolates, at least five bacterial isolates, at least six bacterial isolates, at least seven

bacterial isolates, at least eight bacterial isolates, at least nine bacterial isolates, at least ten bacterial isolates, at least eleven bacterial isolates, at least twelve bacterial isolates, at least thirteen bacterial isolates, at least fourteen bacterial isolates, at least fifteen bacterial isolates, at least sixteen bacterial isolates, at least seventeen bacterial isolates, at least eighteen bacterial isolates, at least nineteen bacterial isolates, at least twenty bacterial isolates, at least twenty one bacterial isolates, at least twenty two bacterial isolates, or at least twenty three bacterial isolates that each comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of at least one of the bacterial isolates provided in Table 4.

Table 4

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence
Faecalibacterium prausnitzii	PI00000329	1
Odoribacter splanchnicus	PI00000072	2
Anaerostipes hadrus	PI00000094	3
Alistipes onderdonkii	IS00004389	4
Parabacteroides merdae	IS00006167	5
Dorea longicatena	IS00006618	6
Faecalibacterium prausnitzii	IS00006632	7
Eubacterium rectale	IS00006864	8
Blautia obeum	PI00000053	9
Bacteroides uniformis	PI00000137	11
Bacteroides vulgatus	PI00000138	12
Bacteroides cellulosilyticus	PI00000316	14
Alistipes finegoldii	PI00000340	15
Bacteroides uniformis	PI00000352	16
Alistipes shahii	PI00000395	18
Akkermansia muciniphila	IS00007180	20
Phascolarctobacterium faecium	PI00000289	21
Subdoligranulum variabile	IS00007359	22
Subdoligranulum variabile	IS00007357	23
Blautia sp.	IS00002788	34
Alistipes putredinis	IS00008139	35
Alistipes putredinis	IS00008142	36
Alistipes putredinis	IS00008177	37

[00170] In an embodiment, a bacterial isolate is identified as suitable for inclusion in a pharmaceutical composition described herein (e.g., comprising a microbial cocktail) based on its correspondence to a bacterial strain that is abundant in healthy versus UC patients in the data set reported in Morgan *et al.*, *Genome Biology* 13 (2012), the entire contents of which are hereby incorporated by reference.

[00171] In an embodiment, a bacterial isolate is identified as suitable for inclusion in a pharmaceutical composition described herein (e.g., comprising a microbial cocktail) based on its correspondence to a bacterial strain that is abundant in healthy versus UC patients in the data set reported in Papa *et al.*, *PLOS ONE* 7, no. 6 (June 29, 2012), the entire contents of which are hereby incorporated by reference.

[00172] In embodiments, a microbial cocktail described herein can contain two or more bacterial isolates which are related bacterial isolates. Herein "related bacterial isolates" have 16S rRNA sequences which typically share at least 95% sequence identity. In certain embodiments, related bacterial isolates have 16S sequences which share at least 97% sequence identity, and thus the bacterial isolates are members of the same species. In embodiments, a microbial cocktail contains two or more related bacterial isolates. In other embodiments, a microbial cocktail does not contain two related bacterial isolates. In embodiments, a first version of a microbial cocktail contains a first bacterial isolate, and a second version of a microbial cocktail contains a second bacterial isolate that is a related bacterial isolate to the first bacterial isolate.

[00173] Examples of related bacterial isolates to those listed in Table 4 that can be included in a microbial cocktail described herein are shown in Table 5. Like the bacterial isolates in Table 4, those in Table 5 correspond to bacterial strains that have a greater abundance in a healthy human subject relative to a patient with UC. Table 5 lists the bacterial isolates' identification numbers, the ID number of the corresponding bacterial isolate in Table 4, the percent identity of the related bacterial strain's 16S sequences to the sequence of the corresponding bacterial isolate in Table 4, and the Sequence Identifier (SEQ ID NO) for its 16S rRNA sequence.

Table 5

ID Number	Related to ID Number of Table 4	% identity of 16S rRNA Sequence to Related ID Number of Table 4	SEQ ID NO for 16S rRNA Sequence
PI00000070	PI00000072	98.6	24
PI00000092	PI00000094	98.1	25
PI00000339	IS00004389	96.6	26
PI00000327	IS00006167	99.4	27
PI00000056	PI00000053	96.2	28
PI00000152	PI00000138	98.7	29
PI00000043	PI00000316	99.2	30
IS00003009	PI00000340	97.6	31

PI00000052	PI00000352	96.6	32
PI00000330	PI00000395	95.3	33

[00174] In embodiments, a pharmaceutical composition (e.g., comprising a microbial cocktail) comprises one or more bacterial isolates having the ability to release (e.g., by secretion) one or more aryl hydrocarbons and/or tryptophan derivatives. Microbial metabolites are produced by the gut microbiota via metabolism of tryptophan from host dietary sources. Such metabolites, which are typically compounds containing an aryl hydrocarbon, can signal through the aryl hydrocarbon receptor (AhR) of a eukaryotic cell (e.g., a cell of a subject administered a pharmaceutical composition (e.g., comprising a microbial cocktail) described herein). AhR is a cytosolic ligand-activated transcription factor that regulates immunity and inflammation, intestinal mucosal barrier health and maintenance of intestinal homeostasis. Once bound by an appropriate cytosolic ligand, AhR translocates to the nucleus and binds to specific DNA sequence elements to regulate transcription. Without wishing to be bound by theory, activation of AhR is associated with a reduction of intestinal inflammation in subjects with inflammatory bowel disease, release of anti-inflammatory cytokines (e.g., IL-10), and induction of regulatory T cells. Pharmaceutical compositions containing one or more bacterial isolates that produce ligands capable of activating the AhR can thus be effective to treat, alleviate, inhibit or prevent dysbiosis of the gut caused by disorders such as IBD (e.g., ulcerative colitis).

[00175] Examples of aryl hydrocarbons (e.g., microbial produced aryl hydrocarbons) capable of activating the AhR are indole and indole derivatives, indole-3-acetic acid (IAA) , indole-3-aldehyde (IAId), indole-3-lactic acid, indole-3-carbinol (I3C), indole-3-acetonitrile (I3ACN), 3,3'-diindolylmethane (DIM), 2-(indol-3-ylmethyl)-3,3'-diindolylmethane (Ltr-1), indolo[3,2-*b*]carbazole (ICZ), 2-(1'H-indole-3'carbonyl)-thiazole-4-carboxylic acid methyl ester (ITE), 3-methyl-indole (skatole), tryptamine, kynurenine, kynurenate, indigo, indirubin, indoxyl-3-sulfate (I3S), xanthurenic acid, cinnabarinic acid, 3-indolepropionic acid (indole-3-propionate), and a combination thereof.

[00176] In an embodiment, an amount, concentration or level of one or more aryl hydrocarbons is measured in a functional assay (i.e., an assay conducted *ex vivo* or *in vivo* and designed to measure the concentration or amount of an aryl hydrocarbon produced by a bacterial isolate, microbial cocktail, a preparation of uncultured fecal bacteria, or an uncultured fecal microbiota during a period of time (e.g., at least 24 hours)). In an embodiment, the aryl hydrocarbon is produced in the intestine of a subject administered a composition described

herein. In an example, the functional assay can comprise incubation of one or more bacterial isolates with tryptophan (or tryptophan derivative) for any period of time sufficient to allow conversion of the tryptophan to an aryl hydrocarbon, for example at least 1 hour, at least 2 hours, at least 3 hours, at least 4 hours, at least 5 hours, at least 6 hours, at least 7 hours, at least 8 hours, at least 9 hours, at least 10 hours, at least 11 hours, at least 12 hours, at least 13 hours, at least 14 hours, at least 15 hours, at least 16 hours, at least 17 hours, at least 18 hours, at least 19 hours, at least 20 hours, at least 21 hours, at least 22 hours, at least 23 hours, at least 24 hours, at least 25 hours, at least 26 hours, at least 27 hours, at least 28 hours, at least 29 hours, at least 30 hours, at least 31 hours, at least 32 hours, at least 33 hours, at least 34 hours, at least 35 hours, at least 36 hours, at least 37 hours, at least 38 hours, at least 39 hours, at least 40 hours, at least 41 hours, at least 42 hours, at least 43 hours, at least 44 hours, at least 45 hours, at least 46 hours, at least 47 hours, at least 48 hours, or greater than 48 hours.

[00177] In embodiments, a functional assay can measure an absolute amount or concentration of one or more aryl hydrocarbons capable of activating an AhR of a host cell. In other embodiments, the functional assay can measure a relative amount of one or more aryl hydrocarbons. In an example, an amount of production of an aryl hydrocarbon by a bacterial isolate can be relative to blank media not containing a bacterial isolate. Alternatively, the functional assay can measure the amount or concentration of an aryl hydrocarbon produced by a bacterial isolate relative to that produced by one or more control bacterial strains. In an embodiment, the control bacterial strain is known to produce an aryl hydrocarbon, for example the aryl hydrocarbon being measured in the assay. Exemplary control strains that can be used in a functional assay to measure one or more aryl hydrocarbons are bacterial strains that are a member of the genus *Peptostreptococcus* (e.g., *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii*) In an embodiment, the functional assay comprises comparison of a level of an aryl hydrocarbon produced by a bacterial isolate of interest over a period of time (e.g., 48 hours) to a level of the same aryl hydrocarbon produced by one or more of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii* over the same period of time. In certain embodiments, a pharmaceutical composition comprises a bacterial isolate capable of producing an aryl hydrocarbon at a level of at least 1.1x, at least 1.2x, at least 1.3x, at least 1.4x, at least 1.5x, at least 1.6x, at least 1.7x, at least 1.8x, at least 1.9x, at least 2x, at least 2.1x, at least 2.2x, at least 2.3x, at least 2.4x, at least 2.5x, at least 2.6x, at least 2.7x, at least 2.8x, at least 2.9x, at least 3x, at least 4x, at least 5x, at least 6x, at least 7x, at least 8x, at least 9x, at least 10x, at least 11x, at least 12x, at least 13x, at least 14x, at least 15x, at least

16x, at least 17x, at least 18x, at least 19x, at least 20x, at least 21x, at least 22x, at least 23x, at least 24x, at least 25x, at least 26x, at least 27x, at least 28x, at least 29x, at least 30x, at least 35x, at least 40x, at least 45x, at least 50x, at least 60x, at least 70x, at least 80x, at least 90x, at least 100x, at least 110x, at least 120x, at least 130x, at least 140x, at least 150x, at least 160x, at least 170x, at least 180x, at least 190x, at least 200x, at least 210x, at least 220x, at least 230x, at least 240x, at least 250x, or greater than 250x relative to a control bacterial strain (e.g. a *Peptostreptococcus* strain such as *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii*)), or compared to blank media alone.

[00178] In embodiments, a pharmaceutical composition comprises a bacterial isolate that produces kynurenate (i.e., kynurenic acid), as measured by a functional assay. For example, a bacterial isolate can produce kynurenate at a concentration of at least 0.01 μM kynurenate, at least 0.02 μM kynurenate, at least 0.03 μM kynurenate, at least 0.04 μM kynurenate, at least 0.05 μM kynurenate, at least 0.06 μM kynurenate, at least 0.07 μM kynurenate, at least 0.08 μM kynurenate, at least 0.09 μM kynurenate, at least 0.1 μM kynurenate, at least 0.2 μM kynurenate, at least 0.3 μM kynurenate, at least 0.4 μM kynurenate, at least 0.5 μM kynurenate, at least 0.6 μM kynurenate, at least 0.7 μM kynurenate, at least 0.8 μM kynurenate, at least 0.9 μM kynurenate, at least 1 μM kynurenate, at least 1.5 μM kynurenate, at least 2 μM kynurenate, at least 2.5 μM kynurenate, at least 3 μM kynurenate, at least 3.5 μM kynurenate, at least 4 μM kynurenate, at least 4.5 μM kynurenate, at least 5 μM kynurenate, or greater than 5 μM kynurenate. In embodiments, a bacterial isolate does not produce kynurenate. In embodiments, the bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the bacterial isolate comprises *Odoribacter splanchnicus* In an embodiment, the bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 2.

[00179] In other embodiments, a bacterial isolate can produce kynurenate at a higher level than blank media or a control bacterial strain (e.g., positive control bacterial strain capable of producing kynurenate, such as a strain that is a member of the *Peptostreptococcus* genus), as measured in a functional assay. For example, a bacterial isolate can produce kynurenate at a higher level than at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii* over a duration of time. In embodiments, a pharmaceutical composition comprises a bacterial isolate that can produce kynurenate at a level that is at least 1.1x, at least 1.2x, at least 1.3x, at least 1.4x, at least 1.5x, at least 1.6x, at least 1.7x, at least

1.8x, at least 1.9x, at least 2x, at least 2.1x, at least 2.2x, at least 2.3x, at least 2.4x, at least 2.5x, at least 2.6x, at least 2.7x, at least 2.8x, at least 2.9x, at least 3x, at least 4x, at least 5x, at least 6x, at least 7x, at least 8x, at least 9x, at least 10x, at least 11x, at least 12x, at least 13x, at least 14x, at least 15x, at least 16x, at least 17x, at least 18x, at least 19x, at least 20x, at least 21x, at least 22x, at least 23x, at least 24x, at least 25x, at least 26x, at least 27x, at least 28x, at least 29x, at least 30x, at least 35x, at least 40x, at least 45x, at least 50x, at least 60x, at least 70x, at least 80x, at least 90x, at least 100x, at least 110x, at least 120x, at least 130x, at least 140x, at least 150x, at least 160x, at least 170x, at least 180x, at least 190x, at least 200x, at least 210x, at least 220x, at least 230x, at least 240x, at least 250x, or greater than 250x relative to at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii*, or relative to blank media alone. In embodiments, the bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the bacterial isolate comprises *Odoribacter splanchnicus* In an embodiment, the bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 2.

[00180] In embodiments, a pharmaceutical composition comprises one or more bacterial isolates that produce indole-3-acetic acid (IAA) capable of activating an AhR in a cell of a subject administered the pharmaceutical composition. For example, a bacterial isolate can produce IAA at a concentration of at least 0.1 μM IAA, at least 0.2 μM IAA, at least 0.3 μM IAA, at least 0.4 μM IAA, at least 0.5 μM IAA, at least 0.6 μM IAA, at least 0.7 μM IAA, at least 0.8 μM IAA, at least 0.9 μM IAA, at least 1 μM IAA, at least 1.5 μM IAA, at least 2 μM IAA, at least 2.5 μM IAA, at least 3 μM IAA, at least 4 μM IAA, at least 5 μM IAA, at least 6 μM IAA, at least 7 μM IAA, at least 8 μM IAA, at least 9 μM IAA, at least 10 μM IAA, at least 20 μM IAA, at least 30 μM IAA, at least 40 μM IAA, at least 50 μM IAA, at least 60 μM IAA, at least 70 μM IAA, at least 80 μM IAA, at least 90 μM IAA, at least 100 μM IAA, at least 110 μM IAA, at least 120 μM IAA, at least 130 μM IAA, at least 140 μM IAA, at least 150 μM IAA, at least 160 μM IAA, at least 170 μM IAA, at least 180 μM IAA, at least 190 μM IAA, at least 200 μM IAA or greater than 200 μM IAA. In embodiments, a bacterial isolate does not produce IAA. In embodiments, the bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the bacterial isolate comprises *Odoribacter splanchnicus* In an embodiment, the bacterial isolate comprises

a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 2. In an embodiment, the bacterial isolate comprises *Clostridium aldenense*. In an embodiment, the bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 10.

[00181] In other embodiments, a bacterial isolate can produce indole-3-acetic acid (IAA) at a higher level than blank media or a control bacterial strain (e.g., positive control bacterial strain capable of producing IAA, such as a strain that is a member of the *Peptostreptococcus* genus), as measured in a functional assay. For example, a bacterial isolate can produce IAA at a higher level than at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii* over a duration of time. In embodiments, a pharmaceutical composition comprises a bacterial isolate that can produce IAA at a level that is at least 1.1x, at least 1.2x, at least 1.3x, at least 1.4x, at least 1.5x, at least 1.6x, at least 1.7x, at least 1.8x, at least 1.9x, at least 2x, at least 2.1x, at least 2.2x, at least 2.3x, at least 2.4x, at least 2.5x, at least 2.6x, at least 2.7x, at least 2.8x, at least 2.9x, at least 3x, at least 4x, at least 5x, at least 6x, at least 7x, at least 8x, at least 9x, at least 10x, at least 11x, at least 12x, at least 13x, at least 14x, at least 15x, at least 16x, at least 17x, at least 18x, at least 19x, at least 20x, at least 21x, at least 22x, at least 23x, at least 24x, at least 25x, at least 26x, at least 27x, at least 28x, at least 29x, at least 30x, at least 35x, at least 40x, at least 45x, at least 50x, at least 60x, at least 70x, at least 80x, at least 90x, at least 100x, at least 110x, at least 120x, at least 130x, at least 140x, at least 150x, at least 160x, at least 170x, at least 180x, at least 190x, at least 200x, at least 210x, at least 220x, at least 230x, at least 240x, at least 250x, or greater than 250x relative to at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii*, or relative to blank media alone. In embodiments, the bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the bacterial isolate comprises *Odoribacter splanchnicus* In an embodiment, the bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 2. In an embodiment, the bacterial isolate comprises *Clostridium aldenense*. In an embodiment, the bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 10.

[00182] In embodiments, a pharmaceutical composition comprises one or more bacterial isolates that produce indole-3-lactic acid capable of activating an AhR of a subject administered the pharmaceutical composition. For example, a bacterial isolate can produce indole-3-lactic

acid at a concentration of at least 0.1 μM indole-3-lactic acid, at least 0.2 μM indole-3-lactic acid, at least 0.3 μM indole-3-lactic acid, at least 0.4 μM indole-3-lactic acid, at least 0.5 μM indole-3-lactic acid, at least 0.6 μM indole-3-lactic acid, at least 0.7 μM indole-3-lactic acid, at least 0.8 μM indole-3-lactic acid, at least 0.9 μM indole-3-lactic acid, at least 1 μM indole-3-lactic acid, at least 1.5 μM indole-3-lactic acid, at least 2 μM indole-3-lactic acid, at least 2.5 μM indole-3-lactic acid, at least 3 μM indole-3-lactic acid, at least 3.5 μM indole-3-lactic acid, at least 4 μM indole-3-lactic acid, at least 4.5 μM indole-3-lactic acid, at least 5 μM indole-3-lactic acid, or greater than 5 μM indole-3-lactic acid. In embodiments, a bacterial isolate does not produce indole-3-lactic acid. In embodiments, the bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6.

[00183] In other embodiments, a bacterial isolate can produce indole-3-lactic acid at a higher level than blank media or a control bacterial strain (e.g., positive control bacterial strain capable of producing indole-3-lactic acid, such as a strain that is a member of the *Peptostreptococcus* genus), as measured in a functional assay. For example, a bacterial isolate can produce indole-3-lactic acid at a higher level than at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii* over a duration of time. In embodiments, a pharmaceutical composition comprises a bacterial isolate that can produce indole-3-lactic acid at a level that is at least 1.1x, at least 1.2x, at least 1.3x, at least 1.4x, at least 1.5x, at least 1.6x, at least 1.7x, at least 1.8x, at least 1.9x, at least 2x, at least 2.1x, at least 2.2x, at least 2.3x, at least 2.4x, at least 2.5x, at least 2.6x, at least 2.7x, at least 2.8x, at least 2.9x, at least 3x, at least 4x, at least 5x, at least 6x, at least 7x, at least 8x, at least 9x, at least 10x, at least 11x, at least 12x, at least 13x, at least 14x, at least 15x, at least 16x, at least 17x, at least 18x, at least 19x, at least 20x, at least 21x, at least 22x, at least 23x, at least 24x, at least 25x, at least 26x, at least 27x, at least 28x, at least 29x, at least 30x, at least 35x, at least 40x, at least 45x, at least 50x, at least 60x, at least 70x, at least 80x, at least 90x, at least 100x, at least 110x, at least 120x, at least 130x, at least 140x, at least 150x, at least 160x, at least 170x, at least 180x, at least 190x, at least 200x, at least 210x, at least 220x, at least 230x, at least 240x, at least 250x, or greater than 250x relative to at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii*, or relative to blank media alone. In embodiments, the bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6.

[00184] In embodiments, a pharmaceutical composition comprises one or more bacterial isolates that produce indole capable of activating an AhR of a subject administered the pharmaceutical composition. For example, a bacterial isolate can produce indole at a concentration of at least 0.1 μM indole, at least 0.2 μM indole, at least 0.3 μM indole, at least 0.4 μM indole, at least 0.5 μM indole, at least 0.6 μM indole, at least 0.7 μM indole, at least 0.8 μM indole, at least 0.9 μM indole, at least 1 μM indole, at least 1.5 μM indole, at least 2 μM indole, at least 2.5 μM indole, at least 3 μM indole, at least 3.5 μM indole, at least 4 μM indole, at least 4.5 μM indole, at least 5 μM indole, or greater than 5 μM indole. In embodiments, a bacterial isolate does not produce indole. In embodiments, the bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the bacterial isolate comprises *Clostridium* sp. (e.g., *Clostridium aldenense*) In an embodiment, the bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 10.

[00185] In other embodiments, a bacterial isolate can produce indole at a higher level than blank media or a control bacterial strain (e.g., positive control bacterial strain capable of producing indole, such as a strain that is a member of the *Peptostreptococcus* genus), as measured in a functional assay. For example, a bacterial isolate can produce indole at a higher level than at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii* over a duration of time. In embodiments, a pharmaceutical composition comprises a bacterial isolate that can produce indole at a level that is at least 1.1x, at least 1.2x, at least 1.3x, at least 1.4x, at least 1.5x, at least 1.6x, at least 1.7x, at least 1.8x, at least 1.9x, at least 2x, at least 2.1x, at least 2.2x, at least 2.3x, at least 2.4x, at least 2.5x, at least 2.6x, at least 2.7x, at least 2.8x, at least 2.9x, at least 3x, at least 4x, at least 5x, at least 6x, at least 7x, at least 8x, at least 9x, at least 10x, at least 11x, at least 12x, at least 13x, at least 14x, at least 15x, at least 16x, at least 17x, at least 18x, at least 19x, at least 20x, at least 21x, at least 22x, at least 23x, at least 24x, at least 25x, at least 26x, at least 27x, at least 28x, at least 29x, at least 30x, at least 35x, at least 40x, at least 45x, at least 50x, at least 60x, at least 70x, at least 80x, at least 90x, at least 100x, at least 110x, at least 120x, at least 130x, at least 140x, at least 150x, at least 160x, at least 170x, at least 180x, at least 190x, at least 200x, at least 210x, at least 220x, at least 230x, at least 240x, at least 250x, or greater than 250x relative to at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii*, or relative to blank media alone. In embodiments, the bacterial isolate is provided in Table 6, or

comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the bacterial isolate comprises *Clostridium* sp. (e.g., *Clostridium aldenense*) In an embodiment, the bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 10.

[00186] In embodiments, a pharmaceutical composition comprises one or more bacterial isolates that produce kynurenine capable of activating an AhR of a subject administered the pharmaceutical composition. For example, a bacterial isolate can produce kynurenine at a concentration of at least 0.1 μM kynurenine, at least 0.2 μM kynurenine, at least 0.3 μM kynurenine, at least 0.4 μM kynurenine, at least 0.5 μM kynurenine, at least 0.6 μM kynurenine, at least 0.7 μM kynurenine, at least 0.8 μM kynurenine, at least 0.9 μM kynurenine, at least 1 μM kynurenine, at least 1.5 μM kynurenine, at least 2 μM kynurenine, at least 2.5 μM kynurenine, at least 3 μM kynurenine, at least 3.5 μM kynurenine, at least 4 μM kynurenine, at least 4.5 μM kynurenine, at least 5 μM kynurenine, or greater than 5 μM kynurenine. In embodiments, a bacterial isolate does not produce kynurenine. In embodiments, the bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the bacterial isolate comprises *Odoribacter splanchnicus* In an embodiment, the bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 2. In an embodiment, the bacterial isolate comprises *Bacteroides stercoris*. In an embodiment, the bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 13.

[00187] In other embodiments, a bacterial isolate can produce kynurenine at a higher level than blank media or a control bacterial strain (e.g., positive control bacterial strain capable of producing kynurenine, such as a strain that is a member of the *Peptostreptococcus* genus), as measured in a functional assay. For example, a bacterial isolate can produce kynurenine at a higher level than at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii* over a duration of time. In embodiments, a pharmaceutical composition comprises a bacterial isolate that can produce kynurenine at a level that is at least 1.1x, at least 1.2x, at least 1.3x, at least 1.4x, at least 1.5x, at least 1.6x, at least 1.7x, at least 1.8x, at least 1.9x, at least 2x, at least 2.1x, at least 2.2x, at least 2.3x, at least 2.4x, at least 2.5x, at least 2.6x, at least 2.7x, at least 2.8x, at least 2.9x, at least 3x, at least 4x, at least 5x, at least 6x, at least 7x, at least 8x, at least 9x, at least 10x, at least 11x, at least 12x, at least 13x, at least

14x, at least 15x, at least 16x, at least 17x, at least 18x, at least 19x, at least 20x, at least 21x, at least 22x, at least 23x, at least 24x, at least 25x, at least 26x, at least 27x, at least 28x, at least 29x, at least 30x, at least 35x, at least 40x, at least 45x, at least 50x, at least 60x, at least 70x, at least 80x, at least 90x, at least 100x, at least 110x, at least 120x, at least 130x, at least 140x, at least 150x, at least 160x, at least 170x, at least 180x, at least 190x, at least 200x, at least 210x, at least 220x, at least 230x, at least 240x, at least 250x, or greater than 250x relative to at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii*, or relative to blank media alone. In an embodiment, the bacterial isolate comprises *Odoribacter splanchnicus*. In an embodiment, the bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 2. In an embodiment, the bacterial isolate comprises *Bacteroides stercoris*. In an embodiment, the bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 13.

[00188] In embodiments, a pharmaceutical composition comprises one or more bacterial isolates that produce tryptamine capable of activating an AhR of a subject administered the pharmaceutical composition. For example, a bacterial isolate can produce tryptamine at a concentration of at least 0.1 μM tryptamine, at least 0.2 μM tryptamine, at least 0.3 μM tryptamine, at least 0.4 μM tryptamine, at least 0.5 μM tryptamine, at least 0.6 μM tryptamine, at least 0.7 μM tryptamine, at least 0.8 μM tryptamine, at least 0.9 μM tryptamine, at least 1 μM tryptamine, at least 1.5 μM tryptamine, at least 2 μM tryptamine, at least 2.5 μM tryptamine, at least 3 μM tryptamine, at least 3.5 μM tryptamine, at least 4 μM tryptamine, at least 4.5 μM tryptamine, at least 5 μM tryptamine, or greater than 5 μM tryptamine. In embodiments, a bacterial isolate does not produce tryptamine. In embodiments, the bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In embodiments, the bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the bacterial isolate comprises *Odoribacter splanchnicus*. In an embodiment, the bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 2.

[00189] In other embodiments, a bacterial isolate can produce tryptamine at a higher level than blank media or a control bacterial strain (e.g., positive control bacterial strain capable of producing tryptamine, such as a strain that is a member of the *Peptostreptococcus* genus), as

measured in a functional assay. For example, a bacterial isolate can produce tryptamine at a higher level than at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii* over a duration of time. In embodiments, a pharmaceutical composition comprises a bacterial isolate that can produce tryptamine at a level that is at least 1.1x, at least 1.2x, at least 1.3x, at least 1.4x, at least 1.5x, at least 1.6x, at least 1.7x, at least 1.8x, at least 1.9x, at least 2x, at least 2.1x, at least 2.2x, at least 2.3x, at least 2.4x, at least 2.5x, at least 2.6x, at least 2.7x, at least 2.8x, at least 2.9x, at least 3x, at least 4x, at least 5x, at least 6x, at least 7x, at least 8x, at least 9x, at least 10x, at least 11x, at least 12x, at least 13x, at least 14x, at least 15x, at least 16x, at least 17x, at least 18x, at least 19x, at least 20x, at least 21x, at least 22x, at least 23x, at least 24x, at least 25x, at least 26x, at least 27x, at least 28x, at least 29x, at least 30x, at least 35x, at least 40x, at least 45x, at least 50x, at least 60x, at least 70x, at least 80x, at least 90x, at least 100x, at least 110x, at least 120x, at least 130x, at least 140x, at least 150x, at least 160x, at least 170x, at least 180x, at least 190x, at least 200x, at least 210x, at least 220x, at least 230x, at least 240x, at least 250x, or greater than 250x relative to at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii*, or relative to blank media alone. In an embodiment, the bacterial isolate comprises *Odoribacter splanchnicus*. In embodiments, the bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the bacterial isolate comprises *Odoribacter splanchnicus*. In an embodiment, the bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 2.

[00190] In embodiments, an aryl hydrocarbon (i.e., AhR ligand) produced and/or released by a bacterial isolate described herein can bind to and/or activate an AhR expressed by a cell of a subject administered a pharmaceutical composition containing the bacterial isolate. Non-limiting examples of host cells that can express an AhR for binding to an aryl hydrocarbon released by a bacterial isolate include intestinal cells and immune cells. Examples of intestinal cells are an intestinal epithelial cell, an intestinal mucosal cell, or an intestinal lamina propria cell. Examples of immune cells include a B cell, a dendritic cell, a granulocyte, an innate lymphoid cell, a megakaryocyte, a monocyte, a macrophage, a myeloid-derived suppressor cell (MDSC), a natural killer cell (NK cell), a T cell, and a thymocyte.

[00191] In embodiments, a functional assay can be utilized to determine an ability of a bacterial isolate and/or an aryl hydrocarbon produced or secreted by a bacterial isolate to

activate AhR. For example, activation of AhR can be determined or measured using an AhR-responsive reporter gene construct, e.g., comprising an AhR-responsive promoter fused to a reporter gene. The AhR-responsive reporter gene construct can then be transfected into cells (e.g., mammalian cell line such as Chinese hamster ovary cells or a human cell line), which can be exposed in the functional assay to a bacterial isolate or a supernatant extracted from the bacterial isolate cells after growth. The ability of an aryl hydrocarbon (e.g., secreted by the bacterial isolate during growth) to activate AhR in the transfected cell can then be measured as reporter gene activity or output. Non-limiting examples of reporter genes include coding sequences for β-galactosidase, Green Fluorescent Protein (GFP), Red Fluorescent Protein (RFP), and luciferase.

[00192] Examples of bacterial isolates having the ability to secrete an aryl hydrocarbon in an appreciable amount are provided in Table 6. Table 6 lists bacterial isolates which can be included in a pharmaceutical composition such as a microbial cocktail; each isolate is identified by Latin name, an Identification Number (ID number), and the Sequence Identifier (SEQ ID NO) for its 16S rRNA sequence. In aspects, a pharmaceutical composition (e.g., comprising a microbial cocktail) comprises at least one bacterial isolate provided in Table 6, or at least one bacterial isolate comprising a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more of the bacterial isolates provided in Table 6. In embodiments, the pharmaceutical composition comprises at least two bacterial isolates, at least three bacterial isolates, at least four bacterial isolates, at least five bacterial isolates, at least six bacterial isolates, or at least seven bacterial isolates, that each comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of at least one of the bacterial isolates provided in Table 6.

Table 6

Isolate Latin Name	ID Number	SEQ ID NO. for 16S rRNA Sequence
Odoribacter splanchnicus	PI00000072	2
Bacteroides stercoris	PI00000146	13
Clostridium aldenense	PI00000097	10
Dorea longicatena	IS00006618	6
Parabacteroides merdae	IS00006167	5
Bacteroides uniformis	PI00000352	16
Bacteroides uniformis	PI00000137	11

[00193] In embodiments, a pharmaceutical composition comprises all or a subset of the bacterial isolates in at least one of Tables 1-4 and 6, or a bacterial isolate having a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of one or more of the bacterial isolates in Tables 1-4 and 6. In embodiments, all bacterial isolates in a pharmaceutical composition (e.g., comprising a microbial cocktail) are found in at least one of Tables 2-4 and 6, or share at least 95% identity in a 16S rRNA sequence to that of a bacterial isolate provided in at least one of Tables 2-4 and 6. In embodiments, all bacterial isolates in a pharmaceutical composition are listed together in one of Tables 2-4 and 6, or share at least 95% identity in a 16S rRNA sequence to that of a bacterial isolate provided in at least one of Tables 2-4 and 6. In an aspect, a pharmaceutical composition does not contain any bacterial isolates from at least one of Tables 2-4 and 6, or does not contain a bacterial isolate that shares 95% identity in a 16S rRNA sequence to that of a bacterial isolate provided in at least one of Tables 2-4 and 6.

[00194] In an aspect, a pharmaceutical composition can comprise one or more bacterial isolates (e.g., at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, or at least 9 bacterial isolates) from Table 2, or comprising a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of one or more of the bacterial isolates provided in Table 2. A microbial cocktail described herein can therefore comprise multiple bacterial isolates capable of generating one or more SCFAs such as butyrate. By providing a microbial cocktail containing multiple bacterial isolates that produce an SCFA such as butyrate in a gut of a subject administered the cocktail, a pharmaceutical composition can induce a spike or elevation or 'burst' of butyrate in the gut of a subject (e.g., which is depleted of SCFAs). Table 7, Table 8 and Table 9 illustrate exemplary microbial cocktails containing bacterial isolates that are all found in Table 2; each isolate is identified by Latin name, an Identification Number (ID number), and the Sequence Identifier (SEQ ID NO) for its 16S rRNA sequence. In certain embodiments, a composition comprises a microbial cocktail comprising each of the bacterial isolates in one of Tables 7-9, or bacterial isolates comprising 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of each of the bacterial isolates in one of Tables 7-9. In embodiments, the pharmaceutical composition comprises at least eight bacterial isolates that each comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of at least one of the bacterial isolates provided in Table 7. In embodiments, the pharmaceutical composition comprises at least six bacterial isolates that each comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of at least one of the bacterial isolates provided in one of Tables 8-9. In certain embodiments, a composition comprises a microbial cocktail

consisting essentially of the bacterial isolates listed in one of Tables 7-9, or bacterial isolates comprising 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of each of the bacterial isolates in one of Tables 7-9. In certain embodiments, a composition comprises a microbial cocktail consisting of the bacterial isolates listed in one of Tables 7-9, or bacterial isolates comprising 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of each of the bacterial isolates in one of Tables 7-9.

Table 7

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence
Odoribacter splanchnicus	PI00000072	2
Subdoligranulum variabile	IS00007359	22
Subdoligranulum variabile	IS00007357	23
Eubacterium rectale	IS00006864	8
Roseburia faecis	PI00000404	19
Faecalibacterium prausnitzii	PI00000329	1
Faecalibacterium prausnitzii	IS00006632	7
Anaerostipes hadrus	PI00000094	3

Table 8

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence
Faecalibacterium prausnitzii	PI00000329	1
Coprococcus comes	PI00000370	17
Anaerostipes hadrus	PI00000094	3
Eubacterium rectale	IS00006864	8
Roseburia faecis	PI00000404	19
Subdoligranulum variabile	IS00007359 OR IS00007357	22 OR 23

Table 9

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence
Faecalibacterium prausnitzii	IS00006632	7
Anaerostipes hadrus	PI00000094	3
Eubacterium rectale	IS00006864	8
Roseburia faecis	PI00000404	19
Coprococcus comes	PI00000370	17
Subdoligranulum variabile	IS00007359	22

	OR IS00007357	OR 23

[00195] In embodiments, a pharmaceutical composition (e.g., comprising a microbial cocktail) can comprise one or more bacterial isolates (e.g., at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, or greater than 15 bacterial isolates) that are not in Table 2. In embodiments, a pharmaceutical composition lacks at least one of the bacterial isolates in Table 2, or lacks bacterial isolates comprising 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of at least one of the bacterial isolates in Table 2. In embodiments, a pharmaceutical composition (e.g., comprising a microbial cocktail) does not contain any bacterial isolate from Table 2. A pharmaceutical composition described herein can therefore comprise or consist of one or more bacterial isolates which substantially do not produce an SCFA in the gut of a subject, and/or does not induce a spike of SCFA in the gut of the subject post-administration. Table 10, Table 11 and Table 12 illustrate exemplary microbial cocktails containing bacterial isolates that are not found in Table 2; each isolate is identified by Latin name, an Identification Number (ID number), and the Sequence Identifier (SEQ ID NO) for its 16S rRNA sequence. In certain embodiments, a composition comprises a microbial cocktail comprising each of the bacterial isolates in one of Tables 10-12, or bacterial isolates comprising 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of each of the bacterial isolates in one of Tables 10-12. In embodiments, the pharmaceutical composition comprises at least eight bacterial isolates that each comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of at least one of the bacterial isolates provided in one of Tables 10-11. In embodiments, the pharmaceutical composition comprises at least six bacterial isolates that each comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of at least one of the bacterial isolates provided in Table 12. In certain embodiments, a composition comprises a microbial cocktail consisting essentially of the bacterial isolates listed in one of Tables 10-12, or bacterial isolates comprising 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of each of the bacterial isolates in one of Tables 10-12. In certain embodiments, a composition comprises a microbial cocktail consisting of the bacterial isolates listed in one of Tables 10-12, or bacterial isolates comprising 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of each of the bacterial isolates in one of Tables 10-12. In an embodiment, a microbial cocktail comprises bacterial isolates comprising 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of each of the bacterial isolates in

one of Tables 10-12, as well as an additional bacterial isolate. For example, the additional bacterial isolate can be a member of the genus *Blautia*.

Table 10

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence
Akkermansia muciniphila	IS00007180	20
Parabacteroides merdae	IS00006167	5
Bacteroides uniformis	PI00000137 OR PI00000352	11 OR 16
Alistipes finegoldii	PI00000340	15
Bacteroides vulgatus	PI00000138	12
Dorea longicatena	IS00006618	6
Blautia obeum	PI00000053	9
Blautia sp.	IS00002788	34

Table 11

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence
Akkermansia muciniphila	IS00007180	20
Parabacteroides merdae	IS00006167	5
Bacteroides uniformis	PI00000137 OR PI00000352	11 OR 16
Alistipes finegoldii	PI00000340	15
Bacteroides vulgatus	PI00000138	12
Dorea longicatena	IS00006618	6
Alistipes onderdonkii	IS00004389	4
Blautia sp.	IS00002788	34

Table 12

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence
Akkermansia muciniphila	IS00007180	20
Bacteroides uniformis	PI00000137 OR PI00000352	11 OR 16
Alistipes finegoldii	PI00000340	15
Bacteroides vulgatus	PI00000138	12
Dorea longicatena	IS00006618	6
Blautia sp.	IS00002788	34

[00196] In embodiments, a pharmaceutical composition (e.g., comprising a microbial cocktail) can comprise one or more bacterial isolates (e.g., at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, or 11 bacterial isolates) from Table 3, and/or one or more bacterial isolates (e.g., at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, or greater than 15 bacterial isolates) comprising a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 3. A microbial cocktail described herein can therefore comprise multiple bacterial isolates capable of modulating production and/or release of one or more cytokines from a eukaryotic cell (e.g., a cell of a subject administered a composition comprising the microbial cocktail).

[00197] In embodiments, a pharmaceutical composition (e.g., comprising a microbial cocktail) can comprise one or more bacterial isolates (e.g., at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, or greater than 15 bacterial isolates) that are not in Table 3. In embodiments, a pharmaceutical composition lacks at least one of the bacterial isolates in Table 3, or lacks bacterial isolates comprising 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of at least one of the bacterial isolates in Table 2. In embodiments, a pharmaceutical composition (e.g., comprising a microbial cocktail) does not contain any bacterial isolate from Table 3. A pharmaceutical composition described herein can therefore comprise or consist of one or more bacterial isolates which do not substantially modulate production and/or release of one or more cytokines from a eukaryotic cell (e.g., a cell of a subject administered a composition comprising the microbial cocktail).

[00198] In embodiments, a pharmaceutical composition can comprise one or more bacterial isolates (e.g., at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, or greater than 15 bacterial isolates) from Table 4 comprising a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 4. A microbial cocktail described herein can therefore comprise multiple bacterial isolates corresponding to bacterial strains more highly abundant in a healthy subject relative to a patient with UC.

[00199] In embodiments, a pharmaceutical composition (e.g., comprising a microbial cocktail) can comprise one or more bacterial isolates (e.g., at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, or greater than 15 bacterial isolates) that are not in Table 4. In embodiments, a pharmaceutical composition lacks at least one of the bacterial isolates in Table 4, or lacks bacterial isolates comprising 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of at least one of the bacterial isolates in Table 4. In embodiments, a pharmaceutical composition (e.g., comprising a microbial cocktail) does not contain any bacterial isolate from Table 4. A pharmaceutical composition described herein can therefore comprise or consist of one or more bacterial isolates which do not correspond to bacterial strains more highly abundant in a healthy subject relative to a patient with UC.

[00200] In embodiments, a pharmaceutical composition can comprise one or more bacterial isolates (e.g., one, two, and three bacterial isolates) from Table 6, and/or one or more bacterial isolates (e.g., at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, or greater than 15 bacterial isolates) comprising a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 6. A microbial cocktail described herein can therefore comprise multiple bacterial isolates that produce an aryl hydrocarbon capable of binding to and activating an AhR receptor.

[00201] In embodiments, a pharmaceutical composition (e.g., comprising a microbial cocktail) can comprise one or more bacterial isolates (e.g., at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, or greater than 15 bacterial isolates) that are not in Table 6. In embodiments, a pharmaceutical composition lacks at least one of the bacterial isolates in Table 6, or lacks bacterial isolates comprising 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of at least one of the bacterial isolates in Table 6. In embodiments, a pharmaceutical composition (e.g., comprising a microbial cocktail) does not contain any bacterial isolate from Table 6. A pharmaceutical composition described herein can therefore comprise or consist of one or more bacterial isolates which do not substantially secrete an aryl hydrocarbon capable of binding to and activating an AhR receptor.

[00202] In embodiments, a microbial cocktail can comprise bacterial isolates comprising 16S rRNA sequences at least 95% identical to 16S rRNA sequences of bacterial isolates provided in more than one of Tables 2-4. Such a microbial cocktail can therefore advantageously

influence the health of a subject administered the cocktail (e.g., in the form of a pharmaceutical composition) via multiple mechanisms. For example, a microbial cocktail can comprise one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 2, and one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 3. In such cases at least one bacterial isolate in the composition can produce one or more SCFAs to increase a level of SCFAs (e.g., butyrate) in the gut of the subject (i.e., 'Table 2 bacterial isolate') and at least one bacterial isolate administered to the subject can modulate production and/or release of a cytokine by a host cell of the subject (i.e., 'Table 3 bacterial isolate').

[00203] In another example, a microbial cocktail can comprise one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 2, and one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 4. In such cases, at least one bacterial isolate in the composition can produce one or more SCFAs to increase a level of SCFAs (e.g., butyrate) in the gut of the subject (i.e., 'Table 2 bacterial isolate') and at least one bacterial isolate in the composition corresponds to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC ('Table 4 bacterial isolate').

[00204] In another example, a microbial cocktail can comprise one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 3, and one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 4. In such cases, at least one bacterial isolate in the composition can modulate production and/or release of a cytokine by a host cell of the subject (i.e., 'Table 3 bacterial isolate') and at least one bacterial isolate in the composition corresponds to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC ('Table 4 bacterial isolate').

[00205] In another example, a microbial cocktail can comprise one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 2, one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 3, and one or more bacterial isolates that comprise a 16S rRNA sequence at

least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 4. In such cases, at least one bacterial isolate in the composition can produce one or more SCFAs to increase a level of SCFAs in the gut of the subject (i.e., 'Table 2 bacterial isolate'), at least one bacterial isolate in the composition can modulate production and/or release of a cytokine by a host cell of the subject (i.e., 'Table 3 bacterial isolate'), and at least one bacterial isolate in the composition corresponds to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC ('Table 4 bacterial isolate').

[00206] In embodiments, a microbial cocktail can comprise bacterial isolates comprising 16S rRNA sequences at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates from Table 6 and one or more bacterial isolates of Tables 2-4. Such a microbial cocktail can therefore advantageously influence the health of a subject administered the cocktail (e.g., in the form of a pharmaceutical composition) via multiple mechanisms. For example, a microbial cocktail can comprise one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 2, and one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 6. In such cases, at least one bacterial isolate in the composition can produce one or more SCFAs to increase a level of SCFAs (e.g., butyrate) in the gut of the subject (i.e., 'Table 2 bacterial isolate'), and at least one bacterial isolate in the composition can produce a compound capable of binding to and activating AhR receptor (i.e., 'Table 6 bacterial isolate'). In another example, a microbial cocktail can comprise one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 4, and one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 6. In such cases, at least one bacterial isolate in the composition corresponds to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC ('Table 4 bacterial isolate'), and at least one bacterial isolate in the composition can produce a ligand capable of binding to an AhR receptor (i.e., 'Table 6 bacterial isolate'). In another example, a microbial cocktail can comprise one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 3, and one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 6. In such cases, at least one bacterial isolate in the composition can modulate production and/or release of a

cytokine by a host cell of the subject (i.e., 'Table 3 bacterial isolate'), and at least one bacterial isolate in the composition can produce a ligand capable of binding to an AhR receptor (i.e., 'Table 6 bacterial isolate').

[00207] In another example, a microbial cocktail can comprise one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 2, one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 3, and one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 6. In such cases, at least one bacterial isolate in the composition can produce one or more SCFAs to increase a level of SCFAs in the gut of the subject (i.e., 'Table 2 bacterial isolate'), at least one bacterial isolate in the composition can modulate production and/or release of a cytokine by a host cell of the subject (i.e., 'Table 3 bacterial isolate'), and at least one bacterial isolate in the composition can produce a ligand capable of binding to an AhR receptor (i.e., 'Table 6 bacterial isolate'). In another example, a microbial cocktail can comprise one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 2, one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 4, and one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 6. In such cases, at least one bacterial isolate in the composition can produce one or more SCFAs to increase a level of SCFAs in the gut of the subject (i.e., 'Table 2 bacterial isolate'), at least one bacterial isolate in the composition corresponds to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC ('Table 4 bacterial isolate'), and at least one bacterial isolate in the composition can produce a ligand capable of binding to an AhR receptor (i.e., 'Table 6 bacterial isolate'). In another example, a microbial cocktail can comprise one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 3, one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 4, and one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 6. In such cases, at least one bacterial isolate in the composition can modulate production and/or release of a cytokine by a

host cell of the subject (i.e., 'Table 3 bacterial isolate'), at least one bacterial isolate in the composition corresponds to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC ('Table 4 bacterial isolate'), and at least one bacterial isolate in the composition can produce a ligand capable of binding to an AhR receptor (i.e., 'Table 6 bacterial isolate').

[00208] In another example, a microbial cocktail can comprise one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 2, one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 3, one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 4, and one or more bacterial isolates that comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more bacterial isolates provided in Table 6. In such cases, at least one bacterial isolate in the composition can produce one or more SCFAs to increase a level of SCFAs in the gut of the subject (i.e., 'Table 2 bacterial isolate'), at least one bacterial in the composition can modulate production and/or release of a cytokine by a host cell of the subject (i.e., 'Table 3 bacterial isolate'), at least one bacterial isolate in the composition corresponds to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC ('Table 4 bacterial isolate'), and at least one bacterial isolate in the composition can produce a ligand capable of binding to an AhR receptor (i.e., 'Table 6 bacterial isolate').

[00209] Tables 13-35 illustrate different exemplary microbial cocktails containing bacterial isolates found in Tables 2-4 and/or 6, such that collectively the bacterial isolates in the microbial cocktail, once administered to a subject, can act to (i) increase a level of SCFAs in the gut of the subject; and (ii) modulate release of a cytokine by a host cell of the subject; and (iii) provide for bacterial isolates in the gut of the subject that correspond to bacterial strains more highly abundant in a healthy subject relative to a patient with UC; and/or (iv) release one or more hydrocarbons capable of binding to and activating an AhR receptor of a host cell of the subject. In each table, isolates are identified by Latin name, an Identification Number (ID number), the Sequence Identifier (SEQ ID NO) for its 16S rRNA sequence, and the above Table(s) (i.e., Table 2, 3, 4 and/or 6) in which the isolate appears.

[00210] In certain embodiments, a composition comprises a microbial cocktail comprising each of the bacterial isolates provided in one of Tables 13-35, or bacterial isolates having 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of each of the bacterial

isolates provided in one of Tables 13-35. In embodiments, the pharmaceutical composition comprises at least one, at least two, at least three, at least four, at least five, at least six, at least seven, or at least eight of the bacterial isolates provided in one of Tables 15-17, 17a, 17b, and 22-29, or at least one, at least two, at least three, at least four, at least five, at least six, at least seven, or at least eight bacterial isolates that each comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of at least one of the bacterial isolates provided in one of Tables 15-17, 17a, 17b, and 22-29. In embodiments, the pharmaceutical composition comprises at least one, at least two, at least three, at least four, at least five, or at least six of the bacterial isolates provided in one of Tables 13, 14, 21 and 30-35, or at least one, at least two, at least three, at least four, at least five, or at least six bacterial isolates that each comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of at least one of the bacterial isolates provided in one of Tables 13, 14, 21 and 30-35. In embodiments, the pharmaceutical composition comprises at least one, at least two, at least three, at least four, at least five, at least six, or at least seven of the bacterial isolates provided in one of Tables 18-20, or at least one, at least two, at least three, at least four, at least five, at least six, or at least seven bacterial isolates that each comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of at least one of the bacterial isolates provided in one of Tables 18-20. In certain embodiments, a composition comprises a microbial cocktail consisting essentially of each of the bacterial isolates provided in one of Tables 13-35, or bacterial isolates having 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of each of the bacterial isolates provided in one of Tables 13-35. In certain embodiments, a composition comprises a microbial cocktail consisting of each of the bacterial isolates provided in one of Tables 13-35, or bacterial isolates having 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of each of the bacterial isolates provided in one of Tables 13-35.

Table 13

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Eubacterium rectale	IS00006864	8	2, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	1 OR 7	2, 3, 4
Alistipes shahii	PI00000395	18	3, 4
Anaerostipes hadrus	PI00000094	3	2, 3, 4
Roseburia faecis	PI00000404	19	2

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.

Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.

Table 14

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Eubacterium rectale	IS00006864	8	2, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	1 OR 7	2, 3, 4
Alistipes shahii	PI00000395	18	3, 4
Blautia obeum	PI00000053	9	4
Roseburia faecis	PI00000404	19	2

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.

Table 15

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table(s)*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Subdoligranulum variabile	IS00007359 OR IS00007357	22 OR 23	2, 4
Eubacterium rectale	IS00006864	8	2, 4
Alistipes shahii	PI00000395	18	3, 4
Phascolarctobacterium faecium	PI00000289	21	4
Bacteroides cellulosilyticus	PI00000316	14	4
Akkermansia muciniphila	IS00007180	20	4
Anaerostipes hadrus	PI00000094	3	2, 3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 16

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table(s)*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Subdoligranulum variabile	IS00007359 OR	22 OR	2, 4

	IS00007357	23	
Eubacterium rectale	IS00006864	8	2, 4
Alistipes onderdonkii	IS00004389	4	4
Phascolarctobacterium faecium	PI00000289	21	4
Bacteroides cellulosilyticus	PI00000316	14	4
Akkermansia muciniphila	IS00007180	20	4
Anaerostipes hadrus	PI00000094	3	2, 3, 4

* Table 2: Bacterial isolates capable of producing SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates capable of producing a ligand for an AhR of a host cell.

Table 17

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table(s)*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Subdoligranulum variabile	IS00007359 OR IS00007357	22 OR 23	2, 4
Eubacterium rectale	IS00006864	8	2, 4
Alistipes finegoldii	PI00000340	15	4
Phascolarctobacterium faecium	PI00000289	21	4
Bacteroides cellulosilyticus	PI00000316	14	4
Akkermansia muciniphila	IS00007180	20	4
Anaerostipes hadrus	PI00000094	3	2, 3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 17a

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Subdoligranulum variabile	IS00007359 OR IS00007357	22 OR 23	2, 4
Eubacterium rectale	IS00006864	8	2, 4
Alistipes shahii	PI00000395	18	3, 4
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	1 OR 7	2, 3, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Akkermansia muciniphila	IS00007180	20	4
Roseburia faecis	PI00000404	19	2

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 17b

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Faecalibacterium prausnitzii	IS00006632	7	2, 3, 4
Eubacterium rectale	IS00006864	8	2, 4
Alistipes shahii	PI00000395	18	3, 4
Faecalibacterium prausnitzii	PI00000329	1	2, 3, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Akkermansia muciniphila	IS00007180	20	4
Roseburia faecis	PI00000404	19	2

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 18

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Subdoligranulum variabile	IS00007359 OR IS00007357	22 OR 23	2, 4
Eubacterium rectale	IS00006864	8	2, 4
Alistipes shahii	PI00000395	18	3, 4
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	1 OR 7	2, 3, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Anaerostipes hadrus	PI00000094	3	2, 3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 19

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6

Subdoligranulum variabile	IS00007359 OR IS00007357	22 OR 23	2, 4
Eubacterium rectale	IS00006864	8	2, 4
Alistipes onderdonkii	IS00004389	4	4
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	1 OR 7	2, 3, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Anaerostipes hadrus	PI00000094	3	2, 3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 20

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Subdoligranulum variabile	IS00007359 OR IS00007357	22 OR 23	2, 4
Eubacterium rectale	IS00006864	8	2, 4
Alistipes finegoldii	PI00000340	15	4
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	1 OR 7	2, 3, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Anaerostipes hadrus	PI00000094	3	2, 3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 21

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Eubacterium rectale	IS00006864	8	2, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	1 OR 7	2, 3, 4
Alistipes shahii	PI00000395	18	3, 4
Blautia obeum	PI00000053	9	4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.

Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 22

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Subdoligranulum variabile	IS00007359 OR IS00007357	22 OR 23	2, 4
Eubacterium rectale	IS00006864	8	2, 4
Alistipes shahii	PI00000395	18	3, 4
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	PI00000329: 1 OR IS00006632: 7	2, 3, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Bacteroides stercoris	PI00000146	13	3, 6
Anaerostipes hadrus	PI00000094	3	2, 3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 23

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Subdoligranulum variabile	IS00007359 OR IS00007357	22 OR 23	2, 4
Eubacterium rectale	IS00006864	8	2, 4
Alistipes shahii	PI00000395	18	3, 4
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	PI00000329: 1 OR IS00006632: 7	2, 3, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Clostridium aldenense	PI00000097	10	3, 6
Anaerostipes hadrus	PI00000094	3	2, 3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 24

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Subdoligranulum variabile	IS00007359 OR IS00007357	22 OR 23	2, 4
Eubacterium rectale	IS00006864	8	2, 4
Alistipes onderdonkii	IS00004389	4	4
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	PI00000329: 1 OR IS00006632: 7	2, 3, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Bacteroides stercoris	PI00000146	13	3, 6
Anaerostipes hadrus	PI00000094	3	2, 3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 25

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Subdoligranulum variabile	IS00007359 OR IS00007357	22 OR 23	2, 4
Eubacterium rectale	IS00006864	8	2, 4
Alistipes onderdonkii	IS00004389	4	4
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	PI00000329: 1 OR IS00006632: 7	2, 3, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Clostridium aldenense	PI00000097	10	3, 6
Anaerostipes hadrus	PI00000094	3	2, 3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 26

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6

Subdoligranulum variabile	IS00007359 OR IS00007357	22 OR 23	2, 4
Eubacterium rectale	IS00006864	8	2, 4
Alistipes finegoldii	PI00000340	15	4
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	PI00000329: 1 OR IS00006632: 7	2, 3, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Bacteroides stercoris	PI00000146	13	3, 6
Anaerostipes hadrus	PI00000094	3	2, 3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 27

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Subdoligranulum variabile	IS00007359 OR IS00007357	22 OR 23	2, 4
Eubacterium rectale	IS00006864	8	2, 4
Alistipes finegoldii	PI00000340	15	4
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	PI00000329: 1 OR IS00006632: 7	2, 3, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Clostridium aldenense	PI00000097	10	3, 6
Anaerostipes hadrus	PI00000094	3	2, 3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 28

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Eubacterium rectale	IS00006864	8	2, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Bacteroides stercoris	PI00000146	13	3, 6
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	PI00000329: 1 OR IS00006632: 7	2, 3, 4

Alistipes shahii	PI00000395	18	3, 4
Anaerostipes hadrus	PI00000094	3	2, 3, 4
Roseburia faecis	PI00000404	19	2

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 29

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Eubacterium rectale	IS00006864	8	2, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Bacteroides stercoris	PI00000146	13	3, 6
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	PI00000329: 1 OR IS00006632: 7	2, 3, 4
Alistipes shahii	PI00000395	18	3, 4
Blautia obeum	PI00000053	9	4
Roseburia faecis	PI00000404	19	2

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 30

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Eubacterium rectale	IS00006864	8	2, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Bacteroides stercoris	PI00000146	13	3, 6
Roseburia faecis	PI00000404	19	2
Alistipes shahii	PI00000395	18	3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 31

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6

Eubacterium rectale	IS00006864	8	2, 4
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	PI00000329: 1 OR IS00006632: 7	2, 3, 4
Bacteroides stercoris	PI00000146	13	3, 6
Roseburia faecis	PI00000404	19	2
Anaerostipes hadrus	PI00000094	3	2, 3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 32

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Bacteroides stercoris	PI00000146	13	3, 6
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	PI00000329: 1 OR IS00006632: 7	2, 3, 4
Alistipes shahii	PI00000395	18	3, 4
Roseburia faecis	PI00000404	19	2
Anaerostipes hadrus	PI00000094	3	2, 3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 33

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Eubacterium rectale	IS00006864	8	2, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Bacteroides stercoris	PI00000146	13	3, 6
Blautia obeum	PI00000053	9	4
Alistipes shahii	PI00000395	18	3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 34

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*

Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Eubacterium rectale	IS00006864	8	2, 4
Bacteroides stercoris	PI00000146	13	3, 6
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	PI00000329: 1 OR IS00006632: 7	2, 3, 4
Blautia obeum	PI00000053	9	4
Roseburia faecis	PI00000404	19	2

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 35

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Eubacterium rectale	IS00006864	8	2, 4
Bacteroides stercoris	PI00000146	13	3, 6
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	PI00000329: 1 OR IS00006632: 7	2, 3, 4
Alistipes shahii	PI00000395	18	3, 4
Roseburia faecis	PI00000404	19	2

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

[00211] Tables 36-43 illustrate different exemplary microbial cocktails containing bacterial isolates found in Tables 2-4 and/or 6, such that collectively the bacterial isolates in the microbial cocktail, once administered to a subject, can act to (i) increase a level of SCFAs in the gut of the subject; (ii) modulate release of a cytokine by a host cell of the subject; (iii) provide for bacterial isolates in the gut of the subject that correspond to bacterial strains more highly abundant in a healthy subject relative to a patient with UC; and/or (iv) release one or more hydrocarbons capable of binding to and activating an AhR receptor of a host cell of the subject. In each table, isolates are identified by Latin name, an Identification Number (ID number), the Sequence Identifier (SEQ ID NO) for its 16S rRNA sequence, and the above Table(s) (i.e., Table 2, 3, 4 and/or 6) in which the isolate appears.

[00212] In certain embodiments, a composition comprises a microbial cocktail comprising each of the bacterial isolates provided in one of Tables 36-43, or bacterial isolates having 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of each of the bacterial isolates provided in one of Tables 36-43. In embodiments, the pharmaceutical composition comprises one or more, two or more, three or more, four or more, five or more, six or more, seven or more, eight or more, or nine of the bacterial isolates provided in one of Tables 36-41, or one or more, two or more, three or more, four or more, five or more, six or more, seven or more, eight or more, or nine bacterial isolates that each comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of at least one of the bacterial isolates provided in one of Tables 36-41. In embodiments, the pharmaceutical composition comprises one or more, two or more, three or more, four or more, five or more, six or more, seven or more, eight or more, or nine or more, or ten of the bacterial isolates provided in one of Tables 41-42, or one or more, two or more, three or more, four or more, five or more, six or more, seven or more, eight or more, or nine or more, or ten bacterial isolates that each comprise a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of at least one of the bacterial isolates provided in one of Tables 41-42.

[00213] In certain embodiments, a composition comprises a microbial cocktail consisting essentially of each of the bacterial isolates provided in one of Tables 36-43, or bacterial isolates having 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of each of the bacterial isolates provided in one of Tables 36-43. In certain embodiments, a composition comprises a microbial cocktail consisting of each of the bacterial isolates provided in one of Tables 36-43, or bacterial isolates having 16S rRNA sequences at least 95% identical to the 16S rRNA sequence of each of the bacterial isolates provided in one of Tables 36-43.

Table 36

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Subdoligranulum variabile	IS00007359 OR IS00007357	22 OR 23	2, 4
Eubacterium rectale	IS00006864	8	2, 4
Alistipes finegoldii	PI00000340	15	4
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	PI00000329: 1 OR IS00006632: 7	2, 3, 4
Bacteroides cellulosilyticus	PI00000316	14	4

Clostridium aldenense	PI00000097	10	3, 6
Akkermansia muciniphila	IS00007180	20	4
Anaerostipes hadrus	PI00000094	3	2, 3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 37

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Subdoligranulum variabile	IS00007359 OR IS00007357	22 OR 23	2, 4
Eubacterium rectale	IS00006864	8	2, 4
Alistipes finegoldii	PI00000340	15	4
Faecalibacterium prausnitzii	PI00000329 OR IS00006632	PI00000329: 1 OR IS00006632: 7	2, 3, 4
Bacteroides cellulosilyticus	PI00000316	14	4
Clostridium aldenense	PI00000097	10	3, 6
Akkermansia muciniphila	IS00007180	20	4
Alistipes shahii	PI00000395	18	3, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 38

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Bacteroides cellulosilyticus	PI00000316	14	4
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Faecalibacterium prausnitzii	IS00006632	7	2, 3, 4
Faecalibacterium prausnitzii	PI00000329	1	2, 3, 4
Akkermansia muciniphila	IS00007180	20	4
Bacteroides stercoris	PI00000146	13	6
Alistipes shahii	PI00000395	18	3, 4
Eubacterium rectale	IS00006864	8	2, 4
Roseburia faecis	PI00000404	19	2

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 39

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Bacteroides cellulosilyticus	PI00000316	14	4
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Faecalibacterium prausnitzii	IS00006632	7	2, 3, 4
Faecalibacterium prausnitzii	PI00000329	1	2, 3, 4
Akkermansia muciniphila	IS00007180	20	4
Clostridium aldenense	PI00000097	10	3, 6
Alistipes shahii	PI00000395	18	3, 4
Eubacterium rectale	IS00006864	8	2, 4
Roseburia faecis	PI00000404	19	2

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 40

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Bacteroides cellulosilyticus	PI00000316	14	4
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Faecalibacterium prausnitzii	IS00006632	7	2, 3, 4
Faecalibacterium prausnitzii	PI00000329	1	2, 3, 4
Bacteroides uniformis	PI00000137	11	3, 4, 6
Bacteroides stercoris	PI00000146	13	6
Alistipes shahii	PI00000395	18	3, 4
Eubacterium rectale	IS00006864	8	2, 4
Roseburia faecis	PI00000404	19	2

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

Table 41

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Bacteroides cellulosilyticus	PI00000316	14	4
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Faecalibacterium prausnitzii	IS00006632	7	2, 3, 4
Faecalibacterium prausnitzii	PI00000329	1	2, 3, 4
Akkermansia muciniphila	IS00007180	20	4
Bacteroides stercoris	PI00000146	13	6
Alistipes shahii	PI00000395	18	3, 4

Eubacterium rectale	IS00006864	8	2, 4
Subdoligranulum variabile	IS00007359	22	2, 4

Table 42

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Bacteroides cellulosilyticus	PI00000316	14	4
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Faecalibacterium prausnitzii	IS00006632	7	2, 3, 4
Faecalibacterium prausnitzii	PI00000329	1	2, 3, 4
Akkermansia muciniphila	IS00007180	20	4
Bacteroides stercoris	PI00000146	13	6
Alistipes shahii	PI00000395	18	3, 4
Eubacterium rectale	IS00006864	8	2, 4
Roseburia faecis	PI00000404	19	2
Subdoligranulum variabile	IS00007359	22	2, 4

Table 43

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Bacteroides cellulosilyticus	PI00000316	14	4
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Faecalibacterium prausnitzii	IS00006632	7	2, 3, 4
Faecalibacterium prausnitzii	PI00000329	1	2, 3, 4
Akkermansia muciniphila	IS00007180	20	4
Bacteroides stercoris	PI00000146	13	6
Alistipes shahii	PI00000395	18	3, 4
Eubacterium rectale	IS00006864	8	2, 4
Roseburia faecis	PI00000404	19	2
Bacteroides uniformis	PI00000137	11	3, 4, 6

[00214] In embodiments, a pharmaceutical composition described herein can comprise a bacterial mixture comprising multiple bacterial isolates that together provide for redundancy of one or more advantageous phenotypes in the bacterial mixture, which may include for example the ability to induce a particular mechanism or pathway in the intestine of the subject when the composition is administered to the subject. Such redundancy can increase the likelihood that a subject administered the composition will benefit from a particular advantageous trait or phenotype in common between the "redundant" isolates of bacteria (e.g. a propensity to increase a level of an SCFA in the gut of the subject). Without intending to be bound by theory, a reason for this is potential variation across subjects in the likelihood of a particular bacterial isolate to engraft in the intestine of each subject, which is typically

necessary for the bacterial isolate to exert its beneficial effects. By formulating a composition comprising genetically distinct isolates that each exhibit the same phenotype of interest (e.g. the production of one or more SCFAs above a threshold level), the composition may exhibit enhanced efficacy across individuals (i.e., compared to a formulation without built-in redundancy), since the likelihood of at least one of the multiple redundant bacterial isolates engrafting is increased compared to the likelihood of engraftment of a single bacterial isolate without a redundant counterpart.

[00215] In an aspect, redundancy can be incorporated into the composition by including in the bacterial mixture multiple bacterial isolates that each possess at least one of the following phenotypes: (i) each of the multiple bacterial isolates produces a level of one or more SCFAs above a threshold level (e.g., by incorporating into the bacterial mixture or administering to the subject multiple bacterial isolates selected from Table 2); (ii) each of the multiple bacterial isolates induces release of a cytokine by a host cell of the subject (e.g., by incorporating into the bacterial mixture or administering to the subject multiple bacterial isolates selected from Table 3); (iii) each of the multiple bacterial isolates corresponds to a bacterial strain that is more highly abundant in a healthy subject relative to a patient with UC (e.g., by incorporating into the bacterial mixture or administering to the subject multiple bacterial isolates selected from Table 4); and/or (iv) each of the multiple bacterial isolates releases one or more aryl hydrocarbons capable of binding to and activating an AhR receptor of a host cell of the subject (e.g., by incorporating into the bacterial mixture or administering to the subject multiple bacterial isolates selected from Table 6).

[00216] In an aspect, a bacterial mixture comprising multiple bacterial isolates that provide for redundancy of phenotypes is shown in Table 38, which contains at least five bacterial isolates that produce significant levels of an SCFA (here butyrate; see Example 2) (i.e., *Odoribacter splanchnicus*, *Eubacterium rectale*, *Roseburia faecis*, and two isolates of *Faecalibacterium prausnitzii*), at least four bacterial isolates that induce release of pro-inflammatory cytokines by human cells (here PBMCs; see Example 3) (i.e., *Odoribacter sphlanchnicus*, *Alistipes shahii*, and two isolates of *Faecalibacterium prausnitzii*), at least two bacterial isolates that release aryl hydrocarbons capable of binding to and activating an AhR receptor of a host cell of the subject (see Example 5) (i.e., *Odoribacter sphlanchnicus* and *Bacteroides stercoris*), and at least seven bacterial isolates that correspond to bacterial strains more highly abundant in a healthy subject relative to a patient with UC (see Example 4) (i.e.,

Bacteroides cellulosilyticus, *Odoribacter splanchnicus*, *Akkermansia muciniphila*, *Alistipes shahii*, *Eubacterium rectale* and two isolates of *Faecalibacterium prausnitzii*).

[00217] In embodiments, a pharmaceutical composition can comprise multiple distinct bacterial isolates that are each a member of a particular genus, or multiple bacterial isolates that are each a member of a particular species. This can be advantageous, for example, by providing redundancy where multiple bacterial isolates of the same genus or species are capable of optimally inducing or influencing a particular mechanism of interest (e.g. by producing SCFA, inducing an anti-inflammatory profile, or producing aryl hydrocarbons). By including multiple taxonomically related bacterial isolates that each exhibit a similar optimal trait or phenotype (e.g. ability to produce high levels of an SCFA) in the same pharmaceutical composition, redundancy is built into the composition such that there is a higher likelihood that a subject administered the composition will benefit from the trait or phenotype. A reason for this is potential variation across subjects in the ability of a particular bacterial isolate to engraft in the intestines of the subjects, which is typically necessary for the bacterial isolate to exert its beneficial effects. For example, a pharmaceutical composition can comprise multiple (e.g. two, three, four, five, or more than five) bacterial isolates that are each a member of the genus *Faecalibacterium*, or multiple (e.g. two, three, four, five, or more than five) bacterial isolates that are each a member of the species *Faecalibacterium prausnitzii* (see e.g. Table 17b or Table 38). In another example, a pharmaceutical composition can comprise multiple (e.g. two, three, four, five, or more than five) bacterial isolates that are each a member of the genus *Bacteroides*, e.g. *B. cellulosilyticus* and *B. stercoris* (see e.g. Tables 26, 28 and 38).

[00218] In embodiments, a pharmaceutical composition can comprise only one bacterial isolate that is a member of a particular genus, or only one bacterial isolate that is a member of a particular species. This can be advantageous, for example, to minimize the total number of bacterial isolates in a pharmaceutical composition (e.g. to reduce costs and resources related to growing and formulating each bacterial isolate), while maintaining a diversity of taxa represented by the bacterial isolates, which can correspond to induction of multiple treatment-related mechanisms (e.g. SCFA production, anti-inflammatory cytokine induction, AhR activation) in a subject administered the composition. For example, a pharmaceutical composition can comprise only one bacterial isolate that is a member of the genus *Bacteroides*. In an embodiment, the single bacterial isolate from the genus *Bacteroides* is *B. cellulosilyticus* (see e.g. Tables 17a and 17b). In another example, a pharmaceutical composition can comprise only one bacterial isolate that is a member of the genus *Eubacterium*, or only one bacterial

isolate that is a member of the species *Eubacterium rectale* (see e.g. Tables 17a and 17b and 38). In another example, a pharmaceutical composition can comprise only one bacterial isolate that is a member of the genus *Roseburia*, or only one bacterial isolate that is a member of *Roseburia faecis* (see e.g. Tables 17a and 17b and 38). In another example, a pharmaceutical composition can comprise only one bacterial isolate that is a member of the genus *Coprococcus*, or only one bacterial isolate that is a member of the species *Coprococcus comes*.

[00219] In another example, a pharmaceutical composition can comprise only one bacterial isolate that is a member of the genus *Alistipes*. In certain embodiments, a pharmaceutical composition comprises a bacterial isolate comprising *Alistipes shahii*, but does not comprise *Alistipes finegoldii* or *Alistipes putredinis* (see e.g. Tables 17a and 17b and 38). The inclusion of *A. shahii* over *A. finegoldii* and *A. putredinis* is consistent with the Examples below, which show that *A. shahii* has a lower cross sectional combined p-value than *A. finegoldii* and *A. putredinis* for (i) enrichment in healthy subjects over patients diagnosed with UC; and/or (ii) association/correlation with clinical remission or response of UC symptoms in UC patients following FMT treatment. In other embodiments, a pharmaceutical composition comprises a bacterial isolate comprising *Alistipes finegoldii*, but does not comprise *Alistipes shahii* or *Alistipes putredinis* (see e.g. Table 17). In certain embodiments, a pharmaceutical composition comprises a bacterial isolate comprising *Alistipes Alistipes putredinis*, but does not comprise *Alistipes shahii* or *Alistipes finegoldii*.

[00220] In embodiments, a pharmaceutical composition can exclude or omit a bacterial genus, species or strain that may not be beneficial, or may be detrimental, for treating a condition related to a gut dysbiosis (e.g., IBD including ulcerative colitis). For example, a pharmaceutical composition can exclude or omit a strain or bacterial isolate from the genus *Escherichia* (e.g., *Escherichia coli*). The below Examples show that *E. coli* produces little or no butyrate and is characterized by a cytokine profile that is pro-inflammatory (i.e. low ratios of IL-10/IL-12 and/or IL-10/TNF-alpha).

[00221] In other examples, a pharmaceutical composition can omit or exclude one or more of the following bacterial taxa: a member of the genus *Adlercreutzia*, *Adlercreutzia equolifaciens*, a member of the genus *Akkermansia*, *Akkermansia muciniphila*, a member of the genus *Alistipes*, *Alistipes finegoldii*, *Alistipes putredinis*, *Alistipes shahii*, a member of the genus *Bacteroides*, *Bacteroides capillosus*, *Bacteroides cellulosilyticus*, *Bacteroides eggerthii*, *Bacteroides ovatus*, *Bacteroides thetaiotaomicron*, *Bacteroides uniformis*, a member of the genus *Bacillus*, *Bacillus circulans*, *Bacillus simplex*, a member of the genus *Bifidobacterium*,

Bifidobacterium longum, a member of the genus *Blautia*, *Blautia hydrogenotrophica*, a member of the genus *Brevibacillus*, *Brevibacillus parabrevis*, a member of the genus *Catabacter*, *Catabacter hongkongensis*, a member of the genus *Catenibacterium*, *Catenibacterium mitsuokai*, a member of the genus *Clostridium*, *Clostridium coccoides*, *Clostridium aldenense*, *Clostridium asparagiforme*, *Clostridium celerecrescens*, *Clostridium hathewayi*, *Clostridium hylemonae*, *Clostridium inocuum*, *Clostridium lavalense*, *Clostridium leptum*, *Clostridium scindens*, *Clostridium staminisolvens*, *Clostridium sulfatireducens*, *Clostridium symbiosum*, *Clostridium thermocellum*, a member of the genus *Collinsella*, *Collinsella aerofaciens*, a member of the genus *Coprococcus*, *Coprococcus catus*, *Coprococcus comes*, *Coprococcus eutactus*, a member of the genus *Dorea*, *Dorea formicigenerans*, *Dorea longicatena*, a member of the genus *Eubacterium*, *Eubacterium biforme*, *Eubacterium callanderi*, *Eubacterium dolichum*, *Eubacterium eligens*, *Eubacterium fissicatena*, *Eubacterium rectale*, *Eubacterium siraeum*, *Eubacterium ventriosum*, *Eubacterium xylanophilum*, a member of the genus *Faecalibacterium*, *Faecalibacterium prausnitzii*, a member of the genus *Holdemania*, *Holdemania filimormis*, a member of the genus *Subdoligranulum*, *Subdoligranulum variabile*, a member of the genus *Microbacterium*, *Microbacterium schleiferi*, *Micrococcus luteus*, a member of the genus *Odoribacter*, *Odoribacter splanchnicus*, a member of the genus *Oscillibacter*, *Oscillibacter valericigenes*, a member of the genus *Parabacteroides*, *Parabacteroides merdae*, *Parabacteroides gordonii*, a member of the genus *Parasutterella*, *Parasutterella excrementihominis*, a member of the genus *Phascolarctobacterium*, *Phascolarctobacterium faecium*, a member of the genus *Roseburia*, *Roseburia faecalis*, *Roseburia faecis*, *Roseburia hominis*, *Roseburia intestinalis*, a member of the genus *Ruminococcus*, *Ruminococcus albus*, *Ruminococcus bromii*, *Ruminococcus lactaris*, *Ruminococcus luti*, *Ruminococcus obeum*, *Ruminococcus torques*, a member of the genus Staphylococcus, *Staphylococcus epidermidis*, a member of the genus *Streptococcus*, *Streptococcus mitis*, *Streptococcus thermophilus*, a member of the genus *Synergistes*, a member of the genus *Turicibacter*, and *Turicibacter sanguinis*.

[00222] In embodiments, a bacterial isolate incorporated into a pharmaceutical composition can act through multiple mechanisms to advantageously impact the health of a subject. Such a bacterial isolate can therefore advantageously influence the health of a subject administered the cocktail (e.g., in the form of a pharmaceutical composition) via multiple mechanisms. For example, a pharmaceutical composition can comprise a bacterial isolate that when administered to a subject can produce one or more SCFAs to increase a level of SCFAs (e.g., butyrate) in

the gut of the subject ('Table 2 bacterial isolate'), and can also modulate production and/or release of a cytokine by a host cell of the subject ('Table 3 bacterial isolate'). In another example, a pharmaceutical composition can comprise a bacterial isolate that when administered to a subject can produce one or more SCFAs to increase a level of SCFAs (e.g., butyrate) in the gut of the subject ('Table 2 bacterial isolate'), and also corresponds to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC ('Table 4 bacterial isolate'). In another example, a pharmaceutical composition can comprise a bacterial isolate that when administered to a subject can modulate production and/or release of a cytokine by a host cell of the subject ('Table 3 bacterial isolate'), and also correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC ('Table 4 bacterial isolate'). In another example, a pharmaceutical composition can comprise a bacterial isolate that when administered to a subject can produce one or more SCFAs to increase a level of SCFAs (e.g., butyrate) in the gut of the subject ('Table 2 bacterial isolate'), can also modulate production and/or release of a cytokine by a host cell of the subject ('Table 3 bacterial isolate'), and also corresponds to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC ('Table 4 bacterial isolate').

[00223] Table 44 illustrates exemplary bacterial isolates capable of positively affecting the health of a subject via multiple mechanisms (e.g., production of SCFAs, induction of cytokine release by host cells, or providing bacteria in the gut that correspond to bacterial strains more highly abundant in a healthy subject relative to a patient with UC). In Table 44, isolates are identified by Latin name, an Identification Number (ID number), the Sequence Identifier (SEQ ID NO) for its 16S rRNA sequence, and the above Tables 2-4 in which the bacterial isolate appears (with Table 2 representing bacterial isolates that secrete SCFAs in the gut of a subject, Table 3 representing bacterial isolates capable of modulating cytokine production by a host cell, Table 4 representing bacterial isolates corresponding to bacterial strains more highly abundant in a healthy subject than a patient with UC), and Table 6 representing bacterial isolates that secrete an aryl hydrocarbon for binding to an AhR of a cell of the subject). In certain embodiments, a pharmaceutical composition (e.g., a microbial cocktail) comprises one or more bacterial isolates provided in Table 44, and/or one or more bacterial isolates having a 16S rRNA sequence that is at least 95% identical to the 16S rRNA sequence of one or more of the bacterial isolates provided in Table 44.

Table 44

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Table*
Faecalibacterium prausnitzii	PI00000329	1	2, 3, 4
Odoribacter splanchnicus	PI00000072	2	2, 3, 4, 6
Anaerostipes hadrus	PI00000094	3	2, 3, 4
Parabacteroides merdae	IS00006167	5	4, 6
Dorea longicatena	IS00006618	6	4, 6
Faecalibacterium prausnitzii	IS00006632	7	2, 3, 4
Eubacterium rectale	IS00006864	8	2, 4
Bacteroides uniformis	PI00000137	11	3, 4, 6
Bacteroides vulgatus	PI00000138	12	3, 4
Bacteroides uniformis	PI00000352	16	3, 4, 6
Coprococcus comes	PI00000370	17	2, 3
Alistipes shahii	PI00000395	18	3, 4
Bacteroides stercoris	PI00000146	13	3, 6
Clostridium aldenense	PI00000097	10	3, 6
Subdoligranulum variabile	IS00007359	22	2, 4
Subdoligranulum variabile	IS00007357	23	2, 4

* Table 2: Bacterial isolates that secrete SCFAs in the gut of a subject.
Table 3: Bacterial isolates capable of modulating cytokine production by a host cell of a subject.
Table 4: Bacterial isolates that correspond to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC.
Table 6: Bacterial isolates that secrete a ligand for an AhR of a host cell.

[00224] In embodiments, a bacterial isolate can comprise a 16S rRNA sequence that is at least 70%, at least 71%, at least 72%, at least 73%, at least 74%, at least 75%, at least 76%, at least 77%, at least 78%, at least 79%, at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the 16S rRNA sequence of at least one of the bacterial isolates provided in Table 1 to Table 44. In embodiments, a bacterial isolate comprises a 16S rRNA sequence that is at least 97% identical to the 16S rRNA sequence of at least one of the bacterial isolates provided in Table 1 to Table 44.

[00225] In embodiments, a pharmaceutical composition (e.g., comprising a microbial cocktail) described herein can comprise at least one bacterial isolate that has been previously identified. For example, in certain embodiments a known type strain (e.g., from the ATCC or DSM archived collections) can comprise a 16S rRNA sequence that is at least 95% identical (e.g., at least 97% identical) to a 16S rRNA sequence of a bacterial isolate provided in Table 1 to Table 44. Exemplary publicly available strains that can be included in a microbial cocktail described

herein are provided in Table 45. In an embodiment, for a particular pharmaceutical composition, one or more bacterial isolates provided in Table 1 to Table 44 can be substituted with the corresponding representative strain (i.e., having the same taxonomic designation) from Table 45.

Table 45

Isolate Latin Name	Representative Strain*
Faecalibacterium prausnitzii	ATCC 27768
Odoribacter splanchnicus	ATCC 29572
Odoribacter laneus	DSM 22474
Anaerostipes hadrus	DSM 3319
Alistipes onderdonkii	ATCC BAA-1178
Parabacteroides merdae	ATCC 43184
Dorea longicatena	DSM 13814
Eubacterium rectale	ATCC 33656
Blautia obeum	DSM 25238
Clostridium aldenense	DSM 19262
Bacteroides uniformis	ATCC 8492
Bacteroides vulgatus	DSM 1447
Bacteroides stercoris	ATCC 43183
Bacteroides cellulosilyticus	DSM 14838
Alistipes finegoldii	DSM 17242
Coprococcus comes	ATCC 27758
Alistipes shahii	ATCC BAA-1179
Roseburia faecis	DSM 16840
Akkermansia muciniphila	DSM 22959
Phascolarctobacterium faecium	DSM 14760
Subdoligranulum variabile	DSM 15176
Alistipes putredinis	ATCC 29800

* DSM: Leibniz Institute DSMZ-German Collection of Microorganisms and Cell Cultures
ATCC: American Type Culture Collection

[00226] In embodiments, a pharmaceutical composition or microbial cocktail comprises a plurality of bacterial isolates isolated or purified from stool samples of multiple different human donors. An advantage of sourcing bacterial isolates from stool samples of multiple human donors, rather than a single donor, is that stool samples of multiple donors offer a larger pool of bacterial strains that can be subjected to functional screens to identify bacterial isolates that optimally induce a particular mechanism of interest. For example, while the stool of one donor may carry one or more bacterial strains that produce a high (optimal) level of an SCFA

(e.g., butyrate), the same donor's stool may carry bacterial isolates that only moderately induce an anti-inflammatory profile (e.g. moderate IL-10:IL-12 ratio) when subjected to a functional screen. Alternatively, a different donor's stool may carry one or more bacterial strains that induce an optimal anti-inflammatory profile (e.g. high IL-10:IL-12 ratio), but not carry bacterial strains that produce high levels of an SCFA.

[00227] Another advantage of using stool from multiple different donors as a basis of selection when identifying bacterial isolates to include within a pharmaceutical composition described herein is that microbiota from multiple donors yields a larger pool of bacterial strains within which to identify a bacterial isolate corresponding to a bacterial strain having (i) a greater relative abundance in a healthy human subject relative to a patient with an intestinal dysbiosis, or (ii) a greater relative abundance in a human subject in remission from an intestinal dysbiosis relative to a patient having the intestinal dysbiosis (i.e., bacterial isolates provided in Table 4). In general, the match between a 16S rRNA sequence of a bacterial strain having (i) or (ii) above and the 16S rRNA sequence of a selected bacterial isolate should be as close as possible (e.g., at least 97%, at least 97.5%, at least 98%, at least 98.5%, at least 99%, at least 99.5%, or at least 100%). The likelihood of identifying the desired match increases with a greater pool of bacterial strains to select from, which is provided by sourcing stool from multiple donors.

[00228] Therefore, in general, the rational mechanism-based selection scheme set out herein to construct a microbial therapeutic favors increasing the pool of bacterial strains beyond those of a single donor to enable selection of optimal bacterial isolates for induction of each mechanism of interest in a subject administered the therapeutic. This multi-donor selection process is therefore advantageous over known approaches which attempt to recreate a synthetic version of a single donor's stool.

[00229] In other embodiments, a pharmaceutical composition or microbial cocktail comprises a plurality of bacterial isolates isolated or purified from a stool sample or stool samples of only a single human donor.

[00230] In various embodiments, a pharmaceutical composition (e.g., comprising a microbial cocktail) comprises one or more bacterial isolates capable of engrafting in a subject's GI tract following administration of the composition to the subject. Herein "engrafting" or "engraftment" refers to the stable presence over time of cells of a bacterial strain or bacterial isolate in the intestinal tract of a subject (e.g., after introducing the bacterial strain or isolate into the subject's intestinal tract by administering a composition described herein, for example,

orally or rectally). Typically, engraftment of a bacterial isolate introduced into the intestine of a patient (e.g. by oral and/or rectal administration) is measured longitudinally, or over time, by comparing the abundance of the bacterial isolate in fecal samples of the subject before and after administration of the bacterial isolate to the subject. In an embodiment, the bacterial isolate introduced into the intestine of the subject was absent prior to the administration. In another embodiment, the bacterial isolate introduced into the intestine of the subject was present in the intestine prior to the administration, but is increased abundance following the administration. In certain embodiments, engraftment is determined by identifying an increase in abundance of a bacterial strain administered to an intestine of the subject after at least 1 day, at least 2 days, at least 3 days, at least 4 days, at least 5 days, at least 6 days, at least 7 days, at least 8 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14, days, at least 1 week, at least 2 weeks, at least 3 weeks, at least 4 weeks, at least 5 weeks, at least 6 weeks, at least 7 weeks, at least 8 weeks, at least 1 month, at least 2 months, at least 3 months, at least 4 months, at least 5 months, at least 6 months, or greater than 6 months following administration of the bacterial strain to the subject.

[00231] In embodiments, engraftment of a bacterial isolate in an intestine of a subject occurs when the bacterial isolate is administered to the subject at or above a threshold dose. In embodiments, engraftment of a bacterial isolate in an intestine of a subject does not occur, or occurs with relative inefficiency (e.g., across patients), when the bacterial isolate is administered to the subject below the threshold dose. For example, engraftment of a bacterial isolate into the intestine of a subject can occur when the bacterial isolate is administered to the subject (e.g., orally or rectally in a pharmaceutical composition described herein) at a dose of at least 10^6 cells, at least 10^7 cells, at least 10^8 cells, at least 10^9 cells, at least 10^{10} cells, at least 10^{11} cells, or at least 10^{12} cells.

[00232] In embodiments, engraftment of a bacterial isolate in an intestine of a subject occurs when the bacterial isolate is administered to the subject at or below a threshold dose. In embodiments, engraftment of a bacterial isolate in an intestine of a subject does not occur, or occurs with relative inefficiency (e.g., across patients), when the bacterial isolate is administered to the subject above the threshold dose. For example, engraftment of a bacterial isolate into the intestine of a subject can occur when the bacterial isolate is administered to the subject (e.g., orally or rectally in a pharmaceutical composition described herein) at a dose of not more than 10^8 cells, not more than 10^9 cells, not more than 10^{10} cells, not more than 10^{11} cells, or not more than 10^{12} cells.

[00233] In embodiments, a dose of one or more bacterial isolates to a patient in need thereof can depend on the engraftment threshold of the bacterial isolate.

[00234] In embodiments, a bacterial isolate in a pharmaceutical composition administered to a subject engrafts in the duodenum of the subject. In embodiments, a bacterial isolate in a pharmaceutical composition administered to a subject engrafts in the jejunum of the subject. In embodiments, a bacterial isolate in a pharmaceutical composition administered to a subject engrafts in the ileum of the subject. In embodiments, a bacterial isolate in a pharmaceutical composition administered to a subject engrafts in the colon of the subject.

[00235] In various embodiments, the present pharmaceutical compositions (e.g., microbial cocktails) includes one or more bacterial isolates that interact, including synergistically, to have an inhibitory effect on the growth and/or survival of a pathogenic bacterium present in a gut of a subject administered the composition. For example, one or more bacterial isolates can have a cytotoxic or cytostatic effect on the pathogenic bacterium. In various embodiments, one or more bacterial isolates exert an inhibitory effect on a pathogenic bacterium present in or entering into the GI tract of a patient. In various embodiments, the one or more bacterial isolates augment growth of at least one type of bacteria not detectably present in a patient's GI tract prior to administration.

[00236] In various embodiments, a pharmaceutical composition (e.g., comprising a microbial cocktail) includes one or more isolated or purified bacterial strains that interact synergistically to have an inhibitory effect on the growth or survival of a pathogenic bacterium (e.g., via cytotoxic and/or cytostatic effects). Illustrative pathogenic bacteria that can be affected by administration of one or more bacterial isolates described herein include *C. difficile, Salmonella* sp., enteropathogenic *E. coli*, multi-drug resistant bacteria such as *Klebsiella*, and *E. coli*, Carbapenem-resistant Enterobacteriaceae (CRE), extended spectrum beta-lactam resistant *Enterococci* (ESBL), and vancomycin-resistant *Enterococci* (VRE). Further illustrative bacteria include *Yersinia, Vibrio, Treponema, Streptococcus, Staphylococcus, Shigella, Salmonella, Rickettsia, Orientia, Pseudomonas, Neisseria, Mycoplasma, Mycobacterium, Listeria, Leptospira, Legionella, Klebsiella, Helicobacter, Haemophilus, Francisella, Escherichia, Ehrlichia, Enterococcus, Coxiella, Corynebacterium, Clostridium, Chlamydia, Chlamydophila, Campylobacter, Burkholderia, Brucella, Borrelia, Bordetella, Bifidobacterium, Bacillus*, multi-drug resistant bacteria, extended spectrum beta-lactam resistant *Enterococci* (ESBL), Carbapenem-resistant Enterobacteriaceae (CRE), and vancomycin-resistant *Enterococci* (VRE). Illustrative pathogenic bacteria include *Aeromonas*

hydrophila, Campylobacter fetus, Plesiomonas shigelloides, Bacillus cereus, Campylobacter jejuni, Clostridium botulinum, Clostridium difficile, Clostridium perfringens, enteroaggregative *Escherichia coli*, enterohemorrhagic *Escherichia coli*, enteroinvasive *Escherichia coli*, enterotoxigenic *Escherichia coli* (such as, but not limited to, LT and/or ST), *Escherichia coli* 0157:H7, *Helicobacter pylori, Klebsiellia pneumonia, Lysteria monocytogenes, Plesiomonas shigelloides, Salmonella* sp., *Salmonella typhi, Salmonella paratyphi, Shigella* sp., *Staphylococcus* sp., *Staphylococcus aureus*, vancomycin-resistant *enterococcus* sp., *Vibrio* sp., *Vibrio cholerae, Vibrio parahaemolyticus, Vibrio vulnificus*, and *Yersinia enterocolitica.*

[00237] In some embodiments, a bacterial isolate is a non-pathogenic bacterial strain. In embodiments, a non-pathogenic bacterial strain comprises a genome that lacks genes, or expression thereof, which cause virulence and/or toxicity. For instance, in some embodiments, a microbial cocktail comprising two or more bacterial isolates is substantially free of organisms or entities (e.g., substantially free of pathogenic bacteria) which are capable of causing a disease or disorder in a subject administered the microbial cocktail.

[00238] In embodiments, the microbial cocktail does not include bacterial cells other than the one or more bacterial isolates incorporated into the microbial cocktail during the manufacturing process. For example, the microbial cocktail can be free of particular species of bacteria, whether cultured or uncultured, including *Bacteroides, Bifidobacterium, Desulfomonas, Clostridium, Escherichia coli, Eubacterium, Fusobacterium, Lactobacillus, Monilia, Peptostreptococcus, Propionibacterium,* or *Ruminococcus.*

[00239] In embodiments, a bacterial isolate can be obtained from a laboratory stock or a bacterial cell bank of a bacterial strain originally obtained from a stool sample of a healthy human donor. For example, a fecal microbiota (e.g., purified from a stool sample using methods described herein) can be used as the source of a bacterial isolate incorporated into a pharmaceutical composition described herein. In certain embodiments, all or a portion of a fecal microbiota of a stool sample is cultured on a solid media substrate and one or more bacterial isolates are identified as single colonies. In other embodiments, all or a portion of a fecal microbiota can be inoculated into liquid culture to produce a mixed bacterial culture that is then serially diluted to produce a culture containing a single cell of a bacterial isolate. In embodiments, an identified bacterial isolate can then be cultured (e.g., in solid or liquid media) using known techniques and expanded. Methods for isolating, purifying, and/or culturing

bacterial strains are described in Sadowsky *et al.*, WO 2012/122478 and described in Borody *et al.*, WO 2012/016287, each of which is incorporated herein by reference.

Uncultured fecal microbiota or preparations of uncultured fecal bacteria

[00240] In one aspect, a pharmaceutical composition administered herein comprises an uncultured fecal microbiota or a preparation of uncultured fecal bacteria. For example, an uncultured fecal microbiota can comprise a substantially complete fecal microbiota (e.g., purified from a healthy human donor).

[00241] In embodiments, the preparation of a fecal microbiota used herein, or the manufacture of a preparation of uncultured fecal bacteria, involves a treatment selected from the group consisting of ethanol treatment, detergent treatment, heat treatment, irradiation, and sonication. In another aspect, the preparation of a fecal microbiota or manufacture of a preparation of uncultured fecal bacteria used herein involves no treatment selected from the group consisting of ethanol treatment, detergent treatment, heat treatment, irradiation, and sonication. In one aspect, the preparation of a fecal microbiota or manufacture of a preparation of uncultured fecal bacteria used herein involves a separation step selected from the group consisting of density gradients, filtration (*e.g.*, sieves, nylon mesh), and chromatography. In another aspect, the preparation of a fecal microbiota or manufacture of a preparation of uncultured fecal bacteria used herein involves no separation step selected from the group consisting of density gradients, filtration (*e.g.*, sieves, nylon mesh), and chromatography. In another aspect, a fecal microbiota or preparation of uncultured fecal bacteria used herein comprises a donor's entire fecal microbiota. In another aspect, a pharmaceutical composition administered herein comprises a fecal microbiota or preparation of uncultured fecal bacteria substantially free of eukaryotic cells.

[00242] In another aspect, a pharmaceutical composition administered herein comprises an uncultured fecal microbiota, or a preparation of uncultured fecal bacteria, further supplemented, spiked, or enhanced with one or more bacterial isolates described herein. In one aspect, an uncultured fecal microbiota is spiked with a bacterial isolate provided in Table 1. In one aspect, an uncultured fecal microbiota, or a preparation of uncultured fecal bacteria, is supplemented with a non-pathogenic (or with attenuated pathogenicity) bacterium of *Clostridium*, *Collinsella*, *Dorea*, *Ruminococcus*, *Coprococcus*, *Prevotella*, *Veillonella*, *Bacteroides*, *Baccillus*, or a combination thereof. In another aspect, a pharmaceutical composition administered herein comprises an uncultured fecal microbiota or a preparation of uncultured fecal bacteria further

supplemented, spiked, or enhanced with a species of *Veillonellaceae*, *Firmicutes*, *Gammaproteobacteria*, *Bacteroidetes*, or a combination thereof. In another aspect, a pharmaceutical composition administered herein comprises an uncultured fecal microbiota or a preparation of uncultured fecal bacteria further supplemented with fecal bacterial spores. In one aspect, fecal bacterial spores are *Clostridium* spores, *Bacillus* spores, or both.

[00243] In an aspect, a pharmaceutical composition comprises an uncultured fecal microbiota a preparation of uncultured fecal bacteria from a subject selected from the group consisting of a human, a bovine, a dairy calf, a ruminant, an ovine, a caprine, or a cervine. In another aspect, a pharmaceutical composition can be administered to a subject selected from the group consisting of a human, a bovine, a dairy calf, a ruminant, an ovine, a caprine, or a cervine. In an aspect, a pharmaceutical composition is substantially or nearly odorless.

[00244] In an aspect, a pharmaceutical composition provided or administered herein comprises an uncultured fecal microbiota a preparation of uncultured fecal bacteria comprising a Shannon Diversity Index of greater than or equal to 0.3, greater than or equal to 0.4, greater than or equal to 0.5, greater than or equal to 0.6, greater than or equal to 0.7, greater than or equal to 0.8, greater than or equal to 0.9, greater than or equal to 1.0, greater than or equal to 1.1, greater than or equal to 1.2, greater than or equal to 1.3, greater than or equal to 1.4, greater than or equal to 1.5, greater than or equal to 1.6, greater than or equal to 1.7, greater than or equal to 1.8, greater than or equal to 1.9, greater than or equal to 2.0, greater than or equal to 2.1, greater than or equal to 2.2, greater than or equal to 2.3, greater than or equal to 2.4, greater than or equal to 2.5, greater than or equal to 3.0, greater than or equal to 3.1, greater than or equal to 3.2, greater than or equal to 3.3, greater than or equal to 3.4, greater than or equal to 3.5, greater than or equal to 3.6, greater than or equal to 3.7, greater than or equal to 3.8, greater than or equal to 3.9, greater than or equal to 4.0, greater than or equal to 4.1, greater than or equal to 4.2, greater than or equal to 4.3, greater than or equal to 4.4, greater than or equal to 4.5, or greater than or equal to 5.0. In another aspect, a pharmaceutical composition comprises fecal microbiota comprising a Shannon Diversity Index of between 0.1 and 3.0, between 0.1 and 2.5, between 0.1 and 2.4, between 0.1 and 2.3, between 0.1 and 2.2, between 0.1 and 2.1, between 0.1 and 2.0, between 0.4 and 2.5, between 0.4 and 3.0, between 0.5 and 5.0, between 0.7 and 5.0, between 0.9 and 5.0, between 1.1 and 5.0, between 1.3 and 5.0, between 1.5 and 5.0, between 1.7 and 5.0, between 1.9 and 5.0, between 2.1 and 5.0, between 2.3 and 5.0, between 2.5 and 5.0, between 2.7 and 5.0, between 2.9 and 5.0, between 3.1 and 5.0, between 3.3 and 5.0, between 3.5 and 5.0, between 3.7 and 5.0, between 31.9 and 5.0, or between 4.1

and 5.0. In one aspect, a Shannon Diversity Index is calculated at the phylum level. In another aspect, a Shannon Diversity Index is calculated at the family level. In one aspect, a Shannon Diversity Index is calculated at the genus level. In another aspect, a Shannon Diversity Index is calculated at the species level. In a further aspect, a pharmaceutical composition comprises a preparation of flora in proportional content that resembles a normal healthy human fecal flora.

[00245] In a further aspect, a pharmaceutical composition comprises fecal bacteria from at least 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 different families. In another aspect, a pharmaceutical composition comprises fecal bacteria from at least 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 different families. In yet another aspect, a pharmaceutical composition comprises fecal bacteria from at least 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 different families. In a further aspect, a pharmaceutical composition comprises fecal bacteria from at least 31, 32, 33, 34, 35, 36, 37, 38, 39, or 40 different families. In another aspect, a pharmaceutical composition comprises fecal bacteria from at least 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 different families. In another aspect, a pharmaceutical composition comprises fecal bacteria from between 1 and 10, between 10 and 20, between 20 and 30, between 30 and 40, between 40 and 50 different families. In an aspect, a pharmaceutical composition provided or administered herein comprises an uncultured fecal microbiota a preparation of uncultured fecal bacteria a preparation of uncultured fecal bacteria comprising no greater than 0.05%, 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, or 10% weight non-living material/weight biological material. In another aspect, a pharmaceutical composition provided or administered herein comprises an uncultured fecal microbiota a preparation of uncultured fecal bacteria comprising no greater than 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95% weight non-living material/weight biological material. In another aspect, a pharmaceutical composition provided or administered herein comprises, consists of, or consists essentially of, particles of non-living material and/or particles of biological material of a fecal sample that passes through a sieve, a column, or a similar filtering device having a sieve, exclusion, or particle filter size of 2.0 mm, 1.0 mm, 0.5 mm, 0.33mm, 0.25 mm, 0.212 mm, 0.180 mm, 0.150 mm, 0.125 mm, 0.106 mm, 0.090 mm, 0.075 mm, 0.063 mm, 0.053 mm, 0.045 mm, 0.038 mm, 0.032 mm, 0.025 mm, 0.020 mm, 0.01 mm, or 0.002 mm. "Non-living material" does not include an excipient, *e.g.*, a pharmaceutically inactive substance, such as a cryoprotectant, added to a processed fecal material. "Biological material" refers to the living material in fecal material, and includes microbes including prokaryotic cells, such as bacteria and archaea (*e.g.*, living prokaryotic cells and spores that can sporulate to

become living prokaryotic cells), eukaryotic cells such as protozoa and fungi, and viruses. In one embodiment, "biological material" refers to the living material, *e.g.*, the microbes, eukaryotic cells, and viruses, which are present in the colon of a normal healthy human. In an aspect, a pharmaceutical composition provided or administered herein comprises an extract of human stool, wherein the composition is substantially odorless. In an aspect, a pharmaceutical composition provided or administered herein comprises fecal material or a fecal floral preparation in a lyophilized, crude, semi-purified or purified formulation.

[00246] In an aspect, an uncultured fecal microbiota or a preparation of uncultured fecal bacteria in a pharmaceutical composition comprises highly refined or purified fecal flora, *e.g.*, substantially free of non-floral fecal material. In an aspect, an uncultured fecal microbiota or a preparation of uncultured fecal bacteria can be further processed, *e.g.*, to undergo microfiltration before, after, or before and after sieving. In another aspect, a highly purified fecal microbiota product is ultra-filtrated to remove large molecules but retain the therapeutic microflora, *e.g.*, bacteria.

[00247] In another aspect, an uncultured fecal microbiota or a preparation of uncultured fecal bacteria in a pharmaceutical composition used herein comprises or consists essentially of a substantially isolated or a purified fecal flora or entire (or substantially entire) microbiota that is (or comprises) an isolate of fecal flora that is at least about 90%, 91 %, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.6%, 99.7%, 99.8% or 99.9% isolated or pure, or having no more than about 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9% or 1.0% or more non-fecal floral material; or, a substantially isolated, purified, or substantially entire microbiota as described in Sadowsky *et al.*, WO 2012/122478 A1, or as described in Borody *et al.*, WO 2012/016287 A2.

[00248] In an aspect, an uncultured fecal microbiota or a preparation of uncultured fecal bacteria in a pharmaceutical composition comprises a donor's substantially entire or non-selected fecal microbiota. In another aspect, the fecal microbiota in a pharmaceutical composition comprises no antibiotic resistant population. In another aspect, a pharmaceutical composition comprises an uncultured fecal microbiota or a preparation of uncultured fecal bacteria and is largely free of extraneous matter (*e.g.*, non-living matter including acellular matter such as residual fiber, DNA, RNA, viral coat material, non-viable material; and living matter such as eukaryotic cells from the fecal matter's donor).

[00249] In an aspect, an uncultured fecal microbiota or a preparation of uncultured fecal bacteria in a pharmaceutical composition used herein is derived from a disease-screened stool sample of a human donor. In an aspect, a stool sample does not include an antibiotic resistant population. For example, a fecal composition can comprise a preparation of viable flora which can in proportional content, resemble normal healthy human fecal flora which does not include antibiotic resistant populations. Suitable microorganisms in a flora can be selected from the following: *Bacteroides*, *Eubacterium*, *Fusobacterium*, *Propionibacterium*, *Lactobacillus*, *Ruminococcus, Escherichia coli, Gemmiger, Clostridium, Desulfomonas, Peptostreptococcus, Bifidobacterium, Collinsella, Coprococcus, Dorea,* and *Ruminococcus.*

[00250] In an aspect, a pharmaceutical composition used in a treatment disclosed herein comprises a sterile fecal filtrate or a non-cellular fecal filtrate. In one aspect, a sterile fecal filtrate originates from a donor stool. In another aspect, a sterile fecal filtrate originates from cultured microorganisms. In another aspect, a sterile fecal filtrate comprises a non-cellular non-particulate fecal component. In one aspect, a sterile fecal filtrate is made as described in WO2014/078911, published May 30, 2014. In another aspect, a sterile fecal filtrate is made as described in Ott *et al., Gastroenterology* 152:799-911(2017).

[00251] In one aspect, a fecal filtrate comprises secreted, excreted or otherwise liquid components or a microbiota, e.g., biologically active molecules (BAMs), which can be antibiotics or anti-inflammatories, are preserved, retained or reconstituted in a flora extract.

[00252] In one aspect, an exemplary pharmaceutical composition comprising a fecal filtrate comprises starting material from a donor from a defined donor pool, where this donor contributes a stool that is centrifuged, then filtered with very high-level filtration using *e.g.*, either metal sieving or Millipore filters, or equivalent, to ultimately permit only cells of bacterial origin to remain, *e.g.*, often less than about 5 micrometers diameter. After the initial centrifugation, the solid material can be separated from the liquid, and the solid is then filtered in progressively reducing size filters and tangential filters, *e.g.*, using a Millipore filtration, and optionally, also comprising use of nano-membrane filtering. The filtering can also be done by sieves as described in WO 2012/122478, but in contrast using sieves that are smaller than .0120 mm, down to about .0110 mm, which ultimately result in having only bacterial cells present.

[00253] The supernatant separated during centrifugation can be filtered progressively in a filtering, e.g., a Millipore filtering or equivalent systems, to produce a liquid which is finely filtered through an about 0.22 micron filter. This removes all particulate matter including all

living matter, including bacteria and viruses. The product then is sterile, but the aim is to remove the bacteria but to keep their secretions, especially antimicrobial bacteriocins, bacteria-derived cytokine-like products and all accompanying Biologically Active Molecules (BAMs), including: thuricin (which is secreted by bacilli in donor stools), bacteriocins (including colicin, troudulixine or putaindicine, or microcin or subtilosin A), lanbiotics (including nisin, subtilin, epidermin, mutacin, mersacidin, actagardine, cinnamycin), lacticins and other antimicrobial or anti-inflammatory compounds.

[00254] In one aspect, a pharmaceutical composition used herein comprises a reconstituted fecal flora consisting essentially of a combination of a purified fecal microbiota and a non-cellular fecal filtrate. In another aspect, a pharmaceutical composition used herein comprises a purified fecal microbiota supplemented with one or more non-cellular non-particulate fecal components. In one aspect, a pharmaceutical composition used here comprises one or more non-cellular non-particulate fecal components. In one aspect, one or more non-cellular non-particulate fecal components comprise synthetic molecules, biologically active molecules produced by a fecal microorganism, or both. In another aspect, one or more non-cellular non-particulate fecal components comprise biologically active proteins or peptides, micronutrients, fats, sugars, small carbohydrates, trace elements, mineral salts, ash, mucous, amino acids, nutrients, vitamins, minerals, or any combination thereof. In one aspect, one or more non-cellular non-particulate fecal components comprise one or more biologically active molecules selected from the group consisting of bacteriocin, lanbiotic, and lacticin. In another aspect, one or more non-cellular non-particulate fecal components comprise one or more bacteriocins selected from the group consisting of colicin, troudulixine, putaindicine, microcin, and subtilosin A. In one aspect, one or more non-cellular non-particulate fecal components comprise one or more lanbiotics selected from the group consisting of thuricin, nisin, subtilin, epidermin, mutacin, mersacidin, actagardine, and cinnamycin. In another aspect, one or more non-cellular non-particulate fecal components comprise an anti-spore compound, an antimicrobial compound, an anti-inflammatory compound, or any combination thereof. In a further aspect, one or more non-cellular non-particulate fecal components comprise an interleukin, a cytokine, a leukotriene, an eicosanoid, or any combination thereof.

[00255] In another aspect, a treatment method provided here comprises the use of both fecal bacterial cells, e.g., a partial or a complete representation of the human GI microbiota, and an isolated, processed, filtered, concentrated, reconstituted and/or artificial liquid component (e.g., fecal filtrate) of the flora (the microbiota) which comprises, among others ingredients, bacterial

secretory products such as *e.g.*, bacteriocins (proteinaceous toxins produced by bacteria, including colicin, troudulixine or putaindicine, or microcin or subtilosin A), lanbiotics (a class of peptide antibiotics that contain a characteristic polycyclic thioether amino acid lanthionine or methyllanthionine, and unsaturated amino acids dehydroalanine and 2-aminoisobutyric acid; which include thuricin (which is secreted by bacilli in donor stools), nisin, subtilin, epidermin, mutacin, mersacidin, actagardine, cinnamycin), a lacticin (a family of pore-forming peptidic toxins) and other antimicrobial or anti-inflammatory compounds and/or additional biologically active molecules (BAMs) produced by bacteria or other microorganisms of the microbiota, and/or which are found in the "liquid component" of a microbiota.

[00256] In one aspect, a fecal bacteria-based pharmaceutical composition is used concurrently with a fecal non-cellular filtrate-based pharmaceutical composition. In another aspect, a patient is treated with a first fecal non-cellular filtrate-based pharmaceutical composition before being given a second fecal bacteria-based pharmaceutical composition, or vice versa. In a further aspect, a treatment method comprises three steps: first, antibiotic pretreatment to non-selectively remove infectious pathogen(s); second, a fecal non-cellular filtrate-based treatment step to further suppress selected infectious pathogen(s); and third, giving the patient a fecal bacteria-based pharmaceutical composition to re-establish a functional intestinal microbiome.

[00257] In an aspect, a treatment method effects a cure, reduction of the symptoms, or a percentage reduction of symptoms of a disorder related to an intestinal dysbiosis. The change of flora can be as "near-complete" as possible and the flora is replaced by viable organisms which will crowd out any remaining, original flora. Typically, the change in enteric flora comprises introduction of an array of predetermined flora into the gastro-intestinal system, and thus in a preferred form the method of treatment comprises substantially or completely displacing pathogenic enteric flora in patients requiring such treatment.

[00258] In an aspect, uncultured fecal microbiota or a preparation of uncultured fecal bacteria for incorporation into a pharmaceutical composition comprises non-pathogenic spores of one or more, two or more, three or more, or four or more *Clostridium* species selected from the group consisting of *Clostridium absonum, Clostridium argentinense, Clostridium baratii, Clostridium botulinum, Clostridium cadaveris, Clostridium carnis, Clostridium celatum, Clostridium chauvoei, Clostridium clostridioforme, Clostridium cochlearium, Clostridium fallax, Clostridium felsineum, Clostridium ghonii, Clostridium glycolicum, Clostridium haemolyticum, Clostridium hastiforme, Clostridium histolyticum, Clostridium indolis, Clostridium irregulare, Clostridium limosum, Clostridium malenominatum, Clostridium novyi,*

Clostridium oroticum, Clostridium paraputrificum, Clostridium perfringens, Clostridium piliforme, Clostridium putrefaciens, Clostridium putrificum, Clostridium sardiniense, Clostridium sartagoforme, Clostridium scindens, Clostridium septicum, Clostridium sordellii, Clostridium sphenoides, Clostridium spiroforme, Clostridium sporogenes, Clostridium subterminale, Clostridium symbiosum, Clostridium tertium, Clostridium tetani, Clostridium welchii, and *Clostridium villosum*.

[00259] In an aspect, uncultured fecal microbiota or a preparation of uncultured fecal bacteria for incorporation into a pharmaceutical composition comprises purified, isolated, or cultured viable non-pathogenic *Clostridium* and a plurality of purified, isolated, or cultured viable non-pathogenic microorganisms from one or more genera selected from the group consisting of *Collinsella, Coprococcus, Dorea, Eubacterium,* and *Ruminococcus*. In another aspect, a pharmaceutical composition comprises a plurality of purified, isolated, or cultured viable non-pathogenic microorganisms from one or more genera selected from the group consisting of *Clostridium, Collinsella, Coprococcus, Dorea, Eubacterium,* and *Ruminococcus*.

[00260] In an aspect, uncultured fecal microbiota or a preparation of uncultured fecal bacteria for incorporation into a pharmaceutical composition comprises two or more genera selected from the group consisting of *Collinsella, Coprococcus, Dorea, Eubacterium,* and *Ruminococcus*. In another aspect, a pharmaceutical composition comprises two or more genera selected from the group consisting of *Coprococcus, Dorea, Eubacterium,* and *Ruminococcus*. In a further aspect, a pharmaceutical composition comprises one or more, two or more, three or more, four or more, or five or more species selected from the group consisting of *Coprococcus catus, Coprococcus comes, Dorea longicatena, Eubacterium eligens, Eubacterium hadrum, Eubacterium hallii, Eubacterium rectale,* and *Ruminococcus torques*.

[00261] In one aspect, an uncultured fecal microbiota or a preparation of uncultured fecal bacteria for incorporation into a pharmaceutical composition described herein comprises at least about 10^5, 10^6, 10^7, 10^8, 10^9, 10^{10}, 10^{11}, 10^{12}, or 10^{13} cfu or total cell count. In another aspect, a pharmaceutical composition comprises at most about 10^5, 10^6, 10^7, 10^8, 10^9, 10^{10}, 10^{11}, 10^{12}, 10^{13} or 10^{14} cfu or total cell count.

[00262] In another aspect, an uncultured fecal microbiota or a preparation of uncultured fecal bacteria comprises at least about 10^5, 10^6, 10^7, 10^8, 10^9, 10^{10}, 10^{11}, 10^{12}, or 10^{13} cells or total cell count. In another aspect, a pharmaceutical composition comprises at most about 10^5, 10^6, 10^7, 10^8, 10^9, 10^{10}, 10^{11}, 10^{12}, 10^{13} or 10^{14} cells or total cell count.

Extraction and purification of bacteria from stool

[00263] The pharmaceutical compositions described here can comprise microbes, e.g. bacteria, derived from a stool sample of a donor, e.g. a healthy human donor. In an aspect, a composition incorporates all or a portion of a fecal microbiota of a stool sample. For example, a composition can incorporate a substantially complete fecal microbiota of a stool sample of a healthy human donor. In an aspect, a composition incorporates a bacterial isolate of a fecal microbiota, wherein the bacterial isolate has been purified and/or cultured from all or a portion of the fecal microbiota. The extraction and/or purification of a fecal microbiota from a stool sample can thus be performed to prepare a composition comprising at least one of a fecal microbiota (e.g., a substantially complete fecal microbiota) or a bacterial isolate.

[00264] In one aspect, an exemplary fecal microbiota for use in preparing a composition described herein comprises starting material from a human donor. In another aspect, an exemplary fecal microbiota comprises material from one or more healthy human donors. In yet another aspect, an exemplary fecal microbiota comprises starting material from a pool of known, defined donors. In another aspect, a donor is an adult male. In a further aspect, a donor is an adult female. In yet another aspect, a donor is an adolescent male. In another aspect, a donor is an adolescent female. In another aspect, a donor is a female toddler. In another aspect, a donor is a male toddler. In another aspect, a donor is healthy. In one aspect, a human donor is a child below about 18, 15, 12, 10, 8, 6, 4, 3, 2, or 1-year-old. In another aspect, a human donor is an elderly individual. In a further aspect, a human donor is an individual above about 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, or 95 years old. In another aspect, a donor is between 1 and 5, between 2 and 10, between 3 and 18, between 21 and 50, between 21 and 40, between 21 and 30, between 50 and 90, between 60 and 90, between 70 and 90, between 60 and 80, or between 65 and 75 years old. In one aspect, a donor is a young old individual (65-74 years). In one aspect, a donor is a middle old individual (75-84 years). In one aspect, a donor is an old individual (>85 years). In yet another aspect, a donor is a carefully screened, healthy, neurotypical human.

[00265] In an aspect, a carefully screened donor undergoes a complete medical history and physical exam. Donors are excluded if they have a risk of infectious agents. Additional exclusion criteria comprise the following:

1. Known viral infection with Hepatitis B, C or HIV
2. Known exposure to HIV or viral hepatitis at any time

3. High risk behaviors including sex for drugs or money, men who have sex with men, more than one sexual partner in the preceding 12 months, any past use of intravenous drugs or intranasal cocaine, history of incarceration.

4. Tattoo or body piercing within 12 months.

5. Travel to areas of the world where risk of traveler's diarrhea is higher than the US.

6. Current communicable disease, e.g., upper respiratory viral infection.

7. History of irritable bowel syndrome. Specific symptoms can include frequent abdominal cramps, excessive gas, bloating, abdominal distension, fecal urgency, diarrhea, constipation.

8. History of inflammatory bowel disease such as Crohn's disease, ulcerative colitis, microscopic colitis.

9. Chronic diarrhea.

10. Chronic constipation or use of laxatives.

11. History of gastrointestinal malignancy or known colon polyposis.

12. History of any abdominal surgery, e.g., gastric bypass, intestinal resection, appendectomy, cholecystectomy, etc.

13. Use of Probiotics or any other over the counter aids used by the potential donor for purpose of regulating digestion. Yogurt and kefir products are allowed if taken merely as food rather than nutritional supplements.

14. Antibiotics for any indication within the preceding 6 months.

15. Any prescribed immunosuppressive or anti-neoplastic medications.

16. Metabolic Syndrome, established or emerging. Criteria used for definition here are stricter than any established criteria. These include history of increased blood pressure, history of diabetes or glucose intolerance.

17. Known systemic autoimmunity, e.g., connective tissue disease, multiple sclerosis.

18. Known atopic diseases including asthma or eczema.

19. Chronic pain syndromes including fibromyalgia, chronic fatigue syndrome.

20. Ongoing (even if intermittent) use of any prescribed medications, including inhalers or topical creams and ointments.

21. Neurologic, neurodevelopmental, and neurodegenerative disorders including autism, Parkinson's disease.

22. General. Body mass index > 26 kg/ m2, central obesity defined by waste:hip ratio > 0.85 (male) and > 0.80 (female).

23. Blood pressure > 135 mmHg systolic and > 85 mmHg diastolic.

24. Skin — presence of a rash, tattoos or body piercing placed within a year, or jaundice

25. Enlarged lymph nodes.

26. Wheezing on auscultation.

27. Hepatomegaly or stigmata of liver disease.

28. Swollen or tender joints. Muscle weakness.

29. Abnormal neurologic examination.

30. Positive stool Clostridium difficile toxin B tested by PCR.

31. Positive stool cultures for any of the routine pathogens including Salmonella, Shigella, Yersinia, Campylobacter, E. coli 0157:H7.

32. Abnormal ova and parasites examination.

33. Positive Giardia, Cryptosporidium, or Helicobacter pylori antigens.

34. Positive screening for any viral illnesses, including HIV 1 and 2, Viral Hepatitis A IgM, Hepatitis surface antigen and core Ab.

35. Abnormal RPR (screen for syphilis).

36. Any abnormal liver function tests including alkaline phosphatase, aspartate aminotransaminase, alanine aminotransferase.

37. Raised serum triglycerides > 150 mg/Dl

38. HDL cholesterol < 40 mg/dL (males) and < 50 mg/dL (females)

39. High sensitivity CRP > 2.4 mg/L

40. Raised fasting plasma glucose (> 100 mg/dL)

[00266] In embodiments, the plurality of bacterial isolates comprises lyophilized bacteria. In embodiments, the plurality of bacterial isolates does not include *Escherichia coli*. In embodiments, the pharmaceutical composition of any of the embodiments disclosed herein is not a stoll sample or a minimally processed version thereof.

[00267] In one aspect, provided herein is a process for preparing fecal flora (*e.g.*, an entire (or substantially entire) microbiota), first comprising a collection from one or more healthy (*e.g.*, screened) donor(s). In one aspect, a fresh stool is transported via a stool collection device, which can provide or comprises a suitably oxygen free (or substantially oxygen free) appropriate container. In one aspect, the container can be made oxygen free by *e.g.*, incorporating into the container a built in or clipped-on oxygen-scavenging mechanism, *e.g.*, oxygen scavenging pellets as described *e.g.*, in U.S. Pat. No: 7,541,091. In another aspect, the container itself is made of an oxygen scavenging material, *e.g.*, oxygen scavenging iron, *e.g.*, as described by O2BLOCK™, or equivalents, which uses a purified and modified layered clay as a performance-enhancing carrier of oxygen-scavenging iron; the active iron is dispersed directly in the polymer. In one aspect, oxygen-scavenging polymers are used to make the container itself or to coat the container, or as pellets to be added; *e.g.*, as described in U.S. Pat. App. Pub. 20110045222, describing polymer blends having one or more unsaturated olefinic homopolymers or copolymers; one or more polyamide homopolymers or copolymers; one or more polyethylene terephthalate homopolymers or copolymers; that exhibit oxygen-scavenging activity. In one aspect, oxygen-scavenging polymers are used to make the container itself or to coat the container, or as pellets to be added; *e.g.*, as described in U.S. Pat. App. Pub. 20110008554, describing compositions comprising a polyester, a copolyester ether and an oxidation catalyst, wherein the copolyester ether comprises a polyether segment comprising poly(tetramethylene-co-alkylene ether). In one aspect, oxygen-scavenging polymers are used to make the container itself or to coat the container, or as pellets to be added; *e.g.*, as described in U.S. Pat. App. Pub. 201000255231, describing a dispersed iron/salt particle in a polymer matrix, and an oxygen scavenging film with oxygen scavenging particulates.

[00268] Alternatively, in addition to or in place of the oxygen-scavenging mechanism, the air in the container can be replaced (completely or substantially) with nitrogen and/or other inert non-reactive gas or gases. In one aspect, the container simulates (creates) partially, substantially or completely an anaerobic environment.

[00269] In one aspect, the stool (*e.g.*, fecal sample) is held in an aesthetically acceptable container that will not leak nor smell yet maintain an anaerobic environment. In one aspect, the container is sterile before receiving the fecal flora.

[00270] In one aspect, a stool sample provided herein is maintained at room temperature during most or all of its transportation and/or storage at *e.g.*, a "stool bank". For example, once delivered to a "processing stool bank" it is stored at ambient temperature, *e.g.*, room temperature. In one aspect, stabilizing agents, such as glycerol, are added to the harvested and/or stored material.

[00271] In one aspect, the stool is tested for various pathogens, as noted above. In one aspect, once cleared of infective agents, a stool sample is homogenized and filtered to remove large particles of matter. In one aspect, the stool is subdivided into desired volumes, *e.g.*, which can be between 5 cc and 3 or more liters. For example, in one aspect, a container comprises a 50 gram (g) stool, which can be held in an appropriate oxygen resistant plastic, *e.g.*, a metallized polyethylene terephthalate polyester film, or a metallized MYLAR™.

[00272] In one aspect, the stool is subject to homogenization by for example, mixing, agitating, stirring or shaking. In certain aspects, a stool sample is diluted with a homogenization buffer prior to homogenization. A homogenization buffer can, for example, contain a cryoprotectant (e.g., trehalose), an antioxidant or reducing agent (e.g., cysteine), and a buffer (e.g., 0.25X PBS at pH 7.4).

[00273] In one aspect, to separate the non-bacterial components from the fecal microbiota, the stool can be homogenized and filtered from rough particulate matter. In one aspect, the microscopic fiber/nonliving matter is then separated from the bacteria. Several methods can be used, including *e.g.*, recurrent filtration with filter sizes, *e.g.*, progressively coming down to the size of a typical bacterium.

[00274] In one aspect, different filters are used to isolate bacterial sp., or a technique as used by Williams in WO 2011/033310A1, which uses a crude technique of filtration with a gauze.

[00275] In one aspect, a filtration procedure for filtering whole stool is suitably used to reach the highest concentration of almost 100% bacteria. In one aspect, the filtering procedure is a two-step procedure suitably using glass fibre depth filters for initial clarification. In one aspect, the stool is filtered under positive pressure. In one aspect, this would be using a combination or sandwich configuration with a 30 micron PVDF filter. In one aspect, this sandwich procedure will be filtering the product under positive pressure. Later, membrane concentration

can, in one aspect, be used as another step to reduce the volume of the filtrate. In one aspect, this can be done prior to freeze drying or spray drying under nitrogen cover.

[00276] Alternative membranes that can be used for filtration include, but not limited to, nylon filters, cellulose nitrate filters, polyethersulfone (PES) filters, polytetrafluorethylene (PTFE) filters, TEFLON™ filters, mixed cellulose Ester filters, polycarbonate filters, polypropylene filters, Polyvinylchloride (PVC) filters or quartz filters. Various combinations of these can be used to achieve a high purity of bacteria with solids and liquid removed.

[00277] In one aspect, a subject in need thereof is administered a pharmaceutical composition comprising fecal microbiota or a preparation of uncultured fecal bacteria of multiple carefully screened, healthy donors. In an aspect, a subject is administered a pharmaceutical composition over a dosing period wherein a first dose comprises at least one pharmaceutical composition comprises fecal microbiota or a preparation of uncultured fecal bacteria of a single donor, and a second dose of a pharmaceutical composition comprises fecal microbiota or a preparation of uncultured fecal bacteria of a single donor different from the donor of the first dose. In another aspect, a first dose comprises a pharmaceutical composition comprising fecal microbiota or a preparation of uncultured fecal bacteria of a single donor and a second dose comprises fecal microbiota or a preparation of uncultured fecal bacteria of a donor pool. The first and second dose do not indicate the order of administration to a subject, but rather that fecal microbiota or preparations of uncultured fecal bacteria from separate donors can be used in a non-blended form.

[00278] In another aspect, the present disclosure provides for methods for treating a subject in need thereof with capsules containing a pharmaceutical composition comprising fecal microbiota from a single donor. In another aspect, a capsule comprises a pharmaceutical composition comprising fecal microbiota from multiple donors. In one aspect a subject is administered two or more pills comprising fecal microbiota from a single but different donor.

[00279] In one aspect, the present disclosure provides for methods for treating a subject in need thereof comprising administering a pharmaceutical composition orally or by infusions through a colonoscope, an enema or via a nasojejunal tube. In another aspect, each administration comprises a pharmaceutical composition comprising fecal microbiota of a single donor similar to or different from a prior administration in a treatment period. In another aspect, a treatment period includes administration of a first dose comprising a pharmaceutical

composition comprising fecal microbiota of a single donor and administration of a second dose comprising a pharmaceutical composition comprising fecal microbiota of multiple donors.

Pharmaceutical compositions, Formulations, and Administration

[00280] Described herein are pharmaceutical compositions comprising one or more bacterial isolates (and/or additional therapeutic agents, e.g. a substantially complete fecal microbiota or preparation of uncultured fecal bacteria) in various formulations. Any pharmaceutical composition (and/or additional therapeutic agents) described herein can take the form of tablets, pills, pellets, capsules, capsules containing liquids, capsules containing multiparticulates, powders, solutions, emulsion, drops, suppositories, emulsions, aerosols, sprays, suspensions, delayed-release formulations, sustained-release formulations, controlled-release formulations, or any other form suitable for use.

[00281] The formulations comprising the pharmaceutical compositions can conveniently be presented in unit dosage forms. For example, the dosage forms can be prepared by methods which include the step of bringing the therapeutic agents into association with a carrier, which constitutes one or more accessory ingredients. For example, the formulations are prepared by uniformly and intimately bringing the therapeutic agent into association with a liquid carrier, a finely divided solid carrier, or both, and then, if necessary, shaping the product into dosage forms of the desired formulation (*e.g.*, wet or dry granulation, powder blends, *etc.*, followed by press tableting).

[00282] In another aspect, a pharmaceutical composition can be provided together with a pharmaceutically acceptable carrier. As used herein, a "pharmaceutically acceptable carrier" refers to a non-toxic solvent, dispersant, excipient, adjuvant, or other material which is mixed with a live bacterium in order to permit the formation of a pharmaceutical composition, *e.g.*, a dosage form capable of administration to the patient. A pharmaceutically acceptable carrier can be liquid (*e.g.*, saline), gel or solid form of diluents, adjuvant, excipients or an acid resistant encapsulated ingredient. Suitable diluents and excipients include pharmaceutical grades of physiological saline, dextrose, glycerol, mannitol, lactose, starch, magnesium stearate, sodium saccharin, cellulose, magnesium carbonate, and the like, and a combination thereof. In another aspect, a pharmaceutical composition can contain auxiliary substances such as wetting or emulsifying agents, stabilizing or pH buffering agents. In an aspect, a pharmaceutical composition contains about 1%-5%, 5%-10%, 10%-15%, 15-20%, 20%-25%, 25-30%, 30-35%, 40-45%, 50%-55%, 1%-95%, 2%-95%, 5%-95%, 10%-95%, 15%-95%, 20%-95%, 25%-

95%, 30%-95%, 35%-95%, 40%-95%, 45%-95%, 50%-95%, 55%-95%, 60%-95%, 65%-95%, 70%-95%, 45%-95%, 80%-95%, or 85%-95% of active ingredient. In an aspect, a pharmaceutical composition contains about 2%-70%, 5%-60%, 10%-50%, 15%-40%, 20%-30%, 25%-60%, 30%-60%, or 35%-60% of active ingredient.

[00283] In an aspect, a pharmaceutical composition can be incorporated into tablets, drenches, boluses, capsules or premixes. Formulation of these active ingredients into such dosage forms can be accomplished by means of methods well known in the pharmaceutical formulation arts. *See, e.g.*, U.S. Pat. No. 4,394,377. Filling gelatin capsules with any desired form of the active ingredients readily produces capsules. If desired, these materials can be diluted with an inert powdered diluent, such as sugar, starch, powdered milk, purified crystalline cellulose, or the like to increase the volume for convenience of filling capsules.

[00284] In an aspect, for preparing solid compositions such as tablets, an active ingredient is mixed with a pharmaceutical carrier, *e.g.*, conventional tableting ingredients such as cornstarch, lactose, sucrose, sorbitol, talc, stearic acid, magnesium stearate, dicalcium phosphate or gums, or other pharmaceutical diluents, *e.g.* water, to form a solid preformulation composition containing a homogeneous mixture of a composition described herein. When referring to these preformulation compositions as homogeneous, it is meant that the active ingredient is dispersed evenly throughout the composition so that the composition can be readily subdivided into equally effective unit dosage forms such as tablets, pills and capsules. This solid preformulation composition is then subdivided into unit dosage forms of the type described above containing a desired amount of an active ingredient (*e.g.*, at least about 10^5, 10^6, 10^7, 10^8, 10^9, 10^{10}, 10^{11}, 10^{12}, or 10^{13} cfu). A pharmaceutical composition used herein can be flavored.

[00285] In one embodiment, a pharmaceutical composition comprising one or more bacterial isolates (and/or additional therapeutic agents) described herein is formulated as a composition adapted for a mode of administration described herein.

[00286] In various embodiments, the administration of the pharmaceutical compositions is any one of oral, intravenous, intraperitoneal, and parenteral. For example, routes of administration include, but are not limited to, oral, intraperitoneal, intravenous, intramuscular, or rectally. In various embodiments, the administration of the pharmaceutical compositions is oral, naso-gastric, antegrade gastrointestinal, retrograde gastrointestinal, endoscopic, or enemic.

[00287] In one embodiment, the pharmaceutical compositions described herein are formulated as a composition adapted for oral administration. Compositions for oral delivery can be in the

form of tablets, lozenges, aqueous or oily suspensions, granules, powders, sprinkles, emulsions, capsules, syrups, or elixirs, for example. Orally administered compositions can comprise one or more agents, for example, sweetening agents such as fructose, aspartame or saccharin; flavoring agents such as peppermint, oil of wintergreen, or cherry; coloring agents; and preserving agents, to provide a pharmaceutically palatable preparation. Moreover, where in tablet or pill form, the compositions can be coated to delay disintegration to provide a sustained action over an extended period of time. Selectively permeable membranes surrounding an osmotically active agent are also suitable for orally administered compositions. In these latter platforms, fluid from the environment surrounding the capsule is imbibed by a driving compound, which swells to displace the agent or agent composition through an aperture. These delivery platforms can provide an essentially zero order delivery profile as opposed to the spiked profiles of immediate release formulations. A time-delay material, such as glycerol monostearate or glycerol stearate, can also be useful. Oral compositions can include standard excipients such as mannitol, lactose, starch, magnesium stearate, sodium saccharin, cellulose, ethacrylic acid and derivative polymers thereof, and magnesium carbonate. In one embodiment, the excipients are of pharmaceutical grade. Suspensions, in addition to the active compounds, can contain suspending agents such as, for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar, tragacanth, *etc.*, and mixtures thereof.

[00288] In various embodiments, the pharmaceutical compositions are formulated as solid dosage forms such as tablets, dispersible powders, granules, and capsules. In one embodiment, the pharmaceutical compositions are formulated as a capsule. In another embodiment, the pharmaceutical compositions are formulated as a tablet. In yet another embodiment, the pharmaceutical compositions are formulated as a soft-gel capsule. In a further embodiment, the pharmaceutical compositions are formulated as a gelatin capsule.

[00289] In an aspect, a pharmaceutical composition is in the form of: an enema composition which can be reconstituted with an appropriate diluent; enteric-coated capsules; enteric-coated microcapsules; acid-resistant tablet; acid-resistant capsules; acid-resistant microcapsules; powder for reconstitution with an appropriate diluent for naso-enteric infusion or colonoscopic infusion; powder for reconstitution with appropriate diluent, flavoring and gastric acid suppression agent for oral ingestion; powder for reconstitution with food or drink; or food or food supplement comprising enteric-coated and/or acid-resistant microcapsules of the composition, powder, jelly, or liquid.

[00290] In various embodiments, formulations can additionally comprise a pharmaceutically acceptable carrier or excipient. As one skilled in the art will recognize, the formulations can be in any suitable form appropriate for the desired use and route of administration.

[00291] In some dosage forms, the pharmaceutical compositions comprising one or more bacterial isolates described herein are mixed with at least one inert, pharmaceutically acceptable excipient or carrier such as sodium citrate, dicalcium phosphate, *etc.*, and/or a) fillers or extenders such as starches, lactose, sucrose, glucose, mannitol, silicic acid, microcrystalline cellulose, and Bakers Special Sugar, *etc.*, b) binders such as, for example, carboxymethylcellulose, alginates, gelatin, polyvinylpyrrolidone, sucrose, acacia, polyvinyl alcohol, polyvinylpyrrolidone, methylcellulose, hydroxypropyl cellulose (HPC), and hydroxymethyl cellulose *etc.*, c) humectants such as glycerol, *etc.*, d) disintegrating agents such as agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates, sodium carbonate, cross-linked polymers such as crospovidone (cross-linked polyvinylpyrrolidone), croscarmellose sodium (cross-linked sodium carboxymethylcellulose), sodium starch glycolate, *etc.*, e) solution retarding agents such as paraffin, *etc.*, f) absorption accelerators such as quaternary ammonium compounds, *etc.*, g) wetting agents such as, for example, cetyl alcohol and glycerol monostearate, *etc.*, h) absorbents such as kaolin and bentonite clay, *etc.*, and i) lubricants such as talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, glyceryl behenate, *etc.*, and mixtures of such excipients. One of skill in the art will recognize that particular excipients can have two or more functions in the oral dosage form. In the case of an oral dosage form, for example, a capsule or a tablet, the dosage form can also comprise buffering agents.

[00292] In embodiments, a pharmaceutical composition comprising one or more bacterial isolates is combined with one or more pharmaceutically acceptable cryoprotectants, lyoprotectants, binders, disintegrants, excipients, fillers, and/or preservatives, acid suppressants, antacids, H2 antagonists, and proton pump inhibitors, or combinations thereof.

[00293] In an aspect, a pharmaceutical composition is combined with other adjuvants such as antacids to dampen bacterial inactivation in the stomach. (*e.g.*, Mylanta, Mucaine, Gastrogel). In another aspect, acid secretion in the stomach could also be pharmacologically suppressed using H2-antagonists or proton pump inhibitors. An example H2-antagonist is ranitidine. An example proton pump inhibitor is omeprazole. In one aspect, an acid suppressant is administered prior to administering, or in co-administration with, a pharmaceutical composition.

[00294] In one aspect, a pharmaceutical composition administered herein further comprises an acid suppressant, an antacid, an H2 antagonist, a proton pump inhibitor or a combination thereof. In one aspect, a pharmaceutical composition administered herein substantially free of non-living matter. In another aspect, a pharmaceutical composition administered herein substantially free of acellular material selected from the group consisting of residual fiber, DNA, viral coat material, and non-viable material. In another aspect, a pharmaceutical composition administered does not comprise an acid suppressant, an antacid, an H2 antagonist, a proton pump inhibitor or a combination thereof. In yet another aspect, a pharmaceutical composition administered does not comprise an acid suppressant. In another aspect, a pharmaceutical composition administered does not comprise an antacid. In another aspect, a pharmaceutical composition administered does not comprise an H2 antagonist. In another aspect, a pharmaceutical composition administered does not comprise a proton pump inhibitor. In another aspect, a pharmaceutical composition administered does not comprise metoclopramide.

[00295] In embodiments, the bacterial mixture is dry, *e.g.*, when it includes lyophilized bacterial cells/spores or comprises dry binders, fillers, and dispersants. Alternately, the microbial cocktail comprising bacterial isolates is aqueous, *e.g.*, when it comprises non-dry binders, fillers, and dispersants.

[00296] In embodiments, a bacterial mixture described herein can be subject to lyophilization. As used herein, "lyophilization" or "freeze drying" refers to the process of drying a material by first freezing it and then encouraging the ice within it to sublimate in a vacuum environment. Disclosed herein is a method of manufacturing a microbial cocktail, the method comprising culturing a first bacterial isolate as a pure culture; culturing a second bacterial isolate as a pure culture; lyophilizing the first bacterial isolate; lyophilizing the second bacterial isolate; and combining the first and second lyophilized bacterial isolates into the microbial cocktail. In another embodiment, disclosed herein is a method of manufacturing a microbial cocktail, the method comprising culturing a first bacterial isolate as a pure culture; culturing a second bacterial isolate as a pure culture; and combining the first bacterial isolate with the second bacterial isolate to form the microbial cocktail. Optionally, the microbial cocktail comprising the first and second bacterial isolates can be lyophilized. It will therefore be understood that a microbial cocktail can be lyophilized or non-lyophilized, and that a lyophilized microbial cocktail can be produced by lyophilizing bacterial isolates that form the cocktail before or after combining the bacterial isolates.

[00297] In one aspect, a bacterial mixture comprises a lyophilized formulation further comprising a reducing agent and/or antioxidant. In certain embodiments, the reducing agent comprises cysteine selected from the group consisting of D-cysteine and L-cysteine. In another aspect, cysteine is at a concentration of at least about 0.025%. In one aspect, cysteine is at a concentration of about 0.025%. In another aspect, cysteine is at a concentration of 0.025%. In another aspect, another reducing agent other than cysteine is used in lieu of, or in combination with cysteine. In an aspect, another reducing agent is selected from the group comprising ascorbic acid, sodium ascorbate, thioglycolic acid, sodium sulfite, sodium bisulfite, sodium metabisulfite, potassium metabisulfite, glutathione, methionine, thioglycerol, and alpha tocopherol.

[00298] In one aspect, cysteine is at a concentration of at least about 0.005%, at least about 0.01%, at least about 0.015%, at least about 0.02%, at least about 0.025%, at least about 0.03%, at least about 0.035%, at least about 0.04%, at least about 0.045%, at least about 0.05%, at least about 0.055%, at least about 0.06%, at least about 0.065%, at least about 0.07%, at least about 0.075%, at least about 0.08%, at least about 0.085%, at least about 0.09%, at least about 0.095%, at least about 0.1%, at least about 0.12%, at least about 0.14%, at least about 0.16%, at least about 0.18%, at least about 0.2%, at least about 0.25%, at least about 0.3%, at least about 0.4%, at least about 0.5%, at least about 0.6%, at least about 0.7%, at least about 0.8%, at least about 0.9%, at least about 1%, at least about 2%, at least about 4%, at least about 6%, at least about 8%, at least about 10%, at least about 12%, at least about 14%, at least about 16%, at least about 18%, at least about 20%, at least about 22%, at least about 24%, or at least about 26%.

[00299] In embodiments, a pharmaceutical composition comprising one or more bacterial isolates comprises a cryoprotectant or mixture of cryoprotectants. As used herein, a "cryoprotectant" refers to a substance that is added to a formulation in order to protect an active ingredient during freezing. For example, a cryoprotectant can comprise, consist essentially of, or consist of polyethylene glycol, skim milk, erythritol, arabitol, sorbitol, glucose, fructose, alanine, glycine, proline, sucrose, lactose, ribose, trehalose, dimethyl sulfoxide (DMSO) or equivalent, a glycerol, a polyethylene glycol (PEG) or equivalent, or an amino acid (e.g., alanine, glycine, proline). In embodiments of the present disclosure, a cryoprotectant can be selected from the group comprising 5% Sucrose; 10% Sucrose; 10% Skim milk; 10% Trehalose with 2.5% sucrose; 5% Trehalose with 2.5% sucrose; 5% Mannitol; 5% Mannitol with 0.1% Polysorbate 80; 10% Mannitol; 10% Mannitol with 0.1% Polysorbate 80; 5% Trehalose; 5%

Trehalose with 0.1% Polysorbate 80; 10% Trehalose; and 10% Trehalose with 0.1% Polysorbate 80.

[00300] In embodiments, a pharmaceutical composition comprising one or more bacterial isolates comprises a lyoprotectant. As used herein, a "lyoprotectant" refers to a substance that is added to a formulation in order to protect an active ingredient during the stage of a lyophilization (also known as freeze-drying). In embodiments, the same substance or the same substance combination is used as both a cryoprotectant and a lyoprotectant. Exemplary lyoprotectants include sugars such as sucrose or trehalose; an amino acid such as monosodium glutamate or histidine; a methylamine such as betaine; a lyotropic salt such as magnesium sulfate; a polyol such as trihydric or higher sugar alcohols, *e.g.* glycerin, erythritol, glycerol, arabitol, xylitol, sorbitol, and mannitol; propylene glycol; polyethylene glycol; Pluronics; and a combination thereof. In embodiments, a lyoprotectant is a non-reducing sugar, such as trehalose or sucrose. In embodiments, a cryoprotectant or a lyoprotectant consists essentially of, or consists of, one or more substances mentioned in this paragraph and the paragraph above.

[00301] In embodiments, a cryoprotectant or a lyoprotectant comprise an intracellular agent, *e.g.*, DMSO, Glycerol, or PEG, which penetrates inside the cell preventing the formation of ice crystals that could result in membrane rupture. In embodiments, a cryoprotectant or a lyoprotectant comprise an extracellular agent, *e.g.*, sucrose, trehalose, or dextrose, which does not penetrate into the cell membrane but acts to improve the osmotic imbalance that occurs during freezing.

[00302] In one aspect, the present disclosure provides a pharmaceutical composition comprising a lyophilized fecal microbe preparation comprising a lyophilization formulation comprising at least about 12.5% trehalose.

[00303] In embodiments, a lyophilized formulation comprises trehalose. In embodiments, a lyophilized formulation comprises 2% to 30%, 3% to 25%, 4% to 20%, 5% to 15%, 6% to 10%, 2% to 30%, 2% to 25%, 2% to 20%, 2% to 15%, or 2% to 10% trehalose. In embodiments, a lyophilized formulation comprises at least 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, or 15% trehalose. In embodiments, a lyophilized formulation comprises at most 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, or 15% trehalose. In embodiments, a lyophilized formulation comprises about 5% trehalose. In embodiments, a lyophilized formulation comprises trehalose and sucrose. In embodiments, a lyophilized formulation comprises between about 8% and 12% trehalose with between about 1.5% and 3.5% sucrose and between about 0.5% and 1.5% NaCl.

[00304] In one aspect, a lyophilization formulation comprises at least about 5%, at least about 7.5%, at least about 10%, at least about 12.5%, at least about 13%, at least about 13.5%, at least about 14%, at least about 14.5%, at least about 15%, at least about 15.5%, at least about 16%, at least about 16.5%, at least about 17%, at least about 17.5%, at least about 18%, at least about 18.5%, at least about 19%, at least about 19.5%, at least about 20%, at least about 22.5%, at least about 25%, at least about 27.5%, at least about 30%, at least about 32.5%, at least about 35%, at least about 37.5%, at least about 40%, at least about 42.5%, at least about 45%, at least about 47.5%, at least about 50%, at least about 52.5%, at least about 55%, at least about 57.5%, or at least about 60% of trehalose.

[00305] In embodiments, a pharmaceutical composition provided here, after at least 12 weeks of storage at ambient temperature or lower, is effective for treating one or more disorders selected from the group consisting of recurrent or primary *C. diff.* infection, ulcerative colitis, Crohn's disease, and irritable bowel syndrome. In embodiments, a pharmaceutical composition remains effective after at least 4, 8, 10, 16, 20, 24, 30, 40, 50, 60, 70, 80 or 100 weeks of storage at ambient temperature or lower.

[00306] In embodiments, a pharmaceutical composition (e.g., comprising a microbial cocktail) described herein can be lyophilized or freeze dried and stored at ambient temperatures (*e.g.*, room temperature), at a freezing temperature, or at between about 2°C and 8°C. In embodiments, freeze-drying allows the majority of cells to remain viable, and produces a powdered form of the product that can be gently pulverized into a powder. The powder, or lyophilized or freeze-dried composition, then can be encapsulated into a carrier, *e.g.*, a tablet, geltab, pill or capsule, *e.g.*, an enteric-coated capsule, or placed into oil-filled capsules for ingestion. Alternatively, the freeze-dried or lyophilized product, or powder, can be reconstituted at ambient temperatures before delivery to an individual in *e.g.*, a fluid, *e.g.*, a sterile fluid, such as saline, a buffer or a media such as a fluid-glucose-cellobiose agar (RGCA) media.

[00307] For freeze-drying, in embodiments, bacterial isolates are held in a liquid that will prevent bursting of cells on thawing. This can include various stabilizers, *e.g.*, glycerol and appropriate buffers, and/or ethylene glycol. In embodiments, the cryoprotecting process uses final concentrations of stabilizer(s) of between about 10% and 80%, 20% and 70%, 30% and 60%, or 40% and 50%, depending on the stabilizer(s) used; in embodiments, this helps stabilize proteins by preventing formation of ice crystals that would otherwise destroy protein structures.

[00308] In embodiments, stabilizers that help reduce destruction of living bacteria include skim milk, erythritol, arabitol, sorbitol, glucose, fructose and other polyols. Polymers such as dextran and polyethylene glycol can also be used to stabilize bacterial cells.

[00309] In embodiments, manufacturing a pharmaceutical composition can comprise steps of: (1) coating the exterior of a dissociated capsule (*i.e.*, comprising separate capsule body and capsule cap) with the exterior enteric coating, (2) filling the capsule body with a pharmaceutical composition (e.g., comprising a microbial cocktail) comprising one or more bacterial isolates, and (3) closing the capsule cap over the capsule body, thereby encapsulating the composition comprising in the exterior, enteric-coated capsule.

[00310] Optionally, manufacturing a pharmaceutical composition can comprise steps of: (1) coating the exterior of a dissociated capsule (*i.e.*, comprising separate capsule body and capsule cap) with the exterior enteric coating, (2) coating the interior of the dissociated capsule with an interior coating, (3) filling the capsule body with a pharmaceutical composition (e.g., comprising a microbial cocktail) comprising one or more bacterial isolates, and (4) closing the capsule cap over the capsule body, thereby encapsulating the composition in the dual-coated capsule.

[00311] Alternately, manufacturing a pharmaceutical composition can comprise step of: (1) coating the interior of the dissociated capsule (*i.e.*, comprising separate capsule body and capsule cap) with an interior coating, (2) coating the exterior of a dissociated capsule with the exterior enteric coating, (3) filling the capsule body with a pharmaceutical composition (e.g., comprising a microbial cocktail) comprising bacterial isolates, and (4) closing the capsule cap over the capsule body, thereby encapsulating the composition in the dual-coated capsule.

[00312] In embodiments, one or more additional therapeutic agents can be combined with a pharmaceutical composition (e.g., comprising a microbial cocktail) and encapsulated by the capsule.

[00313] In embodiments, the bodies and caps of gelatin capsules (*e.g.*, size #00) are separated. An exterior enteric coating suspension is prepared by dispersing one or more enteric coating polymers along with other components in a solution. The exterior enteric coating suspension is applied to the exterior of separated capsule bodies and caps, *e.g.*, using a fluid bed Wurster column coater, Fluid Bed Coater, or an equivalent). The capsules are fluidized in the product bowl and the exterior enteric coating suspension is sprayed to produce the outer coating to a target of between about 2 mg/cm^2 and 6 mg/cm^2, *e.g.*, 3 mg/cm^2. After completion of this step,

the capsules are set to dry, *e.g.*, between about 8 hours and 24 hours. After drying, exemplary capsules are weighed to calculate weight gain from the exterior enteric coating. Capsules can be inspected for irregularities.

[00314] In an embodiment, EUDRAGIT® S100 (poly(methacrylic acid, methylmethacrylate)), starch, triethyl citrate, and PlasACRYL™ T20 are dissolved in a solution of water, ethanol, and n-butanol, mixed, and then charged to a suitable spraying device. The solution is then spray coated on the outer surface of the capsule bodies and capsule caps to a target weight gain. The capsule bodies and capsule caps are allowed to dry for about 8 hours to about 24 hours, or longer, *e.g.*, for a week, a month, or more, before further procession, *e.g.*, filling with a microbial cocktail comprising bacterial isolates.

[00315] In embodiments, it may be desirable to provide an amount of the pharmaceutical composition (e.g., comprising a microbial cocktail) to a capsule's cap in addition to providing the composition in the capsule's body. In this embodiment, more of the composition will be included in a capsule and/or less air will be contained in a closed capsule.

[00316] In embodiments, the interior surface of a capsule is provided an internal coating.

[00317] Any of the above-described compositions (e.g., microbial cocktails), inner coatings, capsules, and outer coatings can be combined into a pharmaceutical composition described herein. A skilled artisan would know how to select an inner coating; capsule, and outer coating according to his/her present need, which could be based, for example, on the specific bacterial isolate(s) and/or the location in a subject (*e.g.*, in the colon) where the bacterial isolate(s) should be delivered.

[00318] Additional relevant teachings are disclosed in WO 2007122374, which is hereby incorporated herein by reference in its entirety.

[00319] In embodiments, during the manufacture of a pharmaceutical composition, a pharmaceutically-acceptable cryoprotectant, lyoprotectant, binder, disintegrant, filler, preservative, acid suppressant, antacid, H2 antagonist, and proton pump inhibitor, or combination thereof can be mixed into the pharmaceutical composition (e.g., comprising a microbial cocktail) to promote desirable properties.

[00320] The pharmaceutical composition can additionally include a surface active agent. Surface active agents suitable for use include, but are not limited to, any pharmaceutically acceptable, non-toxic surfactant. Classes of surfactants suitable for use include, but are not limited to, polyethoxylated fatty acids, PEG-fatty acid diesters, PEG-fatty acid mono- and di-

ester mixtures, polyethylene glycol glycerol fatty acid esters, alcohol-oil transesterification products, polyglycerized fatty acids, propylene glycol fatty acid esters, mixtures of propylene glycol esters-glycerol esters, mono- and diglycerides, sterol and sterol derivatives, polyethylene glycol sorbitan fatty acid esters, polyethylene glycol alkyl ethers, sugar esters, polyethylene glycol alkyl phenols, polyoxyethylene-olyoxypropylene block copolymers, sorbitan fatty acid esters, lower alcohol fatty acid esters, ionic surfactants, and mixtures thereof. In some embodiments, compositions can comprise one or more surfactants including, but not limited to, sodium lauryl sulfate, polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80, and triethyl citrate.

[00321] The pharmaceutical composition can also contain pharmaceutically acceptable plasticizers to obtain the desired mechanical properties such as flexibility and hardness. Such plasticizers include, but are not limited to, triacetin, citric acid esters, triethyl citrate, phthalic acid esters, dibutyl sebacate, cetyl alcohol, polyethylene glycols, polysorbates or other plasticizers.

[00322] The pharmaceutical composition can also include one or more application solvents. Some of the more common solvents that can be used to apply, for example, a delayed-release coating composition include isopropyl alcohol, acetone, methylene chloride and the like.

[00323] The pharmaceutical composition can also include one or more alkaline materials. Alkaline material suitable for use in compositions include, but are not limited to, sodium, potassium, calcium, magnesium and aluminum salts of acids such as phosphoric acid, carbonic acid, citric acid and other aluminum/magnesium compounds. In addition, the alkaline material can be selected from antacid materials such as aluminum hydroxides, calcium hydroxides, magnesium hydroxides and magnesium oxide.

[00324] Besides inert diluents, the oral compositions can also include adjuvants such as sweetening, flavoring, and perfuming agents.

[00325] In various embodiments, the pharmaceutical compositions are formulated for systemic or local delivery. In an embodiment, administration is systemic. In another embodiment, it may be desirable to administer locally to the area in need of treatment.

[00326] Various methods can be used to formulate and/or deliver a pharmaceutical composition (e.g., comprising a microbial cocktail) described herein to a location of interest. For example, the pharmaceutical compositions can be formulated for delivery to the GI tract. The GI tract includes organs of the digestive system such as mouth, esophagus, stomach,

duodenum, small intestine, large intestine and rectum and includes all subsections thereof (*e.g.* the small intestine may include the duodenum, jejunum and ileum; the large intestine may include the colon transversum, colon descendens, colon ascendens, colon sigmoidenum and cecum). For example, the compositions can be formulated for delivery to one or more of the stomach, small intestine, large intestine and rectum and includes all subsections thereof (*e.g.* duodenum, jejunum and ileum, colon transversum, colon descendens, colon ascendens, colon sigmoidenum and cecum). In some embodiments, the compositions described herein can be formulated to deliver to the upper or lower GI tract. In an embodiment, the compositions can be administered to a subject, by, for example, directly or indirectly contacting the mucosal tissues of the GI tract.

[00327] In various embodiments, the administration of the pharmaceutical compositions is into the GI tract via, for example, oral delivery, nasogastral tube, intestinal intubation (*e.g.* an enteral tube or feeding tube such as, for example, a jejunal tube or gastro-jejunal tube, *etc.*), direct infusion (*e.g.*, duodenal infusion), endoscopy, colonoscopy, or enema.

[00328] In one aspect, a method comprises administering a pharmaceutical composition orally, by enema, or via rectal suppository. In one aspect, a pharmaceutical composition administered herein is formulated as an enteric coated (and/or acid-resistant) capsule or microcapsule, or formulated as part of or administered together with a food, a food additive, a dairy-based product, a soy-based product or a derivative thereof, a jelly, flavored liquid, ice block, ice cream, or a yogurt. In another aspect, a pharmaceutical composition administered herein is formulated as an acid-resistant enteric coated capsule. A pharmaceutical composition can be provided as a powder for sale in combination with a food or drink. A food or drink can be a dairy-based product or a soy-based product. In another aspect, a food or food supplement contains enteric-coated and/or acid-resistant microcapsules containing a pharmaceutical composition.

[00329] In an aspect, a pharmaceutical composition comprises a liquid culture. In another aspect, a pharmaceutical composition is homogenized, lyophilized, pulverized and powdered. It can then be infused, dissolved such as in saline, as an enema. Alternatively, the powder can be encapsulated as enteric-coated and/or acid-resistant delayed release capsules for oral administration. In an aspect, the powder can be double encapsulated with acid-resistant/delayed release capsules for oral administration. These capsules can take the form of enteric-coated and/or acid-resistant delayed release microcapsules. A powder can be provided in a palatable form for reconstitution for drinking or for reconstitution as a food additive. In a further aspect,

a food is yogurt. In one aspect, a powder can be reconstituted to be infused via naso-duodenal infusion.

[00330] In another aspect, a pharmaceutical composition administered herein is in a liquid, frozen, freeze-dried, spray-dried, foam-dried, lyophilized, or powder form. In a further aspect, a pharmaceutical composition administered herein is formulated as a delayed or gradual enteric release form. In another aspect, a pharmaceutical composition administered herein comprises an excipient, a saline, a buffer, a buffering agent, or a fluid-glucose-cellobiose agar (RGCA) media. In another aspect, a pharmaceutical composition administered herein comprises a cryoprotectant. In one aspect, a cryoprotectant comprises polyethylene glycol, skim milk, erythritol, arabitol, sorbitol, glucose, fructose, alanine, glycine, proline, sucrose, lactose, ribose, trehalose, dimethyl sulfoxide (DMSO), glycerol, or a combination thereof.

[00331] In various embodiments, provided herein are modified-release formulations comprising one or more bacterial isolates (and/or additional therapeutic agents), wherein the formulation releases a substantial amount of the bacterial isolates (and/or additional therapeutic agents) into one or more regions of the GI tract. For example, the formulation can release at least about 60% of the bacterial isolates after the stomach and into one or more regions of the GI tract.

[00332] In various embodiments, the modified-release formulation can release at least 60% of the bacterial isolates (and/or additional therapeutic agents) after the stomach into one or more regions of the intestine. For example, the modified-release formulation releases at least 60%, at least 61%, at least 62%, at least 63%, at least 64%, at least 65%, at least 66%, at least 67%, at least 68%, at least 69%, at least 70%, at least 71%, at least 72%, at least 73%, at least 74%, at least 75%, at least 76%, at least 77%, at least 78%, at least 79%, at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% of the bacterial isolates (and/or additional therapeutic agents) in the intestines.

[00333] In various embodiments, the modified-release formulation can release at least 60% of the bacterial isolates (and/or additional therapeutic agents) in the small intestine. For example, the modified-release formulation releases at least 60%, at least 61%, at least 62%, at least 63%, at least 64%, at least 65%, at least 66%, at least 67%, at least 68%, at least 69%, at least 70%, at least 71%, at least 72%, at least 73%, at least 74%, at least 75%, at least 76%, at least 77%,

at least 78%, at least 79%, at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% of the bacterial isolates (and/or additional therapeutic agents) in the small intestine (*e.g.*, one or more of duodenum, jejunum, ileum, and ileocecal junction).

[00334] In various embodiments, the modified-release formulation can release at least 60% of the bacterial isolates (and/or additional therapeutic agents) in the large intestine. For example, the modified-release formulation releases at least 60%, at least 61%, at least 62%, at least 63%, at least 64%, at least 65%, at least 66%, at least 67%, at least 68%, at least 69%, at least 70%, at least 71%, at least 72%, at least 73%, at least 74%, at least 75%, at least 76%, at least 77%, at least 78%, at least 79%, at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% of the bacterial isolates (and/or additional therapeutic agents) in the large intestine (*e.g.*, one or more of cecum, ascending, transverse, descending or sigmoid portions of the colon, and rectum).

[00335] In some embodiments, the pharmaceutical composition is formulated for release in the stomach. In other embodiments, the pharmaceutical composition is formulated so as to not substantially release the bacterial isolates in the stomach.

[00336] In certain embodiments, the modified-release formulation releases the bacterial isolates (and/or additional therapeutic agents) at a specific pH. For example, in some embodiments, the modified-release formulation is substantially stable in an acidic environment and substantially unstable (*e.g.*, dissolves rapidly or is physically unstable) in a near neutral to alkaline environment. In some embodiments, stability is indicative of not substantially releasing while instability is indicative of substantially releasing. For example, in some embodiments, the modified-release formulation is substantially stable at a pH of about 7.0 or less, or about 6.5 or less, or about 6.0 or less, or about 5.5 or less, or about 5.0 or less, or about 4.5 or less, or about 4.0 or less, or about 3.5 or less, or about 3.0 or less, or about 2.5 or less, or about 2.0 or less, or about 1.5 or less, or about 1.0 or less. In some embodiments, the present formulations are stable in lower pH areas and therefore do not substantially release in, for example, the stomach. In some embodiments, modified-release formulation is substantially stable at a pH of about 1 to about 4 or lower and substantially unstable at pH values that are greater. In these embodiments, the modified-release formulation does not substantially release

in the stomach. In these embodiments, the modified-release formulation substantially releases in the small intestine (*e.g.* one or more of the duodenum, jejunum, and ileum) and/or large intestine (*e.g.* one or more of the cecum, ascending colon, transverse colon, descending colon, and sigmoid colon). In some embodiments, modified-release formulation is substantially stable at a pH of about 4 to about 5 or lower and consequentially is substantially unstable at pH values that are greater and therefore is not substantially released in the stomach and/or small intestine (*e.g.* one or more of the duodenum, jejunum, and ileum). In these embodiments, the modified-release formulation substantially releases in the large intestine (*e.g.* one or more of the cecum, ascending colon, transverse colon, descending colon, and sigmoid colon). In various embodiments, the pH values recited herein can be adjusted as known in the art to account for the state of the subject, *e.g.* whether in a fasting or postprandial state.

[00337] In some embodiments, the modified-release formulation is substantially stable in gastric fluid and substantially unstable in intestinal fluid and, accordingly, is substantially released in the small intestine (*e.g.* one or more of the duodenum, jejunum, and ileum) and/or large intestine (*e.g.* one or more of the cecum, ascending colon, transverse colon, descending colon, and sigmoid colon).

[00338] In some embodiments, the modified-release formulation is stable in gastric fluid or stable in acidic environments. These modified-release formulations release about 30% or less by weight of the pharmaceutical composition (e.g., comprising bacterial isolates of a microbial cocktail) in the modified-release formulation in gastric fluid with a pH of about 4 to about 5 or less, or simulated gastric fluid with a pH of about 4 to about 5 or less, in about 15, or about 30, or about 45, or about 60, or about 90 minutes. Modified-release formulations of can release from about 0% to about 30%, from about 0% to about 25%, from about 0% to about 20%, from about 0% to about 15%, from about 0% to about 10%, about 5% to about 30%, from about 5% to about 25%, from about 5% to about 20%, from about 5% to about 15%, from about 5% to about 10% by weight of the composition in the modified-release formulation in gastric fluid with a pH of 4-5, or less or simulated gastric fluid with a pH of 4-5 or less, in about 15, or about 30, or about 45, or about 60, or about 90 minutes. Modified-release formulations can release about 1%, about 2%, about 3%, about 4%, about 5%, about 6%, about 7%, about 8%, about 9%, or about 10% by weight of the total composition in the modified-release formulation in gastric fluid with a pH of 5 or less, or simulated gastric fluid with a pH of 5 or less, in about 15, or about 30, or about 45, or about 60, or about 90 minutes.

[00339] In some embodiments, the modified-release formulation is unstable in intestinal fluid. These modified-release formulations release about 70% or more by weight of the bacterial isolates and/or additional therapeutic agent in the modified-release formulation in intestinal fluid or simulated intestinal fluid in about 15, or about 30, or about 45, or about 60, or about 90 minutes. In some embodiments, the modified-release formulation is unstable in near neutral to alkaline environments. These modified-release formulations release about 70% or more by weight of the bacterial isolates and/or additional therapeutic agent in the modified-release formulation in intestinal fluid with a pH of about 4-5 or greater, or simulated intestinal fluid with a pH of about 4-5 or greater, in about 15, or about 30, or about 45, or about 60, or about 90 minutes. A modified-release formulation that is unstable in near neutral or alkaline environments can release 70% or more by weight of the pharmaceutical composition (e.g., comprising a microbial cocktail) in the modified-release formulation in a fluid having a pH greater than about 5 (*e.g.*, a fluid having a pH of from about 5 to about 14, from about 6 to about 14, from about 7 to about 14, from about 8 to about 14, from about 9 to about 14, from about 10 to about 14, or from about 11 to about 14) in from about 5 minutes to about 90 minutes, or from about 10 minutes to about 90 minutes, or from about 15 minutes to about 90 minutes, or from about 20 minutes to about 90 minutes, or from about 25 minutes to about 90 minutes, or from about 30 minutes to about 90 minutes, or from about 5 minutes to about 60 minutes, or from about 10 minutes to about 60 minutes, or from about 15 minutes to about 60 minutes, or from about 20 minutes to about 60 minutes, or from about 25 minutes to about 90 minutes, or from about 30 minutes to about 60 minutes.

[00340] Examples of simulated gastric fluid and simulated intestinal fluid include, but are not limited to, those disclosed in the 2005 Pharmacopeia 23NF/28USP in Test Solutions at page 2858 and/or other simulated gastric fluids and simulated intestinal fluids known to those of skill in the art, for example, simulated gastric fluid and/or intestinal fluid prepared without enzymes.

[00341] In various embodiments, the modified-release formulation can be substantially stable in chyme. For example, there is, in some embodiments, a loss of less about 50% or about 40%, or about 30%, or about 20%, or about 10% of bacterial isolates activity in about 10, or 9, or 8, or 7, or 6, or 5, or 4, or 3, or 2, or 1 hour from administration.

[00342] In various embodiments, the modified-release formulations can be designed for immediate release (*e.g.* upon ingestion). In various embodiments, the modified-release formulations can have sustained-release profiles, *i.e.* slow release of the active ingredient(s) in

the body (*e.g.*, GI tract) over an extended period of time. In various embodiments, the modified-release formulations can have a delayed-release profile, *i.e.* not immediately release the active ingredient(s) upon ingestion; rather, postponement of the release of the active ingredient(s) until the composition is lower in the GI tract; for example, for release in the small intestine (*e.g.*, one or more of duodenum, jejunum, ileum) or the large intestine (*e.g.*, one or more of cecum, ascending, transverse, descending or sigmoid portions of the colon, and rectum). For example, a composition can be enteric coated to delay release of the active ingredient(s) until it reaches the small intestine or large intestine.

[00343] In various embodiments, the modified-release formulations can utilize one or more modified-release coatings such as delayed-release coatings to provide for effective, delayed yet substantial delivery of the bacterial isolates to the GI tract together with, optionally, additional therapeutic agents.

[00344] In one embodiment, the delayed-release coating includes an enteric agent that is substantially stable in acidic environments and substantially unstable in near neutral to alkaline environments. In an embodiment, the delayed-release coating contains an enteric agent that is substantially stable in gastric fluid. The enteric agent can be selected from, for example, solutions or dispersions of methacrylic acid copolymers, cellulose acetate phthalate, hydroxypropylmethyl cellulose phthalate, polyvinyl acetate phthalate, carboxymethylethylcellulose, and EUDRAGIT®-type polymer (poly(methacrylic acid, methylmethacrylate), hydroxypropyl methylcellulose acetate succinate, cellulose acetate trimellitate, shellac or other suitable enteric coating polymers. The EUDRAGIT®-type polymers include, for example, EUDRAGIT® FS 30D, L 30 D-55, L 100-55, L 100, L 12,5, L 12,5 P, RL 30 D, RL PO, RL 100, RL 12,5, RS 30 D, RS PO, RS 100, RS 12,5, NE 30 D, NE 40 D, NM 30 D, S 100, S 12,5, and S 12,5 P. Similar polymers include Kollicoat® MAE 30 DP and Kollicoat® MAE 100 P. In some embodiments, one or more of EUDRAGIT® FS 30D, L 30 D-55, L 100-55, L 100, L 12,5, L 12,5 P RL 30 D, RL PO, RL 100, RL 12,5, RS 30 D, RS PO, RS 100, RS 12,5, NE 30 D, NE 40 D, NM 30 D, S 100, S 12,5 S 12,5 P, Kollicoat® MAE 30 DP and Kollicoat® MAE 100 P is used. In various embodiments, the enteric agent can be a combination of the foregoing solutions or dispersions.

[00345] In certain embodiments, one or more coating system additives are used with the enteric agent. For example, one or more PlasACRYL™ additives can be used as an anti-tacking agent coating additive. Illustrative PlasACRYL™ additives include, but are not limited to, PlasACRYL™ HTP20 and PlasACRYL™ T20.

[00346] In another embodiment, the delayed-release coating can degrade as a function of time when in aqueous solution without regard to the pH and/or presence of enzymes in the solution. Such a coating can comprise a water insoluble polymer. Its solubility in aqueous solution is therefore independent of the pH. The term "pH independent" as used herein means that the water permeability of the polymer and its ability to release pharmaceutical ingredients is not a function of pH and/or is only very slightly dependent on pH. Such coatings can be used to prepare, for example, sustained release formulations. Suitable water insoluble polymers include pharmaceutically acceptable non-toxic polymers that are substantially insoluble in aqueous media, *e.g.*, water, independent of the pH of the solution. Suitable polymers include, but are not limited to, cellulose ethers, cellulose esters, or cellulose ether-esters, *i.e.*, a cellulose derivative in which some of the hydroxy groups on the cellulose skeleton are substituted with alkyl groups and some are modified with alkanoyl groups. Examples include ethyl cellulose, acetyl cellulose, nitrocellulose, and the like. Other examples of insoluble polymers include, but are not limited to, lacquer, and acrylic and/or methacrylic ester polymers, polymers or copolymers of acrylate or methacrylate having a low quaternary ammonium content, or mixture thereof and the like. Other examples of insoluble polymers include EUDRAGIT RS®, EUDRAGIT RL®, and EUDRAGIT NE®. Insoluble polymers can include polyvinyl esters, polyvinyl acetals, polyacrylic acid esters, butadiene styrene copolymers, and the like. In one embodiment, colonic delivery is achieved by use of a slowly eroding wax plug (*e.g.*, various PEGS, including for example, PEG6000).

[00347] In a further embodiment, the delayed-release coating can be degraded by a microbial enzyme present in the gut flora. In one embodiment, the delayed-release coating can be degraded by bacteria present in the small intestine. In another embodiment, the delayed-release coating can be degraded by bacteria present in the large intestine.

[00348] In various embodiments, the modified release formulation can be designed for release in the colon. Various colon-specific delivery approaches can be utilized. For example, the modified release formulation can be formulated using a colon-specific drug delivery system (CODES) as described for example, in Li *et al.*, AAPS PharmSciTech (2002), 3(4): 1-9, the entire contents of which are incorporated herein by reference. Drug release in such a system is triggered by colonic microflora coupled with pH-sensitive polymer coatings. For example, the formulation can be designed as a core tablet with three layers of polymer. The first coating is an acid-soluble polymer (*e.g.*, EUDRAGIT E), the outer coating is enteric, along with a hydroxypropyl methylcellulose barrier layer interposed in between. In another embodiment,

colon delivery can be achieved by formulating the pharmaceutical composition (e.g., comprising a microbial cocktail) with specific polymers that degrade in the colon such as, for example, pectin. The pectin can be further gelled or crosslinked with a cation such as a zinc cation. In an embodiment, the formulation is in the form of ionically crosslinked pectin beads which are further coated with a polymer (*e.g.*, EUDRAGIT polymer). Additional colon specific formulations include, but are not limited to, pressure-controlled drug delivery systems (prepared with, for example, ethylcellulose) and osmotic controlled drug delivery systems (*i.e.*, ORDS-CT).

[00349] Formulations for colon specific delivery of the bacterial isolates (and/or additional therapeutic agents), as described herein, can be evaluated using, for example, *in vitro* dissolution tests. For example, parallel dissolution studies in different buffers can be undertaken to characterize the behavior of the formulations at different pH levels. Alternatively, *in vitro* enzymatic tests can be carried out. For example, the formulations can be incubated in fermenters containing suitable medium for bacteria, and the amount of drug released at different time intervals is determined. Drug release studies can also be done in buffer medium containing enzymes or rat or guinea pig or rabbit cecal contents and the amount of drug released in a particular time is determined. In a further embodiment, *in vivo* evaluations can be carried out using animal models such as dogs, guinea pigs, rats, and pigs. Further, clinical evaluation of colon specific drug delivery formulations can be evaluated by calculating drug delivery index (DDI) which considers the relative ratio of RCE (relative colonic tissue exposure to the drug) to RSC (relative amount of drug in blood *i.e.* that is relative systemic exposure to the drug). Higher drug DDI indicates better colon drug delivery. Absorption of drugs from the colon can be monitored by colonoscopy and intubation.

[00350] In various embodiments, the present formulation provides for substantial uniform delivery of the bacterial isolates (and/or additional therapeutic agent) in the area of release in the GI tract. In an embodiment, the present formulation minimizes patchy or heterogeneous release of the bacterial isolates.

[00351] In various embodiments, the present formulations provide for release of multiple doses of the bacterial isolates along the GI tract. For example, the composition and/or formulation can release multiple doses of the bacterial isolates at different locations along the intestines, at different times, and/or at different pH. The overall release profile of such a formulation can be adjusted using, for example, multiple particle types or multiple layers. For example, in one embodiment, the first dose of the bacterial isolates can be formulated for

release in, for example, the small intestine (*e.g.*, one or more of duodenum, jejunum, ileum), whereas the second dose is formulated for delayed release in, for example, the large intestines (*e.g.*, one or more of cecum, ascending, transverse, descending or sigmoid portions of the colon, and rectum). In another example, the first dose of the bacterial isolates can be formulated for release in, for example, the small intestine (*e.g.*, one or more of duodenum, jejunum, ileum), whereas the second dose is formulated for delayed release in, for example, another part of the small intestine (*e.g.*, one or more of duodenum, jejunum, ileum). In another embodiment, the first dose of the bacterial isolates can be formulated for release in, for example, the large intestine (*e.g.*, one or more of cecum, ascending, transverse, descending or sigmoid portions of the colon, and rectum), whereas the second dose is formulated for delayed release in, for example, another part of the large intestine (*e.g.*, one or more of cecum, ascending, transverse, descending or sigmoid portions of the colon, and rectum). In various embodiments, the composition and/or formulation can release at least one dose, at least two doses, at least three doses, at least four doses, or at least five doses of the bacterial isolates at different locations along the intestines, at different times, and/or at different pH.

[00352] In some embodiments, the bacterial isolates described herein are in the form of live, vegetative cells. In some embodiments, the bacterial isolates described herein are in the form of spores. In some embodiments, the bacterial isolates described herewith are lyophilized. By way of non-limiting example, lyophilization can be via methods known in the art, including those described in US Patent No. 7,799,328, the contents of which are hereby incorporated by reference in their entirety. In some embodiments, lyophilized bacterial isolates described herein are placed in an enterically coated soft gel or capsule.

[00353] In various embodiments, formulations can take the form of those described in one or more of US Patent Nos. 8,535,713 and 8,9117,77 and US Patent Publication Nos. 20120141585, 20120141531, 2006/001896, 2007/0292523, 2008/0020018, 2008/0113031, 2010/0203120, 2010/0255087, 2010/0297221, 2011/0052645, 2013/0243873, 2013/0330411, 2014/0017313, and 2014/0234418, the contents of which are hereby incorporated by reference in their entirety.

[00354] In various embodiments, formulations can take the form of those as described in International Patent Publication No. WO 2008/135090, the contents of which are hereby incorporated by reference in their entirety.

[00355] In various embodiments, formulations can take the form of those described in one or more of US Patent Nos. 4,196,564; 4,196,565; 4,247,006; 4,250,997; 4,268,265; 5,317,849;

6,572,892; 7,712,634; 8,074,835; 8,398,912; 8,440,224; 8,557,294; 8,646,591; 8,739,812; 8,810,259; 8,852,631; and 8,911,788 and US Patent Publication Nos. 2014/0302132; 2014/0227357; 20140088202; 20130287842; 2013/0295188; 2013/0307962; and 20130184290, the contents of which are hereby incorporated by reference in their entirety.

Administration and Dosage

[00356] It will be appreciated that the actual dose of a pharmaceutical composition described herein (e.g., a microbial cocktail comprising bacterial isolates and/or additional therapeutic agents) will vary according to, for example, the particular dosage form and the mode of administration to a subject. Many factors that may modify the action of the bacterial isolates (*e.g.*, body weight, gender, diet, time of administration, route of administration, rate of excretion, condition of the subject, drug combinations, genetic disposition and reaction sensitivities) can be taken into account by those skilled in the art. Administration can be carried out continuously or in one or more discrete doses within the maximum tolerated dose. Optimal administration rates for a given set of conditions can be ascertained by those skilled in the art using conventional dosage administration tests.

[00357] In various embodiments, the dose of the pharmaceutical composition (e.g., comprising a microbial cocktail) is effective to modulate a patient's microbiome to favor an ecological balance, *i.e.* treating or preventing a disorder related to intestinal dysbiosis described herein (including a gastrointestinal disorder).

[00358] In one aspect, a pharmaceutically active or therapeutically effective dose of a bacterial isolate administered to a subject (i.e., in single or multiple administrations) to treat at least one symptom of a disorder related to a gut dysbiosis comprises at least 10^5, at least 10^6, at least 10^7, at least 10^8, at least 10^9, at least 10^{10}, at least 10^{11}, at least 10^{12}, at least 10^{13}, at least 10^{14}, or at least 10^{15} CFUs of the bacterial isolate. In another aspect, a pharmaceutically active or therapeutically effective dose of a bacterial isolate administered to a subject (i.e., in single or multiple administrations) to treat at least one symptom of a disorder related to a gut dysbiosis comprises at most 10^5, at most 10^6, at most 10^7, at most 10^8, at most 10^9, at most 10^{10}, at most 10^{11}, at most 10^{12}, at most 10^{13}, at most 10^{14}, or at most 10^{15} CFUs of the bacterial isolate. In a further aspect, a pharmacologically active or therapeutically effective dose of a bacterial isolate administered to a subject (i.e., in single or multiple administrations) to treat at least one symptom of a disorder related to a gut dysbiosis is selected from the group consisting of: from 10^8 CFUs to 10^{14} CFUs, from 10^9 CFUs to 10^{13} CFUs, from 10^{10} CFUs to 10^{12} CFUs, from

10^{10} CFUs to 10^{11} CFUs, from 10^{9} CFUs to 10^{14} CFUs, from 10^{9} CFUs to 10^{12} CFUs, from 10^{9} CFUs to 10^{11} CFUs, from 10^{9} CFUs to 10^{10} CFUs, from 10^{10} CFUs to 10^{14} CFUs, from 10^{10} CFUs to 10^{13} CFUs, from 10^{11} CFUs to 10^{14} CFUs, from 10^{11} CFUs to 10^{13} CFUs, from 10^{12} CFUs to 10^{14} CFUs, and from 10^{13} CFUs to 10^{14} CFUs of the bacterial isolate.

[00359] In an aspect, a pharmaceutical composition comprises one or more bacterial isolates, with each bacterial isolate present in each unit dose at one of the foregoing pharmaceutically active or therapeutically effective doses in a unit weight of about 0.2, 0.4, 0.6, 0.8 or 1.0 gram, or a unit volume of about 0.2, 0.4, 0.6, 0.8 or 1.0 milliliter.

[00360] In one aspect, a pharmaceutically active or therapeutically effective dose of a bacterial isolate administered to a subject (i.e., in single or multiple administrations) to treat at least one symptom of a disorder related to a gut dysbiosis comprises at least 10^{5}, at least 10^{6}, at least 10^{7}, at least 10^{8}, at least 10^{9}, at least 10^{10}, at least 10^{11}, at least 10^{12}, at least 10^{13}, at least 10^{14}, or at least 10^{15} cells or spores of the bacterial isolate. In another aspect, a pharmaceutically active or therapeutically effective dose of a bacterial isolate administered to a subject i.e. in single or multiple administrations) to treat at least one symptom of a disorder related to a gut dysbiosis comprises at most 10^{5}, at most 10^{6}, at most 10^{7}, at most 10^{8}, at most 10^{9}, at most 10^{10}, at most 10^{11}, at most 10^{12}, at most 10^{13}, at most 10^{14}, or at most 10^{15} total cells or spores of the bacterial isolate. In a further aspect, a pharmacologically active or therapeutically effective dose of a bacterial isolate administered to a subject (i.e., in single or multiple administrations) to treat at least one symptom of a disorder related to a gut dysbiosis is selected from the group consisting of: from 10^{8} to 10^{14}, from 10^{9} to 10^{13}, from 10^{10} to 10^{12}, from 10^{10} to 10^{11}, from 10^{9} to 10^{14}, from 10^{9} to 10^{12}, from 10^{9} to 10^{11}, from 10^{9} to 10^{10}, from 10^{10} to 10^{14}, from 10^{10} to 10^{13}, from 10^{11} to 10^{14}, from 10^{11} to 10^{13}, from 10^{12} to 10^{14}, and from 10^{13} to 10^{14} cells or spores of the bacterial isolate.

[00361] In an aspect, the pharmaceutically active or therapeutically effective dose cell count of a bacterial isolate is directed to live cells. In one aspect, a pharmaceutical composition comprises one or more bacterial isolates, with each bacterial isolates present in each dosage unit at one of the foregoing pharmaceutically active or therapeutically effective doses in a unit weight of about 0.2, 0.4, 0.6, 0.8 or 1.0 gram, or a unit volume of about 0.2, 0.4, 0.6, 0.8 or 1.0 milliliter.

[00362] In an aspect, a pharmaceutical composition described herein is in the form of a capsule, and each capsule comprises at least 10^{5}, at least 10^{6}, at least 10^{7}, at least 10^{8}, at least 10^{9}, at

least 10^{10}, at least 10^{11}, at least 10^{12}, at least 10^{13}, at least 10^{14}, or at least 10^{15} cells or spores. In an aspect, a pharmaceutical composition described herein is in the form of a capsule, and each capsule comprises from 10^{8} to 10^{14}, from 10^{9} to 10^{13}, from 10^{10} to 10^{12}, from 10^{10} to 10^{11}, from 10^{9} to 10^{14}, from 10^{9} to 10^{12}, from 10^{9} to 10^{11}, from 10^{9} to 10^{10}, from 10^{10} to 10^{14}, from 10^{10} to 10^{13}, from 10^{11} to 10^{14}, from 10^{11} to 10^{13}, from 10^{12} to 10^{14}, or from 10^{13} to 10^{14} cells or spores of a bacterial isolate.

[00363] In embodiments, a pharmaceutical composition comprises a microbial cocktail that comprises multiple bacterial isolates. In embodiments, at least two bacterial isolates are present in the microbial cocktail at about the same amounts (e.g., about the same number of total cells and/or about the same number of live cells). In embodiments, at least three bacterial isolates, at least four bacterial isolates, at least five bacterial isolates, at least six bacterial isolates, at least seven bacterial isolates, at least eight bacterial isolates, at least nine bacterial isolates, at least ten bacterial isolates, or more than ten bacterial isolates are present in the pharmaceutical composition at about the same amounts (e.g., about the same number of total cells and/or about the same number of live cells). In embodiments, all of the bacterial isolates of a microbial cocktail are present in about the same amounts.

[00364] In embodiments, at least two bacterial isolates of a microbial cocktail described herein are present in the microbial cocktail at different amounts (e.g., different numbers of total cells and/or different numbers of live cells). In embodiments, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, or more than ten bacterial isolates are present in the microbial cocktail at different amounts.

[00365] In embodiments, first and second bacterial isolates of a microbial cocktail are present in the microbial cocktail at different amounts, and a relative proportion of the first and second bacterial isolates to each other in the microbial cocktail is about the same as the relative proportion of first and second bacterial strains corresponding to the first and second bacterial isolates in a microbiota of a fecal sample of a human (e.g., a fecal microbiota of a donor of one or more of the first and second bacterial isolates or a fecal microbiota of a subject administered the first and second bacterial isolates).

[00366] In embodiments, first and second bacterial isolates of a microbial cocktail are present in the microbial cocktail at different amounts, and a relative proportion of the first and second bacterial isolates to each other in the microbial cocktail is different than or does not resemble a proportion of first and second bacterial strains corresponding to the first and second bacterial

isolates in a microbiota of a fecal sample of a human (e.g., a fecal microbiota of a donor of one or more of the first and second bacterial isolates or a fecal microbiota of a subject administered the first and second bacterial isolates).

[00367] In embodiments, a pharmaceutical composition comprises one or more bacterial isolates at an amount or dosage which is at or above the minimum amount or dosage of the bacterial isolate required to be administered to a subject for engraftment of the bacterial isolate to occur in the intestine of the subject. For example, a minimum dosage of the bacterial isolate required for engraftment of the bacterial isolate into the intestine of the subject can be at least 10^6 cells, at least 10^7 cells, at least 10^8 cells, at least 10^9 cells, at least 10^{10} cells, at least 10^{11} cells, or at least 10^{12} cells. In embodiments a first and second bacterial isolate of a microbial cocktail engraft in the intestine of a subject at different minimal dosages or amounts, and a dosage or amount of each of the first and second bacterial isolate in the microbial cocktail varies corresponding to the respective minimal dosage or amount required for engraftment of the respective bacterial isolate.

[00368] In embodiments, a microbial cocktail comprises *Odoribacter splanchnicus* and *Faecalibacterium prausnitzii*, and the *O. splanchnicus* cells are more abundant in the microbial cocktail than the *F. prausnitzii* cells. In embodiments, a microbial cocktail comprises *O. splanchnicus* and *Faecalibacterium prausnitzii*, and the *O. splanchnicus* cells are less abundant in the microbial cocktail than the *F. prausnitzii* cells. In embodiments, a microbial cocktail comprises *O. splanchnicus* and *Faecalibacterium prausnitzii*, and the *O. splanchnicus* cells are more abundant in the microbial cocktail than the *F. prausnitzii* cells. In embodiments, a microbial cocktail comprises *O. splanchnicus* and *Eubacterium rectale*, and the *O. splanchnicus* cells are less abundant in the microbial cocktail than the *E. rectale* cells. In embodiments, a microbial cocktail comprises *O. splanchnicus* and *Akkermansia muciniphila*, and the *O. splanchnicus* cells are more abundant in the microbial cocktail than the *A. muciniphila* cells. In embodiments, a microbial cocktail comprises *O. splanchnicus* and *Bacteroides cellulosilyticus*, and the *O. splanchnicus* cells are more abundant in the microbial cocktail than the *B. cellulosilyticus* cells. In embodiments, a microbial cocktail comprises *O. splanchnicus* and *Roseburia faecis*, and the *O. splanchnicus* cells are less abundant in the microbial cocktail than the *R. faecis* cells. In embodiments, a microbial cocktail comprises *O. splanchnicus* and *Alistipes shahii*, and the *O. splanchnicus* cells are more abundant in the microbial cocktail than the *A. shahii* cells.

[00369] In embodiments, a microbial cocktail comprises *Eubacterium rectale*, the cells of which are more abundant in the microbial cocktail than the cells of any other single bacterial isolate of the microbial cocktail (i.e., *E. rectale* is the most abundant bacterial isolate in the microbial cocktail). In embodiments, a microbial cocktail comprises *E. rectale* and *F. prausnitzii*, and the *E. rectale* cells are more abundant in the microbial cocktail than the *F. prausnitzii* cells. In embodiments, a microbial cocktail comprises *E. rectale* and *A. shahii*, and the *E. rectale* cells are more abundant in the microbial cocktail than the *A. shahii* cells. In embodiments, a microbial cocktail comprises *E. rectale* and *R. faecis*, and the *E. rectale* cells are more abundant in the microbial cocktail than the *R. faecis* cells. In embodiments, a microbial cocktail comprises *E. rectale* and *A. muciniphila*, and the *E. rectale* cells are more abundant in the microbial cocktail than the *A. muciniphila* cells.

[00370] In embodiments, a microbial cocktail comprises *R. faecis* and *F. prausnitzii*, and the *R. faecis* cells are more abundant than the *F. prausnitzii* cells. In embodiments, a microbial cocktail comprises *R. faecis* and *F. prausnitzii*, and the *R. faecis* cells are more abundant than the *F. prausnitzii* cells. In embodiments, a microbial cocktail comprises *R. faecis* and *A. muciniphila*, and the *R. faecis* cells are more abundant than the *A. muciniphila* cells. In embodiments, a microbial cocktail comprises *R. faecis* and *A. shahii*, and the *R. faecis* cells are more abundant than the *A. shahii* cells. In embodiments, a microbial cocktail comprises *R. faecis* and *B. cellusloilyticus*, and the *R. faecis* cells are more abundant than the *B. cellulosilyticus* cells.

[00371] In embodiments, a microbial cocktail comprises *B. cellulosilyticus*, the cells of which are less abundant in the microbial cocktail than the cells of any other single bacterial isolate of the microbial cocktail (i.e., *B. cellulosilyticus* is the least abundant bacterial isolate in the microbial cocktail). In embodiments, a microbial cocktail comprises *B. cellulosilyticus* and *A. shahii*, and the *B. cellulosilyticus* cells are less abundant than the *A. shahii* cells. In embodiments, a microbial cocktail comprises *B. cellulosilyticus* and *A. muciniphila*, and the *B. cellulosilyticus* cells are less abundant than the *A. muciniphila* cells. In embodiments, a microbial cocktail comprises *B. cellulosilyticus* and *F. prausnitzii*, and the *B. cellulosilyticus* cells are less abundant than the *F. prausnitzii* cells.

[00372] In embodiments, a microbial cocktail comprises *A. shahii* and *A. muciniphila*, and the *A. shahii* cells are less abundant than the *A. muciniphila* cells. In embodiments, a microbial cocktail comprises *A. shahii* and *F. prausnitzii*, and the *A. shahii* cells are less abundant than the *F. prausnitzii* cells.

[00373] In embodiments, a microbial cocktail comprises multiple bacterial isolates belonging to the species *F. prausnitzii*, and the cells of one of the bacterial isolates are more abundant than the cells of at least one of the other bacterial isolates in the microbial cocktail. In embodiments, a microbial cocktail comprises two bacterial isolates belonging to the species *F. prausnitzii*, and the cells of one of the bacterial isolates are more abundant than the cells of the other bacterial isolate of the microbial cocktail.

[00374] In embodiments, a pharmaceutical composition comprises *O. splanchnicus* at a dosage of at least 10^8 cells. In embodiments, a pharmaceutical composition comprises *O. splanchnicus* at a dosage of between 10^8 to 10^9 cells. In embodiments, a pharmaceutical composition comprises *O. splanchnicus* at a dosage of not more than 10^9 cells. In embodiments, a pharmaceutical composition comprises *O. splanchnicus* at a dosage of at least 10^9 cells.

[00375] In embodiments, a pharmaceutical composition comprises *B. cellulosilyticus* at a dosage of at least 10^7 cells. In embodiments, a pharmaceutical composition comprises *B. cellulosilyticus* at a dosage of between 10^7 to 10^8 cells. In embodiments, a pharmaceutical composition comprises *B. cellulosilyticus* at a dosage of at least 10^8 cells. In embodiments, a pharmaceutical composition comprises *B. cellulosilyticus* at a dosage of between 10^8 to 10^9 cells. In embodiments, a pharmaceutical composition comprises *B. cellulosilyticus* at a dosage of not more than 10^9 cells. In embodiments, a pharmaceutical composition comprises *B. cellulosilyticus* at a dosage of at least 10^9 cells.

[00376] In embodiments, a pharmaceutical composition comprises *A. shahii* at a dosage of at least 10^8 cells. In embodiments, a pharmaceutical composition comprises *A. shahii* at a dosage of between 10^8 to 10^9 cells. In embodiments, a pharmaceutical composition comprises *A. shahii* at a dosage of not more than 10^9 cells. In embodiments, a pharmaceutical composition comprises *A. shahii* at a dosage of at least 10^9 cells.

[00377] In embodiments, a pharmaceutical composition comprises *A. muciniphila* at a dosage of at least 10^8 cells. In embodiments, a pharmaceutical composition comprises *A. muciniphila* at a dosage of between 10^8 to 10^9 cells. In embodiments, a pharmaceutical composition comprises *A. muciniphila* at a dosage of not more than 10^9 cells. In embodiments, a pharmaceutical composition comprises *A. muciniphila* at a dosage of at least 10^9 cells.

[00378] In embodiments, a pharmaceutical composition comprises *R. faecis* at a dosage of at least 10^8 cells. In embodiments, a pharmaceutical composition comprises *R. faecis* at a dosage of between 10^8 to 10^9 cells. In embodiments, a pharmaceutical composition comprises *A.*

muciniphila at a dosage of not more than 10^9 cells. In embodiments, a pharmaceutical composition comprises *A. muciniphila* at a dosage of at least 10^9 cells. In embodiments, a pharmaceutical composition comprises *R. faecis* at a dosage of between 10^9 to 10^{10} cells. In embodiments, a pharmaceutical composition comprises *A. muciniphila* at a dosage of not more than 10^{10} cells.

[00379] In embodiments, a pharmaceutical composition comprises *F. prausnitzii* at a dosage of at least 10^8 cells. In embodiments, a pharmaceutical composition comprises *F. prausnitzii* at a dosage of between 10^8 to 10^9 cells. In embodiments, a pharmaceutical composition comprises *F. prausnitzii* at a dosage of not more than 10^9 cells. In embodiments, a pharmaceutical composition comprises *F. prausnitzii* at a dosage of at least 10^9 cells. In embodiments, a pharmaceutical composition comprises *R. faecis* at a dosage of between 10^9 to 10^{10} cells. In embodiments, a pharmaceutical composition comprises *F. prausnitzii* at a dosage of not more than 10^{10} cells. In embodiments, a pharmaceutical composition comprises *F. prausnitzii* at a dosage of at least 10^{10} cells. In embodiments, a pharmaceutical composition comprises *F. prausnitzii* at a dosage of not more than 10^{11} cells.

[00380] In embodiments, a pharmaceutical composition comprises *E. rectale* at a dosage of at least 10^8 cells. In embodiments, a pharmaceutical composition comprises *E. rectale* at a dosage of between 10^8 to 10^9 cells. In embodiments, a pharmaceutical composition comprises *E. rectale* at a dosage of not more than 10^9 cells. In embodiments, a pharmaceutical composition comprises *E. rectale* at a dosage of at least 10^9 cells. In embodiments, a pharmaceutical composition comprises *E. rectale* at a dosage of between 10^9 to 10^{10} cells. In embodiments, a pharmaceutical composition comprises *E. rectale* at a dosage of not more than 10^{10} cells. In embodiments, a pharmaceutical composition comprises *E. rectale* at a dosage of at least 10^{10} cells. In embodiments, a pharmaceutical composition comprises *E. rectale* at a dosage of between 10^{10} to 10^{11} cells. In embodiments, a pharmaceutical composition comprises *E. rectale* at a dosage of not more than 10^{11} cells. In embodiments, a pharmaceutical composition comprises *E. rectale* at a dosage of at least 10^{11} cells.

[00381] In embodiments, every about 200mg of a pharmaceutical composition comprises a pharmacologically active dose. In embodiments, every about 75, 100, 125, 150, 175, 200, 250, 300, 350, 400, 450, 500, 750, 1000, 1500, or 2000 mg of a pharmaceutical composition comprises a pharmacologically active dose.

[00382] Individual doses of the pharmaceutical composition (e.g., comprising a microbial cocktail) can be administered in unit dosage forms (*e.g.*, tablets or capsules) containing, for example, from about 0.01 mg to about 5,000 mg, from about 0.01 mg to about 4,000 mg, from about 0.01 mg to about 3,000 mg, from about 0.01 mg to about 2,000 mg, from about 0.01 mg to about 1,000 mg, from about 0.01 mg to about 950 mg, from about 0.01 mg to about 900 mg, from about 0.01 mg to about 850 mg, from about 0.01 mg to about 800 mg, from about 0.01 mg to about 750 mg, from about 0.01 mg to about 700 mg, from about 0.01 mg to about 650 mg, from about 0.01 mg to about 600 mg, from about 0.01 mg to about 550 mg, from about 0.01 mg to about 500 mg, from about 0.01 mg to about 450 mg, from about 0.01 mg to about 400 mg, from about 0.01 mg to about 350 mg, from about 0.01 mg to about 300 mg, from about 0.01 mg to about 250 mg, from about 0.01 mg to about 200 mg, from about 0.01 mg to about 150 mg, from about 0.01 mg to about 100 mg, from about 0.1 mg to about 90 mg, from about 0.1 mg to about 80 mg, from about 0.1 mg to about 70 mg, from about 0.1 mg to about 60 mg, from about 0.1 mg to about 50 mg, from about 0.1 mg to about 40 mg, from about 0.1 mg to about 30 mg, from about 0.1 mg to about 20 mg, from about 0.1 mg to about 10 mg, from about 0.1 mg to about 5 mg, from about 0.1 mg to about 3 mg, from about 0.1 mg to about 1 mg of the active ingredient per unit dosage form, or from about 5 mg to about 80 mg per unit dosage form. For example, a unit dosage form can include about 0.01 mg, about 0.02 mg, about 0.03 mg, about 0.04 mg, about 0.05 mg, about 0.06 mg, about 0.07 mg, about 0.08 mg, about 0.09 mg, about 0.1 mg, about 0.2 mg, about 0.3 mg, about 0.4 mg, about 0.5 mg, about 0.6 mg, about 0.7 mg, about 0.8 mg, about 0.9 mg, about 1 mg, about 2 mg, about 3 mg, about 4 mg, about 5 mg, about 6 mg, about 7 mg, about 8 mg, about 9 mg about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 35 mg, about 40 mg, about 45 mg, about 50 mg, about 55 mg, about 60 mg, about 65 mg, about 70 mg, about 75 mg, about 80 mg, about 85 mg, about 90 mg, about 95 mg, about 100 mg, about 150 mg, about 200 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, about 700 mg, about 750 mg, about 800 mg, about 850 mg, about 900 mg, about 950 mg, about 1,000 mg, , about 2,000 mg, about 3,000 mg, about 4,000 mg, or about 5,000 mg of the active ingredient, inclusive of all values and ranges therebetween.

[00383] In one embodiment, the pharmaceutical composition (e.g., comprising a microbial cocktail) is administered at an amount of from about 0.01 mg to about 100 mg daily, an amount of from about 0.01 mg to about 5,000 mg daily, about 0.01 mg to about 4,000 mg daily, about 0.01 mg to about 3,000 mg daily, about 0.01 mg to about 2,000 mg daily, about 0.01 mg to

about 1,000 mg daily, from about 0.01 mg to about 950 mg daily, from about 0.01 mg to about 900 mg daily, from about 0.01 mg to about 850 mg daily, from about 0.01 mg to about 800 mg daily, from about 0.01 mg to about 750 mg daily, from about 0.01 mg to about 700 mg daily, from about 0.01 mg to about 650 mg daily, from about 0.01 mg to about 600 mg daily, from about 0.01 mg to about 550 mg daily, from about 0.01 mg to about 500 mg daily, from about 0.01 mg to about 450 mg daily, from about 0.01 mg to about 400 mg daily, from about 0.01 mg to about 350 mg daily, from about 0.01 mg to about 300 mg daily, from about 0.01 mg to about 250 mg daily, from about 0.01 mg to about 200 mg daily, from about 0.01 mg to about 150 mg daily, from about 0.1 mg to about 100 mg daily, from about 0.1 mg to about 95 mg daily, from about 0.1 mg to about 90 mg daily, from about 0.1 mg to about 85 mg daily, from about 0.1 mg to about 80 mg daily, from about 0.1 mg to about 75 mg daily, from about 0.1 mg to about 70 mg daily, from about 0.1 mg to about 65 mg daily, from about 0.1 mg to about 60 mg daily, from about 0.1 mg to about 55 mg daily, from about 0.1 mg to about 50 mg daily, from about 0.1 mg to about 45 mg daily, from about 0.1 mg to about 40 mg daily, from about 0.1 mg to about 35 mg daily, from about 0.1 mg to about 30 mg daily, from about 0.1 mg to about 25 mg daily, from about 0.1 mg to about 20 mg daily, from about 0.1 mg to about 15 mg daily, from about 0.1 mg to about 10 mg daily, from about 0.1 mg to about 5 mg daily, from about 0.1 mg to about 3 mg daily, from about 0.1 mg to about 1 mg daily, or from about 5 mg to about 80 mg daily. In various embodiments, the bacterial isolates (and/or additional therapeutic agents) is administered at a daily dose of about 0.01 mg, about 0.02 mg, about 0.03 mg, about 0.04 mg, about 0.05 mg, about 0.06 mg, about 0.07 mg, about 0.08 mg, about 0.09 mg, about 0.1 mg, about 0.2 mg, about 0.3 mg, about 0.4 mg, about 0.5 mg, about 0.6 mg, about 0.7 mg, about 0.8 mg, about 0.9 mg, about 1 mg, about 2 mg, about 3 mg, about 4 mg, about 5 mg, about 6 mg, about 7 mg, about 8 mg, about 9 mg about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 35 mg, about 40 mg, about 45 mg, about 50 mg, about 55 mg, about 60 mg, about 65 mg, about 70 mg, about 75 mg, about 80 mg, about 85 mg, about 90 mg, about 95 mg, about 100 mg, about 150 mg, about 200 mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 650 mg, about 700 mg, about 750 mg, about 800 mg, about 850 mg, about 900 mg, about 950 mg, about 1,000 mg, about 2,000 mg, about 3,000 mg, about 4,000 mg, or about 5,000 mg inclusive of all values and ranges therebetween.

[00384] In some embodiments, a suitable dosage of the pharmaceutical composition (e.g., comprising a microbial cocktail) is in a range of about 0.01 mg/kg to about 100 mg/kg of body

weight of the subject, for example, about 0.01 mg/kg, about 0.02 mg/kg, about 0.03 mg/kg, about 0.04 mg/kg, about 0.05 mg/kg, about 0.06 mg/kg, about 0.07 mg/kg, about 0.08 mg/kg, about 0.09 mg/kg, about 0.1 mg/kg, about 0.2 mg/kg, about 0.3 mg/kg, about 0.4 mg/kg, about 0.5 mg/kg, about 0.6 mg/kg, about 0.7 mg/kg, about 0.8 mg/kg, about 0.9 mg/kg, about 1 mg/kg, about 1.1 mg/kg, about 1.2 mg/kg, about 1.3 mg/kg, about 1.4 mg/kg, about 1.5 mg/kg, about 1.6 mg/kg, about 1.7 mg/kg, about 1.8 mg/kg, 1.9 mg/kg, about 2 mg/kg, about 3 mg/kg, about 4 mg/kg, about 5 mg/kg, about 6 mg/kg, about 7 mg/kg, about 8 mg/kg, about 9 mg/kg, about 10 mg/kg body weight, about 20 mg/kg body weight, about 30 mg/kg body weight, about 40 mg/kg body weight, about 50 mg/kg body weight, about 60 mg/kg body weight, about 70 mg/kg body weight, about 80 mg/kg body weight, about 90 mg/kg body weight, or about 100 mg/kg body weight, inclusive of all values and ranges therebetween. In other embodiments, a suitable dosage of the composition in a range of about 0.01 mg/kg to about 100 mg/kg of body weight, in a range of about 0.01 mg/kg to about 90 mg/kg of body weight, in a range of about 0.01 mg/kg to about 80 mg/kg of body weight, in a range of about 0.01 mg/kg to about 70 mg/kg of body weight, in a range of about 0.01 mg/kg to about 60 mg/kg of body weight, in a range of about 0.01 mg/kg to about 50 mg/kg of body weight, in a range of about 0.01 mg/kg to about 40 mg/kg of body weight, in a range of about 0.01 mg/kg to about 30 mg/kg of body weight, in a range of about 0.01 mg/kg to about 20 mg/kg of body weight, in a range of about 0.01 mg/kg to about 10 mg/kg of body weight, in a range of about 0.01 mg/kg to about 9 mg/kg of body weight, in a range of about 0.01 mg/kg to about 8 mg/kg of body weight, in a range of about 0.01 mg/kg to about 7 mg/kg of body weight, in a range of 0.01 mg/kg to about 6 mg/kg of body weight, in a range of about 0.05 mg/kg to about 5 mg/kg of body weight, in a range of about 0.05 mg/kg to about 4 mg/kg of body weight, in a range of about 0.05 mg/kg to about 3 mg/kg of body weight, in a range of about 0.05 mg/kg to about 2 mg/kg of body weight, in a range of about 0.05 mg/kg to about 1.5 mg/kg of body weight, or in a range of about 0.05 mg/kg to about 1 mg/kg of body weight.

[00385] In accordance with certain embodiments, the pharmaceutical composition (e.g., comprising a microbial cocktail) can be administered, for example, more than once daily, about once per day, about every other day, about every third day, about once a week, about once every two weeks, about once every month, about once every two months, about once every three months, about once every six months, or about once every year.

[00386] In embodiments, a pharmaceutical composition can be administered to a patient in need thereof at least once daily for at least two consecutive days. In embodiments, a

pharmaceutical composition is administered at least once daily for at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 consecutive days. In embodiments, a pharmaceutical composition is administered at least once daily for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive weeks. In embodiments, a pharmaceutical composition is administered at least twice, three times, four times, or five times per week for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive weeks. In embodiments, a pharmaceutical composition is administered at least once daily for at most 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 consecutive days or weeks. In embodiments, a pharmaceutical composition is administered at least once daily for at most 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive weeks or months. In embodiments, a pharmaceutical composition is administered at least once for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive months or years, chronically for a subject's entire life span, or an indefinite period of time.

[00387] In embodiments, a pharmaceutical composition can be administered to a patient in need thereof at least twice daily for at least two consecutive days. In embodiments, a pharmaceutical composition is administered at least twice daily for at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 consecutive days. In embodiments, a pharmaceutical composition is administered at least twice daily for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive weeks. In embodiments, a pharmaceutical composition is administered at least twice daily for at most 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 consecutive days or week. In embodiments, a pharmaceutical composition is administered at least twice daily for at most 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive weeks or months. In embodiments, a pharmaceutical composition is administered at least twice for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive months or years, chronically for a subject's entire life span, or an indefinite period of time.

[00388] In embodiments, a pharmaceutical composition can be administered to a patient in need thereof at least three times daily for at least two consecutive days. In embodiments, a pharmaceutical composition is administered at least three times daily for at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 consecutive days. In embodiments, a pharmaceutical composition is administered at least three times daily for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive weeks. In embodiments, a pharmaceutical composition is administered at least three times daily for at most 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 consecutive days or weeks. In embodiments, a pharmaceutical composition is administered at least three times daily for at most 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive weeks or

months. In embodiments, a pharmaceutical composition is administered at least three times for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive months or years, chronically for a subject's entire life span, or an indefinite period of time.

[00389] In embodiments, a pharmaceutical composition can be administered to a patient in need thereof at a dosing schedule of at least once or twice daily for at least three consecutive days or weeks. In embodiments, a dose is administered at least once, twice, or three times daily for a period between 1 and 12 weeks, between 2 and 12 weeks, between 3 and 12 weeks, between 4 and 12 weeks, between 5 and 12 weeks, between 6 and 12 weeks, between 7 and 12 weeks, between 8 and 12 weeks, between 9 and 12 weeks, between 10 and 12 weeks, between 1 and 2 weeks, between 2 and 3 weeks, between 3 and 4 weeks, between 4 and 5 weeks, between 5 and 6 weeks, between 6 and 7 weeks, between 7 and 8 weeks, between 8 and 9 weeks, between 9 and 10 weeks, or between 10 and 11 weeks.

[00390] In embodiments, a pharmaceutical composition can be administered to a patient in need thereof at a dosing schedule of once-a-week, twice-a-week, or thrice-a-week. The term "once-a-week" means that a dose is administered typically only once in a week, for example, on the same day of each week. "Twice-a-week" means that a dose is administered typically only two times in a week, for example, on the same two days of each weekly period. "Thrice-a-week" means that a dose is administered typically only three times in a week, for example, on the same three days of each weekly period.

[00391] In embodiments, a pharmaceutical composition can be administered to a patient in need thereof, wherein the administration comprises a first dosing schedule followed by a second dosing schedule. In embodiments, a first dosing schedule comprises a treatment or induction dose. In embodiments, a second dosing schedule comprises a maintenance dose. For example, a pharmaceutically active maintenance dose of a second dosage schedule can be lower than or equal to a pharmaceutically active induction dose of a first dosing schedule. In other examples, a maintenance dose of a second dosing schedule can be higher than an induction dose of a first dosing schedule.

[00392] At least one of a first and second dosing schedule for administering a pharmaceutical composition can comprise administration of the composition at least once daily for at least one day. In embodiments, at least one of a first or second dosing schedule comprises administration of the composition at least once daily for at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 consecutive days. In embodiments, at least one of a first or second dosing schedule comprises

administration of the composition at least once daily for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive weeks. In embodiments, at least one of a first or second dosing schedule comprises administration of the composition for at most 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 consecutive days or weeks. In embodiments, at least one of a first or second dosing schedule comprises administration of the composition for at most 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive weeks or months. In embodiments, at least one of a first or second dosing schedule comprises administration of the composition for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive months or years, chronically for a subject's entire life span, or an indefinite period of time.

[00393] In embodiments, at least one of a first or second dosing schedule used in a method can be once-a-week, twice-a-week, or thrice-a-week.

[00394] In embodiments, at least one of a first and second dosing schedule can last for at least about 2, 4, 6, 8, 10, 12, 18, 24, 36, 48, 72, or 96 months. In embodiments, a second dosing schedule lasts permanently, for a treated subject's entire life span, or an indefinite period of time. In embodiments, at least one of a first and second dosing schedule is a continuous dosing schedule. In embodiments, at least one of a first and second dosing schedule is an intermittent dosing schedule. In embodiments, at least one of a first and second dosing schedule is an intermittent dosing schedule comprising a treatment period of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 days followed by a resting period of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 days. In embodiments, at least one of a first and second dosing schedule comprises administering a dose every other day, every two days, or every 3, 4, 5, 6, 7, 8 days. In embodiments, a dose is administered for an extended period of time with or without titration (or otherwise changing the dosage or dosing schedule).

[00395] In embodiments, the interval between a first and a second dosing schedule is at least about 1, 2, 3, 4, 5, 6, or 7 days, or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 weeks, or at least about 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, or 12 months.

[00396] In embodiments, a second dosing schedule (*e.g.*, a maintenance dose) comprises a dosage about 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 75, 100, 200, 400, 800, 1000, 5000 or more fold lower than the dosage used in a first dosing schedule (*e.g.*, an initial induction dose). In embodiments, a second dosing schedule (*e.g.*, a maintenance dosing schedule) has an equal or lower dosing frequency than a first dosing schedule (*e.g.*, an initial treatment dosing schedule).

In embodiments, a second dosing schedule (*e.g.*, a maintenance dosing schedule) has a higher dosing interval than a first dosing schedule (*e.g.*, an initial treatment dosing schedule).

[00397] In various embodiments, methods described herein are useful in treatment of a human subject. In some embodiments, the human is a pediatric human. In other embodiments, the human is an adult human. In other embodiments, the human is a geriatric human. In other embodiments, the human may be referred to as a patient. In some embodiments, the human is a female. In some embodiments, the human is a male.

[00398] In certain embodiments, the human has an age in a range of from about 1 to about 18 months old, from about 18 to about 36 months old, from about 1 to about 5 years old, from about 5 to about 10 years old, from about 10 to about 15 years old, from about 15 to about 20 years old, from about 20 to about 25 years old, from about 25 to about 30 years old, from about 30 to about 35 years old, from about 35 to about 40 years old, from about 40 to about 45 years old, from about 45 to about 50 years old, from about 50 to about 55 years old, from about 55 to about 60 years old, from about 60 to about 65 years old, from about 65 to about 70 years old, from about 70 to about 75 years old, from about 75 to about 80 years old, from about 80 to about 85 years old, from about 85 to about 90 years old, from about 90 to about 95 years old or from about 95 to about 100 years old.

[00399] In one aspect, a subject being treated is a human patient. In one aspect, a patient is a male patient. In one aspect, a patient is a female patient. In one aspect, a patient is a premature newborn. In one aspect, a patient is a term newborn. In one aspect, a patient is a neonate. In one aspect, a patient is an infant. In one aspect, a patient is a toddler. In one aspect, a patient is a young child. In one aspect, a patient is a child. In one aspect, a patient is an adolescent. In one aspect, a patient is a pediatric patient. In one aspect, a patient is a geriatric patient. In one aspect, a human patient is a child patient below about 18, 15, 12, 10, 8, 6, 4, 3, 2, or 1-year-old. In another aspect, a human patient is an adult patient. In another aspect, a human patient is an elderly patient. In a further aspect, a human patient is a patient above about 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, or 95 years old. In another aspect, a patient is about between 1 and 5, between 2 and 10, between 3 and 18, between 21 and 50, between 21 and 40, between 21 and 30, between 50 and 90, between 60 and 90, between 70 and 90, between 60 and 80, or between 65 and 75 years old. In one aspect, a patient is a young old patient (65-74 years). In one aspect, a patient is a middle old patient (75-84 years). In one aspect, a patient is an old patient (>85 years).

Additional Therapeutic Agents and Combination Therapy or Co-Formulation

[00400] The pharmaceutical compositions described herein can include one or more additional therapeutic agents, which can be administered to a subject in need thereof in a method described herein. The additional therapeutic agent can be administered simultaneous or sequential with a microbial therapeutic (e.g., microbial cocktail) described herein. Further, the present compositions and formulations can comprise the additional therapeutic agent (*e.g.* via co-formulation). For example, the additional therapeutic agent and one or more bacterial isolates can be combined into a single formulation.

[00401] In one embodiment, the additional therapeutic agent and a microbial therapeutic (e.g., one or more bacterial isolates) are administered to a subject simultaneously. The term "simultaneously" as used herein, means that the additional therapeutic agent and the microbial therapeutic are administered with a time separation of no more than about 60 minutes, such as no more than about 30 minutes, no more than about 20 minutes, no more than about 10 minutes, no more than about 5 minutes, or no more than about 1 minute. Administration of the additional therapeutic agent and the microbial therapeutic can be by simultaneous administration of a single formulation (*e.g.*, a formulation comprising the additional therapeutic agent and one or more bacterial isolates) or of separate formulations (*e.g.*, a first formulation including the additional therapeutic agent and a second formulation including one or more bacterial isolates).

[00402] Co-administration does not require an additional therapeutic agent to be administered simultaneously, if the timing of its administration is such that the pharmacological activities of the additional therapeutic agent and the microbial therapeutic (e.g., one or more bacterial isolates) overlap in time. For example, the additional therapeutic agent and the microbial therapeutic can be administered sequentially. The term "sequentially" as used herein means that the additional therapeutic agent and the microbial therapeutic are administered with a time separation of more than about 60 minutes. For example, the time between the sequential administration of the additional therapeutic agent and the microbial therapeutic can be more than about 60 minutes, more than about 2 hours, more than about 5 hours, more than about 10 hours, more than about 1 day, more than about 2 days, more than about 3 days, or more than about 1 week apart. The optimal administration times will depend on the rates of metabolism, excretion, and/or the pharmacodynamic activity of the additional therapeutic agent and the microbial therapeutic being administered. Either of the additional therapeutic agent or the microbial therapeutic (e.g., one or more bacterial isolates) can be administered first.

[00403] In a further embodiment, the additional therapeutic agent and the microbial therapeutic (e.g., one or more bacterial isolates) are administered to a subject simultaneously but the release of additional therapeutic agent and the microbial therapeutic from their respective dosage forms (or single unit dosage form if co-formulated) in the GI tract occurs sequentially.

[00404] Co-administration also does not require multiple additional therapeutic agents to be administered to the subject by the same route of administration. Rather, each additional therapeutic agent can be administered by any appropriate route, for example, parenterally or non-parenterally.

[00405] In some embodiments, the additional therapeutic agent is an agent used in the current standard-of-care induction therapies for IBD such as UC. Such agents include but are not limited to 5-aminosalicylic acid (5-ASA), corticosteroids, or biologics (*e.g.*, Infliximab, Adalimumab or Vedolizumab).

[00406] In some embodiments, the additional therapeutic agent is an anti-inflammatory agent such as steroidal anti-inflammatory agents or non-steroidal anti-inflammatory agents (NSAIDS). Steroids, particularly the adrenal corticosteroids and their synthetic analogues, are well known in the art. Examples of corticosteroids include, without limitation, hydroxyltriamcinolone, alpha-methyl dexamethasone, beta-methyl betamethasone, beclomethasone dipropionate, betamethasone benzoate, betamethasone dipropionate, betamethasone valerate, clobetasol valerate, desonide, desoxymethasone, dexamethasone, diflorasone diacetate, diflucortolone valerate, fluadrenolone, fluclorolone acetonide, flumethasone pivalate, fluosinolone acetonide, fluocinonide, flucortine butylester, fluocortolone, fluprednidene (fluprednylidene) acetate, flurandrenolone, halcinonide, hydrocortisone acetate, hydrocortisone butyrate, methylprednisolone, triamcinolone acetonide, cortisone, cortodoxone, flucetonide, fludrocortisone, difluorosone diacetate, fluradrenolone acetonide, medrysone, amcinafel, amcinafide, betamethasone and the balance of its esters, chloroprednisone, clocortelone, clescinolone, dichlorisone, difluprednate, flucloronide, flunisolide, fluoromethalone, fluperolone, fluprednisolone, hydrocortisone, meprednisone, paramethasone, prednisolone, prednisone, beclomethasone dipropionate. (NSAIDS) that can be used, include but are not limited to, salicylic acid, acetyl salicylic acid, methyl salicylate, glycol salicylate, salicylmides, benzyl-2,5-diacetoxybenzoic acid, ibuprofen, fulindac, naproxen, ketoprofen, etofenamate, phenylbutazone, and indomethacin. Additional anti-

inflammatory agents are described, for example, in U.S. Patent No. 4,537,776, the entire contents of which is incorporated by reference herein.

[00407] In some embodiments, the additional therapeutic agent is a probiotic. Probiotics suitable for use include, but are not limited to, *Saccharomyces boulardii; Lactobacillus rhamnosus* GG; *Lactobacillus plantarum* 299v; *Clostridium butyricum* M588; *Clostridium difficile* VP20621 (non-toxigenic *C.* difficile strain); combination of *Lactobacillus casei*, *Lactobacillus acidophilus* (Bio-K + CL1285); combination of *Lactobacillus casei*, *Lactobacillus bulgaricus*, *Streptococcus thermophilus* (Actimel); combination of *Lactobacillus acidophilus*, *Bifidobacterium bifidum* (Florajen3); combination of *Lactobacillus acidophilus, Lactobacillus bulgaricus delbrueckii subsp. bulgaricus, Lactobacillus bulgaricus casei, Lactobacillus bulgaricus plantarum, Bifidobacterium longum, Bifidobacterium infantis, Bifidobacterium breve, and Streptococcus salivarius subsp.thermophilus* (VSL#3)).

[00408] In an aspect, the present disclosure provides for administering a probiotic prior to administering a pharmaceutical composition comprising a non-selected fecal microbiota. In another aspect, the disclosure provides for co-administering a probiotic and a pharmaceutical composition comprising a non-selected fecal microbiota. In another aspect, the probiotic is selected from the group consisting of one or more *Akkermansia* or *Parabacteroides* species. In another aspect, the probiotic is selected from the group consisting of two or more *Akkermansia* or *Parabacteroides* species. In another aspect, the probiotic is selected from the group consisting of three or more *Akkermansia* or *Parabacteroides* species. In another aspect, the probiotic is selected from the group consisting of four or more *Akkermansia* or *Parabacteroides* species. In another aspect, the probiotic is selected from the group consisting of five or more *Akkermansia* or *Parabacteroides* species. In another aspect, the probiotic is selected from the group consisting of six or more *Akkermansia* or *Parabacteroides* species. In another aspect, the probiotic is selected from the group consisting of 1 to 3, 3 to 5, 5 to 8, or 8 to 10 *Akkermansia* or *Parabacteroides* species. A probiotic can be provided in a single dose or in multiple doses. When provided as a single composition, the single composition can comprise a single probiotic or a mixture of probiotics. When provided in multiple compositions, each composition can comprise a single probiotic or a mixture of probiotics.

[00409] In some embodiments, the additional therapeutic agent is a prebiotic. A prebiotic is a compound or compounds (e.g., comprising one or more nutrients) administered to a subject to promote the growth, proliferation, or activity of one or more microorganisms (e.g., bacteria) in the intestine of the subject (e.g., by providing a substrate to be metabolized by the one or more

microorganisms). Without wishing to be bound by theory, prebiotics can be added to a pharmaceutical composition to nutritionally supplement bacteria in the endogenous microbiome of the subject and/or in the pharmaceutical composition itself, e.g., to stimulate the growth or activity of one or more strains of an uncultured population of fecal bacteria and/or one or more bacterial isolates. Additionally, one or more prebiotics can be added to a composition to buffer against "shock" to bacteria cells when transitioning those cells to a new environment, for example, subsequent to the isolation and/or purification of an uncultured population of fecal bacteria, or before or after freezing, freeze-drying, spray-drying, reconstitution in solution and the like.

[00410] Non-limiting examples of prebiotics that can be added to a pharmaceutical composition or administered to a subject include amino acids, lactic acid, ammonium nitrate, amylose, barley mulch, biotin, carbonate, cellulose, chitin, choline, fructooligosaccharides (FOSs), fructose, galactooligosaccharides (GOSs), glucose, glycerol, heteropolysaccharide, histidine, homopolysaccharide, hydroxyapatite, inulin, isomaltulose, lactose, lactulose, maltodextrins, maltose, mannooligosaccharides, nitrogen, oligodextrose, oligofructoses, oligofructose-enriched inulin, oligosaccharides, pectin, phosphate salts, phosphorus, polydextroses, polyols, potash, potassium, sodium nitrate, starch, sucrose, sulfur, sun fiber, tagatose, thiamine, trans-galactooligosaccharides, trehalose, vitamins, a water-soluble carbohydrate, and/or xylooligosaccharides (XOSs), and a combination thereof. Illustrative prebiotics include complex carbohydrates, amino acids, peptides, or other essential nutritional components for the survival of the bacterial composition.

[00411] In an aspect, a subject is not pretreated with a prebiotic nutrient prior to treatment with a pharmaceutical composition. In another aspect, the pharmaceutical composition is not supplemented with a prebiotic nutrient.

[00412] In embodiments, a prebiotic can be added (e.g., in dry or liquid forms) in a pharmaceutical composition described herein, for example, a composition comprising one or more bacterial isolates.

[00413] Alternately, or additionally, a prebiotic can be included (e.g., in dry or liquid forms) in a distinct pharmaceutical composition lacking a microbial therapeutic.

[00414] A prebiotic can be provided to a subject before, contemporaneously with, and/or after administration of a pharmaceutical composition comprising a microbial therapeutic (e.g., one

or more bacterial isolates), either in the same pharmaceutical composition or in a separate pharmaceutical composition.

[00415] A prebiotic can be provided in a single dose or in multiple doses. When provided as a single composition, the single composition can comprise a single prebiotic or a mixture of prebiotics. When provided in multiple compositions, each composition can comprise a single prebiotic or a mixture of prebiotics.

[00416] As examples, when multiple doses are provided, a first composition comprising a prebiotic can include one specific prebiotic, e.g., inulin, and a second composition can include a second specific prebiotic, e.g., pectin. Alternately, a first composition can include a mixture of prebiotics, e.g., inulin and pectin and a second composition can include different mixture of prebiotics, e.g., inulin and a FOS. A first composition can include a mixture of prebiotics and a second composition can include one specific prebiotic.

[00417] The amount of prebiotic provided to a subject/patient and/or included in a composition depends on the specific prebiotic, the specific bacterial strain of beneficial bacteria, and/or the disease state of the subject/patient.

[00418] In some embodiments, the additional therapeutic agent is an antidiarrheal agent. Antidiarrheal agents suitable for use include, but are not limited to, DPP-IV inhibitors, natural opioids, such as tincture of opium, paregoric, and codeine, synthetic opioids, such as diphenoxylate, difenoxin and loperamide, bismuth subsalicylate, lanreotide, vapreotide and octreotide, motiln antagonists, COX2 inhibitors like celecoxib, glutamine, thalidomide and traditional antidiarrheal remedies, such as kaolin, pectin, berberine and muscarinic agents.

[00419] In some embodiments, the additional therapeutic agent can be an analgesic. Analgesics useful in the compositions and methods described herein include, without limitation, morphine, codeine, heroine, methadone and related compounds, thebaine, orpiavine, and their derivatives, buprenorphine, the piperidines, morphinans, benzomorphans, tetrahydroisoquinolines, thiambutanes, benzylamines, tilidine, viminol, nefopam, capsaicin(8-methyl-N-vanillyl-6E-nonenamide), "synthetic" capsaicin(N-vanillylnonamide), and related compounds.

[00420] In some embodiments, the additional therapeutic agent is an anti-bacterial agent, which includes, but is not limited to, cephalosporin antibiotics (cephalexin, cefuroxime, cefadroxil, cefazolin, cephalothin, cefaclor, cefamandole, cefoxitin, cefprozil, and ceftobiprole); fluoroquinolone antibiotics (cipro, Levaquin, floxin, tequin, avelox, and norflox);

tetracycline antibiotics (tetracycline, minocycline, oxytetracycline, and doxycycline); penicillin antibiotics (amoxicillin, ampicillin, penicillin V, dicloxacillin, carbenicillin, vancomycin, and methicillin); monobactam antibiotics (aztreonam); and carbapenem antibiotics (ertapenem, doripenem, imipenem/cilastatin, and meropenem). In some embodiments, the anti-bacterial agent can be any of the penicillin, cephalosporin, monobactam, and carbapenem antibiotics.

[00421] In one aspect, a method further comprises pretreating a subject with an antibiotic composition prior to administering a therapeutic bacterial or microbiota composition. In one aspect, an antibiotic composition administered herein comprises an antibiotic selected from the group consisting of rifabutin, clarithromycin, clofazimine, vancomycin, rifampicin, nitroimidazole, chloramphenicol, and a combination thereof. In another aspect, an antibiotic composition administered herein comprises an antibiotic selected from the group consisting of rifaximin, rifamycin derivative, rifampicin, rifabutin, rifapentine, rifalazil, bicozamycin, aminoglycoside, gentamycin, neomycin, streptomycin, paromomycin, verdamicin, mutamicin, sisomicin, netilmicin, retymicin, kanamycin, aztreonam, aztreonam macrolide, clarithromycin, dirithromycin, roxithromycin, telithromycin, azithromycin, bismuth subsalicylate, vancomycin, streptomycin, fidaxomicin, amikacin, arbekacin, neomycin, netilmicin, paromomycin, rhodostreptomycin, tobramycin, apramycin, and a combination thereof. In another aspect, a subject is not pretreated with an antibiotic composition prior to administering a therapeutic bacterial or microbiota composition. In another aspect, the pharmaceutical composition is not supplemented with an antibiotic composition. In a further aspect, a method further comprises pretreating a subject with an anti-inflammatory drug prior to administration of a therapeutic bacterial or microbiota composition. In yet another aspect, a subject is not pretreated with an anti-inflammatory drug prior to administering a therapeutic bacterial or microbiota composition. In another aspect, a therapeutic bacterial or microbiota composition is not supplemented with an anti-inflammatory.

[00422] For all additional therapeutic agent compositions and methods, targeting to various parts of the GI tract can be employed as described herein.

Methods of Treatment

[00423] An aspect of the present invention is a method of treating or preventing inflammatory bowel disease (IBD) in a subject in need thereof, the method comprising administering to the subject a plurality of bacterial isolates, wherein the plurality of bacterial

isolates comprises *Bacteroides stercoris*, and at least two of *Bacteroides cellulosilyticus, Bacteroides uniformis, Suboligranulum variabile, Anaerostipes hadrus, Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*, wherein at least two of the plurality of bacterial isolates are isolated from a stool of different human donors.

[00424] In embodiments, the *Bacteroides stercoris* comprises a 16S ribosomal ribonucleic acid (rRNA) sequence that has at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity with the nucleotide sequence of SEQ ID NO: 13. In embodiments, the plurality of bacterial isolates comprises at least one of *Bacteroides cellulosilyticus, Bacteroides uniformis, Odoribacter splanchnicus*, *Roseburia faecis*, *Anaerostipes hadrus, Faecalibacterium prausnitzii*, *Suboligranulum variabile, Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least two, or at least three, or at least four, or at least five, or at least six, or at least seven, or at least eight, or at least nine, or each of *Bacteroides cellulosilyticus, Bacteroides uniformis, Odoribacter splanchnicus*, *Roseburia faecis*, *Anaerostipes hadrus, Faecalibacterium prausnitzii*, *Suboligranulum variabile, Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

[00425] In embodiments, the plurality of bacterial isolates comprises at least four of *Bacteroides cellulosilyticus, Bacteroides uniformis, Odoribacter splanchnicus*, *Roseburia faecis*, *Anaerostipes hadrus, Faecalibacterium prausnitzii*, *Suboligranulum variabile, Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least five of *Bacteroides cellulosilyticus, Bacteroides uniformis, Odoribacter splanchnicus*, *Roseburia faecis*, *Anaerostipes hadrus, Faecalibacterium prausnitzii*, *Suboligranulum variabile, Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least six of *Bacteroides cellulosilyticus, Bacteroides uniformis, Odoribacter splanchnicus*, *Roseburia faecis*, *Anaerostipes hadrus, Faecalibacterium prausnitzii*, *Suboligranulum variabile, Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least seven of *Bacteroides cellulosilyticus, Bacteroides uniformis, Odoribacter splanchnicus*, *Roseburia faecis*, *Anaerostipes hadrus, Faecalibacterium prausnitzii*, *Suboligranulum variabile, Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*. In embodiments, the plurality of bacterial isolates comprises at least eight of *Bacteroides cellulosilyticus, Bacteroides uniformis, Odoribacter splanchnicus*, *Roseburia faecis*, *Anaerostipes hadrus,*

Faecalibacterium prausnitzii, *Suboligranulum variabile*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

[00426] In embodiments, the plurality of bacterial isolates comprises a 16S rRNA sequence that has at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity with nucleotide sequences selected from SEQ ID NOs: 1, 2, 3, 7, 8, 11, 14, 18, 19, 20, 22 and 23.

[00427] In embodiments, the plurality of bacterial isolates comprises: (a) a 16S rRNA sequence that is at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity with nucleotide sequence of SEQ ID NOs: 1 and/or 7, (b) a 16S rRNA sequence that is at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity with nucleotide sequence of SEQ ID NO: 2, (c) a 16S rRNA sequence that is at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity with nucleotide sequence of SEQ ID NO: 3. (d) a 16S rRNA sequence that is at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity with nucleotide sequence of SEQ ID NO: 8, (e) a 16S rRNA sequence that is at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity with nucleotide sequence of SEQ ID NO: 11 (f) a 16S rRNA sequence that is at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity with nucleotide sequence of SEQ ID NO: 13, (g) a 16S rRNA sequence that is at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity with nucleotide sequence of SEQ ID NO: 14, (h) a 16S rRNA sequence that is at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity with nucleotide sequence of SEQ ID NO: 18, (i) a 16S rRNA sequence that is at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity with nucleotide sequence of SEQ ID NO: 19, (j) a 16S rRNA sequence that is at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity with nucleotide sequence of SEQ ID NO: 20, and/or (k) a 16S rRNA sequence that is at least about 95%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity with nucleotide sequence of SEQ ID NOs: 22 and/or 23.

[00428] In embodiments, the plurality of bacterial isolates comprises at least two bacterial isolates comprising *Faecalibacterium prausnitzii*, wherein the at least two bacterial isolates comprise different 16S rRNA sequences. In embodiments, the at least two bacterial isolates comprising *Faecalibacterium prausnitzii* comprise 16S rRNA sequences that are at

least about 95%, or at least about 97%, or at least about 98%, or at least about 99% identity sequence identity with nucleotide sequences of SEQ ID NOs: 1 and/or 7. In embodiments, the at least two bacterial isolates comprising *Faecalibacterim prausnitzii* are isolated from a stool of different human donors.

[00429] Disclosed herein are methods of preventing or treating a disorder related to an intestinal dysbiosis in a subject in need thereof, comprising administering to the subject an effective amount of any herein-disclosed pharmaceutical composition. In embodiments, the disorder is selected from inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), C. difficile infection (CDI), C. difficile-associated disease (CDAD), and antibiotic-induced adverse effect. In embodiments, the disorder is IBD selected from ulcerative colitis (UC), Crohn's disease (CD), and pouchitis. In embodiments, the method treats or prevents a nosocomial infection and/or a secondary emergent infection and/or treats and/or prevents the overgrowth of one or more pathogenic microorganisms in the GI tract of the subject. In embodiments, the method comprises maintenance of a normal intestinal microbiota. In embodiments, the method further comprises administering at least one prebiotic to the subject.

[00430] In various embodiments, provided herein is a method of modulating a microbiome of a subject in need thereof to provide or restore an ecological balance, comprising administering to the subject a composition described herein. For instance, in various embodiments, there is provided methods of diminishing or inhibiting one or more pathogenic bacteria by administering a composition described herein. In various embodiments, admistration of one or more bacterial isolates described herein augments growth of at least one type of bacteria not detectably present in a patient's GI tract prior to administration and, in various embodiments, which is non-pathogenic.

[00431] In various embodiments, provided herein is a method of restoring or enhancing ecological control over gut pathogens or pathobionts in a subject in need thereof, comprising administering to the subject a composition described herein.

[00432] In various embodiments, a method comprises administering a composition described herein to treat a disease or condition associated with GI dysbiosis in a subject in need thereof. In some embodiments, the subject has inflammatory bowel diseases (IBD), for example, Crohn's disease, colitis (*e.g.*, UC or microscopic colitis), or pouchitis. IBD is a group of inflammatory conditions of the large intestine and, in some cases, the small intestine. Examples of IBD that can be treated by the compositions, formulations and methods described herein

include, but are not limited to, Crohn's disease, UC, pouchitis, collagenous colitis, lymphocytic colitis, ischemic colitis, diversion colitis, Behçet's syndrome, infective colitis, and indeterminate colitis. In an embodiment, provided herein is a method of treating UC comprising administering a composition described herein to a subject in need thereof. In another embodiment, provided herein is a method of treating CD comprising administering a composition described herein to a subject in need thereof. In a further embodiment, provided herein is a method of treating pouchitis comprising administering a composition described herein to a subject in need thereof.

[00433] In various embodiments, a method comprises administering a composition described herein to treat UC in a subject in need thereof. UC is one form of IBD. It is a chronic disease of the colon, in which the lining of the colon becomes inflamed and develops tiny open sores, or ulcers, that produce pus and mucous. In some embodiments, methods described herein can ameliorate, reduce, or eliminate the inflammation and/or ulceration associated with UC. In some embodiments, methods described herein can ameliorate, reduce, or eliminate one or more symptoms associated with UC including but not limited to, abdominal discomfort or pain, frequent emptying of the colon, lose and urgent bowel movements, persistent diarrhea, bloody stool, loss of appetite, and weight loss. In some embodiments, methods described herein can reduce or prevent the delay in growth and development in children afflicted with UC.

[00434] In various embodiments, a method comprises administering a composition described herein to treat UC in a subject in need thereof. For example, a successful treatment of the subject can be measured using the indices below, *e.g.*, the present methods cause a subject's activity score threshold to change from severe to moderate, mild, or remission; or cause a patient's score to change from moderate to mild or remission; or cause a patient's score to change from mild to remission:

Index	**Parameters assessed**	**Scoring system**	**Activity score thresholds**			
			Remission	**Mild**	**Moderate**	**Severe**
Mayo score	Stool frequency Rectal bleeding Physician's global assessment Sigmoidoscopy	Cumulative score	0–2	3–5	6–10	11–12

Index	Parameters assessed	Scoring system	Activity score thresholds			
			Remission	Mild	Moderate	Severe
UCDAI	Stool frequency Rectal bleeding Physician's global assessment Sigmoidoscopy	Cumulative score	0–2	3–8		9–12
Rachmilewitz score (CAI)	Bowel movement frequency Blood in stools Physician's global assessment Abdominal pain/cramps Temperature EIMs Laboratory findings (ESR, hemoglobin)	Cumulative score	0–4	5–10	11–17	>17
Powell–Tuck index (St Mark's index)	Well-being Abdominal pain Bowel movement frequency Stool consistency Bleeding Anorexia Nausea/vomiting Abdominal	Cumulative score	≤3	4–10	11–14	>14

Index	Parameters assessed	Scoring system	Activity score thresholds			
			Remission	Mild	Moderate	Severe
	tenderness Eye, joint, mouth, or skin complications Temperature Sigmoidoscopy					
SCCAI (Walmsley)	Bowel movement frequency (day) Bowel movement frequency (night) Urgency of defecation Blood in stool Well-being Extracolonic features	Cumulative score	≤2 <2.5	3–20		
Lichtiger index	Diarrhea frequency Nocturnal diarrhea Visible blood (% of movements) Fecal incontinence Abdominal pain/cramping Well-being Abdominal	Cumulative score	≤3	4–8	9–14	>14

Index	Parameters assessed	Scoring system	Activity score thresholds			
			Remission	Mild	Moderate	Severe
	tenderness Need for antidiarrheal medications					
Sco index	Bowel movement frequency Blood in stool ESR Hemoglobin Albumin	Cumulative score with components given different weightings (+ constant to yield a mean value as close as possible to Truelove–Witts criteria)	<108 <120	<150	150–220	>220

[00435] In some embodiments, a method comprises administering a pharmaceutical composition described herein to treat IBS in a subject in need thereof. IBS is a common disorder that affects the colon and can cause cramping, abdominal pain, bloating, gas, diarrhea and constipation. IBS is classified based on the predominant symptom of diarrhea (IBS with predominant diarrhea, IBS-D), constipation (IBS with predominant constipation, IBS-C) or mixed symptoms (IBS with alternating constipation and diarrhea, IBS-A). Methods described herein can be effective in treating one or more of IBS-D, IBS-C, and/or IBS-A. In some embodiments, methods described herein (e.g., comprising administering a composition described herein) can reduce or eliminate one or more symptoms associated with one or more of IBS-D, IBS-C, and/or IBS-A.

[00436] In embodiments, a method comprises administering a pharmaceutical composition described herein to treat or prevent a disease/disorder associated with the presence of abnormal enteric microflora (e.g. intestinal dysbiosis) in a subject in need thereof. The disease/disorder can be selected from a gastro-intestinal disorder including irritable bowel syndrome or spastic

colon, Functional Bowel Disease (FBD), including constipation predominant FBD, pain predominant FBD, upper abdominal FBD, Nonulcer Dyspepsia (NUD), gastro-esophageal reflux, inflammatory bowel disease including Crohn's disease, ulcerative colitis, indeterminate colitis, collagenous colitis, microscopic colitis, chronic Clostridium difficile infection, pseudomembranous colitis, mucous colitis, antibiotic associated colitis, idiopathic or simple constipation, diverticular disease, AIDS enteropathy, small bowel bacterial overgrowth, coeliac disease, polyposis coil, colonic polyps, chronic idiopathic pseudo obstructive syndrome, and toxic megacolon.

[00437] In embodiments, a method comprises administering a composition described herein to treat or prevent a disorder associated with a liver disorder in a subject in need thereof. Non-limiting examples of a liver disorder include primary biliary cirrhosis, Primary Sclerosing Cholangitis (PSC), fatty liver, and cryptogenic cirrhosis. In embodiments, such diseases/disorders are related to an intestinal dysbiosis of a subject.

[00438] In embodiments, a method comprises administering a composition described herein to treat or prevent a rheumatic disorder in a subject in need thereof. Non-limiting examples of a rheumatic disorder include rheumatoid arthritis, non-rheumatoid arthritis, non-rheumatoid factor positive arthritis, ankylosing spondylitis, Lyme disease, and Reiter's syndrome. In embodiments, such diseases/disorders are related to an intestinal dysbiosis of a subject.

[00439] In embodiments, a method comprises administering a composition described herein to treat or prevent an immune-mediated disorder in a subject in need thereof. Non-limiting examples of an immune-mediated disorder include glomerulonephritis, hemolytic uraemic syndrome, juvenile diabetes mellitus, mixed cryoglobulinaemia, polyarteritis, familial Mediterranean fever, amyloidosis, scleroderma, systemic lupus erythematosus, and Behçets syndrome. In embodiments, such diseases/disorders are related to an intestinal dysbiosis of a subject.

[00440] In embodiments, a method comprises administering a composition described herein to treat or prevent an autoimmune disorder in a subject in need thereof. Non-limiting examples of an autoimmune disorder include Acute Disseminated Encephalomyelitis (ADEM), acute necrotizing hemorrhagic leukoencephalitis, Addison's disease, agammaglobulinemia, alopecia areata, amyloidosis, ankylosing spondylitis, anti-GBM/anti-TBM nephritis, Antiphospholipid Syndrome (APS), autoimmune angioedema, autoimmune aplastic anemia, autoimmune dysautonomia, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune

hyperlipidemia, autoimmune immunodeficiency, Autoimmune Inner Ear Disease (AIED), autoimmune myocarditis, autoimmune oophoritis, autoimmune pancreatitis, autoimmune retinopathy, Autoimmune Thrombocytopenic Purpura (ATP), autoimmune thyroid disease, autoimmune urticarial, axonal & neuronal neuropathies, Balo disease, Behcet's disease, bullous pemphigoid, cardiomyopathy, Castleman disease, celiac disease, Chagas disease, Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Chronic Recurrent Multifocal Ostomyelitis (CRMO), Churg-Strauss syndrome, cicatricial pemphigoid/benign mucosal pemphigoid, Crohn's disease, Cogan's syndrome, cold agglutinin disease, congenital heart block, Coxsackie myocarditis, CREST disease, essential mixed cryoglobulinemia, demyelinating neuropathies, dermatitis herpetiformis, dermatomyositis, Devic's disease (neuromyelitis optica), discoid lupus, Dressler's syndrome, endometriosis, eosinophilic esophagitis, eosinophilic fasciitis, erythema nodosum, experimental allergic encephalomyelitis, Evans syndrome, fibrosing alveolitis, giant cell arteritis (temporal arteritis), giant cell myocarditis, glomerulonephritis, Goodpasture's syndrome, Granulomatosis With Polyangiitis (GPA), Graves' disease, Guillain-Barre syndrome, Hashimoto's encephalitis, Hashimoto's thyroiditis, hemolytic anemia, Henoch-Schonlein purpura, herpes gestationis, hypogammaglobulinemia, idiopathic thrombocytopenic purpura (ITP), IgA nephropathy, IgG4-related sclerosing disease, immunoregulatory lipoproteins, inclusion body myositis, interstitial cystitis, juvenile arthritis, juvenile idiopathic arthritis, juvenile myositis, Kawasaki syndrome, Lambert-Eaton syndrome, leukocytoclastic vasculitis, lichen planus, lichen sclerosus, ligneous conjunctivitis, linear IgA disease (LAD), lupus (systemic lupus erythematosus), chronic Lyme disease, Meniere's disease, microscopic polyangiitis, Mixed Connective Tissue Disease (MCTD), Mooren's ulcer, Mucha-Habermann disease, multiple sclerosis, myasthenia gravis, myositis, narcolepsy, neuromyelitis optica (Devic's), neutropenia, ocular cicatricial pemphigoid, optic neuritis, palindromic rheumatism, PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus), paraneoplastic cerebellar degeneration, Paroxysmal Nocturnal Hemoglobinuria (PNH), Parry Romberg syndrome, Parsonnage-Turner syndrome, pars planitis (peripheral uveitis), pemphigus, peripheral neuropathy, perivenous encephalomyelitis, pernicious anemia, POEMS syndrome, polyarteritis nodosa, type I, II, & III autoimmune polyglandular syndromes, polymyalgia rheumatic, polymyositis, postmyocardial infarction syndrome, postpericardiotomy syndrome, progesterone dermatitis, primary biliary cirrhosis, Primary Sclerosing Cholangitis (PSC), psoriasis, psoriatic arthritis, idiopathic pulmonary fibrosis, pyoderma gangrenosum, pure red cell aplasia, Raynaud's phenomenon, reactive arthritis, reflex sympathetic dystrophy, Reiter's

syndrome, relapsing polychondritis, restless legs syndrome, retroperitoneal fibrosis, rheumatic fever, rheumatoid arthritis, sarcoidosis, Schmidt syndrome, scleritis, scleroderma, Sjögren's syndrome, sperm & testicular autoimmunity, stiff person syndrome, Subacute Bacterial Endocarditis (SBE), Susac's syndrome, sympathetic ophthalmia, Takayasu's arteritis, temporal arteritis/giant cell arteritis, Thrombocytopenic Purpura (TTP), Tolosa-Hunt syndrome, transverse myelitis, type 1 diabetes, asthma, ulcerative colitis, Undifferentiated Connective Tissue Disease (UCTD), uveitis, vasculitis, vesiculobullous dermatosis, vitiligo, and Wegener's granulomatosis. In embodiments, such disorders are related to an intestinal dysbiosis of a subject.

[00441] In embodiments, a method comprises administering a composition described herein to treat or prevent a neurological syndrome in a subject in need thereof. Non-limiting examples of a neurological syndrome include as chronic fatigue syndrome, migraine, multiple sclerosis, amyotrophic lateral sclerosis, myasthenia gravis, Gillain-Barré syndrome, Parkinson's disease, Alzheimer's disease, Chronic Inflammatory Demyelinating Polyneuropathy, and other degenerative disorders. In embodiments, such syndromes are related to an intestinal dysbiosis of a subject.

[00442] In embodiments, a method comprises administering a composition described herein to treat or prevent a psychiatric disorder in a subject in need thereof. Non-limiting examples of a psychiatric disorder include chronic depression, schizophrenia, psychotic disorders, manic depressive illness; regressive disorders including, Asperger's syndrome, Rett syndrome, Attention Deficit Hyperactivity Disorder (ADHD), and Attention Deficit Disorder (ADD); the regressive disorder; autism; Sudden Infant Death Syndrome (SIDS); anorexia nervosa. In embodiments, such diseases/disorders are related to an intestinal dysbiosis of a subject.

[00443] In embodiments, a method comprises administering a composition described herein to treat or prevent a dermatological condition in a subject in need thereof. Non-limiting examples of a dermatological condition include chronic urticaria, acne, dermatitis herpetiformis and vasculitis disorders. In embodiments, such diseases/disorders are related to an intestinal dysbiosis of a subject.

[00444] In embodiments, a method comprises administering a composition described herein to treat or prevent a cardiovascular and/or vascular disorder in a subject in need thereof. In embodiments, such diseases/disorders are related to an intestinal dysbiosis of a subject.

[00445] In embodiments, a method comprises administering a composition described herein to treat or prevent a bloodstream infection (BSI) in a subject in need thereof. Patients at risk for such BSIs include but are not limited to solid organ transplant patients; chronic kidney disease patients, *e.g.*, on hemodialysis; and oncology patients. In embodiments, such BSIs are related to an intestinal dysbiosis of a subject.

[00446] In embodiments, a method comprises administering a composition described herein to treat or prevent a catheter or intravascular-line infection (*e.g.*, central-line infection) in a subject in need thereof. In embodiments, such infections are related to an intestinal dysbiosis of a subject.

[00447] In embodiments, a method comprises administering a composition described herein to treat or prevent a skin or soft tissue infection in a subject in need thereof. In embodiments, such infections are related to an intestinal dysbiosis of a subject.

[00448] In embodiments, a method comprises administering a composition described herein to treat or prevent a surgical-site infection in a subject in need thereof. In embodiments, such infections are related to an intestinal dysbiosis of a subject.

[00449] In embodiments, a method comprises administering a composition described herein to treat or prevent a urinary tract infection (*e.g.*, antibiotic-resistant urinary tract infections and catheter-associated urinary tract infections) in a subject in need thereof. In embodiments, such infections are related to an intestinal dysbiosis of a subject.

[00450] In embodiments, a method comprises administering a composition described herein to treat or prevent a wound infection in a subject in need thereof. In embodiments, such infections are related to an intestinal dysbiosis of a subject.

[00451] In embodiments, a method comprises administering a composition described herein to treat or prevent an infection in a subject in need thereof. Non-limiting examples of an infection include an antibiotic-resistant infection and an antibiotic-sensitive infection. In embodiments, such infections are related to an intestinal dysbiosis of a subject.

[00452] In embodiments, the pharmaceutical compositions and methods described herein can treat or prevent meningitis. In embodiments, the meningitis is related to an intestinal dysbiosis of a subject.

[00453] In embodiments, a method comprises administering a composition described herein to treat or prevent pneumonia, *e.g.*, ventilator-associated pneumonia in a subject in need thereof. In embodiments, the pneumonia is related to an intestinal dysbiosis of a subject.

[00454] In embodiments, the compositions, formulations and methods described herein can be used in patient populations who are in an outpatient setting, hospitalized, and/or in long-term care facilities. Such patient populations are at risk for nosocomial infections. In embodiments, such infections are related to an intestinal dysbiosis of a subject.

[00455] In embodiments, a method comprises administering a composition described herein to treat or prevent Primary Sclerosing Cholangitis (PSC) in a subject in need thereof. For example, one or more bacterial isolates provided in a pharmaceutical composition administered to the subject can replace a dysbiotic gut microbiome with a healthy community, thereby, at least, reducing bile duct inflammation and/or improving liver function.

[00456] In embodiments, a method comprises administering a composition described herein to treat or prevent a diarrheal disease in a subject in need thereof. Non-limiting example s of a diarrheal disease include acute bloody diarrhea (*e.g.*, dysentery), acute watery diarrhea (*e.g.*, cholera), checkpoint inhibitor associated colitis, diarrhea due to food poisoning, persistent diarrhea, and traveler's diarrhea. In embodiments, the diarrhea is related to an intestinal dysbiosis of a subject.

[00457] In various embodiments, administration of a pharmaceutical composition described herein can reduce, ameliorate, or eliminate one or more symptom(s) associated with a herein-described condition, disease, or disorder. Exemplary symptoms include, but are not limited to, diarrhea, bloody stool, mouth sores, perianal disease, abdominal pain, abdominal cramping, fever, fatigue, weight loss, iron deficiency, anemia, appetite loss, weight loss, anorexia, delayed growth, delayed pubertal development, and inflammation of the skin, eyes, joints, liver, and bile ducts. In embodiments, the symptom is related to an intestinal dysbiosis of a subject.

[00458] In some embodiments, a method comprises administering a composition described herein to treat or prevent an infection by pathogenic bacteria and/or inhibiting the growth or decreasing the number of pathogenic bacteria in the GI tract of a subject in need thereof. In an embodiment, the pathogenic bacteria is enterobacteria such as *Salmonella*. In various embodiments, a method comprises administering a composition described herein to mitigate or prevent the overgrowth of various coliforms in a patient's gut (including coliforms that are virulent and/or antibiotic resistant). Illustrative coliforms include *Citrobacter*, *Enterobacter*,

Hafnia, *Kelbsiella*, and *Escherichia*. In some embodiments, the methods and compositions described herein prevent or diminish secondary infections with resistant organisms.

[00459] In still other embodiments, a method comprises administering a composition described herein to treat or prevent an infectious disease of the intestines in a subject in need thereof. Non-limiting examples of an infectious disease of the intestine include CDI and/or a CDAD, nosocomial infection, secondary emergent infection, amebiasis, intestinal tuberculosis, or parasitic disorder. In some embodiments, provided herein are methods for treating or preventing a CDI and/or a CDAD, comprising administering an effective amount of a pharmaceutical composition described herein to a subject or a patient need thereof. In various embodiments, the CDI or CDAD comprises one or more of: *C. difficile* diarrhea (CDD), *C. difficile* intestinal inflammatory disease, colitis, pseudomembranous colitis, fever, abdominal pain, dehydration and disturbances in electrolytes, megacolon, peritonitis, and perforation and/or rupture of the colon.

[00460] In various embodiments, a composition described herein is administered to a subject in need thereof to treat or prevent a disease or condition associated with GI dysbiosis in the context of initial onset or relapse/recurrence (*e.g.* due to continued or restarted antibiotic therapy). For example, in a subject that has previously suffered from a GI dysbiosis, the present pharmaceutical composition or formulation can be administered upon the first symptoms of recurrence in the subject. By way of non-limiting example, symptoms of recurrence include, in a mild case, about 5 to about 10 watery bowel movements per day, no significant fever, and only mild abdominal cramps while blood tests can show a mild rise in the white blood cell count up to about 15,000 (normal levels are up to about 10,000), and, in a severe case, more than about 12 watery stools per day, nausea, vomiting, high fever (*e.g.* about 102-104°F), rectal bleeding, severe abdominal pain (*e.g.* with tenderness), abdominal distention, and a high white blood count (*e.g.* of about 15,000 to about 40,000).

[00461] In some embodiments, the methods described herein can be used to treat a subject or patient who is suffering from, or is susceptible to, a disease or condition associated with GI dysbiosis. For example, the subject can be undergoing or have undergone an initial and/or adjunctive therapy that renders the subject susceptible to a disease or condition associated with GI dysbiosis. In some embodiments, the subject is undergoing treatment, or has undergone treatment, with an antibiotic. For example, the subject can have taken an antibiotic during the past about 30 days and/or have an immune system that is weak (*e.g.* from a chronic illness). In another example, the patient can have recently been in the hospital, including in an intensive

care unit. Accordingly, in some embodiments, a method comprises administering a composition described herein to treat or prevent a nosocomial infection and/or a secondary emergent infection and/or a hospital acquired infection (HAI) in a subject in need thereof.

[00462] In various embodiments, described herein are methods for treating antibiotic-induced adverse effects in the GI tract, comprising administering an effective amount of a microbial therapeutic (e.g., one or more bacterial isolates) to a subject in need thereof. In another embodiment, provided herein are methods for preventing an antibiotic-induced adverse effect in the GI tract, comprising administering an effective amount of a microbial therapeutic to a subject in need thereof.

[00463] In another aspect, a pharmaceutical composition or a plurality of pharmaceutical compositions, as disclosed herein, can be used in the manufacture of a medicament, *e.g.*, for treating a herein-described condition, disease, or disorder in a subject in need thereof. In various embodiments, the bacterial isolates as described herein protect the intestinal microbiome from antibiotics-induced damage. In some embodiments, the methods described herein can treat or prevent an antibiotics-associated adverse effect including but not limited to diarrhea, nausea, vomiting, dysgeusia, colitis, and pseudomembranous colitis disease and/or symptoms. In an embodiment, methods described herein can be used to treat or prevent antibiotic-associated diarrhea (AAD).

[00464] Methods for measuring change and/or improvement in GI tract function can include, but are not limited to: endoscopy for direct examination of epithelium and mucosa; histological evaluation and/or tissue procurement for direct evaluation of structural changes and/or immune biomarkers; urine tests for assessment of permeability with non-absorbable sugars and LPS levels; stool tests for assessment of inflammation and/or microbiota changes (for example by PCR); and/or blood tests for assessment of specific markers, including CD4+ cell counts, Th17 cell counts, and/or LPS levels.

[00465] In embodiments, the present disclosure provides a method for treating a disorder (*e.g.*, *C. difficile* infection, autism spectrum disorder (ASD), inflammatory bowel disease, ulcerative colitis, Crohn's disease, or another indication listed herein) in a subject in need thereof, where the method comprises administering to the subject a pharmaceutically active dose of a pharmaceutical composition described herein. In embodiments, the present disclosure provides a method for treating a disorder (*e.g.*, *C. difficile* infection, ASD, inflammatory bowel disease, ulcerative colitis, or Crohn's disease) in a subject in need thereof, where the method comprises

administering daily to the subject a pharmaceutically active dose of a pharmaceutical composition described herein. In embodiments, a pharmaceutical composition is administered to a patient in need thereof at least once daily for at least two consecutive days. In embodiments, a pharmaceutical composition is administered at least once daily for at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 consecutive days. In embodiments, a pharmaceutical composition is administered at least once daily for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive weeks. In embodiments, a pharmaceutical composition is administered at least twice, three times, four times, or five times per week for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive weeks. In embodiments, a pharmaceutical composition is administered at least once daily for at most 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 consecutive days or weeks. In embodiments, a pharmaceutical composition is administered at least once daily for at most 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive weeks or months. In embodiments, a pharmaceutical composition is administered at least once for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive months or years, chronically for a subject's entire life span, or an indefinite period of time.

[00466] In embodiments, a pharmaceutical composition is administered to a patient in need thereof at least twice daily for at least two consecutive days. In embodiments, a pharmaceutical composition is administered at least twice daily for at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 consecutive days. In embodiments, a pharmaceutical composition is administered at least twice daily for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive weeks. In embodiments, a pharmaceutical composition is administered at least twice daily for at most 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 consecutive days or week. In embodiments, a pharmaceutical composition is administered at least twice daily for at most 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive weeks or months. In embodiments, a pharmaceutical composition is administered at least twice for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive months or years, chronically for a subject's entire life span, or an indefinite period of time.

In embodiments, a pharmaceutical composition is administered to a patient in need thereof at least three times daily for at least two consecutive days. In embodiments, a pharmaceutical composition is administered at least three times daily for at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 consecutive days. In embodiments, a pharmaceutical composition is administered at least three times daily for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive weeks. In embodiments, a pharmaceutical composition is administered at least three times daily for at most 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 consecutive days or weeks. In

embodiments, a pharmaceutical composition is administered at least three times daily for at most 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive weeks or months. In embodiments, a pharmaceutical composition is administered at least three times for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 consecutive months or years, chronically for a subject's entire life span, or an indefinite period of time.

[00467] In embodiments, the present disclosure provides a method for treating a disorder (*e.g.*, *C. difficile* infection, ASD, inflammatory bowel disease, ulcerative colitis, or Crohn's disease) in a subject in need thereof, where the method comprises administering orally to the subject a pharmaceutically active dose of a pharmaceutical composition comprising one or more live, non-pathogenic, bacterial isolates described herein, where the dose is administered at a dosing schedule of at least once or twice daily for at least three consecutive days or weeks. In embodiments, a dose is administered at least once, twice, or three times daily for a period between 1 and 12 weeks, between 2 and 12 weeks, between 3 and 12 weeks, between 4 and 12 weeks, between 5 and 12 weeks, between 6 and 12 weeks, between 7 and 12 weeks, between 8 and 12 weeks, between 9 and 12 weeks, between 10 and 12 weeks, between 1 and 2 weeks, between 2 and 3 weeks, between 3 and 4 weeks, between 4 and 5 weeks, between 5 and 6 weeks, between 6 and 7 weeks, between 7 and 8 weeks, between 8 and 9 weeks, between 9 and 10 weeks, or between 10 and 11 weeks.

[00468] In embodiments, the present disclosure provides a method for treating a disorder (*e.g.*, *C. difficile* infection, ASD, inflammatory bowel disease, ulcerative colitis, or Crohn's disease) in a subject in need thereof, where the method comprises a combination treatment or therapy. For example, the method can comprise a double combination therapy, a triple combination therapy, or a quadruple combination therapy.

[00469] In yet another aspect, described herein is a plurality of pharmaceutical compositions, e.g., two or more pharmaceutical compositions, as disclosed herein, for use in the prevention or treatment a condition, disease, or disorder in a subject in need thereof. In embodiments, a first composition comprises one or more bacterial isolates having a first characteristic and a second composition comprises one or more bacterial isolates having a second characteristic. In embodiments, a first composition comprises one or more bacterial isolates having a first characteristic, a second composition comprises one or more bacterial isolates having a second characteristic, and a third composition comprises one or more bacterial isolates having a third characteristic. In embodiments, a first composition comprises one or more bacterial isolates having a first characteristic, a second composition comprises one or more bacterial isolates

having a second characteristic, a third composition comprises one or more bacterial isolates having a third characteristic, and a fourth composition comprises one or more bacterial isolates having a fourth characteristic. As used herein, a characteristic of a bacterial isolate can include, for example: an ability of a bacterial isolate to produce or enhance production of at least one short-chain fatty acid (SCFA) in a gut of a subject administered the composition (e.g., represented by bacterial isolates provided in Table 2); an ability of a bacterial isolate to modulate cytokine production in a eukaryotic cell (e.g., a host cell of a subject administered the composition) (e.g., represented by bacterial isolates provided in Table 3); a correspondence to a bacterial strain more highly abundant in a healthy subject relative to a patient with UC (e.g., the bacterial isolate comprises a 16S rRNA sequence having at least 97% identity to a 16S rRNA sequence of the bacterial strain) (e.g., represented by bacterial isolates provided in Table 4); an ability to produce an aryl hydrocarbon capable of binding to and activating an AhR of a host cell of the subject (e.g., represented by bacterial isolates provided in Table 6); and a combination thereof.

[00470] Described herein is a method for preventing or treating a condition, disease or disorder in a subject in need thereof, comprising administering to the subject an effective amount of one or more pharmaceutical compositions comprising one or more bacterial isolates disclosed herein. In an embodiment, the method comprises administering to the subject one or more bacterial isolates comprising a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more of the bacterial isolates provided in Table 1. In an embodiment, the method comprises administering to the subject one or more bacterial isolates comprising a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence of one or more of the bacterial isolates provided in any one of Table 2, Table 3, or Table 4. In an embodiment, the method comprises administering to the subject one or more bacterial isolates comprising a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of one or more of the bacterial isolates provided in Table 6.

[00471] In an embodiment, the method comprises administering to the subject a plurality of bacterial isolates comprising 16S rRNA sequences at least 95% identical to 16S rRNA sequences of each of the bacterial isolates provided in any one of Tables 7-43. In an embodiment, the method comprises administering to the subject one or more bacterial isolates comprising a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence of one or more of the bacterial isolates provided in Table 44.

[00472] In embodiments, a plurality of bacterial isolates administered to a subject in a method described herein are administered in the same pharmaceutical composition. In embodiments, a plurality of bacterial isolates administered to a subject in a method described herein are administered in separate pharmaceutical compositions. For example, a method can comprise administering to a subject in need thereof an effective amount of a plurality of pharmaceutical compositions, e.g., two or more pharmaceutical compositions, as disclosed herein. The plurality of pharmaceutical compositions can be provided simultaneously or sequentially. Thus, if a subject is to be treated with, for example, three bacterial isolates, a first composition can comprise two of the bacterial isolates and the second composition can comprise the third bacterial isolate. In a different example, if a subject is to be treated with three bacterial isolates, a first composition can comprise the first bacterial isolate, the second composition can comprise the second bacterial isolate, and the third composition can comprise the third bacterial isolate.

[00473] In embodiments, disclosed herein is a method of treating a disorder, disease, or condition involving a dysbiosis of an intestinal microbiota in a subject in need thereof, the method comprising administering to the subject a pharmaceutical composition described herein, wherein the pharmaceutical composition comprises one or more bacterial isolates, wherein the one or more bacterial isolates are each administered at a particular dose (e.g., a particular number of cells or a particular number of live cells). In an embodiment, the method comprises administering a pharmaceutical composition comprising one or more bacterial isolates, wherein the one or more bacterial isolates comprises one or more of *O. splanchnicus*, *B. cellulosilyticus*, *A. shahii*, *A. muciniphila*, *R. faecis*, *F. prausnitzii*, *E. rectale*, and *S. variabile*, wherein each of the one or more bacterial isolates is administered at a dosage of at least 10^7 cells, between 10^7 to 10^8 cells, not more than10^8 cells, at least 10^8 cells, between 10^8 to 10^9 cells, not more than 10^9 cells, at least 10^9 cells, between 10^9 to 10^{10} cells, not more than 10^{10} cells, at least 10^{10} cells, between 10^{10} to 10^{11} cells, not more than 10^{11} cells, at least 10^{11} cells, between 10^{11} to 10^{12} cells, not more than 10^{12} cells, and at least 10^{12} cells.

[00474] In another aspect, disclosed herein are a plurality of pharmaceutical compositions, e.g., two or more pharmaceutical compositions, as disclosed herein, for use in the prevention or treatment of a condition, disease, or disorder in a subject in need thereof. In embodiments, a first composition comprises one or more bacterial isolates described herein. In embodiments, a second composition comprises an uncultured fecal microbiota (e.g., a substantially complete fecal microbiota purified from a stool sample) or a preparation of uncultured fecal bacteria. A

subject can be treated with the first and second compositions in any order to treat or prevent a disorder. For example, in one embodiment a subject is treated with a composition comprising an uncultured fecal microbiota (or a preparation of uncultured fecal bacteria), followed by a composition comprising one or more bacterial isolates. In another embodiment, a subject is treated with a composition comprising one or more bacterial isolates followed by a composition comprising an uncultured fecal microbiota (or a preparation of uncultured fecal bacteria). In still other embodiments, a subject can be treated with a composition comprising one or more bacterial isolates and a composition comprising an uncultured fecal microbiota (or a preparation of uncultured fecal bacteria) simultaneously (for example, with a composition comprising both the bacterial isolate(s) and uncultured fecal microbiota (or preparation of uncultured fecal bacteria), or with multiple compositions each comprising one of the bacterial isolate(s) or an uncultured fecal microbiota or a preparation of uncultured fecal bacteria).

[00475] In an embodiment, a method for treating or preventing a condition, disease or disorder of a subject comprises administration to the subject of: (i) a pharmaceutical composition comprising one or more bacterial isolates; and (ii) an uncultured fecal microbiota or a preparation of uncultured fecal bacteria. For example, the one or more bacterial isolates can be administered before or after the uncultured fecal microbiota (or preparation of uncultured fecal bacteria), or at the same time (e.g., in different compositions or together in the same composition). In another embodiment, a method for treating a disorder of a subject comprises administration to the subject of: (i) a pharmaceutical composition comprising one or more bacterial isolates; and (ii) one or more antibiotics. For example, the one or more bacterial isolates can be administered before or after the uncultured fecal microbiota (or preparation of uncultured fecal bacteria), or at the same time (e.g., in different compositions or together in the same composition). Typically, the antibiotic is administered to the subject prior to administration of the one or more bacterial isolates, in order to purge the subject's intestine of harmful and/or pathogenic bacteria prior to replenishment of the gut with bacteria from the bacterial isolate(s). In an embodiment, a method for treating a disorder of a subject comprises administration to the subject of: (i) a pharmaceutical composition comprising one or more bacterial isolates; and (ii) a prebiotic. For example, the one or more bacterial isolates can be administered before or after the prebiotic, or at the same time (e.g., in different compositions or together in the same composition). For each of the above examples, it is further understood that any given component in a method of treatment can be administered multiple times. For example, an uncultured fecal microbiota (or a preparation of uncultured fecal bacteria) can be

administered to the subject, followed by one or more bacterial isolates, followed by a second administration of the uncultured fecal microbiota (or preparation of uncultured fecal bacteria).

[00476] In an embodiment, a method for treating or preventing a condition, disease or disorder of a subject comprises administration to the subject of: (i) a pharmaceutical composition comprising one or more bacterial isolates; (ii) an uncultured fecal microbiota (or preparation of uncultured fecal bacteria); and (iii) one or more antibiotics. The different components of (i)-(iii) can be administered to the subject in any order. For example, a subject can be administered one or more antibiotics, followed by an uncultured fecal microbiota (or preparation of uncultured fecal bacteria), followed by one or more bacterial isolates. In another example, the subject can be administered one or more antibiotics, followed by one or more bacterial isolates, followed by an uncultured fecal microbiota (or preparation of uncultured fecal bacteria). For each of the above examples, it is further understood that any given component in a method of treatment can be administered multiple times. For example, an antibiotic can be administered to the subject, followed by an uncultured fecal microbiota, followed by one or more bacterial isolates, followed by a second administration of the uncultured fecal microbiota (or preparation of uncultured fecal bacteria).

[00477] In an embodiment, a method for treating or preventing a condition, disease or disorder of a subject comprises administration to the subject of: (i) a pharmaceutical composition comprising one or more bacterial isolates; (ii) an uncultured fecal microbiota (or preparation of uncultured fecal bacteria); and (iii) one or more prebiotics. The different components of (i)-(iii) can be administered to the subject in any order. For example, a subject can be administered one or more prebiotics, followed by an uncultured fecal microbiota (or preparation of uncultured fecal bacteria), followed by one or more bacterial isolates. In another example, the subject can be administered one or more prebiotics, followed by one or more bacterial isolates, followed by an uncultured fecal microbiota (or preparation of uncultured fecal bacteria). In another example, the subject can be administered one or more prebiotics following administration of one or both of the one or more bacterial isolates and/or the uncultured fecal microbiota (or preparation of uncultured fecal bacteria). For each of the above examples, it is further understood that any given component in a method of treatment can be administered multiple times. For example, an uncultured fecal microbiota (or preparation of uncultured fecal bacteria) can be administered to a subject, followed by a one or more bacterial isolates, followed by a prebiotic, followed by a second administration of the uncultured fecal microbiota (or preparation of uncultured fecal bacteria).

[00478] In an embodiment, a method for treating or preventing a condition, disease or disorder of a subject comprises administration to the subject of: (i) a pharmaceutical composition comprising one or more bacterial isolates; (ii) an uncultured fecal microbiota (or preparation of uncultured fecal bacteria); (iii) one or more prebiotics; and (iv) one or more antibiotics. The different components of (i)-(iv) can be administered to the subject in any order. For example, a subject can be administered one or more antibiotics, followed by one or more prebiotics, followed by an uncultured fecal microbiota (or preparation of uncultured fecal bacteria), followed by one or more bacterial isolates. In another example, the subject can be administered one or more antibiotics, followed by one or more prebiotics, followed by one or more bacterial isolates, followed by an uncultured fecal microbiota (or preparation of uncultured fecal bacteria). In another example, the prebiotic can be administered after one or both of the one or more bacterial isolates and/or the uncultured fecal microbiota (or preparation of uncultured fecal bacteria). For each of the above examples, it is further understood that any given component in a method of treatment can be administered multiple times. For example, an antibiotic can be administered to a subject, followed by an uncultured fecal microbiota (or preparation of uncultured fecal bacteria), followed by one or more bacterial isolates, followed by a prebiotic, followed by a second administration of the uncultured fecal microbiota (or preparation of uncultured fecal bacteria).

[00479] In each of the above combination treatments, the duration of time between different treatments (e.g., between administration of an uncultured fecal microbiota (or preparation of uncultured fecal bacteria) and one or more bacterial isolates) can be at least 1 hour, at least 2 hours, at least 6 hours, at least 12 hours, at least 1 day, at least 2 days, at least 3 days, at least 4 days, at least 5 days, at least 6 days, at least 1 week, at least 2 weeks, at least 3 weeks, at least 4 weeks, at least 5 weeks, at least 6 weeks, at least 7 weeks, at least 8 weeks, or greater than 8 weeks.

[00480] In embodiments, the pharmaceutical composition is used in a method for treating a disorder related to an intestinal dysbiosis in a subject, e.g., a GI disorder.

Kits

[00481] Described herein are kits comprising any herein-disclosed pharmaceutical composition and instructions for use.

[00482] The instructions can describe, for example, dosing information. As examples, the frequency of administration and dose of a composition, e.g., the number of capsules of a

pharmaceutical composition to be administered at a given time, and the number of times of administration per day/week). In embodiments in which the kit comprises more than one composition (e.g., a microbial therapeutic and an additional pharmaceutical composition lacking a microbial therapeutic), the instructions can describe the dosing of each composition. For example, one composition can be administered before another composition, e.g., sequential administration of the two pharmaceutical compositions separated by minutes, hours, days, weeks, months, or longer. Alternately, two compositions can be administered simultaneously.

Methods of manufacture

[00483] Disclosed herein is a method of manufacturing a pharmaceutical composition comprising a microbial cocktail, the method comprising combining two or more bacterial isolates to form the microbial cocktail.

[00484] Disclosed herein is a method of manufacturing a pharmaceutical composition that comprises one or more bacterial isolates, the method comprising selecting the one or more bacterial isolates based on at least one of the following characteristics: (i) an ability to produce a particular amount, concentration or level of one or more short-chain fatty acids (SCFAs) such as butyrate as measured in a functional assay (e.g., represented by bacterial isolates provided in Table 2); (ii) an ability to induce a particular amount, concentration or level of cytokine production or release by a eukaryotic cell incubated with the bacterial isolate in a functional assay (e.g., represented by bacterial isolates provided in Table 3); (iii) a greater relative abundance of the bacterial isolate in a healthy human subject relative to a patient with an intestinal dysbiosis (e.g., ulcerative colitis (UC)), or a greater relative abundance of the bacterial isolate in a human subject in remission from an intestinal dysbiosis (e.g., UC) relative to a patient having the intestinal dysbiosis (e.g., represented by bacterial isolates provided in Table 4); and/or (iv) an ability to produce a particular amount, concentration or level of one or more aryl hydrocarbons as measured in a functional assay, such that the one or more aryl hydrocarbons are capable of inducing an aryl hydrocarbon receptor of a host cell of a subject administered the pharmaceutical composition (e.g., represented by bacterial isolates provided in Table 6). The method can further comprise incorporating the one or more bacterial isolates into the pharmaceutical composition.

[00485] In embodiments, only one bacterial isolate comprising characteristic (i) is selected and incorporated into the pharmaceutical composition. In embodiments, only one bacterial isolate comprising characteristic (ii) is selected and incorporated into the pharmaceutical

composition. In embodiments, only one bacterial isolate comprising characteristic (iii) is selected and incorporated into the pharmaceutical composition. In embodiments, only one bacterial isolate comprising characteristic (iv) is selected and incorporated into the pharmaceutical composition. In embodiments, the pharmaceutical composition comprises only one bacterial isolate.

[00486] Disclosed herein is a method of manufacturing a pharmaceutical composition that comprises a plurality of bacterial isolates, the method comprising selecting the plurality of bacterial isolates based on at least one of the following characteristics: (i) an ability of the bacterial isolate to produce one or more short-chain fatty acids (SCFAs) in a gut of a subject administered the pharmaceutical composition; (ii) an ability of the bacterial isolate to modulate cytokine production in a host cell of a subject administered the pharmaceutical composition; (iii) a greater relative abundance of the bacterial isolate in a healthy human subject relative to a patient with an intestinal dysbiosis (e.g., ulcerative colitis (UC)), or a greater relative abundance of the bacterial isolate in a human subject in remission from an intestinal dysbiosis (e.g., UC) relative to a patient having the intestinal dysbiosis; and/or (iv) an ability to release an aryl hydrocarbon capable of inducing an aryl hydrocarbon receptor of a host cell of a subject administered the pharmaceutical composition. The method can further comprise incorporating the plurality of bacterial isolates into a microbial cocktail, and incorporating the microbial cocktail into the pharmaceutical composition.

[00487] In embodiments, two or more bacterial isolates comprising characteristic (i) can be selected and incorporated into the microbial cocktail; two or more bacterial isolates comprising characteristic (ii) can be selected and incorporated into the microbial cocktail; two or more bacterial isolates comprising characteristic (iii) can be selected and incorporated into the microbial cocktail; and/or two or more bacterial isolates comprising characteristic (iv) can be selected and incorporated into the microbial cocktail.

[00488] In embodiments, at least one bacterial isolate comprising characteristic (i) can be selected and incorporated into the microbial cocktail, and at least one bacterial isolate comprising characteristic (ii) can be selected and incorporated into the microbial cocktail. In embodiments, at least one bacterial isolate comprising characteristic (i) can be selected and incorporated into the microbial cocktail, and at least one bacterial isolate comprising characteristic (iii) can be selected and incorporated into the microbial cocktail. In embodiments, at least one bacterial isolate comprising characteristic (ii) can be selected and incorporated into the microbial cocktail, and at least one bacterial isolate comprising characteristic (iii) can be

selected and incorporated into the microbial cocktail. In embodiments, at least one bacterial isolate comprising characteristic (i) can be selected and incorporated into the microbial cocktail, and at least one bacterial isolate comprising characteristic (iv) can be selected and incorporated into the microbial cocktail. In embodiments, at least one bacterial isolate comprising characteristic (ii) can be selected and incorporated into the microbial cocktail, and at least one bacterial isolate comprising characteristic (iv) can be selected and incorporated into the microbial cocktail. In embodiments, at least one bacterial isolate comprising characteristic (iii) can be selected and incorporated into the microbial cocktail, and at least one bacterial isolate comprising characteristic (iv) can be selected and incorporated into the microbial cocktail.

[00489] In embodiments, at least one bacterial isolate comprising characteristic (i) can be selected and incorporated into the microbial cocktail, at least one bacterial isolate comprising characteristic (ii) can be selected and incorporated into the microbial cocktail, and at least one bacterial isolate comprising characteristic (iii) can be selected and incorporated into the microbial cocktail. In embodiments, at least one bacterial isolate comprising characteristic (i) can be selected and incorporated into the pharmaceutical composition, at least one bacterial isolate comprising characteristic (ii) can be selected and incorporated into the microbial cocktail, and at least one bacterial isolate comprising characteristic (iv) can be selected and incorporated into the microbial cocktail. In embodiments, at least one bacterial isolate comprising characteristic (ii) can be selected and incorporated into the pharmaceutical composition, and at least one bacterial isolate comprising characteristic (iii) can be selected and incorporated into the microbial cocktail, and at least one bacterial isolate comprising characteristic (iv) can be selected and incorporated into the microbial cocktail.

[00490] In embodiments, at least one bacterial isolate comprising characteristic (i) can be selected and incorporated into the microbial cocktail, at least one bacterial isolate comprising characteristic (ii) can be selected and incorporated into the microbial cocktail, at least one bacterial isolate comprising characteristic (iii) can be selected and incorporated into the microbial cocktail, and at least one bacterial isolate comprising characteristic (iv) can be selected and incorporated into the microbial cocktail.

[00491] In embodiments, a bacterial isolate comprising characteristic (i) is not selected. In embodiments, a bacterial isolate comprising characteristic (ii) is not selected. In embodiments, a bacterial isolate comprising characteristic (iii) is not selected. In embodiments, a bacterial isolate comprising characteristic (iv) is not selected.

[00492] In embodiments, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or greater than 20 bacterial isolates are selected based on characteristics (i) to (iv) and incorporated into a microbial cocktail.

[00493] In embodiments, all bacterial isolates incorporated into a microbial cocktail are selected based on at least one of characteristics (i) to (iii). In embodiments, all bacterial isolates incorporated into a microbial cocktail are selected based on at least two of characteristics (i) to (iii). In embodiments, all bacterial isolates incorporated into a microbial cocktail are selected based on all three of characteristics (i) to (iii). In embodiments, all bacterial isolates incorporated into a composition are selected based on characteristic (i). In embodiments, all bacterial isolates incorporated into a composition are selected based on only characteristic (i). In embodiments, all bacterial isolates incorporated into a composition are selected based on characteristic (ii). In embodiments, all bacterial isolates incorporated into a composition are selected based on only characteristic (ii). In embodiments, all bacterial isolates incorporated into a composition are selected based on characteristic (iii). In embodiments, all bacterial isolates incorporated into a composition are selected based on only characteristic (iii). In embodiments, all bacterial isolates incorporated into a microbial cocktail are selected based on at least one of characteristics (i) to (iv). In embodiments, all bacterial isolates incorporated into a microbial cocktail are selected based on at least two of characteristics (i) to (iv). In embodiments, all bacterial isolates incorporated into a microbial cocktail are selected based on at least three of characteristics (i) to (iv). In embodiments, all bacterial isolates incorporated into a microbial cocktail are selected based on all four of characteristics (i) to (iv). In embodiments, all bacterial isolates incorporated into a composition are selected based on characteristic (iv). In embodiments, all bacterial isolates incorporated into a composition are selected based on only characteristic (iv).

[00494] In embodiments, a bacterial isolate comprising *Odoribacter sphlanchnicus* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting at least one of characteristic (i), characteristic (ii), characteristic (iii), and characteristic (iv). In embodiments, a bacterial isolate comprising *Odoribacter sphlanchnicus* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting at least two of characteristic (i), characteristic (ii) characteristic (iii), and characteristic (iv). In embodiments, a bacterial isolate comprising *Odoribacter sphlanchnicus* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial

isolate exhibiting at least three of characteristic (i), characteristic (ii), characteristic (iii) and characteristic (iv). In embodiments, a bacterial isolate comprising *Odoribacter sphlanchnicus* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting each of characteristic (i), characteristic (ii), characteristic (iii), and characteristic (iv).

[00495] In embodiments, a bacterial isolate comprising *Faecalibacterium prausnitzii* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting at least one of characteristic (i), characteristic (ii) and characteristic (iii). In embodiments, a bacterial isolate comprising *Faecalibacterium prausnitzii* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting at least two of characteristics (i), characteristic (ii) and characteristic (iii). In embodiments, a bacterial isolate comprising *Faecalibacterium prausnitzii* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting each of characteristic (i), characteristic (ii) and characteristic (iii).

[00496] In embodiments, a bacterial isolate comprising *Eubacterium rectale* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting at least one of characteristic (i) and characteristic (iii). In embodiments, a bacterial isolate comprising *Eubacterium rectale* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting each of characteristic (i) and characteristic (ii).

[00497] In embodiments, a bacterial isolate comprising *Roseburia faecis* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting characteristic (i).

[00498] In embodiments, a bacterial isolate comprising *Akkermansia muciniphila* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting at least one of characteristic (ii) and characteristic (iii). In embodiments, a bacterial isolate comprising *Akkermansia muciniphila* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting each of characteristic (ii) and characteristic (iii).

[00499] In embodiments, a bacterial isolate comprising *Alistipes shahii* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting at least one of characteristic (ii) and characteristic (iii). In embodiments, a bacterial isolate

comprising *Alistipes shahii* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting each of characteristic (ii) and characteristic (iii).

[00500] In embodiments, a bacterial isolate comprising *Bacteroides cellulosilyticus* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting characteristic (iii).

[00501] In embodiments, a bacterial isolate comprising *Subdoligranulum variabile* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting at least one of characteristic (i), characteristic (ii) and characteristic (iii). In embodiments, a bacterial isolate comprising *Subdoligranulum variabile* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting at least two of characteristics (i), characteristic (ii) and characteristic (iii). In embodiments, a bacterial isolate comprising *Subdoligranulum variabile* is selected and incorporated into a pharmaceutical composition on the basis of the bacterial isolate exhibiting each of characteristic (i), characteristic (ii) and characteristic (iii).

[00502] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on its ability to produce a particular amount or concentration of an SCFA such as butyrate (i.e., based on characteristic (i)) as measured in a functional assay. For example, a series of bacterial isolates can be screened for an ability to produce a threshold concentration of an SCFA when incubated with an organic substrate capable of being converted to an SCFA during a period of time. In embodiments, the substrate can comprise at least one of an oligosaccharide (e.g., a fructooligosaccharide (FOS) or an xylooligosaccharide (XOS)), sunfiber/partially hydrolyzed guar gum (PHGG), or barley malt. The bacterial isolate can be incubated with the substrate for any period of time sufficient to allow conversion of the substrate to the SCFA, for example at least 1 hour, at least 2 hours, at least 3 hours, at least 4 hours, at least 5 hours, at least 6 hours, at least 7 hours, at least 8 hours, at least 9 hours, at least 10 hours, at least 11 hours, at least 12 hours, at least 13 hours, at least 14 hours, at least 15 hours, at least 16 hours, at least 17 hours, at least 18 hours, at least 19 hours, at least 20 hours, at least 21 hours, at least 22 hours, at least 23 hours, at least 24 hours, at least 25 hours, at least 26 hours, at least 27 hours, at least 28 hours, at least 29 hours, at least 30 hours, at least 35 hours, at least 40 hours, at least 44 hours, at least 48 hours, or greater than 48 hours.

[00503] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on a production of SCFA (e.g., butyrate) over a duration of time (e.g., 24 hours) at a level of at least 5 mM, at least 10 mM, at least 15 mM, at least 20 mM, at least 25 mM, at least 30 mM, at least 35 mM, at least 40 mM, at least 45 mM at least 50 mM, at least 60 mM, at least 70 mM, at least 80 mM, at least 90 mM, at least 100 mM, or greater than 100 mM. In embodiments, a bacterial isolate selected for inclusion in a pharmaceutical composition is provided in Table 2, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 2.

[00504] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on its ability to modulate production and/or release of one or more cytokines by a eukaryotic cell incubated with the bacterial isolate (i.e., based on characteristic (ii)), as measured in a functional assay. For example, a series of bacterial isolates can be screened for an ability to modulate production and/or release of one or more cytokines from a eukaryotic cell incubated with each bacterial isolate. Examples of eukaryotic cells that can be used in the functional assay include an intestinal cell, an epithelial cell, an intestinal mucosal cell, an intestinal epithelial cell, an intestinal lamina propria cell, an endothelial cell, fibroblast, a stromal cell, a macrophage, a B lymphocyte, a T lymphocyte, a mast cell, and a peripheral blood mononuclear cell (PBMC). In embodiments, the eukaryotic cell can be a human cell.

[00505] The bacterial isolate can be incubated with the eukaryotic cell for any period of time sufficient to allow modulation of cytokine expression, for example at least 1 hour, at least 2 hours, at least 3 hours, at least 4 hours, at least 5 hours, at least 6 hours, at least 7 hours, at least 8 hours, at least 9 hours, at least 10 hours, at least 11 hours, at least 12 hours, at least 13 hours, at least 14 hours, at least 15 hours, at least 16 hours, at least 17 hours, at least 18 hours, at least 19 hours, at least 20 hours, at least 21 hours, at least 22 hours, at least 23 hours, at least 24 hours, at least 25 hours, at least 26 hours, at least 27 hours, at least 28 hours, at least 29 hours, at least 30 hours, at least 35 hours, at least 40 hours, at least 44 hours, at least 48 hours, or greater than 48 hours.

[00506] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on the induction of IL-10 by a population of eukaryotic cells (e.g., population of PBMCs) incubated with the bacterial isolate during a period of time (e.g., 24 hours), as measured in a functional assay. For example, the bacterial isolate can induce

IL-10 at a concentration of at least 1000 pg/ml, at least 1500 pg/ml, at least 2000 pg/ml, at least 2500 pg/ml, at least 3000 pg/ml, at least 3500 pg/ml, at least 4000 pg/ml, at least 5000 pg/ml, at least 6000 pg/ml, at least 7000 pg/ml, at least 8000 pg/ml, at least 9000 pg/ml, at least 10,000 pg/ml, or greater than 10,000 pg/ml. In embodiments, a bacterial isolate selected for inclusion in a pharmaceutical composition is provided in Table 3, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 3.

[00507] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on a limited production of GM-CSF by a population of eukaryotic cells (e.g., population of PBMCs) incubated with the bacterial isolate during a period of time (e.g., 24 hours), as measured in a functional assay. For example, the bacterial isolate can limit production of GM-CSF to a concentration of no more than 5 pg/ml, 10 pg/ml, 15 pg/ml, 20 pg/ml, 25 pg/ml, 30 pg/ml, 35 pg/ml, 40 pg/ml, 45 pg/ml, 50 pg/ml, 55 pg/ml, 60 pg/ml, 65 pg/ml, 70 pg/ml, 75 pg/ml, 80 pg/ml, 85 pg/ml, 90 pg/ml, 95 pg/ml, 100 pg/ml, 105 pg/ml, 110 pg/ml, 115 pg/ml, 120 pg/ml, 125 pg/ml, 130 pg/ml, 135 pg/ml, 140 pg/ml, 145 pg/ml, 150 pg/ml, 155 pg/ml, 160 pg/ml, 165 pg/ml, 170 pg/ml, 175 pg/ml, 180 pg/ml, 185 pg/ml, 190 pg/ml, 195 pg/ml, or 200 pg/ml. In embodiments, a bacterial isolate selected for inclusion in a pharmaceutical composition is provided in Table 3, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 3.

[00508] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on a limited production of IL-12 by a population of eukaryotic cells (e.g., population of PBMCs) incubated with the bacterial isolate during a period of time (e.g., 24 hours), as measured in a functional assay. For example, the bacterial isolate can limit production of IL-12 to a concentration of no more than 5 pg/ml, 10 pg/ml, 15 pg/ml, 20 pg/ml, 25 pg/ml, 30 pg/ml, 35 pg/ml, 40 pg/ml, 45 pg/ml, 50 pg/ml, 55 pg/ml, 60 pg/ml, 65 pg/ml, 70 pg/ml, 75 pg/ml, 80 pg/ml, 85 pg/ml, 90 pg/ml, 95 pg/ml, 100 pg/ml, 105 pg/ml, 110 pg/ml, 115 pg/ml, 120 pg/ml, 125 pg/ml, 130 pg/ml, 135 pg/ml, 140 pg/ml, 145 pg/ml, 150 pg/ml, 155 pg/ml, 160 pg/ml, 165 pg/ml, 170 pg/ml, 175 pg/ml, 180 pg/ml, 185 pg/ml, 190 pg/ml, 195 pg/ml, or 200 pg/ml. In embodiments, a bacterial isolate selected for inclusion in a pharmaceutical composition is provided in Table 3, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 3.

[00509] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on a limited production of IFN-gamma by a population of eukaryotic cells (e.g., population of PBMCs) incubated with the bacterial isolate during a period of time (e.g., 24 hours), as measured in a functional assay. For example, the bacterial isolate can limit production of IFN-gamma to a concentration of no more than 5 pg/ml, 10 pg/ml, 15 pg/ml, 20 pg/ml, 25 pg/ml, 30 pg/ml, 35 pg/ml, 40 pg/ml, 45 pg/ml, 50 pg/ml, 55 pg/ml, 60 pg/ml, 65 pg/ml, 70 pg/ml, 75 pg/ml, 80 pg/ml, 85 pg/ml, 90 pg/ml, 95 pg/ml, 100 pg/ml, 105 pg/ml, 110 pg/ml, 115 pg/ml, 120 pg/ml, 125 pg/ml, 130 pg/ml, 135 pg/ml, 140 pg/ml, 145 pg/ml, 150 pg/ml, 155 pg/ml, 160 pg/ml, 165 pg/ml, 170 pg/ml, 175 pg/ml, 180 pg/ml, 185 pg/ml, 190 pg/ml, 195 pg/ml, or 200 pg/ml. In embodiments, a bacterial isolate selected for inclusion in a pharmaceutical composition is provided in Table 3, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 3.

[00510] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on a limited production of TNF-alpha by a population of eukaryotic cells (e.g., population of PBMCs) incubated with the bacterial isolate during a period of time (e.g., 24 hours), as measured in a functional assay. For example, the bacterial isolate can limit production of TNF-alpha to a concentration of no more than 20 pg/ml, 30 pg/ml, 40 pg/ml, 50 pg/ml, 75 pg/ml, 100 pg/ml, 150 pg/ml, 200 pg/ml, 250 pg/ml, 300 pg/ml, 350 pg/ml, 400 pg/ml, 450 pg/ml, 500 pg/ml, 550 pg/ml, 600 pg/ml, 650 pg/ml, 700 pg/ml, 750 pg/ml, 800 pg/ml, 850 pg/ml, 900 pg/ml, 950 pg/ml, 1000 pg/ml, 1100 pg/ml, 1200 pg/ml, 1300 pg/ml, 1400 pg/ml, 1500 pg/ml, 1600 pg/ml, 1700 pg/ml, 1800 pg/ml, 1900 pg/ml, 2000 pg/ml, 2100 pg/ml, 2200 pg/ml, 2300 pg/ml, 2400 pg/ml, or 2500 pg/ml. In embodiments, a bacterial isolate selected for inclusion in a pharmaceutical composition is provided in Table 3, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 3.

[00511] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on a limited production of IL-23 by a population of eukaryotic cells (e.g., population of PBMCs) incubated with the bacterial isolate during a period of time (e.g., 24 hours), as measured in a functional assay. For example, the bacterial isolate can limit production of IL-23 to a concentration of no more than 5 pg/ml, 10 pg/ml, 15 pg/ml, 20 pg/ml, 25 pg/ml, 30 pg/ml, 35 pg/ml, 40 pg/ml, 45 pg/ml, 50 pg/ml, 55 pg/ml, 60 pg/ml, 65 pg/ml, 70 pg/ml, 75 pg/ml, 80 pg/ml, 85 pg/ml, 90 pg/ml, 95 pg/ml, 100 pg/ml, 105

pg/ml, 110 pg/ml, 115 pg/ml, 120 pg/ml, 125 pg/ml, 130 pg/ml, 135 pg/ml, 140 pg/ml, 145 pg/ml, 150 pg/ml, 155 pg/ml, 160 pg/ml, 165 pg/ml, 170 pg/ml, 175 pg/ml, 180 pg/ml, 185 pg/ml, 190 pg/ml, 195 pg/ml, 200 pg/ml, 250 pg/ml, or 300 pg/ml. In embodiments, a bacterial isolate selected for inclusion in a pharmaceutical composition is provided in Table 3, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 3.

[00512] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on an IL-10:IL-12 ratio produced by a population of eukaryotic cells (e.g., population of PBMCs) incubated with the bacterial isolate during a period of time (e.g., 24 hours), as measured in a functional assay. For example, the bacterial isolate can generate an IL-10:IL-12 ratio of at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50, at least 55, at least 60, at least 65, at least 70, at least 75, at least 80, at least 85, at least 90, at least 95, at least 100, at least 110, at least 120, at least 130, at least 140, at least 150, at least 160, at least 170, at least 180, at least 190, at least 200, at least 210, at least 220, at least 230, at least 240, at least 250, at least 260, at least 270, at least 280, at least 290, at least 300, at least 325, at least 350, at least 375, at least 400, at least 425, at least 450, at least 475, at least 500, at least 550, at least 600, at least 650, at least 700, at least 750, at least 800, at least 850, at least 900, at least 950, at least 1000, at least 1100, at least 1200, at least 1300, at least 1400, at least 1500, at least 1600, at least 1700, at least 1800, at least 1900, at least 2000, at least 2200, at least 2400, at least 2600, at least 2800, at least 3000, at least 3200, at least 3400, at least 3600, at least 3800, at least 4000, or greater than 4000. In an embodiment, the bacterial isolate is provided in Table 3, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 3.

[00513] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on an IL-10:TNF-alpha ratio produced by a population of eukaryotic cells (e.g., population of PBMCs) incubated with the bacterial isolate during a period of time (e.g., 24 hours), as measured in a functional assay. For example, the bacterial isolate can generate an IL-10:TNF-alpha ratio of at least 0.5, at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, at least 26, at least 27, at least 28, at least 29, at least 30, at least 31, at least 32, at least 33, at least 34, at least 35, at least 36, at least 37, at

least 38, at least 39, at least 40, at least 45, at least 50, at least 55, at least 60, at least 65, at least 70, at least 75, at least 80, at least 85, at least 90, at least 95, or at least 100. In embodiments, a bacterial isolate selected for inclusion in a pharmaceutical composition is provided in Table 3, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 3.

[00514] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on its ability to produce a threshold amount or concentration of one or more aryl hydrocarbons for activating an AhR of a host cell of a subject administered the pharmaceutical composition (i.e., based on characteristic (iv)), as measured in a functional assay. For example, a series of bacterial isolates can be screened for an ability to modulate production and/or release of one or more aryl hydrocarbons after incubation with tryptophan or a tryptophan intermediate in a functional assay. In embodiments, the aryl hydrocarbon is selected from the group consisting of indole, indole-3-acetic acid (IAA), indole-3-aldehyde (IAId), indole-3-lactic acid, indole-3-carbinol (I3C), indole-3-acetonitrile (I3ACN), 3,3'-diindolylmethane (DIM), 2-(indol-3-ylmethyl)-3,3'-diindolylmethane (Ltr-1), indolo[3,2-*b*]carbazole (ICZ), 2-(1'H-indole-3'carbonyl)-thiazole-4-carboxylic acid methyl ester (ITE), 3-methyl-indole (skatole), tryptamine, kynurenine, kynurenate, indigo, indirubin, indoxyl-3-sulfate (I3S), xanthurenic acid, cinnabarinic acid, and any combination thereof.

[00515] The bacterial isolate can be incubated in a functional assay (e.g., in the presence of tryptophan or a tryptophan intermediate) for any period of time sufficient to allow production of the aryl hydrocarbon by the bacterial isolate, for example at least 1 hour, at least 2 hours, at least 3 hours, at least 4 hours, at least 5 hours, at least 6 hours, at least 7 hours, at least 8 hours, at least 9 hours, at least 10 hours, at least 11 hours, at least 12 hours, at least 13 hours, at least 14 hours, at least 15 hours, at least 16 hours, at least 17 hours, at least 18 hours, at least 19 hours, at least 20 hours, at least 21 hours, at least 22 hours, at least 23 hours, at least 24 hours, at least 25 hours, at least 26 hours, at least 27 hours, at least 28 hours, at least 29 hours, at least 30 hours, at least 31 hours, at least 32 hours, at least 33 hours, at least 34 hours, at least 35 hours, at least 36 hours, at least 37 hours, at least 38 hours, at least 39 hours, at least 40 hours, at least 41 hours, at least 42 hours, at least 43 hours, at least 44 hours, at least 45 hours, at least 46 hours, at least 47 hours, at least 48 hours, or greater than 48 hours.

[00516] In embodiments, the functional assay can measure an absolute amount or concentration of one or more aryl hydrocarbons capable of activating an AhR of a host cell. In other embodiments, the functional assay can measure a relative amount of one or more aryl

hydrocarbons. In an example, an amount of production of an aryl hydrocarbon by a bacterial isolate can be relative to blank media not containing a bacterial isolate. Alternatively, the functional assay can measure the amount or concentration of an aryl hydrocarbon produced by a bacterial isolate relative to that produced by one or more control bacterial strains. In an embodiment, the control bacterial strain is known to produce an aryl hydrocarbon, for example the aryl hydrocarbon being measured in the assay. Exemplary control strains that can be used in a functional assay to measure one or more aryl hydrocarbons are bacterial strains that are a member of the genus *Peptostreptococcus* (e.g., *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii*) In an embodiment, the functional assay comprises comparison of a level of an aryl hydrocarbon produced by a bacterial isolate of interest over a period of time (e.g., 48 hours) to a level of the same aryl hydrocarbon produced by one or more of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii* over the same period of time. In certain embodiments, a pharmaceutical composition comprises a bacterial isolate capable of producing an aryl hydrocarbon at a level of at least 1.1x, at least 1.2x, at least 1.3x, at least 1.4x, at least 1.5x, at least 1.6x, at least 1.7x, at least 1.8x, at least 1.9x, at least 2x, at least 2.1x, at least 2.2x, at least 2.3x, at least 2.4x, at least 2.5x, at least 2.6x, at least 2.7x, at least 2.8x, at least 2.9x, at least 3x, at least 4x, at least 5x, at least 6x, at least 7x, at least 8x, at least 9x, at least 10x, at least 11x, at least 12x, at least 13x, at least 14x, at least 15x, at least 16x, at least 17x, at least 18x, at least 19x, at least 20x, at least 21x, at least 22x, at least 23x, at least 24x, at least 25x, at least 26x, at least 27x, at least 28x, at least 29x, at least 30x, at least 35x, at least 40x, at least 45x, at least 50x, at least 60x, at least 70x, at least 80x, at least 90x, at least 100x, at least 110x, at least 120x, at least 130x, at least 140x, at least 150x, at least 160x, at least 170x, at least 180x, at least 190x, at least 200x, at least 210x, at least 220x, at least 230x, at least 240x, at least 250x, or greater than 250x relative to a control bacterial strain (e.g. a *Peptostreptococcus* strain such as *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii*)), or compared to blank media alone.

[00517] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on the production of kynurenate (i.e., kynurenic acid) during a period of time (e.g., 48 hours), as measured in a functional assay. For example, the bacterial isolate can be selected if it can produce kynurenate at a concentration of at least 0.1 μM kynurenate, at least 0.2 μM kynurenate, at least 0.3 μM kynurenate, at least 0.4 μM kynurenate, at least 0.5 μM kynurenate, at least 0.6 μM kynurenate, at least 0.7 μM kynurenate, at least 0.8 μM kynurenate, at least 0.9 μM kynurenate, at least 1 μM kynurenate, at least 1.5

μM kynurenate, at least 2 μM kynurenate, at least 2.5 μM kynurenate, at least 3 μM kynurenate, at least 3.5 μM kynurenate, at least 4 μM kynurenate, at least 4.5 μM kynurenate, at least 5 μM kynurenate, or greater than 5 μM kynurenate. In embodiments, the selected bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the selected bacterial isolate comprises *Odoribacter splanchnicus*. In an embodiment, the selected bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 6.

[00518] In other embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on production of kynurenate at a higher level than blank media or a control bacterial strain (e.g., positive control bacterial strain capable of producing kynurenate, such as a strain that is a member of the *Peptostreptococcus* genus), as measured in a functional assay. For example, a bacterial isolate can be selected if it can produce kynurenate at a higher level than at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii* over a duration of time. In embodiments, a bacterial isolate is selected if it can produce kynurenate at a level of at least 1.1x, at least 1.2x, at least 1.3x, at least 1.4x, at least 1.5x, at least 1.6x, at least 1.7x, at least 1.8x, at least 1.9x, at least 2x, at least 2.1x, at least 2.2x, at least 2.3x, at least 2.4x, at least 2.5x, at least 2.6x, at least 2.7x, at least 2.8x, at least 2.9x, at least 3x, at least 4x, at least 5x, at least 6x, at least 7x, at least 8x, at least 9x, at least 10x, at least 11x, at least 12x, at least 13x, at least 14x, at least 15x, at least 16x, at least 17x, at least 18x, at least 19x, at least 20x, at least 21x, at least 22x, at least 23x, at least 24x, at least 25x, at least 26x, at least 27x, at least 28x, at least 29x, at least 30x, at least 35x, at least 40x, at least 45x, at least 50x, at least 60x, at least 70x, at least 80x, at least 90x, at least 100x, at least 110x, at least 120x, at least 130x, at least 140x, at least 150x, at least 160x, at least 170x, at least 180x, at least 190x, at least 200x, at least 210x, at least 220x, at least 230x, at least 240x, at least 250x, or greater than 250x relative to at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii*, or relative to blank media alone. In embodiments, the bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the bacterial isolate comprises *Odoribacter splanchnicus*. In an embodiment, the bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 2.

[00519] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on the production of indole-3-acetic acid (IAA) during a period of time (e.g., 48 hours), as measured in a functional assay. For example, the bacterial isolate can be selected if it can produce IAA at a concentration of at least 0.1 μM IAA, at least 0.2 μM IAA, at least 0.3 μM IAA, at least 0.4 μM IAA, at least 0.5 μM IAA, at least 0.6 μM IAA, at least 0.7 μM IAA, at least 0.8 μM IAA, at least 0.9 μM IAA, at least 1 μM IAA, at least 1.5 μM IAA, at least 2 μM IAA, at least 2.5 μM IAA, at least 3 μM IAA, at least 4 μM IAA, at least 5 μM IAA, at least 6 μM IAA, at least 7 μM IAA, at least 8 μM IAA, at least 9 μM IAA, at least 10 μM IAA, at least 20 μM IAA, at least 30 μM IAA, at least 40 μM IAA, at least 50 μM IAA, at least 60 μM IAA, at least 70 μM IAA, at least 80 μM IAA, at least 90 μM IAA, at least 100 μM IAA, at least 110 μM IAA, at least 120 μM IAA, at least 130 μM IAA, at least 140 μM IAA, at least 150 μM IAA, at least 160 μM IAA, at least 170 μM IAA, at least 180 μM IAA, at least 190 μM IAA, at least 200 μM IAA or greater than 200 μM IAA. In embodiments, the selected bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the selected bacterial isolate comprises *Odoribacter splanchnicus*. In an embodiment, the selected bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 2. In an embodiment, the selected bacterial isolate comprises *Clostridium aldenense*. In an embodiment, the selected bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 10.

[00520] In other embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on production of indole-3-acetoc acid (IAA) at a higher level than blank media or a control bacterial strain (e.g., positive control bacterial strain capable of producing IAA, such as a strain that is a member of the *Peptostreptococcus* genus), as measured in a functional assay. For example, a bacterial isolate can be selected if it can produce IAA at a higher level than at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii* over a duration of time. In embodiments, a bacterial isolate is selected if it can produce IAA at a level of at least 1.1x, at least 1.2x, at least 1.3x, at least 1.4x, at least 1.5x, at least 1.6x, at least 1.7x, at least 1.8x, at least 1.9x, at least 2x, at least 2.1x, at least 2.2x, at least 2.3x, at least 2.4x, at least 2.5x, at least 2.6x, at least 2.7x, at least 2.8x, at least 2.9x, at least 3x, at least 4x, at least 5x, at least 6x, at least 7x, at least 8x, at least 9x, at least 10x, at least 11x, at least 12x, at least 13x, at least 14x,

at least 15x, at least 16x, at least 17x, at least 18x, at least 19x, at least 20x, at least 21x, at least 22x, at least 23x, at least 24x, at least 25x, at least 26x, at least 27x, at least 28x, at least 29x, at least 30x, at least 35x, at least 40x, at least 45x, at least 50x, at least 60x, at least 70x, at least 80x, at least 90x, at least 100x, at least 110x, at least 120x, at least 130x, at least 140x, at least 150x, at least 160x, at least 170x, at least 180x, at least 190x, at least 200x, at least 210x, at least 220x, at least 230x, at least 240x, at least 250x, or greater than 250x relative to at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii*, or relative to blank media alone. In embodiments, the selected bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the selected bacterial isolate comprises *Odoribacter splanchnicus*. In an embodiment, the selected bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 2. In an embodiment, the selected bacterial isolate comprises *Clostridium aldenense*. In an embodiment, the selected bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 10.

[00521] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on the production of indole-3-lactic acid during a period of time (e.g., 48 hours), as measured in a functional assay. For example, the bacterial isolate can be selected if it can produce indole-3-lactic acid at a concentration of at least 0.1 μM indole-3-lactic acid, at least 0.2 μM indole-3-lactic acid, at least 0.3 μM indole-3-lactic acid, at least 0.4 μM indole-3-lactic acid, at least 0.5 μM indole-3-lactic acid, at least 0.6 μM indole-3-lactic acid, at least 0.7 μM indole-3-lactic acid, at least 0.8 μM indole-3-lactic acid, at least 0.9 μM indole-3-lactic acid, at least 1 μM indole-3-lactic acid, at least 1.5 μM indole-3-lactic acid, at least 2 μM indole-3-lactic acid, at least 2.5 μM indole-3-lactic acid, at least 3 μM indole-3-lactic acid, at least 3.5 μM indole-3-lactic acid, at least 4 μM indole-3-lactic acid, at least 4.5 μM indole-3-lactic acid, at least 5 μM indole-3-lactic acid, or greater than 5 μM indole-3-lactic acid. In embodiments, the selected bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6.

[00522] In other embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on production of indole-3-lactic acid at a higher level than blank media or a control bacterial strain (e.g., positive control bacterial strain

capable of producing indole-3-lactic acid, such as a strain that is a member of the *Peptostreptococcus* genus), as measured in a functional assay. For example, a bacterial isolate can be selected if it can produce indole-3-lactic acid at a higher level than at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii* over a duration of time. In embodiments, a bacterial isolate is selected if it can produce indole-3-lactic acid at a level that is at least 1.1x, at least 1.2x, at least 1.3x, at least 1.4x, at least 1.5x, at least 1.6x, at least 1.7x, at least 1.8x, at least 1.9x, at least 2x, at least 2.1x, at least 2.2x, at least 2.3x, at least 2.4x, at least 2.5x, at least 2.6x, at least 2.7x, at least 2.8x, at least 2.9x, at least 3x, at least 4x, at least 5x, at least 6x, at least 7x, at least 8x, at least 9x, at least 10x, at least 11x, at least 12x, at least 13x, at least 14x, at least 15x, at least 16x, at least 17x, at least 18x, at least 19x, at least 20x, at least 21x, at least 22x, at least 23x, at least 24x, at least 25x, at least 26x, at least 27x, at least 28x, at least 29x, at least 30x, at least 35x, at least 40x, at least 45x, at least 50x, at least 60x, at least 70x, at least 80x, at least 90x, at least 100x, at least 110x, at least 120x, at least 130x, at least 140x, at least 150x, at least 160x, at least 170x, at least 180x, at least 190x, at least 200x, at least 210x, at least 220x, at least 230x, at least 240x, at least 250x, or greater than 250x relative to at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii*, or relative to blank media alone. In embodiments, the selected bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6.

[00523] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on the production of indole during a period of time (e.g., 48 hours), as measured in a functional assay. For example, the bacterial isolate can be selected if it can produce indole at a concentration of at least 0.1 μM indole, at least 0.2 μM indole, at least 0.3 μM indole, at least 0.4 μM indole, at least 0.5 μM indole, at least 0.6 μM indole, at least 0.7 μM indole, at least 0.8 μM indole, at least 0.9 μM indole, at least 1 μM indole, at least 1.5 μM indole, at least 2 μM indole, at least 2.5 μM indole, at least 3 μM indole, at least 3.5 μM indole, at least 4 μM indole, at least 4.5 μM indole, at least 5 μM indole, or greater than 5 μM indole. In embodiments, the selected bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the selected bacterial isolate comprises *Clostridium* sp. (e.g., *Clostridium aldenense*). In an embodiment, the selected

bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 10.

[00524] In other embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on production of indole at a higher level than blank media or a control bacterial strain (e.g., positive control bacterial strain capable of producing indole, such as a strain that is a member of the *Peptostreptococcus* genus), as measured in a functional assay. For example, a bacterial isolate can be selected if it can produce indole at a higher level than at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii* over a duration of time. In embodiments, a bacterial isolate is selected if it can produce indole at a level that is at least 1.1x, at least 1.2x, at least 1.3x, at least 1.4x, at least 1.5x, at least 1.6x, at least 1.7x, at least 1.8x, at least 1.9x, at least 2x, at least 2.1x, at least 2.2x, at least 2.3x, at least 2.4x, at least 2.5x, at least 2.6x, at least 2.7x, at least 2.8x, at least 2.9x, at least 3x, at least 4x, at least 5x, at least 6x, at least 7x, at least 8x, at least 9x, at least 10x, at least 11x, at least 12x, at least 13x, at least 14x, at least 15x, at least 16x, at least 17x, at least 18x, at least 19x, at least 20x, at least 21x, at least 22x, at least 23x, at least 24x, at least 25x, at least 26x, at least 27x, at least 28x, at least 29x, at least 30x, at least 35x, at least 40x, at least 45x, at least 50x, at least 60x, at least 70x, at least 80x, at least 90x, at least 100x, at least 110x, at least 120x, at least 130x, at least 140x, at least 150x, at least 160x, at least 170x, at least 180x, at least 190x, at least 200x, at least 210x, at least 220x, at least 230x, at least 240x, at least 250x, or greater than 250x relative to at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii*, or relative to blank media alone. In embodiments, the selected bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the selected bacterial isolate comprises *Clostridium* sp. (e.g., *Clostridium aldenense*). In an embodiment, the selected bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 10.

[00525] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on the production of kynurenine during a period of time (e.g., 48 hours), as measured in a functional assay. For example, the bacterial isolate can be selected if it can produce kynurenine at a concentration of at least 0.1 μM kynurenine, at least 0.2 μM kynurenine, at least 0.3 μM kynurenine, at least 0.4 μM kynurenine, at least 0.5 μM kynurenine, at least 0.6 μM kynurenine, at least 0.7 μM kynurenine, at least 0.8 μM kynurenine,

at least 0.9 μM kynurenine, at least 1 μM kynurenine, at least 1.5 μM kynurenine, at least 2 μM kynurenine, at least 2.5 μM kynurenine, at least 3 μM kynurenine, at least 3.5 μM kynurenine, at least 4 μM kynurenine, at least 4.5 μM kynurenine, at least 5 μM kynurenine, or greater than 5 μM kynurenine. In embodiments, the selected bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the selected bacterial isolate comprises *Odoribacter splanchnicus*. In an embodiment, the selected bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 2. In an embodiment, the selected bacterial isolate comprises *Bacteroides stercoris*. In an embodiment, the selected bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 13.

[00526] In other embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on production of kynurenine at a higher level than blank media or a control bacterial strain (e.g., positive control bacterial strain capable of producing kynurenine, such as a strain that is a member of the *Peptostreptococcus* genus), as measured in a functional assay. For example, a bacterial isolate can be selected if it can produce kynurenine at a higher level than at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii* over a duration of time. In embodiments, a bacterial isolate is selected if it can produce kynurenine at a level that is at least 1.1x, at least 1.2x, at least 1.3x, at least 1.4x, at least 1.5x, at least 1.6x, at least 1.7x, at least 1.8x, at least 1.9x, at least 2x, at least 2.1x, at least 2.2x, at least 2.3x, at least 2.4x, at least 2.5x, at least 2.6x, at least 2.7x, at least 2.8x, at least 2.9x, at least 3x, at least 4x, at least 5x, at least 6x, at least 7x, at least 8x, at least 9x, at least 10x, at least 11x, at least 12x, at least 13x, at least 14x, at least 15x, at least 16x, at least 17x, at least 18x, at least 19x, at least 20x, at least 21x, at least 22x, at least 23x, at least 24x, at least 25x, at least 26x, at least 27x, at least 28x, at least 29x, at least 30x, at least 35x, at least 40x, at least 45x, at least 50x, at least 60x, at least 70x, at least 80x, at least 90x, at least 100x, at least 110x, at least 120x, at least 130x, at least 140x, at least 150x, at least 160x, at least 170x, at least 180x, at least 190x, at least 200x, at least 210x, at least 220x, at least 230x, at least 240x, at least 250x, or greater than 250x relative to at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii*, or relative to blank media alone. In an embodiment, the selected bacterial isolate comprises *Odoribacter* sp. In an embodiment, the selected bacterial isolate comprises a 16S rRNA sequence at least 95%

identical to the 16S rRNA sequence corresponding to SEQ ID NO: 2. In an embodiment, the selected bacterial isolate comprises *Bacteroides stercoris*. In an embodiment, the selected bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 13.

[00527] In embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on the production of tryptamine during a period of time (e.g., 48 hours), as measured in a functional assay. For example, the bacterial isolate can be selected if it can produce tryptamine at a concentration of at least 0.1 μM tryptamine, at least 0.2 μM tryptamine, at least 0.3 μM tryptamine, at least 0.4 μM tryptamine, at least 0.5 μM tryptamine, at least 0.6 μM tryptamine, at least 0.7 μM tryptamine, at least 0.8 μM tryptamine, at least 0.9 μM tryptamine, at least 1 μM tryptamine, at least 1.5 μM tryptamine, at least 2 μM tryptamine, at least 2.5 μM tryptamine, at least 3 μM tryptamine, at least 3.5 μM tryptamine, at least 4 μM tryptamine, at least 4.5 μM tryptamine, at least 5 μM tryptamine, or greater than 5 μM tryptamine. In embodiments, the selected bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In embodiments, the selected bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the selected bacterial isolate comprises *Odoribacter splanchnicus*. In an embodiment, the selected bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 2.

[00528] In other embodiments, a bacterial isolate can be selected for inclusion in a pharmaceutical composition described herein based on production of tryptamine at a higher level than blank media or a control bacterial strain (e.g., positive control bacterial strain capable of producing tryptamine, such as a strain that is a member of the *Peptostreptococcus* genus), as measured in a functional assay. For example, a bacterial isolate can be selected if it can produce tryptamine at a higher level than at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii* over a duration of time. In embodiments, a bacterial isolate is selected if it can produce tryptamine at a level that is at least 1.1x, at least 1.2x, at least 1.3x, at least 1.4x, at least 1.5x, at least 1.6x, at least 1.7x, at least 1.8x, at least 1.9x, at least 2x, at least 2.1x, at least 2.2x, at least 2.3x, at least 2.4x, at least 2.5x, at least 2.6x, at least 2.7x, at least 2.8x, at least 2.9x, at least 3x, at least 4x, at least 5x, at least 6x, at least 7x, at least 8x, at least 9x, at least 10x, at least 11x, at least 12x, at least 13x, at least 14x, at least 15x,

at least 16x, at least 17x, at least 18x, at least 19x, at least 20x, at least 21x, at least 22x, at least 23x, at least 24x, at least 25x, at least 26x, at least 27x, at least 28x, at least 29x, at least 30x, at least 35x, at least 40x, at least 45x, at least 50x, at least 60x, at least 70x, at least 80x, at least 90x, at least 100x, at least 110x, at least 120x, at least 130x, at least 140x, at least 150x, at least 160x, at least 170x, at least 180x, at least 190x, at least 200x, at least 210x, at least 220x, at least 230x, at least 240x, at least 250x, or greater than 250x relative to at least one of the control strains *Peptostreptococcus anaerobius* or *Peptostreptococcus russellii*, or relative to blank media alone. In an embodiment, the selected bacterial isolate comprises *Odoribacter splanchnicus*. In embodiments, the selected bacterial isolate is provided in Table 6, or comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence corresponding to a SEQ ID NO of a bacterial isolate provided in Table 6. In an embodiment, the selected bacterial isolate comprises *Odoribacter splanchnicus*. In an embodiment, the selected bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence corresponding to SEQ ID NO: 2.

[00529] In an embodiment, a method of manufacture comprises selecting one or more bacterial isolates comprising a 16S rRNA sequence that is at least 95% identical to the 16S rRNA sequence of one or more of the bacterial isolates provided in Table 1, and incorporating the one or more bacterial isolates into a pharmaceutical composition. In an embodiment, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, or greater than 20 bacterial isolates comprising a 16S rRNA sequence that is at least 95% identical to the 16S rRNA sequence of one or more of the bacterial isolates provided in Table 1 are selected and incorporated into a microbial cocktail.

[00530] In an embodiment, a method of manufacture comprises selecting one or more bacterial isolates comprising a 16S rRNA sequence that is at least 95% identical to the 16S rRNA sequence of one or more of the bacterial isolates provided in Tables 2-4, and incorporating the one or more bacterial isolates into a pharmaceutical composition. In an embodiment, a method of manufacture comprises selecting one or more bacterial isolates comprising a 16S rRNA sequence at least 95% identical to the 16S rRNA sequence of one or more of the bacterial isolates provided in Table 6, and incorporating the one or more bacterial isolates into a pharmaceutical composition.

[00531] In an embodiment, a method of manufacture comprises selecting bacterial isolates comprising 16S rRNA sequences at least 95% identical to the 16S rRNA sequences of each of

the bacterial isolates provided in one of Tables 7-44, incorporating the bacterial isolates into a microbial cocktail, and incorporating the microbial cocktail into a pharmaceutical composition.

[00532] In embodiments, one or more bacterial isolates can be rationally selected for inclusion in a pharmaceutical composition described herein based on one or more desired traits or characteristics exhibited or possessed by the isolate. Non-limiting examples of a trait possessed or exhibited by a bacterial isolate that can form the basis of rational selection can include: a coding or non-coding DNA sequence; an RNA sequence; a polypeptide sequence; production or lack of production of a particular RNA or protein product; activity or inactivity of a metabolic pathway; production or lack of production of a particular metabolic product; production or lack of production of a particular ligand or set of ligands; ability to induce or inhibit production of a compound or pathway in a target cell (e.g., eukaryotic cell), association of the presence or abundance of the strain with the existence or severity of a condition or indication (e.g. in a human patient); and the particular taxonomic classification of the strain, including genus or species.

[00533] In embodiments, a method of manufacture comprises selecting a dosage of a bacterial isolate to be incorporated into a pharmaceutical composition, and incorporating the bacterial isolate into the pharmaceutical composition at the selected dosage. In an embodiment, selecting a dosage of a bacterial isolate comprises determining a threshold or minimum dosage required for engraftment of the bacterial isolate in the intestine of a subject administered the bacterial isolate, and selecting a dosage of the bacterial isolate that is above the threshold or minimum dosage.

Embodiments

[00534] Embodiment 1: A pharmaceutical composition comprising a cocktail of at least two bacterial isolates, wherein at least one of the bacterial isolates comprises a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1, and wherein the at least two bacterial isolates are isolated from stool samples of different donors.

[00535] Embodiment 2: The pharmaceutical composition of embodiment 1, wherein at least two of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1.

[00536] Embodiment 3: The pharmaceutical composition of embodiment 1 or embodiment 2, wherein at least three of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1.

[00537] Embodiment 4: The pharmaceutical composition of any one of embodiments 1 to 3, wherein at least four of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1.

[00538] Embodiment 5: The pharmaceutical composition of any one of embodiments 1 to 4, wherein at least five of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1.

[00539] Embodiment 6: The pharmaceutical composition of any one of embodiments 1 to 5, wherein at least six of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1.

[00540] Embodiment 7: The pharmaceutical composition of any one of embodiments 1 to 6, wherein at least seven of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1.

[00541] Embodiment 8: The pharmaceutical composition of any one of embodiments 1 to 7, wherein at least eight of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1.

[00542] Embodiment 9: The pharmaceutical composition of any one of embodiments 1 to 8, wherein at least nine of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1.

[00543] Embodiment 10: The pharmaceutical composition of any one of embodiments 1 to 9, wherein at least ten of the bacterial isolates comprise a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 1.

[00544] Embodiment 11: A pharmaceutical composition comprising a plurality of bacterial isolates, wherein the plurality of bacterial isolates comprises at least two bacterial isolates selected from the group consisting of *Eubacterium rectale*, *Odoribacter splanchnicus* and *Subdoligranulum variabile*, wherein the at least two bacterial isolates are isolated from stool samples of different donors.

[00545] Embodiment 12: The pharmaceutical composition of embodiment 11, wherein the *Subdoligranulum variabile* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 22 or SEQ ID NO: 23.

[00546] Embodiment 13: The pharmaceutical composition of embodiment 11 or embodiment 12, wherein the *Odoribacter* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 2.

[00547] Embodiment 14: The pharmaceutical composition of any one of embodiments 11 to 13, wherein the *Eubacterium rectale* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 8.

[00548] Embodiment 15: The pharmaceutical composition of any one of embodiments 11 to 13, wherein the at least two bacterial isolates do not include *Eubacterium rectale*.

[00549] Embodiment 16: The pharmaceutical composition of any one of embodiment 11, embodiment 12, embodiment 13, or embodiment 14, wherein the at least two bacterial isolates do not include *Odoribacter splanchnicus*.

[00550] Embodiment 17: The pharmaceutical composition of any one of embodiment 11, embodiment 13, or embodiment 14, wherein the at least two bacterial isolates do not include *Subdoligranulum variabile*.

[00551] Embodiment 18: The pharmaceutical composition of any one of embodiments 11 to 14 or embodiment 17, wherein the at least two bacterial isolates comprise *Odoribacter splanchnicus* and *Eubacterium rectale*.

[00552] Embodiment 19: The pharmaceutical composition of embodiment 18, wherein the plurality of bacterial isolates further comprises at least one of *Bacteroides cellulosilyticus*, *Faecalibacterium prausnitzii*, *Alistipes shahii*, and *Blautia obeum*.

[00553] Embodiment 20: The pharmaceutical composition of embodiment 19, wherein the plurality of bacterial isolates further comprises each of *Bacteroides cellulosilyticus*, *Faecalibacterium prausnitzii*, *Alistipes shahii*, and *Blautia obeum*.

[00554] Embodiment 21: The pharmaceutical composition of embodiment 19 or embodiment 20, wherein the *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 14.

[00555] Embodiment 22: The pharmaceutical composition of any one of embodiments 19 to 21, wherein the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7.

[00556] Embodiment 23: The pharmaceutical composition of any one of embodiments 19 to 22, wherein the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 18.

[00557] Embodiment 24: The pharmaceutical composition of any one of embodiments 19 to 23, wherein the *Blautia obeum* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 9.

[00558] Embodiment 25: The pharmaceutical composition of embodiment 18, wherein the plurality of bacterial isolates further comprises at least one of *Bacteroides cellulosilyticus*, *Bacteroides stercoris*, *Faecalibacterium prausnitzii*, *Alistipes shahii*, *Anaerostipes hadrus*, *Roseburia faecis*, and *Blautia obeum*.

[00559] Embodiment 26: The pharmaceutical composition of embodiment 25, wherein the plurality of bacterial isolates further comprises each of *Bacteroides cellulosilyticus*, *Bacteroides stercoris*, *Faecalibacterium prausnitzii*, *Alistipes shahii*, *Anaerostipes hadrus*, and *Roseburia faecis*

[00560] Embodiment 27: The pharmaceutical composition of embodiment 25 or embodiment 26, wherein the *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 14.

[00561] Embodiment 28: The pharmaceutical composition of any one of embodiments 25 to 27, wherein the *Bacteroides stercoris* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 13.

[00562] Embodiment 29: The pharmaceutical composition of any one of embodiments 25 to 28, wherein the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7.

[00563] Embodiment 30: The pharmaceutical composition of any one of embodiments 25 to 29, wherein the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 18.

[00564] Embodiment 31: The pharmaceutical composition of any one of embodiments 25 to 30, wherein the *Anaerostipes hadrus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 3.

[00565] Embodiment 32: The pharmaceutical composition of any one of embodiments 25 to 31, wherein the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19.

[00566] Embodiment 33: The pharmaceutical composition of embodiment 25, wherein the plurality of bacterial isolates does not comprise at least one of *Blautia obeum* and *Anaerostipes hadrus*.

[00567] Embodiment 34: The pharmaceutical composition of embodiment 18, wherein the plurality of bacterial isolates further comprises each of *Bacteroides cellulosilyticus*, *Bacteroides stercoris*, *Faecalibacterium prausnitzii*, *Alistipes shahii*, *Blautia obeum*, and *Roseburia faecis*.

[00568] Embodiment 35: The pharmaceutical composition of embodiment 34, wherein the *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 14.

[00569] Embodiment 36: The pharmaceutical composition of embodiment 34 or embodiment 35, wherein the *Bacteroides stercoris* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 13.

[00570] Embodiment 37: The pharmaceutical composition of any one of embodiments 34 to 36, wherein the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7.

[00571] Embodiment 38: The pharmaceutical composition of any one of embodiments 34 to 37, wherein the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 18.

[00572] Embodiment 39: The pharmaceutical composition of any one of embodiments 34 to 38, wherein the *Blautia obeum* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 9.

[00573] Embodiment 40: The pharmaceutical composition of any one of embodiments 34 to 39, wherein the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19.

[00574] Embodiment 41: The pharmaceutical composition of embodiment 18, wherein the plurality of bacterial isolates further comprises at least one of *Bacteroides cellulosilyticus*, *Bacteroides stercoris*, *Alistipes shahii*, and *Roseburia faecis*.

[00575] Embodiment 42: The pharmaceutical composition of embodiment 41, wherein the plurality of bacterial isolates further comprises each of *Bacteroides cellulosilyticus*, *Bacteroides stercoris*, *Alistipes shahii*, and *Roseburia faecis*.

[00576] Embodiment 43: The pharmaceutical composition of embodiment 41 or embodiment 42, wherein the *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 14.

[00577] Embodiment 44: The pharmaceutical composition of any one of embodiments 41 to 43, wherein the *Bacteroides stercoris* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 13.

[00578] Embodiment 45: The pharmaceutical composition of any one of embodiments 41 to 44, wherein the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19.

[00579] Embodiment 46: The pharmaceutical composition of any one of embodiments 41 to 45, wherein the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 18.

[00580] Embodiment 47: The pharmaceutical composition of embodiment 18, wherein the plurality of bacterial isolates further comprises at least one of *Faecalibacterium prausnitzii*, *Bacteroides stercoris*, *Roseburia faecis*, and *Anaerostipes hadrus*.

[00581] Embodiment 48: The pharmaceutical composition of embodiment 47, wherein the plurality of bacterial isolates further comprises each of *Faecalibacterium prausnitzii*, *Bacteroides stercoris*, *Roseburia faecis*, and *Anaerostipes hadrus*.

[00582] Embodiment 49: The pharmaceutical composition of embodiment 47 or embodiment 48, wherein the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7.

[00583] Embodiment 50: The pharmaceutical composition of any one of embodiment 47 to 49, wherein the *Bacteroides stercoris* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 13.

[00584] Embodiment 51: The pharmaceutical composition of any one of embodiment 47 to 50, wherein the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19.

[00585] Embodiment 52: The pharmaceutical composition of any one of embodiment 47 to 51, wherein the *Anaerostipes hadrus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 3.

[00586] Embodiment 53: The pharmaceutical composition of embodiment 18, wherein the plurality of bacterial isolates further comprises at least one of *Bacteroides cellulosilyticus*, *Bacteroides stercoris*, *Blautia obeum*, and *Alistipes shahii*.

[00587] Embodiment 54: The pharmaceutical composition of embodiment 53, wherein the plurality of bacterial isolates further comprises each of *Bacteroides cellulosilyticus*, *Bacteroides stercoris*, *Blautia obeum*, and *Alistipes shahii*.

[00588] Embodiment 55: The pharmaceutical composition of embodiment 53 or embodiment 54, wherein the *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 14.

[00589] Embodiment 56: The pharmaceutical composition of any one of embodiments 53 to 55, wherein the *Bacteroides stercoris* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 13.

[00590] Embodiment 57: The pharmaceutical composition of any one of embodiments 53 to 56, wherein the *Blautia obeum* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 9.

[00591] Embodiment 58: The pharmaceutical composition of any one of embodiments 53 to 57, wherein the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 18.

[00592] Embodiment 59: The pharmaceutical composition of embodiment 18, wherein the plurality of bacterial isolates further comprises at least one of *Faecalibacterium prausnitzii*, *Bacteroides stercoris*, *Alistipes shahii*, and *Roseburia faecis*.

[00593] Embodiment 60: The pharmaceutical composition of embodiment 59, wherein the plurality of bacterial isolates further comprises each of *Faecalibacterium prausnitzii*, *Bacteroides stercoris*, *Alistipes shahii*, and *Roseburia faecis*.

[00594] Embodiment 61: The pharmaceutical composition of embodiment 59 or embodiment 60, wherein the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7.

[00595] Embodiment 62: The pharmaceutical composition of any one of embodiments 59 to 61, wherein the *Bacteroides stercoris* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 13.

[00596] Embodiment 63: The pharmaceutical composition of any one of embodiments 59 to 62, wherein the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 18.

[00597] Embodiment 64: The pharmaceutical composition of any one of embodiments 59 to 63, wherein the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19.

[00598] Embodiment 65: The pharmaceutical composition of embodiment 18, wherein the plurality of bacterial isolates further comprises at least one of *Faecalibacterium prausnitzii*, *Bacteroides stercoris*, *Blautia obeum*, and *Roseburia faecis*.

[00599] Embodiment 66: The pharmaceutical composition of embodiment 65, wherein the plurality of bacterial isolates further comprises each of *Faecalibacterium prausnitzii*, *Bacteroides stercoris*, *Blautia obeum*, and *Roseburia faecis*.

[00600] Embodiment 67: The pharmaceutical composition of embodiment 65 or embodiment 66, wherein the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7.

[00601] Embodiment 68: The pharmaceutical composition of any one of embodiments 65 to 67, wherein the *Bacteroides stercoris* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 13.

[00602] Embodiment 69: The pharmaceutical composition of any one of embodiments 65 to 68, wherein the *Blautia obeum* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 9.

[00603] Embodiment 70: The pharmaceutical composition of any one of embodiments 65 to 69, wherein the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19.

[00604] Embodiment 71: The pharmaceutical composition of any one of embodiments 1 to 18, wherein the plurality of bacterial isolates comprises at least one of *Bacteroides stercoris* and *Clostridium aldenense*.

[00605] Embodiment 72: The pharmaceutical composition of embodiment 71, wherein the plurality of bacterial isolates produces an aryl hydrocarbon for binding to an aryl hydrocarbon receptor.

[00606] Embodiment 73: The pharmaceutical composition of embodiment 71 or embodiment 72, wherein the aryl hydrocarbon receptor is expressed by a cell of a subject administered the composition.

[00607] Embodiment 74: The pharmaceutical composition of embodiment 73, wherein the cell is an intestinal cell or an immune cell.

[00608] Embodiment 75: The pharmaceutical composition of any one of embodiments 71 to 74, wherein the aryl hydrocarbon is selected from the group consisting of indole, indole-3-acetic acid (IAA), indole-3-aldehyde (IAId), indole-3-lactic acid, indole-3-carbinol (I3C), indole-3-acetonitrile (I3ACN), 3,3'-diindolylmethane (DIM), 2-(indol-3-ylmethyl)-3,3'-diindolylmethane (Ltr-1), indolo[3,2-*b*]carbazole (ICZ), 2-(1'H-indole-3'carbonyl)-thiazole-4-carboxylic acid methyl ester (ITE), 3-methyl-indole (skatole), tryptamine, kynurenine, kynurenate, indigo, indirubin, indoxyl-3-sulfate (I3S), xanthurenic acid, cinnabarinic acid, and any combination thereof.

[00609] Embodiment 76: The pharmaceutical composition of embodiment 75, wherein the aryl hydrocarbon is IAA.

[00610] Embodiment 77: The pharmaceutical composition of embodiment 76, wherein the IAA is secreted at a concentration of at least 1 μM.

[00611] Embodiment 78: The pharmaceutical composition of embodiment 76, wherein the IAA is secreted at a concentration of at least 10 μM.

[00612] Embodiment 79: The pharmaceutical composition of embodiment 76, wherein the IAA is secreted at a concentration of at least 20 μM.

[00613] Embodiment 80: The pharmaceutical composition of embodiment 76, wherein the IAA is secreted at a concentration of at least 40 μM.

[00614] Embodiment 81: The pharmaceutical composition of embodiment 76, wherein the IAA is secreted at a concentration of at least 50 μM.

[00615] Embodiment 82: The pharmaceutical composition of embodiment 76, wherein the IAA is secreted at a concentration of at least 75 μM.

[00616] Embodiment 83: The pharmaceutical composition of embodiment 76, wherein the IAA is secreted at a concentration of at least 100 μM.

[00617] Embodiment 84: The pharmaceutical composition of embodiment 11, wherein the at least two bacterial isolates comprise *Eubacterium rectale* and *Subdoligranulum variabile*.

[00618] Embodiment 85: The pharmaceutical composition of embodiment 84, wherein the plurality of bacterial isolates further comprises at least one of *Faecalibacterium prausnitzii*, *Coprococcus comes*, *Anaerostipes hadrus*, and *Roseburia faecis*.

[00619] Embodiment 86: The pharmaceutical composition of embodiment 84 or embodiment 85, wherein the plurality of bacterial isolates further comprises each of *Faecalibacterium prausnitzii*, *Coprococcus comes*, *Anaerostipes hadrus*, and *Roseburia faecis*.

[00620] Embodiment 87: The pharmaceutical composition of any one of embodiments 84 to 86, wherein the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7.

[00621] Embodiment 88: The pharmaceutical composition of any one of embodiments 84 to 87, wherein the *Anaerostipes hadrus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 3.

[00622] Embodiment 89: The pharmaceutical composition of any one of embodiments 84 to 88, wherein the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19.

[00623] Embodiment 90: The pharmaceutical composition of any one of embodiments 84 to 89, wherein the *Coprococcus comes* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 17.

[00624] Embodiment 91: The pharmaceutical composition of any one of embodiments 1 to 18, wherein the plurality of bacterial strains does not include at least one of *Faecalibacterium prausnitzii*, *Roseburia faecis*, *Bacteroides cellulosilyticus*, *Alistipes shahii*, or *Blautia obeum*.

[00625] Embodiment 92: A pharmaceutical composition comprising a plurality of bacterial isolates, wherein the plurality of bacterial isolates comprises *Roseburia faecis* and *Bacteroides cellulosilyticus*, and at least one of *Faecalibacterium prausnitzii* and *Alistipes shahii*, and wherein at least two of the plurality of bacterial isolates are isolated from stool samples of different donors.

[00626] Embodiment 93: The pharmaceutical composition of embodiment 92, wherein the plurality of bacterial isolates further comprises at least one of *Eubacterium rectale*, *Anaerostipes hadrus*, and *Blautia obeum*.

[00627] Embodiment 94: The pharmaceutical composition of embodiment 92 or embodiment 93, wherein the plurality of bacterial isolates comprises each of *Roseburia faecis*, *Bacteroides cellulosilyticus*, *Faecalibacterium prausnitzii*, *Alistipes shahii*, *Eubacterium rectale*, and *Anaerostipes hadrus*.

[00628] Embodiment 95: The pharmaceutical composition of any one of embodiments 92 to 94, wherein the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19.

[00629] Embodiment 96: The pharmaceutical composition of any one of embodiments 92 to 95, wherein the *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 14.

[00630] Embodiment 97: The pharmaceutical composition of any one of embodiments 92 to 96, wherein the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7.

[00631] Embodiment 98: The pharmaceutical composition of any one of embodiments 92 to 97, wherein the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 18.

[00632] Embodiment 99: The pharmaceutical composition of any one of embodiments 93 to 98, wherein the *Eubacterium rectale* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 8.

[00633] Embodiment 100: The pharmaceutical composition of any one of embodiments 93 to 99, wherein the *Anaerostipes hadrus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 3.

[00634] Embodiment 101: The pharmaceutical composition of any one of embodiments 92 to 100, wherein the plurality of bacterial isolates does not comprise at least one of *Anaerostipes hadrus* and *Blautia obeum*.

[00635] Embodiment 102: The pharmaceutical composition of embodiment 92, wherein the plurality of bacterial isolates comprises each of *Roseburia faecis*, *Bacteroides cellulosilyticus*,

Faecalibacterium prausnitzii, *Alistipes shahii*, and further comprises *Eubacterium rectale* and *Blautia obeum*.

[00636] Embodiment 103: The pharmaceutical composition of embodiment 102, wherein the *Roseburia faecis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 19.

[00637] Embodiment 104: The pharmaceutical composition of embodiment 102 or embodiment 103, wherein the *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 14.

[00638] Embodiment 105: The pharmaceutical composition of any one of embodiments 102 to 104, wherein the *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 1 or SEQ ID NO: 7.

[00639] Embodiment 106: The pharmaceutical composition of any one of embodiments 102 to 105, wherein the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 18.

[00640] Embodiment 107: The pharmaceutical composition of any one of embodiments 102 to 106, wherein the *Eubacterium rectale* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 8.

[00641] Embodiment 108: The pharmaceutical composition of any one of embodiments 102 to 107, wherein the *Blautia obeum* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 9.

[00642] Embodiment 109: The pharmaceutical composition of any one of embodiment 1 to 108, wherein one or more of the plurality of bacterial isolates secretes a short-chain fatty acid (SCFA) in an intestine of a subject administered the composition.

[00643] Embodiment 110: The pharmaceutical composition of embodiment 109, wherein the SCFA is selected from the group consisting of acetic acid, butyric acid, caproic acid, formic acid, heptanoic acid, isobutyric acid, isocaproic acid, isovaleric acid, propionic acid, valeric acid, and a combination thereof.

[00644] Embodiment 111: The pharmaceutical composition of embodiment 109 or embodiment 110, wherein the SCFA is butyric acid.

[00645] Embodiment 112: The pharmaceutical composition of embodiment 111, wherein a level of the butyric acid produced by the one or more bacterial isolates over a period of 24 hours is at least 5 mM.

[00646] Embodiment 113: The pharmaceutical composition of embodiment 111, wherein a level of the butyric acid produced by the one or more bacterial isolates over a period of 24 hours is at least 10 mM.

[00647] Embodiment 114: The pharmaceutical composition of embodiment 111, wherein a level of the butyric acid produced by the one or more bacterial isolates over a period of 24 hours is at least 15 mM.

[00648] Embodiment 115: The pharmaceutical composition of embodiment 111, wherein a level of the butyric acid produced by the one or more bacterial isolates over a period of 24 hours is at least 20 mM.

[00649] Embodiment 116: The pharmaceutical composition of embodiment 111, wherein a level of the butyric acid produced by the one or more bacterial isolates over a period of 24 hours is at least 25 mM.

[00650] Embodiment 117: The pharmaceutical composition of embodiment 111, wherein a level of the butyric acid produced by the one or more bacterial isolates over a period of 24 hours is at least 30 mM.

[00651] Embodiment 118: The pharmaceutical composition of embodiment 111, wherein a level of the butyric acid produced by the one or more bacterial isolates over a period of 24 hours is at least 35 mM.

[00652] Embodiment 119: The pharmaceutical composition of embodiment 111, wherein a level of the butyric acid produced by the one or more bacterial isolates over a period of 24 hours is at least 40 mM.

[00653] Embodiment 120: The pharmaceutical composition of embodiment 111, wherein the one or more bacterial isolates producing at least one SCFA comprises a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 2.

[00654] Embodiment 121: A pharmaceutical composition comprising a plurality of bacterial isolates, wherein the plurality of bacterial isolates comprises a bacterial isolate

comprising *Parabacteroides merdae* and at least one of *Alistipes finegoldii* and *Alistipes onderdonkii*.

[00655] Embodiment 122: The pharmaceutical composition of embodiment 121, wherein the plurality of bacterial isolates comprises both *Alistipes finegoldii* and *Alistipes onderdonkii*.

[00656] Embodiment 123: The pharmaceutical composition of embodiment 122, wherein the plurality of bacterial isolates further comprises at least one of *Akkermansia muciniphila*, *Dorea longicatena*, *Blautia obeum*, *Blautia* sp., *Bacteroides uniformis* or *Bacteroides vulgatus*.

[00657] Embodiment 124: The pharmaceutical composition of embodiment 123, wherein the plurality of bacterial isolates comprises each of *Akkermansia muciniphila*, *Dorea longicatena*, *Blautia* sp., *Bacteroides uniformis* and *Bacteroides vulgatus*.

[00658] Embodiment 125: The pharmaceutical composition of embodiment 123 or embodiment 124, wherein the *Parabacteroides merdae* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 5.

[00659] Embodiment 126: The pharmaceutical composition of any one of embodiments 123 to 125, wherein the *Akkermansia muciniphila* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 20.

[00660] Embodiment 127: The pharmaceutical composition of any one of embodiments 123 to 126, wherein the *Alistipes finegoldii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 15.

[00661] Embodiment 128: The pharmaceutical composition of any one of embodiments 123 to 127, wherein the *Dorea longicatena* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 6.

[00662] Embodiment 129: The pharmaceutical composition of any one of embodiments 123 to 128, wherein the *Alistipes onderdonkii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 4.

[00663] Embodiment 130: The pharmaceutical composition of any one of embodiments 123 to 129, wherein the *Blautia* sp. comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 34.

[00664] Embodiment 131: The pharmaceutical composition of any one of embodiments 123 to 130, wherein the *Bacteroides uniformis* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 11 and SEQ ID NO: 16.

[00665] Embodiment 132: The pharmaceutical composition of any one of embodiments 123 to 131, wherein the *Bacteroides vulgatus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 12.

[00666] Embodiment 133: The pharmaceutical composition of any one of embodiments 121 to 132, wherein the plurality of bacterial isolates does not include one of *Alistipes finegoldii* and *Alistipes onderdonkii*.

[00667] Embodiment 134: The pharmaceutal composition of embodiment 133, wherein the plurality of bacterial isolates does not include *Alistipes finegoldii*.

[00668] Embodiment 135: The pharmaceutical composition of embodiment 121, wherein the plurality of bacterial isolates comprises *Alistipes finegoldii* and further comprises *Akkermansia muciniphila*, *Dorea longicatena*, *Blautia obeum*, *Blautia* sp., *Bacteroides uniformis* and *Bacteroides vulgatus*.

[00669] Embodiment 136: The pharmaceutical composition of embodiment 135, wherein the *Parabacteroides merdae* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 5.

[00670] Embodiment 137: The pharmaceutical composition of embodiment 135 or embodiment 136, wherein the *Akkermansia muciniphila* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 20.

[00671] Embodiment 138: The pharmaceutical composition of any one of embodiments 135 to 137, wherein the *Alistipes finegoldii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 15.

[00672] Embodiment 139: The pharmaceutical composition of any one of embodiments 135 to 138, wherein the *Dorea longicatena* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 6.

[00673] Embodiment 140: The pharmaceutical composition of any one of embodiments 135 to 139, wherein the *Blautia obeum* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 9.

[00674] Embodiment 141: The pharmaceutical composition of any one of embodiments 135 to 140, wherein the *Blautia* sp. comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 34.

[00675] Embodiment 142: The pharmaceutical composition of any one of embodiments 135 to 141, wherein the *Bacteroides uniformis* comprises a 16S rRNA sequence that is at least 95% identical to at least one of SEQ ID NO: 11 and SEQ ID NO: 16.

[00676] Embodiment 143: The pharmaceutical composition of any one of embodiments 135 to 142, wherein the *Bacteroides vulgatus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 12.

[00677] Embodiment 144: A pharmaceutical composition comprising a plurality of bacterial isolates, wherein the plurality of bacterial isolates comprises *Alistipes finegoldii* and at least one of *Bacteroides uniformis* and *Dorea longicatena*.

[00678] Embodiment 145: The pharmaceutical composition of embodiment 144, wherein the plurality of bacterial isolates further comprises at least one of *Akkermansia muciniphila*, *Bacteroides vulgatus*, and *Blautia* sp.

[00679] Embodiment 146: The pharmaceutical composition of embodiment 145, wherein the plurality of bacterial isolates comprises each of *Bacteroides uniformis*, *Dorea longicatena*, *Akkermansia muciniphila*, *Bacteroides vulgatus*, and *Blautia* sp.

[00680] Embodiment 147: The pharmaceutical composition of embodiment 145 or embodiment 146, wherein the *Alistipes finegoldii* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 15.

[00681] Embodiment 148: The pharmaceutical composition of any one of embodiments 145 to 147, wherein the *Bacteroides uniformis* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 11.

[00682] Embodiment 149: The pharmaceutical composition of any one of embodiments 145 to 148, wherein the *Dorea longicatena* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 6.

[00683] Embodiment 150: The pharmaceutical composition of any one of embodiments 145 to 149, wherein the *Akkermansia muciniphila* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 20.

[00684] Embodiment 151: The pharmaceutical composition of any one of embodiments 145 to 150, wherein the *Bacteroides vulgatus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 12.

[00685] Embodiment 152: The pharmaceutical composition of any one of embodiments 145 to 151, wherein the *Blautia* sp. comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 34.

[00686] Embodiment 153: The pharmaceutical composition of any one of embodiments 144 to 152, wherein the plurality of bacterial isolates does not comprise one of *Bacteroides uniformis* or *Dorea longicatena.*

[00687] Embodiment 154: The pharmaceutical composition of any one of embodiments 1 to 153, wherein the plurality of bacterial isolates comprises at least one bacterial isolate provided in Table 3.

[00688] Embodiment 155: The pharmaceutical composition of embodiment 154, wherein the at least one bacterial isolate modulates cytokine production or release by a eukaryotic cell.

[00689] Embodiment 156: The pharmaceutical composition of embodiment 155, wherein the at least one bacterial isolate decreases production or release of a pro-inflammatory cytokine by the eukaryotic cell.

[00690] Embodiment 157: The pharmaceutical composition of embodiment 156, wherein the pro-inflammatory cytokine is selected from the group consisting of: IFNγ, IL-12p70, IL-1 (e.g., IL-1α, IL-1β), IL-6, IL-8, IL-12, IL-17, IL-18, IL-23, MCP1, MIP1α, MIP1β, TNFα, TNF-γ, and a combination thereof.

[00691] Embodiment 158: The pharmaceutical composition of any one of embodiments 155 to 157, wherein the at least one bacterial isolate increases production or release of an anti-inflammatory cytokine by the eukaryotic cell.

[00692] Embodiment 159: The pharmaceutical composition of embodiment 158, wherein the anti-inflammatory cytokine is selected from the group consisting of: IL-10, IL-13, IL-4, IL-5, TGF-β, and a combination thereof.

[00693] Embodiment 160: The pharmaceutical composition of embodiment 159, wherein the anti-inflammatory cytokine is IL-10.

[00694] Embodiment 161: The pharmaceutical composition of embodiment 160, wherein the at least one bacterial isolate induces the eukaryotic cell to produce or release at least 500 pg/ml of IL-10.

[00695] Embodiment 162: The pharmaceutical composition of embodiment 160, wherein the at least one bacterial isolate induces the eukaryotic cell to produce or release at least 1000 pg/ml of IL-10.

[00696] Embodiment 163: The pharmaceutical composition of embodiment 160, wherein the at least one bacterial isolate induces the eukaryotic cell to produce or release at least 1500 pg/ml of IL-10.

[00697] Embodiment 164: The pharmaceutical composition of embodiment 160, wherein the at least one bacterial isolate induces the eukaryotic cell to produce or release at least 2000 pg/ml of IL-10.

[00698] Embodiment 165: The pharmaceutical composition of embodiment 160, wherein the at least one bacterial isolate induces the eukaryotic cell to produce or release at least 2500 pg/ml of IL-10.

[00699] Embodiment 166: The pharmaceutical composition of embodiment 160, wherein the at least one bacterial isolate induces the eukaryotic cell to produce or release at least 3000 pg/ml of IL-10.

[00700] Embodiment 167: The pharmaceutical composition of any one of embodiments 154 to 160, wherein the eukaryotic cell is a cultured cell.

[00701] Embodiment 168: The pharmaceutical composition of embodiment 167, wherein the cultured cell is a peripheral blood mononuclear cell (PBMC).

[00702] Embodiment 169: The pharmaceutical composition of any one of embodiments 154 to 168, wherein the eukaryotic cell is a cell of a subject administered the composition.

[00703] Embodiment 170: The pharmaceutical composition of embodiment 169, wherein the cell of the subject is selected from the group consisting of: an epithelial cell, an intestinal lamina propria cell, an endothelial cell, a fibroblast, a stromal cell, a macrophage, a B lymphocyte, a T lymphocyte, a mast cell, and a peripheral blood mononuclear cell (PBMC).

[00704] Embodiment 171: The pharmaceutical composition of embodiment 170, wherein the cell of the subject is an epithelial cell and the epithelial cell is an intestinal epithelial cell.

[00705] Embodiment 172: The pharmaceutical composition of any one of embodiments 1 to 171, wherein the pharmaceutical composition is formulated as a capsule for oral administration.

[00706] Embodiment 173: The pharmaceutical composition of embodiment 172, wherein the capsule comprises a delayed-release coating.

[00707] Embodiment 174: The pharmaceutical composition of embodiment 172 or embodiment 173, wherein the capsule comprises a hydrophobic coating.

[00708] Embodiment 175: The pharmaceutical composition of any one of embodiments 1 to 173, wherein the pharmaceutical composition is formulated for delivery of the cocktail to the intestine.

[00709] Embodiment 176: The pharmaceutical composition of embodiment 175, wherein the pharmaceutical composition is formulated for delivery of the cocktail to the small intestine.

[00710] Embodiment 177: The pharmaceutical composition of embodiment 175 or embodiment 176, wherein the composition is formulated for delivery of the cocktail to the large intestine.

[00711] Embodiment 178: The pharmaceutical composition of any one of embodiments 1 to 177, wherein the cocktail is lyophilized.

[00712] Embodiment 179: The pharmaceutical composition of any one of embodiments 1 to 178, wherein the pharmaceutical composition further comprises at least one of a pharmaceutically acceptable antioxidant, cryoprotectant, lyoprotectant, binder, disintegrant, excipient, filler, preservative, acid suppressant, antacid, H2 antagonist, and/or proton pump inhibitor.

[00713] Embodiment 180: A method of treating or preventing a disorder related to an intestinal dysbiosis in a subject in need thereof, wherein the method comprises administering to the subject a pharmaceutical composition of any one of embodiments 1 to 179.

[00714] Embodiment 181: The pharmaceutical composition of embodiment 180, wherein the disorder is selected from the group consisting of inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), *C. difficile* infection (CDI), *C. difficile*-associated disease (CDAD), an antibiotic-induced adverse effect, and a combination thereof.

[00715] Embodiment 182: A method of treating or preventing inflammatory bowel disease (IBD) in a subject in need thereof, comprising administering to the subject a plurality of bacterial isolates, wherein one of the bacterial isolates comprises *Bacteroides cellulosilyticus*, and wherein at least two of the plurality of bacterial isolates are isolated from stool samples of different donors.

[00716] Embodiment 183: The method of embodiment 182, wherein the *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 26.

[00717] Embodiment 184: The method of embodiment 182 or embodiment 183, wherein the plurality of bacterial isolates further comprises *Odoribacter splanchnicus*.

[00718] Embodiment 185: A method of manufacturing a cocktail of bacterial isolates, the method comprising selecting a first bacterial isolate based on a level of a short-chain fatty acid (SCFA) produced by the first bacterial isolate; selecting a second bacterial isolate based on a relative abundance of a corresponding bacterial strain in a healthy human subject versus a subject having inflammatory bowel disease, wherein the second bacterial isolate comprises a 16S rRNA sequence at least 97% identical to a 16S rRNA sequence of the corresponding bacterial strain; and combining the first and second bacterial isolates to produce the cocktail of bacterial isolates.

[00719] Embodiment 186: The method of embodiment 185, wherein the first bacterial isolate comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 2.

[00720] Embodiment 187: The method of embodiment 185 or embodiment 186, wherein the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 4.

[00721] Embodiment 188: The method of any one of embodiments 185 to 187, wherein the method further comprises selecting a third bacterial isolate based on a modulation by the bacterial isolate of a level of a cytokine produced by a eukaryotic cell.

[00722] Embodiment 189: The method of embodiment 188, wherein the third bacterial isolate comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 3.

[00723] Embodiment 190: The method of any one of embodiments 185 to 189, wherein the method further comprises selecting a fourth bacterial isolate based on a level of an aryl hydrocarbon produced by the fourth bacterial isolate.

[00724] Embodiment 191: The method of embodiment 190, wherein the fourth bacterial isolate comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 6.

[00725] Embodiment 192: A pharmaceutical composition comprising a microbial cocktail, wherein the microbial cocktail comprises: a first human-derived bacterial isolate which induces an IL-10:IL-12 ratio of at least 50 or an IL-10:TNF-alpha ratio of at least 1when incubated with a population of eukaryotic cells in a first functional assay; and a second human-derived bacterial isolate which produces a short chain fatty acid (SCFA) at a concentration of at least 10 mM as measured by a second functional assay; wherein the first and second bacterial isolates are capable of engrafting into the intestine of a subject following administration of the pharmaceutical composition to the subject.

[00726] Embodiment 193: The pharmaceutical composition of embodiment 192, wherein the IL-10:IL-12 ratio is at least 100.

[00727] Embodiment 194: The pharmaceutical composition of embodiment 192, wherein the IL-10:IL-12 ratio is at least 500.

[00728] Embodiment 195: The pharmaceutical composition of embodiment 192, wherein the IL-10:IL-12 ratio is at least 1000.

[00729] Embodiment 196: The pharmaceutical composition of embodiment 192, wherein the IL-10:IL-12 ratio is at least 2000.

[00730] Embodiment 197: The pharmaceutical composition of embodiment 192, wherein the IL-10:TNF-alpha ratio is at least 2.

[00731] Embodiment 198: The pharmaceutical composition of embodiment 192, wherein the IL-10:TNF-alpha ratio is at least 5.

[00732] Embodiment 199: The pharmaceutical composition of embodiment 192, wherein the IL-10:TNF-alpha ratio is at least 10.

[00733] Embodiment 200: The pharmaceutical composition of embodiment 192, wherein the IL-10:TNF-alpha ratio is at least 20.

[00734] Embodiment 201: The pharmaceutical composition of any one of embodiments 192 to 200, wherein the population of eukaryotic cells comprises a population of PBMCs.

[00735] Embodiment 202: The pharmaceutical composition of any one of embodiments 192 to 201, wherein the first human-derived bacterial isolate is incubated with the population of eukaryotic cells for about 24 hours.

[00736] Embodiment 203: The pharmaceutical composition of any one of embodiments 178 to 188, wherein the SCFA is butyrate.

[00737] Embodiment 204: The pharmaceutical composition of any one of embodiments 192 to 203, wherein the SCFA is produced at a concentration of at least 20 mM.

[00738] Embodiment 205: The pharmaceutical composition of any one of embodiments 192 to 204, wherein the SCFA is produced at a concentration of at least 25 mM.

[00739] Embodiment 206: The pharmaceutical composition of any one of embodiments 192 to 205, wherein the SCFA is produced at a concentration of at least 30 mM.

[00740] Embodiment 207: The pharmaceutical composition of any one of embodiments 192 to 206, wherein the SCFA is produced at a concentration of at least 35 mM.

[00741] Embodiment 208: The pharmaceutical composition of any one of embodiments 192 to 207, wherein the second functional assay comprises incubating the second bacterial isolate with a substrate.

[00742] Embodiment 209: The pharmaceutical composition of embodiment 208, wherein the substrate comprises at least one of an oligosaccharide, sunfiber, or barley malt.

[00743] Embodiment 210: The pharmaceutical composition of embodiment 209, wherein the oligosaccharide comprises at least one of a fructooligosaccharide (FOS) and an xylooligosaccharide (XOS).

[00744] Embodiment 211: The pharmaceutical composition of embodiment 210, wherein the substrate comprises both of a fructooligosaccharide (FOS) and an xylooligosaccharide (XOS).

[00745] Embodiment 212: The pharmaceutical composition of any one of embodiments 192 to 211, wherein the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 2.

[00746] Embodiment 213: The pharmaceutical composition of any one of embodiments 192 to 212, wherein the second bacterial isolate comprises *Anaerostipes* sp.

[00747] Embodiment 214: The pharmaceutical composition of embodiment 213, wherein the *Anaerostipes* sp. is *Anaerostipes hadrus*.

[00748] Embodiment 215: The pharmaceutical composition of any one of embodiments 192 to 214, wherein the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the sequence corresponding to SEQ ID NO: 3.

[00749] Embodiment 216: The pharmaceutical composition of any one of embodiments 192 to 215, wherein the second bacterial isolate comprises *Roseburia* sp.

[00750] Embodiment 217: The pharmaceutical composition of embodiment 216, wherein the *Roseburia* sp. is *Roseburia faecis*.

[00751] Embodiment 218: The pharmaceutical composition of any one of embodiments 192 to 217, wherein the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the sequence corresponding to SEQ ID NO: 19.

[00752] Embodiment 219: The pharmaceutical composition of any one of embodiments 192 to 218, wherein the second bacterial isolate comprises *Eubacterium* sp.

[00753] Embodiment 220: The pharmaceutical composition of embodiment 219, wherein the *Eubacterium* sp. is *Eubacterium rectale*.

[00754] Embodiment 221: The pharmaceutical composition of any one of embodiments 192 to 220, wherein the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the sequence corresponding to SEQ ID NO: 8.

[00755] Embodiment 222: The pharmaceutical composition of any one of embodiments 192 to 221, wherein the second bacterial isolate comprises *Coprococcus* sp.

[00756] Embodiment 223: The pharmaceutical composition of embodiment 222, wherein the *Coprococcus* sp. is *Coprococcus comes*.

[00757] Embodiment 224: The pharmaceutical composition of any one of embodiments 192 to 223, wherein the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to the sequence corresponding to SEQ ID NO: 17.

[00758] Embodiment 211: The pharmaceutical composition of any one of embodiments 192 to 224, wherein the first bacterial isolate comprises a 16S sequence at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 3.

[00759] Embodiment 212: A pharmaceutical composition, comprising a microbial cocktail, wherein the microbial cocktail comprises: a first human-derived bacterial isolate capable of producing a short chain fatty acid (SCFA) at a concentration of at least 10 mM, as measured by a first functional assay; and a second human-derived bacterial isolate capable of producing, as measured by a second functional assay, at least one of: (i) indole at a level at least 5x greater than a level of indole produced by a control bacterial strain; (ii) tryptamine at a level at least 1.4x greater than a level of tryptamine produced by a control bacterial strain; (iii) kynurenate at a level at least 1.4x greater than a level of kynurenate produced by a control bacterial strain; (iv) kynurenine at a level at least 2.5x greater than a level of kynurenine produced by a control bacterial strain; and (v) indole-3-acetic acid at a level at least 2x greater than a level of indole-3-acetic acid produced by a control bacterial strain; wherein the control bacterial strain is selected from at least one of *Peptostreptococcus russellii* and *Peptostreptococcus anaerobius*; wherein the first and second bacterial isolates engraft in the intestine of a subject following administration of the pharmaceutical composition to the subject.

[00760] Embodiment 213: The pharmaceutical composition of embodiment 212, wherein the second functional assay comprises separately incubating the second bacterial isolate and the control strain with tryptophan.

[00761] Embodiment 214: The pharmaceutical composition of embodiment 212 or embodiment 213, wherein the second bacterial isolate produces indole at a level at least 50x greater than the level of indole produced by the control bacterial strain.

[00762] Embodiment 215: The pharmaceutical composition of any one of embodiments 212 to 214, wherein the second bacterial isolate produces indole at a level at least 100x greater than the level of indole produced by the control bacterial strain.

[00763] Embodiment 216: The pharmaceutical composition of any one of embodiments 212 to 215, wherein the second bacterial isolate produces indole at a level at least 150x greater than the level of indole produced by the control bacterial strain.

[00764] Embodiment 217: The pharmaceutical composition of any one of embodiments 214 to 216, wherein the second bacterial isolate comprises *Clostridium aldenense*.

[00765] Embodiment 218: The pharmaceutical composition of any one of embodiments 214 to 217, wherein the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to SEQ ID NO: 10.

[00766] Embodiment 219: The pharmaceutical composition of any one of embodiments 212 to 218, wherein the second bacterial isolate produces tryptamine at a level at least 1.5x greater than the level of tryptamine produced by the control bacterial strain.

[00767] Embodiment 220: The pharmaceutical composition of embodiment 219, wherein the second bacterial isolate comprises *Odoribacter splanchnicus*.

[00768] Embodiment 221: The pharmaceutical composition of embodiment 219 or embodiment 220, wherein the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to SEQ ID NO: 2.

[00769] Embodiment 222: The pharmaceutical composition of any one of embodiments 212 to 218, wherein the second bacterial isolate produces kynurenate at a level at least 1.5x greater than the level of kynurenate produced by the control bacterial strain.

[00770] Embodiment 223: The pharmaceutical composition of embodiment 222, wherein the second bacterial isolate comprises *Odoribacter splanchnicus*.

[00771] Embodiment 224: The pharmaceutical composition of embodiment 222 or embodiment 223, wherein the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to SEQ ID NO: 2.

[00772] Embodiment 225: The pharmaceutical composition of any one of embodiments 212 to 224, wherein the second bacterial isolate produces kynurenine at a level at least 3x greater than the level of tryptamine produced by the control bacterial strain.

[00773] Embodiment 226: The pharmaceutical composition of embodiment 225, wherein the second bacterial isolate comprises *Odoribacter splanchnicus* or *Bacteroides stercoris*.

[00774] Embodiment 227: The pharmaceutical composition of embodiment 225 or embodiment 226, wherein the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to SEQ ID NO: 2 or SEQ ID NO: 13.

[00775] Embodiment 228: The pharmaceutical composition of at least one of embodiments 225 to 227, wherein the control bacterial strain comprises *Peptostreptococcus anaerobius*.

[00776] Embodiment 229: The pharmaceutical composition of any one of embodiments 212 to 228, wherein the second bacterial isolate produces indole-3-acetic acid at a level at least 3x greater than the level of indole-3-acetic acid produced by the control bacterial strain.

[00777] Embodiment 230: The pharmaceutical composition of embodiment 229, wherein the second bacterial isolate produces indole-3-acetic acid at a level at least 8x greater than the level of indole-3-acetic acid produced by the control bacterial strain.

[00778] Embodiment 231: The pharmaceutical composition of embodiment 230, wherein the second bacterial isolate comprises *Odoribacter splanchnicus* or *Clostridium aldenense*.

[00779] Embodiment 232: The pharmaceutical composition of embodiment 230 or embodiment 231, wherein the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to SEQ ID NO: 2 or SEQ ID NO: 10.

[00780] Embodiment 233: The pharmaceutical composition of any one of embodiments 212 to 232, wherein the SCFA is butyrate.

[00781] Embodiment 234: The pharmaceutical composition of any one of embodiments 212 to 233, wherein the SCFA is produced at a concentration of at least 20 mM.

[00782] Embodiment 235: The pharmaceutical composition of any one of embodiments 212 to 234, wherein the SCFA is produced at a concentration of at least 25 mM.

[00783] Embodiment 236: The pharmaceutical composition of any one of embodiments 212 to 235, wherein the SCFA is produced at a concentration of at least 30 mM.

[00784] Embodiment 237: The pharmaceutical composition of any one of embodiments 212 to 236, wherein the SCFA is produced at a concentration of at least 35 mM.

[00785] Embodiment 238: The pharmaceutical composition of any one of embodiments 212 to 237, wherein the second functional assay comprises incubating the second bacterial isolate with a substrate.

[00786] Embodiment 239: The pharmaceutical composition of embodiment 238, wherein the substrate comprises at least one of an oligosaccharide, sunfiber, or barley malt.

[00787] Embodiment 240: The pharmaceutical composition of embodiment 239, wherein the oligosaccharide comprises at least one of a fructooligosaccharide (FOS) and an xylooligosaccharide (XOS).

[00788] Embodiment 241: The pharmaceutical composition of embodiment 240, wherein the substrate comprises both of a fructooligosaccharide (FOS) and an xylooligosaccharide (XOS).

[00789] Embodiment 242: The pharmaceutical composition of any one of embodiments 212 to 241, wherein the second bacterial isolate comprises a 16S rRNA sequence at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in Table 2.

[00790] Embodiment 243: A method of treating inflammatory bowel disease comprising administering the pharmaceutical composition of any one of embodiments 192 to 242 to a subject in need thereof.

[00791] Embodiment 244: The method of embodiment 243, wherein a dosage of at least one of the first bacterial isolate and second bacterial isolate is less than 10^{10} cells/ml.

[00792] Embodiment 245: A pharmaceutical composition comprising a plurality of bacterial isolates, wherein the plurality of bacterial isolates comprises *Bacteroides cellulosilyticus* and at least one of *Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, *Subdoligranulum variabile*, and *Eubacterium rectale*, wherein at least two of the plurality of bacterial isolates are isolated from stool samples of different donors.

[00793] Embodiment 246: The pharmaceutical composition of embodiment 245, wherein the plurality of bacterial isolates comprises *Odoribacter splanchnicus*.

[00794] Embodiment 247: The pharmaceutical composition of embodiment 246, wherein the plurality of bacterial isolates comprises *Faecalibacterium prausnitzii*.

[00795] Embodiment 248: The pharmaceutical composition of embodiment 247, wherein the plurality of bacterial isolates comprises two different bacterial isolates that are each members of the species *Faecalibacterium prausnitzii*.

[00796] Embodiment 249: The pharmaceutical composition of embodiment 247, wherein the plurality of bacterial isolates comprises *Subdoligranulum variabile*.

[00797] Embodiment 250: The pharmaceutical composition of embodiment 248, wherein the plurality of bacterial isolates comprises *Roseburia faecis, Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

[00798] Embodiment 251: The pharmaceutical composition of embodiment 249, wherein the plurality of bacterial isolates comprises *Roseburia faecis, Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

[00799] Embodiment 252: A pharmaceutical composition comprising a plurality of bacterial isolates, wherein the plurality of bacterial isolates comprises two different bacterial isolates that are each members of the species *Faecalibacterium prausnitzii*.

[00800] Embodiment 253: The composition of embodiment 252, wherein the two different bacterial isolates are isolated from stool samples of different human donors.

[00801] Embodiment 254: The composition of embodiment 252, wherein the plurality of bacterial isolates further comprises at least one of *Bacteroides cellulosilyticus*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

[00802] Embodiment 255: The composition of embodiment 252, wherein the plurality of bacterial isolates further comprises each of *Bacteroides cellulosilyticus*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

[00803] Embodiment 256: A method of treating or preventing inflammatory bowel disease (IBD) in a subject in need thereof, comprising administering to the subject a first pharmaceutical composition comprising a bacterial isolate comprising *Bacteroides cellulosilyticus*, and administering to the subject a second pharmaceutical composition comprising a second bacterial isolate.

[00804] Embodiment 257: The method of embodiment 256, wherein the plurality of bacterial isolates further comprises at least one of *Faecalibacterium prausnitzii*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Akkermansia muciniphila*, *Alistipes shahii*, *Subdoligranulum variabile* and *Eubacterium rectale*.

[00805] Embodiment 258: The method of embodiment 256, wherein the plurality of bacterial isolates further comprises each of *Faecalibacterium prausnitzii*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Akkermansia muciniphila*, *Alistipes shahii*, *Subdoligranulum variabile* and *Eubacterium rectale*.

[00806] Embodiment 259: The method of embodiment 256, wherein the plurality of bacterial isolates further comprises each of *Odoribacter splanchnicus*, *Roseburia faecis*,

Akkermansia muciniphila, *Alistipes shahii*, *Eubacterium rectale*, and two different bacterial isolates that are each members of the species *Faecalibacterium prausnitzii*.

[00807] Embodiment 260: A method of manufacture, the method comprising culturing *Bacteroides cellulosilyticus* as a pure culture; and lyophilizing bacteria from the pure culture of *B. cellulosilyticus* to produce a *B. cellulosilyticus* lyophilate.

[00808] Embodiment 261: The method of embodiment 260, further comprising combining the *B. cellulosilyticus* lyophilate with a second lyophilate, wherein the second lyophilate is produced by lyophilizing bacteria from a pure culture of at least one of *Faecalibacterium prausnitzii*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Akkermansia muciniphila*, *Alistipes shahii*, *Subdoligranulum variabile* and *Eubacterium rectale*.

[00809] Embodiment 262: A pharmaceutical composition comprising a plurality of bacterial isolates, wherein an amount of cells of a first bacterial isolate of the plurality of bacterial isolates is at least 1% greater than an amount of cells of a second bacterial isolate of the plurality of bacterial isolates, wherein the plurality of bacterial isolates are selected from the group consisting of: *Bacteroides cellulosilyticus*, *Faecalibacterium prausnitzii*, *Subdogranulum variabile*, *Eubacterium rectale*, *Odoribacter splanchnicus*, *Alistipes shahii*, *Roseburia faecis* and *Akkermansia muciniphila*.

[00810] Embodiment 263: The pharmaceutical composition of embodiment 262, wherein the amount of cells of the first bacterial isolate is at least 10% greater than the amount of cells of the second bacterial isolate.

[00811] Embodiment 264: The pharmaceutical composition of embodiment 262 or 263, wherein the first bacterial isolate comprises one of *Eubacterium rectale* and *Faecalibacterium prausnitzii*.

[00812] Embodiment 265: The pharmaceutical composition of embodiment 262 or 263, wherein the second bacterial isolate comprises one of *Alistipes shahii*, and *Akkermansia muciniphila*.

[00813] Embodiment 266: The pharmaceutical composition of embodiment 262 or 263, wherein each of the first and second bacterial isolates comprises *Faecalibacterium prausnitzii*.

[00814] Embodiment 267: The pharmaceutical composition of embodiment 266, wherein the first bacterial isolate comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 7.

[00815] Embodiment 268: The pharmaceutical composition of embodiment 266 or 267, wherein the second bacterial isolate comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 1.

[00816] Embodiment 269: A pharmaceutical composition comprising a plurality of bacterial isolates, wherein an amount of cells of a first bacterial isolate of the plurality of bacterial isolates is at least 1% greater than an amount of cells of a second bacterial isolate of the plurality of bacterial isolates, wherein each of the first and second bacterial isolates comprises *Faecalibacterium prausnitzii*.

[00817] Embodiment 270: The pharmaceutical composition of embodiment 269, wherein the amount of cells of the first bacterial isolate is at least 10% greater than the amount of cells of the second bacterial isolate.

[00818] Embodiment 271: The pharmaceutical composition of embodiment 269 or 270, wherein the first bacterial isolate comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 7.

[00819] Embodiment 272: The pharmaceutical composition of any one of embodiments 269 to 271, wherein the second bacterial isolate comprises a 16S rRNA sequence that is at least 95% identical to SEQ ID NO: 1.

[00820] Embodiment 273: A pharmaceutical composition comprising a bacterial isolate, wherein the bacterial isolate comprises a 16S rRNA sequence that is at least 97% identical to a 16S rRNA sequence of a bacterial strain that is either (i) enriched in a group of healthy subjects over a group of patients with ulcerative colitis (UC) and/or (ii) correlated with clinical remission of one or more UC symptoms in a group of patients following treatment of each patient of the group of patients with a fecal microbiota transplant, wherein a cross-sectional combined p-value of the bacterial strain is less than $1x10^{-10}$.

[00821] Embodiment 274: The pharmaceutical composition of embodiment 273, wherein the bacterial isolate comprises a 16S rRNA sequence that is at least 99% identical to a 16S rRNA sequence of the bacterial strain.

[00822] Embodiment 275: The pharmaceutical composition of embodiment 273 or 274, wherein the bacterial isolate comprises at least one of *Odoribacter splanchnicus*, *Eubacterium rectale*, *Bacteroides cellulosilyticus* and *Alistipes shahii*.

[00823] Embodiment 276: The pharmaceutical composition of any one of embodiments 273 to 275, wherein the cross-sectional combined p-value of the bacterial strain is less than $1x10^{-14}$.

[00824] Embodiment 277: The pharmaceutical composition of any one of embodiments 273 to 276, wherein the bacterial isolate comprises at least one of *Odoribacter splanchnicus* and *Alistipes shahii*.

[00825] Embodiment 278: The pharmaceutical composition of any one of embodiments 273 to 277, wherein the cross-sectional combined p-value of the bacterial strain is less than $1x10^{-20}$.

[00826] Embodiment 279: The pharmaceutical composition of any one of embodiments 273 to 278, wherein the bacterial isolate comprises *Alistipes shahii*.

[00827] Embodiment 280: The pharmaceutical composition of embodiment 279, wherein the *Alistipes shahii* comprises a 16S rRNA sequence that is at least 97% identical to SEQ ID NO: 18.

[00828] Embodiment 281: A method of treating inflammatory bowel disease comprising administering the pharmaceutical composition of any one of embodiments 245 to 280 to a subject in need thereof.

[00829] Embodiment 282: A pharmaceutical composition comprising a bacterial mixture comprising a plurality of bacterial isolates, wherein the plurality of bacterial isolates comprises two or more bacterial isolates that are each a member of the genus *Bacteroides*, wherein at least one of the two or more bacterial isolates comprises *Bacteroides cellulosilyticus* or *Bacteroides stercoris*.

[00830] Embodiment 283: The pharmaceutical composition of embodiment 282, wherein the two or more bacterial isolates comprise a bacterial isolate comprising *Bacteroides cellulosilyticus* and a bacterial isolate comprising *Bacteroides stercoris*.

[00831] Embodiment 284: The pharmaceutical composition of embodiment 283, wherein the bacterial isolate comprising *Bacteroides cellulosilyticus* comprises a 16S rRNA sequence having the sequence shown in SEQ ID NO: 14.

[00832] Embodiment 285: The pharmaceutical composition of embodiment 284, wherein the bacterial isolate comprising *Bacteroides stercoris* comprises a 16S rRNA sequence having the sequence shown in SEQ ID NO: 13.

[00833] Embodiment 286: The pharmaceutical composition of embodiment 285, wherein the bacterial mixture further comprises two bacterial isolates comprising *Faecalibacterium prausnitzii*.

[00834] Embodiment 287: The pharmaceutical composition of embodiment 286, wherein one of the two bacterial isolates comprising *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence having the sequence shown in SEQ ID NO: 7, and the other of the two bacterial isolates comprising *Faecalibacterium prausnitzii* comprises a 16S rRNA sequence having the sequence shown in SEQ ID NO: 1.

[00835] Embodiment 288: The pharmaceutical composition of embodiment 287, wherein the bacterial mixture further comprises a bacterial isolate comprising *Odoribacter splanchnicus*.

[00836] Embodiment 289: The pharmaceutical composition of embodiment 288, wherein the bacterial isolate comprising *Odoribacter splanchnicus* comprises a 16S rRNA sequence having the sequence shown in SEQ ID NO: 2.

[00837] Embodiment 290: The pharmaceutical composition of embodiment 289, wherein the bacterial mixture further comprises a bacterial isolate comprising *Akkermansia muciniphila*.

[00838] Embodiment 291: The pharmaceutical composition of embodiment 290, wherein the bacterial isolate comprising *Akkermansia muciniphila* comprises a 16S rRNA sequence having the sequence shown in SEQ ID NO: 20.

[00839] Embodiment 292: The pharmaceutical composition of embodiment 291, wherein the bacterial mixture further comprises a bacterial isolate comprising *Eubacterium rectale*.

[00840] Embodiment 293: The pharmaceutical composition of embodiment 292, wherein the bacterial isolate comprising *Eubacterium rectale* comprises a 16S rRNA sequence having the sequence shown in SEQ ID NO: 8.

[00841] Embodiment 294: The pharmaceutical composition of embodiment 293, wherein the bacterial mixture further comprises a bacterial isolate comprising *Roseburia faecis*.

[00842] Embodiment 295: The pharmaceutical composition of embodiment 294, wherein the bacterial isolate comprising *Roseburia faecis* comprises a 16S rRNA sequence having the sequence shown in SEQ ID NO: 19.

[00843] Embodiment 296: The pharmaceutical composition of embodiment 295, wherein the bacterial mixture further comprises a bacterial isolate comprising *Alistipes shahii*.

[00844] Embodiment 297: The pharmaceutical composition of embodiment 296, wherein the bacterial isolate comprising *Alistipes shahii* comprises a 16S rRNA sequence having the sequence shown in SEQ ID NO: 18.

[00845] Embodiment 298: A method of treating inflammatory bowel disease comprising administering the pharmaceutical composition of any one of embodiments 282 to 297 to a subject in need thereof.

[00846] Embodiment 299: A pharmaceutical composition comprising a cocktail of at least two bacterial isolates, wherein at least one of the bacterial isolates comprises a 16S rRNA sequence that is at least 95% identical to a 16S rRNA sequence of a bacterial isolate provided in any one of Tables 1-51, and wherein the at least two bacterial isolates are isolated from stool samples of different donors.

[00847] Embodiment 300: A method of treating inflammatory bowel disease comprising administering the pharmaceutical composition of embodiment 299 to a subject in need thereof.

EXAMPLES

[00848] The examples herein are provided to illustrate advantages and benefits of the present technology and to further assist a person of ordinary skill in the art with preparing or using compositions of the present technology. The examples herein are also presented in order to more fully illustrate the preferred aspects of the present technology. The examples should in no way be construed as limiting the scope of the present disclosure, as defined by the appended claims. The examples can include or incorporate any of the variations, aspects or embodiments of the present technology described above. The variations, aspects or embodiments described above may also further each include or incorporate the variations of any or all other variations, aspects or embodiments of the present technology.

Example 1: Isolating and Growing Bacterial Isolates

[00849] Stool samples from candidate human donors was collected and screened for the presence of pathogens. Six donors whose stool samples did not contain pathogens were selected. Donor stool was then collected in Whirl-Pak® filter bags, suspended in buffer (12.5% glycerol and 0.9% PBS, pH 7.4), and homogenized. Filtrate was diluted ~10^3x in PBS containing 0.05% cysteine and either plated on solid Isolation Media (IM; see below for each strain) or inoculated into IM broth, and grown under anaerobic conditions. Bacterial isolates were purified from plates by picking bacterial colonies and from IM broth by diluting to extinction. Once purified, each bacterial isolate was grown in IM broth under anaerobic conditions for further characterization, and aliquots frozen at -80°C in 20% glycerol to make stocks.

Isolation Media (IM) for Strains

The following IM was used to culture strains used in this study. In each case, agar was omitted for cultures grown in broth.

1. Complex Gut Medium (CGM)

CGM was used to culture bacteria from the following genus and species:

- *Alistipes onderdonkii* (e.g., a bacterial isolate having SEQ ID NO: 4, which was isolated from stool of a disease-screened and healthy human donor ("Donor E"));
- *Bacteroides uniformis* (e.g., a bacterial isolate having SEQ ID NO: 11 or SEQ ID NO:16; which were each isolated from stool of a disease-screened and healthy human donor (respectively "Donor K" and "Donor E")).

Formulation (per liter):

Tryptone	2 g
Peptone from casein	2 g
Yeast extract	1 g
D-glucose	0.4 g
L-cysteine	0.5 g
D-(+)-Cellobiose	1 g
D-(+)-Maltose	1 g
D-(-) Fructose	1 g
Meat extract	5 g
$MgSO_4 \cdot 7H_2O$	0.0025 g
$NaHCO_3$	0.4 g
$NaCl_2$	0.08 g
Phosphate buffer	100 mM
$CaCl_2$	0.8%
Vitamin K (menadione)	5.8 mM
$FeSO_4$	1.44 mM
Histidine hematin	0.1%
Tween80	0.05%
ATCC Vitamin mix	1%
ATCC Trace Mineral mix	1%
Acetic acid	30 mM
Isovaleric acid	1 mM
Propionic acid	8 mM
Butyric acid	4 mM
Resazurin	4 mM
Agar	1.5%

Final pH 7.0 ± 0.2

2. Minimal mucin media (Min muc)

Minimal mucin media was used to culture bacteria from the following genus and species:

- *Dorea longicatena* (e.g., a bacterial isolate having SEQ ID NO: 6, which was isolated from stool of a disease-screened and healthy human donor ("Donor F")).

Formulation (per liter):

5X Minimum salts (see below)	11.28 g
Agar	12 g
Mucin from porcine stomach Type II	2.5 g
Final pH 6.8 ± 0.2	

5X Minimum Salts (HiMedia® M1253) (used in Min muc media)

Formulation (per liter):

Disodium phosphate	33.9 g
Potassium phosphate	15 g
Sodium chloride	2.5 g
Ammonium chloride	5 g

3. Veggie Brain Heart Infusion agar with supplements (vBHI3)

vBHI3 media was used to culture bacteria from the following genus and species:

- *Odoribacter splanchnicus* (e.g., a bacterial isolate having SEQ ID NO: 2, which was isolated from stool of a disease-screened and healthy human donor ("Donor G"));
- *Bacteroides cellulosilyticus* (e.g., a bacterial isolate having SEQ ID NO: 14, which was isolated from stool of a disease-screened and healthy human donor ("Donor G"));
- *Blautia obeum* (e.g., a bacterial isolate having SEQ ID NO: 9, which was isolated from stool of a disease-screened and healthy human donor ("Donor G"));
- *Blautia* sp., (e.g., a bacterial isolate having SEQ ID NO: 34, which was isolated from stool of a disease-screened and healthy human donor ("Donor H");
- *Parabacteroides merdae* (e.g., a bacterial isolate having SEQ ID NO: 5, which was isolated from stool of a disease-screened and healthy human donor ("Donor H")).

Formulation (per liter):

HiVeg™ Peptone No. 3 (HiMedia® RM005V)	10 g
HiVeg™ Special Infusion (HiMedia® RM188V)	7.5 g
HiVeg™ Infusion (HiMedia® RM191V)	10 g
Dextrose	2 g
Sodium Chloride	5 g
Disodium phosphate	2.5 g
Agar	12 g

L-cysteine	0.005 g
Hemin	0.05 mg
Vitamin K	0.0025 mg
Final pH 7.4 ± 0.2	

4. Veggie Brain Heart Infusion agar with supplements and sodium taurocholate (vBHI3 + NaTau)

vBHI3+NaTau media was used to culture bacteria from the following genus and species:

- *Anaerostipes hadrus* (e.g., a bacterial isolate having SEQ ID NO: 3, which was isolated from stool of a disease-screened and healthy human donor ("Donor G"));
- *Clostridium aldenense* (e.g., a bacterial isolate having SEQ ID NO: 10, which was isolated from stool of a disease-screened and healthy human donor ("Donor G")).

Formulation (per liter):
Use recipe for Veggie Brain Heart Infusion agar with supplements (vBHI3)
Plus Sodium taurocholate 1 g
Final pH 7.4 ± 0.2

5. 0.2X Veggie Brain Heart Infusion agar with supplements and mucin (vBHI3 + mucin)

vBHI3+mucin media was used to culture bacteria from the following genus and species:

- *Alistipes finegoldii* (e.g., a bacterial isolate having SEQ ID NO: 15, which was isolated from stool of a disease-screened and healthy human donor ("Donor E")).

Formulation (per liter):

HiVeg™ Peptone No. 3 (HiMedia® RM005V)	2 g
HiVeg™ Special Infusion (HiMedia® RM188V)	1.5 g
HiVeg™ Infusion (HiMedia® RM191V)	2 g
Dextrose	0.4 g
Sodium Chloride	1 g
Disodium phosphate	0.5 g
Agar	12 g
L-cysteine	0.005 g
Hemin	0.05 mg
Vitamin K	0.0025 mg
Mucin from porcine stomach Type II	2.5 g
Final pH 7.4 ± 0.2	

6. Veggie Reinforced Clostridial Medium with rumen (vRCM + rumen)

vRCM+rumen media was used to culture bacteria from the following genus and species:

- *Coprococcus comes* (e.g., a bacterial isolate having SEQ ID NO: 17, which was isolated from stool of a disease-screened and healthy human donor ("Donor J")).

Formulation (per liter):

Differential Reinforced Clostridial HiVeg broth (see below)	29 g
Noble agar	12 g
Rumen fluid	30%
L-cysteine	0.005 g
Final pH 7.2 ± 0.2	

Differential Reinforced Clostridial HiVeg™ broth (HiMedia MV549) (used in vRCM + rumen media)

Formulation (per liter):

HiVeg™ peptone	10 g
HiVeg™ extract	10 g
Yeast extract	1.5 g
Starch	1 g
Sodium acetate	5 g
Glucose	1 g
L-cysteine hydrochloride	0.5 g

7. Wilkins-Chalgren Anaerobe agar with cooked meat (WCA+CM)

WCA+CM media was used to culture bacteria from the following genus and species:

- *Eubacterium rectale* (e.g., a bacterial isolate having SEQ ID NO: 8, which was isolated from stool of a disease-screened and healthy human donor ("Donor F")).

Formulation (per liter):

Wilkins-Chalgren Anaerobe broth (see below)	33 g
Noble agar	12 g
Ground cooked meat granules	10 g
L-cysteine	0.005 g
Hemin	0.05 mg
Vitamin K	0.0025 mg
Final pH 7 ± 0.2	

Wilkins-Chalgren Anaerobe broth (Oxoid CM0643) (used in WCA+CM media)

Formulation (per liter):

Tryptone	10 g
Gelatin peptone	10 g
Yeast extract	5 g
Glucose	1 g
Sodium chloride	5 g
L-Arginine	1 g
Sodium pyruvate	1 g
Menadione	0.0005 g
Haemin	0.005 g
Final pH 7.1 ± 0.2	

8. Yeast Casitone Fatty Acids Agar with Carbohydrates (YCFAC)

YCFAC media was used to culture bacteria from the following genus and species:

- *Faecalibacterium prausnitzii* (e.g., a bacterial isolate having SEQ ID NO: 1 or SEQ ID NO: 7, which were each isolated from stool of a disease-screened and healthy human donor (respectively "Donor E" and "Donor F");
- *Alistipes shahii* (e.g., a bacterial isolate having SEQ ID NO: 18, which was isolated from stool of a disease-screened and healthy human donor ("Donor E");
- *Bacteroides uniformis* (e.g., a bacterial isolate having SEQ ID NO: 11 or SEQ ID NO:16; which were each isolated from stool of a disease-screened and healthy human donor (respectively "Donor K" and "Donor E")).
- *Bacteroides vulgatus* (e.g., a bacterial isolate having SEQ ID NO: 12, which was isolated from stool of a disease-screened and healthy human donor ("Donor K");
- *Roseburia faecis* (e.g., a bacterial isolate having SEQ ID NO: 19, which was isolated from stool of a disease-screened and healthy human donor ("Donor E");
- *Bacteroides stercoris* (e.g., a bacterial isolate having SEQ ID NO: 13, which was isolated from stool of a disease-screened and healthy human donor ("Donor K").

Media was pre-purchased from Anaerobe Systems (Cat # AS-675)

Formulation (per liter):

Casitone	10.00 g
Yeast Extract	2.50 g
Sodium Bicarbonate	4.00 g
Glucose	2.00 g
Cellobiose	2.00 g
Maltose	2.00 g
Potassium Phosphate Monobasic	0.45 g
Potassium Phosphate Dibasic	0.45 g
Sodium Chloride	0.90 g
Ammonium Sulfate	0.90 g
Magnesium Sulfate Heptahydrate	0.09 g
Calcium Chloride	0.09 g
Hemin (0.1% solution)	10.00 mL
Vitamin Mix	10.00 mL
L-Cysteine (25.0% solution)	4.00 mL
Resazurin (0.025% solution)	4.00 mL
Volatile Fatty Acid Solution	2.90 mL
Agar	15.00 g

Final pH 6.8 ± 0.3

9. HiVeg™ Brucella Blood Agar (vBBA)

vBBA media was used to culture bacteria from the following genus and species:

- *Phascolarctobacterium faecium* (e.g., a bacterial isolate having SEQ ID NO: 21, which was isolated from stool of a disease-screened and healthy human donor ("Donor K").

Media can be purchased as a dehydrated mix (Brucella HiVeg Agar Base; HiMedia MV074), followed by addition of L-cysteine and horse serum.

Formulation (per liter):

HiVeg hydrolysate	10 g
HiVeg peptone	10 g
Yeast extract	2 g
Dextrose	1 g
Sodium chloride	5 g
Sodium bisulphite	0.1 g
Agar	15 g
Horse serum	50 mL
L-cysteine	0.005 g
Final pH 7.0 ± 0.2	

10. Minimal Media + Purified Mucin

Minimal media + purified mucin was used to culture bacteria from the following genus and species:

- *Akkermansia muciniphila* (e.g., a bacterial isolate having SEQ ID NO: 20, which was isolated from stool of a disease-screened and healthy human donor ("Donor F").

Formulation (per liter):

Monopotassium phosphate	0.4 g
Disodium phosphate	0.53 g
Ammonium chloride	0.3 g
Sodium chloride	0.3 g
Magnesium chloride	0.047 g
Calcium chloride	0.11 g
Sodium bicarbonate	4 g
Sodium sulfite	0.005 g
L-cysteine	0.005 g
ATCC Trace Mineral solution	10 mL
ATCC Vitamin solution	10 mL
Ethanol-purified Type III mucin	2.5 g

11. M10+rumen fluid+mucin

M10+rumen fluid+mucin was used to culture bacteria from the following genus and species:

- *Subdoligranulum variabile* (e.g., a bacterial isolate having SEQ ID NO: 22, which was isolated from stool of a disease-screened and healthy human donor ("Donor F").
- *Alistipes putredinis* (e.g., a bacterial isolate having SEQ ID NO: 35, which was isolated from stool of a disease-screened and healthy human donor ("Donor #").

Formulation (per liter):

Potassium phosphate monobasic	1.3 mM
Sodium chloride	0.76 mM
Potassium phosphate dibasic	1.7 mM
ATCC Trace Mineral Solution	10 mL
Sodium bicarbonate	1 g
Clarified rumen fluid	300 mL
Type II mucin	5 g
ATCC Vitamin solution	10 mL
Acetic acid	170 µL
Propionic acid	60 µL
Butyric acid	40 µL
Isobutyric acid	10 µL
n-valeric acid	10 µL
Isovaleric acid	10 µL
DL-α-methylbutyric acid	10 µL
L-cysteine	0.005 g
Hemin	0.05 mg
Vitamin K	0.0025 mg
Final pH 6.8 ± 0.2	

Example 2: Bacterial isolates that produce a short-chain fatty acid (SCFA)

[00850] A functional assay was developed for screening bacterial isolates for production of butyrate. Bacterial isolates were isolated from stool samples of healthy human donors and grown in liquid culture as described above. Cells were pelleted by centrifugation and resuspended in deep well plates in 150µL of fresh culture media and 150 µL of assay buffer (0.1M sodium phosphate buffer (pH 7) containing 2 grams/200 mL sodium phosphate buffer of each of fructooligosaccharides (FOS), xylooligosaccharides (XOS), sunfiber/partially hydrolyzed guar gum (PHGG) and barley malt). Plates were incubated at 37°C in an anaerobic chamber for 6 hours or 24 hours on a plate shaker at 200 rpm in order to allow fermentation of carbohydrates to butyrate. Following incubation, cells were pelleted and 100 µl of supernatant was transferred to a fresh vial for SCFA extraction.

[00851] 100 µl of supernatant was mixed with 10 µl of 50% sulfuric acid and 500 µl of diethyl ether containing 5mM 2-methylpentanoic acid in a 2 mL glass vial. Samples were centrifuged at 3,220 g for 10 minutes to obtain a clear phase boundary. SCFA levels were measured using

a Gas Chromatograph (GC) with a Flame Ionization Detector (FID) using the following parameters:

- Injection: A 1 µL sample injected at a sample depth of 8 mm with a fast plunger speed and four sample washes.
- Inlet: Split mode at 225°C with a 20:1 split ratio.
- Carrier Gas: Helium
- Oven: Isothermal temperature program at 140°C for 5 min.
- Column: Nitroterephthalic-acid modified/polyethylene glycol (PEG) capillary column that is 0.25 mm in diameter, approximately 30 m long with a 0.25 µm film thickness. Column kept at a constant flow of 6.0 mL/min.
- Flame Ionization Detector (FID): Temperature set at 225°C. Flow rate for hydrogen is 30.0 mL/min. Flow rate for air is 400.0 mL/min. Makeup flow of helium is 20.0 mL/min.

[00852] Levels of butyrate were determined as net concentrations (t24 – t0, and t6 – t0) and as a percent of total SCFAs produced, on a per carbon basis.

[00853] **FIG. 1A** shows butyrate concentration (mM) produced by bacterial isolates after 24 hours incubation in substrate buffer. For these same bacterial isolates, **FIG. 1B** shows the % butyrate produced of total SCFA production per carbon after 24 hours incubation in substrate buffer. Taxonomic information for each isolate, as well as SEQ ID NOs corresponding to each 16S rRNA sequence, can be found in Table 2. Also shown is data for positive control strains DSM 15176 (*Subdoligranulum variabile*), DSM 17677 (*Faecalibacterium prausnitzii* A2-165), and ATCC 27749 (*Gemmiger formicilis* X2-56). The *E. coli* ATCC 8739 strain, which does not secrete butyrate, was used as a negative control. The two *S. variabile* strains listed in Table 2 (IS00007359 and IS00007357) are also predicted to produce butyrate based on their taxonomic similarity to strain DSM 15176.

[00854] The ability of these bacterial isolates to produce butyrate (e.g., in the gut of a subject administered one or more of the bacterial isolates) makes them excellent candidates for inclusion in a pharmaceutical composition (e.g., microbial cocktail) described herein for the treatment of an intestinal dysbiosis (e.g. IBD or ulcerative colitis) in a subject in need thereof.

Example 3: Bacterial isolates that modulate cytokine production

[00855] Functional assays were developed for screening bacterial isolates for modulation of human immune cells, e.g., by influencing specific cytokine production in human peripheral blood mononuclear cells (PBMC).

[00856] A screen was performed to identify bacterial strains that induce production of anti-inflammatory cytokines while not inducing (or possibly inhibiting) production of pro-inflammatory cytokines from host cells. Bacterial isolates were co-cultured with human PBMCs and the levels of six cytokines measured. The six cytokines were: IL-10, a significant anti-inflammatory cytokine; GM-CSF, which evidence suggests has protective effects on gut immunology; and IL-12p70, IFN-gamma, TNF-alpha, and IL-23 and which are believed to have pro-inflammatory effects.

[00857] Bacterial isolates were cultured in liquid culture as described above and cells were washed and re-suspended at 1 x 10^9 CFU/mL (optionally, stored at -80°C until the later co-culture step). Human PBMCs were seeded into 24-well plates and incubated in 5% CO_2 overnight. Bacterial isolates were added to the PBMCs at a multiplicity of infection (MOI) of 0.4x, 2x, or 10x and co-cultured for 24 hours. The co-culture supernatants were then collected and cytokine levels (of IL-10, IL-12, IFN-gamma, GM-CSF, TNF-alpha, and IL-23) were quantified by Luminex.

[00858] Tables 46 and 46a show the results of the assay for isolates assayed using PBMCs from three human donors (results in pg/ml). Also shown is data for positive control strain DSM 17677 (*Faecalibacterium prausnitzii* A2-165) and negative controls (*E. coli* ATCC 8739, PBMCs alone, and cell culture medium alone). Each of the tested isolates induced an anti-inflammatory profile, characterized by high levels of IL-10 production and/or low levels of IL-12, TNF-alpha, IFN-gamma, and/or IL-23, as shown by the ratios of IL-10/IL-12 and IL-10/TNF-alpha in Tables 46 and 46a. The bacterial isolates identified as beneficial in immunomodulation in the PBMC assay are each identified above in Table 3, along with the Sequence Identifier (SEQ ID NO) for their respective 16S rRNA sequences.

[00859] The ability of these bacterial isolates to induce an anti-inflammatory cytokine profile from host cells (e.g., in the gut of a subject administered one or more of the bacterial isolates) makes them excellent candidates for inclusion in a pharmaceutical composition (e.g., microbial cocktail) described herein for the treatment of an intestinal dysbiosis (e.g. IBD or ulcerative colitis) in a subject in need thereof.

Table 46

ID Number	Taxonomy	IL-10	GM-CSF	IL-12p70	IFN-gamma	TNF-alpha	IL-23	IL-10/IL12	IL-10/TNF-alpha
PI00000072	*O. splanchnicus*	3149	29.32	14.50	13.28	364.1	34.15	217.3	8.65
PI00000395	*A. shahii*	2885	49.93	41.39	13.65	693.3	110.6	69.70	4.16
PI00000094	*A. hadrus*	3453	72.88	8.54	12.55	523.8	114.9	404.5	6.59
PI00000146	*B. stercoris*	1751	76.53	57.68	4.37	1147	465.0	30.35	1.53
PI00000137	*B. uniformis*	2811	91.25	21.38	6.62	1225	226.3	131.5	2.29
PI00000352	*B. uniformis*	3032	64.37	92.60	29.75	2680	309.3	32.74	1.13
PI00000138	*B. vulgatus*	2751	62.21	57.46	21.72	1680	135.0	47.88	1.64
PI00000097	*C. aldenense*	2041	49.93	11.90	3.81	968.0	95.46	171.5	2.11
PI00000370	*C. comes*	3639	117.3	69.71	24.28	2713	180.2	52.20	1.34
PI00000329	*F. prausnitzii*	1672	10.73	0.63	1.72	45.23	7.74	2637	36.96
IS00006632	*F. prausnitzii*	2760	45.88	7.85	3.99	565.8	71.72	351.8	4.88
DSM 17677	*F. prausnitzii*	3949	46.47	23.08	6.24	2398	73.16	171.1	1.65
ATCC 8739	*E. coli*	3585	479.0	351.57	361.42	27867	1999	10.20	0.13
	PBMC only	0.85	13.38	1.66	0.50	2.49	3.72	0.51	0.34
	Cell culture medium only	0.05	0.50	0.04	0.16	0.40	0.07	1.23	0.13

Table 46a

ID Number	Taxonomy	IL-10	GM-CSF	IL-12p70	IFN-gamma	TNF-alpha	IL-23	IL-10/IL12	IL-10/TNF-alpha
IS00007180	*A. muciniphila*	2136	44.53	33.12	12.86	511.2	79.19	64.49	4.18
IS00007359	*S. variabile*	2948	66.14	51.30	14.70	971.8	157.5	57.48	3.03
IS00007357	*S. variabile*	1788	26.46	3.25	2.14	136.7	1.29	550.4	13.08
DSM 17677	*F. prausnitzii*	1790	64.04	20.14	13.58	1249	117	88.89	1.43
ATCC 8739	*E. coli*	2561	180.2	1371	487	10386	4113	1.87	0.25
	PBMC only	2.41	3.34	1.66	3.60	0.53	5.04	1.45	4.52
	Cell culture medium only	0.25	3.34	1.66	3.60	0.13	3.76	0.15	1.95

Example 4: Reduction of Inflammatory Markers

[00860] The anti-inflammatory activity of a microbial cocktail comprising bacterial isolates described herein was tested. The PBMC assay described in Example 3 was modified by co-incubating the PBMCs with viable *E. coli* to induce an inflammatory response, thus generating a sensitized platform incorporating the physiologically and disease (e.g., IBD) relevant PBMC cell type for determining the capacity of a bacterial consortium to reduce inflammation.

[00861] Bacterial isolates were cultured in liquid culture as described above and cells were washed and re-suspended at 1 x 10^9 CFU/mL (optionally, stored at -80°C until the later co-culture step). Human PBMCs were seeded into 24-well plates and incubated in 5% CO_2 overnight. For consortia assays each individual bacterial isolate was added to the PBMCs at a multiplicity of infection (MOI) of 0.4 and co-cultured for 24 hours. The MOI of *E. coli* was kept at 0.4 in all experiments. The co-culture supernatants were then collected and cytokine levels (of IL-10, IL-12, IFN-gamma, TNF-alpha, and IL-23) were quantified by Luminex.

[00862] FIG. 4A-E and FIG. 5A-E shows the anti-inflammatory effects of incubation of the PBMC/E.coli mixture with 8-strain and 7-strain microbial cocktails, respectively. The 8-strain microbial cocktail consisted of *Odoribacter splanchnicus* (PI00000072), two isolates of *Faecalibacterium prausnitzii* (IS00006632 and PI00000329) *Akkermansia muciniphila* (IS00007180), *Bacteroides cellulosilyticus* (PI00000316), *Eubacterium rectale*, (IS00006864) *Alistipes shahii* (PI00000395) and *Roseburia faecis* (PI00000404). The 7-strain microbial cocktail included the same strains, except *B. cellulosilyticus* was removed. Incubation with each microbial cocktail reduced the anti-inflammatory effect of treatment with *E. coli*, as shown by reduced levels of IL-23 (FIGS. 4A and 5A), TNF-α (FIGS. 4B and 5B), IL-10 (FIGS. 4C and 5C), IFN-γ (FIGS. 4D and 5D) and IL12-p70 (FIGS. 4E and 5E).

Example 5: Bacterial isolates enriched in healthy subjects

[00863] A mechanism agnostic empirical approach was developed to identify species associated with reducing the dysbiosis associated with Ulcerative Colitis (UC). 16S ribosomal DNA (rDNA) and shotgun metagenomic sequences were incorporated from interventional (FMT), cross-sectional and time series datasets to develop predictive features associated with either a healthy status or clinical response to FMT. These features were used to rank and select bacterial phylogenetic clades for (i) enrichment in healthy subjects over patients diagnosed with UC; and/or (ii) association/correlation with clinical remission or response of UC

symptoms in UC patients following FMT treatment. Clades were ranked based on a "cross-sectional combined p-value" which compares the presence and abundances of bacterial strains in fecal material between healthy subjects and patients with UC. The lower the value, the more likely the organisms in the clade are having an effect on the treatment, inhibition or prevention of UC based on: (i) depletion of the strain in UC patients and/or (ii) high abundance of the strain in healthy subjects. Isolated bacterial strains were then selected from donor stool samples by 16S rDNA similarity to the ranked phylogenetic clades or by ranking their 16S rDNA directly according to the aforementioned criteria.

[00864] Twenty-three bacterial strains were identified as enriched in healthy subjects relative to UC patients. To identify bacterial isolates corresponding to the twenty-three bacterial strains, microbiota extracted from stool samples of donors were screened for bacteria having at least 97% identity to the 16S rRNA sequence of each identified bacterial strain. Table 47 shows these isolates' taxonomic information, sequence identifier (SEQ ID NO) for its 16S rRNA sequence, and cross-sectional combined p-value.

Table 47

Isolate Latin Name	ID Number	SEQ ID NO for 16S rRNA Sequence	Cross sectional combined p-value
Faecalibacterium prausnitzii	PI00000329	1	8.0E-3
Odoribacter splanchnicus	PI00000072	2	1.31E-15
Anaerostipes hadrus	PI00000094	3	1.37E-04
Alistipes onderdonkii	IS00004389	4	1.35E-17
Parabacteroides merdae	IS00006167	5	1.30E-07
Dorea longicatena	IS00006618	6	2.00E-05
Faecalibacterium prausnitzii	IS00006632	7	0.123420709
Eubacterium rectale	IS00006864	8	2.69E-11
Blautia obeum	PI00000053	9	3.91E-05
Bacteroides uniformis	PI00000137	11	5.38E-06
Bacteroides vulgatus	PI00000138	12	0.001351122
Bacteroides cellulosilyticus	PI00000316	14	4.04E-12
Alistipes finegoldii	PI00000340	15	1.13E-18
Bacteroides uniformis	PI00000352	16	3.66E-06
Alistipes shahii	PI00000395	18	6.30E-21
Akkermansia muciniphila	IS00007180	20	7.0E-8
Phascolarctobacterium faecium	PI00000289	21	7.0E-9
Subdoligranulum variabile	IS00007359	22	1.0E-5
Subdoligranulum variabile	IS00007357	23	1.0E-3
Blautia sp.	IS00002788	34	2.0E-10
Alistipes putredinis	IS00008139	35	1.0E-10
Alistipes putredinis	IS00008142	36	1.0E-10

Alistipes putredinis	IS00008177	37	1.0E-10

[00865] An additional ten bacterial isolates having a 16S rRNA sequence at least 95% identical to a bacterial isolate of Table 47 were also characterized. Table 48 lists each isolates' identification number, the ID number of the related bacterial isolate from Table 47, the percent identity of the isolate's 16S rRNA sequence to the related isolate in Table 47, the cross-sectional combined p value of the isolate, and the isolate's sequence identifier (SEQ ID NO). These data demonstrate that the functionality of the bacterial isolates identified in Table 47 in relieving one or more symptoms of UC is exemplary only and is also possessed by a larger group of related isolates (e.g., sharing at least 95% 16S rRNA sequence identity with the bacterial isolates of Table 47).

Table 48

ID Number	Related to ID Number of Table 47	% identity of 16S to ID Number of Table 47	Cross sectional combined p-value	SEQ ID NO. for 16S rRNA Sequence
PI00000070	PI00000072	98.6	1.31E-15	24
PI00000092	PI00000094	98.1	1.17E-05	25
PI00000339	IS00004389	96.6	1.13E-18	26
PI00000327	IS00006167	99.4	1.13E-07	27
PI00000056	PI00000053	96.2	3.91E-05	28
PI00000152	PI00000138	98.7	0.001351122	29
PI00000043	PI00000316	99.2	2.71E-11	30
IS00003009	PI00000340	97.6	2.15E-11	31
PI00000052	PI00000352	96.6	2.85E-11	32
PI00000330	PI00000395	95.3	1.13E-18	33

Example 6: Production of aryl hydrocarbons by bacterial isolates

[00866] A functional assay was developed for screening bacterial isolates for activation of the aryl hydrocarbon receptor (AhR), e.g., in gut epithelial cells of a subject administered the bacterial isolate.

[00867] AhR is a transcription factor that regulates gene expression. The signaling pathways of the transcription factor AhR are inducible by a number of small molecular weight chemicals, including polycyclic aromatic hydrocarbons, bacterial toxic pigments, and physiological compounds such as tryptophan derivatives or dietary indoles. The most notable of these xenobiotic chemicals are aromatic (aryl) hydrocarbons from which the receptor derives its name.

[00868] Bacteria capable of activating the AhR pathway were identified via two methods: metabolomics analysis and functional screening.

[00869] For metabolomics analysis, an assay was developed to assess the ability of bacterial isolates to produce known AhR ligands. Each isolate to be screened was grown in liquid culture as described above, with all media supplemented with 0.6 mM tryptophan. Cells were pelleted by centrifugation and resuspended in fresh culture media containing 0.6 mM tryptophan. Plates were incubated at 37°C in an anaerobic chamber for 48 hours to allow for growth and production of tryptophan metabolites. Following incubation, cells were pelleted by centrifugation and supernatants were sterile filtered through 0.2 μm filters. 200 μL of sterile filtered supernatant was then shipped to Metabolon, Inc. (Morrisville, NC) for untargeted metabolomics analysis. Metabolomics data for each strain was analyzed to identify production of tryptophan metabolites and AhR ligands. Metabolomics data is reported in relative metabolite abundance.

[00870] For functional screening, the same supernatants generated for untargeted metabolomics were evaluated using a cell-based genetic reporter assay using a luciferase reporter gene to assess AhR response (Indigo Biosciences; State College, PA). Reporter cells were incubated with serially diluted bacterial supernatants with a maximum supernatant concentration of 1% by volume. Fluorescence was measured and compared to the results from a positive control chemical (MeBio), blank media negative control, and supernatants from positive control strains of *Peptostreptococcus russellii* and *Peptostreptococcus anaerobius* to evaluate ability to activate the AhR pathway. Functional screen data is reported in relative fluorescence units.

[00871] **FIG. 2A** to **FIG. 2E** show relative production of the aryl hydrocarbons: indole **(FIG. 2A)**, tryptamine **(FIG. 2B)**, kynurenic acid **(FIG. 2C)**, kynurenine **(FIG. 2D)**, and indole-3-acetic acid **(FIG. 2E)**.

[00872] As shown in **FIG. 2A-FIG. 2E**, all three of the bacterial isolates PI00000072 (*Odoribacter splanchnicus*), PI00000097 (*Clostridium aldenense*), and PI00000146 (*Bacteroides stercoris*) produce aryl hydrocarbons at levels above the blank media control and *Peptostreptococcus* controls. Each of the three bacterial isolates identified as producers of aryl hydrocarbons in the AhR assay are identified above in Table 6, along with the Sequence Identifier (SEQ ID NO) for each 16S rRNA sequence.

[00873] Absolute levels of certain aryl hydrocarbons produced by bacterial isolates were also quantified. Table 49 shows levels of indole-3-acetic acid produced by bacterial isolates described herein, while Table 50 shows levels of kynurenic acid produced by bacterial isolates described herein.

Table 49

Isolate Latin Name	ID Number	SEQ ID NO. for 16S rRNA Sequence	Indole-3-Acetic Acid (μM)
Clostridium aldenense	PI00000097	10	5.9
Dorea longicatena	IS00006618	6	3.45
Parabacteroides merdae	IS00006167	5	2.05
Odoribacter splanchnicus	PI00000072	2	1.45
Blank media	-	-	0.23

Table 50

Isolate Latin Name	ID Number	SEQ ID NO. for 16S rRNA Sequence	Kynurenic Acid (nM)
Bacteroides uniformis	PI00000352	16	58
Bacteroides uniformis	PI00000137	11	49
Odoribacter splanchnicus	PI00000072	2	45
Blank media	-	-	0

Example 7: Induction of AhR by bacterial isolates

[00874] A bacterial isolate or a culture supernatant extracted from cells of the bacterial isolate following growth can be contacted with eukaryotic cultured cells which express AhR, e.g., a mammalian cell line, for characterization of the effects of the one or more aryl hydrocarbons on AhR activity. Pure cultures of bacterial isolates were grown for 48 hours in the respective media shown in Table 1, which was supplemented with 0.6 mM tryptophan. Cultures were centrifuged at 3200xg for 15 minutes and supernatants collected. Supernatants were sterile filtered first through a 0.4 μm filter, followed by a 0.2 μm filter. Supernatants were then tested for an ability to activate AhR using the Indigo Biosciences Human Aryl Receptor Reporter Assay System, using the manufacturer's directions and protocol. Briefly, supernatants were diluted to 4% and incubated for 22-24 hours with a human liver cell line (Huh7) transfected with a luciferase reporter gene functionally linked to an AhR-responsive promoter. Following addition of luciferase substrate, intensity of light emission (in units of Relative Light Units, or RLU) was quantified using a plate-reading luminometer.

[00875] Results of the assay are shown in Table 51 for three bacterial isolates described herein. This shows that the compositions described herein are capable of activating AhR in a cell of a subject administered the composition.

Table 51

Isolate Latin Name	ID Number	SEQ ID NO. for 16S rRNA Sequence	Relative Light Units (RLU)
Odoribacter splanchnicus	PI00000072	2	35849
Clostridium aldenense	PI00000097	10	56627
Bacteroides stercoris	PI00000146	13	30900
Blank media	-	-	8706

Example 8: Engraftment of bacterial isolates

[00876] **FIG. 3** shows the relationship between the dosage of various bacterial strains corresponding by 16S rRNA sequence to bacterial isolates and engraftment of the strains in the gut of subject following administration to the subject of a substantially complete fecal microbiota (i.e., a preparation of uncultured fecal bacteria) containing the strains.

[00877] For each bacterial isolate corresponding to a given strain in the fecal microbiota, number of cells dosed to a patient was calculated by the following formula: frequency of bacteria in the administered composition having a 16S sequence matching the 16S sequence of the bacterial isolate x $9x10^{10}$ (approximate number of cells per gram of the administered composition) x cumulative dose of the composition administered to a patient (in grams). Engraftment of bacteria was measured for each unique 16S sequence by comparing relative abundances in the administered composition, the patient's baseline community, and the patient's post-treatment community. Positive engraftment was called for cases where the abundance in the patient's baseline was <20% of the administered material, and the post-treatment abundance increased at least 5-fold.

[00878] Results show that the minimum dose to achieve engraftment for most bacterial isolates screened (with the exception of the *E. rectale* isolate IS00006864) is below 10^{10} cells.

Example 9: Engraftment of bacterial isolates

[00879] To assess the engraftment of bacterial isolates in the intestine of a subject following administration of a microbial cocktail, germ free C57BL/6 mice were inoculated via gavage with the 8-strain consortium described in Example 4 grown under anaerobic conditions. Fecal

pellets were collected at 7, 14, 21 and 28 days and DNA was isolated for 16srRNA gene sequencing. Relative abundance of strains was determined based on 16S rRNA gene abundance.

[00880] **FIG. 6** shows the engraftment of four bacterial isolates (*Bacteroides cellulosilyticus*, *Akkermansia muciniphila*, *Odoribacter sphlanchnicus*, and *Alistipes shahii*) in the intestine of the germ free mice following administration of the microbial cocktail comprising the isolates.

Example 10: Production of a therapeutic agent

[00881] Bacterial isolates of any one of Tables 7-44 are independently cultured and mixed together before administration. Isolates are independently grown anaerobically in supportive media, *e.g.* at 37° C., pH 7, as shown in Example 1. After each isolate reaches a sufficient biomass, it is optionally preserved for banking by adding 15% glycerol and then frozen at -80°C. in 1 ml cryotubes.

[00882] Each bacterial isolate is then cultivated to a concentration of about 10^{10} CFU/mL, then concentrated 20-fold by tangential flow microfiltration; the spent medium is exchanged by diafiltering with a preservative medium consisting of 2% gelatin, 100 mM trehalose, and 10 mM sodium phosphate buffer, or other suitable preservative medium. The suspension is freeze-dried to a powder and titrated.

[00883] After drying, the powder is blended with microcrystalline cellulose and magnesium stearate and formulated into a 250 mg gelatin capsule containing 10 mg of lyophilized powder (10^8 to 10^{11} bacteria), 160 mg microcrystalline cellulose, 77.5 mg gelatin, and 2.5 mg magnesium stearate.

Example 11: Treatment of Ulcerative Colitis

[00884] A patient with a diagnosis of Ulcerative Colitis (UC) by endoscopy and histology consistent with diagnosis is treated with a pharmaceutical composition disclosed herein.

[00885] Efficacy is monitored as described in Travis, *et al.* Aliment Pharmacol Ther. 2011;34(2):113-124 (which is incorporated by reference in its entirety), including one or more of the following indices (for each index, the associated publication is incorporated by reference in its entirety):

Clinical:

- Truelove and Witts (Truelove SC, Witts LJ. Cortisone in ulcerative colitis. Final report on a therapeutic trial. *BMJ* 1955; 2: 1041–8),

- Powel-Tuck Index (St. Mark's Index; Powell-Tuck J, *et al.* Correlations between defined sigmoidoscopic appearances and other measures of disease activity in ulcerative colitis. *Dig DisSci* 1982; 27: 533–7),
- Clinical Activity Index (CAI; Rachmilewitz D. Coated mesalazine (5-aminosalicylic acid) versus sulphasalazine in the treatment of active ulcerative colitis: a randomised trial. *BMJ* 1989; 298: 82–6),
- Lichtiger Index (S. Lichtiger, D.H. Present Preliminary report: cyclosporin in treatment of severe active ulcerative colitis Lancet, 336 (1990), pp. 16–19),
- Seo Index (Seo M, *et al.* An index of disease activity in patients with ulcerative colitis. *Am J Gastroenterol* 1992; 87: 971–6),
- Physician's Global Assessment (Hanauer S *et al.*, Mesalamine capsules for treatment of active ulcerative colitis: results of a controlled trial Am J Gastroenterol. 1993 Aug;88(8):1188-97),
- Investigator's Global Evaluation (Hanauer SB *et al.*, Budesonide enema for the treatment of active, distal ulcerative colitis and proctitis: a dose-ranging study. U.S. Budesonide enema study group Gastroenterology. 1998 Sep;115(3):525-32).
- Simple Clinical Colitis Activity Index (Walmsley RS, *et al.*, A simple clinical colitis activity index. Gut 1998; 43: 29–32),
- Improvement Based on Individual Symptom Scores (Levine *et al.*, A randomized, double blind, dose-response comparison of balsalazide (6.75 g), balsalazide (2.25 g), and mesalamine (2.4 g) in the treatment of active, mild-to-moderate ulcerative colitis Am J Gastroenterol. 2002 Jun;97(6):1398-407), and
- Patient-defined remission (Higgins P, *et al.* Is endoscopy necessary for the measurement of disease activity in ulcerative colitis. *Am J Gastroenterol* 2005; 100: 355–61).

Endoscopic:

- Truelove Witts Sigmoidoscopic Assessment (Seo M, *et al.* Evaluation of disease activity in patients with moderately active ulcerative colitis: comparisons between a new activity index and Truelove and Witts classification. *Am J Gastroenterol* 1995; 90: 1759–63),

- Baron Score (Baron JH, *et al.* Variation between observers in describing mucosal appearances in proctocolitis. *BMJ* 1964; 1: 89–92),
- Endoscopic Index (Rachmilewitz D. Coated mesalazine (5-aminosalicylic acid) versus sulphasalazine in the treatment of active ulcerative colitis: a randomised trial. BMJ 1989; 298: 82–6),
- Sigmoidoscopic Index (Hanauer S *et al.*, Mesalamine capsules for treatment of active ulcerative colitis: results of a controlled trial Am J Gastroenterol. 1993 Aug;88(8):1188-97),
- Sigmoidoscopic Inflammation Grade Score (Lémann M *et al.*, Comparison of budesonide and 5-aminosalicylic acid enemas in active distal ulcerative colitis Aliment Pharmacol Ther. 1995 Oct;9(5):557-62.),
- Mayo Score Flexible Proctosigmoidoscopy Assessment (Schroeder KW, *et al.* Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study. *NEngl J Med* 1987; 317: 1625–9), and
- Modified Baron Score (Rutgeerts P, *et al.* Infliximab for induction and maintenance therapy for ulcerative colitis. *NEngl J Med* 2005; 353: 2462–76).

Clinical and Endoscopic:

- Mayo Clinic Score (Schroeder KW, *et al.* Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study. *NEngl J Med* 1987; 317: 1625–9) and
- Sutherland Index (Sutherland LR, *et al.* 5-Aminosalicylic acid enema in the treatment of distal ulcerative colitis, proctosigmoiditis, and proctitis. *Gastroenterology* 1987; 92: 1894–8).

Quality of Life:

- Rating form of IBD Patient Concerns (Drossman DA *et al.* Health status and health care use in persons with inflammatory bowel disease. A national sample. Dig Dis Sci. 1991 Dec;36(12):1746-55),
- Inflammatory Bowel Disease Questionnaire (Irvine EJ, *et al.* Quality of life: a valid and reliable measure of outcome for clinical trials in inflammatory bowel disease. Gastroenterology. 1194; 106:287-96), and

- Short Form-36 (Ware JE *et al.* The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection Med Care. 1992 Jun;30(6):473-83).

Histological:

- Riley Index (Riley SA, *et al.* Microscopic activity in ulcerative colitis: what does it mean? *Gut*1991; 32: 174–8),
- Gebboes Index (Geboes K *et al.* A reproducible grading scale for histological assessment of inflammation in ulcerative colitis Gut. 2000 Sep;47(3):404-9), and
- Chicago Index (Rubin DT, *et al.* Increased degree of histological inflammation predicts colectomy and hospitalization in patients with ulcerative colitis. *Gastroenterology* 2007; 132(Suppl. 1): A-19 (Abstract 103)).

Example 12: In vivo testing of a therapeutic agent in mice

[00886] A composition or various compositions comprising the nine isolates of any one of Tables 36-43 are provided. Alternatively, a therapeutic agent, *e.g.*, without limitation, made via the methods of Example 10, comprising the nine isolates of any one of Tables 36-43 is provided.

[00887] A suitable murine model for UC is selected and provided. Illustrative models include chemical models (such as DSS, TNBS, oxazolone, acetic acid, and sulfhydryl inhibitors) and transgenic/knock out models (such as TCR$\alpha^{-/-}$, WASP$^{-/-}$, Mdr1a$^{-/-}$, IL-2$^{-/-}$, Gαi2$^{-/-}$, IL-7 Tg, TRUC, TGFβRIIDN, and C3H/HeJBir). *See World J Gastroenterol.* 2007 Nov 14; 13(42): 5581–5593 and *Drug Des Devel Ther*. 2013; 7: 1341–1357 (2013), the entire contents of which are incorporated by reference.

[00888] Taking DDS as a non-limiting example, oral administration of 3-5% DSS in drinking water to mice is undertaken. For instance, one cycle of 3%-5% DSS administration for 5-7 d, followed by regular water, results in extensive injury with complete crypt depletion (e.g. basal crypt) and relatively slow regeneration of colonic epithelium. Animals which develop UC-like symptoms are treated with the composition or various compositions comprising the nine isolates of any one of Tables 36-43 or a therapeutic agent (alternatively, the bacterial compositions can be administered concurrently with the DSS) and comparison is made to determine therapeutic effect (*e.g.* comparing one or more parameters, such as measuring clinical scores of colitis, including weight change, diarrhea, colorectal bleeding and survival; overall disease severity may be assessed by a clinical scoring system, and a disease activity index (DAI) score may be calculated for each animal). Alternative measures include endoscopy,

histological analyses, microbiota analysis by 16S rRNA sequencing, and the like. A more detailed protocol is found in *Curr Protoc Immunol.* 2014 Feb 4; 104: Unit–15.25, the entire contents of which are incorporated by reference. The present Example allows for variations in the detailed protocol is found in *Curr Protoc Immunol.* 2014 Feb 4; 104: Unit–15.25 as necessary or desired to determine the presence or absence of a therapeutic effect.

Example 13: Treatment of UC

[00889] A composition or various compositions comprising the nine isolates of any one of Tables 36-43 are provided. Alternatively, a therapeutic agent, *e.g.,* without limitation, made via the methods of Example 10, comprising the nine isolates of any one of Tables 36-43 is provided. A study of a UC as described in Example 11 is undertaken with such compositions as the therapeutic agent.

EQUIVALENTS

[00890] While the invention has been described in connection with specific embodiments thereof, it will be understood that it is capable of further modifications and this application is intended to cover any variations, uses, or adaptations of the invention following, in general, the principles of the invention and including such departures from the present disclosure as come within known or customary practice within the art to which the invention pertains and as may be applied to the essential features hereinbefore set forth and as follows in the scope of the appended claims.

[00891] Those skilled in the art will recognize, or be able to ascertain, using no more than routine experimentation, numerous equivalents to the specific embodiments described specifically herein. Such equivalents are intended to be encompassed in the scope of the following claims.

INCORPORATION BY REFERENCE

[00892] All patents and publications referenced herein are hereby incorporated by reference in their entireties.

[00893] The publications discussed herein are provided solely for their disclosure prior to the filing date of the present application. Nothing herein is to be construed as an admission that the present disclosure is not entitled to antedate such publication by virtue of prior invention.

[00894] As used herein, all headings are simply for organization and are not intended to limit the disclosure in any manner. The content of any individual section may be equally applicable to all sections.

Claims

1. Use of a pharmaceutical composition comprising a plurality of bacterial isolates in manufacture of a medicament for treating or preventing inflammatory bowel disease (IBD) in a subject in need thereof, wherein the plurality of bacterial isolates comprises *Bacteroides stercoris and Bacteroides cellulosilyticus*, and at least one of *Bacteroides uniformis*, *Subdoligranulum variabile*, *Anaerostipes hadrus*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Faecalibacterium prausnitzii*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*, wherein the *Bacteroides stercoris* comprises a 16S ribosomal ribonucleic acid (rRNA) sequence that has at least 95%, or at least 97%, or at least 98%, or at least 99% sequence identity with the nucleotide sequence of SEQ ID NO: 13.

2. The use of claim 1, wherein at least two of the plurality of bacterial isolates are isolated from a stool of different human donors.

3. The use of claim 1 or 2, wherein the plurality of bacterial isolates comprises at least two of *Bacteroides uniformis*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Anaerostipes hadrus*, *Faecalibacterium prausnitzii*, *Subdoligranulum variabile*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

4. The use of claim 1 or 2, wherein the plurality of bacterial isolates comprises at least three of *Bacteroides uniformis*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Anaerostipes hadrus*, *Faecalibacterium prausnitzii*, *Subdoligranulum variabile*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

5. The use of claim 1 or 2, wherein the plurality of bacterial isolates comprises at least four of *Bacteroides uniformis*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Anaerostipes hadrus*, *Faecalibacterium prausnitzii*, *Subdoligranulum variabile*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

6. The use of claim 1 or 2, wherein the plurality of bacterial isolates comprises at least five of *Bacteroides uniformis*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Anaerostipes hadrus*, *Faecalibacterium prausnitzii*, *Subdoligranulum variabile*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

7. The use of claim 1 or 2, wherein the plurality of bacterial isolates comprises at least six of *Bacteroides uniformis*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Anaerostipes hadrus*, *Faecalibacterium prausnitzii*, *Subdoligranulum variabile*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

8. The use of claim 1 or 2, wherein the plurality of bacterial isolates comprises at least seven of *Bacteroides uniformis*, *Odoribacter splanchnicus*, *Roseburia faecis*, *Anaerostipes hadrus*, *Faecalibacterium prausnitzii*, *Subdoligranulum variabile*, *Akkermansia muciniphila*, *Alistipes shahii*, and *Eubacterium rectale*.

9. The use of any one of claims 1-8, wherein the plurality of bacterial isolates comprises one or more 16S rRNA sequences that have at least 95%, or at least 97%, or at least 98%, or at least 99% sequence identity with one or more nucleotide sequences selected from SEQ ID NOs: 1, 2, 3, 7, 8, 11, 14, 18, 19, 20, 22 and 23.

10. The use of any one of claims 1-9, wherein the plurality of bacterial isolates comprises at least two bacterial isolates comprising *Faecalibacterium prausnitzii*, wherein the at least two bacterial isolates comprise different 16S rRNA sequences.

11. The use of claim 10, wherein the at least two bacterial isolates comprising *Faecalibacterium prausnitzii* comprise 16S rRNA sequences that have at least 95%, or at least 97%, or at least 98%, or at least 99% sequence identity with nucleotide sequences of SEQ ID NOs: 1 and/or 7.

12. The use of claim 10 or 11, wherein the at least two bacterial isolates comprising *Faecalibacterim prausnitzii* are isolated from a stool of different human donors.

13. The use of any one of claims 1-12, wherein the plurality of bacterial isolates comprises lyophilized bacteria.

14. The use of any one of claims 1-13, wherein the plurality of bacterial isolates does not include *Escherichia coli*.