GLYCAN THERAPEUTICS AND RELATED METHODS THEREOF

BACKGROUND

The microbiota of humans is complex, and varies by individual depending on genetics, age, sex, stress, nutrition and diet. The microbiota perform many activities and may influence the physiology of the host. Changing the numbers and species of gut microbiota can alter community function and interaction with the host. A limited number of probiotic bacteria is known in the art, and some association with health benefits documented when taken by humans. Some foods are considered 'prebiotic' foods that contain substances that may promote the growth of certain bacteria that are thought to be beneficial to the human host. The results of clinical tests with these substances are conflicted with respect to their efficacy, and their influence on human health is generally described as being modest. Thus, there is a need for novel therapeutic inputs that can stimulate beneficial microbiota shifts and improve human health.

SUMMARY OF THE INVENTION

The present disclosure features methods of modulating the abundance of a bacterial taxa in a human subject's gastrointestinal microbiota, the method comprising administering to the human subject a pharmaceutical composition comprising a glycan therapeutic preparation in an amount effective to modulate the abundance of the bacterial taxa, wherein i) the glycan therapeutic preparation comprises a mixture of branched glycans, wherein the average degree of branching (DB, branching points per residue) of the glycans in the preparation is at least 0.01 (e.g., at least 0.05, or at least 0.1), ii) at least 50% of the glycans in the preparation have a degree of polymerization (DP) of at least 3 and less than 30 glycan units, and iii) the ratio of alpha- to beta-glycosidic bonds present in the glycans of the preparation is between about 1:1 to about 5:1 overall. In some embodiments, the bacterial taxa comprises at least a first and a second bacterial taxa.

In some embodiments, the preparation comprises branched oligosaccharides. In some embodiments, the average degree of branching in the preparation (DB) is at least 0.05 (e.g., at least 0.1).

In some embodiments, the present disclosure features a method of reducing a drug- or treatment-induced symptom in a human subject, comprising administering to the human subject a glycan therapeutic preparation in an amount effective to reduce a symptom induced by a drug or treatment, wherein i) the glycan therapeutic preparation comprises a mixture of branched glycans, wherein the average degree of branching (DB) of the glycans in the preparation is at least 0.01 (e.g., at least 0.05, or at least 0.1), ii) at least 50% of the glycans in the preparation have a degree of polymerization (DP) of at least 3 and less than 30 glycan units, and iii) the ratio of alpha- to beta-glycosidic bonds present in the glycans of the preparation is between about 1:1 to about 5:1 overall.

In some embodiments, the drug- or treatment-induced symptom is selected from the group of bloating, diarrhea, vomiting, nausea, and constipation. In some embodiments, the drug- or treatment-induced is diarrhea. In some embodiments, the drug- or treatment-induced symptom is constipation.

In some embodiments, the composition reduces drug-induced symptoms and the composition is administered prior to, concomitant with, or after administration of the drug. In some embodiments, the drug is an anti-diabetic drug, an immune-suppressive drug, an antimicrobial drug, a chemotherapeutic drug, an anti-psychotic drug, a proton pump inhibitor drug, or a non-steroid anti-inflammatory drug (NSAID). In some embodiments, the drug is selected from the group of ciprofloxacin, clindamycin, amoxicillin-clavulanate, cefixime, ephalosporins, fluoroquinolones, azithromycin, clarithromycin, erythromycin, tetracycline, azithromycin, irinotecan (camptosar), 5-fluorouracil, leucovorin, oxaliplatin, bortezomib, imatinib, lenalidomide, imbruvica, ipilimumab, pertuzumab, capecitabine, docetaxel, lapatinib, erlotinib, carmustine, etoposide, aracytine, melphalan, cytarabine, daunorubicine, amsacrine, mitoxantrone, olanzapine, ranitidine, famotidine, cimetidine, omeprazole, sucralfate, esomeprazole, naproxen, diclofenac, indomethacin, ibuprofen, ketoprofen, piroxicam, celecoxib, nimesulid, aspirin, metformin, paroxetine, valproic acid, and clozapine.

In some embodiments, the composition reduces treatment-induced symptoms and the treatment comprises radiation treatment or surgery.

In some embodiments, the drug- or treatment-induced symptom is exhibited by the subject during a treatment regimen. In some embodiments, the reducing the one or more

symptom increases compliance by the subject to the treatment regimen. In some embodiments, the reducing the one or more symptom increases the subject's tolerance to a higher dose of the drug to be administered during the treatment regimen.

In some embodiments, the present disclosure features a method for modulating microbial diversity in a human subject's gastrointestinal tract, the composition comprising a glycan therapeutic preparation in an amount effective to modulate the microbial diversity, wherein i) the glycan therapeutic preparation comprises a mixture of branched glycans, wherein the average degree of branching (DB, branching points per residue) of the glycans in the preparation is at least 0.01 (e.g., at least 0.05, or at least 0.1), ii) at least 50% of the glycans in the preparation have a degree of polymerization (DP) of at least 3 and less than 30 glycan units; and iii) the ratio of alpha- to beta-glycosidic bonds present in the glycans of the preparation is between about 1:1 to about 5:1 overall. In some embodiments, the microbial diversity comprises bacterial diversity. In some embodiments, the modulating comprises an increase or a decrease in microbial diversity.

In some embodiments, the microbial diversity is determined (e.g., measured) by or expressed through use of the Shannon Diversity Index. In some embodiments, the Shannon Diversity is increased or decreased by at least about 5%. In some embodiments, the Shannon Diversity is increased or decreased by at least about 15%. In some embodiments, the Shannon Diversity is increased or decreased by at least about 0.3 log-fold. In some embodiments, Shannon Diversity is increased or decreased by at least about 0.6 log-fold. In some embodiments, Shannon Diversity is increased or decreased by at least about 1 log-fold.

In some embodiments, the abundance of at least one bacterial taxa selected from the group of genus Prevotella, Akkermansia, Bacteroides, Clostridium (Erysipelotrichaceae), Clostridium (Clostridiaceae), Bifidobacterium, Aggregatibacter, Clostridium (Peptostreptococcaveae), Parabacteroides, Lactobacillus, and Enterococcus is modulated. In some embodiments, the abundance of at least one bacterial taxa selected from the group of genus Prevotella, Akkermansia, Bacteroides, Clostridium (Erysipelotrichaceae), Clostridium (Clostridiaceae), Bifidobacterium, Aggregatibacter, Clostridium (Peptostreptococcaveae), Parabacteroides, Lactobacillus, and Enterococcus is increased by at least about 5%.

In some embodiments, the abundance of at least two bacterial taxa selected from the group of genus Prevotella, Akkermansia, Bacteroides, Clostridium (Erysipelotrichaceae), Clostridium (Clostridiaceae), Bifidobacterium, Aggregatibacter, Clostridium (Peptostreptococcaveae), Parabacteroides, Lactobacillus, and Enterococcus is modulated. In some embodiments, the abundance of at least two bacterial taxa selected from the group of genus Prevotella, Akkermansia, Bacteroides, Clostridium (Erysipelotrichaceae), Clostridium (Clostridiaceae), Bifidobacterium, Aggregatibacter, Clostridium (Peptostreptococcaveae), Parabacteroides, Lactobacillus, and Enterococcus is increased by at least about 5%.

In some embodiments, the abundance of at least one bacterial taxa selected from the group of genus Akkermansia, Bacteroides, Bifidobacterium, Lactobacillus, and Parabacteroides is modulated. In some embodiments, the abundance of at least two bacterial taxa selected from the group of genus Akkermansia, Bacteroides, Bifidobacterium, Lactobacillus, and Parabacteroides is modulated. In some embodiments, the abundance of at least one bacterial taxa selected from the group of genus Akkermansia and Blautia is modulated. In some embodiments, the abundance of both of the bacterial genera Akkermansia and Blautia is modulated. In some embodiments, the modulating the microbial diversity treats a dysbiosis.

In some embodiments, the present disclosure features a method of treating a human subject in need thereof, the method comprising: a) identifying a human subject in need of treatment for dysbiosis, and b) administering to the human subject a pharmaceutical composition comprising a glycan therapeutic preparation in an amount effective to treat the dysbiosis, wherein i) the glycan therapeutic preparation comprises a mixture of branched glycans, wherein the average degree of branching (DB) of the glycans in the preparation is at least 0.01 (e.g., at least 0.05, or at least 0.1), ii) at least 50% of the glycans in the preparation have a degree of polymerization (DP) of at least 3 and less than 30 glycan units, and iii) the ratio of alpha- to beta-glycosidic bonds present in the glycans of the preparation is between about 1:1 to about 5:1 overall.

In some embodiments, the human subject has an infectious disease, disorder or condition. In some embodiments, the infectious disease, disorder or condition is selected from the group of *Clostridium difficile* infection (CDI); Vancomycin-resistant enterococci (VRE) infection, infectious colitis, or *C. difficile* colitis. In some embodiments, the infectious disease, disorder or

In some embodiments, the composition is administered daily. In some embodiments, the composition is administered each day for a predetermined number of days (the treatment period). In some embodiments, the treatment period comprises between about 1 day and about 30 days. In some embodiments, the treatment period comprises between about 1 month and about 6 months. In some embodiments, the subject is administered the composition for a single treatment period. In some embodiments, the subject is administered the composition for more than one treatment period.

In some embodiments, by treating the dysbiosis the disease of the human subject is treated.

In some embodiments, the present disclosure features a method of modulating a functional pathway of the microbiota of a human subject's gastrointestinal tract, the composition comprising a glycan therapeutic preparation in an amount effective to modulate the functional pathway, wherein i) the glycan therapeutic preparation comprises a mixture of branched glycans, wherein the average degree of branching (DB) of the glycans in the preparation is at least 0.01 (e.g., at least 0.05, or at least 0.1); ii) at least 50% of the glycans in the preparation have a degree of polymerization (DP) of at least 3 and less than 30 glycan units; and
iii) the ratio of alpha- to beta-glycosidic bonds present in the glycans of the preparation is between about 1:1 to about 5:1 overall.

In some embodiments, the functional pathway modulates the production of an anti-microbial agent, a secondary bile acid, a short-chain fatty acid, a siderophore, or a metabolite listed in Table 2 by the microbiota. In some embodiments, the antimicrobial agent comprises a bacteriocin or hydrogen peroxide. In some embodiments, the short-chain fatty acid comprises formate, butyrate, acetate, propionate, or valerate. In some embodiments, the metabolite comprises 2-hydroxyisobutyrate, 3-hydroxyisovalerate, 3-methylcrotonylglycine, 3-methylcrotonylglycine, allantoin, betaine, formate, mannitol, p-cresol glucuronide, phenylacetylglycine, sarcosine, taurine, acetic acid, acetylaldehyde, ascorbic acid, butanedione, butyric acid, deoxycholic acid, ethylphenyl sulfate, formic acid, indole, isobutyric acid, isovaleric acid, propionic acid, serotonin, succinic acid, succinate, TMAO, tryptophan, valeric acid, ursodeoxycholic acid, lactate, lactic acid, or hydrogen peroxide.

In some embodiments, the functional pathway modulates the level of an inflammatory or immunomodulatory cytokine in the human subject. In some embodiments, the inflammatory and immunomodulatory cytokine comprises interleukin-1α (IL-1α), IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12, IL-13, IL-17A, IL-17F, IL-22, IL-23, tumor necrosis factor (TNF), chemokine (C-C motif) ligand 5 (CCL5, also known as RANTES), transforming growth factor beta (TGF-β), or interferon gamma (IFN-γ).

In some embodiments, the functional pathway increases the level of a short-chain fatty acid in the subject. In some embodiments, the increase in the short-chain fatty acid induces the generation of regulatory T (Treg) cells by the subject. In some embodiments, the increase in the short-chain fatty acid reduces the permeability of the intestinal or plasma endotoxin level in the subject. In some embodiments, the increase of a short-chain fatty acid reduces the inflammatory response of the subject. In some embodiments, the short-chain fatty acid is produced by at least one bacterial species of the *Ruminococcaceae* and/or *Lachnospiraceae* family.

In some embodiments, the subject is obese.

In some embodiments, the present disclosure features a method of preventing a relapse of a *Clostridium difficile* infection in a human subject previously administered a drug for the treatment of a *C. difficile* infection, the method comprising administering a glycan therapeutic preparation in an amount effective to prevent the relapse, wherein i) the glycan therapeutic preparation comprises a mixture of branched glycans, wherein the average degree of branching (DB) of the glycans in the preparation is at least 0.01 (e.g., at least 0.05, or at least 0.1); ii) at least 50% of the glycans in the preparation have a degree of polymerization (DP) of at least 3 and less than 30 glycan units; and iii) the ratio of alpha- to beta-glycosidic bonds present in the glycans is between about 1:1 to about 5:1 overall.

In some embodiments, the relapse comprises the recurrence of one or more symptoms associated with a *C. difficile* infection. In some embodiments, the relapse occurs during or after a first-line or standard of care drug treatment regimen.

In some embodiments, the drug for the treatment of a *C. difficile* infection is an antibiotic. In some embodiments, the antibiotic is selected from the group of vancomycin, metronidazole,

and fidaxomicin. In some embodiments, the composition is administered concurrently or after administration of the drug for the treatment of a *C. difficile* infection.

In some embodiments, the composition is administered in combination with a second drug or treatment. In some embodiments, the second drug or treatment comprises an antibiotic. In some embodiments, the antibiotic is selected from the group of vancomycin, metronidazole, and fidaxomicin.

In some embodiments, administration of the composition results in a reduction of the severity of a symptom associated with a *C. difficile* infection in the subject but does not eliminate the population of *C. difficile* in the subject. In some embodiments, administration of the composition results in a reduction of the severity of a symptom associated with a *C. difficile* infection in the subject but does not change the level of the population of *C. difficile* in the subject.

In one aspect, the present disclosure features a method of making a pharmaceutical composition, the method comprising: (a) providing a preparation comprising a mixture of synthetic glycans, (b) acquiring a value for the following characteristics of the preparation: (i) the degree of polymerization (DP), (ii) the average degree of branching (DB), (iii) the ratio of alpha- glycosidic to beta-glycosidic bonds, and (c) formulating the preparation as a pharmaceutical composition if the following criteria are met: (i) at least 50% of the glycans in the preparation have a DP of at least 3 and less than 30 glycan units, (ii) the average degree of branching (DB) of the glycans in the preparation is at least 0.01, (iii) the ratio of alpha- to beta-glycosidic bonds present in the glycans of the preparation is between about 1:1 to about 5:1.

In some embodiments, the present disclosure features a method of making a pharmaceutical composition, the method comprising a) providing a preparation comprising a mixture of synthetic glycans, b) acquiring a value for one or more of the following characteristics of the preparation, c) the degree of polymerization (DP), d) the average degree of branching (DB), e) the ratio of alpha- glycosidic to beta-glycosidic bonds, and f) formulating the preparation as a pharmaceutical composition if one or more of the following criteria are met: i) at least 50% of the glycans in the preparation have a DP of at least 3 and less than 30 glycan units, ii) the average degree of branching (DB) of the glycans in the preparation is at least 0.01 (e.g., at

least 0.05, or at least 0.1), iii) the ratio of alpha- to beta-glycosidic bonds present in the glycans of the preparation is between about 1:1 to about 5:1 overall.

In some embodiments, the method further comprises a) acquiring a value for any one or both additional characteristics of the preparation: i) the identity of the glycan units, ii) the ratio of glycan units, and b) formulating the preparation as a pharmaceutical composition if: iii) the glycan unit ratio in the preparation is about the same as the ratio of the glycan unit input.

In some embodiments, the method further comprises: b) acquiring a value for any one or both additional characteristics of the preparation: iv) the level of bacterial growth, in media

supplemented with the preparation, of commensal strains selected from the group consisting of *Bacteroides caccae* ATCC 43185, *Prevotella copri* DSM 18205, *Bacteroides thetaiotamicron* ATCC 29741, *Bacteroides cellulosilyticus* DSM 14838, *Clostridium scindens* ATCC 35704, *Ruminococcus obeum* ATCC 29714, *Clostridium nexile* ATCC 27757, and *Parabacteroides distasonis* ATCC 8503, v) the level of bacterial growth, in media supplemented with the preparation, of pathogenic strains selected from the group consisting of *Clostridium difficile* ATCC BAA-1382, *Clostridium difficile* ATCC 43255, *Enterococcus faecium* ATCC 700221, and *Salmonella enterica* ATCC 27869, and c) formulating the preparation as a pharmaceutical composition if one or both of the following criteria are met: vi) promotion by the media supplemented with the preparation of growth of at least 5 commensal strains, vii) promotion by the media supplemented with the preparation of growth of no more than 2 pathogenic strain. In some embodiments, step (b) may be performed prior to, concurrently with, another step in the process.

In some embodiments, the step of formulating the preparation as a pharmaceutical composition comprises one or more of: i) removing unwanted constituents from the preparation, ii) reducing the volume of the preparation, iii) sterilizing the preparation, iv) admixing the preparation with a pharmaceutically acceptable excipient or carrier, v) admixing the preparation with a second drug or pharmaceutical agent, vi) formulating the preparation into a aqueous solution or syrup, vii) formulating the preparation into a tablet or pill, and viii) formulating the preparation into a capsule.

In some embodiments, the step of formulating the preparation as a pharmaceutical composition comprises one or more of ix) packaging the preparation, x) labeling the packaged preparation, and xi) selling or offering for sale the packaged and labeled preparation.

In some embodiments, the present disclosure features a method of making a pharmaceutical composition, the method comprising: (i) providing a therapeutic glycan preparation comprising at least one glycan unit selected from the group consisting of glucose, galactose, fucose, xylose, arabinose, rhamnose, and mannose, (ii) determining if a preselected NMR peak or group of NMR peaks is associated with the glycan preparation, and (iii) if the preselected peak or group of peaks is present, formulating the preparation as a pharmaceutical composition.

comprising galactose, the peaks comprise at least two, at least three, at least four, or more 1H-13C HSQC peaks selected from 5.37, 92.9; 5.24, 93.1; 5.14, 96.0; 4.96, 99.3; 5.31, 98.7; 5.39, 101.4; 5.00, 101.8; 4.80, 101.3; 4.63, 97.0; 4.56, 97.2; 4.53, 103.1; 4.43, 104.1 1H shift (ppm) and 13C shift (ppm) or a corresponding peak; iii) for glycans comprising fucose, the peaks comprise at least two, at least three, at least four, or more 1H-13C HSQC peaks selected from 5.18, 92.9; 5.33, 92.4; 5.04, 96.3; 4.90, 99.7; 4.52, 97.0; 4.39, 103.6 1H shift (ppm) and 13C shift (ppm) or a corresponding peak; iv) for glycans comprising xylose, the peaks comprise at least two, at least three, at least four, or more 1H-13C HSQC peaks selected from 5.18, 93.0; 5.10, 94.3; 5.34, 98.2; 5.31, 99.6; 5.11, 100.8; 4.91, 99.4; 4.56, 97.3; 4.64, 104.2; 4.54, 103.4; 4.44, 102.6; 4.44, 104.1 1H shift (ppm) and 13C shift (ppm) or a corresponding peak; v) for glycans comprising arabinose, the peaks comprise at least two, at least three, at least four, or more 1H-13C HSQC peaks selected from 5.22, 93.2; 5.13, 93.2;5.29, 96.0; 5.26, 97.2; 5.12, 96.6; 5.18, 99.6; 5.06, 99.2; 4.99, 100.0; 5.26, 101.9; 5.06, 102.1; 4.55, 97.4; 4.54, 105.2; 4.50, 105.5; 4.38, 103.9 1H shift (ppm) and 13C shift (ppm) or a corresponding peak; vi) for glycans comprising rhamnose, the peaks comprise at least two, at least three, at least four, or more 1H-13C HSQC peaks selected from 5.21, 93.2; 5.10, 94.5; 4.85, 94.1; 5.01, 95.8; 5.35, 100.5; 5.15, 102.2; 5.04, 102.9; 4.78, 97.9; 4.71, 99.0; 4.72, 101.0 1H shift (ppm) and 13C shift (ppm) or a corresponding peak; vii) for glycans comprising mannose, the peaks comprise at least two, at least three, at least four, or more 1H-13C HSQC peaks selected from 5.37, 93.0; 5.16, 94.6; 4.88, 94.2; 5.39, 101.7; 5.24, 101.9; 5.13, 102.8; 5.03, 102.7; 5.24, 105.6; 5.09, 108.0; 4.88, 94.2; 4.89, 100.0; 4.70, 101.1 1H shift (ppm) and 13C shift (ppm) or a corresponding peak.

In another aspect, the present disclosure features a pharmaceutical composition comprising a therapeutic glycan preparation comprising a mixture of branched glycans, wherein the average degree of branching (DB) of the glycans in the preparation is at least 0.01, wherein i) at least 50% of the glycans in the preparation have a degree of polymerization (DP) of at least 3 and less than 30 glycan units, ii) the glycan preparation comprises both alpha- and beta-glycosidic bonds, iii) at least one of the glycosidic bonds present in the glycans of the preparation comprise a 1->2 glycosidic bond, a 1->3 glycosidic bond, a 1->4 glycosidic bond, or a 1->6 glycosidic bond, and iv) the ratio of alpha-

Ruminococcus, Bilophila, Akkermansia, Cryocola, Mycobacterium, Enterococcus, Lactococcus, Streptococcus, Turicibacter, Blautia, Coprococcus, Holdemania, Pseudoramibacter, Eubacterium, Agrobacterium, Sphingomonas, Achromobacter, Burkholderia, and Ralstonia.

In some embodiments, the present disclosure features a pharmaceutical kit comprising a) a glycan therapeutic preparation in an amount effective to modulate the abundance of the bacterial taxa, wherein i) the glycan therapeutic preparation comprises a mixture of branched glycans, wherein the average degree of branching (DB) of the glycans in the preparation is at least 0.01; ii) at least 50% of the glycans in the preparation have a degree of polymerization (DP) of at least 3 and less than 30 glycan units; and iii) the ratio of alpha- to beta-glycosidic bonds present in the glycans of the preparation is between about 1:1 to about 5:1, b) at least a second constituent selected from the group of a preparation of polyphenols, a preparation of probiotic bacteria, a drug or therapeutic agent, and a dietary component, c) instructional material, and d) packaging.

In another aspect, the present disclosure features a pharmaceutical kit comprising: i) the pharmaceutical composition as disclosed herein, ii) at least a second constituent selected from the group of a preparation of polyphenols, a preparation of probiotic bacteria, a drug or therapeutic agent, and a dietary component, iii) instructional material, and iv) packaging.

In some embodiments, the present disclosure features a pharmaceutical composition comprising a therapeutic glycan preparation comprising at least one glycan unit selected from the group of: glucose, galactose, fucose, xylose, arabinose, rhamnose, and mannose, wherein the preparation comprises a glycan unit associated with one or more of the following 1H-13C HSQC peaks: i) for glycans comprising glucose, the peaks comprise at least one of an 1H-13C HSQC peak selected from 5.42, 92.5; 5.21, 92.8; 5.18, 93.9; 5.08, 97.0; 5.36, 98.4; 5.34, 99.8; 5.38, 100.3; 4.95, 98.6; 4.62, 96.6; 4.70, 103.6; 4.49, 103.4 1H shift (ppm) and 13C shift (ppm) or a corresponding peak; ii) for glycans comprising galactose, the peaks comprise at least one of an 1H-13C HSQC peak selected from 5.37, 92.9; 5.24, 93.1; 5.14, 96.0; 4.96, 99.3; 5.31, 98.7; 5.39, 101.4; 5.00, 101.8; 4.80, 101.3; 4.63, 97.0; 4.56, 97.2; 4.53, 103.1; 4.43, 104.1 1H shift (ppm) and 13C shift (ppm) or a corresponding peak; iii) for glycans

comprising fucose, the peaks comprise at least one of an 1H-13C HSQC peak selected from 5.18, 92.9; 5.33, 92.4; 5.04, 96.3; 4.90, 99.7; 4.52, 97.0; 4.39, 103.6 1H shift (ppm) and 13C shift (ppm) or a corresponding peak; iv) for glycans comprising xylose, the peaks comprise at least one of an 1H-13C HSQC peak selected from 5.18, 93.0; 5.10, 94.3; 5.34, 98.2; 5.31, 99.6; 5.11, 100.8; 4.91, 99.4; 4.56, 97.3; 4.64, 104.2; 4.54, 103.4; 4.44, 102.6; 4.44, 104.1 1H shift (ppm) and 13C shift (ppm) or a corresponding peak; v) for glycans comprising arabinose, the peaks comprise at least one of an

97.4; 4.54, 105.2; 4.50, 105.5; 4.38, 103.9 1H shift (ppm) and 13C shift (ppm) or a corresponding peak; vi) for glycans comprising rhamnose, the peaks comprise at least two, at least three, at least four, or more 1H-13C HSQC peaks selected from 5.21, 93.2; 5.10, 94.5; 4.85, 94.1; 5.01, 95.8; 5.35, 100.5; 5.15, 102.2; 5.04, 102.9; 4.78, 97.9; 4.71, 99.0; 4.72, 101.0 1H shift (ppm) and 13C shift (ppm) or a corresponding peak; vii) for glycans comprising mannose, the peaks comprise at least two, at least three, at least four, or more 1H-13C HSQC peaks selected from 5.37, 93.0; 5.16, 94.6; 4.88, 94.2; 5.39, 101.7; 5.24, 101.9; 5.13, 102.8; 5.03, 102.7; 5.24, 105.6; 5.09, 108.0; 4.88, 94.2; 4.89, 100.0; 4.70, 101.1 1H shift (ppm) and 13C shift (ppm) or a corresponding peak.

In some embodiments, the present disclosure features a pharmaceutical composition for use in modulating the abundance of a bacterial taxa in a human subject's gastrointestinal microbiota, the composition comprising a glycan therapeutic preparation in an amount effective to modulate the abundance of the bacterial taxa, wherein i) the glycan therapeutic preparation comprises a mixture of branched glycans, wherein the average degree of branching (DB, branching points per residue) of the glycans in the preparation is at least 0.01 (e.g., at least 0.05, or at least 0.1), ii) at least 50% of the glycans in the preparation have a degree of polymerization (DP) of at least 3 and less than 30 glycan units, and iii) the ratio of alpha- to beta-glycosidic bonds present in the glycans of the preparation is between about 1:1 to about 5:1 overall. In some embodiments, the bacterial taxa comprises at least a first and a second bacterial taxa.

In some embodiments, the preparation comprises branched oligosaccharides. In some embodiments, the average degree of branching in the preparation (DB) is at least 0.05 (e.g., at least 0.1).

In some embodiments, at least one, at least two, at least three, at least four, or more of the glycosidic bonds independently comprise a 1->2 glycosidic bond, a 1->3 glycosidic bond, a 1->4 glycosidic bond, or a 1->6 glycosidic bond. In some embodiments, one or more, two or more, or three or more glycosidic bonds are present in both alpha and beta configuration.

In some embodiments, a glycan unit comprises at least one, at least two, at least three, or more of a monosaccharide selected from the group of a tetrose, a pentose, a hexose, and a heptose. In some embodiments, a glycan unit comprises at least one, at least two, at least three,

Akkermansia, Bacteroides, Clostridium (Erysipelotrichaceae), Clostridium (Clostridiaceae), Bifidobacterium, Aggregatibacter, Clostridium (Peptostreptococcaveae), Parabacteroides, Lactobacillus, and Enterococcus. In some embodiments, the bacterial taxa (e.g., a first and a second bacterial taxa) comprises a genus selected from the group of Akkermansia, Bacteroides, Bifidobacterium, Lactobacillus, and Parabacteroides. In some embodiments, the bacterial taxa (e.g., a first and a second bacterial taxa) comprises a genus selected from the group of Akkermansia and Blautia.

In some embodiments, the bacterial taxa (e.g., a first and a second bacterial taxa) comprises a taxa predominant in the small intestine or large intestine. In some embodiments, the bacterial taxa (e.g., a first and a second bacterial taxa) predominant in the small intestine comprises a genus selected from the group of Achromobacter, Agrobacterium, Blautia, Burkholderia, Coprococcus, Cryocola, Enterococcus, Eubacterium, Holdemania, Lactococcus, Mycobacterium, Pseudoramibacter, Ralstonia, Sphingomonas, Streptococcus, and Turicibacter. In some embodiments, the bacterial taxa (e.g., a first and a second bacterial taxa) predominant in the large intestine comprises a genus selected from the group of Anaerotruncus, Akkermansia, Bacteroides, Bilophila, Butyricimonas, Odoribacter, Parabacteroides, Phascolarctobacterium, Prevotella, and Ruminococcus.

In some embodiments, the pharmaceutical composition further comprises a polyphenol preparation. In some embodiments, the polyphenol preparation comprises a plant polyphenol isolated from a plant source material. In some embodiments, the plant source material comprises blueberry, cranberry, grape, peach, plum, pomegranate, soy, red wine, black tea, or green tea.

In some embodiments, the modulating the abundance of a bacterial taxa (e.g., a first and a second bacterial taxa) treats a dysbiosis, e.g., a dysbiosis described herein.

In some embodiments, the present disclosure features a pharmaceutical composition for use in reducing a drug- or treatment-induced symptom in a human subject, comprising administering to the human subject a glycan therapeutic preparation in an amount effective to reduce a symptom induced by a drug or treatment, wherein i) the glycan therapeutic preparation comprises a mixture of branched glycans, wherein the average degree of branching (DB) of the glycans in the preparation is at least 0.01 (e.g., at least 0.05, or at least 0.1), ii) at least 50% of the glycans in the

preparation have a degree of polymerization (DP) of at least 3 and less than 30 glycan units, and iii) the ratio of alpha- to beta-glycosidic bonds present in the glycans of the preparation is between about 1:1 to about 5:1 overall.

In some embodiments, the drug- or treatment-induced symptom is selected from the group of bloating, diarrhea, vomiting, nausea, and constipation. In some embodiments, the drug- or treatment-induced is diarrhea. In some embodiments, the drug- or treatment-induced symptom is constipation.

In some embodiments, the composition reduces drug-induced symptoms and the composition is administered prior to, concomitant with, or after administration of the drug. In some embodiments, the drug is an anti-diabetic drug, an immune-suppressive drug, an antimicrobial drug, a chemotherapeutic drug, an anti-psychotic drug, a proton pump inhibitor drug, or a non-steroid anti-inflammatory drug (NSAID). In some embodiments, the drug is selected from the group of ciprofloxacin, clindamycin, amoxicillin-clavulanate, cefixime, ephalosporins, fluoroquinolones, azithromycin, clarithromycin, erythromycin, tetracycline, azithromycin, irinotecan (camptosar), 5-fluorouracil, leucovorin, oxaliplatin, bortezomib, imatinib, lenalidomide, imbruvica, ipilimumab, pertuzumab, capecitabine, docetaxel, lapatinib, erlotinib, carmustine, etoposide, aracytine, melphalan, cytarabine, daunorubicine, amsacrine, mitoxantrone, olanzapine, ranitidine, famotidine, cimetidine, omeprazole, sucralfate, esomeprazole, naproxen, diclofenac, indomethacin, ibuprofen, ketoprofen, piroxicam, celecoxib, nimesulid, aspirin, metformin, paroxetine, valproic acid, and clozapine.

In some embodiments, the composition reduces treatment-induced symptoms and the treatment comprises radiation treatment or surgery.

In some embodiments, the drug- or treatment-induced symptom is exhibited by the subject during a treatment regimen. In some embodiments, the reducing the one or more symptom increases compliance by the subject to the treatment regimen. In some embodiments, the reducing the one or more symptom increases the subject's tolerance to a higher dose of the drug to be administered during the treatment regimen.

In some embodiments, the present disclosure features a pharmaceutical composition for use in modulating microbial diversity in a human subject's gastrointestinal tract, the composition

(Clostridiaceae), Bifidobacterium, Aggregatibacter, Clostridium (Peptostreptococcaveae), Parabacteroides, Lactobacillus, and Enterococcus is increased by at least about 5%.

In some embodiments, the abundance of at least one bacterial taxa selected from the group of genus Akkermansia, Bacteroides, Bifidobacterium, Lactobacillus, and Parabacteroides is modulated. In some embodiments, the abundance of at least two bacterial taxa selected from the group of genus Akkermansia, Bacteroides, Bifidobacterium, Lactobacillus, and Parabacteroides is modulated. In some embodiments, the abundance of at least one bacterial taxa selected from the group of genus Akkermansia and Blautia is modulated. In some embodiments, the abundance of both of the bacterial genera Akkermansia and Blautia is modulated. In some embodiments, the modulating the microbial diversity treats a dysbiosis.

In some embodiments, the present disclosure features a pharmaceutical composition for use in treating a human subject in need thereof, the treating comprising: a) identifying a human subject in need of treatment for dysbiosis, and b) administering to the human subject a pharmaceutical composition comprising a glycan therapeutic preparation in an amount effective to treat the dysbiosis, wherein i) the glycan therapeutic preparation comprises a mixture of branched glycans, wherein the average degree of branching (DB) of the glycans in the preparation is at least 0.01 (e.g., at least 0.05, or at least 0.1), ii) at least 50% of the glycans in the preparation have a degree of polymerization (DP) of at least 3 and less than 30 glycan units, and iii) the ratio of alpha- to beta-glycosidic bonds present in the glycans of the preparation is between about 1:1 to about 5:1 overall.

In some embodiments, the human subject has an infectious disease, disorder or condition. In some embodiments, the infectious disease, disorder or condition is selected from the group of *Clostridium difficile* infection (CDI); Vancomycin-resistant enterococci (VRE) infection, infectious colitis, or *C. difficile* colitis. In some embodiments, the infectious disease, disorder or condition is diarrhea selected from the group of *Clostridium difficile* associated diarrhea (CDAD), antibiotic-associated diarrhea (AAD), antibiotic-induced diarrhea, travelers' diarrhea (TD), pediatric diarrhea, and (acute) infectious diarrhea.

In some embodiments, the human subject has a metabolic disease, disorder or condition. In some embodiments, the metabolic disease, disorder or condition is selected from the group of

treatment period. In some embodiments, the subject is administered the composition for more than one treatment period.

In some embodiments, by treating the dysbiosis the disease of the human subject is treated.

In some embodiments, the present disclosure features a pharmaceutical composition for use in modulating a functional pathway of the microbiota of a human subject's gastrointestinal tract, the composition comprising a glycan therapeutic preparation in an amount effective to modulate the functional pathway, wherein i) the glycan therapeutic preparation comprises a mixture of branched glycans, wherein the average degree of branching (DB) of the glycans in the preparation is at least 0.01 (e.g., at least 0.05, or at least 0.1); ii) at least 50% of the glycans in the preparation have a degree of polymerization (DP) of at least 3 and less than 30 glycan units; and iii) the ratio of alpha- to beta-glycosidic bonds present in the glycans of the preparation is between about 1:1 to about 5:1 overall.

In some embodiments, the functional pathway modulates the production of an anti-microbial agent, a secondary bile acid, a short-chain fatty acid, a siderophore, or a metabolite listed in Table 2 by the microbiota. In some embodiments, the antimicrobial agent comprises a bacteriocin or hydrogen peroxide. In some embodiments, the short-chain fatty acid comprises formate, butyrate, acetate, propionate, or valerate. In some embodiments, the metabolite comprises 2-hydroxyisobutyrate, 3-hydroxyisovalerate, 3-methylcrotonylglycine, 3-methylcrotonylglycine, allantoin, betaine, formate, mannitol, p-cresol glucuronide, phenylacetylglycine, sarcosine, taurine, acetic acid, acetylaldehyde, ascorbic acid, butanedione, butyric acid, deoxycholic acid, ethylphenyl sulfate, formic acid, indole, isobutyric acid, isovaleric acid, propionic acid, serotonin, succinic acid, succinate, TMAO, tryptophan, valeric acid, ursodeoxycholic acid, lactate, lactic acid, or hydrogen peroxide.

In some embodiments, the functional pathway modulates the level of an inflammatory or immunomodulatory cytokine in the human subject. In some embodiments, the inflammatory and immunomodulatory cytokine comprises interleukin-1α (IL-1α), IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12, IL-13, IL-17A, IL-17F, IL-22, IL-23, tumor necrosis factor (TNF), chemokine (C-C

motif) ligand 5 (CCL5, also known as RANTES), transforming growth factor beta (TGF-β), or interferon gamma (IFN-γ).

In some embodiments, the functional pathway increases the level of a short-chain fatty acid in the subject. In some embodiments, the increase in the short-chain fatty acid induces the generation of regulatory T (Treg) cells by the subject. In some embodiments, the increase in the short-chain fatty acid reduces the permeability of the intestinal or plasma endotoxin level in the subject. In some embodiments, the increase of a short-chain fatty acid reduces the inflammatory response of the subject. In some embodiments, the short-chain fatty acid is produced by at least one bacterial species of the *Ruminocaccaceae* and/or *Lachnospiraceae* family.

In some embodiments, the subject is obese.

In some embodiments, the present disclosure features a pharmaceutical composition for use in preventing a relapse of a *Clostridium difficile* infection in a human subject previously administered a drug for the treatment of a *C. difficile* infection, the composition comprising a glycan therapeutic preparation in an amount effective to prevent the relapse, wherein i) the glycan therapeutic preparation comprises a mixture of branched glycans, wherein the average degree of branching (DB) of the glycans in the preparation is at least 0.01 (e.g., at least 0.05, or at least 0.1); ii) at least 50% of the glycans in the preparation have a degree of polymerization (DP) of at least 3 and less than 30 glycan units; and iii) the ratio of alpha- to beta-glycosidic bonds present in the glycans is between about 1:1 to about 5:1 overall.

In some embodiments, the relapse comprises the recurrence of one or more symptoms associated with a *C. difficile* infection. In some embodiments, the relapse occurs during or after a first-line or standard of care drug treatment regimen.

In some embodiments, the drug for the treatment of a *C. difficile* infection is an antibiotic. In some embodiments, the antibiotic is selected from the group of vancomycin, metronidazole, and fidaxomicin. In some embodiments, the composition is administered concurrently or after administration of the drug for the treatment of a *C. difficile* infection.

In some embodiments, the composition is administered in combination with a second drug or treatment. In some embodiments, the second drug or treatment comprises an antibiotic.

We claim:

1. A method of making a pharmaceutical composition, the method comprising:
   (a) providing a preparation comprising a mixture of synthetic glycans,
   (b) acquiring a value for the following characteristics of the preparation:
      (i) the degree of polymerization (DP),
      (ii) the average degree of branching (DB),
      (iii) the ratio of alpha- glycosidic to beta-glycosidic bonds, and
   (c) formulating the preparation as a pharmaceutical composition if the following criteria are met:
      (i) at least 50% of the glycans in the preparation have a DP of at least 3 and less than 30 glycan units,
      (ii) the average degree of branching (DB) of the glycans in the preparation is at least 0.01,
      (iii) the ratio of alpha- to beta-glycosidic bonds present in the glycans of the preparation is between about 1:1 to about 5:1.

2. The method of claim 1, further comprising:
   b) acquiring a value for any one or both additional characteristics of the preparation:
      (iv) the identity of the glycan units,
      (v) the ratio of glycan units, and
   c) formulating the preparation as a pharmaceutical composition if:
      (vi) the glycan unit ratio in the preparation is about the same as the ratio of the glycan unit input.

3. The method of either of claims 1 or 2, further comprising:
   b) acquiring a value for any one or both additional characteristics of the preparation:
      (iv) the level of bacterial growth, in media supplemented with the preparation, of commensal strains selected from the group consisting of *Bacteroides caccae* ATCC 43185, *Prevotella copri* DSM 18205, *Bacteroides thetaiotamicron* ATCC 29741, *Bacteroides cellulosilyticus* DSM 14838, *Clostridium scindens*

ATCC 35704, *Ruminococcus obeum* ATCC 29714, *Clostridium nexile* ATCC 27757, and *Parabacteroides distasonis* ATCC 8503,

(v) the level of bacterial growth, in media supplemented with the preparation, of pathogenic strains selected from the group consisting of *Clostridium difficile* ATCC BAA-1382, *Clostridium difficile* ATCC 43255, *Enterococcusfaecium* ATCC 700221, and *Salmonella enterica* ATCC 27869, and

c) formulating the preparation as a pharmaceutical composition if one or both of the following criteria are met:

(vi) promotion by the media supplemented with the preparation of growth of at least 5 commensal strains,

(v) promotion by the media supplemented with the preparation of growth of no more than 2 pathogenic strain.

4. The method of any one of claims 1-3, wherein step (b) is performed prior to, concurrently with, or after step (b) of claim 1, but prior to step (c) of claim 1.

5. The method of any one of claims 1-4, wherein the step of formulating the preparation as a pharmaceutical composition comprises one or more of:

i) removing unwanted constituents from the preparation,

ii) reducing the volume of the preparation,

iii) sterilizing the preparation,

iv) admixing the preparation with a pharmaceutically acceptable excipient or carrier,

v) admixing the preparation with a second drug or pharmaceutical agent,

vi) formulating the preparation into a aqueous solution or syrup,

vii) formulating the preparation into a tablet or pill,

viii) formulating the preparation into a capsule,

ix) packaging the preparation,

x) labeling the package preparation of ix), and

xi) selling or offering for sale the packaged and labeled preparation of x).

6. The method of claim 1, the method comprising:

(i) providing a therapeutic glycan preparation comprising at least one glycan unit selected from the group consisting of glucose, galactose, fucose, xylose, arabinose, rhamnose, and mannose,

(ii) determining if a preselected NMR peak or group of NMR peaks is associated with the glycan preparation, and

(iii) if the preselected peak or group of peaks is present, formulating the preparation as a pharmaceutical composition.

7. The method of claim 6, wherein the peak is a 1H-13C HSQC NMR peak, and wherein determining optionally comprises: acquiring a value for the identity of an 1H-13C HSQC peak or group of peaks associated with the preparation, and if a preselected peak is present, formulating the preparation as a pharmaceutical composition.

8. The method of either of claims 6 or 7, wherein

(i) for glycans comprising glucose, the peaks comprise at least one or at least two 1H-13C HSQC peaks selected from 5.42, 92.5; 5.21, 92.8; 5.18, 93.9; 5.08, 97.0; 5.36, 98.4; 5.34, 99.8; 5.38, 100.3; 4.95, 98.6; 4.62, 96.6; 4.70, 103.6; 4.49, 103.4 1H shift (ppm) and 13C shift (ppm) or a corresponding peak;

(ii) for glycans comprising galactose, the peaks comprise at least one or at least two 1H-13C HSQC peaks selected from 5.37, 92.9; 5.24, 93.1; 5.14, 96.0; 4.96, 99.3; 5.31, 98.7; 5.39, 101.4; 5.00, 101.8; 4.80, 101.3; 4.63, 97.0; 4.56, 97.2; 4.53, 103.1; 4.43, 104.1 1H shift (ppm) and 13C shift (ppm) or a corresponding peak;

(iii) for glycans comprising fucose, the peaks comprise at least one or at least two 1H-13C HSQC peaks selected from 5.18, 92.9; 5.33, 92.4; 5.04, 96.3; 4.90, 99.7; 4.52, 97.0; 4.39, 103.6 1H shift (ppm) and 13C shift (ppm) or a corresponding peak;

(iv) for glycans comprising xylose, the peaks comprise at least one or at least two 1H-13C HSQC peaks selected from 5.18, 93.0; 5.10, 94.3; 5.34, 98.2; 5.31, 99.6; 5.11, 100.8; 4.91, 99.4; 4.56, 97.3; 4.64, 104.2; 4.54, 103.4; 4.44, 102.6; 4.44, 104.1 1H shift (ppm) and 13C shift (ppm) or a corresponding peak;

(v) for glycans comprising arabinose, the peaks comprise at least one or at least two 1H-13C HSQC peaks selected from 5.22, 93.2; 5.13, 93.2;5.29, 96.0; 5.26, 97.2; 5.12, 96.6; 5.18, 99.6; 5.06, 99.2; 4.99, 100.0; 5.26, 101.9; 5.06, 102.1; 4.55, 97.4; 4.54, 105.2; 4.50, 105.5; 4.38, 103.9 1H shift (ppm) and 13C shift (ppm) or a corresponding peak;

(vi) for glycans comprising rhamnose, the peaks comprise at least one or at least two 1H-13C HSQC peaks selected from 5.21, 93.2; 5.10, 94.5; 4.85, 94.1; 5.01, 95.8; 5.35, 100.5; 5.15, 102.2; 5.04, 102.9; 4.78, 97.9; 4.71, 99.0; 4.72, 101.0 1H shift (ppm) and 13C shift (ppm) or a corresponding peak;

(vii) for glycans comprising mannose, the peaks comprise at least one or at least two 1H-13C HSQC peaks selected from 5.37, 93.0; 5.16, 94.6; 4.88, 94.2; 5.39, 101.7; 5.24, 101.9; 5.13, 102.8; 5.03, 102.7; 5.24, 105.6; 5.09, 108.0; 4.88, 94.2; 4.89, 100.0; 4.70, 101.1 1H shift (ppm) and 13C shift (ppm) or a corresponding peak.

9. A pharmaceutical composition comprising a therapeutic glycan preparation comprising a mixture of branched glycans, wherein the average degree of branching (DB) of the glycans in the preparation is at least 0.01, wherein

i) at least 50% of the glycans in the preparation have a degree of polymerization (DP) of at least 3 and less than 30 glycan units,

ii) the glycan preparation comprises both alpha- and beta-glycosidic bonds,

iii) at least one of the glycosidic bonds present in the glycans of the preparation comprise a 1->2 glycosidic bond, a 1->3 glycosidic bond, a 1->4 glycosidic bond, or a 1->6 glycosidic bond,

iv) the ratio of alpha- to beta-glycosidic bonds present in the glycans of the preparation is between about 1:1 to about 5:1.

10. The composition of claim 9, wherein at least two or at least three of the glycosidic bonds independently comprise a 1->2 glycosidic bond, a 1->3 glycosidic bond, a 1->4 glycosidic bond, or a 1->6 glycosidic bond.

11. The composition of either of claims 9 or 10, wherein the glycan unit comprises at least one of a monosaccharide selected from the group of glucose, galactose, arabinose, mannose, fructose, xylose, fucose, and rhamnose.

12. The composition of any one of claims 9-11, wherein the glycan therapeutic preparation is synthetic and not isolated from a natural oligosaccharide or polysaccharide source.

13. The composition of any one of claims 9-12, further comprising one or more of (i) a polyphenol preparation, (ii) a preparation of probiotic bacteria, (iii) a drug or therapeutic agent, and (iv) a pharmaceutically acceptable excipient.

14. The composition of any one of claims 9-13, wherein the composition is formulated as a unit-dosage form, and wherein optionally: (i) the unit-dosage form is formulated for oral delivery; or (ii) the unit-dosage form is formulated to dissolve in an aqueous solution and is orally administered as a beverage, syrup, solution, or suspension.

15. The pharmaceutical composition of claim 9 comprising at least one glycan unit selected from the group of: glucose, galactose, fucose, xylose, arabinose, rhamnose, and mannose, wherein the preparation comprises a glycan unit associated with one or more of the following 1H-13C HSQC peaks:

(i) for glycans comprising glucose, the peaks comprise at least one or at least two 1H-13C HSQC peaks selected from 5.42, 92.5; 5.21, 92.8; 5.18, 93.9; 5.08, 97.0; 5.36, 98.4; 5.34, 99.8; 5.38, 100.3; 4.95, 98.6; 4.62, 96.6; 4.70,

103.6; 4.49, 103.4 1H shift (ppm) and 13C shift (ppm) or a corresponding peak;

(ii) for glycans comprising galactose, the peaks comprise at least one or at least two 1H-13C HSQC peaks selected from 5.37, 92.9; 5.24, 93.1; 5.14, 96.0; 4.96, 99.3; 5.31, 98.7; 5.39, 101.4; 5.00, 101.8; 4.80, 101.3; 4.63, 97.0; 4.56, 97.2; 4.53, 103.1; 4.43, 104.1 1H shift (ppm) and 13C shift (ppm) or a corresponding peak;

(iii) for glycans comprising fucose, the peaks comprise at least one or at least two 1H-13C HSQC peaks selected from 5.18, 92.9; 5.33, 92.4; 5.04, 96.3; 4.90, 99.7; 4.52, 97.0; 4.39, 103.6 1H shift (ppm) and 13C shift (ppm) or a corresponding peak;

(iv) for glycans comprising xylose, the peaks comprise at least one or at least two 1H-13C HSQC peaks selected from 5.18, 93.0; 5.10, 94.3; 5.34, 98.2; 5.31, 99.6; 5.11, 100.8; 4.91, 99.4; 4.56, 97.3; 4.64, 104.2; 4.54, 103.4; 4.44, 102.6; 4.44, 104.1 1H shift (ppm) and 13C shift (ppm) or a corresponding peak;

(v) for glycans comprising arabinose, the peaks comprise at least one or at least two 1H-13C HSQC peaks selected from 5.22, 93.2; 5.13, 93.2;5.29, 96.0; 5.26, 97.2; 5.12, 96.6; 5.18, 99.6; 5.06, 99.2; 4.99, 100.0; 5.26, 101.9; 5.06, 102.1; 4.55, 97.4; 4.54, 105.2; 4.50, 105.5; 4.38, 103.9 1H shift (ppm) and 13C shift (ppm) or a corresponding peak;

(vi) for glycans comprising rhamnose, the peaks comprise at least one or at least two 1H-13C HSQC peaks selected from 5.21, 93.2; 5.10, 94.5; 4.85, 94.1; 5.01, 95.8; 5.35, 100.5; 5.15, 102.2; 5.04, 102.9; 4.78, 97.9; 4.71, 99.0; 4.72, 101.0 1H shift (ppm) and 13C shift (ppm) or a corresponding peak;

(vii) for glycans comprising mannose, the peaks comprise at least one or at least two 1H-13C HSQC peaks selected from 5.37, 93.0; 5.16, 94.6; 4.88, 94.2; 5.39, 101.7; 5.24, 101.9; 5.13, 102.8; 5.03, 102.7; 5.24, 105.6; 5.09,

108.0; 4.88, 94.2; 4.89, 100.0; 4.70, 101.1 1H shift (ppm) and 13C shift (ppm) or a corresponding peak.

16. A pharmaceutical kit comprising:

i) the pharmaceutical composition of any one of claims 9-15,

ii) at least a second constituent selected from the group of a preparation of polyphenols, a preparation of probiotic bacteria, a drug or therapeutic agent, and a dietary component,

iii) instructional material, and

iv) packaging.