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(71) Applicant: **EVELO BIOSCIENCES, INC.** [US/US]; 620 Memorial Drive, Cambridge, MA 02139 (US).

(72) Inventors: **JAHIC, Mehmedalija**; C/o Evelo Biosciences, Inc., 620 Memorial Drive, Cambridge, MA 02139 (US). **MCKENNA, Collin**; C/o Evelo Biosciences, Inc., 620 Memorial Drive, Cambridge, MA 02139 (US).

(74) Agent: **JONES, Brendan, T.** et al.; Foley Hoag LLP, 155 Seaport Boulevard, Boston, MA 02210-2600 (US).

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(54) Title: PHARMACEUTICAL COMPOSITION CONTAINING BACTERIA

(57) Abstract: Methods and compositions related to pharmaceutical agents containing bacteria are provided herein.

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PHARMACEUTICAL COMPOSITION CONTAINING BACTERIA

Cross Reference to Related Applications

[001] This application claims the benefit of the following U.S. Provisional Application Nos.: 63/172,370, filed April 8, 2021, and 63/197,000 filed June 4, 2021, and the entire contents of each of which are incorporated herein by reference.

Summary

[002] In certain aspects, provided herein are pharmaceutical agents (e.g., powders) comprising bacteria (e.g., freeze dried bacteria), wherein the bacteria in the pharmaceutical agent are present at a total cell count (TCC) of at least $1x10^{11}$ cells/gram of the pharmaceutical agent. In some embodiments, the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of at least $3.3x10^{11}$ cells/gram of the pharmaceutical agent. In some embodiments, the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of at least $5x10^{11}$ cells/gram of the pharmaceutical agent. In some embodiments, the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of at least $7x10^{11}$ cells/gram of the pharmaceutical agent. In some embodiments, the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of at least $1x10^{12}$ cells/gram of the pharmaceutical agent. In some embodiments, the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of at least $2x10^{12}$ cells/gram of the pharmaceutical agent. In some embodiments, the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of between about $1x10^{11}$ cells/gram to about $2.5x10^{12}$ cells/gram of the pharmaceutical agent. In some embodiments, the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of between about $3.3x10^{11}$ cells/gram to about $2.5x10^{12}$ cells/gram of the pharmaceutical agent. In some embodiments, the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of between about $5x10^{11}$ cells/gram to about $2.5x10^{12}$ cells/gram of the pharmaceutical agent. In some embodiments, the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of between about $7x10^{11}$ cells/gram to about $2.4x10^{12}$ cells/gram of the pharmaceutical agent. In some embodiments, the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of about $2x10^{12}$ cells/gram of the pharmaceutical agent. In some embodiments, the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of between about $1x10^{12}$ cells/gram

to about $2x10^{12}$ cells/gram of the pharmaceutical agent. In some embodiments, the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of between about $1.3x10^{12}$ cells/gram to about $2.4x10^{12}$ cells/gram of the pharmaceutical agent. In some embodiments, the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of about $2.5x10^{12}$ cells/gram of the pharmaceutical agent. In some embodiments, the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of about $1.2x10^{12}$ cells/gram of the pharmaceutical agent. In some embodiments, the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of about $1.5x10^{12}$ cells/gram of the pharmaceutical agent. In some embodiments, the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of about $6x10^{11}$ cells/gram of the pharmaceutical agent.

[003] In certain aspects, provided herein are pharmaceutical agents (e.g., powders) comprising bacteria (e.g., freeze dried bacteria) and a cryoprotectant.

[004] In some embodiments, the cryoprotectant comprises sucrose. In some embodiments, the cryoprotectant comprises dextran. In some embodiments, the cryoprotectant comprises sucrose and dextran. In some embodiments, the cryoprotectant comprises sucrose and dextran in equivalent amounts (e.g., on a percent weight by weight basis). In some embodiments, the cryoprotectant comprises sucrose, and dextran. In some embodiments, the cryoprotectant comprises sucrose, dextran, and L-cysteine HCl (e.g., a form of L-cysteine). In some embodiments, the cryoprotectant does not comprise L-cysteine HCl.

[005] In some embodiments, the pharmaceutical agent comprises about 6% to about 12% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 8% to about 12% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 11% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 6% to about 12% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 8% to about 12% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 11% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 6% to about 12% (weight/weight) sucrose and about 6% to about 12% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 8% to about 12% (weight/weight) sucrose and about 8% to about 12% (weight/weight) dextran. In some

embodiments, the pharmaceutical agent comprises about 11% (weight/weight) sucrose and about 11% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 0.1% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.1% to about 0.3% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.15% to about 0.25% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 10% to about 0.25% or about 0.15% to about 0.35% (weight/weight) L-cysteine HCl.

[006] In some embodiments, the pharmaceutical agent comprises about 7% to about 21% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 10% to about 19% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 15% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 7% to about 21% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 10% to about 19% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 15% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 7% to about 21% (weight/weight) sucrose and about 7% to about 21% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 10% to about 19% (weight/weight) sucrose and about 10% to about 19% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 15% (weight/weight) sucrose and about 15% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 0.01% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.1% to about 0.4% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.15% to about 0.35% (weight/weight) L-cysteine HCl.

[007] In some embodiments, the cryoprotectant comprises a dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the cryoprotectant comprises sucrose. In some embodiments, the cryoprotectant comprises dextrose (also referred to as glucose). In some embodiments, the cryoprotectant comprises monosodium glutamate. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose

equivalent (DE) of 21 (such as Glucidex 21) and sucrose. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and sucrose in equivalent amounts (e.g., on a percent weight by weight basis). In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, and dextrose. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, and monosodium glutamate. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, dextrose, and monosodium glutamate. In some embodiments, the cryoprotectant comprises dextrose and monosodium glutamate in equivalent amounts (e.g., on a percent weight by weight basis). In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, dextrose, monosodium glutamate, and L-cysteine HCl (e.g., a form of L-cysteine). In some embodiments, the cryoprotectant does not comprise L-cysteine HCl.

[008] In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the pharmaceutical agent comprises about 26% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the pharmaceutical agent comprises about 21% to about 29% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 23% to about 27% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 25% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 6% to about 11%

(weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 7% to about 10% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 9% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 4% to about 10% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 5% to about 9% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 7% (weight/weight) glutamate.

[009] In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 21% to about 29% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 23% to about 27% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl.

[010] In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 21% to about 29% (weight/weight) sucrose; and about 6% to about 11% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 21% to about 29% (weight/weight) sucrose; and about 4% to about 10% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 21% to about 29% (weight/weight) sucrose; about 6% to about 11% (weight/weight) dextrose; and about 4% to about 10% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as

Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 23% to about 27% (weight/weight) sucrose; and about 7% to about 10% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); 23% to about 27% (weight/weight) sucrose; and about 5% to about 9% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); 23% to about 27% (weight/weight) sucrose; about 7% to about 1% (weight/weight) dextrose; and about 5% to about 9% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl.

[011] In certain embodiments, the pharmaceutical agent comprises about 40% to about 75% (weight/weight) bacteria (e.g., freeze dried bacteria). In certain embodiments, the pharmaceutical agent comprises about 35% to about 70% (weight/weight) bacteria (e.g., freeze dried bacteria). In certain embodiments, the pharmaceutical agent comprises about 64% (weight/weight) bacteria (e.g., freeze dried bacteria).

[012] In certain embodiments, the pharmaceutical agent comprises about 15% to about 35% (weight/weight) bacteria (e.g., freeze dried bacteria). In certain embodiments, the pharmaceutical agent comprises about 18% to about 30% (weight/weight) bacteria (e.g., freeze dried bacteria). In certain embodiments, the pharmaceutical agent comprises about 25% (weight/weight) bacteria (e.g., freeze dried bacteria).

[013] In certain embodiments, the pharmaceutical agent comprises *Prevotella* bacteria.

[014] In certain embodiments, the pharmaceutical agent comprises *Veillonella* bacteria.

[015] In some embodiments, the pharmaceutical agent has a fine and smooth granulated powder appearance.

[016] In some embodiments, the pharmaceutical agent has an off-white to brown, fine powder appearance.

[017] In some aspects, the disclosure provides a pharmaceutical composition that comprises a pharmaceutical agent (e.g., powder) described herein and one or more excipients.

[018] In some aspects, the disclosure provides a method comprising combining bacteria (e.g., a pellet comprising bacteria) with a cryoprotectant solution, thereby preparing a formulated paste. In some embodiments, the disclosure provides a formulated paste prepared by this method.

[019] In some embodiments, the method further comprises freeze drying the formulated paste, to thereby prepare a freeze-dried product. In some embodiments, the freeze drying comprises primary drying. In some embodiments, the freeze drying comprises primary drying and secondary drying. In some embodiments, the disclosure provides a freeze-dried product prepared by this method.

[020] In some embodiments, the method further comprises milling the freeze-dried product, to thereby prepare a freeze-dried powder (e.g., powder, e.g., pharmaceutical agent). In some embodiments, the disclosure provides a pharmaceutical agent prepared by this method.

[021] In some embodiments, the method further comprises combining the freeze-dried powder with one or more excipients to thereby prepare a pharmaceutical composition. In some embodiments, the disclosure provides a pharmaceutical composition prepared by this method.

[022] In some embodiments, the cryoprotectant solution is mixed with the pellet in a ratio of about 0.2 to about 0.5 gram (g) cryoprotectant solution per gram of pellet; about 0.05 to about 0.25 gram (g) cryoprotectant solution per gram of pellet; about 0.06 to about 0.1 gram (g) cryoprotectant solution per gram of pellet; or about 0.15 to about 0.2 gram (g) cryoprotectant solution per gram of pellet. In some embodiments, the cryoprotectant solution is mixed with the pellet in a ratio of about 0.4 gram (g) cryoprotectant solution per gram of pellet. In some embodiments, the cryoprotectant solution is mixed with the pellet in a ratio of about 0.18 gram (g) cryoprotectant solution per gram of pellet. In some embodiments, the cryoprotectant solution is mixed with the pellet in a ratio of about 0.1 (e.g., 0.08) gram (g) of cryoprotectant solution per gram of pellet.

[023] In some embodiments, the cryoprotectant solution is mixed with the pellet at a ratio of 4% to 10% (volume/volume), e.g., 5 % to 8% (volume/volume). In some

embodiments, the cryoprotectant solution is mixed with the pellet at a ratio of about 6.5% (volume/volume).

[024] In some embodiments, the cryoprotectant solution comprises sucrose. In some embodiments, the cryoprotectant solution comprises dextran. In some embodiments, the cryoprotectant solution comprises sucrose and dextran. In some embodiments, the cryoprotectant solution comprises sucrose and dextran in equivalent amounts (e.g., on a percent weight by weight basis). In some embodiments, the cryoprotectant solution comprises sucrose, dextran, and L-cysteine HCl (e.g., a form of L-cysteine). In some embodiments, the cryoprotectant solution does not comprise L-cysteine HCl.

[025] In some embodiments, the cryoprotectant solution comprises about 10% to about 30% (weight/weight) sucrose. In some embodiments, the cryoprotectant solution comprises about 15% to about 35% (weight/weight) sucrose. In some embodiments, the cryoprotectant solution comprises about 20% (weight/weight) sucrose.

[026] In some embodiments, the cryoprotectant solution comprises about 10% to about 30% (weight/weight) dextran. In some embodiments, the cryoprotectant solution comprises about 15% to about 35% (weight/weight) dextran. In some embodiments, the cryoprotectant solution comprises about 20% (weight/weight) dextran.

[027] In some embodiments, the cryoprotectant solution comprises about 10% to about 30% (weight/weight) sucrose and about 10% to about 30% (weight/weight) dextran. In some embodiments, the cryoprotectant solution comprises about 15% to about 35% (weight/weight) sucrose and about 15% to about 35% (weight/weight) dextran. In some embodiments, the cryoprotectant solution comprises about 20% (weight/weight) sucrose and about 20% (weight/weight) dextran.

[028] In some embodiments, the cryoprotectant solution comprises about 40% to about 80% (weight/weight) water. In some embodiments, the cryoprotectant solution comprises about 50% to about 70% (weight/weight) water. In some embodiments, the cryoprotectant solution comprises about 55% to about 65% (weight/weight) water. In some embodiments, the cryoprotectant solution comprises about 60% (weight/weight) water.

[029] In some embodiments, the cryoprotectant solution comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl (e.g., a form of L-cysteine). In some embodiments, the cryoprotectant solution comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant solution comprises about 0.15% to about 0.45% (weight/weight) L-cysteine HCl. In some

embodiments, the pharmaceutical agent comprises about .1% to about 0.25% or about 0.15% to about 0.35% (weight/weight) L-cysteine HCl.

[030] In some embodiments, the cryoprotectant solution comprises about 0.2% (weight/weight) L-cysteine HCl.

[031] In some embodiments, the cryoprotectant solution comprises about 59.8% (weight/weight) water.

[032] In some embodiments, the cryoprotectant solution comprises about 0.4% (weight/weight) L-cysteine HCl.

[033] In some embodiments, the cryoprotectant solution comprises about 59.6% (weight/weight) water.

[034] In certain embodiments, the cryoprotectant solution provided herein comprises: (i) about 20% (weight/weight) sucrose; (ii) about 20% (weight/weight) dextran; (iii) about 0.4% (weight/weight) L-cysteine HCl; and (iv) about 59.6% (weight/weight) water.

[035] In certain embodiments, the cryoprotectant solution provided herein comprises: (i) about 20% (weight/weight) sucrose; (ii) about 20% (weight/weight) dextran; (iii) about 0.2% (weight/weight) L-cysteine HCl; and (iv) about 59.8% (weight/weight) water.

[036] In certain embodiments, the cryoprotectant solution provided herein comprises: (i) about 20% (weight/weight) sucrose; (ii) about 20% (weight/weight) dextran; and (iii) about 60% (weight/weight) water.

[037] In some embodiments, the cryoprotectant (e.g., dry composition not containing water) comprises about 40% to about 60% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 45% to about 55% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 50% (weight/weight) sucrose.

[038] In some embodiments, the cryoprotectant comprises about 40% to about 60% (weight/weight) dextran. In some embodiments, the cryoprotectant comprises about 45% to about 55% (weight/weight) dextran. In some embodiments, the cryoprotectant comprises about 50% (weight/weight) dextran.

[039] In some embodiments, the cryoprotectant comprises about 40% to about 60% (weight/weight) sucrose and 40% to about 60% (weight/weight) dextran. In some embodiments, the cryoprotectant comprises about 45% to about 55% (weight/weight) sucrose and about 45% to about 55% (weight/weight) dextran. In some embodiments, the

cryoprotectant comprises about 50% (weight/weight) sucrose and about 50% (weight/weight) dextran.

[040] In some embodiments, the cryoprotectant comprises about 0.25% to about 5% (weight/weight) L-cysteine HCl (e.g., a form of L-cysteine). In some embodiments, the cryoprotectant comprises about 0.5% to about 2.5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant comprises about 0.75% to about 1.5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant comprises about 1% (weight/weight) L-cysteine HCl.

[041] In certain embodiments, the cryoprotectant provided herein comprises: (i) about 50% (weight/weight) sucrose; (ii) about 50% (weight/weight) dextran; and (iii) about 1% (weight/weight) L-cysteine HCl.

[042] In certain embodiments, the cryoprotectant provided herein comprises: (i) about 50% (weight/weight) sucrose; and (ii) about 50% (weight/weight) dextran.

[043] In some embodiments, the cryoprotectant comprises a dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the cryoprotectant comprises sucrose. In some embodiments, the cryoprotectant comprises dextrose (also referred to as glucose). In some embodiments, the cryoprotectant comprises monosodium glutamate. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and sucrose. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and sucrose in equivalent amounts (e.g., on a percent weight by weight basis). In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, and dextrose. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, and monosodium glutamate. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, dextrose, and monosodium glutamate. In some embodiments, the

cryoprotectant comprises dextrose and monosodium glutamate in equivalent amounts (e.g., on a percent weight by weight basis). In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, dextrose, monosodium glutamate, and L-cysteine HCl (e.g., a form of L-cysteine). In some embodiments, the cryoprotectant does not comprise L-cysteine HCl.

[044] In some embodiments, the cryoprotectant (e.g., dry composition not containing water) comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21).

[045] In some embodiments, the cryoprotectant (e.g., dry composition not containing water) comprises about 27% to about 47% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) sucrose.

[046] In some embodiments, the cryoprotectant comprises about 8% to about 18% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 11% to about 15% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 13% (weight/weight) dextrose.

[047] In some embodiments, the cryoprotectant comprises about 8% to about 18% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 11% to about 15% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 13% (weight/weight) monosodium glutamate.

[048] In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21)

and about 27% to about 47% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 32% to about 42% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 37% (weight/weight) sucrose.

[049] In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 27% to about 47% (weight/weight) sucrose; and about 8% to about 18% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 27% to about 47% (weight/weight) sucrose; and about 8% to about 18% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 27% to about 47% (weight/weight) sucrose; about 8% to about 18% (weight/weight) dextrose; and about 8% to about 18% (weight/weight) monosodium glutamate.

[050] In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 32% to about 42% (weight/weight) sucrose; and about 11% to about 15% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 32% to about 42% (weight/weight) sucrose; and about 11% to about 15% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent

(DE) of 21 (such as Glucidex 21); about 32% to about 42% (weight/weight) sucrose; about 11% to about 15% (weight/weight) dextrose; and about 11% to about 15% (weight/weight) monosodium glutamate.

[051] In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 37% (weight/weight) sucrose; and about 13% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 37% (weight/weight) sucrose; and about 13% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 37% (weight/weight) sucrose; about 13% (weight/weight) dextrose; and about 13% (weight/weight) monosodium glutamate.

[052] In some embodiments, the cryoprotectant comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl (e.g., a form of L-cysteine). In some embodiments, the cryoprotectant comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant comprises about 0.1% to about 0.25% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant comprises about 0.2% (weight/weight) L-cysteine HCl.

[053] In certain embodiments, the cryoprotectant provided herein comprises: (i) about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); (ii) about 37% (weight/weight) sucrose; (iii) about 13% (weight/weight) dextrose; (iv) about 13% (weight/weight) monosodium glutamate; and (v) about 0.2% (weight/weight) L-cysteine HCl.

[054] In certain embodiments, the cryoprotectant provided herein comprises: (i) about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); (ii) about 37% (weight/weight) sucrose; (iii) about 13% (weight/weight) dextrose; and (iv) about 13% (weight/weight) monosodium glutamate.

[055] In certain aspects provided herein are pharmaceutical agents that comprise bacteria. In certain embodiments, the pharmaceutical agents maintain their stability, e.g., for three, six, twelve, eighteen and/or twenty-four months under long-term (2-8°C) and/or accelerated (23-27°C (optionally at 60% relative humidity (RH))) storage conditions, e.g., as determined by total cell count (TCC), e.g., as determined by Coulter counter and described herein. In certain embodiments, the pharmaceutical agents maintain their stability, e.g., for three, six, twelve, eighteen and/or twenty-four months under long-term (-20°C) and/or accelerated (2-8°C) storage conditions, e.g., as determined by total cell count (TCC), e.g., as determined by Coulter counter and described herein.

[056] In certain aspects provided herein are pharmaceutical agents that comprise bacteria. In some embodiments, the water content of the pharmaceutical agents is between about 0.5% and about 9%, between about 1% and about 8%, between about 1% and about 6%, (e.g., about 1.7%, e.g., 1.8%, e.g., about 2%, e.g., about 2.2%, e.g., about 2.3%, e.g., about 2.4%, e.g., about 2.8%, e.g., about 2.9%, e.g., about 3%, e.g., about 3.1%, e.g., about 3.2%, e.g., about 3.3%, e.g., about 3.5%, e.g., about 3.6%, e.g., about 4%, e.g., about 4.5%, e.g., about 5%, e.g., about 5.3%, e.g., about 5.4%, or e.g., about 7.8%), e.g., as determined by the Karl-Fischer method for water content analysis provided in Ph. Eur. method 2.5.12, and as described herein. In some embodiments, the pharmaceutical agents maintain their water content, e.g., for three, six, twelve, eighteen and/or twenty-four months under long-term (2-8°C) and/or accelerated (25°C (optionally at 60% RH)) storage conditions. In some embodiments, the pharmaceutical agents maintain their water content, e.g., for three, six, twelve, eighteen and/or twenty-four months under long-term (-20°C) and/or accelerated (2-8°C) storage conditions.

[057] The pharmaceutical agent can be of bacterial origin (e.g., mixture of selected strains or agents (e.g., components) thereof. The pharmaceutical agent can be of bacterial origin (e.g., a single selected strain and/or agents (e.g., components) thereof. The pharmaceutical agent can be a powder that comprises the bacteria and/or components thereof, and can comprise additional agents such as, e.g., cryoprotectant. For example, in some embodiments, the pharmaceutical agent is a freeze dried (e.g., lyophilized) powder of bacteria and/or components thereof that optionally, further comprise additional agents, such as a cryoprotectant.

[058] In some aspects, the disclosure provides a solid dosage form (e.g., capsule, tablet, or minitablet) that comprises a pharmaceutical agent (e.g., powder) described herein. The solid dosage form can be enteric coated.

[059] In certain embodiments, the solid dosage form comprises a capsule. In some embodiments, the capsule is a size 00, size 0, size 1, size 2, size 3, size 4, or size 5 capsule. In some embodiments, the capsule is a size 0 capsule.

[060] In some embodiments, the solid dosage form comprises a tablet. In some embodiments, the tablet (e.g., enterically coated tablet) is a 5mm, 6mm, 7mm, 8mm, 9mm, 10mm, 11mm, 12mm, 13mm, 14mm, 15mm, 16mm, 17mm, or 18mm tablet.

[061] In some embodiments, the solid dosage form comprises a minitablet. In some embodiments, the minitablet (e.g., enterically coated minitablet) is a 1mm minitablet, 1.5 mm minitablet, 2mm minitablet, 3mm minitablet, or 4mm minitablet. In some embodiments, a plurality of enterically coated minitablets are contained in a capsule (e.g., a size 0 capsule can contain about 31 to about 35 (e.g., 33) minitablets, wherein the minitablets are 3mm in size). In some embodiments, the capsule is a size 00, size 0, size 1, size 2, size 3, size 4, or size 5 capsule. In some embodiments, the capsule comprises HPMC (hydroxyl propyl methyl cellulose) or gelatin.

[062] In some embodiments, the enteric coating comprises one enteric coating.

[063] In some embodiments, the enteric coating comprises an inner enteric coating and an outer enteric coating. In some embodiments, the enteric coating comprises an inner enteric coating and an outer enteric coating, and wherein the inner and outer enteric coatings are not identical (e.g., the inner and outer enteric coatings do not contain identical components in identical amounts).

[064] In some embodiments, the enteric coating (e.g., the one enteric coating or the inner enteric coating and/or the outer enteric coating) comprises a polymethacrylate-based copolymer.

[065] In some embodiments, the enteric coating (e.g., the one enteric coating or the inner enteric coating and/or the outer enteric coating) comprises a methacrylic acid ethyl acrylate (MAE) copolymer (1:1).

[066] In some embodiments, the one enteric coating comprises methacrylic acid ethyl acrylate (MAE) copolymer (1:1) (such as Kollicoat MAE 100P).

[067] In some embodiments, the one enteric coating comprises a Eudragit copolymer, e.g., a Eudragit L (e.g., Eudragit L 100-55; Eudragit L 30 D-55), a Eudragit S, a Eudragit RL, a Eudragit RS, a Eudragit E, or a Eudragit FS (e.g., Eudragit FS 30 D).

[068] In some embodiments, the enteric coating (e.g., the one enteric coating or the inner enteric coating and/or the outer enteric coating) comprises cellulose acetate phthalate (CAP), cellulose acetate trimellitate (CAT), poly(vinyl acetate phthalate) (PVAP), hydroxypropyl methylcellulose phthalate (HPMCP), a fatty acid, a wax, shellac (esters of aleurtic acid), a plastic, a plant fiber, zein, Aqua-Zein (an aqueous zein formulation containing no alcohol), amylose starch, a starch derivative, a dextrin, a methyl acrylate-methacrylic acid copolymer, cellulose acetate succinate, hydroxypropyl methyl cellulose acetate succinate (hypromellose acetate succinate), a methyl methacrylate-methacrylic acid copolymer, or sodium alginate.

[069] In some embodiments, the enteric coating (e.g., the one enteric coating or the inner enteric coating and/or the outer enteric coating) comprises an anionic polymeric material.

[070] In some embodiments, the pharmaceutical agent comprises bacteria.

[071] In some embodiments, the pharmaceutical agent has one or more beneficial immune effects outside the gastrointestinal tract, e.g., when the solid dosage form is orally administered.

[072] In some embodiments, the pharmaceutical agent modulates immune effects outside the gastrointestinal tract in the subject, e.g., when the solid dosage form is orally administered.

[073] In some embodiments, the pharmaceutical agent causes a systemic effect (e.g., an effect outside of the gastrointestinal tract), e.g., when the solid dosage form is orally administered.

[074] In some embodiments, the pharmaceutical agent acts on immune cells and/or epithelial cells in the small intestine (e.g., causing a systemic effect (e.g., an effect outside of the gastrointestinal tract), e.g., when the solid dosage form is orally administered.

[075] In some embodiments, the pharmaceutical agent comprises isolated bacteria (e.g., from one or more strains of bacteria (e.g., bacteria of interest) (e.g., a therapeutically effective amount thereof)). E.g., wherein at least 5%, at least 10%, at least 25%, at least 50%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 99%

of the content of the pharmaceutical agent is the isolated bacteria (e.g., bacteria of interest).

[076] In some embodiments, the pharmaceutical agent comprises bacteria that have been gamma irradiated, UV irradiated, heat inactivated, acid treated, or oxygen sparged.

[077] In some embodiments, the pharmaceutical agent comprises live bacteria.

[078] In some embodiments, the pharmaceutical agent comprises dead bacteria.

[079] In some embodiments, the pharmaceutical agent comprises non-replicating bacteria.

[080] In some embodiments, the pharmaceutical agent comprises bacteria from one strain of bacteria.

[081] In some embodiments, the bacteria are lyophilized (e.g., the lyophilized product further comprises a pharmaceutically acceptable excipient) (e.g., a powder form).

[082] In some embodiments, the bacteria are gamma irradiated.

[083] In some embodiments, the bacteria are UV irradiated.

[084] In some embodiments, the bacteria are heat inactivated (e.g., at 50°C for two hours or at 90°C for two hours).

[085] In some embodiments, the bacteria are acid treated.

[086] In some embodiments, the bacteria are oxygen sparged (e.g., at 0.1 vvm for two hours).

[087] In some embodiments, the bacteria are Gram positive bacteria.

[088] In some embodiments, the bacteria are Gram negative bacteria.

[089] In some embodiments, the bacteria are aerobic bacteria.

[090] In some embodiments, the bacteria are anaerobic bacteria. In some embodiments, the anaerobic bacteria comprise obligate anaerobes. In some embodiments, the anaerobic bacteria comprise facultative anaerobes. In some embodiments, the bacteria are acidophile bacteria.

[091] In some embodiments, the bacteria are alkaliphile bacteria.

[092] In some embodiments, the bacteria are neutralophile bacteria.

[093] In some embodiments, the bacteria are fastidious bacteria.

[094] In some embodiments, the bacteria are nonfastidious bacteria.

[095] In some embodiments, the bacteria are of a taxonomic group (e.g., class, order, family, genus, species or strain) listed in Table 1, Table 2, Table 3, or Table 4.

[096] In some embodiments, the bacteria are a bacterial strain listed in Table 1, Table 2, Table 3, or Table 4.

[097] In some embodiments, the bacteria are of a taxonomic group (e.g., class, order, family, genus, species or strain) listed in Table J.

[098] In some embodiments, the bacteria are a bacterial strain listed in Table J.

[099] In some embodiments, the Gram negative bacteria belong to class *Negativicutes*.

[100] In some embodiments, the Gram negative bacteria belong to family *Veillonellaceae, Selenomonadaceae, Acidaminococcaceae*, or *Sporomusaceae*.

[101] In some embodiments, the bacteria of the genus *Megasphaera, Selenomonas, Propionospora,* or *Acidaminococcus.*

[102] In some embodiments, the bacteria are *Megasphaera* sp., *Selenomonas felix*, *Acidaminococcus intestini*, or *Propionospora* sp. bacteria.

[103] In some embodiments, the bacteria are of the genus *Lactococcus, Prevotella, Bifidobacterium,* or *Veillonell*a.

[104] In some embodiments, the bacteria are *Lactococcus lactis cremoris* bacteria.

[105] In some embodiments, the bacteria are *Prevotella histicola* bacteria.

[106] In some embodiments, the bacteria are *Bifidobacterium animalis* bacteria.

[107] In some embodiments, the bacteria are *Veillonella parvula* bacteria.

[108] In some embodiments, the bacteria are *Lactococcus lactis cremoris* bacteria. In some embodiments, the *Lactococcus lactis cremoris* bacteria are a strain comprising at least 90% (or at least 97%) genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Lactococcus lactis* cremoris Strain A (ATCC designation number PTA-125368). In some embodiments, the *Lactococcus* bacteria are a strain comprising at least 99% genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Lactococcus lactis cremoris* Strain A (ATCC designation number PTA-125368). In some embodiments, the *Lactococcus* bacteria are *Lactococcus lactis cremoris* Strain A (ATCC designation number PTA-125368).

[109] In some embodiments, the bacteria are *Prevotella* bacteria. In some embodiments, the *Prevotella* bacteria are a strain comprising at least 90% (or at least 97%) genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Prevotella* Strain B 50329 (NRRL accession number B 50329). In some embodiments, the *Prevotella* bacteria are a strain comprising at least 99% genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Prevotella* Strain B 50329 (NRRL accession

number B 50329). In some embodiments, the *Prevotella* bacteria are *Prevotella* Strain B 50329 (NRRL accession number B 50329).

[110] In some embodiments, the bacteria are *Bifidobacterium* bacteria. In some embodiments, the *Bifidobacterium* bacteria are from a strain comprising at least 90% (or at least 97%) genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Bifidobacterium* bacteria deposited as ATCC designation number PTA-125097. In some embodiments, the *Bifidobacterium* bacteria are a strain comprising at least 99% genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Bifidobacterium* bacteria deposited as ATCC designation number PTA-125097. In some embodiments, the *Bifidobacterium* bacteria are *Bifidobacterium* bacteria deposited as ATCC designation number PTA-125097.

[111] In some embodiments, the bacteria are *Veillonella* bacteria. In some embodiments, the *Veillonella* bacteria are a strain comprising at least 90% (or at least 97%) genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Veillonell*a bacteria deposited as ATCC designation number PTA-125691. In some embodiments, the *Veillonella* bacteria are a strain comprising at least 99% genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Veillonella* bacteria deposited as ATCC designation number PTA-125691. In some embodiments, the *Veillonella* bacteria are *Veillonella* bacteria deposited as ATCC designation number PTA-125691.

[112] In some embodiments, the bacteria are from *Ruminococcus gnavus* bacteria. In some embodiments, the *Ruminococcus gnavus* bacteria are a strain comprising at least 90% (or at least 97%) genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Ruminococcus gnavus* bacteria deposited as ATCC designation number PTA-126695. In some embodiments, the *Ruminococcus gnavus* bacteria are a strain comprising at least 99% genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Ruminococcus gnavus* bacteria deposited as ATCC designation number PTA-126695. In some embodiments, the *Ruminococcus gnavus* bacteria are *Ruminococcus gnavus* bacteria deposited as ATCC designation number PTA-126695.

[113] In some embodiments, the bacteria are *Megasphaera sp.* bacteria. In some embodiments, the *Megasphaera sp.* bacteria are a strain comprising at least 90% (or at least 97%) genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Megasphaera sp.* bacteria deposited as ATCC designation number PTA-126770. In some embodiments, the *Megasphaera sp.* bacteria are a strain comprising at least 99%

genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Megasphaera sp.* bacteria deposited as ATCC designation number PTA-126770. In some embodiments, the *Megasphaera sp.* bacteria are *Megasphaera sp.* bacteria deposited as ATCC designation number PTA-126770.

[114] In some embodiments, the bacteria are *Fournierella massiliensis* bacteria. In some embodiments, the *Fournierella massiliensis* bacteria are a strain comprising at least 90% (or at least 97%) genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Fournierella massiliensis* bacteria deposited as ATCC designation number PTA-126696. In some embodiments, the *Fournierella massiliensis* bacteria are a strain comprising at least 99% genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Fournierella massiliensis* bacteria deposited as ATCC designation number PTA-126696. In some embodiments, the *Fournierella massiliensis* bacteria are *Fournierella massiliensis* bacteria deposited as ATCC designation number PTA-126696.

[115] In some embodiments, the bacteria are *Harryflintia acetispora* bacteria. In some embodiments, the *Harryflintia acetispora* bacteria are a strain comprising at least 90% (or at least 97%) genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Harryflintia acetispora* bacteria deposited as ATCC designation number PTA-126694. In some embodiments, the *Harryflintia acetispora* bacteria are a strain comprising at least 99% genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Harryflintia acetispora* bacteria deposited as ATCC designation number PTA-126694. In some embodiments, the *Harryflintia acetispora* bacteria are *Harryflintia acetispora* bacteria deposited as ATCC designation number PTA-126694.

[116] In some embodiments, the bacteria are of the family *Acidaminococcaceae, Alcaligenaceae, Akkermansiaceae, Bacteriodaceae, Bifidobacteriaceae, Burkholderiaceae, Catabacteriaceae, Clostridiaceae, Coriobacteriaceae, Enterobacteriaceae, Enterococcaceae, Fusobacteriaceae, Lachnospiraceae, Listeraceae, Mycobacteriaceae, Neisseriaceae, Odoribacteraceae, Oscillospiraceae, Peptococcaceae, Peptostreptococcaceae, Porphyromonadaceae, Prevotellaceae, Propionibacteraceae, Rikenellaceae, Ruminococcaceae, Selenomonadaceae, Sporomusaceae, Streptococcaceae, Streptomycetaceae, Sutterellaceae, Synergistaceae,* or *Veillonellaceae*.

[117] In some embodiments, the bacteria are of the genus *Akkermansia, Christensenella, Blautia, Enterococcus, Eubacterium, Roseburia, Bacteroides, Parabacteroides*, or *Erysipelatoclostridium*.

[118] In some embodiments, the bacteria are *Blautia hydrogenotrophica, Blautia stercoris, Blautia wexlerae, Eubacterium faecium, Eubacterium contortum, Eubacterium rectale, Enterococcus faecalis, Enterococcus durans, Enterococcus villorum, Enterococcus gallinarum; Bifidobacterium lactis, Bifidobacterium bifidium, Bifidobacterium longum, Bifidobacterium animalis,* or *Bifidobacterium breve* bacteria.

[119] In some embodiments, the bacteria are *BCG (bacillus Calmette-Guerin), Parabacteroides, Blautia, Veillonella, Lactobacillus salivarius, Agathobaculum, Ruminococcus gnavus, Paraclostridium benzoelyticum, Turicibacter sanguinus, Burkholderia, Klebsiella quasipneumoniae ssp similpneumoniae, Klebsiella oxytoca, Tyzzerela nexilis*, or *Neisseria* bacteria.

[120] In some embodiments, the bacteria are *Blautia hydrogenotrophica* bacteria.

[121] In some embodiments, the bacteria are *Blautia stercoris* bacteria.

[122] In some embodiments, the bacteria are *Blautia wexlerae* bacteria.

[123] In some embodiments, the bacteria are *Enterococcus gallinarum* bacteria.

[124] In some embodiments, the bacteria are *Enterococcus faecium* bacteria.

[125] In some embodiments, the bacteria are *Bifidobacterium bifidium* bacteria.

[126] In some embodiments, the bacteria are *Bifidobacterium breve* bacteria.

[127] In some embodiments, the bacteria are *Bifidobacterium longum* bacteria.

[128] In some embodiments, the bacteria are *Roseburia hominis* bacteria.

[129] In some embodiments, the bacteria are *Bacteroides thetaiotaomicron* bacteria.

[130] In some embodiments, the bacteria are *Bacteroides coprocola* bacteria.

[131] In some embodiments, the bacteria are *Erysipelatoclostridium ramosum* bacteria.

[132] In some embodiments, the bacteria are *Megasphera massiliensis* bacteria.

[133] In some embodiments, the bacteria are *Eubacterium* bacteria.

[134] In some embodiments, the bacteria are *Parabacteroides distasonis* bacteria.

[135] In some embodiments, the bacteria are *Lactobacillus plantarum* bacteria.

[136] In some embodiments, the bacteria are bacteria of the *Negativicutes* class.

[137] In some embodiments, the bacteria are of the *Veillonellaceae* family.

[138] In some embodiments, the bacteria are of the *Selenomonadaceae* family.

[139] In some embodiments, the bacteria are of the *Acidaminococcaceae* family.

[140] In some embodiments, the bacteria are of the *Sporomusaceae* family.

[141] In some embodiments, the bacteria are of the *Megasphaera* genus.

[142] In some embodiments, the bacteria are of the *Selenomonas* genus.

[143] In some embodiments, the bacteria are of the *Propionospora* genus.

[144] In some embodiments, the bacteria are of the *Acidaminococcus* genus.

[145] In some embodiments, the bacteria are *Megasphaera sp.* bacteria.

[146] In some embodiments, the bacteria are *Selenomonas felix* bacteria.

[147] In some embodiments, the bacteria are *Acidaminococcus intestini* bacteria.

[148] In some embodiments, the bacteria are *Propionospora sp.* bacteria.

[149] In some embodiments, the bacteria are bacteria of the *Clostridia* class.

[150] In some embodiments, the bacteria are of the *Oscillospriraceae* family.

[151] In some embodiments, the bacteria are of the *Faecalibacterium* genus.

[152] In some embodiments, the bacteria are of the *Fournierella* genus.

[153] In some embodiments, the bacteria are of the *Harryflintia* genus.

[154] In some embodiments, the bacteria are of the *Agathobaculum* genus.

[155] In some embodiments, the bacteria are *Faecalibacterium prausnitzii* (e.g., *Faecalibacterium prausnitzii* Strain A) bacteria.

[156] In some embodiments, the bacteria are *Fournierella massiliensis* (e.g., *Fournierella massiliensis* Strain A) bacteria.

[157] In some embodiments, the bacteria are *Harryflintia acetispora* (e.g., *Harryflintia acetispora* Strain A) bacteria.

[158] In some embodiments, the bacteria are *Agathobaculum sp.* (e.g., *Agathobaculum sp.* Strain A) bacteria.

[159] In some embodiments, the bacteria are a strain of *Agathobaculum sp.* In some embodiments, the Agathobaculum *sp.* strain is a strain comprising at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity (e.g., at least 99.5% sequence identity, at least 99.6% sequence identity, at least 99.7% sequence identity, at least 99.8% sequence identity, at least 99.9% sequence identity) to the nucleotide sequence (e.g., genomic sequence, 16S sequence, CRISPR sequence) of the *Agathobaculum sp.* Strain A (ATCC Deposit Number PTA-125892). In some embodiments, the *Agathobaculum sp.* strain is the Agathobaculum sp. Strain A (ATCC Deposit Number PTA- 125892).

[160] In some embodiments, the bacteria are of the class *Bacteroidia* [phylum *Bacteroidota*]. In some embodiments, the bacteria are of order *Bacteroidales*. In some embodiments, the bacteria are of the family *Porphyromonoadaceae*. In some embodiments, the bacteria are of the family *Prevotellaceae*. In some embodiments, the bacteria are of the class *Bacteroidia* wherein the cell envelope structure of the bacteria is diderm. In some embodiments, the bacteria are of the class *Bacteroidia* that stain Gram negative. In some embodiments, the bacteria are of the class *Bacteroidia* wherein the bacteria is diderm and the bacteria stain Gram negative.

[161] In some embodiments, the bacteria are of the class *Clostridia* [phylum *Firmicutes*]. In some embodiments, the bacteria are of the order *Eubacteriales*. In some embodiments, the bacteria are of the family *Oscillispiraceae*. In some embodiments, the bacteria are of the family *Lachnospiraceae*. In some embodiments, the bacteria are of the family *Peptostreptococcaceae*. In some embodiments, the bacteria are of the family *Clostridiales family XIII/ Incertae sedis 41*. In some embodiments, the bacteria are of the class *Clostridia* wherein the cell envelope structure of the bacteria is monoderm. In some embodiments, the bacteria are of the class *Clostridia* that stain Gram negative. In some embodiments, the bacteria are of the class *Clostridia* that stain Gram positive. In some embodiments, the bacteria are of the class *Clostridia* wherein the cell envelope structure of the bacteria is monoderm and the bacteria stain Gram negative. In some embodiments, the bacteria are of the class *Clostridia* wherein the cell envelope structure of the bacteria is monoderm and the bacteria stain Gram positive.

[162] In some embodiments, the bacteria are of the class *Negativicutes* [phylum *Firmicutes*]. In some embodiments, the bacteria are of the order *Veillonellales*. In some embodiments, the bacteria are of the family *Veillonelloceae*. In some embodiments, the bacteria are of the order *Selenomonadales*. In some embodiments, the bacteria are of the family *Selenomonadaceae*. In some embodiments, the bacteria are of the family *Sporomusaceae*. In some embodiments, the bacteria are of the class *Negativicutes* wherein the cell envelope structure of the bacteria is diderm. In some embodiments, the bacteria are of the class *Negativicutes* that stain Gram negative. In some embodiments, the bacteria are of the class *Negativicutes* wherein the cell envelope structure of the bacteria is diderm and the bacteria stain Gram negative.

[163] In some embodiments, the bacteria are of the class *Synergistia* [phylum *Synergistota*]. In some embodiments, the bacteria are of the order *Synergistales*. In some

embodiments, the bacteria are of the family *Synergistaceae*. In some embodiments, the bacteria are of the class *Synergistia* wherein the cell envelope structure of the bacteria is diderm. In some embodiments, the bacteria are of the class *Synergistia* that stain Gram negative. In some embodiments, the bacteria are of the class *Synergistia* wherein the cell envelope structure of the bacteria is diderm and the bacteria stain Gram negative.

[164] In some embodiments, the bacteria are bacteria that produce metabolites, e.g., the bacteria produce butyrate, iosine, proprionate, or tryptophan metabolites.

[165] In some embodiments, the bacteria produce butyrate. In some embodiments, the bacteria are from the genus *Blautia; Christensella; Copracoccus; Eubacterium; Lachnosperacea; Megasphaera;* or *Roseburia*.

[166] In some embodiments, the bacteria produce iosine. In some embodiments, the bacteria are from the genus *Bifidobacterium; Lactobacillus;* or *Olsenella*.

[167] In some embodiments, the bacteria produce proprionate. In some embodiments, the bacteria are from the genus *Akkermansia; Bacteriodes; Dialister; Eubacterium; Megasphaera; Parabacteriodes; Prevotella; Ruminococcus*; or *Veillonella*.

[168] In some embodiments, the bacteria produce tryptophan metabolites. In some embodiments, the bacteria are from the genus *Lactobacillus* or *Peptostreptococcus*.

[169] In some embodiments, the bacteria are bacteria that produce inhibitors of histone deacetylase 3 (HDAC3). In some embodiments, the bacteria are from the species *Bariatricus massiliensis, Faecalibacterium prausnitzii, Megasphaera massiliensis* or *Roseburia intestinalis.*

[170] In some embodiments, the bacteria are of the genus *Cutibacterium*.

[171] In some embodiments, the bacteria are *Cutibacterium avidum.*

[172] In some embodiments, the bacteria are from the genus *Lactobacillus*.

[173] In some embodiments, the bacteria are from the species *Lactobacillus gasseri*.

[174] In some embodiments, the bacteria are from the genus *Dysosmobacter*.

[175] In some embodiments, the bacteria are from the species *Dysosmobacter welbionis*.

[176] In some embodiments, the bacteria of the genus *Leuconostoc*.

[177] In some embodiments, the bacteria of the genus *Lactobacillus*.

[178] In some embodiments, the bacteria are of the genus *Akkermansia*; *Bacillus*; *Blautia*; *Cupriavidus*; *Enhydrobacter*; *Faecalibacterium*; *Lactobacillus*; *Lactococcus*; *Micrococcus*; *Morganella*; *Propionibacterium*; *Proteus*; *Rhizobium*; or *Streptococcus*.

[179] In some embodiments, the bacteria are *Leuconostoc holzapfelii* bacteria.

[180] In some embodiments, the bacteria are *Akkermansia muciniphila*; *Cupriavidus metallidurans*; *Faecalibacterium prausnitzii*; *Lactobacillus casei*; *Lactobacillus plantarum*; *Lactobacillus paracasei*; *Lactobacillus plantarum*; *Lactobacillus rhamnosus*; *Lactobacillus sakei*; or *Streptococcus pyogenes* bacteria.

[181] In some embodiments, the bacteria are *Lactobacillus casei*; *Lactobacillus plantarum*; *Lactobacillus paracasei*; *Lactobacillus plantarum*; *Lactobacillus rhamnosus*; or *Lactobacillus sakei* bacteria.

[182] In some embodiments, the bacteria are *Megasphaera sp.* bacteria (e.g., from the strain with accession number NCIMB 43385, NCIMB 43386 or NCIMB 43387).

[183] In some embodiments, the bacteria are *Megasphaera massiliensis* bacteria (e.g., from the strain with accession number NCIMB 42787, NCIMB 43388 or NCIMB 43389).

[184] In some embodiments, the bacteria are *Megasphaera massiliensis* bacteria (e.g., from the strain with accession number DSM 26228).

[185] In some embodiments, the bacteria are *Bacillus amyloliquefaciens* bacteria (e.g., from the strain with accession number NCIMB 43088, NCIMB 43087, or NCIMB 43086).

[186] In some embodiments, the bacteria are *Parabacteroides distasonis* bacteria (e.g., from the strain with accession number NCIMB 42382).

[187] In some embodiments, the bacteria are *Megasphaera massiliensis* bacteria (e.g., from the strain with accession number NCIMB 43388 or NCIMB 43389), or a derivative thereof. See, e.g., WO 2020/120714. In some embodiments, the *Megasphaera massiliensis* bacteria is a strain comprising at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity (e.g., at least 99.5% sequence identity, at least 99.6% sequence identity, at least 99.7% sequence identity, at least 99.8% sequence identity, at least 99.9% sequence identity) to the nucleotide sequence (e.g., genomic sequence, 16S sequence, and/or CRISPR sequence) of *Megasphaera massiliensis* bacteria from the strain with accession number NCIMB 43388 or NCIMB 43389. In some embodiments, the *Megasphaera massiliensis* bacteria is the strain with accession number NCIMB 43388 or NCIMB 43389.

[188] In some embodiments, the bacteria are *Megasphaera massiliensis* bacteria strain deposited under accession number NCIMB 42787, or a derivative thereof. See, e.g., WO 2018/229216. In some embodiments, the *Megasphaera massiliensis* bacteria is a strain comprising at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least

97%, at least 98%, or at least 99% sequence identity (e.g., at least 99.5% sequence identity, at least 99.6% sequence identity, at least 99.7% sequence identity, at least 99.8% sequence identity, at least 99.9% sequence identity) to the nucleotide sequence (e.g., genomic sequence, 16S sequence, and/or CRISPR sequence) of the *Megasphaera massiliensis* bacteria strain deposited under accession number NCIMB 42787. In some embodiments, the *Megasphaera massiliensis* bacteria is the strain deposited under accession number NCIMB 42787.

[189] In some embodiments, the bacteria are *Megasphaera spp.* bacteria from the strain with accession number NCIMB 43385, NCIMB 43386 or NCIMB 43387, or a derivative thereof. See, e.g., WO 2020/120714. In some embodiments, the *Megasphaera sp.* bacteria is a strain comprising at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity (e.g., at least 99.5% sequence identity, at least 99.6% sequence identity, at least 99.7% sequence identity, at least 99.8% sequence identity, at least 99.9% sequence identity) to the nucleotide sequence (e.g., genomic sequence, 16S sequence, and/or CRISPR sequence) of the *Megasphaera sp.* from a strain with accession number NCIMB 43385, NCIMB 43386 or NCIMB 43387. In some embodiments, the *Megasphaera sp.* bacteria is the strain with accession number NCIMB 43385, NCIMB 43386 or NCIMB 43387.

[190] In some embodiments, the bacteria are *Parabacteroides distasonis* bacteria deposited under accession number NCIMB 42382, or a derivative thereof. See, e.g., WO 2018/229216. In some embodiments, the *Parabacteroides distasonis* bacteria is a strain comprising at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity (e.g., at least 99.5% sequence identity, at least 99.6% sequence identity, at least 99.7% sequence identity, at least 99.8% sequence identity, at least 99.9% sequence identity) to the nucleotide sequence (e.g., genomic sequence, 16S sequence, and/or CRISPR sequence) of the *Parabacteroides distasonis* bacteria deposited under accession number NCIMB 42382. In some embodiments, the *Parabacteroides distasonis* bacteria is the strain deposited under accession number NCIMB 42382.

[191] In some embodiments, the bacteria are *Megasphaera massiliensis* bacteria deposited under accession number DSM 26228, or a derivative thereof. See, e.g., WO 2018/229216. In some embodiments, the *Megasphaera massiliensis* bacteria is a strain comprising at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least

97%, at least 98%, or at least 99% sequence identity (e.g., at least 99.5% sequence identity, at least 99.6% sequence identity, at least 99.7% sequence identity, at least 99.8% sequence identity, at least 99.9% sequence identity) to the nucleotide sequence (e.g., genomic sequence, 16S sequence, and/or CRISPR sequence) of *Megasphaera massiliensis* bacteria deposited under accession number DSM 26228. In some embodiments, the *Megasphaera massiliensis* bacteria is the strain deposited under accession number DSM 26228.

[192] In some embodiments, the bacteria are *Bacillus amyloliquefaciens* bacteria (e.g., from the strain with accession number NCIMB 43088, NCIMB 43087, or NCIMB 43086, or a derivative thereof. See, e.g., WO 2019/236806. In some embodiments, the *Bacillus amyloliquefaciens* bacteria is a strain comprising at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity (e.g., at least 99.5% sequence identity, at least 99.6% sequence identity, at least 99.7% sequence identity, at least 99.8% sequence identity, at least 99.9% sequence identity) to the nucleotide sequence (e.g., genomic sequence, 16S sequence, and/or CRISPR sequence) of *Bacillus amyloliquefaciens* bacteria from the strain with accession number NCIMB 43088, NCIMB 43087, or NCIMB 43086. In some embodiments, the *Bacillus amyloliquefaciens* bacteria is the strain with accession number NCIMB 43088, NCIMB 43087, or NCIMB 43086. In some embodiments, the *Bacillus amyloliquefaciens* bacteria is the strain with accession number NCIMB 43088.

[193] In some embodiments, the pharmaceutical agent comprises bacteria and the dose of bacteria is about 1×10^7 to about 2×10^{12} (e.g., about 3×10^{10} or about 1.5×10^{11} or about 1.5×10^{12}) cells (e.g., wherein cell number is determined by total cell count, which is determined by Coulter counter), wherein the dose is per capsule or tablet or per total number of minitablets in a capsule. In some embodiments, the pharmaceutical agent comprises bacteria and the dose of bacteria is about 1×10^{10} to about 2×10^{12} (e.g., about 1.6×10^{11} or about 8×10^{11} or about 9.6×10^{11} about 12.8×10^{11} or about 1.6×10^{12}) cells (e.g., wherein cell number is determined by total cell count, which is determined by Coulter counter), wherein the dose is per capsule or tablet or per total number of minitablets in a capsule.

[194] In some embodiments, the pharmaceutical agent comprises bacteria and the dose of bacteria is about 1×10^9, about 3×10^9, about 5×10^9, about 1.5×10^{10}, about 3×10^{10},

about 5 x 10^{10}, about 1.5 x 10^{11}, about 1.5 x 10^{12}, or about 2 x 10^{12} cells, wherein the dose is per capsule or tablet or per total number of minitablets in a capsule.

[195] In some embodiments, the pharmaceutical agent comprises a powder comprising bacteria and the dose of the pharmaceutical agent (e.g., a powder comprising bacteria) is about 10 mg to about 3500 mg, wherein the dose is per capsule or tablet or per total number of minitablets in a capsule.

[196] In some embodiments, the pharmaceutical agent comprises a powder comprising bacteria and the dose of the pharmaceutical agent (e.g., a powder comprising bacteria) is about 30 mg to about 1300 mg (by weight of bacteria powder) (about 25, about 30, about 35, about 50, about 75, about 100, about 120, about 150, about 250, about 300, about 350, about 400, about 500, about 600, about 700, about 750, about 800, about 900, about 1000, about 1100, about 1200, about 1250, about 1300, about 2000, about 2500, about 3000, or about 3500 mg wherein the dose is per capsule or tablet or per total number of minitablets in a capsule.

[197] In some embodiments, the pharmaceutical agent comprises bacteria and the dose of pharmaceutical agent (e.g., bacteria) is about 2x10^{6} to about 2x10^{16} particles (e.g., wherein particle count is determined by NTA (nanoparticle tracking analysis)), wherein the dose is per capsule or tablet or per total number of minitablets in a capsule.

[198] In some embodiments, the pharmaceutical agent comprises bacteria and the dose of pharmaceutical agent (e.g., bacteria) is about 5 mg to about 900 mg total protein (e.g., wherein total protein is determined by Bradford assay or BCA), wherein the dose is per capsule or tablet or per total number of minitablets in a capsule.

[199] In some embodiments, the solid dosage form further comprises one or more additional therapeutic agents.

[200] In some aspects, the disclosure provides a method of treating a subject (e.g., human) (e.g., a subject in need of treatment), the method comprising administering to the subject a pharmaceutical agent, a pharmaceutical composition or a solid dosage form provided herein. In some aspects, the disclosure provides use of a pharmaceutical agent, a pharmaceutical composition or a solid dosage form provided herein for the preparation of a medicament for treating a subject (e.g., human) (e.g., a subject in need of treatment).

[201] In some embodiments, the pharmaceutical agent, pharmaceutical composition or solid dosage form is orally administered (e.g., is for oral administration).

[202] In some embodiments, the pharmaceutical agent, pharmaceutical composition or solid dosage form is administered to a subject that is in a fed or fasting state. In some embodiments, the pharmaceutical agent, pharmaceutical composition or solid dosage form is administered to a subject on an empty stomach (e.g., one hour before eating or two hours after eating). In some embodiments, the pharmaceutical agent, pharmaceutical composition or solid dosage form is administered to a subject one hour before eating. In some embodiments, the pharmaceutical agent, pharmaceutical composition or solid dosage form is administered to a subject two hours after eating.

[203] In some embodiments, the pharmaceutical agent, pharmaceutical composition or solid dosage form is administered (e.g., is for administration) 1, 2, 3, or 4 times a day.

[204] In some embodiments, the pharmaceutical composition or solid dosage form provides release of the pharmaceutical agent in the small intestine, e.g., in the upper small intestine, of the pharmaceutical agent contained in the solid dosage form.

[205] In some embodiments, the pharmaceutical composition or solid dosage form delivers the pharmaceutical agent to the small intestine, wherein the pharmaceutical agent can act on immune cells and/or epithelial cells in the small intestine, e.g., in the upper small intestine, e.g., to cause effects throughout the body (e.g., systemic effect).

[206] In some embodiments, the pharmaceutical agent provides one or more beneficial immune effects outside the gastrointestinal tract, e.g., when orally administered.

[207] In some embodiments, the pharmaceutical agent modulates immune effects outside the gastrointestinal tract in the subject, e.g., when orally administered.

[208] In some embodiments, the pharmaceutical agent causes a systemic effect (e.g., an effect outside of the gastrointestinal tract), e.g., when orally administered.

[209] In some embodiments, the pharmaceutical agent acts on immune cells and/or epithelial cells in the small intestine (e.g., upper small intestine) (e.g., causing a systemic effect (e.g., an effect outside of the gastrointestinal tract), e.g., when orally administered.

[210] In some embodiments, the pharmaceutical agent, pharmaceutical composition or solid dosage form is administered orally and has one or more beneficial immune effects outside the gastrointestinal tract (e.g., interaction between the agent and cells in the small intestine modulates a systemic immune response).

[211] In some embodiments, the pharmaceutical agent, pharmaceutical composition or solid dosage form is administered orally and modulates immune effects outside the

gastrointestinal tract (e.g., interaction between agent and cells in the small intestine (e.g., upper small intestine) modulates a systemic immune response).

[212] In some embodiments, the pharmaceutical agent, pharmaceutical composition or solid dosage form is administered orally and activates innate antigen presenting cells (e.g., in the small intestine, e.g., upper small intestine).

[213] In some embodiments, the subject is in need of treatment (and/or prevention) of a cancer.

[214] In some embodiments, the subject is in need of treatment (and/or prevention) of an autoimmune disease.

[215] In some embodiments, the subject is in need of treatment (and/or prevention) of an inflammatory disease.

[216] In some embodiments, the subject is in need of treatment (and/or prevention) of a metabolic disease.

[217] In some embodiments, the subject is in need of treatment (and/or prevention) of a dysbiosis.

[218] In some embodiments, the pharmaceutical agent, pharmaceutical composition or solid dosage form is administered in combination with a therapeutic agent (e.g., additional therapeutic agent).

[219] In some aspects, the disclosure provides a cryoprotectant solution, e.g., for use in preparing a pharmaceutical agent, e.g, that comprises bacteria, as described herein.

[220] In some aspects, the disclosure provides a method comprising combining bacteria (e.g., a pellet comprising bacteria) with a cryoprotectant solution, thereby preparing a formulated paste. In some embodiments, the disclosure provides a formulated paste prepared by this method.

[221] In some embodiments, the method further comprises freeze drying the formulated paste, to thereby prepare a freeze-dried product. In some embodiments, the freeze drying comprises primary drying. In some embodiments, the freeze drying comprises primary drying and secondary drying. In some embodiments, the disclosure provides a freeze-dried product prepared by this method.

[222] In some embodiments, the method further comprises milling the freeze-dried product, to thereby prepare a freeze-dried powder (e.g., powder, e.g., pharmaceutical agent). In some embodiments, the disclosure provides a pharmaceutical agent prepared by this method.

[223] In some embodiments, the method further comprises combining the freeze-dried powder with one or more excipients to thereby prepare a pharmaceutical composition. In some embodiments, the disclosure provides a pharmaceutical composition prepared by this method.

[224] In some embodiments, the cryoprotectant solution is mixed with the pellet in a ratio of about 0.2 to about 0.5 gram (g) cryoprotectant solution per gram of pellet; about 0.05 to about 0.25 gram (g) cryoprotectant solution per gram of pellet; about 0.06 to about 0.1 gram (g) cryoprotectant solution per gram of pellet; or about 0.15 to about 0.2 gram (g) cryoprotectant solution per gram of pellet. In some embodiments, the cryoprotectant solution is mixed with the pellet in a ratio of about 0.4 gram (g) cryoprotectant solution per gram of pellet. In some embodiments, the cryoprotectant solution is mixed with the pellet in a ratio of about 0.18 gram (g) cryoprotectant solution per gram of pellet. In some embodiments, the cryoprotectant solution is mixed with the pellet in a ratio of about 0.1 gram (g) cryoprotectant solution per gram of pellet. In some embodiments, the cryoprotectant solution is mixed with the pellet in a ratio of about 0.08 gram (g) cryoprotectant solution per gram of pellet.

[225] In some embodiments, the cryoprotectant solution is mixed with the pellet at a ratio of 4 % to 10% (volume/volume), e.g., 5 % to 8% (volume/volume). In some embodiments, the cryoprotectant solution is mixed with the pellet at a ratio of about 6.5% (volume/volume).

[226] In some embodiments, the cryoprotectant solution comprises sucrose. In some embodiments, the cryoprotectant solution comprises dextran. In some embodiments, the cryoprotectant solution comprises sucrose and dextran. In some embodiments, the cryoprotectant solution comprises sucrose and dextran in equivalent amounts (e.g., on a percent weight by weight basis). In some embodiments, the cryoprotectant solution comprises sucrose, dextran, and L-cysteine HCl. In some embodiments, the cryoprotectant solution does not comprise L-cysteine HCl.

[227] In some embodiments, the cryoprotectant solution comprises about 10% to about 30% (weight/weight) sucrose. In some embodiments, the cryoprotectant solution comprises about 15% to about 35% (weight/weight) sucrose. In some embodiments, the cryoprotectant solution comprises about 20% (weight/weight) sucrose.

[228] In some embodiments, the cryoprotectant solution comprises about 10% to about 30% (weight/weight) dextran. In some embodiments, the cryoprotectant solution

comprises about 15% to about 35% (weight/weight) dextran. In some embodiments, the cryoprotectant solution comprises about 20% (weight/weight) dextran.

[229] In some embodiments, the cryoprotectant solution comprises about 10% to about 30% (weight/weight) sucrose and about 10% to about 30% (weight/weight) dextran. In some embodiments, the cryoprotectant solution comprises about 15% to about 35% (weight/weight) sucrose and about 15% to about 35% (weight/weight) dextran. In some embodiments, the cryoprotectant solution comprises about 20% (weight/weight) sucrose and about 20% (weight/weight) dextran.

[230] In some embodiments, the cryoprotectant solution comprises about 40% to about 80% (weight/weight) water. In some embodiments, the cryoprotectant solution comprises about 50% to about 70% (weight/weight) water. In some embodiments, the cryoprotectant solution comprises about 55% to about 65% (weight/weight) water. In some embodiments, the cryoprotectant solution comprises about 60% (weight/weight) water.

[231] In some embodiments, the cryoprotectant solution comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant solution comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant solution comprises about 0.15% to about 0.45% (weight/weight) L-cysteine HCl.

[232] In some embodiments, the cryoprotectant solution comprises about 0.2% (weight/weight) L-cysteine HCl.

[233] In some embodiments, the cryoprotectant solution comprises about 59.8% (weight/weight) water.

[234] In some embodiments, the cryoprotectant solution comprises about 0.4% (weight/weight) L-cysteine HCl.

[235] In some embodiments, the cryoprotectant solution comprises about 59.6% (weight/weight) water.

[236] In certain embodiments, the cryoprotectant solution provided herein comprises: (i) about 20% (weight/weight) sucrose; (ii) about 20% (weight/weight) dextran; (iii) about 0.4% (weight/weight) L-cysteine HCl; and (iv) about 59.6% (weight/weight) water.

[237] In certain embodiments, the cryoprotectant solution provided herein comprises: (i) about 20% (weight/weight) sucrose; (ii) about 20% (weight/weight) dextran; (iii) about 0.2% (weight/weight) L-cysteine HCl; and (iv) about 59.8% (weight/weight) water.

[238] In certain embodiments, the cryoprotectant solution provided herein comprises: (i) about 20% (weight/weight) sucrose; (ii) about 20% (weight/weight) dextran; and (iii) about 60% (weight/weight) water.

[239] In some embodiments, the cryoprotectant (e.g., dry composition not containing water) comprises about 40% to about 60% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 45% to about 55% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 50% (weight/weight) sucrose.

[240] In some embodiments, the cryoprotectant comprises about 40% to about 60% (weight/weight) dextran. In some embodiments, the cryoprotectant comprises about 45% to about 55% (weight/weight) dextran. In some embodiments, the cryoprotectant comprises about 50% (weight/weight) dextran.

[241] In some embodiments, the cryoprotectant comprises about 40% to about 60% (weight/weight) sucrose and 40% to about 60% (weight/weight) dextran. In some embodiments, the cryoprotectant comprises about 45% to about 55% (weight/weight) sucrose and about 45% to about 55% (weight/weight) dextran. In some embodiments, the cryoprotectant comprises about 50% (weight/weight) sucrose and about 50% (weight/weight) dextran.

[242] In some embodiments, the cryoprotectant comprises about 0.25% to about 5% (weight/weight) L-cysteine HCl (e.g., a form of L-cysteine). In some embodiments, the cryoprotectant comprises about 0.5% to about 2.5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant comprises about 0.75% to about 1.5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant comprises about 1% (weight/weight) L-cysteine HCl.

[243] In certain embodiments, the cryoprotectant provided herein comprises: (i) about 50% (weight/weight) sucrose; (ii) about 50% (weight/weight) dextran; and (iii) about 1% (weight/weight) L-cysteine HCl.

[244] In certain embodiments, the cryoprotectant provided herein comprises: (i) about 50% (weight/weight) sucrose; and (ii) about 50% (weight/weight) dextran.

[245] In some embodiments, the freeze-dried powder comprises about 6% to about 12% (weight/weight) sucrose. In some embodiments, the freeze-dried powder comprises about 8% to about 12% (weight/weight) sucrose. In some embodiments, the freeze-dried powder comprises about 11% (weight/weight) sucrose. In some embodiments, the freeze-

dried powder comprises about 6% to about 12% (weight/weight) dextran. In some embodiments, the freeze-dried powder comprises about 8% to about 12% (weight/weight) dextran. In some embodiments, the freeze-dried powder comprises about 11% (weight/weight) dextran. In some embodiments, the freeze-dried powder comprises about 6% to about 12% (weight/weight) sucrose and about 6% to about 12% (weight/weight) dextran. In some embodiments, the freeze-dried powder comprises about 8% to about 12% (weight/weight) sucrose and about 8% to about 12% (weight/weight) dextran. In some embodiments, the freeze-dried powder comprises about 11% (weight/weight) sucrose and about 11% (weight/weight) dextran. In some embodiments, the freeze-dried powder comprises about 0.01% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.1% to about 0.3% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.15% to about 0.25% (weight/weight) L-cysteine HCl.

[246] In some embodiments, the pharmaceutical agent comprises about 7% to about 21% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 10% to about 19% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 15% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 7% to about 21% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 10% to about 19% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 15% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 7% to about 21% (weight/weight) sucrose and about 7% to about 21% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 10% to about 19% (weight/weight) sucrose and about 10% to about 19% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 15% (weight/weight) sucrose and about 15% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 0.01% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.1% to about 0.4% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.15% to about 0.35% (weight/weight) L-cysteine HCl.

[247] In some embodiments, the freeze-dried powder comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as

a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the freeze-dried powder comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the freeze-dried powder comprises about 26% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the freeze-dried powder comprises about 21% to about 29% (weight/weight) sucrose. In some embodiments, the freeze-dried powder comprises about 23% to about 27% (weight/weight) sucrose. In some embodiments, the freeze-dried powder comprises about 25% (weight/weight) sucrose. In some embodiments, the freeze-dried powder comprises about 6% to about 11% (weight/weight) dextrose. In some embodiments, the freeze-dried powder comprises about 7% to about 10% (weight/weight) dextrose. In some embodiments, the freeze-dried powder comprises about 9% (weight/weight) dextrose. In some embodiments, the freeze-dried powder comprises about 4% to about 10% (weight/weight) glutamate. In some embodiments, the freeze-dried powder comprises about 5% to about 9% (weight/weight) glutamate. In some embodiments, the freeze-dried powder comprises about 7% (weight/weight) glutamate.

[248] In some embodiments, the freeze-dried powder comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 21% to about 29% (weight/weight) sucrose. In some embodiments, the freeze-dried powder comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 23% to about 27% (weight/weight) sucrose. In some embodiments, the freeze-dried powder comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl. In some embodiments, the freeze-dried powder comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl.

[249] In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 21% to about 29% (weight/weight) sucrose; and about 6% to about 11% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises

about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 21% to about 29% (weight/weight) sucrose; and about 4% to about 10% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 21% to about 29% (weight/weight) sucrose; about 6% to about 11% (weight/weight) dextrose; and about 4% to about 10% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 23% to about 27% (weight/weight) sucrose; and about 7% to about 10% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); 23% to about 27% (weight/weight) sucrose; and about 5% to about 9% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); 23% to about 27% (weight/weight) sucrose; about 7% to about 1% (weight/weight) dextrose; and about 5% to about 9% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl.

[250] In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the pharmaceutical agent comprises about 26% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose

syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the pharmaceutical agent comprises about 21% to about 29% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 23% to about 27% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 25% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 6% to about 11% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 7% to about 10% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 9% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 4% to about 10% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 5% to about 9% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 7% (weight/weight) glutamate.

[251] In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 21% to about 29% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 23% to about 27% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl.

[252] In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 21% to about 29% (weight/weight) sucrose; and about 6% to about 11% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 21% to about 29% (weight/weight) sucrose; and about 4% to about 10% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent

comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 21% to about 29% (weight/weight) sucrose; about 6% to about 11% (weight/weight) dextrose; and about 4% to about 10% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 23% to about 27% (weight/weight) sucrose; and about 7% to about 10% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); 23% to about 27% (weight/weight) sucrose; and about 5% to about 9% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); 23% to about 27% (weight/weight) sucrose; about 7% to about 1% (weight/weight) dextrose; and about 5% to about 9% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl.

[253] In some embodiments, the cryoprotectant comprises a dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the cryoprotectant comprises sucrose. In some embodiments, the cryoprotectant comprises dextrose (also referred to as glucose). In some embodiments, the cryoprotectant comprises monosodium glutamate. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and sucrose. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and sucrose in equivalent amounts (e.g., on a percent weight by weight basis). In some embodiments, the cryoprotectant comprises dried (dehydrated) maize

glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, and dextrose. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, and monosodium glutamate. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, dextrose, and monosodium glutamate. In some embodiments, the cryoprotectant comprises dextrose and monosodium glutamate in equivalent amounts (e.g., on a percent weight by weight basis). In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, dextrose, monosodium glutamate, and L-cysteine HCl (e.g., a form of L-cysteine). In some embodiments, the cryoprotectant does not comprise L-cysteine HCl.

[254] In some embodiments, the cryoprotectant (e.g., dry composition not containing water) comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21).

[255] In some embodiments, the cryoprotectant (e.g., dry composition not containing water) comprises about 27% to about 47% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) sucrose.

[256] In some embodiments, the cryoprotectant comprises about 8% to about 18% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 11% to about 15% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 13% (weight/weight) dextrose.

[257] In some embodiments, the cryoprotectant comprises about 8% to about 18% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 11% to about 15% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 13% (weight/weight) monosodium glutamate.

[258] In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 27% to about 47% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 32% to about 42% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 37% (weight/weight) sucrose.

[259] In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 27% to about 47% (weight/weight) sucrose; and about 8% to about 18% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 27% to about 47% (weight/weight) sucrose; and about 8% to about 18% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 27% to about 47% (weight/weight) sucrose; about 8% to about 18% (weight/weight) dextrose; and about 8% to about 18% (weight/weight) monosodium glutamate.

[260] In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21);

about 32% to about 42% (weight/weight) sucrose; and about 11% to about 15% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 32% to about 42% (weight/weight) sucrose; and about 11% to about 15% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 32% to about 42% (weight/weight) sucrose; about 11% to about 15% (weight/weight) dextrose; and about 11% to about 15% (weight/weight) monosodium glutamate.

[261] In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 37% (weight/weight) sucrose; and about 13% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 37% (weight/weight) sucrose; and about 13% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 37% (weight/weight) sucrose; about 13% (weight/weight) dextrose; and about 13% (weight/weight) monosodium glutamate.

[262] In some embodiments, the cryoprotectant comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl (e.g., a form of L-cysteine). In some embodiments, the cryoprotectant comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant comprises about 0.1% to about 0.25% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant comprises about 0.2% (weight/weight) L-cysteine HCl.

[263] In certain embodiments, the cryoprotectant provided herein comprises: (i) about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); (ii) about 37% (weight/weight) sucrose; (iii) about 13% (weight/weight) dextrose; (iv)

about 13% (weight/weight) monosodium glutamate; and (v) about 0.2% (weight/weight) L-cysteine HCl.

[264] In certain embodiments, the cryoprotectant provided herein comprises: (i) about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); (ii) about 37% (weight/weight) sucrose; (iii) about 13% (weight/weight) dextrose; and (iv) about 13% (weight/weight) monosodium glutamate.

[265] In certain embodiments, the freeze-dried powder comprises about 40% to about 70% (weight/weight) dried bacteria. In certain embodiments, the pharmaceutical agent comprises about 35% to about 70% (weight/weight) bacteria (e.g., freeze dried bacteria).

[266] In certain embodiments, the freeze-dried powder comprises about 64% (weight/weight) dried bacteria.

[267] In certain embodiments, the freeze-dried powder comprises about 15% to about 35% (weight/weight) bacteria (e.g., freeze dried bacteria). In certain embodiments, the freeze-dried powder comprises about 18% to about 30% (weight/weight) bacteria (e.g., freeze dried bacteria). In certain embodiments, the freeze-dried powder comprises about 25% (weight/weight) bacteria (e.g., freeze dried bacteria).

[268] In certain embodiments, the freeze-dried powder comprises *Prevotella* bacteria.

[269] In certain embodiments, the freeze-dried powder comprises *Veillonella* bacteria.

Brief Description of the Drawings

[270] Figure 1 is a graph showing Total Cells/ Gram Stability Profile over time long-term (2-8°C (abbreviation: 5°C)) and accelerated (25°C (abbreviation: 25°C)) storage conditions for *Prevotella histicola* Strain Batch 1. The lower trace in the graph provides values for accelerated (25°C) storage conditions. The upper trace in the graph provides values for long-term (2-8°C (abbreviation: 5°C)) storage conditions. Total Cell Count (TCC) was determined by Coulter counter.

[271] Figure 2 is a graph showing Water Content Stability Profile over time long-term (2-8°C) and accelerated (25°C) storage conditions for for *Prevotella histicola* Strain B Batch 1. Water content was determined by the Karl Fisher method.

[272] Figure 3 is a graph showing Total Cells/ Gram Stability Profile over time long-term (2-8°C (abbreviation: 5°C)) and accelerated (25°C (abbreviation: 25°C)) storage

conditions for *Prevotella histicola* Strain B Batch 2. Total Cell Count (TCC) was determined by Coulter counter.

[273] Figure 4 is a graph showing Water Content Stability Profile over time long-term (2-8°C (abbreviation: 5°C)) and accelerated (25°C) storage conditions for for *Prevotella histicola* Strain B Batch 2. The upper trace in the graph provides values for accelerated (25°C) storage conditions. The lower trace in the graph provides values for long-term (2-8°C (abbreviation: 5°C)) storage conditions. Water content was determined by the Karl Fisher method.

[274] Figure 5 is a graph showing Total Cells/ Gram Stability Profile over time long-term (2-8°C (abbreviation: 5°C)) and accelerated (25°C / 60% RH (abbreviation: 25°C)) storage conditions for *Veillonella parvula* Strain A Batch A. The trace to 6 months in the graph provides values for accelerated (25°C) storage conditions. The trace to 12 months in the graph provides values for long-term (2-8°C (abbreviation: 5°C)) storage conditions. Total Cell Count (TCC) was determined by Coulter counter.

[275] Figure 6 is a graph showing Water Content Stability Profile over time long-term (2-8°C) and accelerated (25°C) storage conditions for for *Veillonella parvula* Strain A Batch A. The trace to 6 months in the graph provides values for accelerated (25°C) storage conditions. The trace to 12 months in the graph provides values for long-term (2-8°C (abbreviation: 5°C)) storage conditions. Water content was determined by the Karl Fisher method.

[276] Figure 7 is a graph showing Total Cells/ Gram Stability Profile over time long-term (2-8°C (abbreviation: 5°C)) and accelerated (25°C / 60% RH (abbreviation: 25°C)) storage conditions for *Veillonella parvula* Strain A Batch D. The lower trace in the graph provides values for accelerated (25°C) storage conditions. The upper trace in the graph provides values for long-term (2-8°C (abbreviation: 5°C)) storage conditions. Total Cell Count (TCC) was determined by Coulter counter.

[277] Figure 8 is a graph showing Water Content Stability Profile over time long-term (2-8°C (abbreviation: 5°C)) and accelerated (25°C) storage conditions for for *Veillonella parvula* Strain A Batch D. Water content was determined by the Karl Fisher method.

[278] Figure 9 is a graph showing Total Cells/ Gram Stability Profile over time long-term (2-8°C (abbreviation: 5°C)) and accelerated (25°C (abbreviation: 25°C)) storage conditions for *Prevotella histicola* Strain Batch 1. The trace to 6 months in the graph provides values for accelerated (25°C) storage conditions. The trace to 18 months in the

graph provides values for long-term (2-8°C (abbreviation: 5°C)) storage conditions. Total Cell Count (TCC) was determined by Coulter counter.

[279] Figure 10 is a graph showing Water Content Stability Profile over time long-term (2-8°C) and accelerated (25°C) storage conditions for for *Prevotella histicola* Strain B Batch 1. Water content was determined by the Karl Fisher method.

[280] Figure 11 is a graph showing Total Cells/ Gram Stability Profile over time long-term (2-8°C (abbreviation: 5°C)) and accelerated (25°C (abbreviation: 25°C)) storage conditions for *Prevotella histicola* Strain Batch 2. The trace to 6 months in the graph provides values for accelerated (25°C) storage conditions. The trace to 18 months in the graph provides values for long-term (2-8°C (abbreviation: 5°C)) storage conditions. Total Cell Count (TCC) was determined by Coulter counter.

[281] Figure 12 is a graph showing Water Content Stability Profile over time long-term (2-8°C) and accelerated (25°C) storage conditions for for *Prevotella histicola* Strain B Batch 2. Water content was determined by the Karl Fisher method.

[282] Figure 13 is a graph showing Total Cells/ Gram Stability Profile over time long-term (2-8°C (abbreviation: 5°C)) and accelerated (25°C (abbreviation: 25°C)) storage conditions for *Prevotella histicola* Strain Batch 4. Total Cell Count (TCC) was determined by Coulter counter.

[283] Figure 14 is a graph showing Water Content Stability Profile over time long-term (2-8°C) and accelerated (25°C) storage conditions for for *Prevotella histicola* Strain B Batch 4. Water content was determined by the Karl Fisher method.

[284] Figure 15 is a graph showing Total Cells/ Gram Stability Profile over time long-term (2-8°C (abbreviation: 5°C)) and accelerated (25°C (abbreviation: 25°C)) storage conditions for *Prevotella histicola* Strain Batch 5. Total Cell Count (TCC) was determined by Coulter counter.

[285] Figure 16 is a graph showing Water Content Stability Profile over time long-term (2-8°C) and accelerated (25°C) storage conditions for for *Prevotella histicola* Strain B Batch 5. Water content was determined by the Karl Fisher method.

[286] Figure 17 is a graph showing Total Cells/ Gram Stability Profile over time long-term (-20°C) and accelerated ((2-8°C (abbreviation: 5°C)) storage conditions for *Prevotella histicola* Strain Batch i. The trace to 6 months in the graph provides values for accelerated (2-8°C (abbreviation: 5°C)) storage conditions. The trace to 24 months in the

graph provides values for long-term ((-20°C) storage conditions. Total Cell Count (TCC) was determined by Coulter counter.

[287] Figure 18 is a graph showing Water Content Stability Profile over time long-term (-20°C) and accelerated (2-8°C (abbreviation: 5°C)) storage conditions for for *Prevotella histicola* Strain B Batch i. Water content was determined by the Karl Fisher method.

Detailed Description

[288] In certain aspects, provided herein are pharmaceutical agents (such as powders) comprising bacteria (e.g., freeze dried bacteria), wherein the bacteria in the pharmaceutical agent are present at a total cell count (TCC) of at least $1x10^{11}$ cells/gram of the pharmaceutical agent.

[289] In certain aspects provided herein are pharmaceutical agents (such as powders) that comprise bacteria. In certain embodiments, the pharmaceutical agents maintain their stability, e.g., for three, six, twelve, eighteen and/or twenty-four months under long-term (2-8°C) and/or accelerated (23-27°C (optionally at 60% relative humidity (RH))) storage conditions, e.g., as determined by total cell count (TCC), e.g., as determined by Coulter counter and described herein. In certain embodiments, the pharmaceutical agents maintain their stability, e.g., for three, six, twelve, eighteen and/or twenty-four months under long-term (-20 °C) and/or accelerated (2-8°C) storage conditions, e.g., as determined by total cell count (TCC), e.g., as determined by Coulter counter and described herein.

[290] In certain aspects provided herein are pharmaceutical agents (such as powders) that comprise bacteria. In some embodiments, the water content of the pharmaceutical agents is between about 0.5% and about 9%, between about 1% and about 8%, between about 1% and about 6%, (e.g., about 1.7%, e.g., 1.8%, e.g., about 2%, e.g., about 2.2%, e.g., about 2.3%, e.g., about 2.4%, e.g., about 2.8%, e.g., about 2.9%, e.g., about 3%, e.g., about 3.1%, e.g., about 3.2%, e.g., about 3.3%, e.g., about 3.5%, e.g., about 3.6%, e.g., about 4%, e.g., about 4.5%, e.g., about 5%, e.g., about 5.3%, e.g., about 5.4%, or e.g., about 7.8%), e.g., as determined by the Karl-Fischer method for water content analysis provided in Ph. Eur. method 2.5.12, and as described herein. In some embodiments, the pharmaceutical agents maintain their water content, e.g., for three, six, twelve, eighteen and/or twenty-four months under long-term (2-8°C) and/or accelerated (25°C (optionally at 60% RH)) storage conditions. In certain embodiments, the pharmaceutical agents maintain their water content, e.g., for three, six, twelve, eighteen and/or twenty-four

months under long-term (-20) and/or accelerated (2-8°C) storage conditions, e.g., as determined by total cell count (TCC), e.g., as determined by Coulter counter and described herein.

[291] In certain aspects provided herein are pharmaceutical agents (such as powders) that comprise bacteria and a cryoprotectant.

Definitions

[292] The term "about" when used before a numerical value indicates that the value may vary within a reasonable range, such as within ± 10%, ± 5% or ± 1% of the stated value.

[293] "Adjuvant" or "Adjuvant therapy" broadly refers to an agent that affects an immunological or physiological response in a subject (e.g., human). For example, an adjuvant might increase the presence of an antigen over time or to an area of interest like a tumor, help absorb an antigen presenting cell antigen, activate macrophages and lymphocytes and support the production of cytokines. By changing an immune response, an adjuvant might permit a smaller dose of an immune interacting agent to increase the effectiveness or safety of a particular dose of the immune interacting agent. For example, an adjuvant might prevent T cell exhaustion and thus increase the effectiveness or safety of a particular immune interacting agent.

[294] "Administration" broadly refers to a route of administration of a composition (e.g., a pharmaceutical composition such as a solid dosage form of a pharmaceutical agent as described herein) to a subject. Examples of routes of administration include oral administration, rectal administration, topical administration, inhalation (nasal) or injection. Administration by injection includes intravenous (IV), intramuscular (IM), intratumoral (IT) and subcutaneous (SC) administration. A pharmaceutical composition described herein can be administered in any form by any effective route, including but not limited to intratumoral, oral, parenteral, enteral, intravenous, intraperitoneal, topical, transdermal (e.g., using any standard patch), intradermal, ophthalmic, (intra)nasally, local, non-oral, such as aerosol, inhalation, subcutaneous, intramuscular, buccal, sublingual, (trans)rectal, vaginal, intra-arterial, and intrathecal, transmucosal (e.g., sublingual, lingual, (trans)buccal, (trans)urethral, vaginal (e.g., trans- and perivaginally), implanted, intravesical, intrapulmonary, intraduodenal, intragastrical, and intrabronchial. In preferred embodiments, a pharmaceutical composition described herein is administered orally, rectally, intratumorally, topically, intravesically, by injection into or adjacent to a draining lymph node, intravenously, by inhalation or aerosol, or subcutaneously. In

another preferred embodiment, a pharmaceutical composition described herein is administered orally, intratumorally, or intravenously. In another embodiment, a pharmaceutical composition described herein is administered orally.

[295] As used herein, the term "antibody" may refer to both an intact antibody and an antigen binding fragment thereof. Intact antibodies are glycoproteins that include at least two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds. Each heavy chain includes a heavy chain variable region (abbreviated herein as V_H) and a heavy chain constant region. Each light chain includes a light chain variable region (abbreviated herein as V_L) and a light chain constant region. The V_H and V_L regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDR), interspersed with regions that are more conserved, termed framework regions (FR). Each V_H and V_L is composed of three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. The variable regions of the heavy and light chains contain a binding domain that interacts with an antigen. The term "antibody" includes, for example, monoclonal antibodies, polyclonal antibodies, chimeric antibodies, humanized antibodies, human antibodies, multispecific antibodies (*e.g.,* bispecific antibodies), single-chain antibodies and antigen-binding antibody fragments.

[296] The terms "antigen binding fragment" and "antigen-binding portion" of an antibody, as used herein, refer to one or more fragments of an antibody that retain the ability to bind to an antigen. Examples of binding fragments encompassed within the term "antigen-binding fragment" of an antibody include Fab, Fab', $F(ab')_2$, Fv, scFv, disulfide linked Fv, Fd, diabodies, single-chain antibodies, NANOBODIES®, isolated CDRH3, and other antibody fragments that retain at least a portion of the variable region of an intact antibody. These antibody fragments can be obtained using conventional recombinant and/or enzymatic techniques and can be screened for antigen binding in the same manner as intact antibodies.

[297] "Cancer" broadly refers to an uncontrolled, abnormal growth of a host's own cells leading to invasion of surrounding tissue and potentially tissue distal to the initial site of abnormal cell growth in the host. Major classes include carcinomas which are cancers of the epithelial tissue (*e.g.*, skin, squamous cells); sarcomas which are cancers of the connective tissue (*e.g.*, bone, cartilage, fat, muscle, blood vessels, etc.); leukemias which are cancers of blood forming tissue (*e.g.*, bone marrow tissue); lymphomas and myelomas

which are cancers of immune cells; and central nervous system cancers which include cancers from brain and spinal tissue. "Cancer(s)" and "neoplasm(s)" are used herein interchangeably. As used herein, "cancer" refers to all types of cancer or neoplasm or malignant tumors including leukemias, carcinomas and sarcomas, whether new or recurring. Specific examples of cancers are: carcinomas, sarcomas, myelomas, leukemias, lymphomas and mixed type tumors. Non-limiting examples of cancers are new or recurring cancers of the brain, melanoma, bladder, breast, cervix, colon, head and neck, kidney, lung, non-small cell lung, mesothelioma, ovary, prostate, sarcoma, stomach, uterus and medulloblastoma. In some embodiments, the cancer comprises a solid tumor. In some embodiments, the cancer comprises a metastasis.

[298] A "carbohydrate" refers to a sugar or polymer of sugars. The terms "saccharide," "polysaccharide," "carbohydrate," and "oligosaccharide" may be used interchangeably. Most carbohydrates are aldehydes or ketones with many hydroxyl groups, usually one on each carbon atom of the molecule. Carbohydrates generally have the molecular formula $C_nH_{2n}O_n$. A carbohydrate may be a monosaccharide, a disaccharide, trisaccharide, oligosaccharide, or polysaccharide. The most basic carbohydrate is a monosaccharide, such as glucose, sucrose, galactose, mannose, ribose, arabinose, xylose, and fructose. Disaccharides are two joined monosaccharides. Exemplary disaccharides include sucrose, maltose, cellobiose, and lactose. Typically, an oligosaccharide includes between three and six monosaccharide units (e.g., raffinose, stachyose), and polysaccharides include six or more monosaccharide units. Exemplary polysaccharides include starch, glycogen, and cellulose. Carbohydrates may contain modified saccharide units such as 2'-deoxyribose wherein a hydroxyl group is removed, 2'-fluororibose wherein a hydroxyl group is replaced with a fluorine, or N-acetylglucosamine, a nitrogen-containing form of glucose (e.g., 2'-fluororibose, deoxyribose, and hexose). Carbohydrates may exist in many different forms, for example, conformers, cyclic forms, acyclic forms, stereoisomers, tautomers, anomers, and isomers.

[299] "Cellular augmentation" broadly refers to the influx of cells or expansion of cells in an environment that are not substantially present in the environment prior to administration of a composition and not present in the composition itself. Cells that augment the environment include immune cells, stromal cells, bacterial and fungal cells. Environments of particular interest are the microenvironments where cancer cells reside or locate. In some instances, the microenvironment is a tumor microenvironment or a

tumor draining lymph node. In other instances, the microenvironment is a pre-cancerous tissue site or the site of local administration of a composition or a site where the composition will accumulate after remote administration.

[300] "Clade" refers to the OTUs or members of a phylogenetic tree that are downstream of a statistically valid node in a phylogenetic tree. The clade comprises a set of terminal leaves in the phylogenetic tree that is a distinct monophyletic evolutionary unit and that share some extent of sequence similarity.

[301] A "combination" of bacteria from two or more strains includes the physical co-existence of the 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 bacteria from the two or more strains.

[302] The term "decrease" or "deplete" means a change, such that the difference is, depending on circumstances, at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 1/100, 1/1000, 1/10,000, 1/100,000, 1/1,000,000 or undetectable after treatment when compared to a pre-treatment state. Properties that may be decreased include the number of immune cells, bacterial cells, stromal cells, myeloid derived suppressor cells, fibroblasts, metabolites; the level of a cytokine; or another physical parameter (such as ear thickness (e.g., in a DTH animal model) or tumor size).

[303] "Dysbiosis" refers to a state of the microbiota or microbiome of the gut or other body area, including, e.g., mucosal or skin surfaces (or any other microbiome niche) in which the normal diversity and/or function of the host gut microbiome ecological networks "microbiome") are disrupted. A state of dysbiosis may result in a diseased state, or it may be unhealthy under only certain conditions or only if present for a prolonged period. Dysbiosis may be due to a variety of factors, including, environmental factors, infectious agents, host genotype, host diet and/or stress. A dysbiosis may result in: a change (e.g., increase or decrease) in the prevalence of one or more bacteria types (e.g., anaerobic), species and/or strains, change (e.g., increase or decrease) in diversity of the host microbiome population composition; a change (e.g., increase or reduction) of one or more populations of symbiont organisms resulting in a reduction or loss of one or more beneficial effects; overgrowth of one or more populations of pathogens (e.g., pathogenic bacteria); and/or the presence of, and/or overgrowth of, symbiotic organisms that cause disease only when certain conditions are present.

[304] The term "ecological consortium" is a group of bacteria which trades metabolites and positively co-regulates one another, in contrast to two bacteria which induce host synergy through activating complementary host pathways for improved efficacy.

[305] The term "effective dose" or "effective amount" is an amount of a pharmaceutical agent that is effective to achieve a desired therapeutic response in a subject for a particular agent, composition, and mode of administration.

[306] As used herein, "engineered bacteria" are any bacteria that have been genetically altered from their natural state by human activities, and the progeny of any such bacteria. Engineered bacteria include, for example, the products of targeted genetic modification, the products of random mutagenesis screens and the products of directed evolution.

[307] The term "epitope" means a protein determinant capable of specific binding to an antibody or T cell receptor. Epitopes usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains. Certain epitopes can be defined by a particular sequence of amino acids to which an antibody is capable of binding.

[308] The term "gene" is used broadly to refer to any nucleic acid associated with a biological function. The term "gene" applies to a specific genomic sequence, as well as to a cDNA or an mRNA encoded by that genomic sequence.

[309] "Identity" as between nucleic acid sequences of two nucleic acid molecules can be determined as a percentage of identity using known computer algorithms such as the "FASTA" program, using for example, the default parameters as in Pearson *et al.* (1988) Proc. Natl. Acad. Sci. USA 85:2444 (other programs include the GCG program package (Devereux, J., *et al.*, Nucleic Acids Research 12(I):387 (1984)), BLASTP, BLASTN, FASTA Atschul, S. F., *et al.*, J Molec Biol 215:403 (1990); Guide to Huge Computers, Mrtin J. Bishop, ed., Academic Press, San Diego, 1994, and Carillo *et al.* (1988) SIAM J Applied Math 48:1073). For example, the BLAST function of the National Center for Biotechnology Information database can be used to determine identity. Other commercially or publicly available programs include, DNAStar "MegAlign" program (Madison, Wis.) and the University of Wisconsin Genetics Computer Group (UWG) "Gap" program (Madison Wis.)).

[310] As used herein, the term "immune disorder" refers to any disease, disorder or disease symptom caused by an activity of the immune system, including autoimmune diseases, inflammatory diseases and allergies. Immune disorders include, but are not

limited to, autoimmune diseases (e.g., psoriasis, atopic dermatitis, lupus, scleroderma, hemolytic anemia, vasculitis, type one diabetes, Grave's disease, rheumatoid arthritis, multiple sclerosis, Goodpasture's syndrome, pernicious anemia and/or myopathy), inflammatory diseases (e.g., acne vulgaris, asthma, celiac disease, chronic prostatitis, glomerulonephritis, inflammatory bowel disease, pelvic inflammatory disease, reperfusion injury, rheumatoid arthritis, sarcoidosis, transplant rejection, vasculitis and/or interstitial cystitis), and/or an allergies (e.g., food allergies, drug allergies and/or environmental allergies).

[311] "Immunotherapy" is treatment that uses a subject's immune system to treat disease (e.g., immune disease, inflammatory disease, metabolic disease, cancer) and includes, for example, checkpoint inhibitors, cancer vaccines, cytokines, cell therapy, CAR-T cells, and dendritic cell therapy.

[312] The term "increase" means a change, such that the difference is, depending on circumstances, at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 2-fold, 4-fold, 10-fold, 100-fold, 10^3 fold, 10^4 fold, 10^5 fold, 10^6 fold, and/or 10^7 fold greater after treatment when compared to a pre-treatment state. Properties that may be increased include the number of immune cells, bacterial cells, stromal cells, myeloid derived suppressor cells, fibroblasts, metabolites; the level of a cytokine; or another physical parameter (such as ear thickness (e.g., in a DTH animal model) or tumor size).

[313] "Innate immune agonists" or "immuno-adjuvants" are small molecules, proteins, or other agents that specifically target innate immune receptors including Toll-Like Receptors (TLR), NOD receptors, RLRs, C-type lectin receptors, STING-cGAS Pathway components, inflammasome complexes. For example, LPS is a TLR-4 agonist that is bacterially derived or synthesized and aluminum can be used as an immune stimulating adjuvant. immuno-adjuvants are a specific class of broader adjuvant or adjuvant therapy. Examples of STING agonists include, but are not limited to, 2'3'- cGAMP, 3'3'-cGAMP, c-di-AMP, c-di-GMP, 2'2'-cGAMP, and 2'3'-cGAM(PS)2 (Rp/Sp) (Rp, Sp-isomers of the bis-phosphorothioate analog of 2'3'-cGAMP). Examples of TLR agonists include, but are not limited to, TLRl, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLRlO and TLRI l. Examples of NOD agonists include, but are not limited to, N-acetylmuramyl-L-alanyl-D-isoglutamine (muramyldipeptide (MDP)), gamma-D-glutamyl-meso-diaminopimelic acid (iE-DAP), and desmuramylpeptides (DMP).

[314] The "internal transcribed spacer" or " ITS" is a piece of non-functional RNA located between structural ribosomal RNAs (rRNA) on a common precursor transcript often used for identification of eukaryotic species in particular fungi. The rRNA of fungi that forms the core of the ribosome is transcribed as a signal gene and consists of the 8S, 5.8S and 28S regions with ITS4 and 5 between the 8S and 5.8S and 5.8S and 28S regions, respectively. These two intercistronic segments between the 18S and 5.8S and 5.8S and 28S regions are removed by splicing and contain significant variation between species for barcoding purposes as previously described (Schoch et al Nuclear ribosomal internal transcribed spacer (ITS) region as a universal DNA barcode marker for Fungi. PNAS 109:6241-6246. 2012). 18S rDNA is traditionally used for phylogenetic reconstruction however the ITS can serve this function as it is generally highly conserved but contains hypervariable regions that harbor sufficient nucleotide diversity to differentiate genera and species of most fungus.

[315] The term "isolated" or "enriched" encompasses a microbe (such as 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 microbes may 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. In some embodiments, isolated microbes are more than about 80%, about 85%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or more than about 99% pure. As used herein, a substance is "pure" if it is substantially free of other components. The terms "purify," "purifying" and "purified" refer to a microbe or other material that has been separated from at least some of the components with which it was associated either when initially produced or generated (e.g., whether in nature or in an experimental setting), or during any time after its initial production. A microbe or a microbial population may be considered purified if it is isolated at or after production, such as from a material or environment containing the microbe or microbial population, and a purified microbe or microbial population may contain other materials up to about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, or above about 90% and still be considered "isolated." In some embodiments, purified microbes or microbial population

are more than about 80%, about 85%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or more than about 99% pure. In the instance of microbial compositions provided herein, the one or more microbial types present in the composition can be independently purified from one or more other microbes produced and/or present in the material or environment containing the microbial type. Microbial compositions and the microbial components thereof are generally purified from residual habitat products.

[316] As used herein a "lipid" includes fats, oils, triglycerides, cholesterol, phospholipids, fatty acids in any form including free fatty acids. Fats, oils and fatty acids can be saturated, unsaturated (cis or trans) or partially unsaturated (cis or trans).

[317] The term "LPS mutant or lipopolysaccharide mutant" broadly refers to selected bacteria that comprises loss of LPS. Loss of LPS might be due to mutations or disruption to genes involved in lipid A biosynthesis, such as *lpxA*, *lpxC*, and *lpxD*. Bacteria comprising LPS mutants can be resistant to aminoglycosides and polymyxins (polymyxin B and colistin).

[318] "Metabolite" as used herein refers to any and all molecular compounds, compositions, molecules, ions, co-factors, catalysts or nutrients used as substrates in any cellular or microbial metabolic reaction or resulting as product compounds, compositions, molecules, ions, co-factors, catalysts or nutrients from any cellular or microbial metabolic reaction.

[319] "Microbe" refers to any natural or engineered organism characterized as a archaeaon, parasite, bacterium, fungus, microscopic alga, protozoan, and the stages of development or life cycle stages (e.g., vegetative, spore (including sporulation, dormancy, and germination), latent, biofilm) associated with the organism. Examples of gut microbes include: *Actinomyces graevenitzii, Actinomyces odontolyticus, Akkermansia muciniphila, Bacteroides caccae, Bacteroides fragilis, Bacteroides putredinis, Bacteroides thetaiotaomicron, Bacteroides vultagus, Bifidobacterium adolescentis, Bifidobacterium bifidum, Bilophila wadsworthia, Blautia, Butyrivibrio, Campylobacter gracilis, Clostridia cluster III, Clostridia cluster IV, Clostridia cluster IX (Acidaminococcaceae group), Clostridia cluster XI, Clostridia cluster XIII (Peptostreptococcus group), Clostridia cluster XIV, Clostridia cluster XV, Collinsella aerofaciens, Coprococcus, Corynebacterium sunsvallense, Desulfomonas pigra, Dorea formicigenerans, Dorea longicatena, Escherichia coli, Eubacterium hadrum,*

Eubacterium rectale, Faecalibacteria prausnitzii, Gemella, Lactococcus, Lanchnospira, Mollicutes cluster XVI, Mollicutes cluster XVIII, Prevotella, Rothia mucilaginosa, Ruminococcus callidus, Ruminococcus gnavus, Ruminococcus torques, and *Streptococcus.*

[320] "Microbiome" broadly refers to the microbes residing on or in body site of a subject or patient. Microbes in a microbiome may include bacteria, viruses, eukaryotic microorganisms, and/or viruses. Individual microbes in a microbiome may be metabolically active, dormant, latent, or exist as spores, may exist planktonically or in biofilms, or may be present in the microbiome in sustainable or transient manner. The microbiome may be a commensal or healthy-state microbiome or a disease-state microbiome. The microbiome may be native to the subject or patient, or components of the microbiome may be modulated, introduced, or depleted due to changes in health state (*e.g.*, precancerous or cancerous state) or treatment conditions (*e.g.*, antibiotic treatment, exposure to different microbes). In some aspects, the microbiome occurs at a mucosal surface. In some aspects, the microbiome is a gut microbiome. In some aspects, the microbiome is a tumor microbiome.

[321] A "microbiome profile" or a "microbiome signature" of a tissue or sample refers to an at least partial characterization of the bacterial makeup of a microbiome. In some embodiments, a microbiome profile indicates whether at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100 or more bacterial strains are present or absent in a microbiome. In some embodiments, a microbiome profile indicates whether at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100 or more cancer-associated bacterial strains are present in a sample. In some embodiments, the microbiome profile indicates the relative or absolute amount of each bacterial strain detected in the sample. In some embodiments, the microbiome profile is a cancer-associated microbiome profile. A cancer-associated microbiome profile is a microbiome profile that occurs with greater frequency in a subject who has cancer than in the general population. In some embodiments, the cancer-associated microbiome profile comprises a greater number of or amount of cancer-associated bacteria than is normally present in a microbiome of an otherwise equivalent tissue or sample taken from an individual who does not have cancer.

[322] "Modified" in reference to a bacteria broadly refers to a bacteria that has undergone a change from its wild-type form. Bacterial modification can result from

engineering bacteria. Examples of bacterial modifications include genetic modification, gene expression modification, phenotype modification, formulation modification, chemical modification, and dose or concentration. Examples of improved properties are described throughout this specification and include, e.g., attenuation, auxotrophy, homing, or antigenicity. Phenotype modification might include, by way of example, bacteria growth in media that modify the phenotype of a bacterium such that it increases or decreases virulence.

[323] An "oncobiome" as used herein comprises tumorigenic and/or cancer-associated microbiota, wherein the microbiota comprises one or more of a virus, a bacterium, a fungus, a protist, a parasite, or another microbe.

[324] "Oncotrophic" or "oncophilic" microbes and bacteria are microbes that are highly associated or present in a cancer microenvironment. They may be preferentially selected for within the environment, preferentially grow in a cancer microenvironment or hone to a said environment.

[325] "Operational taxonomic units" and "OTU(s)" refer to a terminal leaf in a phylogenetic tree and is defined by a nucleic acid sequence, e.g., the entire genome, or a specific genetic sequence, and all sequences that share sequence identity to this nucleic acid sequence at the level of species. In some embodiments the specific genetic sequence may be the 16S sequence or a portion of the 16S sequence. In other embodiments, the entire genomes of two entities are sequenced and compared. In another embodiment, select regions such as multilocus sequence tags (MLST), specific genes, or sets of genes may be genetically compared. For 16S, OTUs that share ≥ 97% average nucleotide identity across the entire 16S or some variable region of the 16S are considered the same OTU. See e.g., Claesson MJ, Wang Q, O'Sullivan O, Greene-Diniz R, Cole JR, Ross RP, and O'Toole PW. 2010. Comparison of two next-generation sequencing technologies for resolving highly complex microbiota composition using tandem variable 16S rRNA gene regions. Nucleic Acids Res 38: e200. Konstantinidis KT, Ramette A, and Tiedje JM. 2006. The bacterial species definition in the genomic era. Philos Trans R Soc Lond B Biol Sci 361: 1929–1940. For complete genomes, MLSTs, specific genes, other than 16S, or sets of genes OTUs that share ≥ 95% average nucleotide identity are considered the same OTU. See e.g., Achtman M, and Wagner M. 2008. Microbial diversity and the genetic nature of microbial species. Nat. Rev. Microbiol. 6: 431–440. Konstantinidis KT, Ramette A, and Tiedje JM. 2006. The bacterial species definition in the genomic era.

Philos Trans R Soc Lond B Biol Sci 361: 1929–1940. OTUs are frequently defined by comparing sequences between organisms. Generally, sequences with no more than 95% sequence identity are not considered to form part of the same OTU. OTUs may also be characterized by any combination of nucleotide markers or genes, in particular highly conserved genes (e.g., "house-keeping" genes), or a combination thereof. Operational Taxonomic Units (OTUs) with taxonomic assignments made to, e.g., genus, species, and phylogenetic clade are provided herein.

[326] As used herein, a gene is "overexpressed" in a bacteria if it is expressed at a higher level in an engineered bacteria under at least some conditions than it is expressed by a wild-type bacteria of the same species under the same conditions. Similarly, a gene is "underexpressed" in a bacteria if it is expressed at a lower level in an engineered bacteria under at least some conditions than it is expressed by a wild-type bacteria of the same species under the same conditions.

[327] As used herein, the term "pharmaceutical agent" refers to an agent for therapeutic use. In some embodiments, a pharmaceutical agent is a composition comprising bacteria that can be used to treat and/or prevent a disease and/or condition. In some embodiments, a medicinal product, medical food, a food product, or a dietary supplement comprises a pharmaceutical agent. In some embodiments, the pharmaceutical agent is a powder that contains the bacteria. The powder can include one or more additional components in addition to the bacteria, such as a cryoprotectant.

[328] The terms "polynucleotide," and "nucleic acid" are used interchangeably. They refer to a polymeric form of nucleotides of any length, either deoxyribonucleotides or ribonucleotides, or analogs thereof. Polynucleotides may have any three-dimensional structure, and may perform any function. The following are non-limiting examples of polynucleotides: coding or non-coding regions of a gene or gene fragment, loci (locus) defined from linkage analysis, exons, introns, messenger RNA (mRNA), micro RNA (miRNA), silencing RNA (siRNA), transfer RNA, ribosomal RNA, ribozymes, cDNA, recombinant polynucleotides, branched polynucleotides, plasmids, vectors, isolated DNA of any sequence, isolated RNA of any sequence, nucleic acid probes, and primers. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and nucleotide analogs. If present, modifications to the nucleotide structure may be imparted before or after assembly of the polymer. A polynucleotide may be further modified, such

as by conjugation with a labeling component. In all nucleic acid sequences provided herein, U nucleotides are interchangeable with T nucleotides.

[329] As used herein, the term "preventing" a disease or condition in a subject refers to administering to the subject to a pharmaceutical treatment, e.g., the administration of one or more agents (e.g., pharmaceutical agent), such that onset of at least one symptom of the disease or condition is delayed or prevented.

[330] As used herein, a substance is "pure" if it is substantially free of other components. The terms "purify," "purifying" and "purified" refer to a microbe preparation or other material that has been separated from at least some of the components with which it was associated either when initially produced or generated (e.g., whether in nature or in an experimental setting), or during any time after its initial production. A microbe preparation or compositions may be considered purified if it is isolated at or after production, such as from one or more other bacterial components, and a purified microbe or microbial population may contain other materials up to about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, or above about 90% and still be considered "purified." In some embodiments, purified microbes are more than about 80%, about 85%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or more than about 99% pure. Microbe compositions (or preparations) are, e.g., purified from residual habitat products.

[331] "Residual habitat products" refers to material derived from the habitat for microbiota within or on a subject. For example, fermentation cultures of microbes can contain contaminants, e.g., other microbe strains or forms (e.g., bacteria, virus, mycoplasm, and/or fungus). For example, microbes live in feces in the gastrointestinal tract, on the skin itself, in saliva, mucus of the respiratory tract, or secretions of the genitourinary tract (i.e., biological matter associated with the microbial community). Substantially free of residual habitat products means that the microbial composition no longer contains the biological matter associated with the microbial environment on or in the culture or human or animal subject and is 100% free, 99% free, 98% free, 97% free, 96% free, or 95% free of any contaminating biological matter associated with the microbial community. Residual habitat products can include abiotic materials (including undigested food) or it can include unwanted microorganisms. Substantially free of residual habitat products may also mean that the microbial composition contains no

detectable cells from a culture contaminant or a human or animal and that only microbial cells are detectable. In one embodiment, substantially free of residual habitat products may also mean that the microbial composition contains no detectable viral (including bacteria, viruses (e.g., phage)), fungal, mycoplasmal contaminants. In another embodiment, it means that fewer than $1x10^{-2}$%, $1x10^{-3}$%, $1x10^{-4}$%, $1x10^{-5}$%, $1x10^{-6}$%, $1x10^{-7}$%, $1x10^{-8}$% of the viable cells in the microbial composition are human or animal, as compared to microbial cells. There are multiple ways to accomplish this degree of purity, none of which are limiting. Thus, contamination may be reduced by isolating desired constituents through multiple steps of streaking to single colonies on solid media until replicate (such as, but not limited to, two) streaks from serial single colonies have shown only a single colony morphology. Alternatively, reduction of contamination can be accomplished by multiple rounds of serial dilutions to single desired cells (e.g., a dilution of 10^{-8} or 10^{-9}), such as through multiple 10-fold serial dilutions. This can further be confirmed by showing that multiple isolated colonies have similar cell shapes and Gram staining behavior. Other methods for confirming adequate purity include genetic analysis (e.g., PCR, DNA sequencing), serology and antigen analysis, enzymatic and metabolic analysis, and methods using instrumentation such as flow cytometry with reagents that distinguish desired constituents from contaminants.

[332] As used herein, "specific binding" refers to the ability of an antibody to bind to a predetermined antigen or the ability of a polypeptide to bind to its predetermined binding partner. Typically, an antibody or polypeptide specifically binds to its predetermined antigen or binding partner with an affinity corresponding to a K_D of about 10^{-7} M or less, and binds to the predetermined antigen/binding partner with an affinity (as expressed by K_D) that is at least 10 fold less, at least 100 fold less or at least 1000 fold no more than its affinity for binding to a non-specific and unrelated antigen/binding partner (e.g., BSA, casein). Alternatively, specific binding applies more broadly to a two component system where one component is a protein, lipid, or carbohydrate or combination thereof and engages with the second component which is a protein, lipid, carbohydrate or combination thereof in a specific way.

[333] "Strain" refers to a member of a bacterial species with a genetic signature such that it may be differentiated from closely-related members of the same bacterial species. The genetic signature may be the absence of all or part of at least one gene, the absence of all or part of at least on regulatory region (e.g., a promoter, a terminator, a riboswitch, a

ribosome binding site), the absence ("curing") of at least one native plasmid, the presence of at least one recombinant gene, the presence of at least one mutated gene, the presence of at least one foreign gene (a gene derived from another species), the presence at least one mutated regulatory region (e.g., a promoter, a terminator, a riboswitch, a ribosome binding site), the presence of at least one non-native plasmid, the presence of at least one antibiotic resistance cassette, or a combination thereof. Genetic signatures between different strains may be identified by PCR amplification optionally followed by DNA sequencing of the genomic region(s) of interest or of the whole genome. In the case in which one strain (compared with another of the same species) has gained or lost antibiotic resistance or gained or lost a biosynthetic capability (such as an auxotrophic strain), strains may be differentiated by selection or counter-selection using an antibiotic or nutrient/metabolite, respectively.

[334] The terms "subject" or "patient" refers to any mammal. A subject or a patient described as "in need thereof" refers to one in need of a treatment (or prevention) for a disease. Mammals (i.e., mammalian animals) include humans, laboratory animals (e.g., primates, rats, mice), livestock (e.g., cows, sheep, goats, pigs), and household pets (e.g., dogs, cats, rodents). The subject may be a human. The subject may be a non-human mammal including but not limited to of a dog, a cat, a cow, a horse, a pig, a donkey, a goat, a camel, a mouse, a rat, a guinea pig, a sheep, a llama, a monkey, a gorilla or a chimpanzee. The subject may be healthy, or may be suffering from a cancer at any developmental stage, wherein any of the stages are either caused by or opportunistically supported of a cancer associated or causative pathogen, or may be at risk of developing a cancer, or transmitting to others a cancer associated or cancer causative pathogen. In some embodiments, a subject has lung cancer, bladder cancer, prostate cancer, plasmacytoma, colorectal cancer, rectal cancer, Merkel Cell carcinoma, salivary gland carcinoma, ovarian cancer, and/or melanoma. The subject may have a tumor. The subject may have a tumor that shows enhanced macropinocytosis with the underlying genomics of this process including Ras activation. In other embodiments, the subject has another cancer. In some embodiments, the subject has undergone a cancer therapy.

[335] As used herein, a "systemic effect" in a subject treated with a pharmaceutical composition containing bacteria (e.g., a pharmaceutical agent comprising bacteria) of the instant invention means a physiological effect occurring at one or more sites outside the gastrointestinal tract. Systemic effect(s) can result from immune modulation (e.g., via an

increase and/or a reduction of one or more immune cell types or subtypes (e.g., CD8+ T cells) and/or one or more cytokines). Such systemic effect(s) may be the result of the modulation by bacteria of the instant invention on immune or other cells (such as epithelial cells) in the gastrointestinal tract which then, directly or indirectly, result in the alteration of activity (activation and/or deactivation) of one or more biochemical pathways outside the gastrointestinal tract. The systemic effect may include treating or preventing a disease or condition in a subject.

[336] As used herein, the term "treating" a disease in a subject or "treating" a subject having or suspected of having a disease refers to administering to the subject to a pharmaceutical treatment, *e.g.*, the administration of one or more agents, such that at least one symptom of the disease is decreased or prevented from worsening. Thus, in one embodiment, "treating" refers inter alia to delaying progression, expediting remission, inducing remission, augmenting remission, speeding recovery, increasing efficacy of or decreasing resistance to alternative therapeutics, or a combination thereof.

[337] As used herein, a value is "greater than" another value if it is higher by any amount (e.g., each of 100, 50, 20, 12, 11, 10.6, 10.1, 10.01, and 10.001 is at least 10). Similarly, as used herein, a value is "less than" another value if it is lower by any amount (e.g., each of 1, 2, 4, 6, 8, 9, 9.2, 9.4, 9.6, 9.8, 9.9, 9.99, 9.999 is no more than 10). In contrast, as used herein, a test value "is" an anchor value when the test value rounds to the anchor value (e.g., if "an ingredient mass is 10% of a total mass," in which case 10% is the anchor value, the test values of 9.5, 9.6, 9.7, 9.8, 9.9, 10, 10.1, 10.2, 10.3, and 10.4 would also meet the "ingredient mass is 10% of the total mass" feature).

Bacteria

[338] The pharmaceutical agent (e.g., and pharmaceutical compositions comprising the same) disclosed herein can comprise bacteria. For example, the pharmaceutical agent disclosed herein can comprise a powder comprising bacteria. Within a pharmaceutical agent that contains bacteria, the pharmaceutical agent can contain bacteria from one or more strains.

[339] In some embodiments, the bacteria of the pharmaceutical agent are obtained are modified to reduce toxicity or other adverse effects, to enhance delivery) (e.g., oral delivery) (e.g., by improving acid resistance, muco-adherence and/or penetration and/or resistance to bile acids, digestive enzymes, resistance to anti-microbial peptides and/or

antibody neutralization), to target desired cell types (e.g., M-cells, goblet cells, enterocytes, dendritic cells, macrophages), to enhance their immunomodulatory and/or therapeutic effect of the bacteria (e.g., either alone or in combination with another therapeutic agent), and/or to enhance immune activation or suppression by the bacteria (e.g., through modified production of polysaccharides, pili, fimbriae, adhesins). In some embodiments, the engineered bacteria described herein are modified to improve bacteria manufacturing (e.g., higher oxygen tolerance, stability, improved freeze-thaw tolerance, shorter generation times). For example, in some embodiments, the engineered bacteria described include bacteria harboring one or more genetic changes, such change being an insertion, deletion, translocation, or substitution, or any combination thereof, of one or more nucleotides contained on the bacterial chromosome or endogenous plasmid and/or one or more foreign plasmids, wherein the genetic change may result in the overexpression and/or underexpression of one or more genes. The engineered bacteria may be produced using any technique known in the art, including but not limited to site-directed mutagenesis, transposon mutagenesis, knock-outs, knock-ins, polymerase chain reaction mutagenesis, chemical mutagenesis, ultraviolet light mutagenesis, transformation (chemically or by electroporation), phage transduction, directed evolution, or any combination thereof.

[340] Examples of taxonomic groups (e.g., class, order, family, genus, species or strain) of bacteria that can be used as a source of bacteria for a pharmaceutical agent described herein are provided herein (e.g., listed in Table 1, Table 2, Table 3, and/or Table 4and/or elsewhere in the specification (e.g., Table J)). In some embodiments, the bacterial strain is a bacterial strain having a genome that has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8% or 99.9% sequence identity to a strain listed herein. In some embodiments, the bacteria of the pharmaceutical agent are oncotrophic bacteria. In some embodiments, the bacteria of the pharmaceutical agent are immunomodulatory bacteria. In some embodiments, the bacteria of the pharmaceutical agent are immunostimulatory bacteria. In some embodiments, the bacteria of the pharmaceutical agent are immunosuppressive bacteria. In some embodiments, the bacteria of the pharmaceutical agent are immunomodulatory bacteria. In certain embodiments, the bacteria of the pharmaceutical agent are generated from a combination of bacterial strains provided herein. In some embodiments, the combination is a combination of at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12,

13, 14, 15, 20, 25, 30, 35, 40, 45 or 50 bacterial strains. In some embodiments, the combination includes the bacteria of the pharmaceutical agent are from bacterial strains listed herein and/or bacterial strains having a genome that has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8% or 99.9% sequence identity to a strain listed herein (e.g., listed in Table 1, Table 2, Table 3, and/or Table 4 and/or elsewhere in the specification (e.g., Table J)). In certain embodiments, the bacteria of the pharmaceutical agent are generated from a bacterial strain provided herein. In some embodiments, the bacteria of the pharmaceutical agent are from a bacterial strain listed herein (e.g., listed in Table 1, Table 2, Table 3, and/or Table 4and/or elsewhere in the specification (e.g., Table J))and/or a bacterial strain having a genome that has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.1%, 99.2%, 99.3%, 99.4%, 99.5%, 99.6%, 99.7%, 99.8% or 99.9% sequence identity to a strain listed herein (e.g., listed in Table 1, Table 2, Table 3, and/or Table 4 and/or elsewhere in the specification (e.g., Table J)).

[341] In some embodiments, the bacteria of the pharmaceutical agent are Gram negative bacteria.

[342] In some embodiments, the Gram negative bacteria belong to the class *Negativicutes*. The *Negativicutes* represent a unique class of microorganisms as they are the only diderm members of the *Firmicutes* phylum. These anaerobic organisms can be found in the environment and are normal commensals of the oral cavity and GI tract of humans. The *Negativicutes* class includes the families *Veillonellaceae, Selenomonadaceae, Acidaminococcaceae*, and *Sporomusaceae*. The *Negativicutes* class includes the genera *Megasphaera, Selenomonas, Propionospora,* and *Acidaminococcus*. Exemplary *Negativicutes* species include, but are not limited to, *Megasphaera sp., Selenomonas felix, Acidaminococcus intestine,* and *Propionospora sp.*

[343] In some embodiments, the bacteria of the pharmaceutical agent are Gram positive bacteria.

[344] In some embodiments, the bacteria of the pharmaceutical agent are aerobic bacteria.

[345] In some embodiments, the bacteria of the pharmaceutical agent are anaerobic bacteria. In some embodiments, the anaerobic bacteria comprise obligate anaerobes. In some embodiments, the anaerobic bacteria comprise facultative anaerobes.

[346] In some embodiments, the bacteria of the pharmaceutical agent are acidophile bacteria.

[347] In some embodiments, the bacteria of the pharmaceutical agent are alkaliphile bacteria.

[348] In some embodiments, the bacteria of the pharmaceutical agent are neutralophile bacteria.

[349] In some embodiments, the bacteria of the pharmaceutical agent are fastidious bacteria.

[350] In some embodiments, the bacteria of the pharmaceutical agent are nonfastidious bacteria.

[351] In some embodiments, the bacteria of the pharmaceutical agent are lyophilized.

[352] In some embodiments, the bacteria of the pharmaceutical agent are gamma irradiated (e.g., at 17.5 or 25 kGy).

[353] In some embodiments, the bacteria of the pharmaceutical agent are UV irradiated.

[354] In some embodiments, the bacteria of the pharmaceutical agent are heat inactivated (e.g., at 50°C for two hours or at 90°C for two hours).

[355] In some embodiments, the bacteria of the pharmaceutical agent are acid treated.

[356] In some embodiments, the bacteria of the pharmaceutical agent are oxygen sparged (e.g., at 0.1 vvm for two hours).

[357] The phase of growth can affect the amount or properties of bacteria. For example, bacteria can be isolated at the start of the log phase of growth, midway through the log phase, and/or once stationary phase growth has been reached for a bacterial culture.

[358] In certain embodiments, the bacteria of the pharmaceutical agent are obligate anaerobic bacteria. Examples of obligate anaerobic bacteria include gram-negative rods (including the genera of *Bacteroides*, *Prevotella*, *Porphyromonas*, *Fusobacterium*, *Bilophila* and *Sutterella spp.*), gram-positive cocci (primarily *Peptostreptococcus spp.*), gram-positive spore-forming (*Clostridium spp.*), non-spore-forming bacilli (*Actinomyces*, *Propionibacterium*, *Eubacterium*, *Lactobacillus* and *Bifidobacterium spp.*), and gram-negative cocci (mainly *Veillonella spp.*). In some embodiments, the obligate anaerobic bacteria are of a genus selected from the group consisting of *Agathobaculum, Atopobium, Blautia, Burkholderia, Dielma, Longicatena, Paraclostridium, Turicibacter,* and *Tyzzerella*.

[359] The Negativicutes class includes the families *Veillonellaceae, Selenomonadaceae, Acidaminococcaceae*, and *Sporomusaceae*. The *Negativicutes* class includes the genera *Megasphaera, Selenomonas, Propionospora*, and *Acidaminococcus*. Exemplary *Negativicutes* species include, but are not limited to, *Megasphaera* sp., *Selenomonas felix, Acidaminococcus intestini*, and *Propionospora* sp.

[360] In some embodiments, the bacteria of the pharmaceutical agent are of the *Negativicutes* class.

[361] In some embodiments, the bacteria of the pharmaceutical agent are of the *Veillonellaceae* family.

[362] In some embodiments, the bacteria of the pharmaceutical agent are of the *Selenomonadaceae* family.

[363] In some embodiments, the bacteria of the pharmaceutical agent are of the *Acidaminococcaceae* family.

[364] In some embodiments, the bacteria of the pharmaceutical agent are of the *Sporomusaceae* family.

[365] In some embodiments, the bacteria of the pharmaceutical agent are of the *Megasphaera* genus.

[366] In some embodiments, the bacteria of the pharmaceutical agent are of the *Selenomonas* genus.

[367] In some embodiments, the bacteria of the pharmaceutical agent are of the *Propionospora* genus.

[368] In some embodiments, the bacteria of the pharmaceutical agent are of the *Acidaminococcus* genus.

[369] In some embodiments, the bacteria of the pharmaceutical agent are *Megasphaera sp.* bacteria.

[370] In some embodiments, the bacteria of the pharmaceutical agent are *Selenomonas felix* bacteria.

[371] In some embodiments, the bacteria of the pharmaceutical agent are *Acidaminococcus intestini* bacteria.

[372] In some embodiments, the bacteria of the pharmaceutical agent are *Propionospora sp.* bacteria.

[373] The Oscillospriraceae family within the *Clostridia* class of microorganisms are common commensal organisms of vertebrates.

[374] In some embodiments, the bacteria of the pharmaceutical agent are of the *Clostridia* class.

[375] In some embodiments, the bacteria of the pharmaceutical agent are of the *Oscillospriraceae* family.

[376] In some embodiments, the bacteria of the pharmaceutical agent are of the *Faecalibacterium* genus.

[377] In some embodiments, the bacteria of the pharmaceutical agent are of the *Fournierella* genus.

[378] In some embodiments, the bacteria of the pharmaceutical agent are of the *Harryflintia* genus.

[379] In some embodiments, the bacteria of the pharmaceutical agent are of the *Agathobaculum* genus.

[380] In some embodiments, the bacteria of the pharmaceutical agent are *Faecalibacterium prausnitzii* (e.g., *Faecalibacterium prausnitzii* Strain A) bacteria.

[381] In some embodiments, the bacteria of the pharmaceutical agent are *Fournierella massiliensis* (e.g., *Fournierella massiliensis* Strain A) bacteria.

[382] In some embodiments, the bacteria of the pharmaceutical agent are *Harryflintia acetispora* (e.g., *Harryflintia acetispora* Strain A) bacteria.

[383] In some embodiments, the bacteria of the pharmaceutical agent are *Agathobaculum sp.* (e.g., *Agathobaculum sp.* Strain A) bacteria.

[384] In some embodiments, the bacteria of the pharmaceutical agent are bacteria of a genus selected from the group consisting of *Escherichia, Klebsiella, Lactobacillus, Shigella,* and *Staphylococcus*.

[385] In some embodiments, the bacteria of the pharmaceutical agent are a species selected from the group consisting of *Blautia massiliensis*, *Paraclostridium benzoelyticum*, *Dielma fastidiosa*, *Longicatena caecimuris*, *Lactococcus lactis cremoris*, *Tyzzerella nexilis*, *Hungatella effluvia*, *Klebsiella quasipneumoniae subsp. Similipneumoniae, Klebsiella oxytoca,* and *Veillonella tobetsuensis*.

[386] In some embodiments, the bacteria of the pharmaceutical agent are a *Prevotella* bacteria selected from the group consisting of *Prevotella albensis, Prevotella amnii, Prevotella bergensis, Prevotella bivia,* Prevotella *brevis, Prevotella bryantii, Prevotella buccae, Prevotella buccalis, Prevotella copri, Prevotella dentalis, Prevotella denticola, Prevotella disiens, Prevotella histicola, Prevotella intermedia, Prevotella maculosa,*

Prevotella marshii, Prevotella melaninogenica, Prevotella micans, Prevotella multiformis, Prevotella nigrescens, Prevotella oralis, Prevotella oris, Prevotella oulorum, Prevotella pallens, Prevotella salivae, Prevotella stercorea, Prevotella tannerae, Prevotella timonensis, Prevotella jejuni, Prevotella aurantiaca, Prevotella baroniae, Prevotella colorans, Prevotella corporis, Prevotella dentasini, Prevotella enoeca, Prevotella falsenii, Prevotella fusca, Prevotella heparinolytica, Prevotella loescheii, Prevotella multisaccharivorax, Prevotella nanceiensis, Prevotella oryzae, Prevotella paludivivens, Prevotella pleuritidis, Prevotella ruminicola, Prevotella saccharolytica, Prevotella scopos, Prevotella shahii, Prevotella zoogleoformans, and *Prevotella veroralis.*

[387] In some embodiments, the bacteria of the pharmaceutical agent are a strain of bacteria comprising a genomic sequence that is 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%, or at least 99% sequence identity (*e.g.,* at least 99.5% sequence identity, at least 99.6% sequence identity, at least 99.7% sequence identity, at least 99.8% sequence identity, at least 99.9% sequence identity) to the genomic sequence of the strain of bacteria deposited with the ATCC Deposit number as provided in Table 3. In some embodiments, the bacteria of the pharmaceutical agent are a strain of bacteria comprising a 16S sequence that is 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%, or at least 99% sequence identity (e.g., at least 99.5% sequence identity, at least 99.6% sequence identity, at least 99.7% sequence identity, at least 99.8% sequence identity, at least 99.9% sequence identity) to the 16S sequence of the strain of bacteria deposited with the ATCC Deposit number as provided in Table 3.

[388] The *Negativicutes* class includes the families *Veillonellaceae, Selenomonadaceae, Acidaminococcaceae*, and *Sporomusaceae*. The *Negativicutes* class includes the genera *Megasphaera, Selenomonas, Propionospora*, and *Acidaminococcus*. Exemplary *Negativicutes* species include, but are not limited to, *Megasphaera sp., Selenomonas felix, Acidaminococcus intestini*, and *Propionospora* sp.

[389] In some embodiments, the bacteria of the pharmaceutical agent are of the *Negativicutes* class.

[390] In some embodiments, the bacteria of the pharmaceutical agent are of the *Veillonellaceae* family.

[391] In some embodiments, the bacteria of the pharmaceutical agent are of the *Selenomonadaceae* family.

[392] In some embodiments, the bacteria of the pharmaceutical agent are of the *Acidaminococcaceae* family.

[393] In some embodiments, the bacteria of the pharmaceutical agent are of the *Sporomusaceae* family.

[394] In some embodiments, the bacteria of the pharmaceutical agent are of the *Megasphaera* genus.

[395] In some embodiments, the bacteria of the pharmaceutical agent are of the *Selenomonas* genus.

[396] In some embodiments, the bacteria of the pharmaceutical agent are of the *Propionospora* genus.

[397] In some embodiments, the bacteria of the pharmaceutical agent are of the *Acidaminococcus* genus.

[398] In some embodiments, the bacteria of the pharmaceutical agent are *Megasphaera sp.* bacteria.

[399] In some embodiments, the bacteria of the pharmaceutical agent are *Selenomonas felix* bacteria.

[400] In some embodiments, the bacteria of the pharmaceutical agent are *Acidaminococcus intestini* bacteria.

[401] In some embodiments, the bacteria of the pharmaceutical agent are *Propionospora sp.* bacteria.

[402] The *Oscillospriraceae* family within the *Clostridia* class of microorganisms are common commensal organisms of vertebrates.

[403] In some embodiments, the bacteria of the pharmaceutical agent are of the *Clostridia* class.

[404] In some embodiments, the bacteria of the pharmaceutical agent are of the *Oscillospriraceae* family.

[405] In some embodiments, the bacteria of the pharmaceutical agent are of the *Faecalibacterium* genus.

[406] In some embodiments, the bacteria of the pharmaceutical agent are of the *Fournierella* genus.

[407] In some embodiments, the bacteria of the pharmaceutical agent are of the *Harryflintia* genus.

[408] In some embodiments, the bacteria of the pharmaceutical agent are of the *Agathobaculum* genus.

[409] In some embodiments, the bacteria of the pharmaceutical agent are *Faecalibacterium prausnitzii* (e.g., *Faecalibacterium prausnitzii* Strain A) bacteria.

[410] In some embodiments, the bacteria of the pharmaceutical agent are *Fournierella massiliensis* (e.g., *Fournierella massiliensis* Strain A) bacteria.

[411] In some embodiments, the bacteria of the pharmaceutical agent are *Harryflintia acetispora* (e.g., *Harryflintia acetispora* Strain A) bacteria.

[412] In some embodiments, the bacteria of the pharmaceutical agent are *Agathobaculum sp.* (e.g., *Agathobaculum sp.* Strain A) bacteria.

[413] In some embodiments, the bacteria of the pharmaceutical agent are a strain of *Agathobaculum sp*. In some embodiments, the *Agathobaculum sp.* strain is a strain comprising at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity (e.g., at least 99.5% sequence identity, at least 99.6% sequence identity, at least 99.7% sequence identity, at least 99.8% sequence identity, at least 99.9% sequence identity) to the nucleotide sequence (e.g., genomic sequence, 16S sequence, CRISPR sequence) of the *Agathobaculum sp.* Strain A (ATCC Deposit Number PTA-125892). In some embodiments, the *Agathobaculum sp.* strain is the Agathobaculum sp. Strain A (ATCC Deposit Number PTA- 125892).

[414] In some embodiments, the bacteria of the pharmaceutical agent are of the class *Bacteroidia* [phylum *Bacteroidota*]. In some embodiments, the bacteria of the pharmaceutical agent are bacteria of order Bacteroidales. In some embodiments, the bacteria of the pharmaceutical agent are of the family *Porphyromonoadaceae*. In some embodiments, the bacteria of the pharmaceutical agent are of the family *Prevotellaceae*. In some embodiments, the bacteria of the pharmaceutical agent are bacteria of the class *Bacteroidia* wherein the cell envelope structure of the bacteria is diderm. In some embodiments, the bacteria of the pharmaceutical agent are bacteria of the class *Bacteroidia* that stain Gram negative. In some embodiments, the bacteria of the pharmaceutical agent are bacteria of the class *Bacteroidia* wherein the bacteria is diderm and the bacteria stain Gram negative.

[415] In some embodiments, the bacteria of the pharmaceutical agent are bacteria of the class *Clostridia* [phylum *Firmicutes*]. In some embodiments, the bacteria of the pharmaceutical agent are of the order *Eubacteriales*. In some embodiments, the bacteria of the pharmaceutical agent are of the family *Oscillispiraceae*. In some embodiments, the bacteria of the pharmaceutical agent are of the family *Lachnospiraceae*. In some embodiments, the bacteria of the pharmaceutical agent are of the family *Peptostreptococcaceae*. In some embodiments, the bacteria of the pharmaceutical agent are of the family *Clostridiales family XIII/ Incertae sedis 41*. In some embodiments, the bacteria of the pharmaceutical agent are of the class *Clostridia* wherein the cell envelope structure of the bacteria is monoderm. In some embodiments, the bacteria of the pharmaceutical agent are of the class *Clostridia* that stain Gram negative. In some embodiments, the bacteria of the pharmaceutical agent are of the class *Clostridia* that stain Gram positive. In some embodiments, the bacteria of the pharmaceutical agent are of the class *Clostridia* wherein the cell envelope structure of the bacteria is monoderm and the bacteria stain Gram negative. In some embodiments, the bacteria of the pharmaceutical agent are of the class *Clostridia* wherein the cell envelope structure of the bacteria is monoderm and the bacteria stain Gram positive.

[416] In some embodiments, the bacteria of the pharmaceutical agent are of the class *Negativicutes* [phylum *Firmicutes*]. In some embodiments, the bacteria of the pharmaceutical agent are of the order *Veillonellales*. In some embodiments, the bacteria of the pharmaceutical agent are of the family *Veillonelloceae*. In some embodiments, the bacteria of the pharmaceutical agent are of the order *Selenomonadales*. In some embodiments, the bacteria of the pharmaceutical agent are bacteria of the family *Selenomonadaceae*. In some embodiments, the bacteria of the pharmaceutical agent are of the family *Sporomusaceae*. In some embodiments, t the bacteria of the pharmaceutical agent are of the class *Negativicutes* wherein the cell envelope structure of the bacteria is diderm. In some embodiments, the bacteria of the pharmaceutical agent are from bacteria of the class *Negativicutes* wherein the cell envelope structure of the bacteria is diderm and the bacteria stain Gram negative.

[417] In some embodiments, the bacteria of the pharmaceutical agent are of the class *Synergistia* [phylum *Synergistota*]. In some embodiments, the bacteria of the pharmaceutical agent are of the order *Synergistales*. In some embodiments, the bacteria of the pharmaceutical agent are of the family *Synergistaceae*. In some embodiments, the

bacteria of the pharmaceutical agent are of the class *Synergistia* wherein the cell envelope structure of the bacteria is diderm. In some embodiments, the bacteria of the pharmaceutical agent are of the class *Synergistia* that stain Gram negative. In some embodiments, the bacteria of the pharmaceutical agent are of the class *Synergistia* wherein the cell envelope structure of the bacteria is diderm and the bacteria stain Gram negative.

[418] In some embodiments, the bacteria of the pharmaceutical agent from one strain of bacteria, e.g., a strain provided herein.

[419] In some embodiments, the bacteria of the pharmaceutical agent are from one strain of bacteria (e.g., a strain provided herein) or from more than one strain provided herein.

[420] In some embodiments, the bacteria of the pharmaceutical agent are *Lactococcus lactis cremoris* bacteria, e.g., a strain comprising at least 90% or at least 99% genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Lactococcus lactis cremoris* Strain A (ATCC designation number PTA-125368). In some embodiments, the bacteria of the pharmaceutical agent are *Lactococcus* bacteria, e.g., *Lactococcus lactis cremoris* Strain A (ATCC designation number PTA-125368).

[421] In some embodiments, the bacteria of the pharmaceutical agent are *Prevotella* bacteria, e.g., a strain comprising at least 90% or at least 99% genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Prevotella* Strain B 50329 (NRRL accession number B 50329). In some embodiments, the bacteria of the pharmaceutical agent are *Prevotella* bacteria, e.g., *Prevotella* Strain B 50329 (NRRL accession number B 50329).

[422] In some embodiments, the bacteria of the pharmaceutical agent are *Bifidobacterium* bacteria, e.g., a strain comprising at least 90% or at least 99% genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Bifidobacterium* bacteria deposited as ATCC designation number PTA-125097. In some embodiments, the bacteria of the pharmaceutical agent are *Bifidobacterium* bacteria, e.g., *Bifidobacterium* bacteria deposited as ATCC designation number PTA-125097.

[423] In some embodiments, the bacteria of the pharmaceutical agent are *Veillonella* bacteria, e.g., a strain comprising at least 90% or at least 99% genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Veillonella* bacteria deposited as ATCC designation number PTA-125691. In some embodiments, the bacteria

of the pharmaceutical agent are *Veillonella* bacteria, e.g., *Veillonella* bacteria deposited as ATCC designation number PTA-125691.

[424] In some embodiments, the bacteria of the pharmaceutical agent are *Ruminococcus gnavus* bacteria. In some embodiments, the *Ruminococcus gnavus* bacteria are a strain comprising at least 90% (or at least 97%) genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Ruminococcus gnavus* bacteria deposited as ATCC designation number PTA-126695. In some embodiments, the *Ruminococcus gnavus* bacteria are a strain comprising at least 99% genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Ruminococcus gnavus* bacteria deposited as ATCC designation number PTA-126695. In some embodiments, the *Ruminococcus gnavus* bacteria are *Ruminococcus gnavus* bacteria deposited as ATCC designation number PTA-126695.

[425] In some embodiments, the bacteria of the pharmaceutical agent are *Megasphaera sp.* bacteria. In some embodiments, the *Megasphaera sp.* bacteria are a strain comprising at least 90% (or at least 97%) genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Megasphaera sp.* bacteria deposited as ATCC designation number PTA-126770. In some embodiments, the *Megasphaera sp.* bacteria are a strain comprising at least 99% genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Megasphaera sp.* bacteria deposited as ATCC designation number PTA-126770. In some embodiments, the *Megasphaera sp.* bacteria are *Megasphaera sp.* bacteria deposited as ATCC designation number PTA-126770.

[426] In some embodiments, the bacteria of the pharmaceutical agent are *Fournierella massiliensis* bacteria. In some embodiments, the *Fournierella massiliensis* bacteria are a strain comprising at least 90% (or at least 97%) genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Fournierella massiliensis* bacteria deposited as ATCC designation number PTA-126696. In some embodiments, the *Fournierella massiliensis* bacteria are a strain comprising at least 99% genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Fournierella massiliensis* bacteria deposited as ATCC designation number PTA-126696. In some embodiments, the *Fournierella massiliensis* bacteria are *Fournierella massiliensis* bacteria deposited as ATCC designation number PTA-126696.

[427] In some embodiments, the bacteria of the pharmaceutical agent are *Harryflintia acetispora* bacteria. In some embodiments, the *Harryflintia acetispora* bacteria are a

strain comprising at least 90% (or at least 97%) genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Harryflintia acetispora* bacteria deposited as ATCC designation number PTA-126694. In some embodiments, the *Harryflintia acetispora* bacteria are a strain comprising at least 99% genomic, 16S and/or CRISPR sequence identity to the nucleotide sequence of the *Harryflintia acetispora* bacteria deposited as ATCC designation number PTA-126694. In some embodiments, the *Harryflintia acetispora* bacteria are *Harryflintia acetispora* bacteria deposited as ATCC designation number PTA-126694.

[428] In some embodiments, the bacteria of the pharmaceutical agent are bacteria that produce metabolites, e.g., the bacteria produce butyrate, iosine, proprionate, or tryptophan metabolites.

[429] In some embodiments, the bacteria produce butyrate. In some embodiments, the bacteria are from the genus *Blautia; Christensella; Copracoccus; Eubacterium; Lachnosperacea; Megasphaera;* or *Roseburia*.

[430] In some embodiments, the bacteria produce iosine. In some embodiments, the bacteria are from the genus *Bifidobacterium; Lactobacillus;* or *Olsenella*.

[431] In some embodiments, the bacteria produce proprionate. In some embodiments, the bacteria are from the genus *Akkermansia; Bacteriodes; Dialister; Eubacterium; Megasphaera; Parabacteriodes; Prevotella; Ruminococcus*; or *Veillonella*.

[432] In some embodiments, the bacteria produce tryptophan metabolites. In some embodiments, the bacteria are from the genus *Lactobacillus* or *Peptostreptococcus*.

[433] In some embodiments, the bacteria of the pharmaceutical agent are bacteria that produce inhibitors of histone deacetylase 3 (HDAC3). In some embodiments, the bacteria are from the species *Bariatricus massiliensis, Faecalibacterium prausnitzii, Megasphaera massiliensis* or *Roseburia intestinalis.*

[434] In some embodiments, the bacteria are of the genus *Cutibacterium*.

[435] In some embodiments, the bacteria are *Cutibacterium avidum.*

[436] In some embodiments, the bacteria are from the genus *Lactobacillus*.

[437] In some embodiments, the bacteria are from the species *Lactobacillus gasseri*.

[438] In some embodiments, the bacteria are from the genus *Dysosmobacter*.

[439] In some embodiments, the bacteria are from the species *Dysosmobacter welbionis*.

[440] In some embodiments, the bacteria of the genus *Leuconostoc*.

[441] In some embodiments, the bacteria of the genus *Lactobacillus*.

[442] In some embodiments, the bacteria are of the genus *Akkermansia*; *Bacillus*; *Blautia*; *Cupriavidus*; *Enhydrobacter*; *Faecalibacterium*; *Lactobacillus*; *Lactococcus*; *Micrococcus*; *Morganella*; *Propionibacterium*; *Proteus*; *Rhizobium*; or *Streptococcus*.

[443] In some embodiments, the bacteria are *Leuconostoc holzapfelii* bacteria.

[444] In some embodiments, the bacteria are *Akkermansia muciniphila*; *Cupriavidus metallidurans*; *Faecalibacterium prausnitzii*; *Lactobacillus casei*; *Lactobacillus plantarum*; *Lactobacillus paracasei*; *Lactobacillus plantarum*; *Lactobacillus rhamnosus*; *Lactobacillus sakei*; or *Streptococcus pyogenes* bacteria.

[445] In some embodiments, the bacteria are *Lactobacillus casei*; *Lactobacillus plantarum*; *Lactobacillus paracasei*; *Lactobacillus plantarum*; *Lactobacillus rhamnosus*; or *Lactobacillus sakei* bacteria.

[446] In some embodiments, the bacteria are *Megasphaera sp.* bacteria (e.g., from the strain with accession number NCIMB 43385, NCIMB 43386 or NCIMB 43387).

[447] In some embodiments, the bacteria are *Megasphaera massiliensis* bacteria (e.g., from the strain with accession number NCIMB 42787, NCIMB 43388 or NCIMB 43389).

[448] In some embodiments, the bacteria are *Megasphaera massiliensis* bacteria (e.g., from the strain with accession number DSM 26228).

[449] In some embodiments, the bacteria are *Bacillus amyloliquefaciens* bacteria (e.g., from the strain with accession number NCIMB 43088, NCIMB 43087, or NCIMB 43086).

[450] In some embodiments, the bacteria are *Parabacteroides distasonis* bacteria (e.g., from the strain with accession number NCIMB 42382).

[451] In some embodiments, the bacteria are *Megasphaera massiliensis* bacteria (e.g., from the strain with accession number NCIMB 43388 or NCIMB 43389), or a derivative thereof. See, e.g., WO 2020/120714. In some embodiments, the *Megasphaera massiliensis* bacteria is a strain comprising at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity (e.g., at least 99.5% sequence identity, at least 99.6% sequence identity, at least 99.7% sequence identity, at least 99.8% sequence identity, at least 99.9% sequence identity) to the nucleotide sequence (e.g., genomic sequence, 16S sequence, and/or CRISPR sequence) of *Megasphaera massiliensis* bacteria from the strain with accession number NCIMB 43388 or NCIMB 43389. In some embodiments, the *Megasphaera massiliensis* bacteria is the strain with accession number NCIMB 43388 or NCIMB 43389.

[452] In some embodiments, the bacteria are *Megasphaera massiliensis* bacteria strain deposited under accession number NCIMB 42787, or a derivative thereof. See, e.g., WO 2018/229216. In some embodiments, the *Megasphaera massiliensis* bacteria is a strain comprising at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity (e.g., at least 99.5% sequence identity, at least 99.6% sequence identity, at least 99.7% sequence identity, at least 99.8% sequence identity, at least 99.9% sequence identity) to the nucleotide sequence (e.g., genomic sequence, 16S sequence, and/or CRISPR sequence) of the *Megasphaera massiliensis* bacteria strain deposited under accession number NCIMB 42787. In some embodiments, the *Megasphaera massiliensis* bacteria is the strain deposited under accession number NCIMB 42787.

[453] In some embodiments, the bacteria are *Megasphaera spp.* bacteria from the strain with accession number NCIMB 43385, NCIMB 43386 or NCIMB 43387, or a derivative thereof. See, e.g., WO 2020/120714. In some embodiments, the *Megasphaera sp.* bacteria is a strain comprising at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity (e.g., at least 99.5% sequence identity, at least 99.6% sequence identity, at least 99.7% sequence identity, at least 99.8% sequence identity, at least 99.9% sequence identity) to the nucleotide sequence (e.g., genomic sequence, 16S sequence, and/or CRISPR sequence) of the *Megasphaera sp.* from a strain with accession number NCIMB 43385, NCIMB 43386 or NCIMB 43387. In some embodiments, the *Megasphaera sp.* bacteria is the strain with accession number NCIMB 43385, NCIMB 43386 or NCIMB 43387.

[454] In some embodiments, the bacteria are *Parabacteroides distasonis* bacteria deposited under accession number NCIMB 42382, or a derivative thereof. See, e.g., WO 2018/229216. In some embodiments, the *Parabacteroides distasonis* bacteria is a strain comprising at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity (e.g., at least 99.5% sequence identity, at least 99.6% sequence identity, at least 99.7% sequence identity, at least 99.8% sequence identity, at least 99.9% sequence identity) to the nucleotide sequence (e.g., genomic sequence, 16S sequence, and/or CRISPR sequence) of the *Parabacteroides distasonis* bacteria deposited under accession number NCIMB 42382. In some embodiments, the *Parabacteroides distasonis* bacteria is the strain deposited under accession number NCIMB 42382.

[455] In some embodiments, the bacteria are *Megasphaera massiliensis* bacteria deposited under accession number DSM 26228, or a derivative thereof. See, e.g., WO 2018/229216. In some embodiments, the *Megasphaera massiliensis* bacteria is a strain comprising at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity (e.g., at least 99.5% sequence identity, at least 99.6% sequence identity, at least 99.7% sequence identity, at least 99.8% sequence identity, at least 99.9% sequence identity) to the nucleotide sequence (e.g., genomic sequence, 16S sequence, and/or CRISPR sequence) of *Megasphaera massiliensis* bacteria deposited under accession number DSM 26228. In some embodiments, the *Megasphaera massiliensis* bacteria is the strain deposited under accession number DSM 26228.

[456] In some embodiments, the bacteria are *Bacillus amyloliquefaciens* bacteria (e.g., from the strain with accession number NCIMB 43088, NCIMB 43087, or NCIMB 43086, or a derivative thereof. See, e.g., WO 2019/236806. In some embodiments, the *Bacillus amyloliquefaciens* bacteria is a strain comprising at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% sequence identity (e.g., at least 99.5% sequence identity, at least 99.6% sequence identity, at least 99.7% sequence identity, at least 99.8% sequence identity, at least 99.9% sequence identity) to the nucleotide sequence (e.g., genomic sequence, 16S sequence, and/or CRISPR sequence) of *Bacillus amyloliquefaciens* bacteria from the strain with accession number NCIMB 43088, NCIMB 43087, or NCIMB 43086. In some embodiments, the *Bacillus amyloliquefaciens* bacteria is the strain with accession number NCIMB 43088, NCIMB 43087, or NCIMB 43086. In some embodiments, the *Bacillus amyloliquefaciens* bacteria is the strain with accession number NCIMB 43088.

Table 1: Bacteria by Class

Class	Order	Family	Genus*	Species
Actinobacter	*Actinomycetales*	*Mycobacteriaceae*	*Mycobacterium*	
		Streptomycetaceae	*Streptomyces (S.)*	*S. lividans, S coelicolor, S sudanesis, S somaliensis*
	Bifidobacteriales	*Bifidobacteriaceae*	*Bifidobacterium (B.)*	*B. adolescentis, B.animalis, B.bifidum, B. breve, B. lactis, B. longum, B. pseudocatenulatum*
	Coriobacteriales	*Coriobacteriaceae*	***Collinsella***	*Collinsella aerofaciens*
			Olsenella	*Olsenella faecalis*

	Propionibacteriales	*Propionibacteraceae*	*Propionibacterium*	
			Cutibacterium	*Cutibacterium avidum*
Bacilli	*Bacillales*	*Bacillales incertae sedis family XI*	*Gemella (G.)*	*G. haemolysans, G. morbillorum*
		Listeraceae	*Listeria (L.)*	*L. monocytogenes, L. welshimeri*
	Lactobacillales	*Enterococcaceae*	*Enterococcus (E.)*	*E. durans, E. faecium, E. faecalis, E. gallinarum, E. villorum,*
			Lactobacillus (L.)	*L. casei, L. fermentum, L. mucosae, L. plantarum, L. reuteri, L. rhamnosus, L. salvarius, L. gasseri*
		Streptococcaceae	*Lactococcus*	*Lactococcus lactis cremoris*
			Staphylococcus	*Staphylococcus aureus*
			Streptococcus (S.)	*S. agalactiae, S. aureus, S. australi, S. mutans, S. parasanguinis, S. pneumoniae, S. pyogenes, S. salivarius*
Bacteriodes	*Bacteroidales*	*Bacteriodaceae*	*Bacteriodes (B.)*	*B. caccae, B. cellulosilyticus, B. coprocola, B. dorei, B. fragilis, B. ovatus, B. putredinis, B. salanitronis, B. thetaiotaomicron, B. vulgatus*
		Odoribacteraceae	*Odoribacter*	*Odoribacter splanchnicus*
		Porphyromonadaceae	*Parabacteriodes (P.)*	*P. distasonis, P. goldsteinii, P. merdae*
			Porphyromonas	*Porphyromonas gingivalis*
		Prevotellaceae	*Prevotella (P.)*	*P. albensis, P. amnii, P. aurantiaca, P. baroniae, P. bergensis, P. bivia, P. brevis, P. bryantii, P. buccae, P. buccalis, P. colorans, P. corporis, P. copri, P. dentalis, P. dentasini, P. denticola, P. disiens,, P. enoeca, P. falsenii, P. fusca, P. heparinolytica, P. histicola, P. intermedia, P. jejuni, , P. loescheii, P. maculosa, P. marshii, P. melaninogenica, P.*

				micans, P. multiformis, P. multisaccharivorax, P. nanceiensis, P. nigrescens, P. oralis, P. oris, , P. oryzae, P. oulorum, P. pallens, P. paludivivens, P. pleuritidis P. ruminicola, P. saccharolytica, P. salivae, P. scopos, P. shahii, P. stercorea, P. tannerae, P. timonensis, P. veroralis, P. zoogleoformans
		Rikenellaceae	*Alstipes (A.)*	*A. communis, A. dispar, A. finegoldii, A. indistinctus, A. ihumii, A. inops, A. massiliensis, A. megaguti, A. obesi , A. onderdonkii, A. provencensis, A. putredinis, A. senegalensis, A. shahii, A. timonensis*
Betaproteobacteria	*Burkholderiales*	*Alcaligenaceae*	*Paenalcaligenes*	*Paenalcaligenes hominis*
			Bordella	*Bordella pertussis*
		Burkholderiaceae	*Burkholderia (B.)*	*B. mallei, B. pseudomallei*
			Ralstonia	*Ralstonia solanacearum*
		Neisseriaceae	*Neisseria*	***Neisseria meningitidis***
		Sutterellaceae	*Sutterella (S.)*	*S. parvirubra, S. stercoricanis, S. wadsworthensis*
Clostridia	*Clostridiales*	*Catabacteriaceae*	*Catabacter*	*Catabacter hongkongensis*
		Clostridiaceae	*Aminiphila*	*Anaerosphaera aminiphila*
			Christensenellacea e (C.)	*C. massiliensis, C. minuta, C. timonensis*
			Hungatella	*Hungatella effluvia*
		Eubacteriaceae	*Eubacterium (E.)*	*E. contortum, E. eligens, E. faecium, E. hadrum, E. hallii, E.*

				limosum, E. ramulus, E. rectale
		Lachnospiraceae	*Anaerostipes (A.)*	*A. caccae, A. hadrus*
			Blautia (B.)	*B. hydrogenotrophica, B. massiliensis, B. stercoris, B. wexlerae*
			Catonella	*Catonella morbi*
			Coprococcus (C.)	*C. catus, C. comes, C. eutactus*
			Dialister (D.)	*D. invisus, D. micraeophilus, D. succinatiphilus*
			Dorea (D.)	*D. formicigenerans, D. longicatena*
			Johnsonella	*Johnsonella ignava*
			Oribacterium (O.)	*O. parvum, O. sinus*
			Lachnobacterium	
			Lachnoclostridium	
			Lacrimispora (L.)	*L. sacchaarolytica*
			Roseburia (R.)	*R. hominis, R. intestinalis*
			Tyzzerella	*Tyzzerella nexilis*
		Oscillospiraceae	*Oscillibacter*	*Oscillibacter valericigenes*
			Harryflintia	*Harryflinta acetispora*
			Dysosmobacter	*Dysosmobacter welbionis*
		Peptococcaceae		
		Peptostreptococcaceae	*Paraclostridium*	*Paraclostridium benzoelyticum*
			Peptostreptococcus	*Peptostreptococcus russellii*
		Ruminococcaceae	*Agathobaculum*	*Agathobaculum sp.*
			Fournierella	*Fournierella masssiliensis*
			Ruminococcus (R.)	*R. albus, R. bromii, R. callidus, R. gnavus, R. inulinivorans, R. obeum, R. torques*
			Faecalibacterium	*Faecalibacterium prasusnitzii*
		Clostridiales family XIII/ Incertae sedis		*Intestimonas butyriciproducens*
Fusobacteria	*Fusobacteriales*	*Fusobacteriaceae*	*Fusobacterium (F.)*	*F. nucleatum, F. naviforme*
		Leptotrichiaceae	*Leptotrichia*	
			Sneathia	
Gammaproteobacteria	*Enterobacterales*	*Enterobacteriaceae*	*Klebsiella (K.)*	*K. oxytoca, K. pneumoniae, K. quasipneumoniae*

				subsp. Similipneumoniae,
			Escherichia (E.)	*E. coli strain Nissle 1917 (EcN), E. coli strain ECOR12, E. coli strain ECOR63*
			Shigella	
Negativicutes		*Acidaminococcaceae*	*Acidaminococcus (A.)*	*A. fermentans, A. intestine*
			Phascolarctobacterium (P.)	*P. faecium, P. succinatutens*
		Selenomonadaceae	*Selenomonas (S.)*	*S. felix, S. incertae sedis, S. sputigena*
		Sporomusaceae	*Selenomonadales*	
		Veillonellaceae	*Allisonella*	
			Anaeroglobus	*Anaeroglobus germinatus*
			Caecibacter	
			Colibacter	
			Megasphaera (M.)	*M. elsedenii, M. massiliensis, M. micronuciformis, Megasphaera sp*
			Massilibacillus	*Massilibacillus massiliensis*
			Propionispira	
			Negativicoccus	*Negativicoccus succinicivornas*
			Veillonella (V.)	*V. dispar, V. parvula, V. ratti, V. tobetsuensis*
	Synergistales	*Synergistaceae*	*Aminobacterium*	*Aminobacterium mobile*
			Cloacibacillus	*Cloacibacillus evryensis*
			Rarimicrobium	*Rarimicrobium hominis*
Verrucomicrobia	*Verrucomicrobiales*	*Akkermansiaceae*	*Akkermansia*	*Akkermansia mucinophila*

Table 2: Exemplary Bacterial Strains

OTU	Public DB Accession	OTU	Public DB Accession
Actinobacillus actinomycetemcomitans	AY362885	*Lactobacillus murinus*	NR_042231
Actinobacillus minor	ACFT01000025	*Lactobacillus nodensis*	NR_041629
Actinobacillus pleuropneumoniae	NR_074857	*Lactobacillus oeni*	NR_043095
Actinobacillus succinogenes	CP000746	*Lactobacillus oris*	AEKL01000077
Actinobacillus ureae	AEVG01000167	*Lactobacillus parabrevis*	NR_042456
Actinobaculum massiliae	AF487679	*Lactobacillus parabuchneri*	NR_041294
Actinobaculum schaalii	AY957507	*Lactobacillus paracasei*	ABQV01000067

Actinobaculum sp. BM#101342	AY282578	*Lactobacillus parakefiri*	NR_029039
Actinobaculum sp. P2P_19 P1	AY207066	*Lactobacillus pentosus*	JN813103
Akkermansia muciniphila	CP001071	*Lactobacillus perolens*	NR_029360
Alistipes finegoldii	NR_043064	*Lactobacillus plantarum*	ACGZ02000033
Alistipes indistinctus	AB490804	*Lactobacillus pontis*	HM218420
Alistipes onderdonkii	NR_043318	*Lactobacillus reuteri*	ACGW02000012
Alistipes putredinis	ABFK02000017	*Lactobacillus rhamnosus*	ABWJ01000068
Alistipes shahii	FP929032	*Lactobacillus rogosae*	GU269544
Alistipes sp. HGB5	AENZ01000082	*Lactobacillus ruminis*	ACGS02000043
Alistipes sp. JC50	JF824804	*Lactobacillus sakei*	DQ989236
Alistipes sp. RMA 9912	GQ140629	*Lactobacillus salivarius*	AEBA01000145
Anaerostipes caccae	ABAX03000023	*Lactobacillus saniviri*	AB602569
Anaerostipes sp. 3_2_56FAA	ACWB01000002	*Lactobacillus senioris*	AB602570
Bacillus aeolius	NR_025557	*Lactobacillus sp. 66c*	FR681900
Bacillus aerophilus	NR_042339	*Lactobacillus sp. BT6*	HQ616370
Bacillus aestuarii	GQ980243	*Lactobacillus sp. KLDS 1.0701*	EU600905
Bacillus alcalophilus	X76436	*Lactobacillus sp. KLDS 1.0702*	EU600906
Bacillus amyloliquefaciens	NR_075005	*Lactobacillus sp. KLDS 1.0703*	EU600907
Bacillus anthracis	AAEN01000020	*Lactobacillus sp. KLDS 1.0704*	EU600908
Bacillus atrophaeus	NR_075016	*Lactobacillus sp. KLDS 1.0705*	EU600909
Bacillus badius	NR_036893	*Lactobacillus sp. KLDS 1.0707*	EU600911
Bacillus cereus	ABDJ01000015	*Lactobacillus sp. KLDS 1.0709*	EU600913
Bacillus circulans	AB271747	*Lactobacillus sp. KLDS 1.0711*	EU600915
Bacillus clausii	FN397477	*Lactobacillus sp. KLDS 1.0712*	EU600916
Bacillus coagulans	DQ297928	*Lactobacillus sp. KLDS 1.0713*	EU600917
Bacillus firmus	NR_025842	*Lactobacillus sp. KLDS 1.0716*	EU600921
Bacillus flexus	NR_024691	*Lactobacillus sp. KLDS 1.0718*	EU600922
Bacillus fordii	NR_025786	*Lactobacillus sp. KLDS 1.0719*	EU600923
Bacillus gelatini	NR_025595	*Lactobacillus sp. oral clone HT002*	AY349382
Bacillus halmapalus	NR_026144	*Lactobacillus sp. oral clone HT070*	AY349383
Bacillus halodurans	AY144582	*Lactobacillus sp. oral taxon 052*	GQ422710
Bacillus herbersteinensis	NR_042286	*Lactobacillus tucceti*	NR_042194
Bacillus horti	NR_036860	*Lactobacillus ultunensis*	ACGU01000081
Bacillus idriensis	NR_043268	*Lactobacillus vaginalis*	ACGV01000168
Bacillus lentus	NR_040792	*Lactobacillus vini*	NR_042196
Bacillus licheniformis	NC_006270	*Lactobacillus vitulinus*	NR_041305
Bacillus megaterium	GU252124	*Lactobacillus zeae*	NR_037122
Bacillus nealsonii	NR_044546	*Lactococcus garvieae*	AF061005
Bacillus niabensis	NR_043334	*Lactococcus lactis*	CP002365
Bacillus niacini	NR_024695	*Lactococcus raffinolactis*	NR_044359
Bacillus pocheonensis	NR_041377	*Listeria grayi*	ACCR02000003
Bacillus pumilus	NR_074977	*Listeria innocua*	JF967625
Bacillus safensis	JQ624766	*Listeria ivanovii*	X56151
Bacillus simplex	NR_042136	*Listeria monocytogenes*	CP002003
Bacillus sonorensis	NR_025130	*Listeria welshimeri*	AM263198
Bacillus sp. 10403023 MM10403188	CAET01000089	*Megasphaera elsdenii*	AY038996
Bacillus sp. 2_A_57_CT2	ACWD01000095	*Megasphaera genomosp. C1*	AY278622
Bacillus sp. 2008724126	GU252108	*Megasphaera genomosp. type_1*	ADGP01000010
Bacillus sp. 2008724139	GU252111	*Megasphaera micronuciformis*	AECS01000020
Bacillus sp. 7_16AIA	FN397518	*Megasphaera sp. BLPYG_07*	HM990964
Bacillus sp. 9_3AIA	FN397519	*Megasphaera sp. UPII 199_6*	AFIJ01000040

Bacillus sp. AP8	JX101689	*Microbacterium gubbeenense*	NR_025098
Bacillus sp. B27(2008)	EU362173	*Microbacterium lacticum*	EU714351
Bacillus sp. BT1B_CT2	ACWC01000034	*Mitsuokella jalaludinii*	NR_028840
Bacillus sp. GB1.1	FJ897765	*Mitsuokella multacida*	ABWK02000005
Bacillus sp. GB9	FJ897766	*Mitsuokella sp. oral taxon 521*	GU413658
Bacillus sp. HU19.1	FJ897769	*Mitsuokella sp. oral taxon G68*	GU432166
Bacillus sp. HU29	FJ897771	*Mycobacterium abscessus*	AGQU01000002
Bacillus sp. HU33.1	FJ897772	*Mycobacterium africanum*	AF480605
Bacillus sp. JC6	JF824800	*Mycobacterium alsiensis*	AJ938169
Bacillus sp. oral taxon F26	HM099642	*Mycobacterium avium*	CP000479
Bacillus sp. oral taxon F28	HM099650	*Mycobacterium chelonae*	AB548610
Bacillus sp. oral taxon F79	HM099654	*Mycobacterium colombiense*	AM062764
Bacillus sp. SRC_DSF1	GU797283	*Mycobacterium elephantis*	AF385898
Bacillus sp. SRC_DSF10	GU797292	*Mycobacterium gordonae*	GU142930
Bacillus sp. SRC_DSF2	GU797284	*Mycobacterium intracellulare*	GQ153276
Bacillus sp. SRC_DSF6	GU797288	*Mycobacterium kansasii*	AF480601
Bacillus sp. tc09	HQ844242	*Mycobacterium lacus*	NR_025175
Bacillus sp. zh168	FJ851424	*Mycobacterium leprae*	FM211192
Bacillus sphaericus	DQ286318	*Mycobacterium lepromatosis*	EU203590
Bacillus sporothermodurans	NR_026010	*Mycobacterium mageritense*	FR798914
Bacillus subtilis	EU627588	*Mycobacterium mantenii*	FJ042897
Bacillus thermoamylovorans	NR_029151	*Mycobacterium marinum*	NC_010612
Bacillus weihenstephanensis	NR_074926	*Mycobacterium microti*	NR_025234
Bacteroidales bacterium ph8	JN837494	*Mycobacterium neoaurum*	AF268445
Bacteroidales genomosp. P1	AY341819	*Mycobacterium parascrofulaceum*	ADNV01000350
Bacteroidales genomosp. P2 oral clone MB1_G13	DQ003613	*Mycobacterium paraterrae*	EU919229
Bacteroidales genomosp. P3 oral clone MB1_G34	DQ003615	*Mycobacterium phlei*	GU142920
Bacteroidales genomosp. P4 oral clone MB2_G17	DQ003617	*Mycobacterium seoulense*	DQ536403
Bacteroidales genomosp. P5 oral clone MB2_P04	DQ003619	*Mycobacterium smegmatis*	CP000480
Bacteroidales genomosp. P6 oral clone MB3_C19	DQ003634	*Mycobacterium sp. 1761*	EU703150
Bacteroidales genomosp. P7 oral clone MB3_P19	DQ003623	*Mycobacterium sp. 1776*	EU703152
Bacteroidales genomosp. P8 oral clone MB4_G15	DQ003626	*Mycobacterium sp. 1781*	EU703147
Bacteroides acidifaciens	NR_028607	*Mycobacterium sp. 1791*	EU703148
Bacteroides barnesiae	NR_041446	*Mycobacterium sp. 1797*	EU703149
Bacteroides caccae	EU136686	*Mycobacterium sp. AQ1GA4*	HM210417
Bacteroides cellulosilyticus	ACCH01000108	*Mycobacterium sp. B10_07.09.0206*	HQ174245
Bacteroides clarus	AFBM01000011	*Mycobacterium sp. GN_10546*	FJ497243
Bacteroides coagulans	AB547639	*Mycobacterium sp. GN_10827*	FJ497247
Bacteroides coprocola	ABIY02000050	*Mycobacterium sp. GN_11124*	FJ652846
Bacteroides coprophilus	ACBW01000012	*Mycobacterium sp. GN_9188*	FJ497240
Bacteroides dorei	ABWZ01000093	*Mycobacterium sp. GR_2007_210*	FJ555538
Bacteroides eggerthii	ACWG01000065	*Mycobacterium sp. HE5*	AJ012738
Bacteroides faecis	GQ496624	*Mycobacterium sp. NLA001000736*	HM627011
Bacteroides finegoldii	AB222699	*Mycobacterium sp. W*	DQ437715
Bacteroides fluxus	AFBN01000029	*Mycobacterium tuberculosis*	CP001658

Bacteroides fragilis	AP006841	*Mycobacterium ulcerans*	AB548725
Bacteroides galacturonicus	DQ497994	*Mycobacterium vulneris*	EU834055
Bacteroides helcogenes	CP002352	*Mycoplasma agalactiae*	AF010477
Bacteroides heparinolyticus	JN867284	*Mycoplasma amphoriforme*	AY531656
Bacteroides intestinalis	ABJL02000006	*Mycoplasma arthritidis*	NC_011025
Bacteroides massiliensis	AB200226	*Mycoplasma bovoculi*	NR_025987
Bacteroides nordii	NR_043017	*Mycoplasma faucium*	NR_024983
Bacteroides oleiciplenus	AB547644	*Mycoplasma fermentans*	CP002458
Bacteroides ovatus	ACWH01000036	*Mycoplasma flocculare*	X62699
Bacteroides pectinophilus	ABVQ01000036	*Mycoplasma genitalium*	L43967
Bacteroides plebeius	AB200218	*Mycoplasma hominis*	AF443616
Bacteroides pyogenes	NR_041280	*Mycoplasma orale*	AY796060
Bacteroides salanitronis	CP002530	*Mycoplasma ovipneumoniae*	NR_025989
Bacteroides salyersiae	EU136690	*Mycoplasma penetrans*	NC_004432
Bacteroides sp. 1_1_14	ACRP01000155	*Mycoplasma pneumoniae*	NC_000912
Bacteroides sp. 1_1_30	ADCL01000128	*Mycoplasma putrefaciens*	U26055
Bacteroides sp. 1_1_6	ACIC01000215	*Mycoplasma salivarium*	M24661
Bacteroides sp. 2_1_22	ACPQ01000117	*Mycoplasmataceae genomosp. P1 oral clone MB1_G23*	DQ003614
Bacteroides sp. 2_1_56FAA	ACWI01000065	*Neisseria bacilliformis*	AFAY01000058
Bacteroides sp. 2_2_4	ABZZ01000168	*Neisseria cinerea*	ACDY01000037
Bacteroides sp. 20_3	ACRQ01000064	*Neisseria elongata*	ADBF01000003
Bacteroides sp. 3_1_19	ADCJ01000062	*Neisseria flavescens*	ACQV01000025
Bacteroides sp. 3_1_23	ACRS01000081	*Neisseria genomosp. P2 oral clone MB5_P15*	DQ003630
Bacteroides sp. 3_1_33FAA	ACPS01000085	*Neisseria gonorrhoeae*	CP002440
Bacteroides sp. 3_1_40A	ACRT01000136	*Neisseria lactamica*	ACEQ01000095
Bacteroides sp. 3_2_5	ACIB01000079	*Neisseria macacae*	AFQE01000146
Bacteroides sp. 315_5	FJ848547	*Neisseria meningitidis*	NC_003112
Bacteroides sp. 31SF15	AJ583248	*Neisseria mucosa*	ACDX01000110
Bacteroides sp. 31SF18	AJ583249	*Neisseria pharyngis*	AJ239281
Bacteroides sp. 35AE31	AJ583244	*Neisseria polysaccharea*	ADBE01000137
Bacteroides sp. 35AE37	AJ583245	*Neisseria sicca*	ACKO02000016
Bacteroides sp. 35BE34	AJ583246	*Neisseria sp. KEM232*	GQ203291
Bacteroides sp. 35BE35	AJ583247	*Neisseria sp. oral clone AP132*	AY005027
Bacteroides sp. 4_1_36	ACTC01000133	*Neisseria sp. oral clone JC012*	AY349388
Bacteroides sp. 4_3_47FAA	ACDR02000029	*Neisseria sp. oral strain B33KA*	AY005028
Bacteroides sp. 9_1_42FAA	ACAA01000096	*Neisseria sp. oral taxon 014*	ADEA01000039
Bacteroides sp. AR20	AF139524	*Neisseria sp. SMC_A9199*	FJ763637
Bacteroides sp. AR29	AF139525	*Neisseria sp. TM10_1*	DQ279352
Bacteroides sp. B2	EU722733	*Neisseria subflava*	ACEO01000067
Bacteroides sp. D1	ACAB02000030	*Odoribacter laneus*	AB490805
Bacteroides sp. D2	ACGA01000077	*Odoribacter splanchnicus*	CP002544
Bacteroides sp. D20	ACPT01000052	*Oscillibacter sp. G2*	HM626173
Bacteroides sp. D22	ADCK01000151	*Oscillibacter valericigenes*	NR_074793
Bacteroides sp. F_4	AB470322	*Oscillospira guilliermondii*	AB040495
Bacteroides sp. NB_8	AB117565	*Paenibacillus barcinonensis*	NR_042272
Bacteroides sp. WH2	AY895180	*Paenibacillus barengoltzii*	NR_042756
Bacteroides sp. XB12B	AM230648	*Paenibacillus chibensis*	NR_040885
Bacteroides sp. XB44A	AM230649	*Paenibacillus cookii*	NR_025372
Bacteroides stercoris	ABFZ02000022	*Paenibacillus durus*	NR_037017
Bacteroides thetaiotaomicron	NR_074277	*Paenibacillus glucanolyticus*	D78470

Bacteroides uniformis	AB050110	*Paenibacillus lactis*	NR_025739
Bacteroides ureolyticus	GQ167666	*Paenibacillus lautus*	NR_040882
Bacteroides vulgatus	CP000139	*Paenibacillus pabuli*	NR_040853
Bacteroides xylanisolvens	ADKP01000087	*Paenibacillus polymyxa*	NR_037006
Bacteroidetes bacterium oral taxon D27	HM099638	*Paenibacillus popilliae*	NR_040888
Bacteroidetes bacterium oral taxon F31	HM099643	*Paenibacillus sp. CIP 101062*	HM212646
Bacteroidetes bacterium oral taxon F44	HM099649	*Parabacteroides distasonis*	CP000140
Barnesiella intestinihominis	AB370251	*Parabacteroides goldsteinii*	AY974070
Bifidobacteriaceae genomosp. C1	AY278612	*Parabacteroides gordonii*	AB470344
Bifidobacterium adolescentis	AAXD02000018	*Parabacteroides johnsonii*	ABYH01000014
Bifidobacterium angulatum	ABYS02000004	*Parabacteroides merdae*	EU136685
Bifidobacterium animalis	CP001606	*Parabacteroides sp. D13*	ACPW01000017
Bifidobacterium bifidum	ABQP01000027	*Parabacteroides sp. NS31_3*	JN029805
Bifidobacterium breve	CP002743	*Peptococcus niger*	NR_029221
Bifidobacterium catenulatum	ABXY01000019	*Peptococcus sp. oral clone JM048*	AY349389
Bifidobacterium dentium	CP001750	*Peptococcus sp. oral taxon 167*	GQ422727
Bifidobacterium gallicum	ABXB03000004	*Peptoniphilus asaccharolyticus*	D14145
Bifidobacterium infantis	AY151398	*Peptoniphilus duerdenii*	EU526290
Bifidobacterium kashiwanohense	AB491757	*Peptoniphilus harei*	NR_026358
Bifidobacterium longum	ABQQ01000041	*Peptoniphilus indolicus*	AY153431
Bifidobacterium pseudocatenulatum	ABXX02000002	*Peptoniphilus ivorii*	Y07840
Bifidobacterium pseudolongum	NR_043442	*Peptoniphilus lacrimalis*	ADDO01000050
Bifidobacterium scardovii	AJ307005	*Peptoniphilus sp. gpac007*	AM176517
Bifidobacterium sp. HM2	AB425276	*Peptoniphilus sp. gpac018A*	AM176519
Bifidobacterium sp. HMLN12	JF519685	*Peptoniphilus sp. gpac077*	AM176527
Bifidobacterium sp. M45	HM626176	*Peptoniphilus sp. gpac148*	AM176535
Bifidobacterium sp. MSX5B	HQ616382	*Peptoniphilus sp. JC140*	JF824803
Bifidobacterium sp. TM_7	AB218972	*Peptoniphilus sp. oral taxon 386*	ADCS01000031
Bifidobacterium thermophilum	DQ340557	*Peptoniphilus sp. oral taxon 836*	AEAA01000090
Bifidobacterium urinalis	AJ278695	*Peptostreptococcaceae bacterium ph1*	JN837495
Blautia coccoides	AB571656	*Peptostreptococcus anaerobius*	AY326462
Blautia glucerasea	AB588023	*Peptostreptococcus micros*	AM176538
Blautia glucerasei	AB439724	*Peptostreptococcus sp. 9succ1*	X90471
Blautia hansenii	ABYU02000037	*Peptostreptococcus sp. oral clone AP24*	AB175072
Blautia hydrogenotrophica	ACBZ01000217	*Peptostreptococcus sp. oral clone FJ023*	AY349390
Blautia luti	AB691576	*Peptostreptococcus sp. P4P_31 P3*	AY207059
Blautia producta	AB600998	*Peptostreptococcus stomatis*	ADGQ01000048
Blautia schinkii	NR_026312	*Porphyromonadaceae bacterium NML 060648*	EF184292
Blautia sp. M25	HM626178	*Porphyromonas asaccharolytica*	AENO01000048
Blautia stercoris	HM626177	*Porphyromonas endodontalis*	ACNN01000021
Blautia wexlerae	EF036467	*Porphyromonas gingivalis*	AE015924
Bordetella bronchiseptica	NR_025949	*Porphyromonas levii*	NR_025907
Bordetella holmesii	AB683187	*Porphyromonas macacae*	NR_025908
Bordetella parapertussis	NR_025950	*Porphyromonas somerae*	AB547667

Bordetella pertussis	BX640418	*Porphyromonas sp. oral clone BB134*	AY005068
Borrelia afzelii	ABCU01000001	*Porphyromonas sp. oral clone F016*	AY005069
Borrelia burgdorferi	ABGI01000001	*Porphyromonas sp. oral clone P2PB_52 P1*	AY207054
Borrelia crocidurae	DQ057990	*Porphyromonas sp. oral clone P4GB_100 P2*	AY207057
Borrelia duttonii	NC_011229	*Porphyromonas sp. UQD 301*	EU012301
Borrelia garinii	ABJV01000001	*Porphyromonas uenonis*	ACLR01000152
Borrelia hermsii	AY597657	*Prevotella albensis*	NR_025300
Borrelia hispanica	DQ057988	*Prevotella amnii*	AB547670
Borrelia persica	HM161645	*Prevotella bergensis*	ACKS01000100
Borrelia recurrentis	AF107367	*Prevotella bivia*	ADFO01000096
Borrelia sp. NE49	AJ224142	*Prevotella brevis*	NR_041954
Borrelia spielmanii	ABKB01000002	*Prevotella buccae*	ACRB01000001
Borrelia turicatae	NC_008710	*Prevotella buccalis*	JN867261
Borrelia valaisiana	ABCY01000002	*Prevotella copri*	ACBX02000014
Brucella ovis	NC_009504	*Prevotella corporis*	L16465
Brucella sp. 83_13	ACBQ01000040	*Prevotella dentalis*	AB547678
Brucella sp. BO1	EU053207	*Prevotella denticola*	CP002589
Brucella suis	ACBK01000034	*Prevotella disiens*	AEDO01000026
Burkholderia ambifaria	AAUZ01000009	*Prevotella genomosp. C1*	AY278624
Burkholderia cenocepacia	AAHI01000060	*Prevotella genomosp. C2*	AY278625
Burkholderia cepacia	NR_041719	*Prevotella genomosp. P7 oral clone MB2_P31*	DQ003620
Burkholderia mallei	CP000547	*Prevotella genomosp. P8 oral clone MB3_P13*	DQ003622
Burkholderia multivorans	NC_010086	*Prevotella genomosp. P9 oral clone MB7_G16*	DQ003633
Burkholderia oklahomensis	DQ108388	*Prevotella heparinolytica*	GQ422742
Burkholderia pseudomallei	CP001408	*Prevotella histicola*	JN867315
Burkholderia rhizoxinica	HQ005410	*Prevotella intermedia*	AF414829
Burkholderia sp. 383	CP000151	*Prevotella loescheii*	JN867231
Burkholderia xenovorans	U86373	*Prevotella maculosa*	AGEK01000035
Burkholderiales bacterium 1_1_47	ADCQ01000066	*Prevotella marshii*	AEEI01000070
Butyrivibrio crossotus	ABWN01000012	*Prevotella melaninogenica*	CP002122
Butyrivibrio fibrisolvens	U41172	*Prevotella micans*	AGWK01000061
Chlamydia muridarum	AE002160	*Prevotella multiformis*	AEWX01000054
Chlamydia psittaci	NR_036864	*Prevotella multisaccharivorax*	AFJE01000016
Chlamydia trachomatis	U68443	*Prevotella nanceiensis*	JN867228
Chlamydiales bacterium NS11	JN606074	*Prevotella nigrescens*	AFPX01000069
Citrobacter amalonaticus	FR870441	*Prevotella oralis*	AEPE01000021
Citrobacter braakii	NR_028687	*Prevotella oris*	ADDV01000091
Citrobacter farmeri	AF025371	*Prevotella oulorum*	L16472
Citrobacter freundii	NR_028894	*Prevotella pallens*	AFPY01000135
Citrobacter gillenii	AF025367	*Prevotella ruminicola*	CP002006
Citrobacter koseri	NC_009792	*Prevotella salivae*	AB108826
Citrobacter murliniae	AF025369	*Prevotella sp. BI_42*	AJ581354
Citrobacter rodentium	NR_074903	*Prevotella sp. CM38*	HQ610181
Citrobacter sedlakii	AF025364	*Prevotella sp. ICM1*	HQ616385
Citrobacter sp. 30_2	ACDJ01000053	*Prevotella sp. ICM55*	HQ616399
Citrobacter sp. KMSI_3	GQ468398	*Prevotella sp. JCM 6330*	AB547699

Citrobacter werkmanii	AF025373	*Prevotella sp. oral clone AA020*	AY005057
Citrobacter youngae	ABWL02000011	*Prevotella sp. oral clone ASCG10*	AY923148
Cloacibacillus evryensis	GQ258966	*Prevotella sp. oral clone ASCG12*	DQ272511
Clostridiaceae bacterium END_2	EF451053	*Prevotella sp. oral clone AU069*	AY005062
Clostridiaceae bacterium JC13	JF824807	*Prevotella sp. oral clone CY006*	AY005063
Clostridiales bacterium 1_7_47FAA	ABQR01000074	*Prevotella sp. oral clone DA058*	AY005065
Clostridiales bacterium 9400853	HM587320	*Prevotella sp. oral clone FL019*	AY349392
Clostridiales bacterium 9403326	HM587324	*Prevotella sp. oral clone FU048*	AY349393
Clostridiales bacterium oral clone P4PA_66 P1	AY207065	*Prevotella sp. oral clone FW035*	AY349394
Clostridiales bacterium oral taxon 093	GQ422712	*Prevotella sp. oral clone GI030*	AY349395
Clostridiales bacterium oral taxon F32	HM099644	*Prevotella sp. oral clone GI032*	AY349396
Clostridiales bacterium ph2	JN837487	*Prevotella sp. oral clone GI059*	AY349397
Clostridiales bacterium SY8519	AB477431	*Prevotella sp. oral clone GU027*	AY349398
Clostridiales genomosp. BVAB3	CP001850	*Prevotella sp. oral clone HF050*	AY349399
Clostridiales sp. SM4_1	FP929060	*Prevotella sp. oral clone ID019*	AY349400
Clostridiales sp. SS3_4	AY305316	*Prevotella sp. oral clone IDR_CEC_0055*	AY550997
Clostridiales sp. SSC_2	FP929061	*Prevotella sp. oral clone IK053*	AY349401
Clostridium acetobutylicum	NR_074511	*Prevotella sp. oral clone IK062*	AY349402
Clostridium aerotolerans	X76163	*Prevotella sp. oral clone P4PB_83 P2*	AY207050
Clostridium aldenense	NR_043680	*Prevotella sp. oral taxon 292*	GQ422735
Clostridium aldrichii	NR_026099	*Prevotella sp. oral taxon 299*	ACWZ01000026
Clostridium algidicarnis	NR_041746	*Prevotella sp. oral taxon 300*	GU409549
Clostridium algidixylanolyticum	NR_028726	*Prevotella sp. oral taxon 302*	ACZK01000043
Clostridium aminovalericum	NR_029245	*Prevotella sp. oral taxon 310*	GQ422737
Clostridium amygdalinum	AY353957	*Prevotella sp. oral taxon 317*	ACQH01000158
Clostridium argentinense	NR_029232	*Prevotella sp. oral taxon 472*	ACZS01000106
Clostridium asparagiforme	ACCJ01000522	*Prevotella sp. oral taxon 781*	GQ422744
Clostridium baratii	NR_029229	*Prevotella sp. oral taxon 782*	GQ422745
Clostridium bartlettii	ABEZ02000012	*Prevotella sp. oral taxon F68*	HM099652
Clostridium beijerinckii	NR_074434	*Prevotella sp. oral taxon G60*	GU432133
Clostridium bifermentans	X73437	*Prevotella sp. oral taxon G70*	GU432179
Clostridium bolteae	ABCC02000039	*Prevotella sp. oral taxon G71*	GU432180
Clostridium botulinum	NC_010723	*Prevotella sp. SEQ053*	JN867222
Clostridium butyricum	ABDT01000017	*Prevotella sp. SEQ065*	JN867234
Clostridium cadaveris	AB542932	*Prevotella sp. SEQ072*	JN867238
Clostridium carboxidivorans	FR733710	*Prevotella sp. SEQ116*	JN867246
Clostridium carnis	NR_044716	*Prevotella sp. SG12*	GU561343
Clostridium celatum	X77844	*Prevotella sp. sp24*	AB003384
Clostridium celerecrescens	JQ246092	*Prevotella sp. sp34*	AB003385
Clostridium cellulosi	NR_044624	*Prevotella stercorea*	AB244774
Clostridium chauvoei	EU106372	*Prevotella tannerae*	ACIJ02000018
Clostridium citroniae	ADLJ01000059	*Prevotella timonensis*	ADEF01000012
Clostridium clariflavum	NR_041235	*Prevotella veroralis*	ACVA01000027
Clostridium clostridiiformes	M59089	*Prevotellaceae bacterium P4P_62 P1*	AY207061
Clostridium clostridioforme	NR_044715	*Propionibacteriaceae bacterium NML 02_0265*	EF599122
Clostridium coccoides	EF025906	*Propionibacterium acidipropionici*	NC_019395

Clostridium cochlearium	NR_044717	*Propionibacterium acnes*	ADJM01000010
Clostridium cocleatum	NR_026495	*Propionibacterium avidum*	AJ003055
Clostridium colicanis	FJ957863	*Propionibacterium freudenreichii*	NR_036972
Clostridium colinum	NR_026151	*Propionibacterium granulosum*	FJ785716
Clostridium difficile	NC_013315	*Propionibacterium jensenii*	NR_042269
Clostridium disporicum	NR_026491	*Propionibacterium propionicum*	NR_025277
Clostridium estertheticum	NR_042153	*Propionibacterium sp. 434_HC2*	AFIL01000035
Clostridium fallax	NR_044714	*Propionibacterium sp. H456*	AB177643
Clostridium favososporum	X76749	*Propionibacterium sp. LG*	AY354921
Clostridium felsineum	AF270502	*Propionibacterium sp. oral taxon 192*	GQ422728
Clostridium frigidicarnis	NR_024919	*Propionibacterium sp. S555a*	AB264622
Clostridium gasigenes	NR_024945	*Propionibacterium thoenii*	NR_042270
Clostridium ghonii	AB542933	*Pseudomonas aeruginosa*	AABQ07000001
Clostridium glycolicum	FJ384385	*Pseudomonas fluorescens*	AY622220
Clostridium glycyrrhizinilyticum	AB233029	*Pseudomonas gessardii*	FJ943496
Clostridium haemolyticum	NR_024749	*Pseudomonas mendocina*	AAUL01000021
Clostridium hathewayi	AY552788	*Pseudomonas monteilii*	NR_024910
Clostridium hiranonis	AB023970	*Pseudomonas poae*	GU188951
Clostridium histolyticum	HF558362	*Pseudomonas pseudoalcaligenes*	NR_037000
Clostridium hylemonae	AB023973	*Pseudomonas putida*	AF094741
Clostridium indolis	AF028351	*Pseudomonas sp. 2_1_26*	ACWU01000257
Clostridium innocuum	M23732	*Pseudomonas sp. G1229*	DQ910482
Clostridium irregulare	NR_029249	*Pseudomonas sp. NP522b*	EU723211
Clostridium isatidis	NR_026347	*Pseudomonas stutzeri*	AM905854
Clostridium kluyveri	NR_074165	*Pseudomonas tolaasii*	AF320988
Clostridium lactatifermentans	NR_025651	*Pseudomonas viridiflava*	NR_042764
Clostridium lavalense	EF564277	*Ralstonia pickettii*	NC_010682
Clostridium leptum	AJ305238	*Ralstonia sp. 5_7_47FAA*	ACUF01000076
Clostridium limosum	FR870444	*Roseburia cecicola*	GU233441
Clostridium magnum	X77835	*Roseburia faecalis*	AY804149
Clostridium malenominatum	FR749893	*Roseburia faecis*	AY305310
Clostridium mayombei	FR733682	*Roseburia hominis*	AJ270482
Clostridium methylpentosum	ACEC01000059	*Roseburia intestinalis*	FP929050
Clostridium nexile	X73443	*Roseburia inulinivorans*	AJ270473
Clostridium novyi	NR_074343	*Roseburia sp. 11SE37*	FM954975
Clostridium orbiscindens	Y18187	*Roseburia sp. 11SE38*	FM954976
Clostridium oroticum	FR749922	*Rothia aeria*	DQ673320
Clostridium paraputrificum	AB536771	*Rothia dentocariosa*	ADDW01000024
Clostridium perfringens	ABDW01000023	*Rothia mucilaginosa*	ACVO01000020
Clostridium phytofermentans	NR_074652	*Rothia nasimurium*	NR_025310
Clostridium piliforme	D14639	*Rothia sp. oral taxon 188*	GU470892
Clostridium putrefaciens	NR_024995	*Ruminobacter amylophilus*	NR_026450
Clostridium quinii	NR_026149	*Ruminococcaceae bacterium D16*	ADDX01000083
Clostridium ramosum	M23731	*Ruminococcus albus*	AY445600
Clostridium rectum	NR_029271	*Ruminococcus bromii*	EU266549
Clostridium saccharogumia	DQ100445	*Ruminococcus callidus*	NR_029160
Clostridium saccharolyticum	CP002109	*Ruminococcus champanellensis*	FP929052
Clostridium sardiniense	NR_041006	*Ruminococcus flavefaciens*	NR_025931
Clostridium sartagoforme	NR_026490	*Ruminococcus gnavus*	X94967
Clostridium scindens	AF262238	*Ruminococcus hansenii*	M59114
Clostridium septicum	NR_026020	*Ruminococcus lactaris*	ABOU02000049

Clostridium sordellii	AB448946	*Ruminococcus obeum*	AY169419
Clostridium sp. 7_2_43FAA	ACDK01000101	*Ruminococcus sp. 18P13*	AJ515913
Clostridium sp. D5	ADBG01000142	*Ruminococcus sp. 5_1_39BFAA*	ACII01000172
Clostridium sp. HGF2	AENW01000022	*Ruminococcus sp. 9SE51*	FM954974
Clostridium sp. HPB_46	AY862516	*Ruminococcus sp. ID8*	AY960564
Clostridium sp. JC122	CAEV01000127	*Ruminococcus sp. K_1*	AB222208
Clostridium sp. L2_50	AAYW02000018	*Ruminococcus torques*	AAVP02000002
Clostridium sp. LMG 16094	X95274	*Salmonella bongori*	NR_041699
Clostridium sp. M62_1	ACFX02000046	*Salmonella enterica*	NC_011149
Clostridium sp. MLG055	AF304435	*Salmonella enterica*	NC_011205
Clostridium sp. MT4 E	FJ159523	*Salmonella enterica*	DQ344532
Clostridium sp. NMBHI_1	JN093130	*Salmonella enterica*	ABEH02000004
Clostridium sp. NML 04A032	EU815224	*Salmonella enterica*	ABAK02000001
Clostridium sp. SS2_1	ABGC03000041	*Salmonella enterica*	NC_011080
Clostridium sp. SY8519	AP012212	*Salmonella enterica*	EU118094
Clostridium sp. TM_40	AB249652	*Salmonella enterica*	NC_011094
Clostridium sp. YIT 12069	AB491207	*Salmonella enterica*	AE014613
Clostridium sp. YIT 12070	AB491208	*Salmonella enterica*	ABFH02000001
Clostridium sphenoides	X73449	*Salmonella enterica*	ABEM01000001
Clostridium spiroforme	X73441	*Salmonella enterica*	ABAM02000001
Clostridium sporogenes	ABKW02000003	*Salmonella typhimurium*	DQ344533
Clostridium sporosphaeroides	NR_044835	*Salmonella typhimurium*	AF170176
Clostridium stercorarium	NR_025100	*Selenomonas artemidis*	HM596274
Clostridium sticklandii	L04167	*Selenomonas dianae*	GQ422719
Clostridium straminisolvens	NR_024829	*Selenomonas flueggei*	AF287803
Clostridium subterminale	NR_041795	*Selenomonas genomosp. C1*	AY278627
Clostridium sulfidigenes	NR_044161	*Selenomonas genomosp. C2*	AY278628
Clostridium symbiosum	ADLQ01000114	*Selenomonas genomosp. P5*	AY341820
Clostridium tertium	Y18174	*Selenomonas genomosp. P6 oral clone MB3_C41*	DQ003636
Clostridium tetani	NC_004557	*Selenomonas genomosp. P7 oral clone MB5_C08*	DQ003627
Clostridium thermocellum	NR_074629	*Selenomonas genomosp. P8 oral clone MB5_P06*	DQ003628
Clostridium tyrobutyricum	NR_044718	*Selenomonas infelix*	AF287802
Clostridium viride	NR_026204	*Selenomonas noxia*	GU470909
Clostridium xylanolyticum	NR_037068	*Selenomonas ruminantium*	NR_075026
Collinsella aerofaciens	AAVN02000007	*Selenomonas sp. FOBRC9*	HQ616378
Collinsella intestinalis	ABXH02000037	*Selenomonas sp. oral clone FT050*	AY349403
Collinsella stercoris	ABXJ01000150	*Selenomonas sp. oral clone GI064*	AY349404
Collinsella tanakaei	AB490807	*Selenomonas sp. oral clone GT010*	AY349405
Coprobacillus cateniformis	AB030218	*Selenomonas sp. oral clone HU051*	AY349406
Coprobacillus sp. 29_1	ADKX01000057	*Selenomonas sp. oral clone IK004*	AY349407
Coprobacillus sp. D7	ACDT01000199	*Selenomonas sp. oral clone IQ048*	AY349408
Coprococcus catus	EU266552	*Selenomonas sp. oral clone JI021*	AY349409
Coprococcus comes	ABVR01000038	*Selenomonas sp. oral clone JS031*	AY349410
Coprococcus eutactus	EF031543	*Selenomonas sp. oral clone OH4A*	AY947498
Coprococcus sp. ART55_1	AY350746	*Selenomonas sp. oral clone P2PA_80 P4*	AY207052
Dialister invisus	ACIM02000001	*Selenomonas sp. oral taxon 137*	AENV01000007
Dialister micraerophilus	AFBB01000028	*Selenomonas sp. oral taxon 149*	AEEJ01000007
Dialister microaerophilus	AENT01000008	*Selenomonas sputigena*	ACKP02000033

Dialister pneumosintes	HM596297	*Serratia fonticola*	NR_025339
Dialister propionicifaciens	NR_043231	*Serratia liquefaciens*	NR_042062
Dialister sp. oral taxon 502	GQ422739	*Serratia marcescens*	GU826157
Dialister succinatiphilus	AB370249	*Serratia odorifera*	ADBY01000001
Dorea formicigenerans	AAXA02000006	*Serratia proteamaculans*	AAUN01000015
Dorea longicatena	AJ132842	*Shigella boydii*	AAKA01000007
Enhydrobacter aerosaccus	ACYI01000081	*Shigella dysenteriae*	NC_007606
Enterobacter aerogenes	AJ251468	*Shigella flexneri*	AE005674
Enterobacter asburiae	NR_024640	*Shigella sonnei*	NC_007384
Enterobacter cancerogenus	Z96078	*Sphingobacterium faecium*	NR_025537
Enterobacter cloacae	FP929040	*Sphingobacterium mizutaii*	JF708889
Enterobacter cowanii	NR_025566	*Sphingobacterium multivorum*	NR_040953
Enterobacter hormaechei	AFHR01000079	*Sphingobacterium spiritivorum*	ACHA02000013
Enterobacter sp. 247BMC	HQ122932	*Sphingomonas echinoides*	NR_024700
Enterobacter sp. 638	NR_074777	*Sphingomonas sp. oral clone FI012*	AY349411
Enterobacter sp. JC163	JN657217	*Sphingomonas sp. oral clone FZ016*	AY349412
Enterobacter sp. SCSS	HM007811	*Sphingomonas sp. oral taxon A09*	HM099639
Enterobacter sp. TSE38	HM156134	*Sphingomonas sp. oral taxon F71*	HM099645
Enterobacteriaceae bacterium 9_2_54FAA	ADCU01000033	*Staphylococcaceae bacterium NML 92_0017*	AY841362
Enterobacteriaceae bacterium CF01Ent_1	AJ489826	*Staphylococcus aureus*	CP002643
Enterobacteriaceae bacterium Smarlab 3302238	AY538694	*Staphylococcus auricularis*	JQ624774
Enterococcus avium	AF133535	*Staphylococcus capitis*	ACFR01000029
Enterococcus caccae	AY943820	*Staphylococcus caprae*	ACRH01000033
Enterococcus casseliflavus	AEWT01000047	*Staphylococcus carnosus*	NR_075003
Enterococcus durans	AJ276354	*Staphylococcus cohnii*	JN175375
Enterococcus faecalis	AE016830	*Staphylococcus condimenti*	NR_029345
Enterococcus faecium	AM157434	*Staphylococcus epidermidis*	ACHE01000056
Enterococcus gallinarum	AB269767	*Staphylococcus equorum*	NR_027520
Enterococcus gilvus	AY033814	*Staphylococcus fleurettii*	NR_041326
Enterococcus hawaiiensis	AY321377	*Staphylococcus haemolyticus*	NC_007168
Enterococcus hirae	AF061011	*Staphylococcus hominis*	AM157418
Enterococcus italicus	AEPV01000109	*Staphylococcus lugdunensis*	AEQA01000024
Enterococcus mundtii	NR_024906	*Staphylococcus pasteuri*	FJ189773
Enterococcus raffinosus	FN600541	*Staphylococcus pseudintermedius*	CP002439
Enterococcus sp. BV2CASA2	JN809766	*Staphylococcus saccharolyticus*	NR_029158
Enterococcus sp. CCRI_16620	GU457263	*Staphylococcus saprophyticus*	NC_007350
Enterococcus sp. F95	FJ463817	*Staphylococcus sciuri*	NR_025520
Enterococcus sp. RfL6	AJ133478	*Staphylococcus sp. clone bottae7*	AF467424
Enterococcus thailandicus	AY321376	*Staphylococcus sp. H292*	AB177642
Erysipelotrichaceae bacterium 3_1_53	ACTJ01000113	*Staphylococcus sp. H780*	AB177644
Erysipelotrichaceae bacterium 5_2_54FAA	ACZW01000054	*Staphylococcus succinus*	NR_028667
Escherichia albertii	ABKX01000012	*Staphylococcus vitulinus*	NR_024670
Escherichia coli	NC_008563	*Staphylococcus warneri*	ACPZ01000009
Escherichia fergusonii	CU928158	*Staphylococcus xylosus*	AY395016
Escherichia hermannii	HQ407266	*Streptobacillus moniliformis*	NR_027615
Escherichia sp. 1_1_43	ACID01000033	*Streptococcus agalactiae*	AAJO01000130
Escherichia sp. 4_1_40B	ACDM02000056	*Streptococcus alactolyticus*	NR_041781

Escherichia sp. B4	EU722735	*Streptococcus anginosus*	AECT01000011
Escherichia vulneris	NR_041927	*Streptococcus australis*	AEQR01000024
Eubacteriaceae bacterium P4P_50 P4	AY207060	*Streptococcus bovis*	AEEL01000030
Eubacterium barkeri	NR_044661	*Streptococcus canis*	AJ413203
Eubacterium biforme	ABYT01000002	*Streptococcus constellatus*	AY277942
Eubacterium brachy	U13038	*Streptococcus cristatus*	AEVC01000028
Eubacterium budayi	NR_024682	*Streptococcus downei*	AEKN01000002
Eubacterium callanderi	NR_026330	*Streptococcus dysgalactiae*	AP010935
Eubacterium cellulosolvens	AY178842	*Streptococcus equi*	CP001129
Eubacterium contortum	FR749946	*Streptococcus equinus*	AEVB01000043
Eubacterium coprostanoligenes	HM037995	*Streptococcus gallolyticus*	FR824043
Eubacterium cylindroides	FP929041	*Streptococcus genomosp. C1*	AY278629
Eubacterium desmolans	NR_044644	*Streptococcus genomosp. C2*	AY278630
Eubacterium dolichum	L34682	*Streptococcus genomosp. C3*	AY278631
Eubacterium eligens	CP001104	*Streptococcus genomosp. C4*	AY278632
Eubacterium fissicatena	FR749935	*Streptococcus genomosp. C5*	AY278633
Eubacterium hadrum	FR749933	*Streptococcus genomosp. C6*	AY278634
Eubacterium hallii	L34621	*Streptococcus genomosp. C7*	AY278635
Eubacterium infirmum	U13039	*Streptococcus genomosp. C8*	AY278609
Eubacterium limosum	CP002273	*Streptococcus gordonii*	NC_009785
Eubacterium moniliforme	HF558373	*Streptococcus infantarius*	ABJK02000017
Eubacterium multiforme	NR_024683	*Streptococcus infantis*	AFNN01000024
Eubacterium nitritogenes	NR_024684	*Streptococcus intermedius*	NR_028736
Eubacterium nodatum	U13041	*Streptococcus lutetiensis*	NR_037096
Eubacterium ramulus	AJ011522	*Streptococcus massiliensis*	AY769997
Eubacterium rectale	FP929042	*Streptococcus milleri*	X81023
Eubacterium ruminantium	NR_024661	*Streptococcus mitis*	AM157420
Eubacterium saburreum	AB525414	*Streptococcus mutans*	AP010655
Eubacterium saphenum	NR_026031	*Streptococcus oligofermentans*	AY099095
Eubacterium siraeum	ABCA03000054	*Streptococcus oralis*	ADMV01000001
Eubacterium sp. 3_1_31	ACTL01000045	*Streptococcus parasanguinis*	AEKM01000012
Eubacterium sp. AS15b	HQ616364	*Streptococcus pasteurianus*	AP012054
Eubacterium sp. OBRC9	HQ616354	*Streptococcus peroris*	AEVF01000016
Eubacterium sp. oral clone GI038	AY349374	*Streptococcus pneumoniae*	AE008537
Eubacterium sp. oral clone IR009	AY349376	*Streptococcus porcinus*	EF121439
Eubacterium sp. oral clone JH012	AY349373	*Streptococcus pseudopneumoniae*	FJ827123
Eubacterium sp. oral clone JI012	AY349379	*Streptococcus pseudoporcinus*	AENS01000003
Eubacterium sp. oral clone JN088	AY349377	*Streptococcus pyogenes*	AE006496
Eubacterium sp. oral clone JS001	AY349378	*Streptococcus ratti*	X58304
Eubacterium sp. oral clone OH3A	AY947497	*Streptococcus salivarius*	AGBV01000001
Eubacterium sp. WAL 14571	FJ687606	*Streptococcus sanguinis*	NR_074974
Eubacterium tenue	M59118	*Streptococcus sinensis*	AF432857
Eubacterium tortuosum	NR_044648	*Streptococcus sp. 16362*	JN590019
Eubacterium ventriosum	L34421	*Streptococcus sp. 2_1_36FAA*	ACOI01000028
Eubacterium xylanophilum	L34628	*Streptococcus sp. 2285_97*	AJ131965
Eubacterium yurii	AEES01000073	*Streptococcus sp. 69130*	X78825
Fusobacterium canifelinum	AY162222	*Streptococcus sp. AC15*	HQ616356
Fusobacterium genomosp. C1	AY278616	*Streptococcus sp. ACS2*	HQ616360
Fusobacterium genomosp. C2	AY278617	*Streptococcus sp. AS20*	HQ616366
Fusobacterium gonidiaformans	ACET01000043	*Streptococcus sp. BS35a*	HQ616369
Fusobacterium mortiferum	ACDB02000034	*Streptococcus sp. C150*	ACRI01000045

Fusobacterium naviforme	HQ223106	*Streptococcus sp. CM6*	HQ616372
Fusobacterium necrogenes	X55408	*Streptococcus sp. CM7*	HQ616373
Fusobacterium necrophorum	AM905356	*Streptococcus sp. ICM10*	HQ616389
Fusobacterium nucleatum	ADVK01000034	*Streptococcus sp. ICM12*	HQ616390
Fusobacterium periodonticum	ACJY01000002	*Streptococcus sp. ICM2*	HQ616386
Fusobacterium russii	NR_044687	*Streptococcus sp. ICM4*	HQ616387
Fusobacterium sp. 1_1_41FAA	ADGG01000053	*Streptococcus sp. ICM45*	HQ616394
Fusobacterium sp. 11_3_2	ACUO01000052	*Streptococcus sp. M143*	ACRK01000025
Fusobacterium sp. 12_1B	AGWJ01000070	*Streptococcus sp. M334*	ACRL01000052
Fusobacterium sp. 2_1_31	ACDC02000018	*Streptococcus sp. OBRC6*	HQ616352
Fusobacterium sp. 3_1_27	ADGF01000045	*Streptococcus sp. oral clone ASB02*	AY923121
Fusobacterium sp. 3_1_33	ACQE01000178	*Streptococcus sp. oral clone ASCA03*	DQ272504
Fusobacterium sp. 3_1_36A2	ACPU01000044	*Streptococcus sp. oral clone ASCA04*	AY923116
Fusobacterium sp. 3_1_5R	ACDD01000078	*Streptococcus sp. oral clone ASCA09*	AY923119
Fusobacterium sp. AC18	HQ616357	*Streptococcus sp. oral clone ASCB04*	AY923123
Fusobacterium sp. ACB2	HQ616358	*Streptococcus sp. oral clone ASCB06*	AY923124
Fusobacterium sp. AS2	HQ616361	*Streptococcus sp. oral clone ASCC04*	AY923127
Fusobacterium sp. CM1	HQ616371	*Streptococcus sp. oral clone ASCC05*	AY923128
Fusobacterium sp. CM21	HQ616375	*Streptococcus sp. oral clone ASCC12*	DQ272507
Fusobacterium sp. CM22	HQ616376	*Streptococcus sp. oral clone ASCD01*	AY923129
Fusobacterium sp. D12	ACDG02000036	*Streptococcus sp. oral clone ASCD09*	AY923130
Fusobacterium sp. oral clone ASCF06	AY923141	*Streptococcus sp. oral clone ASCD10*	DQ272509
Fusobacterium sp. oral clone ASCF11	AY953256	*Streptococcus sp. oral clone ASCE03*	AY923134
Fusobacterium ulcerans	ACDH01000090	*Streptococcus sp. oral clone ASCE04*	AY953253
Fusobacterium varium	ACIE01000009	*Streptococcus sp. oral clone ASCE05*	DQ272510
Gemella haemolysans	ACDZ02000012	*Streptococcus sp. oral clone ASCE06*	AY923135
Gemella morbillorum	NR_025904	*Streptococcus sp. oral clone ASCE09*	AY923136
Gemella morbillorum	ACRX01000010	*Streptococcus sp. oral clone ASCE10*	AY923137
Gemella sanguinis	ACRY01000057	*Streptococcus sp. oral clone ASCE12*	AY923138
Gemella sp. oral clone ASCE02	AY923133	*Streptococcus sp. oral clone ASCF05*	AY923140
Gemella sp. oral clone ASCF04	AY923139	*Streptococcus sp. oral clone ASCF07*	AY953255
Gemella sp. oral clone ASCF12	AY923143	*Streptococcus sp. oral clone ASCF09*	AY923142
Gemella sp. WAL 1945J	EU427463	*Streptococcus sp. oral clone ASCG04*	AY923145
Klebsiella oxytoca	AY292871	*Streptococcus sp. oral clone BW009*	AY005042

Klebsiella pneumoniae	CP000647	*Streptococcus sp. oral clone CH016*	AY005044
Klebsiella sp. AS10	HQ616362	*Streptococcus sp. oral clone GK051*	AY349413
Klebsiella sp. Co9935	DQ068764	*Streptococcus sp. oral clone GM006*	AY349414
Klebsiella sp. enrichment culture clone SRC_DSD25	HM195210	*Streptococcus sp. oral clone P2PA_41 P2*	AY207051
Klebsiella sp. OBRC7	HQ616353	*Streptococcus sp. oral clone P4PA_30 P4*	AY207064
Klebsiella sp. SP_BA	FJ999767	*Streptococcus sp. oral taxon 071*	AEEP01000019
Klebsiella sp. SRC_DSD1	GU797254	*Streptococcus sp. oral taxon G59*	GU432132
Klebsiella sp. SRC_DSD11	GU797263	*Streptococcus sp. oral taxon G62*	GU432146
Klebsiella sp. SRC_DSD12	GU797264	*Streptococcus sp. oral taxon G63*	GU432150
Klebsiella sp. SRC_DSD15	GU797267	*Streptococcus sp. SHV515*	Y07601
Klebsiella sp. SRC_DSD2	GU797253	*Streptococcus suis*	FM252032
Klebsiella sp. SRC_DSD6	GU797258	*Streptococcus thermophilus*	CP000419
Klebsiella variicola	CP001891	*Streptococcus uberis*	HQ391900
Lachnobacterium bovis	GU324407	*Streptococcus urinalis*	DQ303194
Lachnospira multipara	FR733699	*Streptococcus vestibularis*	AEKO01000008
Lachnospira pectinoschiza	L14675	*Streptococcus viridans*	AF076036
Lachnospiraceae bacterium 1_1_57FAA	ACTM01000065	*Sutterella morbirenis*	AJ832129
Lachnospiraceae bacterium 1_4_56FAA	ACTN01000028	*Sutterella parvirubra*	AB300989
Lachnospiraceae bacterium 2_1_46FAA	ADLB01000035	*Sutterella sanguinus*	AJ748647
Lachnospiraceae bacterium 2_1_58FAA	ACTO01000052	*Sutterella sp. YIT 12072*	AB491210
Lachnospiraceae bacterium 3_1_57FAA_CT1	ACTP01000124	*Sutterella stercoricanis*	NR_025600
Lachnospiraceae bacterium 4_1_37FAA	ADCR01000030	*Sutterella wadsworthensis*	ADMF01000048
Lachnospiraceae bacterium 5_1_57FAA	ACTR01000020	*Synergistes genomosp. C1*	AY278615
Lachnospiraceae bacterium 5_1_63FAA	ACTS01000081	*Synergistes sp. RMA 14551*	DQ412722
Lachnospiraceae bacterium 6_1_63FAA	ACTV01000014	*Synergistetes bacterium ADV897*	GQ258968
Lachnospiraceae bacterium 8_1_57FAA	ACWQ01000079	*Synergistetes bacterium LBVCM1157*	GQ258969
Lachnospiraceae bacterium 9_1_43BFAA	ACTX01000023	*Synergistetes bacterium oral taxon 362*	GU410752
Lachnospiraceae bacterium A4	DQ789118	*Synergistetes bacterium oral taxon D48*	GU430992
Lachnospiraceae bacterium DJF VP30	EU728771	*Turicibacter sanguinis*	AF349724
Lachnospiraceae bacterium ICM62	HQ616401	*Veillonella atypica*	AEDS01000059
Lachnospiraceae bacterium MSX33	HQ616384	*Veillonella dispar*	ACIK02000021
Lachnospiraceae bacterium oral taxon 107	ADDS01000069	*Veillonella genomosp. P1 oral clone MB5_P17*	DQ003631
Lachnospiraceae bacterium oral taxon F15	HM099641	*Veillonella montpellierensis*	AF473836
Lachnospiraceae genomosp. C1	AY278618	*Veillonella parvula*	ADFU01000009
Lactobacillus acidipiscis	NR_024718	*Veillonella sp. 3_1_44*	ADCV01000019
Lactobacillus acidophilus	CP000033	*Veillonella sp. 6_1_27*	ADCW01000016

Lactobacillus alimentarius	NR_044701	*Veillonella sp. ACP1*	HQ616359
Lactobacillus amylolyticus	ADNY01000006	*Veillonella sp. AS16*	HQ616365
Lactobacillus amylovorus	CP002338	*Veillonella sp. BS32b*	HQ616368
Lactobacillus antri	ACLL01000037	*Veillonella sp. ICM51a*	HQ616396
Lactobacillus brevis	EU194349	*Veillonella sp. MSA12*	HQ616381
Lactobacillus buchneri	ACGH01000101	*Veillonella sp. NVG 100cf*	EF108443
Lactobacillus casei	CP000423	*Veillonella sp. OK11*	JN695650
Lactobacillus catenaformis	M23729	*Veillonella sp. oral clone ASCA08*	AY923118
Lactobacillus coleohominis	ACOH01000030	*Veillonella sp. oral clone ASCB03*	AY923122
Lactobacillus coryniformis	NR_044705	*Veillonella sp. oral clone ASCG01*	AY923144
Lactobacillus crispatus	ACOG01000151	*Veillonella sp. oral clone ASCG02*	AY953257
Lactobacillus curvatus	NR_042437	*Veillonella sp. oral clone OH1A*	AY947495
Lactobacillus delbrueckii	CP002341	*Veillonella sp. oral taxon 158*	AENU01000007
Lactobacillus dextrinicus	NR_036861	*Veillonellaceae bacterium oral taxon 131*	GU402916
Lactobacillus farciminis	NR_044707	*Veillonellaceae bacterium oral taxon 155*	GU470897
Lactobacillus fermentum	CP002033	*Vibrio cholerae*	AAUR01000095
Lactobacillus gasseri	ACOZ01000018	*Vibrio fluvialis*	X76335
Lactobacillus gastricus	AICN01000060	*Vibrio furnissii*	CP002377
Lactobacillus genomosp. C1	AY278619	*Vibrio mimicus*	ADAF01000001
Lactobacillus genomosp. C2	AY278620	*Vibrio parahaemolyticus*	AAWQ01000116
Lactobacillus helveticus	ACLM01000202	*Vibrio sp. RC341*	ACZT01000024
Lactobacillus hilgardii	ACGP01000200	*Vibrio vulnificus*	AE016796
Lactobacillus hominis	FR681902	*Yersinia aldovae*	AJ871363
Lactobacillus iners	AEKJ01000002	*Yersinia aleksiciae*	AJ627597
Lactobacillus jensenii	ACQD01000066	*Yersinia bercovieri*	AF366377
Lactobacillus johnsonii	AE017198	*Yersinia enterocolitica*	FR729477
Lactobacillus kalixensis	NR_029083	*Yersinia frederiksenii*	AF366379
Lactobacillus kefiranofaciens	NR_042440	*Yersinia intermedia*	AF366380
Lactobacillus kefiri	NR_042230	*Yersinia kristensenii*	ACCA01000078
Lactobacillus kimchii	NR_025045	*Yersinia mollaretii*	NR_027546
Lactobacillus leichmannii	JX986966	*Yersinia pestis*	AE013632
Lactobacillus mucosae	FR693800	*Yersinia pseudotuberculosis*	NC_009708
		Yersinia rohdei	ACCD01000071

Table 3: Exemplary Bacterial Strains

Strain	Deposit Number
Parabacteroides goldsteinii	PTA-126574
Bifidobacterium animalis ssp. lactis Strain A	PTA-125097
Blautia Massiliensis Strain A	PTA-125134
Prevotella Strain B	NRRL accession Number B 50329
Prevotella Histicola	PTA-126140
Blautia Strain A	PTA-125346
Lactococcus lactis cremoris Strain A	PTA-125368
Lactobacillus salivarius	PTA-125893
Ruminococcus gnavus strain	PTA-125706
Tyzzerella nexilis strain	PTA-125707
Paraclostridium benzoelyticum	PTA-125894

Ruminococcus gnavus (also referred to as Mediterraneibacter gnavus)	PTA-126695
Veillonella parvula	PTA-125710
Veillonella atypica Strain A	PTA-125709
Veillonella atypica Strain B	PTA-125711
Veillonella parvula Strain A	PTA-125691
Veillonella parvula Strain B	PTA-125711
Veillonella tobetsuensis Strain A	PTA-125708
Agathobaculum sp.	PTA-125892
Turicibacter sanguinis	PTA-125889
Klebsiella quasipneumoniae subsp. similipneumoniae	PTA-125891
Klebsiella oxytoca	PTA-125890
Megasphaera Sp. Strain A	PTA-126770
Megasphaera Sp.	PTA-126837
Harryflintia acetispora	PTA-126694
Fournierella massiliensis	PTA-126696

Table 4. Exemplary Bacterial Strains

Escherichia coli	NCIMB 12210
Enterococcus faecalis	NCIMB 13280
Bacteroides fragilis	DSM 2151
Bacteroides vulgatus	DSM 1447
Bacteroides ovatus	DSM 1896
Megasphaera massiliensis	DSM 26228
Megasphaera elsdenii	NCIMB 8927
Megasphaera massiliensis	NCIMB 42787
Bifidobacterium breve	DSM 20213
Bifidobacterium longum subsp. longum	DSM 20219
Faecalibacterium prausnitzii	DSM17677
Anaerostipes hadrus	DSM 3319
Blautia coccoides	DSM 935
Dorea longicatena	DSM 13814
Parabacteroides distasonis	DSM 20701
Faecalicatena contorta	DSM3982
Ruminococcus gnavus	ATCC29149
Megasphaera massiliensis	NCIMB 43388
Megasphaera massiliensis	NCIMB 43389
Megasphaera spp.	NCIMB 43385
Megasphaera spp.	NCIMB 43386
Megasphaera spp.	NCIMB 43387
Parabacteroides distasonis (also referred to as "Parabacteroides sp 755")	NCIMB 42382
Bacillus amyloliquefaciens	NCIMB 43088
Bacillus amyloliquefaciens	NCIMB 43087
Bacillus amyloliquefaciens	NCIMB 43086

Modified Bacteria

[457] In some aspects, the bacteria described herein are modified such that they comprise, are linked to, and/or are bound by a therapeutic moiety.

[458] In some embodiments, the therapeutic moiety is a cancer-specific moiety. In some embodiments, the cancer-specific moiety has binding specificity for a cancer cell (e.g., has binding specificity for a cancer-specific antigen). In some embodiments, the cancer-specific moiety comprises an antibody or antigen binding fragment thereof. In some embodiments, the cancer-specific moiety comprises a T cell receptor or a chimeric antigen receptor (CAR). In some embodiments, the cancer-specific moiety comprises a ligand for a receptor expressed on the surface of a cancer cell or a receptor-binding fragment thereof. In some embodiments, the cancer-specific moiety is a bipartite fusion protein that has two parts: a first part that binds to and/or is linked to the bacterium and a second part that is capable of binding to a cancer cell (e.g., by having binding specificity for a cancer-specific antigen). In some embodiments, the first part is a fragment of or a full-length peptidoglycan recognition protein, such as PGRP. In some embodiments the first part has binding specificity for the bacteria (e.g., by having binding specificity for a bacterial antigen). In some embodiments, the first and/or second part comprises an antibody or antigen binding fragment thereof. In some embodiments, the first and/or second part comprises a T cell receptor or a chimeric antigen receptor (CAR). In some embodiments, the first and/or second part comprises a ligand for a receptor expressed on the surface of a cancer cell or a receptor-binding fragment thereof. In certain embodiments, co-administration of the cancer-specific moiety with the pharmaceutical agent (either in combination or in separate administrations) increases the targeting of the pharmaceutical agent to the cancer cells.

[459] In some embodiments, the bacteria described herein can be modified such that they comprise, are linked to, and/or are bound by a magnetic and/or paramagnetic moiety (e.g., a magnetic bead). In some embodiments, the magnetic and/or paramagnetic moiety is comprised by and/or directly linked to the bacteria. In some embodiments, the magnetic and/or paramagnetic moiety is linked to and/or a part of a bacteria-binding moiety that binds to the bacteria. In some embodiments, the bacteria-binding moiety is a fragment of or a full-length peptidoglycan recognition protein, such as PGRP. In some embodiments the bacteria-binding moiety has binding specificity for the bacteria (e.g., by having binding specificity for a bacterial antigen). In some embodiments, the bacteria-binding

moiety comprises an antibody or antigen binding fragment thereof. In some embodiments, the bacteria-binding moiety comprises a T cell receptor or a chimeric antigen receptor (CAR). In some embodiments, the bacteria-binding moiety comprises a ligand for a receptor expressed on the surface of a cancer cell or a receptor-binding fragment thereof. In certain embodiments, co-administration of the magnetic and/or paramagnetic moiety with the bacteria (either together or in separate administrations) can be used to increase the targeting of the bacteria (e.g., to cancer cells and/or a part of a subject where cancer cells are present.

Pharmaceutical Agents and Compositions

[460] In certain embodiments, provided herein are pharmaceutical compositions and/or solid dosage forms (e.g., pharmaceutical products having a solid dosage form) comprising a pharmaceutical agent that contains bacteria. The bacteria can be live bacteria; non-live (dead) bacteria; non replicating bacteria; gamma irradiated bacteria; and/or lyophilized bacteria.

[461] In certain embodiments, provided herein are pharmaceutical agents that contain bacteria. In some embodiments, the pharmaceutical agent can optionally contain one or more additional components, such as a cryoprotectant. The pharmaceutical agent can be lyophilized (e.g., resulting in a powder). The pharmaceutical agent can be combined with one or more excipients (e.g., pharmaceutically acceptable excipients) in the pharmaceutical composition and/or solid dosage form (e.g., solid dose form).

[462] In some embodiments, the pharmaceutical agent has a fine and smooth granulated powder appearance.

[463] In some embodiments, the pharmaceutical agent has an off-white to brown, fine powder appearance.

[464] In certain embodiments, provided herein are pharmaceutical compositions and/or solid dosage forms comprising a pharmaceutical agent that contains bacteria. The bacteria can be live bacteria The bacteria can be live bacteria; non-live (dead) bacteria; non replicating bacteria; gamma irradiated bacteria; and/or lyophilized bacteria.

[465] In some embodiments, the pharmaceutical agents comprise bacteria (e.g., whole bacteria) (e.g., live bacteria, killed bacteria, attenuated bacteria). In some embodiments, the pharmaceutical agents comprise bacteria from one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more) of the bacteria strains or species or taxonomic groups listed herein. In

some embodiments, the pharmaceutical agents comprise bacteria from one of the bacteria strains or species or taxonomic groups listed herein. In some embodiments, the pharmaceutical agents comprise freeze dried (e.g., lyophilized) bacteria. In some embodiments, the pharmaceutical agent comprises gamma irradiated bacteria. In some embodiments, the pharmaceutical agents comprise bacteria from one of the bacteria strains or species described herein, e.g., *Lactococcus, Prevotella, Bifidobacterium, Veillonella, Fournierella, Harryflintia, Megasphaera; e.g., Lactococcus lactis cremoris; Prevotella histicola; Bifidobacterium animalis lactis; Veillonella parvula; Fournierella massiliensis; Harryflintia acetispora; or Megasphaera sp.*

[466] In some embodiments, to quantify the numbers of bacteria present in a sample, electron microscopy (e.g., EM of ultrathin frozen sections) can be used to visualize the bacteria and count their relative numbers. Alternatively, nanoparticle tracking analysis (NTA), Coulter counting, or dynamic light scattering (DLS) or a combination of these techniques can be used. NTA and the Coulter counter count particles and show their sizes. DLS gives the size distribution of particles, but not the concentration. Bacteria frequently have diameters of 1-2 um (microns). The full range is 0.2-20 um. Combined results from Coulter counting and NTA can reveal the numbers of bacteria in a given sample. Coulter counting reveals the numbers of particles with diameters of 0.7-10 um. For most bacterial samples, the Coulter counter alone can reveal the number of bacteria in a sample. For NTA, a Nanosight instrument can be obtained from Malvern Pananlytical. For example, the NS300 can visualize and measure particles in suspension in the size range 10-2000 nm. NTA allows for counting of the numbers of particles that are, for example, 50-1000 nm in diameter. DLS reveals the distribution of particles of different diameters within an approximate range of 1 nm – 3 um.

[467] In some embodiments, the bacteria may be quantified based on total cell count (TCC), e.g, by Coulter counter.

[468] In some embodiments, the bacteria may be quantified based on particle count. For example, total particle count of a bacteria preparation can be measured using NTA.

[469] In some embodiments, the bacteria may be quantified based on the amount of protein, lipid, or carbohydrate. For example, total protein content of a bacteria and/or preparation can be measured using the Bradford assay or BCA.

[470] In some embodiments, bacteria are isolated away from one or more other bacterial components of the source bacterial culture. In some embodiments, the pharmaceutical agent further comprises other bacterial components.

[471] In certain aspects, provided herein are pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms that comprise bacteria useful for the treatment and/or prevention of disease (e.g., a cancer, an autoimmune disease, an inflammatory disease, a metabolic disease, or a dysbiosis), as well as methods of making and/or identifying such bacteria, and methods of using pharmaceutical agents, pharmaceutical compositions and solid dosage forms thereof (e.g., for the treatment of a cancer, an autoimmune disease, an inflammatory disease, or a metabolic disease, either alone or in combination with other therapeutics). In some embodiments, the pharmaceutical agents comprise bacteria (e.g., whole bacteria) (e.g., live bacteria, dead (e.g., killed) bacteria, non-replicating bacteria, attenuated bacteria). In some embodiments, the pharmaceutical agents comprise bacteria from one or more of the bacteria strains or species or taxonomic groups listed herein. In some embodiments, the pharmaceutical agents bacteria from one of the bacteria strains or species or taxonomic groups listed herein. In some embodiments, the pharmaceutical agents comprise bacteria from one of the bacteria strains or species described herein, e.g., *Lactococcus, Prevotella, Bifidobacterium, Veillonella, Fournierella, Harryflintia, Megasphaera; e.g., Lactococcus lactis cremoris; Prevotella histicola; Bifidobacterium animalis lactis; Veillonella parvula; Fournierella massiliensis; Harryflintia acetispora; or Megasphaera sp.*

[472] In certain aspects, provided are pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms for administration to a subject (e.g., human subject). In some embodiments, the pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms are combined with additional active and/or inactive materials in order to produce a final product, which may be in single dosage unit or in a multi-dose format. In some embodiments, the pharmaceutical agent is combined with an adjuvant such as an immuno-adjuvant (e.g., a STING agonist, a TLR agonist, or a NOD agonist).

[473] In some embodiments, the pharmaceutical agent, pharmaceutical composition and/or solid dosage form comprises at least one carbohydrate.

[474] In some embodiments, the pharmaceutical agent, pharmaceutical composition and/or solid dosage form comprises at least one lipid. In some embodiments, the lipid comprises at least one fatty acid selected from lauric acid (12:0), myristic acid (14:0),

palmitic acid (16:0), palmitoleic acid (16:1), margaric acid (17:0), heptadecenoic acid (17:1), stearic acid (18:0), oleic acid (18:1), linoleic acid (18:2), linolenic acid (18:3), octadecatetraenoic acid (18:4), arachidic acid (20:0), eicosenoic acid (20:1), eicosadienoic acid (20:2), eicosatetraenoic acid (20:4), eicosapentaenoic acid (20:5) (EPA), docosanoic acid (22:0), docosenoic acid (22:1), docosapentaenoic acid (22:5), docosahexaenoic acid (22:6) (DHA), and tetracosanoic acid (24:0).

[475] In some embodiments, the pharmaceutical agent, pharmaceutical composition and/or solid dosage form comprises at least one mineral or mineral source. Examples of minerals include, without limitation: chloride, sodium, calcium, iron, chromium, copper, iodine, zinc, magnesium, manganese, molybdenum, phosphorus, potassium, and selenium. Suitable forms of any of the foregoing minerals include soluble mineral salts, slightly soluble mineral salts, insoluble mineral salts, chelated minerals, mineral complexes, non-reactive minerals such as carbonyl minerals, and reduced minerals, and combinations thereof.

[476] In some embodiments, the pharmaceutical agent, pharmaceutical composition and/or solid dosage form comprises at least one vitamin. The at least one vitamin can be fat-soluble or water-soluble vitamins. Suitable vitamins include but are not limited to vitamin C, vitamin A, vitamin E, vitamin B12, vitamin K, riboflavin, niacin, vitamin D, vitamin B6, folic acid, pyridoxine, thiamine, pantothenic acid, and biotin. Suitable forms of any of the foregoing are salts of the vitamin, derivatives of the vitamin, compounds having the same or similar activity of the vitamin, and metabolites of the vitamin.

[477] In some embodiments, the pharmaceutical agent, pharmaceutical composition and/or solid dosage form comprises an excipient. Non-limiting examples of suitable excipients include a buffering agent, a preservative, a stabilizer, a binder, a compaction agent, a lubricant, a dispersion enhancer, a disintegration agent, a flavoring agent, a sweetener, and a coloring agent.

[478] Suitable excipients that can be included in the pharmaceutical agent, pharmaceutical composition and/or solid dosage form can be one or more pharmaceutically acceptable excipients known in the art. For example, see Rowe, Sheskey, and Quinn, eds., *Handbook of Pharmaceutical Excipients*, sixth ed.; 2009; Pharmaceutical Press and American Pharmacists Association.

Solid Dosage Forms

[479] The pharmaceutical agent can be formulated into a solid dosage form. The solid dosage form described herein can be, e.g., a tablet or a minitablet. Further, a plurality of minitablets can be in (e.g., loaded into) a capsule.

[480] In certain embodiments, the solid dosage form comprises a capsule. In some embodiments, the capsule is a size 00, size 0, size 1, size 2, size 3, size 4, or size 5 capsule. In some embodiments, the capsule is a size 0 capsule. As used herein, the size of the capsule refers to the size of the tablet prior to application of an enteric coating. In some embodiments, the capsule is banded after loading (and prior to enterically coating the capsule). In some embodiments, the capsule is banded with an HPMC-based banding solution.

[481] In some embodiments, the solid dosage form comprises a tablet (> 4mm) (e.g., 5mm-17mm). For example, the tablet is a 5mm, 6mm, 7mm, 8mm, 9mm, 10mm, 11mm, 12mm, 13mm, 14mm, 15mm, 16mm, 17mm, or 18mm tablet. The size refers to the diameter of the tablet, as is known in the art. As used herein, the size of the tablet refers to the size of the tablet prior to application of an enteric coating.

[482] In some embodiments, the solid dosage form comprises a minitablet. The minitablet can be in the size range of 1mm-4 mm range. E.g., the minitablet can be a 1mm minitablet, 1.5 mm minitablet, 2mm minitablet, 3mm minitablet, or 4mm minitablet. The size refers to the diameter of the minitablet, as is known in the art. As used herein, the size of the minitablet refers to the size of the minitablet prior to application of an enteric coating.

[483] The minitablets can be in a capsule. The capsule can be a size 00, size 0, size 1, size 2, size 3, size 4, or size 5 capsule. The capsule that contains the minitablets can comprise HPMC (hydroxyl propyl methyl cellulose) or gelatin. The minitablets can be inside a capsule: the number of minitablets inside a capsule will depend on the size of the capsule and the size of the minitablets. As an example, a size 0 capsule can contain 31-35 (an average of 33) minitablets that are 3mm minitablets. In some embodiments, the capsule is banded after loading. In some embodiments, the capsule is banded with an HPMC-based banding solution.

Coating

[484] The solid dosage form (e.g., tablet or minitablet) described herein can be enterically coated, e.g., with one enteric coating layer or with two layers of enteric coating, e.g., an inner enteric coating and an outer enteric coating. The inner enteric coating and outer enteric coating are not identical (e.g., the inner enteric coating and outer enteric coating do not contain the same components in the same amounts). The enteric coating allows for release of the pharmaceutical agent, e.g., in the small intestine, e.g., upper small intestine, e.g., duodenum and/or jejunum.

[485] Release of the pharmaceutical agent in the small intestine, e.g., in the upper small intestine, e.g., in the duodenum, or in the jejunum, allows the pharmaceutical agent to target and affect cells (e.g., epithelial cells and/or immune cells) located at these specific locations, e.g., which can cause a local effect in the small intestine and/or cause a systemic effect (e.g., an effect outside of the gastrointestinal tract).

[486] EUDRAGIT is the brand name for a diverse range of polymethacrylate-based copolymers. It includes anionic, cationic, and neutral copolymers based on methacrylic acid and methacrylic/acrylic esters or their derivatives.

[487] Examples of other materials that can be used in the enteric coating (e.g., the one enteric coating or the inner enteric coating and/or the outer enteric coating) include cellulose acetate phthalate (CAP), cellulose acetate trimellitate (CAT), poly(vinyl acetate phthalate) (PVAP), hydroxypropyl methylcellulose phthalate (HPMCP), fatty acids, waxes, shellac (esters of aleurtic acid), plastics, plant fibers, zein, AQUA-ZEIN® (an aqueous zein formulation containing no alcohol), amylose starch, starch derivatives, dextrins, methyl acrylate-methacrylic acid copolymers, cellulose acetate succinate, hydroxypropyl methyl cellulose acetate succinate (hypromellose acetate succinate), methyl methacrylate-methacrylic acid copolymers, and/or sodium alginate.

[488] The enteric coating (e.g., the one enteric coating or the inner enteric coating and/or the outer enteric coating) can include a methacrylic acid ethyl acrylate (MAE) copolymer (1:1).

[489] The one enteric coating can include methacrylic acid ethyl acrylate (MAE) copolymer (1:1) (such as Kollicoat MAE 100P).

[490] The one enteric coating can include a Eudragit coplymer, e.g., a Eudragit L (e.g., Eudragit L 100-55; Eudragit L 30 D-55), a Eudragit S, a Eudragit RL, a Eudragit RS, a Eudragit E, or a Eudragit FS (e.g., Eudragit FS 30 D).

[491] Other examples of materials that can be used in the enteric coating (e.g., the one enteric coating or the inner enteric coating and/or the outer enteric coating) include those described in, e.g., U.S. 6312728; U.S. 6623759; U.S. 4775536; U.S. 5047258; U.S. 5292522; U.S. 6555124; U.S. 6638534; U.S. 2006/0210631; U.S. 2008/200482; U.S. 2005/0271778; U.S. 2004/0028737; WO 2005/044240.

[492] See also, e.g., U.S. 9233074, which provides pH dependent, enteric polymers that can be used with the solid dosage forms provided herein, including methacrylic acid copolymers, polyvinylacetate phthalate, hydroxypropylmethyl cellulose acetate succinate, hydroxypropylmethyl cellulose phthalate and cellulose acetate phthalate; suitable methacrylic acid copolymers include: poly(methacrylic acid, methyl methacrylate) 1:1 sold, for example, under the Eudragit L100 trade name; poly(methacrylic acid, ethyl acrylate) 1:1 sold, for example, under the Eudragit L100-55 trade name; partially-neutralized poly(methacrylic acid, ethyl acrylate) 1:1 sold, for example, under the Kollicoat MAE-100P trade name; and poly(methacrylic acid, methyl methacrylate) 1:2 sold, for example, under the Eudragit S100 trade name.

[493] In certain aspects, the solid dosage form (e.g., tablet or minitablet) described herein further comprises a sub-coating. In some embodiments, the solid dosage form comprises a sub-coating, e.g., in addition to the enteric coating, e.g., the sub-coating is beneath the enteric coating (e.g., between the solid dosage form and the enteric coating). In some embodiments, the sub-coating comprises Opadry QX, e.g., Opadry QX Blue. The sub-coat can be used, e.g., to visually mask the appearance of the therapeutic agent.

Dose

[494] The dose of the pharmaceutical agent (e.g., for human subjects) is the dose per solid dosage form, such as per capsule or tablet or per total number of minitablets used in a capsule.

[495] In embodiments where dose is determined by total cell count, total cell count can be determined by Coulter counter.

[496] In some embodiments, the pharmaceutical agent comprises bacteria and the dose of bacteria is about 1×10^7 to about 2×10^{12} (e.g., about 3×10^{10} or about 1.5×10^{11} or about 1.5×10^{12}) cells (e.g., wherein cell number is determined by total cell count, which is determined by Coulter counter), wherein the dose is per capsule or tablet or per total number of minitablets in a capsule. In some embodiments, the pharmaceutical agent

comprises bacteria and the dose of bacteria is about 1 x 10^{10} to about 2 x 10^{12} (e.g., about 1.6 x 10^{11} or about 8 x 10^{11} or about 9.6 x 10^{11} about 12.8 x 10^{11} or about 1.6 x 10^{12}) cells (e.g., wherein cell number is determined by total cell count, which is determined by Coulter counter), wherein the dose is per capsule or tablet or per total number of minitablets in a capsule.

[497] In some embodiments, the pharmaceutical agent comprises bacteria and the dose of bacteria is about 1 x 10^{9}, about 3 x 10^{9}, about 5 x 10^{9}, about 1.5 x 10^{10}, about 3 x 10^{10}, about 5 x 10^{10}, about 1.5 x 10^{11}, about 1.5 x 10^{12}, or about 2 x 10^{12} cells, wherein the dose is per capsule or tablet or per total number of minitablets in a capsule.

[498] In some embodiments, the pharmaceutical agent dose can be a milligram (mg) dose determined by weight the pharmaceutical agent (e.g., a powder comprising bacteria). The dose of the pharmaceutical agent is per capsule or tablet or per total number of minitablets, e.g., in a capsule.

[499] For example, to administer a 1x dose of the pharmaceutical agent of about 400 mg, about 200 mg of the pharmaceutical agent is present per capsule and two capsules are administered, resulting in a dose of about 400 mg. The two capsules can be administered, for example, 1x or 2x daily.

[500] For example, for a minitablet: about 0.1 to about 3.5 mg (0.1, 0.35, 1.0, 3.5 mg) of the pharmaceutical agent can be contained per minitablet. The minitablets can be inside a capsule: the number of minitablets inside a capsule will depend on the size of the capsule and the size of the minitablets. For example, an average of 33 (range of 31-35) 3 mm minitablets fit inside a size 0 capsule. As an example, 0.1- 3.5 mg of the pharmaceutical agent per minitablet, the dose range will be 3.3 mg- 115.5 mg (for 33 minitablets in size 0 capsule) per capsule (3.1 mg- 108.5 mg for 31 minitablets in size 0 capsule) (3.5 mg- 122.5 mg for 35 minitablets in size 0 capsule). Multiple capsules and/or larger capsule(s) can be administered to increase the administered dose and/or can be administered one or more times per day to increase the administered dose.

[501] In some embodiments, the dose can be about 3 mg to about 125 mg of the pharmaceutical agent, per capsule or tablet or per total number of minitablets, e.g., in a capsule.

[502] In some embodiments, the dose can be about 35 mg to about 1200 mg (e.g., about 35 mg, about 125 mg, about 350 mg, or about 1200 mg) of the pharmaceutical agent.

[503] In some embodiments, the dose of the pharmaceutical agent can be about 30 mg to about 3500 mg (about 25, about 50, about 75, about 100, about 150, about 250, about 300, about 350, about 400, about 500, about 600, about 750, about 1000, about 1250, about 1300, about 2000, about 2500, about 3000, or about 3500 mg).

[504] A human dose can be calculated appropriately based on allometric scaling of a dose administered to a model organism (e.g., mouse).

[505] In some embodiments, one or two tablets capsules can be administered one or two times a day.

[506] The pharmaceutical agent contains the bacteria, or contains a powder comprising bacteria, and can also contain one or more additional components, such as a cryoprotectant.

[507] In some embodiments, the mg (by weight) dose of the pharmaceutical agent is, e.g., about 1 mg to about 500 mg per capsule, or per tablet, or per total number of minitablets, e.g., used in a capsule.

Methods of Use

[508] The pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein allow, e.g., for oral administration of a pharmaceutical agent contained therein.

[509] The pharmaceutical agent can be combined with (for example, mixed into) a liquid (for example, a buffer, juice, or water), e.g., for oral administration of a pharmaceutical agent contained therein.

[510] The pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein can be used in the treatment and/or prevention of a cancer, inflammation, autoimmunity, a metabolic condition, or a dysbiosis.

[511] Methods of using a pharmaceutical agent, pharmaceutical composition, and/or solid dosage form (e.g., for oral administration) (e.g., for pharmaceutical use), wherein the pharmaceutical agent comprises bacteria, are described herein.

[512] The methods and administered pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein allow, e.g., for oral administration of a pharmaceutical agent contained therein. The pharmaceutical agent, pharmaceutical composition, and/or solid dosage form can be administered to a subject is a fed or fasting state. The pharmaceutical agent, pharmaceutical composition, and/or solid

dosage form can be administered, e.g., on an empty stomach (e.g., one hour before eating or two hours after eating). The pharmaceutical agent, pharmaceutical composition, and/or solid dosage form can be administered one hour before eating. The pharmaceutical agent, pharmaceutical composition, and/or solid dosage form can be administered two hours after eating.

[513] A pharmaceutical agent, pharmaceutical composition, and/or solid dosage form for use in the treatment and/or prevention of a cancer, inflammation, autoimmunity, a metabolic condition, or a dysbiosis is provided herein.

[514] Use of a pharmaceutical agent, pharmaceutical composition, and/or solid dosage form for the preparation of a medicament for the treatment and/or prevention of a cancer, inflammation, autoimmunity, a metabolic condition, or a dysbiosis is provided herein.

Methods of Making Pharmaceutical Agents

[515] In some aspects, the disclosure provides a method of preparing a pharmaceutical agent, wherein the pharmaceutical agent comprises bacteria (e.g., freeze dried bacteria). The pharmaceutical agent can be a powder, e.g., a freeze-dried powder.

[516] The method can comprise combining bacteria (e.g., a pellet comprising bacteria) with a cryoprotectant solution, thereby preparing a formulated paste.

[517] In some embodiments, the method further comprises freeze drying the formulated paste, to thereby prepare a freeze-dried product. In some embodiments, the freeze drying comprises primary drying. In some embodiments, the freeze drying comprises primary drying and secondary drying.

[518] In some embodiments, the method further comprises milling the freeze-dried product, to thereby prepare a freeze-dried powder (e.g., powder, e.g., pharmaceutical agent).

[519] In some embodiments, the cryoprotectant solution is mixed with the pellet in a ratio of about 0.2 to about 0.5 gram (g) cryoprotectant solution per gram of pellet; about 0.05 to about 0.25 gram (g) cryoprotectant solution per gram of pellet; about 0.06 to about 0.1 gram (g) cryoprotectant solution per gram of pellet; or about 0.15 to about 0.2 gram (g) cryoprotectant solution per gram of pellet. In some embodiments, the cryoprotectant solution is mixed with the pellet in a ratio of about 0.4 gram (g) cryoprotectant solution per gram of pellet. In some embodiments, the cryoprotectant solution is mixed with the pellet in a ratio of about 0.18 gram (g) cryoprotectant solution per gram of pellet. In some

embodiments, the cryoprotectant solution is mixed with the pellet in a ratio of about 0.1 gram (g) (such as 0.08 g) cryoprotectant solution per gram of pellet.

[520] In some embodiments, the cryoprotectant solution is mixed with the pellet at a ratio of 6.5% (volume/volume).

[521] In some embodiments, the cryoprotectant solution comprises sucrose. In some embodiments, the cryoprotectant solution comprises dextran. In some embodiments, the cryoprotectant solution comprises sucrose and dextran. In some embodiments, the cryoprotectant solution comprises sucrose and dextran in equivalent amounts (e.g., on a percent weight by weight basis). In some embodiments, the cryoprotectant solution comprises sucrose, dextran, and L-cysteine HCl. In some embodiments, the cryoprotectant solution does not comprise L-cysteine HCl.

[522] In some embodiments, the cryoprotectant solution comprises about 10% to about 30% (weight/weight) sucrose. In some embodiments, the cryoprotectant solution comprises about 15% to about 35% (weight/weight) sucrose. In some embodiments, the cryoprotectant solution comprises about 20% (weight/weight) sucrose.

[523] In some embodiments, the cryoprotectant solution comprises about 10% to about 30% (weight/weight) dextran. In some embodiments, the cryoprotectant solution comprises about 15% to about 35% (weight/weight) dextran. In some embodiments, the cryoprotectant solution comprises about 20% (weight/weight) dextran.

[524] In some embodiments, the cryoprotectant solution comprises about 10% to about 30% (weight/weight) sucrose and about 10% to about 30% (weight/weight) dextran. In some embodiments, the cryoprotectant solution comprises about 15% to about 35% (weight/weight) sucrose and about 15% to about 35% (weight/weight) dextran. In some embodiments, the cryoprotectant solution comprises about 20% (weight/weight) sucrose and about 20% (weight/weight) dextran.

[525] In some embodiments, the cryoprotectant solution comprises about 40% to about 80% (weight/weight) water. In some embodiments, the cryoprotectant solution comprises about 50% to about 70% (weight/weight) water. In some embodiments, the cryoprotectant solution comprises about 55% to about 65% (weight/weight) water. In some embodiments, the cryoprotectant solution comprises about 60% (weight/weight) water.

[526] In some embodiments, the cryoprotectant solution comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant solution comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl. In some

embodiments, the cryoprotectant solution comprises about 0.15% to about 0.45% (weight/weight) L-cysteine HCl.

[527] In some embodiments, the cryoprotectant solution comprises about 0.2% (weight/weight) L-cysteine HCl.

[528] In some embodiments, the cryoprotectant solution comprises about 59.8% (weight/weight) water.

[529] In some embodiments, the cryoprotectant solution comprises about 0.4% (weight/weight) L-cysteine HCl.

[530] In some embodiments, the cryoprotectant solution comprises about 59.6% (weight/weight) water.

[531] In certain embodiments, the cryoprotectant solution provided herein comprises: (i) about 20% (weight/weight) sucrose; (ii) about 20% (weight/weight) dextran; (iii) about 0.4% (weight/weight) L-cysteine HCl; and (iv) about 59.6% (weight/weight) water.

[532] In certain embodiments, the cryoprotectant solution provided herein comprises: (i) about 20% (weight/weight) sucrose; (ii) about 20% (weight/weight) dextran; (iii) about 0.2% (weight/weight) L-cysteine HCl; and (iv) about 59.8% (weight/weight) water.

[533] In certain embodiments, the cryoprotectant solution provided herein comprises: (i) about 20% (weight/weight) sucrose; (ii) about 20% (weight/weight) dextran; and (iii) about 60% (weight/weight) water.

[534] In some embodiments, the cryoprotectant (e.g., dry composition not containing water) comprises about 40% to about 60% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 45% to about 55% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 50% (weight/weight) sucrose.

[535] In some embodiments, the cryoprotectant comprises about 40% to about 60% (weight/weight) dextran. In some embodiments, the cryoprotectant comprises about 45% to about 55% (weight/weight) dextran. In some embodiments, the cryoprotectant comprises about 50% (weight/weight) dextran.

[536] In some embodiments, the cryoprotectant comprises about 40% to about 60% (weight/weight) sucrose and 40% to about 60% (weight/weight) dextran. In some embodiments, the cryoprotectant comprises about 45% to about 55% (weight/weight) sucrose and about 45% to about 55% (weight/weight) dextran. In some embodiments, the

cryoprotectant comprises about 50% (weight/weight) sucrose and about 50% (weight/weight) dextran.

[537] In some embodiments, the cryoprotectant comprises about 0.25% to about 5% (weight/weight) L-cysteine HCl (e.g., a form of L-cysteine). In some embodiments, the cryoprotectant comprises about 0.5% to about 2.5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant comprises about 0.75% to about 1.5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant comprises about 1% (weight/weight) L-cysteine HCl.

[538] In certain embodiments, the cryoprotectant provided herein comprises: (i) about 50% (weight/weight) sucrose; (ii) about 50% (weight/weight) dextran; and (iii) about 1% (weight/weight) L-cysteine HCl.

[539] In certain embodiments, the cryoprotectant provided herein comprises: (i) about 50% (weight/weight) sucrose; and (ii) about 50% (weight/weight) dextran.

[540] In some embodiments, the freeze-dried powder comprises about 6% to about 12% (weight/weight) sucrose. In some embodiments, the freeze-dried powder comprises about 8% to about 12% (weight/weight) sucrose. In some embodiments, the freeze-dried powder comprises about 11% (weight/weight) sucrose. In some embodiments, the freeze-dried powder comprises about 6% to about 12% (weight/weight) dextran. In some embodiments, the freeze-dried powder comprises about 8% to about 12% (weight/weight) dextran. In some embodiments, the freeze-dried powder comprises about 11% (weight/weight) dextran. In some embodiments, the freeze-dried powder comprises about 6% to about 12% (weight/weight) sucrose and about 6% to about 12% (weight/weight) dextran. In some embodiments, the freeze-dried powder comprises about 8% to about 12% (weight/weight) sucrose and about 8% to about 12% (weight/weight) dextran. In some embodiments, the freeze-dried powder comprises about 11% (weight/weight) sucrose and about 11% (weight/weight) dextran. In some embodiments, the freeze-dried powder comprises about 0.01% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.1% to about 0.3% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.15% to about 0.25% (weight/weight) L-cysteine HCl.

[541] In some embodiments, the pharmaceutical agent comprises about 7% to about 21% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 10% to about 19% (weight/weight) sucrose. In some embodiments, the

pharmaceutical agent comprises about 15% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 7% to about 21% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 10% to about 19% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 15% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 7% to about 21% (weight/weight) sucrose and about 7% to about 21% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 10% to about 19% (weight/weight) sucrose and about 10% to about 19% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 15% (weight/weight) sucrose and about 15% (weight/weight) dextran. In some embodiments, the pharmaceutical agent comprises about 0.01% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.1% to about 0.4% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.15% to about 0.35% (weight/weight) L-cysteine HCl.

[542] In certain embodiments, the freeze-dried powder comprises about 40% to about 70% (weight/weight) dried bacteria. In certain embodiments, the pharmaceutical agent comprises about 35% to about 70% (weight/weight) bacteria (e.g., freeze dried bacteria).

[543] In certain embodiments, the freeze-dried powder comprises about 64% (weight/weight) dried bacteria.

[544] In some embodiments, the cryoprotectant comprises a dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the cryoprotectant comprises sucrose. In some embodiments, the cryoprotectant comprises dextrose (also referred to as glucose). In some embodiments, the cryoprotectant comprises monosodium glutamate. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and sucrose. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and sucrose in equivalent amounts (e.g., on a percent weight by weight basis). In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose

equivalent (DE) of 21 (such as Glucidex 21), sucrose, and dextrose. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, and monosodium glutamate. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, dextrose, and monosodium glutamate. In some embodiments, the cryoprotectant comprises dextrose and monosodium glutamate in equivalent amounts (e.g., on a percent weight by weight basis). In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, dextrose, monosodium glutamate, and L-cysteine HCl (e.g., a form of L-cysteine). In some embodiments, the cryoprotectant does not comprise L-cysteine HCl.

[545] In some embodiments, the cryoprotectant (e.g., dry composition not containing water) comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21).

[546] In some embodiments, the cryoprotectant (e.g., dry composition not containing water) comprises about 27% to about 47% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) sucrose.

[547] In some embodiments, the cryoprotectant comprises about 8% to about 18% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 11% to about 15% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 13% (weight/weight) dextrose.

[548] In some embodiments, the cryoprotectant comprises about 8% to about 18% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 11% to about 15% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 13% (weight/weight) monosodium glutamate.

[549] In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 27% to about 47% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 32% to about 42% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 37% (weight/weight) sucrose.

[550] In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 27% to about 47% (weight/weight) sucrose; and about 8% to about 18% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 27% to about 47% (weight/weight) sucrose; and about 8% to about 18% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 27% to about 47% (weight/weight) sucrose; about 8% to about 18% (weight/weight) dextrose; and about 8% to about 18% (weight/weight) monosodium glutamate.

[551] In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21);

about 32% to about 42% (weight/weight) sucrose; and about 11% to about 15% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 32% to about 42% (weight/weight) sucrose; and about 11% to about 15% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 32% to about 42% (weight/weight) sucrose; about 11% to about 15% (weight/weight) dextrose; and about 11% to about 15% (weight/weight) monosodium glutamate.

[552] In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 37% (weight/weight) sucrose; and about 13% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 37% (weight/weight) sucrose; and about 13% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 37% (weight/weight) sucrose; about 13% (weight/weight) dextrose; and about 13% (weight/weight) monosodium glutamate.

[553] In some embodiments, the cryoprotectant comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl (e.g., a form of L-cysteine). In some embodiments, the cryoprotectant comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant comprises about 0.1% to about 0.25% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant comprises about 0.2% (weight/weight) L-cysteine HCl.

[554] In certain embodiments, the cryoprotectant provided herein comprises: (i) about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); (ii) about 37% (weight/weight) sucrose; (iii) about 13% (weight/weight) dextrose; (iv)

about 13% (weight/weight) monosodium glutamate; and (v) about 0.2% (weight/weight) L-cysteine HCl.

[555] In certain embodiments, the cryoprotectant provided herein comprises: (i) about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); (ii) about 37% (weight/weight) sucrose; (iii) about 13% (weight/weight) dextrose; and (iv) about 13% (weight/weight) monosodium glutamate.

[556] In some embodiments, the freeze-dried powder comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the freeze-dried powder comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the freeze-dried powder comprises about 26% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the freeze-dried powder comprises about 21% to about 29% (weight/weight) sucrose. In some embodiments, the freeze-dried powder comprises about 23% to about 27% (weight/weight) sucrose. In some embodiments, the freeze-dried powder comprises about 25% (weight/weight) sucrose. In some embodiments, the freeze-dried powder comprises about 6% to about 11% (weight/weight) dextrose. In some embodiments, the freeze-dried powder comprises about 7% to about 10% (weight/weight) dextrose. In some embodiments, the freeze-dried powder comprises about 9% (weight/weight) dextrose. In some embodiments, the freeze-dried powder comprises about 4% to about 10% (weight/weight) glutamate. In some embodiments, the freeze-dried powder comprises about 5% to about 9% (weight/weight) glutamate. In some embodiments, the freeze-dried powder comprises about 7% (weight/weight) glutamate.

[557] In some embodiments, the freeze-dried powder comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 21% to about 29% (weight/weight) sucrose. In some embodiments, the freeze-dried powder comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a

dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 23% to about 27% (weight/weight) sucrose. In some embodiments, the freeze-dried powder comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl. In some embodiments, the freeze-dried powder comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl.

[558] In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 21% to about 29% (weight/weight) sucrose; and about 6% to about 11% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 21% to about 29% (weight/weight) sucrose; and about 4% to about 10% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 21% to about 29% (weight/weight) sucrose; about 6% to about 11% (weight/weight) dextrose; and about 4% to about 10% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 23% to about 27% (weight/weight) sucrose; and about 7% to about 10% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); 23% to about 27% (weight/weight) sucrose; and about 5% to about 9% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); 23% to about 27% (weight/weight) sucrose; about 7% to about 1% (weight/weight) dextrose; and about 5% to about 9% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl. In some embodiments, the

pharmaceutical agent comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl.

[559] In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the pharmaceutical agent comprises about 26% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the pharmaceutical agent comprises about 21% to about 29% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 23% to about 27% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 25% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 6% to about 11% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 7% to about 10% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 9% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 4% to about 10% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 5% to about 9% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 7% (weight/weight) glutamate.

[560] In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 21% to about 29% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 23% to about 27% (weight/weight) sucrose. In some embodiments, the pharmaceutical agent comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl. In some embodiments, the

pharmaceutical agent comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl.

[561] In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 21% to about 29% (weight/weight) sucrose; and about 6% to about 11% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 21% to about 29% (weight/weight) sucrose; and about 4% to about 10% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 23% to about 30% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 21% to about 29% (weight/weight) sucrose; about 6% to about 11% (weight/weight) dextrose; and about 4% to about 10% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 23% to about 27% (weight/weight) sucrose; and about 7% to about 10% (weight/weight) dextrose. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); 23% to about 27% (weight/weight) sucrose; and about 5% to about 9% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 24% to about 28% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); 23% to about 27% (weight/weight) sucrose; about 7% to about 1% (weight/weight) dextrose; and about 5% to about 9% (weight/weight) glutamate. In some embodiments, the pharmaceutical agent comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl. In some embodiments, the pharmaceutical agent comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl.

[562] In some embodiments, the cryoprotectant comprises a dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the cryoprotectant comprises sucrose. In some embodiments, the cryoprotectant comprises dextrose (also referred to as glucose). In some embodiments, the cryoprotectant comprises monosodium glutamate. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and sucrose. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and sucrose in equivalent amounts (e.g., on a percent weight by weight basis). In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, and dextrose. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, and monosodium glutamate. In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, dextrose, and monosodium glutamate. In some embodiments, the cryoprotectant comprises dextrose and monosodium glutamate in equivalent amounts (e.g., on a percent weight by weight basis). In some embodiments, the cryoprotectant comprises dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), sucrose, dextrose, monosodium glutamate, and L-cysteine HCl (e.g., a form of L-cysteine). In some embodiments, the cryoprotectant does not comprise L-cysteine HCl.

[563] In some embodiments, the cryoprotectant (e.g., dry composition not containing water) comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the cryoprotectant comprises

about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21).

[564] In some embodiments, the cryoprotectant (e.g., dry composition not containing water) comprises about 27% to about 47% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) sucrose.

[565] In some embodiments, the cryoprotectant comprises about 8% to about 18% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 11% to about 15% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 13% (weight/weight) dextrose.

[566] In some embodiments, the cryoprotectant comprises about 8% to about 18% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 11% to about 15% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 13% (weight/weight) monosodium glutamate.

[567] In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 27% to about 47% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 32% to about 42% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 37% (weight/weight) sucrose.

[568] In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 27% to about 47% (weight/weight) sucrose; and about 8% to about 18% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 27%

to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 27% to about 47% (weight/weight) sucrose; and about 8% to about 18% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 27% to about 47% (weight/weight) sucrose; about 8% to about 18% (weight/weight) dextrose; and about 8% to about 18% (weight/weight) monosodium glutamate.

[569] In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 32% to about 42% (weight/weight) sucrose; and about 11% to about 15% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 32% to about 42% (weight/weight) sucrose; and about 11% to about 15% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 32% to about 42% (weight/weight) sucrose; about 11% to about 15% (weight/weight) dextrose; and about 11% to about 15% (weight/weight) monosodium glutamate.

[570] In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 37% (weight/weight) sucrose; and about 13% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 37% (weight/weight) sucrose; and about 13% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent

(DE) of 21 (such as Glucidex 21); about 37% (weight/weight) sucrose; about 13% (weight/weight) dextrose; and about 13% (weight/weight) monosodium glutamate.

[571] In some embodiments, the cryoprotectant comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl (e.g., a form of L-cysteine). In some embodiments, the cryoprotectant comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant comprises about 0.1% to about 0.25% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant comprises about 0.2% (weight/weight) L-cysteine HCl.

[572] In certain embodiments, the cryoprotectant provided herein comprises: (i) about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); (ii) about 37% (weight/weight) sucrose; (iii) about 13% (weight/weight) dextrose; (iv) about 13% (weight/weight) monosodium glutamate; and (v) about 0.2% (weight/weight) L-cysteine HCl.

[573] In certain embodiments, the cryoprotectant provided herein comprises: (i) about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); (ii) about 37% (weight/weight) sucrose; (iii) about 13% (weight/weight) dextrose; and (iv) about 13% (weight/weight) monosodium glutamate.

[574] In certain embodiments, the freeze-dried powder comprises about 15% to about 35% (weight/weight) bacteria (e.g., freeze dried bacteria). In certain embodiments, the freeze-dried powder comprises about 18% to about 30% (weight/weight) bacteria (e.g., freeze dried bacteria). In certain embodiments, the freeze-dried powder comprises about 25% (weight/weight) bacteria (e.g., freeze dried bacteria).

[575] In certain embodiments, the freeze-dried powder comprises *Prevotella* bacteria.

[576] In certain embodiments, the freeze-dried powder comprises *Veillonella* bacteria.

[577] As one example of a method of preparing a pharmaceutical agent, the method can include one or more of the following steps: centrifuging (e.g., using continuous centrifugation) a fermentation broth that contains bacteria to prepare a pellet that comprises bacteria; combining a cryoprotectant solution with the pellet to prepare a formulated paste; and freeze drying the formulated paste to prepare a freeze-dried product. The freeze drying can include primary drying (e.g., at -5 °C). Freeze drying can include secondary drying (e.g., at 25 °C). The total drying time can be, e.g., at least 48

hours. The freeze-dried product can be milling (e.g., using a milling machine) to prepare a freeze-dried powder, e.g., pharmaceutical agent. The freeze-dried powder can optionally be gamma irradiated.

[578] In some embodiments, the method can further comprise combining the freeze-dried powder with one or more excipients to thereby prepare a pharmaceutical composition. The pharmaceutical composition can be used in methods as described herein. The pharmaceutical composition can be prepared as a solid dosage form (e.g., capsule, tablet, and/or mini-tablet) as described herein. The solid dosage form can be coated, e.g., enterically coated, e.g., as described herein.

[579] In some embodiments, the disclosure provides a pharmaceutical agent prepared by a method described herein.

Additional Aspects of the Solid Dosage Forms

[580] The solid dosage forms, e.g., as described herein, comprising a pharmaceutical agent (e.g., a therapeutically effective amount thereof), wherein the pharmaceutical agent comprises bacteria, and wherein the solid dosage form further comprises excipients, can provide a therapeutically effective amount of the pharmaceutical agent to a subject, e.g., a human.

[581] The solid dosage forms, e.g., as described herein, comprising a pharmaceutical agent (e.g., a therapeutically effective amount thereof), wherein the pharmaceutical agent comprises bacteria, and wherein the solid dosage form further comprises excipients, can provide a non-natural amount of the therapeutically effective components (e.g., present in the pharmaceutical agent) to a subject, e.g., a human.

[582] The solid dosage forms, e.g., as described herein, comprising a pharmaceutical agent (e.g., a therapeutically effective amount thereof), wherein the pharmaceutical agent comprises bacteria, and wherein the solid dosage form further comprises excipients, can provide an unnatural quantity of the therapeutically effective components (e.g., present in the pharmaceutical agent) to a subject, e.g., a human.

[583] The solid dosage forms, e.g., as described herein, comprising a pharmaceutical agent (e.g., a therapeutically effective amount thereof), wherein the pharmaceutical agent comprises bacteria, and wherein the solid dosage form further comprises excipients, can bring about one or more changes to a subject, e.g., human, e.g., to treat or prevent a disease or a health disorder.

[584] The solid dosage forms, e.g., as described herein, comprising a pharmaceutical agent (e.g., a therapeutically effective amount thereof), wherein the pharmaceutical agent comprises bacteria, and wherein the solid dosage form further comprises excipients, has potential for significant utility, e.g., to affect a subject, e.g., a human, e.g., to treat or prevent a disease or a health disorder.

Additional Therapeutic Agents

[585] In certain aspects, the methods provided herein include the administration to a subject of a pharmaceutical agent, pharmaceutical composition, and/or solid dosage form described herein either alone or in combination with an additional therapeutic agent. In some embodiments, the additional therapeutic agent is an immunosuppressant, an anti-inflammatory agent, a steroid, and/or a cancer therapeutic.

[586] In some embodiments, the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form is administered to the subject before the additional therapeutic agent is administered (e.g., at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23 or 24 hours before or at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 days before). In some embodiments, the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form is administered to the subject after the additional therapeutic agent is administered (e.g., at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23 or 24 hours after or at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 days after). In some embodiments, the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form and the additional therapeutic agent are administered to the subject simultaneously or nearly simultaneously (e.g., administrations occur within an hour of each other).

[587] In some embodiments, an antibiotic is administered to the subject before the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form is administered to the subject (e.g., at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23 or 24 hours before or at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 days before). In some embodiments, an antibiotic is administered to the subject after the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form is administered to the subject (e.g., at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21,

22, 23 or 24 hours before or at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 days after). In some embodiments, the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form and the antibiotic are administered to the subject simultaneously or nearly simultaneously (e.g., administrations occur within an hour of each other).

[588] In some embodiments, the additional therapeutic agent is a cancer therapeutic. In some embodiments, the cancer therapeutic is a chemotherapeutic agent. Examples of such chemotherapeutic agents include, but are not limited to, alkylating agents such as thiotepa and cyclosphosphamide; alkyl sulfonates such as busulfan, improsulfan and piposulfan; aziridines such as benzodopa, carboquone, meturedopa, and uredopa; ethylenimines and methylamelamines including altretamine, triethylenemelamine, trietylenephosphoramide, triethiylenethiophosphoramide and trimethylolomelamine; acetogenins (especially bullatacin and bullatacinone); a camptothecin (including the synthetic analogue topotecan); bryostatin; callystatin; CC-1065 (including its adozelesin, carzelesin and bizelesin synthetic analogues); cryptophycins (particularly cryptophycin 1 and cryptophycin 8); dolastatin; duocarmycin (including the synthetic analogues, KW-2189 and CB1-TM1); eleutherobin; pancratistatin; a sarcodictyin; spongistatin; nitrogen mustards such as chlorambucil, chlornaphazine, cholophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard; nitrosureas such as carmustine, chlorozotocin, fotemustine, lomustine, nimustine, and ranimnustine; antibiotics such as the enediyne antibiotics (e.g., calicheamicin, especially calicheamicin gammaII and calicheamicin omegaI1; dynemicin, including dynemicin A; bisphosphonates, such as clodronate; an esperamicin; as well as neocarzinostatin chromophore and related chromoprotein enediyne antibiotic chromophores, aclacinomysins, actinomycin, authrarnycin, azaserine, bleomycins, cactinomycin, carabicin, caminomycin, carzinophilin, chromomycinis, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, doxorubicin (including morpholino-doxorubicin, cyanomorpholino-doxorubicin, 2-pyrrolino-doxorubicin and deoxydoxorubicin), epirubicin, esorubicin, idarubicin, marcellomycin, mitomycins such as mitomycin C, mycophenolic acid, nogalamycin, olivomycins, peplomycin, potfiromycin, puromycin, quelamycin, rodorubicin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin; anti-metabolites such as methotrexate and 5-

fluorouracil (5-FU); folic acid analogues such as denopterin, methotrexate, pteropterin, trimetrexate; purine analogs such as fludarabine, 6-mercaptopurine, thiamiprine, thioguanine; pyrimidine analogs such as ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine; androgens such as calusterone, dromostanolone propionate, epitiostanol, mepitiostane, testolactone; anti-adrenals such as aminoglutethimide, mitotane, trilostane; folic acid replenisher such as frolinic acid; aceglatone; aldophosphamide glycoside; aminolevulinic acid; eniluracil; amsacrine; bestrabucil; bisantrene; edatraxate; defofamine; demecolcine; diaziquone; elformithine; elliptinium acetate; an epothilone; etoglucid; gallium nitrate; hydroxyurea; lentinan; lonidainine; maytansinoids such as maytansine and ansamitocins; mitoguazone; mitoxantrone; mopidanmol; nitraerine; pentostatin; phenamet; pirarubicin; losoxantrone; podophyllinic acid; 2-ethylhydrazide; procarbazine; PSK polysaccharide complex); razoxane; rhizoxin; sizofuran; spirogermanium; tenuazonic acid; triaziquone; 2,2',2''-trichlorotriethylamine; trichothecenes (especially T-2 toxin, verracurin A, roridin A and anguidine); urethan; vindesine; dacarbazine; mannomustine; mitobronitol; mitolactol; pipobroman; gacytosine; arabinoside ("Ara-C"); cyclophosphamide; thiotepa; taxoids, e.g., paclitaxel and doxetaxel; chlorambucil; gemcitabine; 6-thioguanine; mercaptopurine; methotrexate; platinum coordination complexes such as cisplatin, oxaliplatin and carboplatin; vinblastine; platinum; etoposide (VP-16); ifosfamide; mitoxantrone; vincristine; vinorelbine; novantrone; teniposide; edatrexate; daunomycin; aminopterin; xeloda; ibandronate; irinotecan (e.g., CPT-11); topoisomerase inhibitor RFS 2000; difluoromethylomithine (DMFO); retinoids such as retinoic acid; capecitabine; and pharmaceutically acceptable salts, acids or derivatives of any of the above.

[589] In some embodiments, the cancer therapeutic is a cancer immunotherapy agent. Immunotherapy refers to a treatment that uses a subject's immune system to treat cancer, e.g., checkpoint inhibitors, cancer vaccines, cytokines, cell therapy, CAR-T cells, and dendritic cell therapy. Non-limiting examples of immunotherapies are checkpoint inhibitors include Nivolumab (BMS, anti-PD-1), Pembrolizumab (Merck, anti-PD-1), Ipilimumab (BMS, anti-CTLA-4), MEDI4736 (AstraZeneca, anti-PD-L1), and MPDL3280A (Roche, anti-PD-L1). Other immunotherapies may be tumor vaccines, such as Gardail, Cervarix, BCG, sipulencel-T, Gp100:209-217, AGS-003, DCVax-L, Algenpantucel-L, Tergenpantucel-L, TG4010, ProstAtak, Prostvac-V/R-TRICOM, Rindopepimul, E75 peptide acetate, IMA901, POL-103A, Belagenpumatucel-L,

GSK1572932A, MDX-1279, GV1001, and Tecemotide. The immunotherapy agent may be administered via injection (e.g., intravenously, intratumorally, subcutaneously, or into lymph nodes), but may also be administered orally, topically, or via aerosol. Immunotherapies may comprise adjuvants such as cytokines.

[590] In some embodiments, the immunotherapy agent is an immune checkpoint inhibitor. Immune checkpoint inhibition broadly refers to inhibiting the checkpoints that cancer cells can produce to prevent or downregulate an immune response. Examples of immune checkpoint proteins include, but are not limited to, CTLA4, PD-1, PD-L1, PD-L2, A2AR, B7-H3, B7-H4, BTLA, KIR, LAG3, TIM-3 or VISTA. Immune checkpoint inhibitors can be antibodies or antigen binding fragments thereof that bind to and inhibit an immune checkpoint protein. Examples of immune checkpoint inhibitors include, but are not limited to, nivolumab, pembrolizumab, pidilizumab, AMP-224, AMP-514, STI-A1110, TSR-042, RG-7446, BMS-936559, MEDI-4736, MSB-0020718C, AUR-012 and STI-A1010.

[591] In some embodiments, the methods provided herein include the administration of a pharmaceutical agent, pharmaceutical composition, and/or solid dosage form described herein in combination with one or more additional therapeutic agents. In some embodiments, the methods disclosed herein include the administration of two immunotherapy agents (e.g., immune checkpoint inhibitor). For example, the methods provided herein include the administration of a pharmaceutical agent, pharmaceutical composition, and/or solid dosage form described herein in combination with a PD-1 inhibitor (such as pemrolizumab or nivolumab or pidilizumab) or a CLTA-4 inhibitor (such as ipilimumab) or a PD-L1 inhibitor.

[592] In some embodiments, the immunotherapy agent is an antibody or antigen binding fragment thereof that, for example, binds to a cancer-associated antigen. Examples of cancer-associated antigens include, but are not limited to, adipophilin, AIM-2, ALDH1A1, alpha-actinin-4, alpha-fetoprotein ("AFP"), ARTC1, B-RAF, BAGE-1, BCLX (L), BCR-ABL fusion protein b3a2, beta-catenin, BING-4, CA-125, CALCA, carcinoembryonic antigen ("CEA"), CASP-5, CASP-8, CD274, CD45, Cdc27, CDK12, CDK4, CDKN2A, CEA, CLPP, COA-1, CPSF, CSNK1A1, CTAG1, CTAG2, cyclin D1, Cyclin-A1, dek-can fusion protein, DKK1, EFTUD2, Elongation factor 2, ENAH (hMena), Ep-CAM, EpCAM, EphA3, epithelial tumor antigen ("ETA"), ETV6-AML1 fusion protein, EZH2, FGF5, FLT3-ITD, FN1, G250/MN/CAIX, GAGE-1,2,8, GAGE-

3,4,5,6,7, GAS7, glypican-3, GnTV, gp100/Pmel17, GPNMB, HAUS3, Hepsin, HER-2/neu, HERV-K-MEL, HLA-A11, HLA-A2, HLA-DOB, hsp70-2, IDO1, IGF2B3, IL13Ralpha2, Intestinal carboxyl esterase, K-ras, Kallikrein 4, KIF20A, KK-LC-1, KKLC1, KM-HN-1, KMHN1 also known as CCDC110, LAGE-1, LDLR-fucosyltransferaseAS fusion protein, Lengsin, M-CSF, MAGE-A1, MAGE-A10, MAGE-A12, MAGE-A2, MAGE-A3, MAGE-A4, MAGE-A6, MAGE-A9, MAGE-C1, MAGE-C2, malic enzyme, mammaglobin-A, MART2, MATN, MC1R, MCSP, mdm-2, ME1, Melan-A/MART-1, Meloe, Midkine, MMP-2, MMP-7, MUC1, MUC5AC, mucin, MUM-1, MUM-2, MUM-3, Myosin, Myosin class I, N-raw, NA88-A, neo-PAP, NFYC, NY-BR-1, NY-ESO-1/LAGE-2, OA1, OGT, OS-9, P polypeptide, p53, PAP, PAX5, PBF, pml-RARalpha fusion protein, polymorphic epithelial mucin ("PEM"), PPP1R3B, PRAME, PRDX5, PSA, PSMA, PTPRK, RAB38/NY-MEL-1, RAGE-1, RBAF600, RGS5, RhoC, RNF43, RU2AS, SAGE, secernin 1, SIRT2, SNRPD1, SOX10, Sp17, SPA17, SSX-2, SSX-4, STEAP1, survivin, SYT-SSX1 or -SSX2 fusion protein, TAG-1, TAG-2, Telomerase, TGF-betaRII, TPBG, TRAG-3, Triosephosphate isomerase, TRP-1/gp75, TRP-2, TRP2-INT2, tyrosinase, tyrosinase ("TYR"), VEGF, WT1, XAGE-1b/GAGED2a. In some embodiments, the antigen is a neo-antigen.

[593] In some embodiments, the immunotherapy agent is a cancer vaccine and/or a component of a cancer vaccine (e.g., an antigenic peptide and/or protein). The cancer vaccine can be a protein vaccine, a nucleic acid vaccine or a combination thereof. For example, in some embodiments, the cancer vaccine comprises a polypeptide comprising an epitope of a cancer-associated antigen. In some embodiments, the cancer vaccine comprises a nucleic acid (e.g., DNA or RNA, such as mRNA) that encodes an epitope of a cancer-associated antigen. Examples of cancer-associated antigens include, but are not limited to, adipophilin, AIM-2, ALDH1A1, alpha-actinin-4, alpha-fetoprotein ("AFP"), ARTC1, B-RAF, BAGE-1, BCLX (L), BCR-ABL fusion protein b3a2, beta-catenin, BING-4, CA-125, CALCA, carcinoembryonic antigen ("CEA"), CASP-5, CASP-8, CD274, CD45, Cdc27, CDK12, CDK4, CDKN2A, CEA, CLPP, COA-1, CPSF, CSNK1A1, CTAG1, CTAG2, cyclin D1, Cyclin-A1, dek-can fusion protein, DKK1, EFTUD2, Elongation factor 2, ENAH (hMena), Ep-CAM, EpCAM, EphA3, epithelial tumor antigen ("ETA"), ETV6-AML1 fusion protein, EZH2, FGF5, FLT3-ITD, FN1, G250/MN/CAIX, GAGE-1,2,8, GAGE-3,4,5,6,7, GAS7, glypican-3, GnTV, gp100/Pmel17, GPNMB, HAUS3, Hepsin, HER-2/neu, HERV-K-MEL, HLA-A11,

HLA-A2, HLA-DOB, hsp70-2, IDO1, IGF2B3, IL13Ralpha2, Intestinal carboxyl esterase, K-ras, Kallikrein 4, KIF20A, KK-LC-1, KKLC1, KM-HN-1, KMHN1 also known as CCDC110, LAGE-1, LDLR-fucosyltransferaseAS fusion protein, Lengsin, M-CSF, MAGE-A1, MAGE-A10, MAGE-A12, MAGE-A2, MAGE-A3, MAGE-A4, MAGE-A6, MAGE-A9, MAGE-C1, MAGE-C2, malic enzyme, mammaglobin-A, MART2, MATN, MC1R, MCSP, mdm-2, ME1, Melan-A/MART-1, Meloe, Midkine, MMP-2, MMP-7, MUC1, MUC5AC, mucin, MUM-1, MUM-2, MUM-3, Myosin, Myosin class I, N-raw, NA88-A, neo-PAP, NFYC, NY-BR-1, NY-ESO-1/LAGE-2, OA1, OGT, OS-9, P polypeptide, p53, PAP, PAX5, PBF, pml-RARalpha fusion protein, polymorphic epithelial mucin ("PEM"), PPP1R3B, PRAME, PRDX5, PSA, PSMA, PTPRK, RAB38/NY-MEL-1, RAGE-1, RBAF600, RGS5, RhoC, RNF43, RU2AS, SAGE, secernin 1, SIRT2, SNRPD1, SOX10, Sp17, SPA17, SSX-2, SSX-4, STEAP1, survivin, SYT-SSX1 or -SSX2 fusion protein, TAG-1, TAG-2, Telomerase, TGF-betaRII, TPBG, TRAG-3, Triosephosphate isomerase, TRP-1/gp75, TRP-2, TRP2-INT2, tyrosinase, tyrosinase ("TYR"), VEGF, WT1, XAGE-1b/GAGED2a. In some embodiments, the antigen is a neo-antigen. In some embodiments, the cancer vaccine is administered with an adjuvant. Examples of adjuvants include, but are not limited to, an immune modulatory protein, Adjuvant 65, α-GalCer, aluminum phosphate, aluminum hydroxide, calcium phosphate, β-Glucan Peptide, CpG ODN DNA, GPI-0100, lipid A, lipopolysaccharide, Lipovant, Montanide, N-acetyl-muramyl-L-alanyl-D-isoglutamine, Pam3CSK4, quil A , cholera toxin (CT) and heat-labile toxin from enterotoxigenic *Escherichia coli* (LT) including derivatives of these (CTB, mmCT, CTA1-DD, LTB, LTK63, LTR72, dmLT) and trehalose dimycolate.

[594] In some embodiments, the immunotherapy agent is an immune modulating protein to the subject. In some embodiments, the immune modulatory protein is a cytokine or chemokine. Examples of immune modulating proteins include, but are not limited to, B lymphocyte chemoattractant ("BLC"), C-C motif chemokine 11 ("Eotaxin-1"), Eosinophil chemotactic protein 2 ("Eotaxin-2"), Granulocyte colony-stimulating factor ("G-CSF"), Granulocyte macrophage colony-stimulating factor ("GM-CSF"), 1-309, Intercellular Adhesion Molecule 1 ("ICAM-1"), Interferon alpha ("IFN-alpha"), Interferon beta ("IFN-beta") Interferon gamma ("IFN-gamma"), Interlukin-1 alpha ("IL-1 alpha"), Interlukin-1 beta ("IL-1 beta"), Interleukin 1 receptor antagonist ("IL-1 ra"), Interleukin-2 ("IL-2"), Interleukin-4 ("IL-4"), Interleukin-5 ("IL-5"), Interleukin-6 ("IL-6"), Interleukin-6 soluble

receptor ("IL-6 sR"), Interleukin-7 ("IL-7"), Interleukin-8 ("IL-8"), Interleukin- 10 ("IL-10"), Interleukin- 11 ("IL-11"), Subunit beta of Interleukin- 12 ("IL-12 p40" or "IL-12 p70"), Interleukin-13 ("IL-13"), Interleukin-15 ("IL-15"), Interleukin-16 ("IL-16"), Interleukin-17A-F ("IL-17A-F"), Interleukin-18 ("IL-18"), Interleukin-21 ("IL-21"), Interleukin-22 ("IL-22"), Interleukin-23 ("IL-23"), Interleukin-33 ("IL-33"), Chemokine (C-C motif) Ligand 2 ("MCP-1"), Macrophage colony-stimulating factor ("M-CSF"), Monokine induced by gamma interferon ("MIG"), Chemokine (C-C motif) ligand 2 ("MIP-1 alpha"), Chemokine (C-C motif) ligand 4 ("MIP-1 beta"), Macrophage inflammatory protein- 1 -delta ("MIP-1 delta"), Platelet-derived growth factor subunit B ("PDGF-BB"), Chemokine (C-C motif) ligand 5, Regulated on Activation, Normal T cell Expressed and Secreted ("RANTES"), TIMP metallopeptidase inhibitor 1 ("TIMP-1"), TIMP metallopeptidase inhibitor 2 ("TIMP-2"), Tumor necrosis factor, lymphotoxin-alpha ("TNF alpha"), Tumor necrosis factor, lymphotoxin-beta ("TNF beta"), Soluble TNF receptor type 1 ("sTNFRI"), sTNFRIIAR, Brain-derived neurotrophic factor ("BDNF"), Basic fibroblast growth factor ("bFGF"), Bone morphogenetic protein 4 ("BMP-4"), Bone morphogenetic protein 5 ("BMP-5"), Bone morphogenetic protein 7 ("BMP-7"), Nerve growth factor ("b-NGF"), Epidermal growth factor ("EGF"), Epidermal growth factor receptor ("EGFR"), Endocrine-gland-derived vascular endothelial growth factor ("EG-VEGF"), Fibroblast growth factor 4 ("FGF-4"), Keratinocyte growth factor ("FGF-7"), Growth differentiation factor 15 ("GDF-15"), Glial cell-derived neurotrophic factor ("GDNF"), Growth Hormone, Heparin-binding EGF-like growth factor ("HB-EGF"), Hepatocyte growth factor ("HGF"), Insulin-like growth factor binding protein 1 ("IGFBP-1"), Insulin-like growth factor binding protein 2 ("IGFBP-2"), Insulin-like growth factor binding protein 3 (" IGFBP-3"), Insulin-like growth factor binding protein 4 ("IGFBP-4"), Insulin-like growth factor binding protein 6 ("IGFBP-6"), Insulin-like growth factor 1 ("IGF-1"), Insulin, Macrophage colony-stimulating factor ("M-CSF R"), Nerve growth factor receptor ("NGF R"), Neurotrophin-3 ("NT-3"), Neurotrophin-4 ("NT-4"), Osteoclastogenesis inhibitory factor ("Osteoprotegerin"), Platelet-derived growth factor receptors ("PDGF-AA"), Phosphatidylinositol-glycan biosynthesis ("PIGF"), Skp, Cullin, F-box containing comples ("SCF"), Stem cell factor receptor ("SCF R"), Transforming growth factor alpha ("TGFalpha"), Transforming growth factor beta-1 ("TGF beta 1"), Transforming growth factor beta-3 ("TGF beta 3"), Vascular endothelial growth factor ("VEGF"), Vascular

endothelial growth factor receptor 2 ("VEGFR2"), Vascular endothelial growth factor receptor 3 ("VEGFR3"), VEGF-D 6Ckine, Tyrosine-protein kinase receptor UFO ("Axl"), Betacellulin ("BTC"), Mucosae-associated epithelial chemokine ("CCL28"), Chemokine (C-C motif) ligand 27 ("CTACK"), Chemokine (C-X-C motif) ligand 16 ("CXCL16"), C-X-C motif chemokine 5 ("ENA-78"), Chemokine (C-C motif) ligand 26 ("Eotaxin-3"), Granulocyte chemotactic protein 2 ("GCP-2"), GRO, Chemokine (C-C motif) ligand 14 ("HCC-l"), Chemokine (C-C motif) ligand 16 ("HCC-4"), Interleukin-9 ("IL-9"), Interleukin-17 F ("IL-17F"), Interleukin- 18-binding protein ("IL-18 BPa"), Interleukin-28 A ("IL-28A"), Interleukin 29 ("IL-29"), Interleukin 31 ("IL-31"), C-X-C motif chemokine 10 ("IP-10"), Chemokine receptor CXCR3 ("I-TAC"), Leukemia inhibitory factor ("LIF"), Light, Chemokine (C motif) ligand ("Lymphotactin"), Monocyte chemoattractant protein 2 ("MCP-2"), Monocyte chemoattractant protein 3 ("MCP-3"), Monocyte chemoattractant protein 4 ("MCP-4"), Macrophage-derived chemokine ("MDC"), Macrophage migration inhibitory factor ("MIF"), Chemokine (C-C motif) ligand 20 ("MIP-3 alpha"), C-C motif chemokine 19 ("MIP-3 beta"), Chemokine (C-C motif) ligand 23 ("MPIF-1"), Macrophage stimulating protein alpha chain ("MSPalpha"), Nucleosome assembly protein 1-like 4 ("NAP-2"), Secreted phosphoprotein 1 ("Osteopontin"), Pulmonary and activation-regulated cytokine ("PARC"), Platelet factor 4 ("PF4"), Stroma cell-derived factor- 1 alpha ("SDF-1 alpha"), Chemokine (C-C motif) ligand 17 ("TARC"), Thymus-expressed chemokine ("TECK"), Thymic stromal lymphopoietin ("TSLP 4- IBB"), CD 166 antigen ("ALCAM"), Cluster of Differentiation 80 ("B7-1"), Tumor necrosis factor receptor superfamily member 17 ("BCMA"), Cluster of Differentiation 14 ("CD14"), Cluster of Differentiation 30 ("CD30"), Cluster of Differentiation 40 ("CD40 Ligand"), Carcinoembryonic antigen-related cell adhesion molecule 1 (biliary glycoprotein) ("CEACAM-1"), Death Receptor 6 ("DR6"), Deoxythymidine kinase ("Dtk"), Type 1 membrane glycoprotein ("Endoglin"), Receptor tyrosine-protein kinase erbB-3 ("ErbB3"), Endothelial-leukocyte adhesion molecule 1 ("E-Selectin"), Apoptosis antigen 1 ("Fas"), Fms-like tyrosine kinase 3 ("Flt-3L"), Tumor necrosis factor receptor superfamily member 1 ("GITR"), Tumor necrosis factor receptor superfamily member 14 ("HVEM"), Intercellular adhesion molecule 3 ("ICAM-3"), IL-1 R4, IL-1 RI, IL-10 Rbeta, IL-17R, IL-2Rgamma, IL-21R, Lysosome membrane protein 2 ("LIMPII"), Neutrophil gelatinase-associated lipocalin ("Lipocalin-2"), CD62L ("L-Selectin"), Lymphatic endothelium ("LYVE-1"), MHC class I

polypeptide-related sequence A ("MICA"), MHC class I polypeptide-related sequence B ("MICB"), NRGl-betal, Beta-type platelet-derived growth factor receptor ("PDGF Rbeta"), Platelet endothelial cell adhesion molecule ("PECAM-1"), RAGE, Hepatitis A virus cellular receptor 1 ("TIM-1"), Tumor necrosis factor receptor superfamily member IOC ("TRAIL R3"), Trappin protein transglutaminase binding domain ("Trappin-2"), Urokinase receptor ("uPAR"), Vascular cell adhesion protein 1 ("VCAM-1"), XEDARActivin A, Agouti-related protein ("AgRP"), Ribonuclease 5 ("Angiogenin"), Angiopoietin 1, Angiostatin, Catheprin S, CD40, Cryptic family protein IB ("Cripto-1"), DAN, Dickkopf-related protein 1 ("DKK-1"), E-Cadherin, Epithelial cell adhesion molecule ("EpCAM"), Fas Ligand (FasL or CD95L), Fcg RIIB/C, FoUistatin, Galectin-7, Intercellular adhesion molecule 2 ("ICAM-2"), IL-13 Rl, IL-13R2, IL-17B, IL-2 Ra, IL-2 Rb, IL-23, LAP, Neuronal cell adhesion molecule ("NrCAM"), Plasminogen activator inhibitor- 1 ("PAI-1"), Platelet derived growth factor receptors ("PDGF-AB"), Resistin, stromal cell-derived factor 1 ("SDF-1 beta"), sgpl30, Secreted frizzled-related protein 2 ("ShhN"), Sialic acid-binding immunoglobulin-type lectins ("Siglec-5"), ST2, Transforming growth factor-beta 2 ("TGF beta 2"), Tie-2, Thrombopoietin ("TPO"), Tumor necrosis factor receptor superfamily member 10D ("TRAIL R4"), Triggering receptor expressed on myeloid cells 1 ("TREM-1"), Vascular endothelial growth factor C ("VEGF-C"), VEGFRlAdiponectin, Adipsin ("AND"), Alpha-fetoprotein ("AFP"), Angiopoietin-like 4 ("ANGPTL4"), Beta-2-microglobulin ("B2M"), Basal cell adhesion molecule ("BCAM"), Carbohydrate antigen 125 ("CA125"), Cancer Antigen 15-3 ("CA15-3"), Carcinoembryonic antigen ("CEA"), cAMP receptor protein ("CRP"), Human Epidermal Growth Factor Receptor 2 ("ErbB2"), Follistatin, Follicle-stimulating hormone ("FSH"), Chemokine (C-X-C motif) ligand 1 ("GRO alpha"), human chorionic gonadotropin ("beta HCG"), Insulin-like growth factor 1 receptor ("IGF-1 sR"), IL-1 sRII, IL-3, IL-18 Rb, IL-21, Leptin, Matrix metalloproteinase-1 ("MMP-1"), Matrix metalloproteinase-2 ("MMP-2"), Matrix metalloproteinase-3 ("MMP-3"), Matrix metalloproteinase-8 ("MMP-8"), Matrix metalloproteinase-9 ("MMP-9"), Matrix metalloproteinase-10 ("MMP-10"), Matrix metalloproteinase-13 ("MMP-13"), Neural Cell Adhesion Molecule ("NCAM-1"), Entactin ("Nidogen-1"), Neuron specific enolase ("NSE"), Oncostatin M ("OSM"), Procalcitonin, Prolactin, Prostate specific antigen ("PSA"), Sialic acid-binding Ig-like lectin 9 ("Siglec-9"), ADAM 17 endopeptidase ("TACE"), Thyroglobulin, Metalloproteinase inhibitor 4 ("TIMP-4"), TSH2B4,

Disintegrin and metalloproteinase domain-containing protein 9 ("ADAM-9"), Angiopoietin 2, Tumor necrosis factor ligand superfamily member 13/ Acidic leucine-rich nuclear phosphoprotein 32 family member B ("APRIL"), Bone morphogenetic protein 2 ("BMP-2"), Bone morphogenetic protein 9 ("BMP-9"), Complement component 5a ("C5a"), Cathepsin L, CD200, CD97, Chemerin, Tumor necrosis factor receptor superfamily member 6B ("DcR3"), Fatty acid-binding protein 2 ("FABP2"), Fibroblast activation protein, alpha ("FAP"), Fibroblast growth factor 19 ("FGF-19"), Galectin-3, Hepatocyte growth factor receptor ("HGF R"), IFN-gammalpha/beta R2, Insulin-like growth factor 2 ("IGF-2"), Insulin-like growth factor 2 receptor ("IGF-2 R"), Interleukin-1 receptor 6 ("IL-1R6"), Interleukin 24 ("IL-24"), Interleukin 33 ("IL-33", Kallikrein 14, Asparaginyl endopeptidase ("Legumain"), Oxidized low-density lipoprotein receptor 1 ("LOX-1"), Mannose-binding lectin ("MBL"), Neprilysin ("NEP"), Notch homolog 1, translocation-associated (Drosophila) ("Notch-1"), Nephroblastoma overexpressed ("NOV"), Osteoactivin, Programmed cell death protein 1 ("PD-1"), N-acetylmuramoyl-L-alanine amidase ("PGRP-5"), Serpin A4, Secreted frizzled related protein 3 ("sFRP-3"), Thrombomodulin, Tolllike receptor 2 ("TLR2"), Tumor necrosis factor receptor superfamily member 10A ("TRAIL Rl"), Transferrin ("TRF"), WIF-lACE-2, Albumin, AMICA, Angiopoietin 4, B-cell activating factor ("BAFF"), Carbohydrate antigen 19-9 ("CA19-9"), CD 163 , Clusterin, CRT AM, Chemokine (C-X-C motif) ligand 14 ("CXCL14"), Cystatin C, Decorin ("DCN"), Dickkopf-related protein 3 ("Dkk-3"), Delta-like protein 1 ("DLL1"), Fetuin A, Heparin-binding growth factor 1 ("aFGF"), Folate receptor alpha ("FOLR1"), Furin, GPCR-associated sorting protein 1 ("GASP-1"), GPCR-associated sorting protein 2 ("GASP-2"), Granulocyte colony-stimulating factor receptor ("GCSF R"), Serine protease hepsin ("HAI-2"), Interleukin-17B Receptor ("IL-17B R"), Interleukin 27 ("IL-27"), Lymphocyte-activation gene 3 ("LAG-3"), Apolipoprotein A-V ("LDL R"), Pepsinogen I, Retinol binding protein 4 ("RBP4"), SOST, Heparan sulfate proteoglycan ("Syndecan-1"), Tumor necrosis factor receptor superfamily member 13B ("TACI"), Tissue factor pathway inhibitor ("TFPI"), TSP-1, Tumor necrosis factor receptor superfamily, member 10b ("TRAIL R2"), TRANCE, Troponin I, Urokinase Plasminogen Activator ("uPA"), Cadherin 5, type 2 or VE-cadherin (vascular endothelial) also known as CD144 ("VE-Cadherin"), WNTl-inducible-signaling pathway protein 1 ("WISP-1"), and Receptor Activator of Nuclear Factor κ B ("RANK").

[595] In some embodiments, the cancer therapeutic is an anti-cancer compound. Exemplary anti-cancer compounds include, but are not limited to, Alemtuzumab (Campath®), Alitretinoin (Panretin®), Anastrozole (Arimidex®), Bevacizumab (Avastin®), Bexarotene (Targretin®), Bortezomib (Velcade®), Bosutinib (Bosulif®), Brentuximab vedotin (Adcetris®), Cabozantinib (Cometriq™), Carfilzomib (Kyprolis™), Cetuximab (Erbitux®), Crizotinib (Xalkori®), Dasatinib (Sprycel®), Denileukin diftitox (Ontak®), Erlotinib hydrochloride (Tarceva®), Everolimus (Afinitor®), Exemestane (Aromasin®), Fulvestrant (Faslodex®), Gefitinib (Iressa®), Ibritumomab tiuxetan (Zevalin®), Imatinib mesylate (Gleevec®), Ipilimumab (Yervoy™), Lapatinib ditosylate (Tykerb®), Letrozole (Femara®), Nilotinib (Tasigna®), Ofatumumab (Arzerra®), Panitumumab (Vectibix®), Pazopanib hydrochloride (Votrient®), Pertuzumab (Perjeta™), Pralatrexate (Folotyn®), Regorafenib (Stivarga®), Rituximab (Rituxan®), Romidepsin (Istodax®), Sorafenib tosylate (Nexavar®), Sunitinib malate (Sutent®), Tamoxifen, Temsirolimus (Torisel®), Toremifene (Fareston®), Tositumomab and 131I-tositumomab (Bexxar®), Trastuzumab (Herceptin®), Tretinoin (Vesanoid®), Vandetanib (Caprelsa®), Vemurafenib (Zelboraf®), Vorinostat (Zolinza®), and Ziv-aflibercept (Zaltrap®).

[596] Exemplary anti-cancer compounds that modify the function of proteins that regulate gene expression and other cellular functions (e.g., HDAC inhibitors, retinoid receptor ligants) are Vorinostat (Zolinza®), Bexarotene (Targretin®) and Romidepsin (Istodax®), Alitretinoin (Panretin®), and Tretinoin (Vesanoid®).

[597] Exemplary anti-cancer compounds that induce apoptosis (e.g., proteasome inhibitors, antifolates) are Bortezomib (Velcade®), Carfilzomib (Kyprolis™), and Pralatrexate (Folotyn®).

[598] Exemplary anti-cancer compounds that increase anti-tumor immune response (e.g., anti CD20, anti CD52; anti-cytotoxic T-lymphocyte-associated antigen-4) are Rituximab (Rituxan®), Alemtuzumab (Campath®), Ofatumumab (Arzerra®), and Ipilimumab (Yervoy™).

[599] Exemplary anti-cancer compounds that deliver toxic agents to cancer cells (e.g., anti-CD20-radionuclide fusions; IL-2-diphtheria toxin fusions; anti-CD30-monomethylauristatin E (MMAE)-fusions) are Tositumomab and 131I-tositumomab (Bexxar®)and Ibritumomab tiuxetan (Zevalin®), Denileukin diftitox (Ontak®), and Brentuximab vedotin (Adcetris®).

[600] Other exemplary anti-cancer compounds are small molecule inhibitors and conjugates thereof of, e.g., Janus kinase, ALK, Bcl-2, PARP, PI3K, VEGF receptor, Braf, MEK, CDK, and HSP90.

[601] Exemplary platinum-based anti-cancer compounds include, for example, cisplatin, carboplatin, oxaliplatin, satraplatin, picoplatin, Nedaplatin, Triplatin, and Lipoplatin. Other metal-based drugs suitable for treatment include, but are not limited to ruthenium-based compounds, ferrocene derivatives, titanium-based compounds, and gallium-based compounds.

[602] In some embodiments, the cancer therapeutic is a radioactive moiety that comprises a radionuclide. Exemplary radionuclides include, but are not limited to Cr-51, Cs-131, Ce-134, Se-75, Ru-97, I-125, Eu-149, Os-189m, Sb-119, I-123, Ho-161, Sb-117, Ce-139, In-111, Rh-103m, Ga-67, Tl-201, Pd-103, Au-195, Hg-197, Sr-87m, Pt-191, P-33, Er-169, Ru-103, Yb-169, Au-199, Sn-121, Tm-167, Yb-175, In-113m, Sn-113, Lu-177, Rh-105, Sn-117m, Cu-67, Sc-47, Pt-195m, Ce-141, I-131, Tb-161, As-77, Pt-197, Sm-153, Gd-159, Tm-173, Pr-143, Au-198, Tm-170, Re-186, Ag-111, Pd-109, Ga-73, Dy-165, Pm-149, Sn-123, Sr-89, Ho-166, P-32, Re-188, Pr-142, Ir-194, In-114m/In-114, and Y-90.

[603] In some embodiments, the additional therapeutic is an antibiotic. For example, if the presence of a disease-associated bacteria and/or a disease-associated microbiome profile is detected, antibiotics can be administered, e.g., to eliminate the disease-associated bacteria from the subject. In some embodiments, the cancer therapeutic is an antibiotic. For example, if the presence of a cancer-associated bacteria and/or a cancer-associated microbiome profile is detected according to the methods provided herein, antibiotics can be administered to eliminate the cancer-associated bacteria from the subject. "Antibiotics" broadly refers to compounds capable of inhibiting or preventing a bacterial infection. Antibiotics can be classified in a number of ways, including their use for specific infections, their mechanism of action, their bioavailability, or their spectrum of target microbe (e.g., Gram-negative vs. Gram-positive bacteria, aerobic vs. anaerobic bacteria, etc.) and these may be used to kill specific bacteria in specific areas of the host ("niches") (Leekha, et al 2011. General Principles of Antimicrobial Therapy. Mayo Clin Proc. 86(2): 156-167). In certain embodiments, antibiotics can be used to selectively target bacteria of a specific niche. In some embodiments, antibiotics known to treat a particular infection that includes a disease (such as cancer) niche may be used to target

disease-associated microbes, including disease-associated bacteria in that niche. In other embodiments, antibiotics are administered after the solid dosage form. In some embodiments, antibiotics are administered before the solid dosage form.

[604] In some aspects, antibiotics can be selected based on their bactericidal or bacteriostatic properties. Bactericidal antibiotics include mechanisms of action that disrupt the cell wall (e.g., β-lactams), the cell membrane (e.g., daptomycin), or bacterial DNA (e.g., fluoroquinolones). Bacteriostatic agents inhibit bacterial replication and include sulfonamides, tetracyclines, and macrolides, and act by inhibiting protein synthesis. Furthermore, while some drugs can be bactericidal in certain organisms and bacteriostatic in others, knowing the target organism allows one skilled in the art to select an antibiotic with the appropriate properties. In certain treatment conditions, bacteriostatic antibiotics inhibit the activity of bactericidal antibiotics. Thus, in certain embodiments, bactericidal and bacteriostatic antibiotics are not combined.

[605] Antibiotics include, but are not limited to aminoglycosides, ansamycins, carbacephems, carbapenems, cephalosporins, glycopeptides, lincosamides, lipopeptides, macrolides, monobactams, nitrofurans, oxazolidonones, penicillins, polypeptide antibiotics, quinolones, fluoroquinolone, sulfonamides, tetracyclines, and anti-mycobacterial compounds, and combinations thereof.

[606] Aminoglycosides include, but are not limited to Amikacin, Gentamicin, Kanamycin, Neomycin, Netilmicin, Tobramycin, Paromomycin, and Spectinomycin. Aminoglycosides are effective, e.g., against Gram-negative bacteria, such as *Escherichia coli*, *Klebsiella*, *Pseudomonas aeruginosa*, and *Francisella tularensis*, and against certain aerobic bacteria but less effective against obligate/facultative anaerobes. Aminoglycosides are believed to bind to the bacterial 30S or 50S ribosomal subunit thereby inhibiting bacterial protein synthesis.

[607] Ansamycins include, but are not limited to, Geldanamycin, Herbimycin, Rifamycin, and Streptovaricin. Geldanamycin and Herbimycin are believed to inhibit or alter the function of Heat Shock Protein 90.

[608] Carbacephems include, but are not limited to, Loracarbef. Carbacephems are believed to inhibit bacterial cell wall synthesis.

[609] Carbapenems include, but are not limited to, Ertapenem, Doripenem, Imipenem/Cilastatin, and Meropenem. Carbapenems are bactericidal for both Gram-

positive and Gram-negative bacteria as broad-spectrum antibiotics. Carbapenems are believed to inhibit bacterial cell wall synthesis.

[610] Cephalosporins include, but are not limited to, Cefadroxil, Cefazolin, Cefalotin, Cefalothin, Cefalexin, Cefaclor, Cefamandole, Cefoxitin, Cefprozil, Cefuroxime, Cefixime, Cefdinir, Cefditoren, Cefoperazone, Cefotaxime, Cefpodoxime, Ceftazidime, Ceftibuten, Ceftizoxime, Ceftriaxone, Cefepime, Ceftaroline fosamil, and Ceftobiprole. Selected Cephalosporins are effective, e.g., against Gram-negative bacteria and against Gram-positive bacteria, including *Pseudomonas*, certain Cephalosporins are effective against methicillin-resistant *Staphylococcus aureus* (MRSA). Cephalosporins are believed to inhibit bacterial cell wall synthesis by disrupting synthesis of the peptidoglycan layer of bacterial cell walls.

[611] Glycopeptides include, but are not limited to, Teicoplanin, Vancomycin, and Telavancin. Glycopeptides are effective, e.g., against aerobic and anaerobic Gram-positive bacteria including MRSA and *Clostridium difficile*. Glycopeptides are believed to inhibit bacterial cell wall synthesis by disrupting synthesis of the peptidoglycan layer of bacterial cell walls.

[612] Lincosamides include, but are not limited to, Clindamycin and Lincomycin. Lincosamides are effective, e.g., against anaerobic bacteria, as well as *Staphylococcus*, and *Streptococcus*. Lincosamides are believed to bind to the bacterial 50S ribosomal subunit thereby inhibiting bacterial protein synthesis.

[613] Lipopeptides include, but are not limited to, Daptomycin. Lipopeptides are effective, e.g., against Gram-positive bacteria. Lipopeptides are believed to bind to the bacterial membrane and cause rapid depolarization.

[614] Macrolides include, but are not limited to, Azithromycin, Clarithromycin, Dirithromycin, Erythromycin, Roxithromycin, Troleandomycin, Telithromycin, and Spiramycin. Macrolides are effective, e.g., against *Streptococcus* and *Mycoplasma*. Macrolides are believed to bind to the bacterial or 50S ribosomal subunit, thereby inhibiting bacterial protein synthesis.

[615] Monobactams include, but are not limited to, Aztreonam. Monobactams are effective, e.g., against Gram-negative bacteria. Monobactams are believed to inhibit bacterial cell wall synthesis by disrupting synthesis of the peptidoglycan layer of bacterial cell walls.

[616] Nitrofurans include, but are not limited to, Furazolidone and Nitrofurantoin.

[617] Oxazolidonones include, but are not limited to, Linezolid, Posizolid, Radezolid, and Torezolid. Oxazolidonones are believed to be protein synthesis inhibitors.

[618] Penicillins include, but are not limited to, Amoxicillin, Ampicillin, Azlocillin, Carbenicillin, Cloxacillin, Dicloxacillin, Flucloxacillin, Mezlocillin, Methicillin, Nafcillin, Oxacillin, Penicillin G, Penicillin V, Piperacillin, Temocillin and Ticarcillin. Penicillins are effective, e.g., against Gram-positive bacteria, facultative anaerobes, e.g., *Streptococcus*, *Borrelia*, and *Treponema*. Penicillins are believed to inhibit bacterial cell wall synthesis by disrupting synthesis of the peptidoglycan layer of bacterial cell walls.

[619] Penicillin combinations include, but are not limited to, Amoxicillin/clavulanate, Ampicillin/sulbactam, Piperacillin/tazobactam, and Ticarcillin/clavulanate.

[620] Polypeptide antibiotics include, but are not limited to, Bacitracin, Colistin, and Polymyxin B and E. Polypeptide Antibiotics are effective, e.g., against Gram-negative bacteria. Certain polypeptide antibiotics are believed to inhibit isoprenyl pyrophosphate involved in synthesis of the peptidoglycan layer of bacterial cell walls, while others destabilize the bacterial outer membrane by displacing bacterial counter-ions.

[621] Quinolones and Fluoroquinolone include, but are not limited to, Ciprofloxacin, Enoxacin, Gatifloxacin, Gemifloxacin, Levofloxacin, Lomefloxacin, Moxifloxacin, Nalidixic acid, Norfloxacin, Ofloxacin, Trovafloxacin, Grepafloxacin, Sparfloxacin, and Temafloxacin. Quinolones/Fluoroquinolone are effective, e.g., against *Streptococcus* and *Neisseria*. Quinolones/Fluoroquinolone are believed to inhibit the bacterial DNA gyrase or topoisomerase IV, thereby inhibiting DNA replication and transcription.

[622] Sulfonamides include, but are not limited to, Mafenide, Sulfacetamide, Sulfadiazine, Silver sulfadiazine, Sulfadimethoxine, Sulfamethizole, Sulfamethoxazole, Sulfanilimide, Sulfasalazine, Sulfisoxazole, Trimethoprim-Sulfamethoxazole (Co-trimoxazole), and Sulfonamidochrysoidine. Sulfonamides are believed to inhibit folate synthesis by competitive inhibition of dihydropteroate synthetase, thereby inhibiting nucleic acid synthesis.

[623] Tetracyclines include, but are not limited to, Demeclocycline, Doxycycline, Minocycline, Oxytetracycline, and Tetracycline. Tetracyclines are effective, e.g., against Gram-negative bacteria. Tetracyclines are believed to bind to the bacterial 30S ribosomal subunit thereby inhibiting bacterial protein synthesis.

[624] Anti-mycobacterial compounds include, but are not limited to, Clofazimine, Dapsone, Capreomycin, Cycloserine, Ethambutol, Ethionamide, Isoniazid, Pyrazinamide, Rifampicin, Rifabutin, Rifapentine, and Streptomycin.

[625] Suitable antibiotics also include arsphenamine, chloramphenicol, fosfomycin, fusidic acid, metronidazole, mupirocin, platensimycin, quinupristin/dalfopristin, tigecycline, tinidazole, trimethoprim amoxicillin/clavulanate, ampicillin/sulbactam, amphomycin ristocetin, azithromycin, bacitracin, buforin II, carbomycin, cecropin Pl, clarithromycin, erythromycins, furazolidone, fusidic acid, Na fusidate, gramicidin, imipenem, indolicidin, josamycin, magainan II, metronidazole, nitroimidazoles, mikamycin, mutacin B-Ny266, mutacin B-JHl 140, mutacin J-T8, nisin, nisin A, novobiocin, oleandomycin, ostreogrycin, piperacillin/tazobactam, pristinamycin, ramoplanin, ranalexin, reuterin, rifaximin, rosamicin, rosaramicin, spectinomycin, spiramycin, staphylomycin, streptogramin, streptogramin A, synergistin, taurolidine, teicoplanin, telithromycin, ticarcillin/clavulanic acid, triacetyloleandomycin, tylosin, tyrocidin, tyrothricin, vancomycin, vemamycin, and virginiamycin.

[626] In some embodiments, the additional therapeutic agent is an immunosuppressive agent, a DMARD, a pain-control drug, a steroid, a non-steroidal antiinflammatory drug (NSAID), or a cytokine antagonist, and combinations thereof. Representative agents include, but are not limited to, cyclosporin, retinoids, corticosteroids, propionic acid derivative, acetic acid derivative, enolic acid derivatives, fenamic acid derivatives, Cox-2 inhibitors, lumiracoxib, ibuprophen, cholin magnesium salicylate, fenoprofen, salsalate, difunisal, tolmetin, ketoprofen, flurbiprofen, oxaprozin, indomethacin, sulindac, etodolac, ketorolac, nabumetone, naproxen, valdecoxib, etoricoxib, MK0966; rofecoxib, acetominophen, Celecoxib, Diclofenac, tramadol, piroxicam, meloxicam, tenoxicam, droxicam, lornoxicam, isoxicam, mefanamic acid, meclofenamic acid, flufenamic acid, tolfenamic, valdecoxib, parecoxib, etodolac, indomethacin, aspirin, ibuprophen, firocoxib, methotrexate (MTX), antimalarial drugs (e.g., hydroxychloroquine and chloroquine), sulfasalazine, Leflunomide, azathioprine, cyclosporin, gold salts, minocycline, cyclophosphamide, D-penicillamine, minocycline, auranofin, tacrolimus, myocrisin, chlorambucil, TNF alpha antagonists (e.g., TNF alpha antagonists or TNF alpha receptor antagonists), e.g., ADALIMUMAB (Humira®), ETANERCEPT (Enbrel®), INFLIXIMAB (Remicade®; TA-650), CERTOLIZUMAB PEGOL (Cimzia®; CDP870), GOLIMUMAB (Simpom®; CNTO 148), ANAKINRA (Kineret®),

RITUXIMAB (Rituxan®; MabThera®), ABATACEPT (Orencia®), TOCILIZUMAB (RoActemra /Actemra®), integrin antagonists (TYSABRI® (natalizumab)), IL-1 antagonists (ACZ885 (Ilaris)), Anakinra (Kineret®)), CD4 antagonists, IL-23 antagonists, IL-20 antagonists, IL-6 antagonists, BLyS antagonists (e.g., Atacicept, Benlysta®/ LymphoStat-B® (belimumab)), p38 Inhibitors, CD20 antagonists (Ocrelizumab, Ofatumumab (Arzerra®)), interferon gamma antagonists (Fontolizumab), prednisolone, Prednisone, dexamethasone, Cortisol, cortisone, hydrocortisone, methylprednisolone, betamethasone, triamcinolone, beclometasome, fludrocortisone, deoxycorticosterone, aldosterone, Doxycycline, vancomycin, pioglitazone, SBI-087, SCIO-469, Cura-100, Oncoxin + Viusid, TwHF, Methoxsalen, Vitamin D - ergocalciferol, Milnacipran, Paclitaxel, rosig tazone, Tacrolimus (Prograf®), RADOOl, rapamune, rapamycin, fostamatinib, Fentanyl, XOMA 052, Fostamatinib disodium,rosightazone, Curcumin (Longvida™), Rosuvastatin, Maraviroc, ramipnl, Milnacipran, Cobiprostone, somatropin, tgAAC94 gene therapy vector, MK0359, GW856553, esomeprazole, everolimus, trastuzumab, JAKl and JAK2 inhibitors, pan JAK inhibitors, e.g., tetracyclic pyridone 6 (P6), 325, PF-956980, denosumab, IL-6 antagonists, CD20 antagonistis, CTLA4 antagonists, IL-8 antagonists, IL-21 antagonists, IL-22 antagonist, integrin antagonists (Tysarbri® (natalizumab)), VGEF antagnosits, CXCL antagonists, MMP antagonists, defensin antagonists, IL-1 antagonists (including IL-1 beta antagonsits), and IL-23 antagonists (e.g., receptor decoys, antagonistic antibodies, etc.).

[627] In some embodiments, the additional therapeutic agent is an immunosuppressive agent. Examples of immunosuppressive agents include, but are not limited to, corticosteroids, mesalazine, mesalamine, sulfasalazine, sulfasalazine derivatives, immunosuppressive drugs, cyclosporin A, mercaptopurine, azathiopurine, prednisone, methotrexate, antihistamines, glucocorticoids, epinephrine, theophylline, cromolyn sodium, anti-leukotrienes, anti-cholinergic drugs for rhinitis, TLR antagonists, inflammasome inhibitors, anti-cholinergic decongestants, mast-cell stabilizers, monoclonal anti-IgE antibodies, vaccines (e.g., vaccines used for vaccination where the amount of an allergen is gradually increased), cytokine inhibitors, such as anti-IL-6 antibodies, TNF inhibitors such as infliximab, adalimumab, certolizumab pegol, golimumab, or etanercept, and combinations thereof.

[628] In some embodiments, the additional therapeutic agent is an RNA molecule, such as a double stranded RNA.

[629] In some embodiments, the additional therapeutic agent is an anti-sense oligonucleotide.

Administration

[630] In certain aspects, provided herein is a method of delivering a pharmaceutical agent, pharmaceutical composition, and/or solid dosage form described herein to a subject. In some embodiments of the methods provided herein, the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form that comprises bacteria is administered in conjunction with the administration of an additional therapeutic agent. In some embodiments, in the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form, a pharmaceutical agent is co-formulated with the additional therapeutic agent. In some embodiments, the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form is co-administered with the additional therapeutic agent. In some embodiments, the additional therapeutic agent is administered to the subject before administration of the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form (e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50 or 55 minutes before, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22 or 23 hours before, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 days before). In some embodiments, the additional therapeutic agent is administered to the subject after administration of the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form (e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50 or 55 minutes after, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22 or 23 hours after, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 days after). In some embodiments, the same mode of delivery is used to deliver both the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form and the additional therapeutic agent. In some embodiments, different modes of delivery are used to administer the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form and the additional therapeutic agent. For example, in some embodiments the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form is administered orally while the additional therapeutic agent is administered via injection (e.g., an intravenous, intramuscular and/or intratumoral injection).

[631] In certain embodiments, the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form described herein can be administered in conjunction with any

other conventional anti-cancer treatment, such as, for example, radiation therapy and surgical resection of the tumor. These treatments may be applied as necessary and/or as indicated and may occur before, concurrent with or after administration of the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form described herein.

[632] The dosage regimen can be any of a variety of methods and amounts, and can be determined by one skilled in the art according to known clinical factors. As is known in the medical arts, dosages for any one patient can depend on many factors, including the subject's species, size, body surface area, age, sex, immunocompetence, and general health, the particular microorganism to be administered, duration and route of administration, the kind and stage of the disease, for example, tumor size, and other compounds such as drugs being administered concurrently or near-concurrently. In addition to the above factors, such levels can be affected by the infectivity of the microorganism, and the nature of the microorganism, as can be determined by one skilled in the art. In the present methods, appropriate minimum dosage levels of microorganisms can be levels sufficient for the microorganism to survive, grow and replicate. The dose of a pharmaceutical agent (e.g., in a solid dosage form) described herein may be appropriately set or adjusted in accordance with the dosage form, the route of administration, the degree or stage of a target disease, and the like.

[633] In some embodiments, the dose administered to a subject is sufficient to prevent disease (e.g., autoimmune disease, inflammatory disease, metabolic disease, dysbiosis, or cancer), delay its onset, or slow or stop its progression, or relieve one or more symptoms of the disease. One skilled in the art will recognize that dosage will depend upon a variety of factors including the strength of the particular agent (e.g., pharmaceutical agent) employed, as well as the age, species, condition, and body weight of the subject. The size of the dose will also be determined by the route, timing, and frequency of administration as well as the existence, nature, and extent of any adverse side-effects that might accompany the administration of a particular pharmaceutical agent and the desired physiological effect.

[634] Suitable doses and dosage regimens can be determined by conventional range-finding techniques known to those of ordinary skill in the art. Generally, treatment is initiated with smaller dosages, which are no more than the optimum dose of the compound. Thereafter, the dosage is increased by small increments until the optimum

effect under the circumstances is reached. An effective dosage and treatment protocol can be determined by routine and conventional means, starting e.g., with a low dose in laboratory animals and then increasing the dosage while monitoring the effects, and systematically varying the dosage regimen as well. Animal studies are commonly used to determine the maximal tolerable dose ("MTD") of bioactive agent per kilogram weight. Those skilled in the art regularly extrapolate doses for efficacy, while avoiding toxicity, in other species, including humans.

[635] In accordance with the above, in therapeutic applications, the dosages of the pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms used in accordance with the invention vary depending on the active agent, the age, weight, and clinical condition of the recipient patient, and the experience and judgment of the clinician or practitioner administering the therapy, among other factors affecting the selected dosage. For example, for cancer treatment, the dose should be sufficient to result in slowing, and preferably regressing, the growth of a tumor and most preferably causing complete regression of the cancer, or reduction in the size or number of metastases As another example, the dose should be sufficient to result in slowing of progression of the disease for which the subject is being treated, and preferably amelioration of one or more symptoms of the disease for which the subject is being treated.

[636] Separate administrations can include any number of two or more administrations, including two, three, four, five or six administrations. One skilled in the art can readily determine the number of administrations to perform or the desirability of performing one or more additional administrations according to methods known in the art for monitoring therapeutic methods and other monitoring methods provided herein. Accordingly, the methods provided herein include methods of providing to the subject one or more administrations of a pharmaceutical agent, pharmaceutical composition, and/or solid dosage form, where the number of administrations can be determined by monitoring the subject, and, based on the results of the monitoring, determining whether or not to provide one or more additional administrations. Deciding on whether or not to provide one or more additional administrations can be based on a variety of monitoring results.

[637] The time period between administrations can be any of a variety of time periods. The time period between administrations can be a function of any of a variety of factors, including monitoring steps, as described in relation to the number of administrations, the time period for a subject to mount an immune response. In one example, the time period

can be a function of the time period for a subject to mount an immune response; for example, the time period can be more than the time period for a subject to mount an immune response, such as more than about one week, more than about ten days, more than about two weeks, or more than about a month; in another example, the time period can be no more than the time period for a subject to mount an immune response, such as no more than about one week, no more than about ten days, no more than about two weeks, or no more than about a month.

[638] In some embodiments, the delivery of an additional therapeutic agent in combination with the pharmaceutical agent, pharmaceutical composition, and/or solid dosage form described herein reduces the adverse effects and/or improves the efficacy of the additional therapeutic agent.

[639] The effective dose of an additional therapeutic agent described herein is the amount of the additional therapeutic agent that is effective to achieve the desired therapeutic response for a particular subject, composition, and mode of administration, with the least toxicity to the subject. The effective dosage level can be identified using the methods described herein and will depend upon a variety of pharmacokinetic factors including the activity of the particular compositions or agents administered, the route of administration, the time of administration, the rate of excretion of the particular compound being employed, the duration of the treatment, other drugs, compounds and/or materials used in combination with the particular compositions employed, the age, sex, weight, condition, general health and prior medical history of the subject being treated, and like factors well known in the medical arts. In general, an effective dose of an additional therapeutic agent will be the amount of the additional therapeutic agent which is the lowest dose effective to produce a therapeutic effect. Such an effective dose will generally depend upon the factors described above.

[640] The toxicity of an additional therapeutic agent is the level of adverse effects experienced by the subject during and following treatment. Adverse events associated with additional therapy toxicity can include, but are not limited to, abdominal pain, acid indigestion, acid reflux, allergic reactions, alopecia, anaphylasix, anemia, anxiety, lack of appetite, arthralgias, asthenia, ataxia, azotemia, loss of balance, bone pain, bleeding, blood clots, low blood pressure, elevated blood pressure, difficulty breathing, bronchitis, bruising, low white blood cell count, low red blood cell count, low platelet count, cardiotoxicity, cystitis, hemorrhagic cystitis, arrhythmias, heart valve disease,

cardiomyopathy, coronary artery disease, cataracts, central neurotoxicity, cognitive impairment, confusion, conjunctivitis, constipation, coughing, cramping, cystitis, deep vein thrombosis, dehydration, depression, diarrhea, dizziness, dry mouth, dry skin, dyspepsia, dyspnea, edema, electrolyte imbalance, esophagitis, fatigue, loss of fertility, fever, flatulence, flushing, gastric reflux, gastroesophageal reflux disease, genital pain, granulocytopenia, gynecomastia, glaucoma, hair loss, hand-foot syndrome, headache, hearing loss, heart failure, heart palpitations, heartburn, hematoma, hemorrhagic cystitis, hepatotoxicity, hyperamylasemia, hypercalcemia, hyperchloremia, hyperglycemia, hyperkalemia, hyperlipasemia, hypermagnesemia, hypernatremia, hyperphosphatemia, hyperpigmentation, hypertriglyceridemia, hyperuricemia, hypoalbuminemia, hypocalcemia, hypochloremia, hypoglycemia, hypokalemia, hypomagnesemia, hyponatremia, hypophosphatemia, impotence, infection, injection site reactions, insomnia, iron deficiency, itching, joint pain, kidney failure, leukopenia, liver dysfunction, memory loss, menopause, mouth sores, mucositis, muscle pain, myalgias, myelosuppression, myocarditis, neutropenic fever, nausea, nephrotoxicity, neutropenia, nosebleeds, numbness, ototoxicity, pain, palmar-plantar erythrodysesthesia, pancytopenia, pericarditis, peripheral neuropathy, pharyngitis, photophobia, photosensitivity, pneumonia, pneumonitis, proteinuria, pulmonary embolus, pulmonary fibrosis, pulmonary toxicity, rash, rapid heart beat, rectal bleeding, restlessness, rhinitis, seizures, shortness of breath, sinusitis, thrombocytopenia, tinnitus, urinary tract infection, vaginal bleeding, vaginal dryness, vertigo, water retention, weakness, weight loss, weight gain, and xerostomia. In general, toxicity is acceptable if the benefits to the subject achieved through the therapy outweigh the adverse events experienced by the subject due to the therapy.

Immune Disorders

[641] In some embodiments, the methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein relate to the treatment or prevention of a disease or disorder associated a pathological immune response, such as an autoimmune disease, an allergic reaction and/or an inflammatory disease. In some embodiments, the disease or disorder is an inflammatory bowel disease (e.g., Crohn's disease or ulcerative colitis). In some embodiments, the disease or disorder is psoriasis. In some embodiments, the disease or disorder is atopic dermatitis.

[642] The methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein can be used to treat any subject in need thereof. As used herein, a "subject in need thereof" includes any subject that has a disease or disorder associated with a pathological immune response (e.g., an inflammatory bowel disease), as well as any subject with an increased likelihood of acquiring such a disease or disorder.

[643] The pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein can be used, for example, for preventing or treating (reducing, partially or completely, the adverse effects of) an autoimmune disease, such as chronic inflammatory bowel disease, systemic lupus erythematosus, psoriasis, muckle-wells syndrome, rheumatoid arthritis, multiple sclerosis, or Hashimoto's disease; an allergic disease, such as a food allergy, pollenosis, or asthma; an infectious disease, such as an infection with *Clostridium difficile*; an inflammatory disease such as a TNF-mediated inflammatory disease (e.g., an inflammatory disease of the gastrointestinal tract, such as pouchitis, a cardiovascular inflammatory condition, such as atherosclerosis, or an inflammatory lung disease, such as chronic obstructive pulmonary disease); a pharmaceutical composition for suppressing rejection in organ transplantation or other situations in which tissue rejection might occur; a supplement, food, or beverage for improving immune functions; or a reagent for suppressing the proliferation or function of immune cells.

[644] In some embodiments, the methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms provided herein are useful for the treatment of inflammation. In certain embodiments, the inflammation of any tissue and organs of the body, including musculoskeletal inflammation, vascular inflammation, neural inflammation, digestive system inflammation, ocular inflammation, inflammation of the reproductive system, and other inflammation, as discussed below.

[645] Immune disorders of the musculoskeletal system include, but are not limited, to those conditions affecting skeletal joints, including joints of the hand, wrist, elbow, shoulder, jaw, spine, neck, hip, knew, ankle, and foot, and conditions affecting tissues connecting muscles to bones such as tendons. Examples of such immune disorders, which may be treated with the methods and compositions described herein include, but are not limited to, arthritis (including, for example, osteoarthritis, rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, acute and chronic infectious arthritis, arthritis associated with gout and pseudogout, and juvenile idiopathic arthritis), tendonitis, synovitis,

tenosynovitis, bursitis, fibrositis (fibromyalgia), epicondylitis, myositis, and osteitis (including, for example, Paget's disease, osteitis pubis, and osteitis fibrosa cystic).

[646] Ocular immune disorders refers to an immune disorder that affects any structure of the eye, including the eye lids. Examples of ocular immune disorders which may be treated with the methods and compositions described herein include, but are not limited to, blepharitis, blepharochalasis, conjunctivitis, dacryoadenitis, keratitis, keratoconjunctivitis sicca (dry eye), scleritis, trichiasis, and uveitis.

[647] Examples of nervous system immune disorders which may be treated with the methods and solid dosage forms described herein include, but are not limited to, encephalitis, Guillain-Barre syndrome, meningitis, neuromyotonia, narcolepsy, multiple sclerosis, myelitis and schizophrenia. Examples of inflammation of the vasculature or lymphatic system which may be treated with the methods and compositions described herein include, but are not limited to, arthrosclerosis, arthritis, phlebitis, vasculitis, and lymphangitis.

[648] Examples of digestive system immune disorders which may be treated with the methods and solid dosage forms described herein include, but are not limited to, cholangitis, cholecystitis, enteritis, enterocolitis, gastritis, gastroenteritis, inflammatory bowel disease, ileitis, and proctitis. Inflammatory bowel diseases include, for example, certain art-recognized forms of a group of related conditions. Several major forms of inflammatory bowel diseases are known, with Crohn's disease (regional bowel disease, e.g., inactive and active forms) and ulcerative colitis (e.g., inactive and active forms) the most common of these disorders. In addition, the inflammatory bowel disease encompasses irritable bowel syndrome, microscopic colitis, lymphocytic-plasmocytic enteritis, coeliac disease, collagenous colitis, lymphocytic colitis and eosinophilic enterocolitis. Other less common forms of IBD include indeterminate colitis, pseudomembranous colitis (necrotizing colitis), ischemic inflammatory bowel disease, Behcet’s disease, sarcoidosis, scleroderma, IBD-associated dysplasia, dysplasia associated masses or lesions, and primary sclerosing cholangitis.

[649] Examples of reproductive system immune disorders which may be treated with the methods and solid dosage forms described herein include, but are not limited to, cervicitis, chorioamnionitis, endometritis, epididymitis, omphalitis, oophoritis, orchitis, salpingitis, tubo-ovarian abscess, urethritis, vaginitis, vulvitis, and vulvodynia.

[650] The methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein may be used to treat autoimmune conditions having an inflammatory component. Such conditions include, but are not limited to, acute disseminated alopecia universalise, Behcet's disease, Chagas' disease, chronic fatigue syndrome, dysautonomia, encephalomyelitis, ankylosing spondylitis, aplastic anemia, hidradenitis suppurativa, autoimmune hepatitis, autoimmune oophoritis, celiac disease, Crohn's disease, diabetes mellitus type 1, giant cell arteritis, Goodpasture's syndrome, Grave's disease, Guillain-Barre syndrome, Hashimoto's disease, Henoch-Schonlein purpura, Kawasaki's disease, lupus erythematosus, microscopic colitis, microscopic polyarteritis, mixed connective tissue disease, Muckle-Wells syndrome, multiple sclerosis, myasthenia gravis, opsoclonus myoclonus syndrome, optic neuritis, Ord's thyroiditis, pemphigus, polyarteritis nodosa, polymyalgia, rheumatoid arthritis, Reiter's syndrome, Sjogren's syndrome, temporal arteritis, Wegener's granulomatosis, warm autoimmune haemolytic anemia, interstitial cystitis, Lyme disease, morphea, psoriasis, sarcoidosis, scleroderma, ulcerative colitis, and vitiligo.

[651] The methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein may be used to treat T-cell mediated hypersensitivity diseases having an inflammatory component. Such conditions include, but are not limited to, contact hypersensitivity, contact dermatitis (including that due to poison ivy), uticaria, skin allergies, respiratory allergies (hay fever, allergic rhinitis, house dustmite allergy) and gluten-sensitive enteropathy (Celiac disease).

[652] Other immune disorders which may be treated with the methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms include, for example, appendicitis, dermatitis, dermatomyositis, endocarditis, fibrositis, gingivitis, glossitis, hepatitis, hidradenitis suppurativa, iritis, laryngitis, mastitis, myocarditis, nephritis, otitis, pancreatitis, parotitis, percarditis, peritonoitis, pharyngitis, pleuritis, pneumonitis, prostatistis, pyelonephritis, and stomatisi, transplant rejection (involving organs such as kidney, liver, heart, lung, pancreas (e.g., islet cells), bone marrow, cornea, small bowel, skin allografts, skin homografts, and heart valve xengrafts, sewrum sickness, and graft vs host disease), acute pancreatitis, chronic pancreatitis, acute respiratory distress syndrome, Sexary's syndrome, congenital adrenal hyperplasis, nonsuppurative thyroiditis, hypercalcemia associated with cancer, pemphigus, bullous dermatitis herpetiformis, severe erythema multiforme, exfoliative dermatitis, seborrheic dermatitis,

seasonal or perennial allergic rhinitis, bronchial asthma, contact dermatitis, atopic dermatitis, drug hypersensistivity reactions, allergic conjunctivitis, keratitis, herpes zoster ophthalmicus, iritis and oiridocyclitis, chorioretinitis, optic neuritis, symptomatic sarcoidosis, fulminating or disseminated pulmonary tuberculosis chemotherapy, idiopathic thrombocytopenic purpura in adults, secondary thrombocytopenia in adults, acquired (autoimmune) haemolytic anemia, leukaemia and lymphomas in adults, acute leukaemia of childhood, regional enteritis, autoimmune vasculitis, multiple sclerosis, chronic obstructive pulmonary disease, solid organ transplant rejection, sepsis. Preferred treatments include treatment of transplant rejection, rheumatoid arthritis, psoriatic arthritis, multiple sclerosis, Type 1 diabetes, asthma, inflammatory bowel disease, systemic lupus erythematosus, psoriasis, chronic obstructive pulmonary disease, and inflammation accompanying infectious conditions (e.g., sepsis).

Metabolic Disorders

[653] In some embodiments, the methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein relate to the treatment or prevention of a metabolic disease or disorder a, such as type II diabetes, impaired glucose tolerance, insulin resistance, obesity, hyperglycemia, hyperinsulinemia, fatty liver, non-alcoholic steatohepatitis, hypercholesterolemia, hypertension, hyperlipoproteinemia, hyperlipidemia, hypertriglylceridemia, ketoacidosis, hypoglycemia, thrombotic disorders, dyslipidemia, non-alcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH) or a related disease. In some embodiments, the related disease is cardiovascular disease, atherosclerosis, kidney disease, nephropathy, diabetic neuropathy, diabetic retinopathy, sexual dysfunction, dermatopathy, dyspepsia, or edema. In some embodiments, the methods and pharmaceutical compositions described herein relate to the treatment of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH).

[654] The methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein can be used to treat any subject in need thereof. As used herein, a "subject in need thereof" includes any subject that has a metabolic disease or disorder, as well as any subject with an increased likelihood of acquiring such a disease or disorder.

[655] The pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein can be used, for example, for preventing or treating (reducing, partially or completely, the adverse effects of) a metabolic disease, such as type II diabetes, impaired glucose tolerance, insulin resistance, obesity, hyperglycemia, hyperinsulinemia, fatty liver, non-alcoholic steatohepatitis, hypercholesterolemia, hypertension, hyperlipoproteinemia, hyperlipidemia, hypertriglylceridemia, ketoacidosis, hypoglycemia, thrombotic disorders, dyslipidemia, non-alcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), or a related disease. In some embodiments, the related disease is cardiovascular disease, atherosclerosis, kidney disease, nephropathy, diabetic neuropathy, diabetic retinopathy, sexual dysfunction, dermatopathy, dyspepsia, or edema.

Cancer

[656] In some embodiments, the methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein relate to the treatment of cancer. In some embodiments, any cancer can be treated using the methods described herein. Examples of cancers that may treated by methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein include, but are not limited to, cancer cells from the bladder, blood, bone, bone marrow, brain, breast, colon, esophagus, gastrointestine, gum, head, kidney, liver, lung, nasopharynx, neck, ovary, prostate, skin, stomach, testis, tongue, or uterus. In addition, the cancer may specifically be of the following histological type, though it is not limited to these: neoplasm, malignant; carcinoma; carcinoma, undifferentiated; giant and spindle cell carcinoma; small cell carcinoma; papillary carcinoma; squamous cell carcinoma; lymphoepithelial carcinoma; basal cell carcinoma; pilomatrix carcinoma; transitional cell carcinoma; papillary transitional cell carcinoma; adenocarcinoma; gastrinoma, malignant; cholangiocarcinoma; hepatocellular carcinoma; combined hepatocellular carcinoma and cholangiocarcinoma; trabecular adenocarcinoma; adenoid cystic carcinoma; adenocarcinoma in adenomatous polyp; adenocarcinoma, familial polyposis coli; solid carcinoma; carcinoid tumor, malignant; branchiolo-alveolar adenocarcinoma; papillary adenocarcinoma; chromophobe carcinoma; acidophil carcinoma; oxyphilic adenocarcinoma; basophil carcinoma; clear cell adenocarcinoma; granular cell carcinoma; follicular adenocarcinoma; papillary and follicular adenocarcinoma; nonencapsulating

sclerosing carcinoma; adrenal cortical carcinoma; endometroid carcinoma; skin appendage carcinoma; apocrine adenocarcinoma; sebaceous adenocarcinoma; ceruminous adenocarcinoma; mucoepidermoid carcinoma; cystadenocarcinoma; papillary cystadenocarcinoma; papillary serous cystadenocarcinoma; mucinous cystadenocarcinoma; mucinous adenocarcinoma; signet ring cell carcinoma; infiltrating duct carcinoma; medullary carcinoma; lobular carcinoma; inflammatory carcinoma; paget's disease, mammary; acinar cell carcinoma; adenosquamous carcinoma; adenocarcinoma w/squamous metaplasia; thymoma, malignant; ovarian stromal tumor, malignant; thecoma, malignant; granulosa cell tumor, malignant; and roblastoma, malignant; sertoli cell carcinoma; leydig cell tumor, malignant; lipid cell tumor, malignant; paraganglioma, malignant; extra-mammary paraganglioma, malignant; pheochromocytoma; glomangiosarcoma; malignant melanoma; amelanotic melanoma; superficial spreading melanoma; malig melanoma in giant pigmented nevus; epithelioid cell melanoma; blue nevus, malignant; sarcoma; fibrosarcoma; fibrous histiocytoma, malignant; myxosarcoma; liposarcoma; leiomyosarcoma; rhabdomyosarcoma; embryonal rhabdomyosarcoma; alveolar rhabdomyosarcoma; stromal sarcoma; mixed tumor, malignant; mullerian mixed tumor; nephroblastoma; hepatoblastoma; carcinosarcoma; mesenchymoma, malignant; brenner tumor, malignant; phyllodes tumor, malignant; synovial sarcoma; mesothelioma, malignant; dysgerminoma; embryonal carcinoma; teratoma, malignant; struma ovarii, malignant; choriocarcinoma; mesonephroma, malignant; hemangiosarcoma; hemangioendothelioma, malignant; kaposi's sarcoma; hemangiopericytoma, malignant; lymphangiosarcoma; osteosarcoma; juxtacortical osteosarcoma; chondrosarcoma; chondroblastoma, malignant; mesenchymal chondrosarcoma; giant cell tumor of bone; ewing's sarcoma; odontogenic tumor, malignant; ameloblastic odontosarcoma; ameloblastoma, malignant; ameloblastic fibrosarcoma; pinealoma, malignant; chordoma; glioma, malignant; ependymoma; astrocytoma; protoplasmic astrocytoma; fibrillary astrocytoma; astroblastoma; glioblastoma; oligodendroglioma; oligodendroblastoma; primitive neuroectodermal; cerebellar sarcoma; ganglioneuroblastoma; neuroblastoma; retinoblastoma; olfactory neurogenic tumor; meningioma, malignant; neurofibrosarcoma; neurilemmoma, malignant; granular cell tumor, malignant; malignant lymphoma; Hodgkin's disease; Hodgkin's lymphoma; paragranuloma; malignant lymphoma, small lymphocytic; malignant lymphoma, large cell, diffuse; malignant lymphoma, follicular; mycosis

fungoides; other specified non-Hodgkin's lymphomas; malignant histiocytosis; multiple myeloma; mast cell sarcoma; immunoproliferative small intestinal disease; leukemia; lymphoid leukemia; plasma cell leukemia; erythroleukemia; lymphosarcoma cell leukemia; myeloid leukemia; basophilic leukemia; eosinophilic leukemia; monocytic leukemia; mast cell leukemia; megakaryoblastic leukemia; myeloid sarcoma; and hairy cell leukemia.

[657] In some embodiments, the cancer comprises breast cancer (e.g., triple negative breast cancer).

[658] In some embodiments, the cancer comprises colorectal cancer (e.g., microsatellite stable (MSS) colorectal cancer).

[659] In some embodiments, the cancer comprises renal cell carcinoma.

[660] In some embodiments, the cancer comprises lung cancer (e.g., non-small cell lung cancer).

[661] In some embodiments, the cancer comprises bladder cancer.

[662] In some embodiments, the cancer comprises gastroesophageal cancer.

[663] In some embodiments, the methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms provided herein relate to the treatment of a leukemia. The term "leukemia" includes broadly progressive, malignant diseases of the hematopoietic organs/systems and is generally characterized by a distorted proliferation and development of leukocytes and their precursors in the blood and bone marrow. Non-limiting examples of leukemia diseases include, acute nonlymphocytic leukemia, chronic lymphocytic leukemia, acute granulocytic leukemia, chronic granulocytic leukemia, acute promyelocytic leukemia, adult T-cell leukemia, aleukemic leukemia, a leukocythemic leukemia, basophilic leukemia, blast cell leukemia, bovine leukemia, chronic myelocytic leukemia, leukemia cutis, embryonal leukemia, eosinophilic leukemia, Gross' leukemia, Rieder cell leukemia, Schilling's leukemia, stem cell leukemia, subleukemic leukemia, undifferentiated cell leukemia, hairy-cell leukemia, hemoblastic leukemia, hemocytoblastic leukemia, histiocytic leukemia, stem cell leukemia, acute monocytic leukemia, leukopenic leukemia, lymphatic leukemia, lymphoblastic leukemia, lymphocytic leukemia, lymphogenous leukemia, lymphoid leukemia, lymphosarcoma cell leukemia, mast cell leukemia, megakaryocytic leukemia, micromyeloblastic leukemia, monocytic leukemia, myeloblastic leukemia, myelocytic leukemia, myeloid granulocytic

leukemia, myelomonocytic leukemia, Naegeli leukemia, plasma cell leukemia, plasmacytic leukemia, and promyelocytic leukemia.

[664] In some embodiments, the methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms provided herein relate to the treatment of a carcinoma. The term "carcinoma" refers to a malignant growth made up of epithelial cells tending to infiltrate the surrounding tissues, and/or resist physiological and non-physiological cell death signals and gives rise to metastases. Non-limiting exemplary types of carcinomas include, acinar carcinoma, acinous carcinoma, adenocystic carcinoma, adenoid cystic carcinoma, carcinoma adenomatosum, carcinoma of adrenal cortex, alveolar carcinoma, alveolar cell carcinoma, basal cell carcinoma, carcinoma basocellulare, basaloid carcinoma, basosquamous cell carcinoma, bronchioalveolar carcinoma, bronchiolar carcinoma, bronchogenic carcinoma, cerebriform carcinoma, cholangiocellular carcinoma, chorionic carcinoma, colloid carcinoma, comedo carcinoma, corpus carcinoma, cribriform carcinoma, carcinoma en cuirasse, carcinoma cutaneum, cylindrical carcinoma, cylindrical cell carcinoma, duct carcinoma, carcinoma durum, embryonal carcinoma, encephaloid carcinoma, epiennoid carcinoma, carcinoma epitheliale adenoides, exophytic carcinoma, carcinoma ex ulcere, carcinoma fibrosum, gelatiniform carcinoma, gelatinous carcinoma, giant cell carcinoma, signet-ring cell carcinoma, carcinoma simplex, small-cell carcinoma, solanoid carcinoma, spheroidal cell carcinoma, spindle cell carcinoma, carcinoma spongiosum, squamous carcinoma, squamous cell carcinoma, string carcinoma, carcinoma telangiectaticum, carcinoma telangiectodes, transitional cell carcinoma, carcinoma tuberosum, tuberous carcinoma, verrucous carcinoma, carcinoma villosum, carcinoma gigantocellulare, glandular carcinoma, granulosa cell carcinoma, hair-matrix carcinoma, hematoid carcinoma, hepatocellular carcinoma, Hurthle cell carcinoma, hyaline carcinoma, hypernephroid carcinoma, infantile embryonal carcinoma, carcinoma in situ, intraepidermal carcinoma, intraepithelial carcinoma, Krompecher's carcinoma, Kulchitzky-cell carcinoma, large-cell carcinoma, lenticular carcinoma, carcinoma lenticulare, lipomatous carcinoma, lymphoepithelial carcinoma, carcinoma medullare, medullary carcinoma, melanotic carcinoma, carcinoma molle, mucinous carcinoma, carcinoma muciparum, carcinoma mucocellulare, mucoepidermoid carcinoma, carcinoma mucosum, mucous carcinoma, carcinoma myxomatodes, naspharyngeal carcinoma, oat cell carcinoma, carcinoma ossificans, osteoid carcinoma, papillary carcinoma, periportal carcinoma, preinvasive

carcinoma, prickle cell carcinoma, pultaceous carcinoma, renal cell carcinoma of kidney, reserve cell carcinoma, carcinoma sarcomatodes, schneiderian carcinoma, scirrhous carcinoma, and carcinoma scroti.

[665] In some embodiments, the methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms provided herein relate to the treatment of a sarcoma. The term "sarcoma" generally refers to a tumor which is made up of a substance like the embryonic connective tissue and is generally composed of closely packed cells embedded in a fibrillar, heterogeneous, or homogeneous substance. Sarcomas include, but are not limited to, chondrosarcoma, fibrosarcoma, lymphosarcoma, melanosarcoma, myxosarcoma, osteosarcoma, endometrial sarcoma, stromal sarcoma, Ewing' s sarcoma, fascial sarcoma, fibroblastic sarcoma, giant cell sarcoma, Abemethy's sarcoma, adipose sarcoma, liposarcoma, alveolar soft part sarcoma, ameloblastic sarcoma, botryoid sarcoma, chloroma sarcoma, chorio carcinoma, embryonal sarcoma, Wilms' tumor sarcoma, granulocytic sarcoma, Hodgkin's sarcoma, idiopathic multiple pigmented hemorrhagic sarcoma, immunoblastic sarcoma of B cells, lymphoma, immunoblastic sarcoma of T-cells, Jensen's sarcoma, Kaposi's sarcoma, Kupffer cell sarcoma, angiosarcoma, leukosarcoma, malignant mesenchymoma sarcoma, parosteal sarcoma, reticulocytic sarcoma, Rous sarcoma, serocystic sarcoma, synovial sarcoma, and telangiectaltic sarcoma.

[666] Additional exemplary neoplasias that can be treated using the methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein include Hodgkin's Disease, Non-Hodgkin's Lymphoma, multiple myeloma, neuroblastoma, breast cancer, ovarian cancer, lung cancer, rhabdomyosarcoma, primary thrombocytosis, primary macroglobulinemia, small-cell lung tumors, primary brain tumors, stomach cancer, colon cancer, malignant pancreatic insulanoma, malignant carcinoid, premalignant skin lesions, testicular cancer, lymphomas, thyroid cancer, neuroblastoma, esophageal cancer, genitourinary tract cancer, malignant hypercalcemia, cervical cancer, endometrial cancer, plasmacytoma, colorectal cancer, rectal cancer, and adrenal cortical cancer.

[667] In some embodiments, the cancer treated is a melanoma. The term "melanoma" is taken to mean a tumor arising from the melanocytic system of the skin and other organs. Non-limiting examples of melanomas are Harding-Passey melanoma, juvenile melanoma, lentigo maligna melanoma, malignant melanoma, acral-lentiginous melanoma, amelanotic

melanoma, benign juvenile melanoma, Cloudman's melanoma, S91 melanoma, nodular melanoma subungal melanoma, and superficial spreading melanoma.

[668] Particular categories of tumors that can be treated using methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein include lymphoproliferative disorders, breast cancer, ovarian cancer, prostate cancer, cervical cancer, endometrial cancer, bone cancer, liver cancer, stomach cancer, colon cancer, pancreatic cancer, cancer of the thyroid, head and neck cancer, cancer of the central nervous system, cancer of the peripheral nervous system, skin cancer, kidney cancer, as well as metastases of all the above. Particular types of tumors include hepatocellular carcinoma, hepatoma, hepatoblastoma, rhabdomyosarcoma, esophageal carcinoma, thyroid carcinoma, ganglioblastoma, fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, Ewing's tumor, leimyosarcoma, rhabdotheliosarcoma, invasive ductal carcinoma, papillary adenocarcinoma, melanoma, pulmonary squamous cell carcinoma, basal cell carcinoma, adenocarcinoma (well differentiated, moderately differentiated, poorly differentiated or undifferentiated), bronchioloalveolar carcinoma, renal cell carcinoma, hypernephroma, hypernephroid adenocarcinoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, testicular tumor, lung carcinoma including small cell, non-small and large cell lung carcinoma, bladder carcinoma, glioma, astrocyoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, retinoblastoma, neuroblastoma, colon carcinoma, rectal carcinoma, hematopoietic malignancies including all types of leukemia and lymphoma including: acute myelogenous leukemia, acute myelocytic leukemia, acute lymphocytic leukemia, chronic myelogenous leukemia, chronic lymphocytic leukemia, mast cell leukemia, multiple myeloma, myeloid lymphoma, Hodgkin' s lymphoma, non-Hodgkin' s lymphoma, plasmacytoma, colorectal cancer, and rectal cancer.

[669] Cancers treated in certain embodiments also include precancerous lesions, e.g., actinic keratosis (solar keratosis), moles (dysplastic nevi), acitinic chelitis (farmer's lip), cutaneous horns, Barrett's esophagus, atrophic gastritis, dyskeratosis congenita, sideropenic dysphagia, lichen planus, oral submucous fibrosis, actinic (solar) elastosis and cervical dysplasia.

[670] Cancers treated in some embodiments include non-cancerous or benign tumors, e.g., of endodermal, ectodermal or mesenchymal origin, including, but not limited to

cholangioma, colonic polyp, adenoma, papilloma, cystadenoma, liver cell adenoma, hydatidiform mole, renal tubular adenoma, squamous cell papilloma, gastric polyp, hemangioma, osteoma, chondroma, lipoma, fibroma, lymphangioma, leiomyoma, rhabdomyoma, astrocytoma, nevus, meningioma, and ganglioneuroma.

Other Diseases and Disorders

[671] In some embodiments, the methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein relate to the treatment of liver diseases. Such diseases include, but are not limited to, Alagille Syndrome, Alcohol-Related Liver Disease, Alpha-1 Antitrypsin Deficiency, Autoimmune Hepatitis, Benign Liver Tumors, Biliary Atresia, Cirrhosis, Galactosemia, Gilbert Syndrome, Hemochromatosis, Hepatitis A, Hepatitis B, Hepatitis C, Hepatic Encephalopathy, Intrahepatic Cholestasis of Pregnancy (ICP), Lysosomal Acid Lipase Deficiency (LAL-D), Liver Cysts, Liver Cancer, Newborn Jaundice, Primary Biliary Cholangitis (PBC), Primary Sclerosing Cholangitis (PSC), Reye Syndrome, Type I Glycogen Storage Disease, and Wilson Disease.

[672] The methods and pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms described herein may be used to treat neurodegenerative and neurological diseases. In certain embodiments, the neurodegenerative and/or neurological disease is Parkinson's disease, Alzheimer's disease, prion disease, Huntington's disease, motor neuron diseases (MND), spinocerebellar ataxia, spinal muscular atrophy, dystonia, idiopathicintracranial hypertension, epilepsy, nervous system disease, central nervous system disease, movement disorders, multiple sclerosis, encephalopathy, peripheral neuropathy or post-operative cognitive dysfunction.

Dysbiosis

[673] In recent years, it has become increasingly clear that the gut microbiome (also called the "gut microbiota") can have a significant impact on an individual's health through microbial activity and influence (local and/or distal) on immune and other cells of the host (Walker, W.A., Dysbiosis. The Microbiota in Gastrointestinal Pathophysiology. Chapter 25. 2017; Weiss and Thierry, Mechanisms and consequences of intestinal dysbiosis. *Cellular and Molecular Life Sciences*. (2017) 74(16):2959-2977. Zurich Open Repository and Archive, doi: https://doi.org/10.1007/s00018-017-2509-x)).

[674] A healthy host-gut microbiome homeostasis is sometimes referred to as a "eubiosis" or "normobiosis," whereas a detrimental change in the host microbiome composition and/or its diversity can lead to an unhealthy imbalance in the microbiome, or a "dysbiosis" (Hooks and O'Malley. *Dysbiosis and its discontents*. American Society for Microbiology. Oct 2017. Vol. 8. Issue 5. mBio 8:e01492-17. https://doi.org/10.1128/mBio.01492-17). Dysbiosis, and associated local or distal host inflammatory or immune effects, may occur where microbiome homeostasis is lost or diminished, resulting in: increased susceptibility to pathogens; altered host bacterial metabolic activity; induction of host proinflammatory activity and/or reduction of host anti-inflammatory activity. Such effects are mediated in part by interactions between host immune cells (e.g., T cells, dendritic cells, mast cells, NK cells, intestinal epithelial lymphocytes (IEC), macrophages and phagocytes) and cytokines, and other substances released by such cells and other host cells.

[675] A dysbiosis may occur within the gastrointestinal tract (a "gastrointestinal dysbiosis" or "gut dysbiosis") or may occur outside the lumen of the gastrointestinal tract (a "distal dysbiosis"). Gastrointestinal dysbiosis is often associated with a reduction in integrity of the intestinal epithelial barrier, reduced tight junction integrity and increased intestinal permeability. Citi, S. Intestinal Barriers protect against disease, *Science* 359:1098-99 (2018); Srinivasan et al., TEER measurement techniques for in vitro barrier model systems. *J. Lab. Autom.* 20:107-126 (2015). A gastrointestinal dysbiosis can have physiological and immune effects within and outside the gastrointestinal tract.

[676] The presence of a dysbiosis has been associated with a wide variety of diseases and conditions including: infection, cancer, autoimmune disorders (e.g., systemic lupus erythematosus (SLE)) or inflammatory disorders (e.g., functional gastrointestinal disorders such as inflammatory bowel disease (IBD), ulcerative colitis, and Crohn's disease), neuroinflammatory diseases (e.g., multiple sclerosis), transplant disorders (e.g., graft-versus-host disease), fatty liver disease, type I diabetes, rheumatoid arthritis, Sjögren's syndrome, celiac disease, cystic fibrosis, chronic obstructive pulmonary disorder (COPD), and other diseases and conditions associated with immune dysfunction. Lynch et al., The Human Microbiome in Health and Disease, *N. Engl. J. Med* .375:2369-79 (2016), Carding et al., Dysbiosis of the gut microbiota in disease. *Microb. Ecol. Health Dis.* (2015); 26: 10: 3402/mehd.v26.2619; Levy et al, Dysbiosis and the Immune System, *Nature Reviews Immunology* 17:219 (April 2017).

[677] Exemplary pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms disclosed herein can treat a dysbiosis and its effects by modifying the immune activity present at the site of dysbiosis. As described herein, such compositions can modify a dysbiosis via effects on host immune cells, resulting in, e.g., an increase in secretion of anti-inflammatory cytokines and/or a decrease in secretion of pro-inflammatory cytokines, reducing inflammation in the subject recipient or via changes in metabolite production.

[678] Exemplary pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms disclosed herein that are useful for treatment of disorders associated with a dysbiosis contain one or more types of immunomodulatory bacteria (*e.g.*, anti-inflammatory bacteria). Such compositions are capable of affecting the recipient host's immune function, in the gastrointestinal tract, and/or a systemic effect at distal sites outside the subject's gastrointestinal tract.

[679] Exemplary pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms disclosed herein that are useful for treatment of disorders associated with a dysbiosis contain a population of immunomodulatory bacteria of a single bacterial species (e.g., a single strain) (*e.g.*, anti-inflammatory bacteria). Such compositions are capable of affecting the recipient host's immune function, in the gastrointestinal tract, and /or a systemic effect at distal sites outside the subject's gastrointestinal tract.

[680] In one embodiment, pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms containing an isolated population of immunomodulatory bacteria (e.g., anti-inflammatory bacterial cells) are administered (e.g., orally) to a mammalian recipient in an amount effective to treat a dysbiosis and one or more of its effects in the recipient. The dysbiosis may be a gastrointestinal tract dysbiosis or a distal dysbiosis.

[681] In another embodiment, pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms of the instant invention can treat a gastrointestinal dysbiosis and one or more of its effects on host immune cells, resulting in an increase in secretion of anti-inflammatory cytokines and/or a decrease in secretion of pro-inflammatory cytokines, reducing inflammation in the subject recipient.

[682] In another embodiment, the pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms can treat a gastrointestinal dysbiosis and one or more of its effects by modulating the recipient immune response via cellular and cytokine

modulation to reduce gut permeability by increasing the integrity of the intestinal epithelial barrier.

[683] In another embodiment, the pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms can treat a distal dysbiosis and one or more of its effects by modulating the recipient immune response at the site of dysbiosis via modulation of host immune cells.

[684] Other exemplary pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms are useful for treatment of disorders associated with a dysbiosis, which compositions contain one or more types of bacteria capable of altering the relative proportions of host immune cell subpopulations, e.g., subpopulations of T cells, immune lymphoid cells, dendritic cells, NK cells and other immune cells, or the function thereof, in the recipient.

[685] Other exemplary pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms are useful for treatment of disorders associated with a dysbiosis, which compositions contain a population of immunomodulatory bacteria of a single bacterial species e.g., a single strain) capable of altering the relative proportions of immune cell subpopulations, e.g., T cell subpopulations, immune lymphoid cells, NK cells and other immune cells, or the function thereof, in the recipient subject.

[686] In one embodiment, the invention provides methods of treating a gastrointestinal dysbiosis and one or more of its effects by orally administering to a subject in need thereof a pharmaceutical agent, pharmaceutical composition, and/or solid dosage form which alters the microbiome population existing at the site of the dysbiosis. The pharmaceutical agent, pharmaceutical composition, and/or solid dosage form can contain one or more types of immunomodulatory bacteria or a population of immunomodulatory bacteria of a single bacterial species (e.g., a single strain).

[687] In one embodiment, the invention provides methods of treating a distal dysbiosis and one or more of its effects by orally administering to a subject in need thereof a pharmaceutical agent, pharmaceutical composition, and/or solid dosage form which alters the subject's immune response outside the gastrointestinal tract. The pharmaceutical agent, pharmaceutical composition, and/or solid dosage form can contain one or more types of immunomodulatory bacteria or a population of immunomodulatory bacteria of a single bacterial species (e.g., a single strain).

[688] In exemplary embodiments, pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms useful for treatment of disorders associated with a dysbiosis stimulate secretion of one or more anti-inflammatory cytokines by host immune cells. Anti-inflammatory cytokines include, but are not limited to, IL-10, IL-13, IL-9, IL-4, IL-5, TGFβ, and combinations thereof. In other exemplary embodiments, pharmaceutical agents, pharmaceutical compositions, and/or solid dosage forms useful for treatment of disorders associated with a dysbiosis that decrease (e.g., inhibit) secretion of one or more pro-inflammatory cytokines by host immune cells. Pro-inflammatory cytokines include, but are not limited to, IFNγ, IL-12p70, IL-1α, IL-6, IL-8, MCP1, MIP1α, MIP1β, TNFα, and combinations thereof. Other exemplary cytokines are known in the art and are described herein.

[689] In another aspect, the invention provides a method of treating or preventing a disorder associated with a dysbiosis in a subject in need thereof, comprising administering (e.g., orally administering) to the subject a therapeutic composition in the form of a probiotic or medical food comprising bacteria in an amount sufficient to alter the microbiome at a site of the dysbiosis, such that the disorder associated with the dysbiosis is treated.

[690] In another embodiment, a therapeutic composition of the instant invention in the form of a probiotic or medical food may be used to prevent or delay the onset of a dysbiosis in a subject at risk for developing a dysbiosis.

Methods of Making Enhanced Bacteria

[691] In certain aspects, provided herein are methods of making engineered bacteria for the production of the bacteria described herein. In some embodiments, the engineered bacteria are modified to enhance certain desirable properties. For example, in some embodiments, the engineered bacteria are modified to enhance the immunomodulatory and/or therapeutic effect of the bacteria (e.g., either alone or in combination with another therapeutic agent), to reduce toxicity and/or to improve bacterial manufacturing (e.g., higher oxygen tolerance, improved freeze-thaw tolerance, shorter generation times). The engineered bacteria may be produced using any technique known in the art, including but not limited to site-directed mutagenesis, transposon mutagenesis, knock-outs, knock-ins, polymerase chain reaction mutagenesis, chemical mutagenesis, ultraviolet light

mutagenesis, transformation (chemically or by electroporation), phage transduction, directed evolution, CRISPR/Cas9, or any combination thereof.

[692] In some embodiments of the methods provided herein, the bacterium is modified by directed evolution. In some embodiments, the directed evolution comprises exposure of the bacterium to an environmental condition and selection of bacterium with improved survival and/or growth under the environmental condition. In some embodiments, the method comprises a screen of mutagenized bacteria using an assay that identifies enhanced bacterium. In some embodiments, the method further comprises mutagenizing the bacteria (e.g., by exposure to chemical mutagens and/or UV radiation) or exposing them to a therapeutic agent (e.g., antibiotic) followed by an assay to detect bacteria having the desired phenotype (e.g., an *in vivo* assay, an *ex vivo* assay, or an *in vitro* assay).

Gamma- Irradiation: Sample Protocol:

[693] Powders are gamma-irradiated at 17.5 kGy radiation unit at ambient temperature. Frozen biomasses are gamma-irradiated at 25 kGy radiation unit in the presence of dry ice.

Frozen Biomass Preparation: Sample Protocol

[694] After a desired level of bacterial culture growth is achieved, centrifuge cultures, discard the supernatant, leaving the pellet as dry as possible. Vortex the pellet to loosen the biomass. Resuspend pellet in desired cryoprotectant solution, transfer to cryogenic tube and snap freeze in liquid nitrogen. Store in -80 degree C freezer.

Powder Preparation: Sample Protocol

[695] After desired level of bacterial culture growth is achieved, centrifuge cultures, discard the supernatant, leaving the pellet as dry as possible. Resuspend pellet in desired cryoprotectant solution to create a formulated paste. The cryoprotectant solution may contain, e.g., maltodextrin, sodium ascorbate, sodium glutamate, and/or calcium chloride or e.g., sucrose, dextran, and L-cysteine HCl. Load the formulated paste onto stainless steel trays and load into a freeze drier (e.g., operating in automated mode with defined cycle parameters) to prepare a freeze dried product. The freeze dried product is fed into a milling machine and the resulting powder is collected.

[696] Powders can be stored (e.g., in vacuum sealed bags) at 2-8 degrees C (e.g., at 4 degrees C), e.g., in a desiccator.

Exemplary Embodiments

[697] Embodiment 1. A pharmaceutical agent (e.g., powder) comprising bacteria (e.g., freeze dried bacteria), wherein the bacteria in the pharmaceutical agent are present at a total cell count (TCC) of at least $1x10^{11}$ cells/gram of the pharmaceutical agent (e.g., the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of at least $3.3x10^{11}$ cells/gram, at least $5x10^{11}$ cells/gram, at least $7x10^{11}$ cells/gram, at least $1x10^{12}$ cells/gram, at least $2x10^{12}$ cells/gram, between about $1x10^{11}$ cells/gram to about $2.5x10^{12}$ cells/gram, between about $3.3x10^{11}$ cells/gram to about $2.5x10^{12}$ cells/gram, between about $5x10^{11}$ cells/gram to about $2.5x10^{12}$ cells/gram, between about $7x10^{11}$ cells/gram to about $2.4x10^{12}$ cells/gram, about $2x10^{12}$ cells/gram, between about $1x10^{12}$ cells/gram to about $2x10^{12}$ cells/gram, between about $1.3x10^{12}$ cells/gram to about $2.4x10^{12}$ cells/gram, about $2.5x10^{12}$ cells/gram, about $1.2x10^{12}$ cells/gram, about $1.5x10^{12}$ cells/gram, or about $6x10^{11}$ cells/gram of the pharmaceutical agent).

[698] Embodiment 2. The pharmaceutical agent of embodiment 1,wherein the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of between about $1x10^{11}$ cells/gram to about $2.5x10^{12}$ cells/gram of the pharmaceutical agent.

[699] Embodiment 3. A pharmaceutical agent (e.g., powder) comprising bacteria and a cryoprotectant.

[700] Embodiment 4. The pharmaceutical agent of embodiment 3, wherein the cryoprotectant comprises sucrose, dextran, or a combination thereof, optionally the cryoprotectant comprises sucrose and dextran in equivalent amounts.

[701] Embodiment 5. The pharmaceutical agent of embodiment 3, wherein the cryoprotectant comprises sucrose, dextran, and L-cysteine HCl.

[702] Embodiment 6. The pharmaceutical agent of embodiment 3, wherein the cryoprotectant does not comprise L-cysteine HCl.

[703] Embodiment 7. The pharmaceutical agent of embodiment 3, wherein the pharmaceutical agent comprises about 6% to about 12% or about 7% to about 21% (weight/weight) sucrose; about 6% to about 12% or about 7% to about 21% (weight/weight) dextran; or about 6% to about 12% (weight/weight) sucrose and about 6% to about 12% (weight/weight) dextran, or about 7% to about 21% (weight/weight)

sucrose and about 7% to about 21% (weight/weight) dextran (e.g., wherein the pharmaceutical agent comprises about 8% to about 12% or about 10% to about 19% (weight/weight) sucrose, the pharmaceutical agent comprises about 11% (weight/weight) sucrose, the pharmaceutical agent comprises about 6% to about 12% or about 7% to about 21% (weight/weight) dextran, the pharmaceutical agent comprises about 8% to about 12% or about 10% to about 19% (weight/weight) dextran. , the pharmaceutical agent comprises about 11% (weight/weight) dextran, the pharmaceutical agent comprises about 6% to about 12% (weight/weight) sucrose and about 6% to about 12% (weight/weight) dextran, or about 7% to about 21% (weight/weight) sucrose and about 7% to about 21% (weight/weight) dextran, the pharmaceutical agent comprises about 8% to about 12% (weight/weight) sucrose and about 8% to about 12% (weight/weight) dextran, or about 10% to about 19% (weight/weight) sucrose and about 10% to about 19% (weight/weight) dextran, or the pharmaceutical agent comprises about 11% (weight/weight) sucrose and about 11% (weight/weight) dextran).

[704] Embodiment 8. The pharmaceutical agent of embodiment 3, wherein the pharmaceutical agent comprises about 0.10% to about 0.25% or about 0.15% to about 0.35% (weight/weight) L-cysteine HCl.

[705] Embodiment 9. A pharmaceutical composition that comprises a pharmaceutical agent (e.g., powder) of any one of embodiments 1 to 10 and one or more excipients.

[706] Embodiment 10. A method comprising combining bacteria (e.g., a pellet comprising bacteria) with a cryoprotectant, optionally the cryoprotectant is a cryoprotectant solution, thereby preparing a formulated paste.

[707] Embodiment 11. The method of embodiment 10, further comprising: (a) freeze drying the formulated paste, to thereby prepare a freeze-dried product; (b) milling the freeze-dried product, to thereby prepare a freeze-dried powder; and/or (c) combining the freeze-dried powder with one or more excipients to thereby prepare a pharmaceutical composition.

[708] Embodiment 12. The method of embodiment 10 or 11, wherein the cryoprotectant is mixed with the pellet in a ratio of 0.1 to 0.25 gram (g) cryoprotectant per gram of pellet (e.g., a ratio of 0.15 to 0.2 gram (g) cryoprotectant solution per gram of pellet, a ratio of about 0.18 gram (g) cryoprotectant solution per gram of pellet); or a ratio of 4 % to 10% (volume/volume) (e.g., 5 % to 8% (volume/volume), a ratio of about 6.5% (volume/volume)).

[709] **Embodiment 13.** The method of any one of embodiments 10 to 12, wherein the cryoprotectant comprises sucrose, dextran, or a combination thereof, optionally the cryoprotectant comprises sucrose and dextran in equivalent amounts.

[710] **Embodiment 14.** The method of any one of embodiments 10 to 12, wherein the cryoprotectant comprises sucrose, dextran, and L-cysteine HCl.

[711] **Embodiment 15.** The method of any one of embodiments 10 to 12, wherein the cryoprotectant does not comprise L-cysteine HCl.

[712] **Embodiment 16.** The method of any one of embodiments 10 to 12, wherein the cryoprotectant comprises about 10% to about 30% (weight/weight) sucrose (e.g., about 15% to about 35% (weight/weight), about 20% (weight/weight)); about 10% to about 30% (weight/weight) dextran (e.g., about 15% to about 35% (weight/weight), about 20% (weight/weight)); or about 10% to about 30% (weight/weight) sucrose and about 10% to about 30% (weight/weight) dextran (e.g., about 15% to about 35% (weight/weight) sucrose and about 15% to about 35% (weight/weight) dextran, about 20% (weight/weight) sucrose and about 20% (weight/weight) dextran).

[713] **Embodiment 17.** The method of any one of embodiments 10 to 12, wherein the cryoprotectant comprises about 40% to about 80% (weight/weight) water (e.g., about 50% to about 70% (weight/weight) water, about 55% to about 65% (weight/weight) water, about 60% (weight/weight) water), about 59.8% (weight/weight) water, about 59.6% (weight/weight) water).

[714] **Embodiment 18.** The method of any one of embodiments 10 to 12, wherein the cryoprotectant comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl (e.g., about 0.1% to about 0.5% (weight/weight) L-cysteine HCl, about 0.15% to about 0.45% (weight/weight) L-cysteine HCl, about 0.2% (weight/weight) L-cysteine HCl, about 0.4% (weight/weight) L-cysteine HCl, about 0.1% (weight/weight) L-cysteine HCl).

[715] **Embodiment 19.** The method of any one of embodiments 10 to 12, wherein the cryoprotectant comprises about 0.25% to about 5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant solution provided herein comprises: (i) about 20% (weight/weight) sucrose; (ii) about 20% (weight/weight) dextran; (iii) about 0.4% (weight/weight) L-cysteine HCl; and (iv) about 59.6% (weight/weight) water. In some embodiments, the cryoprotectant solution provided herein comprises: (i) about 20% (weight/weight) sucrose; (ii) about 20% (weight/weight) dextran; (iii) about 0.2%

(weight/weight) L-cysteine HCl; and (iv) about 59.8% (weight/weight) water. In some embodiments, the cryoprotectant solution provided herein comprises: (i) about 20% (weight/weight) sucrose; (ii) about 20% (weight/weight) dextran; and (iii) about 60% (weight/weight) water. In some embodiments, the cryoprotectant of the cryoprotectant solution comprises about 40% to about 60% (weight/weight) sucrose. In some embodiments, the cryoprotectant of the cryoprotectant solution comprises about 45% to about 55% (weight/weight) sucrose. In some embodiments, the cryoprotectant of the cryoprotectant solution comprises about 50% (weight/weight) sucrose. In some embodiments, the cryoprotectant of the cryoprotectant solution comprises about 40% to about 60% (weight/weight) dextran. In some embodiments, the cryoprotectant of the cryoprotectant solution comprises about 45% to about 55% (weight/weight) dextran. In some embodiments, the cryoprotectant of the cryoprotectant solution comprises about 50% (weight/weight) dextran. In some embodiments, the cryoprotectant of the cryoprotectant solution comprises about 40% to about 60% (weight/weight) sucrose and about 40% to about 60% (weight/weight) dextran. In some embodiments, the cryoprotectant of the cryoprotectant solution comprises about 45% to about 55% (weight/weight) sucrose and about 45% to about 55% (weight/weight) dextran. In some embodiments, the cryoprotectant of the cryoprotectant solution comprises about 50% (weight/weight) sucrose and about 50% (weight/weight) dextran. In some embodiments, the cryoprotectant of the cryoprotectant solution comprises about 0.25% to about 5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant of the cryoprotectant solution comprises about 0.5% to about 2.5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant of the cryoprotectant solution comprises about 0.75% to about 1.5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant of the cryoprotectant solution comprises about 1% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant of the cryoprotectant solution provided herein comprises: (i) about 50% (weight/weight) sucrose; (ii) about 50% (weight/weight) dextran; and (iii) about 1% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant of the cryoprotectant solution provided herein comprises: (i) about 50% (weight/weight) sucrose; and (ii) about 50% (weight/weight) dextran.

[716] Embodiment 20. A pharmaceutical agent that comprises bacteria, wherein the pharmaceutical agent maintains its stability (e.g., e.g., for three, six, twelve, eighteen

and/or twenty-four months under long-term (2-8°C) and/or accelerated (23-27°C (optionally at 60% relative humidity (RH))) storage conditions, e.g., as determined by total cell count (TCC), e.g., as determined by Coulter counter and described herein).

[717] Embodiment 21. The pharmaceutical agent of embodiment 20, wherein the water content of the pharmaceutical agent is between about 0.5% and about 9% (e.g., between about 1% and about 8%, between about 1% and about 6%, (e.g., about 1.7%, e.g., 1.8%, e.g., about 2%, e.g., about 2.2%, e.g., about 2.3%, e.g., about 2.4%, e.g., about 2.8%, e.g., about 2.9%, e.g., about 3%, e.g., about 3.1%, e.g., about 3.2%, e.g., about 3.3%, e.g., about 3.5%, e.g., about 3.6%, e.g., about 4%, e.g., about 4.5%, e.g., about 5%, e.g., about 5.3%, e.g., about 5.4%, or e.g., about 7.8%), e.g., as determined by the Karl-Fischer method for water content analysis provided in Ph. Eur. method 2.5.12).

[718] Embodiment 22. The pharmaceutical agent of embodiment 20 or 21, wherein the pharmaceutical agent maintains its water content (e.g., e.g., for three, six, twelve, eighteen and/or twenty-four months under long-term (2-8°C) and/or accelerated (25°C (optionally at 60% RH)) storage conditions).

[719] Embodiment 23. The pharmaceutical agent of any one of embodiments 20 to 22, wherein the pharmaceutical agent is of bacterial origin (e.g., mixture of selected strains or agents (e.g., components) or a single selected strain and/or agents (e.g., components), ; the pharmaceutical agent is a powder that comprises the bacteria and/or components thereof; comprises additional agents (e.g., cryoprotectant); and/or the pharmaceutical agent is a freeze dried (e.g., lyophilized) powder of bacteria and/or components thereof that optionally, further comprise additional agents (e.g., cryoprotectant).

[720] Embodiment 24. A solid dosage form that comprises a pharmaceutical agent of any one of embodiments 1 to 8 or 20 to 23.

[721] Embodiment 25. The solid dosage form of embodiment 24, wherein the solid dosage form is enteric coated; comprises a capsule; the capsule is a size 00, size 0, size 1, size 2, size 3, size 4, or size 5 capsule; the solid dosage form comprises a tablet (e.g., enterically coated tablet), optionally the tablet is a 5mm, 6mm, 7mm, 8mm, 9mm, 10mm, 11mm, 12mm, 13mm, 14mm, 15mm, 16mm, 17mm, or 18mm tablet; the solid dosage form comprises a minitablet, optionally the minitablet (e.g., enterically coated minitablet) is about a 1mm minitablet to a 4mm minitablet; a plurality of enterically coated minitablets are contained in a capsule (e.g., a size 0 capsule can contain about 31 to about 35 (e.g., 33) minitablets, wherein the minitablets are 3mm in size), optionally the

minitablets are 3mm in size; and/or the capsule comprises HPMC (hydroxyl propyl methyl cellulose) or gelatin.

[722] Embodiment 26. The solid dosage form of embodiment 24 or 25, wherein the enteric coating comprises one enteric coating; the enteric coating comprises an inner enteric coating and an outer enteric coating; the enteric coating comprises an inner enteric coating and an outer enteric coating, and wherein the inner and outer enteric coatings are not identical (e.g., the inner and outer enteric coatings do not contain identical components in identical amounts); the enteric coating (e.g., the one enteric coating or the inner enteric coating and/or the outer enteric coating) comprises a polymethacrylate-based copolymer; the enteric coating e.g., the one enteric coating or the inner enteric coating and/or the outer enteric coating) comprises a methacrylic acid ethyl acrylate (MAE) copolymer (1:1); the one enteric coating comprises methacrylic acid ethyl acrylate (MAE) copolymer (1:1); the one enteric coating comprises a Eudragit copolymer, e.g., a Eudragit, a Eudragit S, a Eudragit RL, a Eudragit RS, a Eudragit E, or a Eudragit FS; the enteric coating (e.g., the one enteric coating or the inner enteric coating and/or the outer enteric coating) comprises cellulose acetate phthalate (CAP), cellulose acetate trimellitate (CAT), poly(vinyl acetate phthalate) (PVAP), hydroxypropyl methylcellulose phthalate (HPMCP), a fatty acid, a wax, shellac (esters of aleurtic acid), a plastic, a plant fiber, zein, Aqua-Zein (an aqueous zein formulation containing no alcohol), amylose starch, a starch derivative, a dextrin, a methyl acrylate-methacrylic acid copolymer, cellulose acetate succinate, hydroxypropyl methyl cellulose acetate succinate (hypromellose acetate succinate), a methyl methacrylate-methacrylic acid copolymer, or sodium alginate; or the enteric coating (e.g., the one enteric coating or the inner enteric coating and/or the outer enteric coating) comprises an anionic polymeric material.

[723] Embodiment 27. The solid dosage form of any one of embodiments 24 to 26 or pharmaceutical agent of any one of embodiments 1 to 8 or 20 to 23, or pharmaceutical composition of embodiment 9 or the method of any one of embodiments 10 to 19, wherein the bacteria are of the genus *Lactococcus*, *Prevotella*, *Bifidobacterium*, or *Veillonella*.

[724] Embodiment 28. The solid dosage form of any one of embodiments 24 to 26 or pharmaceutical agent of any one of embodiments 1 to 8 or 20 to 23, or pharmaceutical composition of embodiment 9 or the method of any one of embodiments 10 to 19, wherein the bacteria are of the species *Lactococcus lactis cremoris*, optionally the

Lactococcus lactis cremoris is *Lactococcus lactis cremoris* Strain A (ATCC designation number PTA-125368); the bacteria are of the species *Veillonella parvula*, optionally the *Veillonella parvula* is *Veillonella parvula* (ATCC designation number PTA-125691); the bacteria are of the species *Prevotella histicola*, optionally the *Prevotella histicola* is *Prevotella histicola* Strain B 50329 (NRRL accession number B 50329); or the bacteria are of the species *Bifidobacterium animalis*, optionally the *Bifidobacterium animalis* is *Bifidobacterium animalis ssp. lactis* (ATCC designation number PTA-125097).

[725] Embodiment 29. The solid dosage form of any one of embodiments 24 to 26 or pharmaceutical agent of any one of embodiments 1 to 8 or 20 to 23, or pharmaceutical composition of embodiment 9 or the method of any one of embodiments 10 to 19, wherein the freeze-dried powder comprises *Prevotella* bacteria or *Veillonella* bacteria; the bacteria are a species listed in Table 1, Table 2, Table 3, or Table 4, optionally the bacteria are a bacterial strain that has at least 95% genomic, 16S ribosomal ribonucleic acid, or clustered regularly interspaced short palindromic repeats sequence identity with a strain listed in Table 1 or Table 3; the bacterial are live, attenuated, or dead; the bacteria are of a taxonomic group listed in Table 1, Table 2, Table 3, or Table 4; the bacteria are a bacterial strain listed in Table 1, Table 2, Table 3, or Table 4; the bacteria are of a taxonomic group (e.g., class, order, family, genus, species or strain) listed in Table J; or the bacteria are a bacterial strain listed in Table J.

[726] Embodiment 30. A method of preventing or treating a disease of a subject, the method comprising administering to the subject a solid dosage form of any one of embodiments 24 to 26.

[727] Embodiment 31. Use of a pharmaceutical agent of any one of embodiments 1 to 8 or 20 to 23, or pharmaceutical composition of embodiment 9, or solid dosage form of any one of embodiments 24 to 26 for the treatment or prevention of a disease of a subject.

[728] Embodiment 32. Use of a pharmaceutical agent of any one of embodiments 1 to 8 or 20 to 23, or pharmaceutical composition of embodiment 9, or solid dosage form of any one of embodiments 24 to 26 for the preparation of a medicament for treating or preventing a disease in a subject.

[729] Embodiment 33. A pharmaceutical agent of any one of embodiments 1 to 8 or 20 to 23, or pharmaceutical composition of embodiment 9, or solid dosage form of any one of embodiments 24 to 26 for use in the treatment or prevention of a disease of a subject.

[730] Embodiment 34. A cryoprotectant for use in preparing a pharmaceutical agent that comprises bacteria, optionally the cryoprotectant is a cryoprotectant solution.

[731] Embodiment 35. A method of preparing a pharmaceutical agent, the method comprising combining bacteria with a cryoprotectant, optionally the cryoprotectant is a cryoprotectant solution, thereby preparing a formulated paste.

[732] Embodiment 36. The method of embodiment 35, further comprising freeze drying the formulated paste, to thereby prepare a freeze-dried product; further comprising milling the freeze-dried product, to thereby prepare a freeze-dried powder; and/or further comprising combining the freeze-dried powder with one or more excipients to thereby prepare a pharmaceutical composition; wherein the cryoprotectant is mixed with the pellet in a ratio of 0.05 to 0.25 gram (g) cryoprotectant per gram of pellet (e.g., ratio of 0.15 to 0.2 gram (g) cryoprotectant solution per gram of pellet, ratio of about 0.18 gram (g) cryoprotectant solution per gram of pellet); or the cryoprotectant is mixed with the pellet at a ratio of 4 % to 10% (volume/volume), (e.g., a ratio of about 5 % to 8% (volume/volume), a ratio of about 6.5% (volume/volume)).

[733] Embodiment 37. The cryoprotectant of embodiment 34 or the method of embodiment 35 or 36, wherein the cryoprotectant comprises sucrose; the cryoprotectant comprises dextran; the cryoprotectant comprises sucrose and dextran, optionally the cryoprotectant comprises sucrose and dextran in equivalent amounts; the cryoprotectant comprises sucrose, dextran, and L-cysteine HCl; or the cryoprotectant does not comprise L-cysteine HCl.

[734] Embodiment 38. The cryoprotectant of embodiment 34 or the method of embodiment 35 or 36, wherein the cryoprotectant comprises about 10% to about 30% (weight/weight) sucrose (e.g. about 15% to about 35% (weight/weight) sucrose, about 20% (weight/weight) sucrose); the cryoprotectant comprises about 10% to about 30% (weight/weight) dextran (e.g., about 15% to about 35% (weight/weight) dextran, about 20% (weight/weight) dextran); the cryoprotectant comprises about 10% to about 30% (weight/weight) sucrose and about 10% to about 30% (weight/weight) dextran (e.g., about 15% to about 35% (weight/weight) sucrose and about 15% to about 35% (weight/weight) dextran, about 20% (weight/weight) sucrose and about 20% (weight/weight) dextran); the cryoprotectant comprises about 40% to about 80% (weight/weight) water (e.g., about 50% to about 70% (weight/weight) water, about 55% to about 65% (weight/weight) water, about 60% (weight/weight) water, about 59.8% (weight/weight) water, about

59.6% (weight/weight) water); the cryoprotectant comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl (e.g., about 0.1% to about 0.5% (weight/weight) L-cysteine HCl, about 0.2% (weight/weight) L-cysteine HCl, about 0.4% (weight/weight) L-cysteine HCl); or the cryoprotectant comprises about 0.25% to about 5% (weight/weight) L-cysteine HCl. In some emodiments, the cryoprotectant provided herein comprises: (i) about 20% (weight/weight) sucrose; (ii) about 20% (weight/weight) dextran; (iii) about 0.4% (weight/weight) L-cysteine HCl; and (iv) about 59.6% (weight/weight) water. In some emodiments, the cryoprotectant provided herein comprises: (i) about 20% (weight/weight) sucrose; (ii) about 20% (weight/weight) dextran; (iii) about 0.2% (weight/weight) L-cysteine HCl; and (iv) about 59.8% (weight/weight) water. In some emodiments, the cryoprotectant provided herein comprises: (i) about 20% (weight/weight) sucrose; (ii) about 20% (weight/weight) dextran; and (iii) about 60% (weight/weight) water. In some emodiments, the cryoprotectant comprises about 40% to about 60% (weight/weight) sucrose. In some emodiments, the cryoprotectant comprises about 45% to about 55% (weight/weight) sucrose. In some emodiments, the cryoprotectant comprises about 50% (weight/weight) sucrose. In some emodiments, the cryoprotectant comprises about 40% to about 60% (weight/weight) dextran. In some emodiments, the cryoprotectant comprises about 45% to about 55% (weight/weight) dextran. In some emodiments, the cryoprotectant comprises about 50% (weight/weight) dextran. In some emodiments, the cryoprotectant comprises about 40% to about 60% (weight/weight) sucrose and about 40% to about 60% (weight/weight) dextran. In some emodiments, the cryoprotectant comprises about 45% to about 55% (weight/weight) sucrose and about 45% to about 55% (weight/weight) dextran. In some emodiments, the cryoprotectant comprises about 50% (weight/weight) sucrose and about 50% (weight/weight) dextran. In some emodiments, the cryoprotectant comprises about 0.25% to about 5% (weight/weight) L-cysteine HCl. In some emodiments, the cryoprotectant comprises about 0.5% to about 2.5% (weight/weight) L-cysteine HCl. In some emodiments, the cryoprotectant comprises about 0.75% to about 1.5% (weight/weight) L-cysteine HCl. In some emodiments, the cryoprotectant comprises about 1% (weight/weight) L-cysteine HCl. In some emodiments, the cryoprotectant comprises: (i) about 50% (weight/weight) sucrose; (ii) about 50% (weight/weight) dextran; and (iii) about 1% (weight/weight) L-cysteine HCl. In some emodiments, the

cryoprotectant provided herein comprises: (i) about 50% (weight/weight) sucrose; and (ii) about 50% (weight/weight) dextran.

[735] Embodiment 39. The cryoprotectant of embodiment 34 or the method of embodiment 35 or 36, wherein the cryoprotectant comprises a dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21), optionally wherein the cryoprotectant further comprises sucrose, optionally wherein the cryoprotectant further comprises dextrose (also referred to as glucose). Optionally wherein the cryoprotectant further comprises monosodium glutamate.

[736] Embodiment 40. The cryoprotectant of embodiment 34 or the method of embodiment 35 or 36, wherein the cryoprotectant (e.g., dry composition not containing water) comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21). In some embodiments, the cryoprotectant (e.g., dry composition not containing water) comprises about 27% to about 47% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 8% to about 18% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 11% to about 15% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 13% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 8% to about 18% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 11% to about 15% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 13% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent

(DE) of 21 (such as Glucidex 21) and about 27% to about 47% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 32% to about 42% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21) and about 37% (weight/weight) sucrose. In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 27% to about 47% (weight/weight) sucrose; and about 8% to about 18% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 27% to about 47% (weight/weight) sucrose; and about 8% to about 18% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 27% to about 47% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 27% to about 47% (weight/weight) sucrose; about 8% to about 18% (weight/weight) dextrose; and about 8% to about 18% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 32% to about 42% (weight/weight) sucrose; and about 11% to about 15% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 32% to about 42% (weight/weight) sucrose; and about 11% to about 15% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 32% to about 42% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21);

about 32% to about 42% (weight/weight) sucrose; about 11% to about 15% (weight/weight) dextrose; and about 11% to about 15% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 37% (weight/weight) sucrose; and about 13% (weight/weight) dextrose. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 37% (weight/weight) sucrose; and about 13% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); about 37% (weight/weight) sucrose; about 13% (weight/weight) dextrose; and about 13% (weight/weight) monosodium glutamate. In some embodiments, the cryoprotectant comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl (e.g., a form of L-cysteine). In some embodiments, the cryoprotectant comprises about 0.1% to about 0.5% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant comprises about 0.1% to about 0.25% (weight/weight) L-cysteine HCl. In some embodiments, the cryoprotectant comprises about 0.2% (weight/weight) L-cysteine HCl. In certain embodiments, the cryoprotectant provided herein comprises: (i) about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); (ii) about 37% (weight/weight) sucrose; (iii) about 13% (weight/weight) dextrose; (iv) about 13% (weight/weight) monosodium glutamate; and (v) about 0.2% (weight/weight) L-cysteine HCl. In certain embodiments, the cryoprotectant provided herein comprises: (i) about 37% (weight/weight) dried (dehydrated) maize glucose syrup (such as Glucidex), such as a dried maize glucose syrup with a dextrose equivalent (DE) of 21 (such as Glucidex 21); (ii) about 37% (weight/weight) sucrose; (iii) about 13% (weight/weight) dextrose; and (iv) about 13% (weight/weight) monosodium glutamate.

[737] Embodiment 41. The method of any one of embodiments 10 to 19 or 36, wherein the freeze-dried powder comprises about 35% to about 75% (weight/weight) dried bacteria (e.g. about 40% to about 70% (weight/weight) dried bacteria).

[738] Embodiment 42. The method of any one of embodiments 10 to 19, 36, or 41 wherein the bacteria comprise *Prevotella* bacteria or *Veillonella* bacteria.

Examples

Example 1: *Prevotella histicola* Pharmaceutical Agent

[739] Pharmaceutical agent comprising *Prevotella histicola* Strain B was prepared as follows. *Prevotella histicola* Strain B has been deposited as *Prevotella histicola* Strain B (NRRL accession number B 50329).

[740] Once a desired level of growth was achieved, centrifugation (using continuous centrifugation) was performed on fermentation broth that contained bacteria to prepare a pellet. A cryoprotectant solution was combined with the pellet to prepare a formulated paste. The components of the cryoprotectant solution are provided in Table 5A (Table 5B provides the percentages of the non-water (dry) components). The cryoprotectant solution was added to the concentrated cells (pellet) at a ratio of 6.5% (v/v) and mixed to give a formulated cell paste. The formulated cell paste was loaded onto disposable trays inside stainless-steel trays. The formulated paste was freeze dried to prepare a freeze-dried product. The freeze drying included primary drying (shelf temperature -5 °C) and secondary drying (shelf temperature 25 °C). The total drying time was at least 48 hours. The freeze-dried product was milled (e.g., using a milling machine) to prepare a freeze-dried powder, e.g., pharmaceutical agent. The pharmaceutical agent was collected into polyethylene bags. Each bag was thereafter sealed under vacuum and then placed in a metalized polyethylene bag, then stored at about 5°C.

Table 5A: Cryoprotectant solution components

Components	Percent (w/w)
Sucrose	20%
Dextran	20%
L-Cysteine-HCL	0.4%
Water	59.6%

Table 5B: Cryoprotectant components (dry)

Components	Percent (w/w)
Sucrose	49.5%
Dextran	49.5%
L-Cysteine-HCL	1.0%

Example 2: Properties of Pharmaceutical Agent containing *Prevotella histicola*

[741] Five batches of pharmaceutical agent comprising *Prevotella histicola* Strain B were prepared according to Example 1 and evaluated.

[742] Batch 1: Upon evaluation, the pharmaceutical agent had a TCC of 2.4 x 10^{12} cells/gram as determined by Coulter counter, and a water content of 1.7%, as determined by Karl Fisher (Ph. Eur. 2.5.12). The acceptable TCC value is set at > 5x10^{11} cells/gram.

[743] Batch 2: Upon evaluation, the pharmaceutical agent had a TCC of 2 x 10^{12} cells/gram as determined by Coulter counter, and a water content of 2.0%, as determined by Karl Fisher (Ph. Eur. 2.5.12). The acceptable TCC value is set at > 5x10^{11} cells/gram.

[744] Batch 3: Upon evaluation, the pharmaceutical agent had a TCC of 2.1 x 10^{12} cells/gram as determined by Coulter counter, and a water content of 3.0%, as determined by Karl Fisher (Ph. Eur. 2.5.12). The acceptable TCC value is set at ≥ 5x10^{11} cells/gram.

[745] Batch 4: Upon evaluation, the pharmaceutical agent had a TCC of 1.5 x 10^{12} cells/gram as determined by Coulter counter, and a water content of 2.0%, as determined by Karl Fisher (Ph. Eur. 2.5.12). The acceptable TCC value is set at ≥ 5x10^{11} cells/gram.

[746] Batch 5: Upon evaluation, the pharmaceutical agent had a TCC of 1.3 x 10^{12} cells/gram as determined by Coulter counter, and a water content of 4.0%, as determined by Karl Fisher (Ph. Eur. 2.5.12). The acceptable TCC value is set at ≥ 5x10^{11} cells/gram.

Example 3: Stability of *Prevotella histicola* Batch 1

[747] Batch 1 of pharmaceutical agent comprising *Prevotella histicola* Strain B was prepared as described in Example 1, and evaluated as described in Example 2.

[748] Stability study samples were packaged using a vacuum sealed polyethylene bag and then placed inside a secondary metalized polyethylene bag.

[749] The stability of Batch 1 pharmaceutical agent was assessed.

Content and Potency: Total Cell Count (TCC)/gram:

[750] The total cells/gram was determined for the batch for the durations shown at long-term (2-8°C) and accelerated (25°C) storage conditions. TCC was determined by Coulter counter. The data are presented in **Figure 1**. The data collected for up to 6 months showed stable total cell count profile with the analytical variability, and suggested that the product content and potency of pharmaceutical agent will be maintained during long term storage condition at 5°C. The data collected for up to 18 months are presented in **Figure 9**.

Water Content:

[751] The water content was determined for the batch for the durations shown for both long-term (2-8°C) and accelerated (25°C) storage conditions for the durations shown. The results are shown in **Figure 2.** No significant change in moisture content was observed for up to 6 months. The data collected for up to 18 months are presented in **Figure 10**.

Example 4: Stability of *Prevotella histicola* Batch 2

[752] Batch 2 of pharmaceutical agent comprising Prevotella histicola Strain B was prepared as described in Example 1, and evaluated as described in Example 2.

[753] Stability study samples were packaged using a vacuum sealed polyethylene bag and then placed inside a metalized polyethylene bag.

[754] The stability of Batch 2 pharmaceutical agent was assessed.

Content and Potency: Total Cell Count (TCC)/gram:

[755] The total cells/gram was determined for the batch for the durations shown at long-term (2-8°C) and accelerated (25°C) storage conditions. TCC was determined by Coulter counter. The data are presented in **Figure 3**. Total cell count stability profiles of the batch at 3 months showed no adverse trend. In addition, the total cell count values are comparable between the 5°C (long-term) and 25°C (accelerated) conditions for all the time points. These data provide support that the product content and potency will be maintained during storage. The data collected for up to 18 months are presented in **Figure 11**.

Water Content:

[756] The water content was determined for the batch for the durations shown for both long-term (2-8°C) and accelerated (25°C) storage conditions for the durations shown. The results are shown in **Figure 4**. No significant change in moisture content was observed for up to 3 months. The data collected for up to 18 months are presented in **Figure 12**.

Example 5: *Veillonella parvula* Pharmaceutical Agent

[757] Pharmaceutical agent comprising *Veillonella parvula* Strain A was prepared as follows. *Veillonella* parvula Strain A has been deposited as *Veillonella parvula* Strain A (ATCC Deposit Number PTA-125691).

[758] Once a desired level of growth was achieved, centrifugation (using continuous centrifugation) was performed on fermentation broth that contained bacteria to prepare a

pellet. A cryoprotectant solution was combined with the pellet to prepare a formulated paste. The components of the cryoprotectant solution are provided in Table 6. The cryoprotectant was mixed with the cell pellet in a ratio of 0.18 g cryoprotectant per g of cell pellet to give a formulated cell paste. The formulated cell paste was loaded onto stainless-steel trays. The formulated paste was freeze dried to prepare a freeze-dried product. The freeze drying included primary drying (shelf temperature -5 °C) and secondary drying (shelf temperature 25 °C). The total drying time was at least 48 hours. The freeze-dried product was milled (e.g., using a milling machine) to prepare a freeze-dried powder, e.g., pharmaceutical agent. The pharmaceutical agent was collected into polyethylene bags. The polyethylene bags with approximately 0.5kg of freeze-dried powder were vacuum sealed and placed inside a polyethylene bag with aluminum foil, then stored at about 5°C. The freeze-dried material in polyethylene bags with aluminum foil were transferred to boxes and gamma-irradiated within a dose rage of 20-35 kGy. After the gamma irradiation step pharmaceutical agent release assays were performed.

Table 6: Cryoprotectant solution components

Components	Percent (w/w)
Sucrose	20%
Dextran	20%
L-Cysteine-HCL	0.2%
Water	59.8%

Example 6: Properties of Pharmaceutical Agent containing *Veillonella parvula*

[759] Six batches of pharmaceutical agent comprising *Veillonella parvula* Strain A were prepared according to Example 5 and evaluated.

[760] Batch A: Upon evaluation, the pharmaceutical agent had a TCC of 2.4×10^{12} cells/gram as determined by Coulter counter, and a water content of 3.2%, as determined by Karl Fisher (Ph. Eur. 2.5.12). The acceptable TCC value is set at $\geq 3.3 \times 10^{11}$ cells/gram.

[761] Batch B: Upon evaluation, the pharmaceutical agent had a TCC of 1.5×10^{12} cells/gram as determined by Coulter counter, and water content was not determined. The acceptable TCC value is set at $\geq 3.3 \times 10^{11}$ cells/gram.

[762] Batch C: Upon evaluation, the pharmaceutical agent had a TCC of 2.2×10^{12} cells/gram as determined by Coulter counter, and water content was not determined. The acceptable TCC value is set at $\geq 3.3 \times 10^{11}$ cells/gram.

[763] Batch D: Upon evaluation, the pharmaceutical agent had a TCC of 12.1 x 10^{11} cells/gram as determined by Coulter counter, and a water content of 2.2%, as determined by Karl Fisher (Ph. Eur. 2.5.12). The acceptable TCC value is set at $\geq 3.3x10^{11}$ cells/gram.

[764] Batch E: Upon evaluation, the pharmaceutical agent had a TCC of 7.7 x 10^{11} cells/gram as determined by Coulter counter, and a water content of 3.0%, as determined by Karl Fisher (Ph. Eur. 2.5.12). The acceptable TCC value is set at > 3.3x1011 cells/gram.

[765] Batch F: Upon evaluation, the pharmaceutical agent had a TCC of 11.4 x 10^{11} cells/gram as determined by Coulter counter, and a water content of 2.8%, as determined by Karl Fisher (Ph. Eur. 2.5.12). The acceptable TCC value is set at $\geq 3.3x10^{11}$ cells/gram.

Example 7: Stability of *Veillonella parvula* Batch A

[766] Batch A of pharmaceutical agent comprising Veillonella parvula Strain A was prepared as described in Example 5, and evaluated as described in Example 6.

[767] Stability study samples were packaged using a polyethylene bag, vacuum sealed and then placed inside another polyethylene bag with aluminum foil.

[768] The stability of Batch A pharmaceutical agent was assessed.

Content and Potency: Total Cell Count (TCC)/gram:

[769] The total cells/gram was determined for the batch for the durations shown at long-term (2-8°C) and accelerated (25°C (± 2 °C) / 60% (±5%) RH (relative humidity)) (abbreviation: 25°C)) storage conditions. TCC was determined by Coulter counter. The data are presented in **Figure 5**. The data collected for up to 12 months showed stable total cell count profile for the batch at 5°C and 25°C, which suggest that the product content and potency of the pharmaceutical agent will be maintained during long term storage conditions.

Water Content:

[770] The water content was determined for the batch for the durations shown for both long-term (2-8°C) and accelerated (25°C) storage conditions for the durations shown. The results are shown in **Figure 6**. No significant change in moisture content was observed for up to 12 months. With an initial upward trend at 1 month (5.0% to 5.4%), the moisture

content remained unchanged at about 3% for up to 6 months. There was a slight increase in moisture content at 12 months, which could be due to normal variability.

Example 8: Stability of *Veillonella parvula* Batch D

[771] Batch D of pharmaceutical agent comprising *Veillonella parvula* Strain A was prepared as described in Example 5, and evaluated as described in Example 6.

[772] Stability study samples were packaged using a polyethylene bag, vacuum sealed and then placed inside another polyethylene bag with aluminum foil.

[773] The stability of Batch A pharmaceutical agent was assessed.

Content and Potency: Total Cell Count (TCC)/gram:

[774] The total cells/gram was determined for the batch for the durations shown at long-term (2-8°C) and accelerated (25°C (± 2 °C) / 60% (±5%) RH (relative humidity)) (abbreviation: 25°C)) storage conditions. TCC was determined by Coulter counter. The data are presented in **Figure 7**. Total cell count stability profiles of the batch at 6 months showed no adverse trend. In addition, the total cell count values are comparable between the 5°C (long-term) and 25°C (accelerated) conditions for all the time points. These data provide support that the product content and potency will be maintained during storage.

Water Content:

[775] The water content was determined for the batch for the durations shown for both long-term (2-8°C) and accelerated (25°C) storage conditions for the durations shown. The results are shown in **Figure 8**. No significant change in moisture content was observed for up to 12 months. No changes in moisture content was observed for the batch for up to 6 months.

Example 9: Representative Strains

[776] Bacteria of the taxonomic groups listed in Table J (e.g., class, order, family, genus, species or strain) can be used in the pharmaceutical agents described herein.

[777] Information on the Gram staining, cell wall structure, and taxonomic classification for each strain is also provided in Table J.

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Table J: Representative Strains

Strain	Gram-stain	Cell envelope structure	Phylum	Class	Order	Family
Parabacteroides distasonis DRLU022118 A ILEUM-6	*Gram-stain-negative*	*diderm*	Bacteroidota	Bacteroidia	Bacteroidales	*Porphyromonadaceae*
Parabacteroides goldsteinii S4	*Gram-stain-negative*	*diderm*	Bacteroidota	Bacteroidia	Bacteroidales	*Porphyromonadaceae*
Prevotella histicola	*Gram-stain-negative*	*diderm*	Bacteroidota	Bacteroidia	Bacteroidales	*Prevotellaceae*
Prevotella histicola	*Gram-stain-negative*	*diderm*	Bacteroidota	Bacteroidia	Bacteroidales	*Prevotellaceae*
Fournierella massiliensis S10 GIMucosa-297	*Gram-stain-negative*	*monoderm*	Firmicutes	Clostridia	Eubacteriales	*Oscillospiraceae (formely Ruminococcaceae)*
Harryflintia acetispora S4-M5	*Gram-stain-negative*	*monoderm*	Firmicutes	Clostridia	Eubacteriales	*Oscillospiraceae*
Blautia massiliensis S1046-4A5	*Gram-stain-negative*	*monoderm*	Firmicutes	Clostridia	Eubacteriales	*Lachnospiraceae*
Mediterraneibacter/[*Ruminococcus*] *gnavus* S10 GIMucosa-412	*Gram-stain-negative*	*monoderm*	Firmicutes	Clostridia	Eubacteriales	*Lachnospiraceae*
Clostridioides difficile S10 GImucosa-525	*Gram-stain-positive*	*monoderm*	Firmicutes	Clostridia	Eubacteriales	*Peptostreptococcaceae*
Aminipila sp. S16-M4	*Gram-stain-positive*	*monoderm*	Firmicutes	Clostridia	Eubacteriales	Clostridiales Family XIII/Incertae sedis 41/[Eubacteriales, no family]
Megasphaera sp. S29-N3	*Gram-stain-negative*	*diderm*	Firmicutes	Negativicutes	Veillonellales	*Veillonellaceae*
Megasphaera sp. S1007	*Gram-stain-negative*	*diderm*	Firmicutes	Negativicutes	Veillonellales	*Veillonellaceae*
Selenomonas felix S34N-300R	*Gram-stain-negative*	*diderm*	Firmicutes	Negativicutes	Selenomonadales	*Selenomonadaceae*
Veillonella parvula S14Ileum-201	*Gram-stain-negative*	*diderm*	Firmicutes	Negativicutes	Veillonellales	*Veillonellaceae*
Propionispora sp. DSM100705-1A	*Gram-stain-negative*	*diderm*	Firmicutes	Negativicutes	Selenomonadales	*Sporomusaceae*
Rarimicrobium hominis S24RS2-T2-5	*Gram-stain-negative*	*diderm*	Synergistota	Synergistia	Synergistales	*Synergistaceae*
Cloacibacillus evryensis S29-M8	*Gram-stain-negative*	*diderm*	Synergistota	Synergistia	Synergistales	*Synergistaceae*
Veillonella parvula S14-205	*Gram-stain-negative*	*diderm*	Firmicutes	Negativicutes	Veillonellales	*Veillonellaceae*
Veillonella sp/*dispar* ECD01-DP-201	*Gram-stain-negative*	*diderm*	Firmicutes	Negativicutes	Veillonellales	*Veillonellaceae*
Veillonella parvula/dispar ECD01-DP-223	*Gram-stain-negative*	*diderm*	Firmicutes	Negativicutes	Veillonellales	*Veillonellaceae*
Veillonella parvula S16 GIMucosa-95	*Gram-stain-negative*	*diderm*	Firmicutes	Negativicutes	Veillonellales	*Veillonellaceae*

Example 10: Pharmaceutical Agents

[778] Pharmaceutical agents containing *Prevotella histicola* Strain B or *Veillonella parvula* Strain A were prepared using cryoprotectant solutions of the recipes provided in Table 5A (for *Prevotella histicola* Strain B) and Table 6 (for *Veillonella parvula* Strain A).

[779] Models were run to estimate the amounts (weight/weight (gram/gram)) of dry cells, sucrose, dextran and L-cysteine HCl in batches of pharmaceutical agent (powder) containing *Prevotella histicola* Strain B. The calculated amounts are provided in Tables 7A and 7B. The amount of L-cysteine HCl includes not only the contribution from the cryoprotectant solution but also a contribution from cell culturing conditions.

Table 7A:

	Batch 1'	Batch 2'	Batch 3'	Batch 4'	Batch 5'	Batch 6'
Dry Cells (*Prevotella histicola*)	64%	58%	47%	60%	54%	43%
Sucrose	11%	10%	8%	12%	11%	9%
Dextran 40k	11%	10%	8%	12%	11%	9%
Cysteine-HCl	0.22%	0.20%	0.17%	0.24%	0.22%	0.19%

Table 7B:

	Batch 7'	Batch 8'	Batch 9'	Batch 10'	Batch 11'	Batch 12'
Dry Cells (*Prevotella histicola*)	71%	65%	55%	67%	61%	51%
Sucrose	9%	8%	7%	10%	9%	7%
Dextran 40k	9%	8%	7%	10%	9%	7%
Cysteine-HCl	0.18%	0.17%	0.15%	0.20%	0.19%	0.16%

[780] Models were run to estimate the amounts (weight/weight (gram/gram)) of dry cells, sucrose, dextran and L-cysteine HCl in batches of pharmaceutical agent (powder) containing *Veillonella parvula* Strain A. The calculated amounts are provided in Tables 8A and 8B. The amount of L-cysteine HCl includes not only the contribution from the cryoprotectant solution but also a contribution from cell culturing conditions.

Table 8A:	Batch 1"	Batch 2"	Batch 3"	Batch 4"	Batch 5"	Batch 6"	Batch 7"	Batch 8"	Batch 9"
Dry Cells (*Veillonella parvula*)	66%	63%	55%	59%	56%	48%	49%	46%	38%
Sucrose	13%	12%	10%	15%	14%	12%	19%	17%	14%
Dextran 40k	13%	12%	10%	15%	14%	12%	19%	17%	14%
Cysteine-HCl	0.17%	0.20%	0.24%	0.21%	0.23%	0.28%	0.26%	0.28%	0.33%

Table 8B:	Batch 10"	Batch 11"	Batch 12"	Batch 13"	Batch 14"	Batch 15"	Batch 16"	Batch 17"	Batch 18"
Dry Cells (*Veillonella parvula*)	65%	61%	54%	58%	54%	47%	48%	44%	37%
Sucrose	13%	12%	11%	15%	14%	12%	19%	18%	15%
Dextran 40k	13%	12%	11%	15%	14%	12%	19%	18%	15%
Cysteine-HCl	0.18%	0.20%	0.25%	0.22%	0.24%	0.28%	0.27%	0.29%	0.34%

Example 11: Stability of *Prevotella histicola* Batch 4

[781] Batch 4 of pharmaceutical agent comprising *Prevotella histicola* Strain B was prepared as described in Example 1, and evaluated as described in Example 2.

[782] Stability study samples were packaged using a vacuum sealed polyethylene bag and then placed inside a secondary metalized polyethylene bag.

[783] The stability of Batch 4 pharmaceutical agent was assessed.

Content and Potency: Total Cell Count (TCC)/gram:

[784] The total cells/gram was determined for the batch for the durations shown at long-term (2-8°C) and accelerated (25°C) storage conditions. TCC was determined by Coulter counter. The data are presented in **Figure 13**.

Water Content:

[785] The water content was determined for the batch for the durations shown for both long-term (2-8°C) and accelerated (25°C) storage conditions for the durations shown. The results are shown in **Figure 14**.

Example 12: Stability of *Prevotella histicola* Batch 5

[786] Batch 5 of pharmaceutical agent comprising *Prevotella histicola* Strain B was prepared as described in Example 1, and evaluated as described in Example 2.

[787] Stability study samples were packaged using a vacuum sealed polyethylene bag and then placed inside a secondary metalized polyethylene bag.

[788] The stability of Batch 5 pharmaceutical agent was assessed.

Content and Potency: Total Cell Count (TCC)/gram:

[789] The total cells/gram was determined for the batch for the durations shown at long-term (2-8°C) and accelerated (25°C) storage conditions. TCC was determined by Coulter counter. The data are presented in **Figure 15**.

Water Content:

[790] The water content was determined for the batch for the durations shown for both long-term (2-8°C) and accelerated (25°C) storage conditions for the durations shown. The results are shown in **Figure 16**.

Example 13: *Prevotella histicola* Pharmaceutical Agent

[791] Pharmaceutical agent comprising *Prevotella histicola* Strain B was prepared as follows. *Prevotella histicola* Strain B has been deposited as *Prevotella histicola* Strain B (NRRL accession number B 50329).

[792] Once a desired level of growth was achieved, centrifugation (using continuous centrifugation) was performed on fermentation broth that contained bacteria to prepare a pellet. A cryoprotectant solution was combined with the pellet to prepare a formulated paste. The components (percentages of the non-water (dry) components) of the cryoprotectant solution are provided in Table 9. The cryoprotectant solution was added to the concentrated cells (pellet) and mixed to give a formulated cell paste. The formulated cell paste was loaded onto disposable trays inside stainless-steel trays. The formulated paste was freeze dried to prepare a freeze-dried product. The freeze drying included primary drying (shelf temperature -20 °C) and secondary drying (shelf temperature 20 °C). The total drying time was at least 48 hours. The freeze-dried product was milled (e.g., using a milling machine) to prepare a freeze-dried powder, e.g., pharmaceutical agent. The pharmaceutical agent was collected into polyethylene bags. Each bag was thereafter sealed under vacuum and then placed in another polyethylene bag, then stored at about -20 °C.

Table 9: Cryoprotectant components (dry)

Components	Percent (w/w)
Glucidex 21	36.9%
Sucrose	36.9%
Dextrose	13.0%
Mono sodium Glutamate	13.0%
L-Cysteine-HCl	0.2%

Example 14: Properties of Pharmaceutical Agent containing *Prevotella histicola*

[793] A batch (Batch i) of pharmaceutical agent comprising *Prevotella histicola* Strain B was prepared according to Example 13 and evaluated.

[794] Batch i: Upon evaluation, the pharmaceutical agent had a TCC of 5.9 x 10^{11} cells/gram as determined by Coulter counter, and a water content of 4%, as determined by Karl Fisher (Ph. Eur. 2.5.12). The acceptable TCC value is set at $\geq$ 1x10^{11} cells/gram.

Example 15: Stability of *Prevotella histicola* Batch i

[795] Batch i of pharmaceutical agent comprising *Prevotella histicola* Strain B was prepared as described in Example 13, and evaluated as described in Example 14.

[796] Stability study samples were packaged using a vacuum sealed polyethylene bag and then placed inside another polyethylene bag.

[797] The stability of Batch i pharmaceutical agent was assessed.

Content and Potency: Total Cell Count (TCC)/gram:

[798] The total cells/gram was determined for the batch for the durations shown at long-term (-20°C) and accelerated (2-8°C) storage conditions. TCC was determined by Coulter counter. The data are presented in **Figure 17**. The data collected for up to 24 months showed stable total cell count profile with the analytical variability, and suggested that the product content and potency of pharmaceutical agent will be maintained during long term storage condition at -20°C. The data suggest the pharmace4uetical agent is stable for 24 months at accelerated temp of 5°C.

Water Content:

[799] The water content was determined for the batch for the durations shown for both long-term (-20°C) and accelerated (2-8°C) storage conditions for the durations shown. The results are shown in **Figure 18.** The moisture content remained steady at about 4% as observed at for up to 24 months at -20°C and up to 6 months at 5°C.

Example 16: Pharmaceutical Agents

[800] Pharmaceutical agents containing *Prevotella histicola* Strain B were prepared using cryoprotectant solution of the recipe provided in Table 9.

[801] Models were run to estimate the amounts (weight/weight (gram/gram)) of dry cells, Glucidex 21, sucrose, dextrose (also referred to as glucose), glutamate, and L-

cysteine HCl in batches of pharmaceutical agent (powder) containing *Prevotella histicola* Strain B. The calculated amounts are provided in Table 10. The amount of L-cysteine HCl includes not only the contribution from the cryoprotectant solution but also a contribution from cell culturing conditions.

Table 10:

	Batch 1'''	Batch 2'''	Batch 3'''	Batch 4'''	Batch 5'''	Batch 6'''
Dry Cells (*Prevotella histicola*)	28%	25%	22%	23%	22%	19%
Sucrose	24%	25%	22%	27%	26%	23%
Glucidex 21D	24.7%	26.2%	25.0%	27.9%	27.3%	25.9%
Glucose	9.2%	8.5%	8.9%	8.7%	8.9%	9.2%
Glutamate	8.26%	7.19%	6.48%	7.84%	7.48%	6.71%
Cysteine-HCl	0.14%	0.50%	0.45%	0.54%	0.52%	0.47%

Incorporation by Reference

[802] All publications patent applications mentioned herein are hereby incorporated by reference in their entirety as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference. In case of conflict, the present application, including any definitions herein, will control.

Equivalents

[803] Those skilled in the art will recognize or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

Claims

What is claimed is:

1. A pharmaceutical agent comprising bacteria, wherein the bacteria in the pharmaceutical agent are present at a total cell count (TCC) of at least $1x10^{11}$ cells/gram of the pharmaceutical agent.

2. The pharmaceutical agent of claim 1, wherein the bacteria are present in the pharmaceutical agent at a total cell count (TCC) of from about $1x10^{11}$ cells/gram to about $2.5x10^{12}$ cells/gram of the pharmaceutical agent.

3. A pharmaceutical agent (e.g., powder) comprising bacteria and a cryoprotectant.

4. The pharmaceutical agent of claim 3, wherein the cryoprotectant comprises sucrose, dextran, or a combination thereof, optionally wherein the cryoprotectant comprises sucrose and dextran in equivalent amounts.

5. The pharmaceutical agent of claim 3, wherein the cryoprotectant comprises sucrose, dextran, and L-cysteine HCl.

6. The pharmaceutical agent of claim 3, wherein the cryoprotectant does not comprise L-cysteine HCl.

7. The pharmaceutical agent of claim 3, wherein the pharmaceutical agent comprises about 6% to about 12% (weight/weight) or about 7% to about 21% (weight/weight) sucrose;

about 6% to about 12% (weight/weight) or about 7% to about 21% (weight/weight) dextran; or

about 6% to about 12% (weight/weight) sucrose and about 6% to about 12% (weight/weight) dextran, or about 7% to about 21% (weight/weight) sucrose and about 7% to about 21% (weight/weight) dextran.

8. The pharmaceutical agent of claim 3, wherein the pharmaceutical agent comprises about 0.10% to about 0.25% (weight/weight) or about 0.15% to about 0.35% (weight/weight) L-cysteine HCl.

9. A pharmaceutical composition comprising a pharmaceutical agent of any one of claims 1 to 8 and one or more excipients.

10. A method of making a formulated paste comprising combining bacteria with a cryoprotectant, optionally wherein the cryoprotectant is a cryoprotectant solution, thereby preparing a formulated paste.

11. A method of preparing a pharmaceutical composition comprising:

(a) performing the method of claim 10 to make a formulated paste;

(b) freeze drying the formulated paste to prepare a freeze-dried product;

(c) milling the freeze-dried product to prepare a freeze-dried powder; and

(d) combining the freeze-dried powder with one or more excipients to prepare a pharmaceutical composition.

12. The method of claim 10 or 11, wherein the cryoprotectant is mixed with the pellet in a ratio of 0.1 to 0.25 gram (g) cryoprotectant per gram of pellet; or a ratio of 4 % to 10% (volume/volume).

13. The method of any one of claims 10 to 12, wherein the cryoprotectant comprises sucrose, dextran, or a combination thereof, optionally wherein the cryoprotectant comprises sucrose and dextran in equivalent amounts.

14. The method of any one of claims 10 to 13, wherein the cryoprotectant comprises sucrose, dextran, and L-cysteine HCl.

15. The method of any one of claims 10 to 13, wherein the cryoprotectant does not comprise L-cysteine HCl.

16. The method of any one of claims 10 to 15, wherein the cryoprotectant comprises about 10% to about 30% (weight/weight) sucrose;

about 10% to about 30% (weight/weight) dextran; or

about 10% to about 30% (weight/weight) sucrose and about 10% to about 30% (weight/weight) dextran.

17. The method of any one of claims 10 to 16, wherein the cryoprotectant comprises about 40% to about 80% (weight/weight) water.

18. The method of any one of claims 10 to 14, wherein the cryoprotectant comprises about 0.05% to about 0.6% (weight/weight) L-cysteine HCl.

19. The method of any one of claims 10 to 14, wherein the cryoprotectant comprises about 0.25% to about 5% (weight/weight) L-cysteine HCl.

20. A pharmaceutical agent comprising bacteria, wherein the pharmaceutical agent maintains its stability.

21. The pharmaceutical agent of claim 20, wherein the water content of the pharmaceutical agent is between about 0.5% and about 9%.

22. The pharmaceutical agent of claim 20 or 21, wherein the pharmaceutical agent maintains its water content.

23. The pharmaceutical agent of any one of claims 20 to 22, wherein the pharmaceutical agent is of bacterial origin;

the pharmaceutical agent is a powder that comprises the bacteria and/or components thereof; comprises additional agents; and/or

the pharmaceutical agent is a freeze dried powder of bacteria and/or components thereof that optionally, further comprise additional agents.

24. A solid dosage form comprising a pharmaceutical agent of any one of claims 1 to 8 or 20 to 23.

25. The solid dosage form of claim 24, wherein the solid dosage form is enteric coated;

optionally wherein the solid dosage form comprises a capsule; optionally wherein the capsule is a size 00, size 0, size 1, size 2, size 3, size 4, or size 5 capsule, optionally wherein the capsule comprises HPMC (hydroxyl propyl methyl cellulose) or gelatin;

optionally wherein the solid dosage form comprises a tablet, optionally wherein the tablet is a 5mm, 6mm, 7mm, 8mm, 9mm, 10mm, 11mm, 12mm, 13mm, 14mm, 15mm, 16mm, 17mm, or 18mm tablet;

optionally wherein the solid dosage form comprises a minitablet, optionally wherein the minitablet is about a 1mm minitablet to a 4mm minitablet; and/or

optionally wherein the solid dosage form comprises a plurality of enterically coated minitablets contained in a capsule, optionally wherein the minitablets are 3mm in size, optionally wherein the capsule comprises HPMC (hydroxyl propyl methyl cellulose) or gelatin.

26. The solid dosage form of claim 25, wherein:

the enteric coating comprises one enteric coating;

the enteric coating comprises an inner enteric coating and an outer enteric coating;

the enteric coating comprises an inner enteric coating and an outer enteric coating, and wherein the inner and outer enteric coatings are not identical;

the enteric coating comprises a polymethacrylate-based copolymer;

the enteric coating comprises a methacrylic acid ethyl acrylate (MAE) copolymer (1:1);

the one enteric coating comprises methacrylic acid ethyl acrylate (MAE) copolymer (1:1);

the one enteric coating comprises a Eudragit copolymer;

the enteric coating comprises cellulose acetate phthalate (CAP), cellulose acetate trimellitate (CAT), poly(vinyl acetate phthalate) (PVAP), hydroxypropyl methylcellulose phthalate (HPMCP), a fatty acid, a wax, shellac (esters of aleurtic acid), a plastic, a plant fiber, zein, Aqua-Zein (an aqueous zein formulation containing no alcohol), amylose starch, a starch derivative, a dextrin, a methyl acrylate-methacrylic acid copolymer, cellulose acetate succinate, hydroxypropyl methyl cellulose acetate succinate (hypromellose acetate succinate), a methyl methacrylate-methacrylic acid copolymer, or sodium alginate; and/or

the enteric coating comprises an anionic polymeric material.

27. The solid dosage form of any one of claims 24 to 26 or pharmaceutical agent of any one of claims 1 to 8 or 20 to 23, or pharmaceutical composition of claim 9 or the method of any one of claims 10 to 19, wherein the bacteria are of the genus *Lactococcus*, *Prevotella*, *Bifidobacterium*, or *Veillonella*.

28. The solid dosage form of any one of claims 24 to 26 or pharmaceutical agent of any one of claims 1 to 8 or 20 to 23, or pharmaceutical composition of claim 9 or the method of any one of claims 10 to 19, wherein the bacteria are of the species *Lactococcus lactis cremoris*, optionally the *Lactococcus lactis cremoris* is *Lactococcus lactis cremoris* Strain A (ATCC designation number PTA-125368); the bacteria are of the species *Veillonella parvula*, optionally the *Veillonella parvula* is *Veillonella parvula* (ATCC

designation number PTA-125691); the bacteria are of the species *Prevotella histicola*, optionally the *Prevotella histicola* is *Prevotella histicola* Strain B 50329 (NRRL accession number B 50329); or the bacteria are of the species *Bifidobacterium animalis*, optionally the *Bifidobacterium animalis* is *Bifidobacterium animalis ssp. lactis* (ATCC designation number PTA-125097).

29. The solid dosage form of any one of claims 24 to 26 or pharmaceutical agent of any one of claims 1 to 8 or 20 to 23, or pharmaceutical composition of claim 9 or the method of any one of claims 10 to 19, wherein the freeze-dried powder comprises *Prevotella* bacteria or *Veillonella* bacteria;

the bacteria are a species listed in Table 1, Table 2, Table 3, or Table 4, optionally the bacteria are a bacterial strain that has at least 95% genomic, 16S ribosomal ribonucleic acid, or clustered regularly interspaced short palindromic repeats sequence identity with a strain listed in Table 1 or Table 3;

the bacteria are of a taxonomic group listed in Table 1, Table 2, Table 3, or Table 4;

the bacteria are a bacterial strain listed in Table 1, Table 2, Table 3, or Table 4;

the bacteria are of a taxonomic group listed in Table J; and/or

the bacteria are a bacterial strain listed in Table J.

30. A method of preventing or treating a disease of a subject, the method comprising administering to the subject a solid dosage form of any one of claims 24 to 26.

31. Use of a pharmaceutical agent of any one of claims 1 to 8 or 20 to 23, or pharmaceutical composition of claim 9, or solid dosage form of any one of claims 24 to 26 for the treatment or prevention of a disease of a subject.

32. Use of a pharmaceutical agent of any one of claims 1 to 8 or 20 to 23, or pharmaceutical composition of claim 9, or solid dosage form of any one of claims 24 to 26 for the preparation of a medicament for treating or preventing a disease in a subject.

33. A pharmaceutical agent of any one of claims 1 to 8 or 20 to 23, or pharmaceutical composition of claim 9, or solid dosage form of any one of claims 24 to 26 for use in the treatment or prevention of a disease of a subject.

34. A cryoprotectant for use in preparing a pharmaceutical agent that comprises bacteria, optionally wherein the cryoprotectant is a cryoprotectant solution.

35. A method of preparing a pharmaceutical agent, the method comprising combining bacteria with a cryoprotectant, optionally wherein the cryoprotectant is a cryoprotectant solution, thereby preparing a formulated paste.

36. The cryoprotectant of claim 34 or the method of claim 35 or 36, wherein:

the cryoprotectant comprises sucrose;

the cryoprotectant comprises dextran;

the cryoprotectant comprises sucrose and dextran, optionally the cryoprotectant comprises sucrose and dextran in equivalent amounts;

the cryoprotectant comprises sucrose, dextran, and L-cysteine HCl; and/or

the cryoprotectant does not comprise L-cysteine HCl.

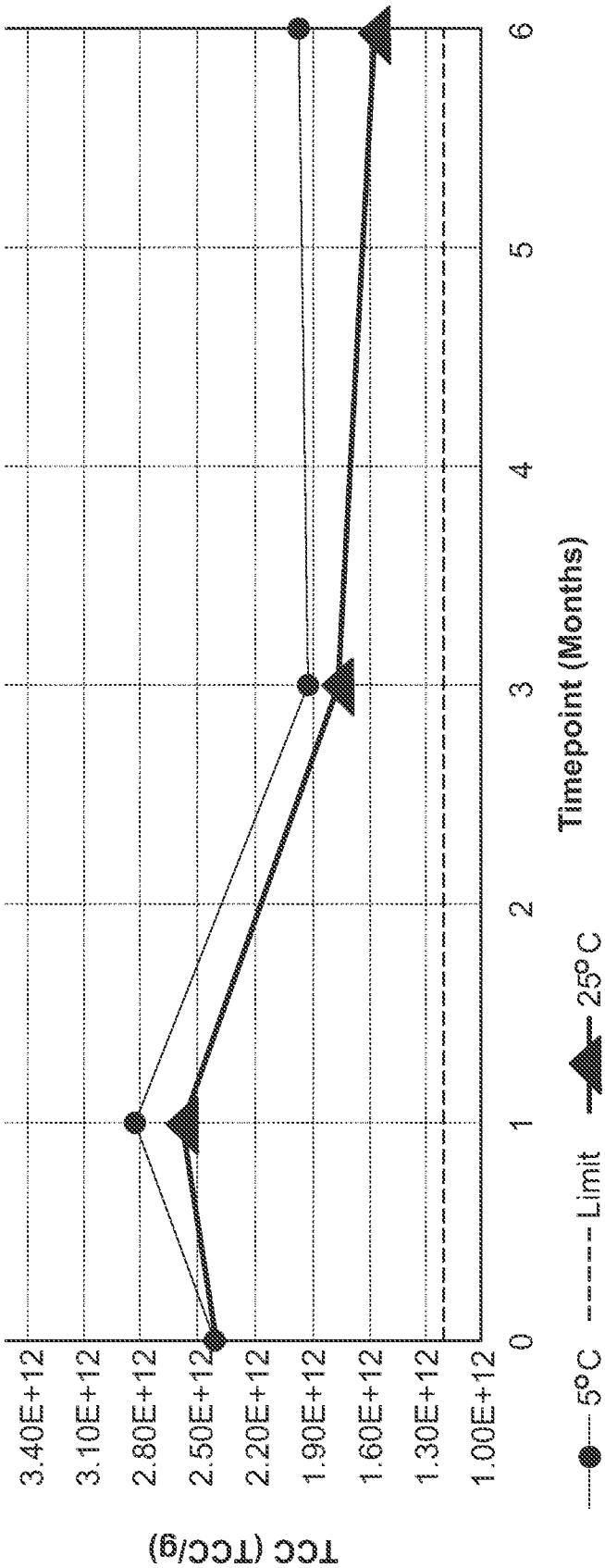

TCC (TCC/g)
3.40E+12
3.10E+12
2.80E+12
2.50E+12
2.20E+12
1.90E+12
1.60E+12
1.30E+12
1.00E+12
0
1
2
3
4
5
6
Timepoint (Months)
5°C
Limit
25°C

FIG. 1

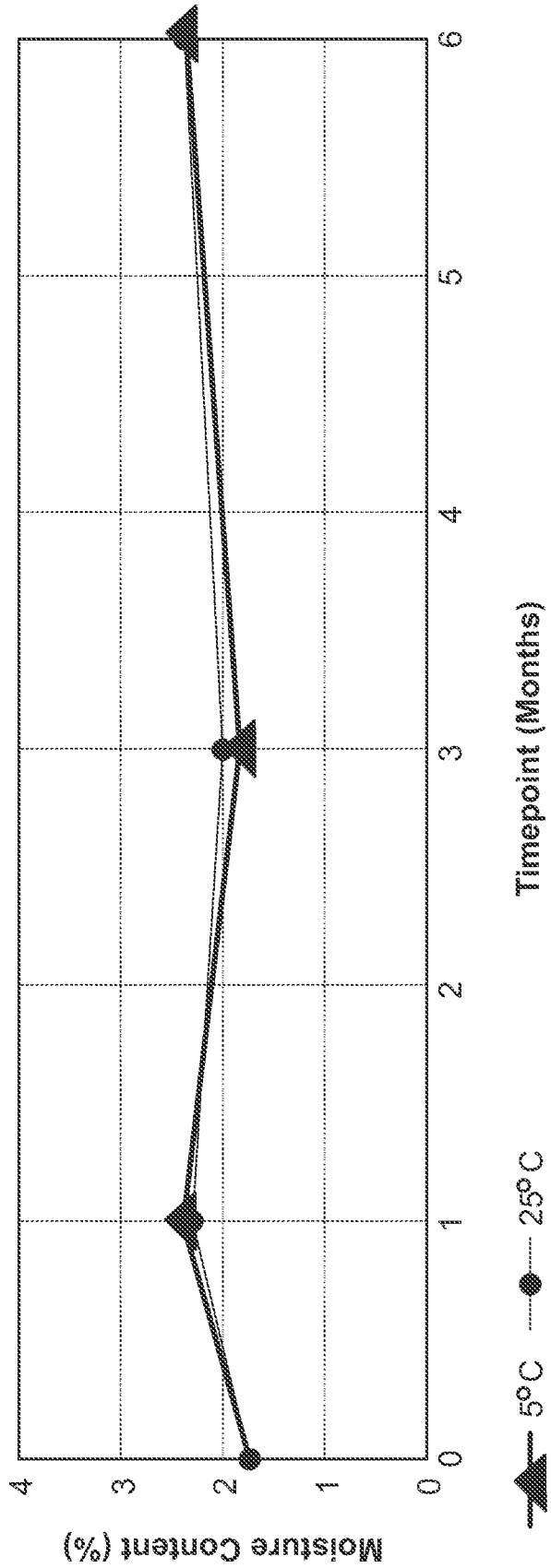


FIG. 2

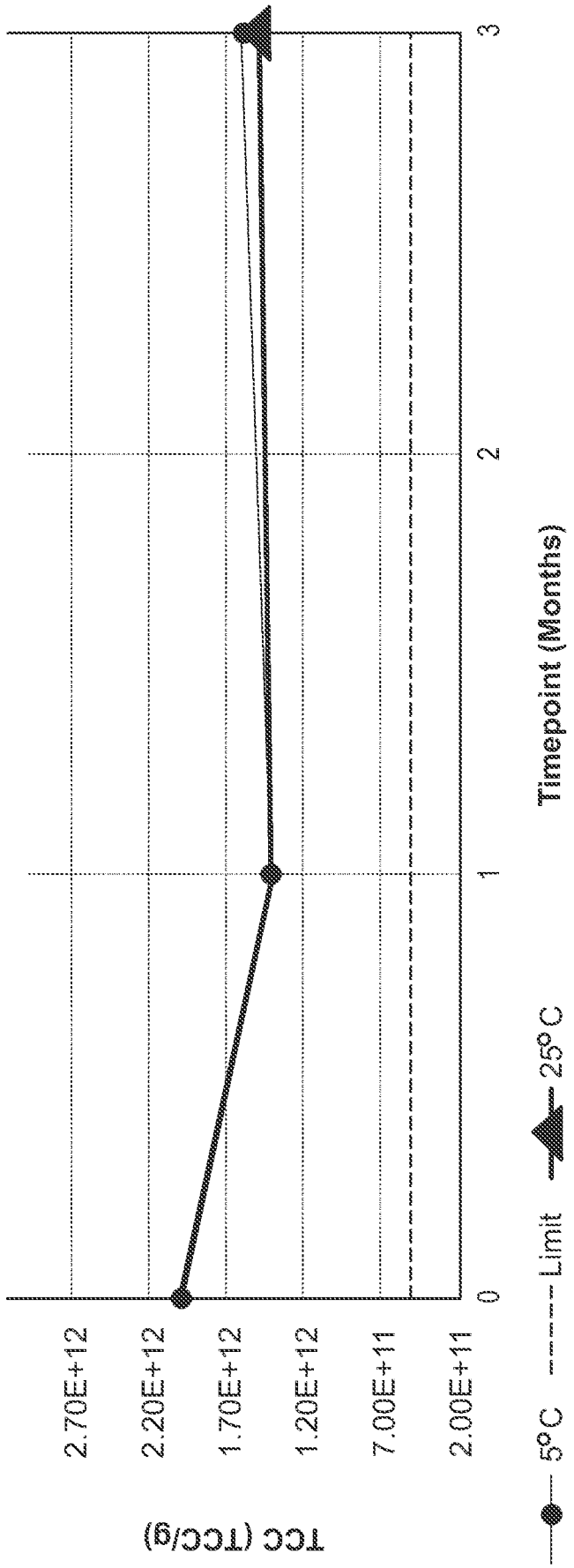

TCC (TCC/g)
2.70E+12
2.20E+12
1.70E+12
1.20E+12
7.00E+11
2.00E+11
0
1
2
3
Timepoint (Months)
5°C
Limit
25°C

FIG. 3

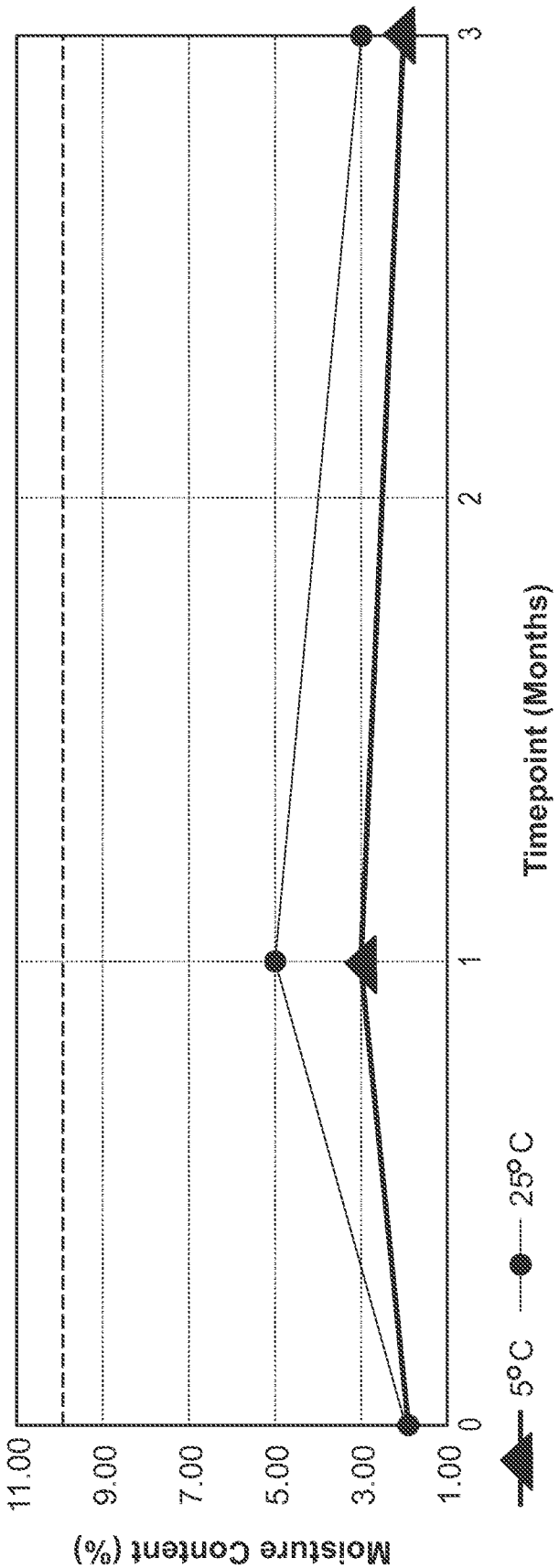

Moisture Content (%)
11.00
9.00
7.00
5.00
3.00
1.00
0
1
2
3
Timepoint (Months)
5°C
25°C

FIG. 4

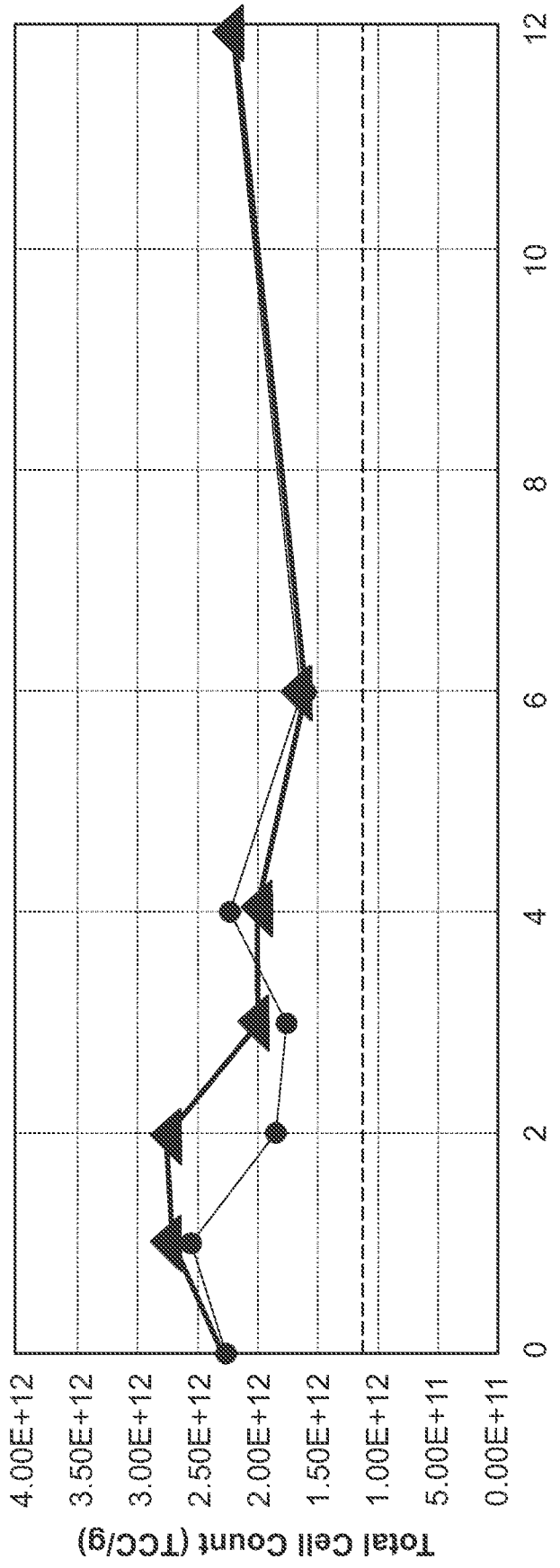

Total cell Count (TCC/g)
4.00E+12
3.50E+12
3.00E+12
2.50E+12
2.00E+12
1.50E+12
1.00E+12
5.00E+11
0.00E+11
0
2
4
6
8
10
12
Timepoint (Months)
5°C
25°C
Limit

FIG. 5

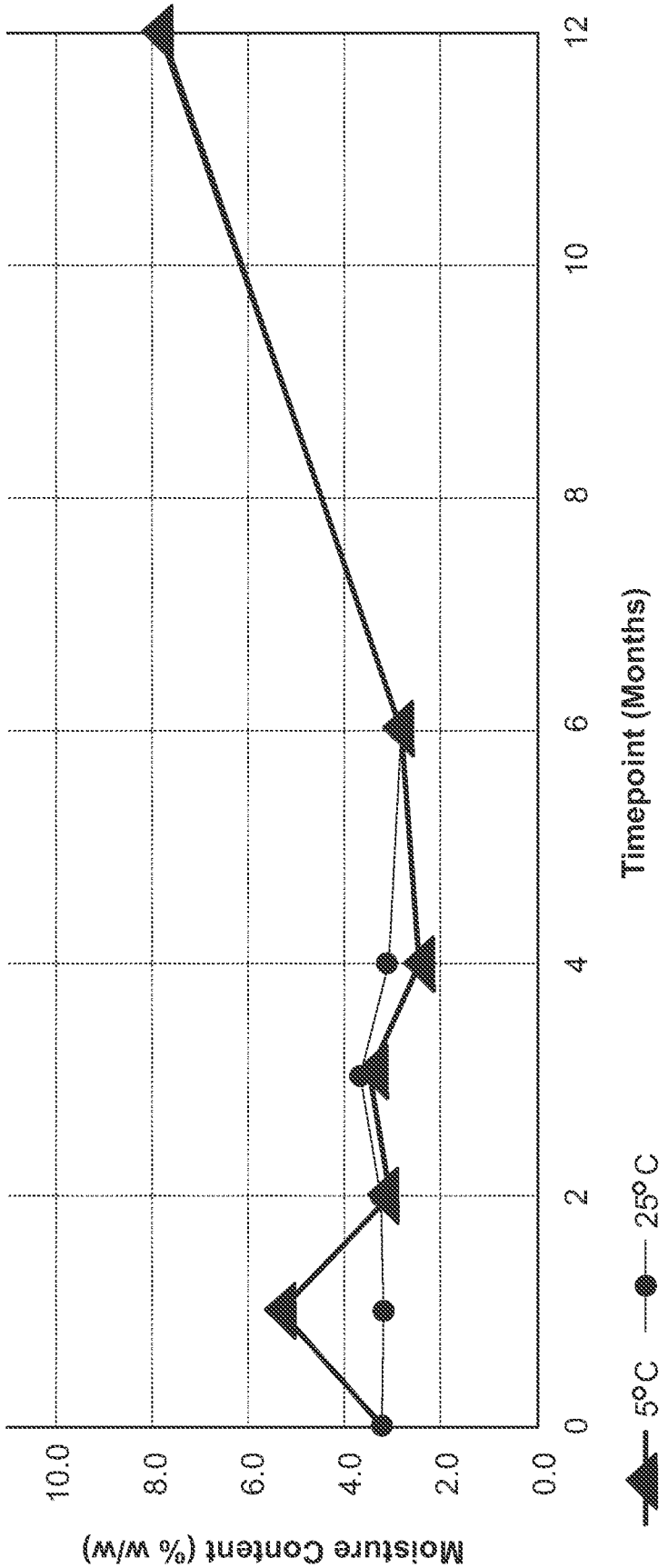

Moisture Content (% w/w)
10.0
8.0
6.0
4.0
2.0
0.0
0
2
4
6
8
10
12
Timepoint (Months)
5°C
25°C

FIG. 6

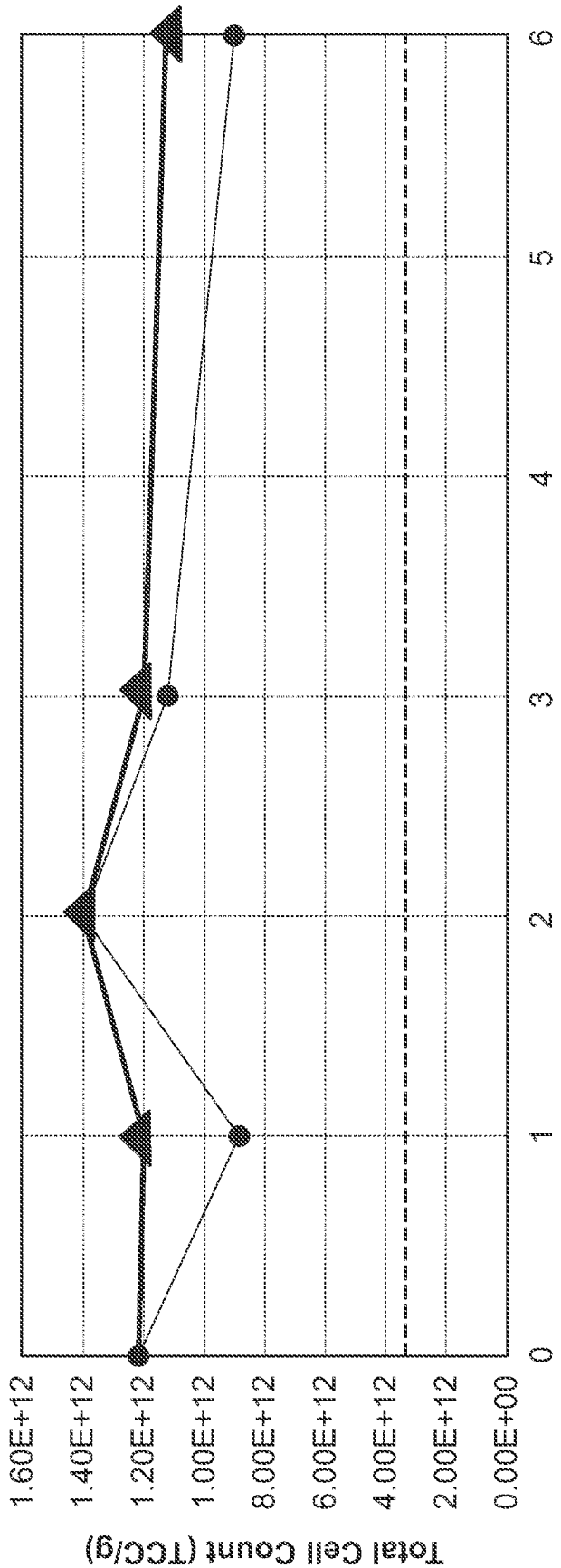

Total Cell Count (TCC/g)
1.60E+12
1.40E+12
1.20E+12
1.00E+12
8.00E+12
6.00E+12
4.00E+12
2.00E+12
0.00E+00
0
1
2
3
4
5
6
Timepoint (Months)
5°C
25°C
Limit

FIG. 7

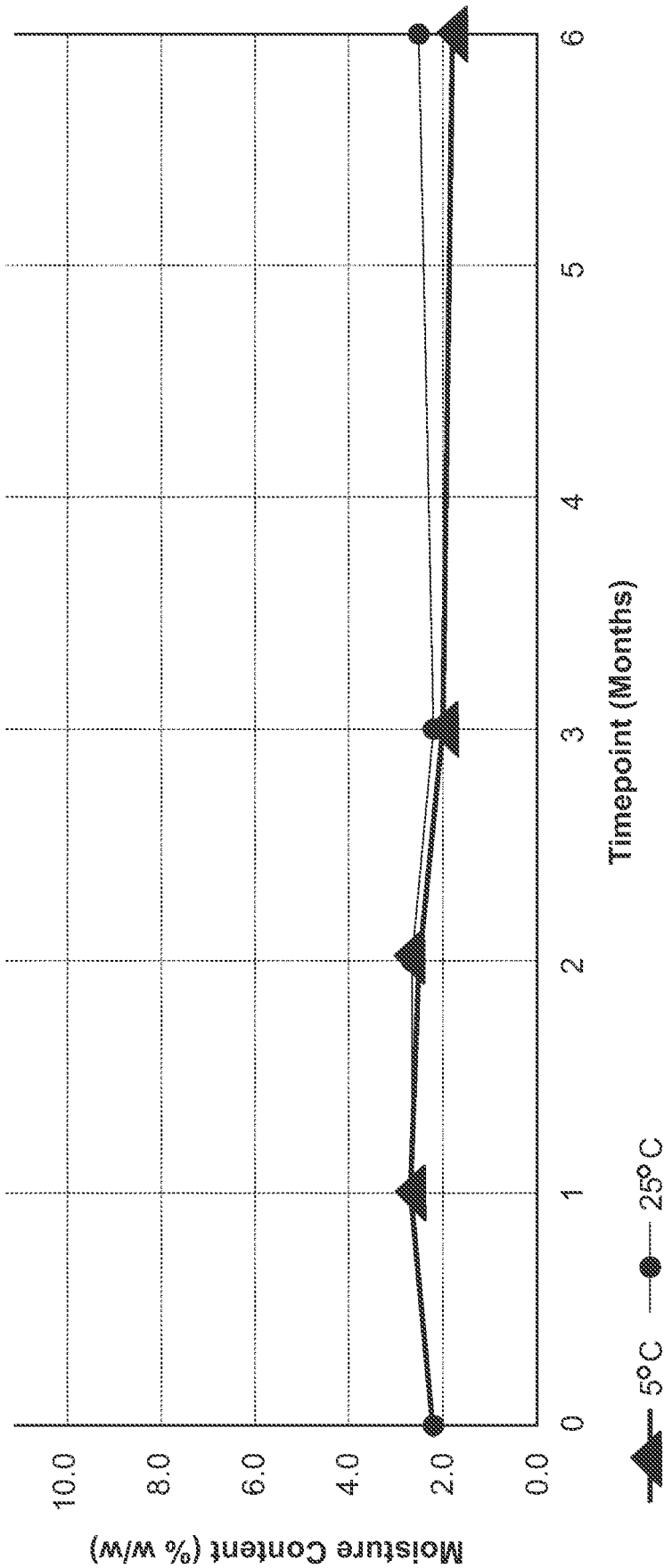

Moisture Content (% w/w)
10.0
8.0
6.0
4.0
2.0
0.0
0
1
2
3
4
5
6
Timepoint (Months)
5°C
25°C

FIG. 8

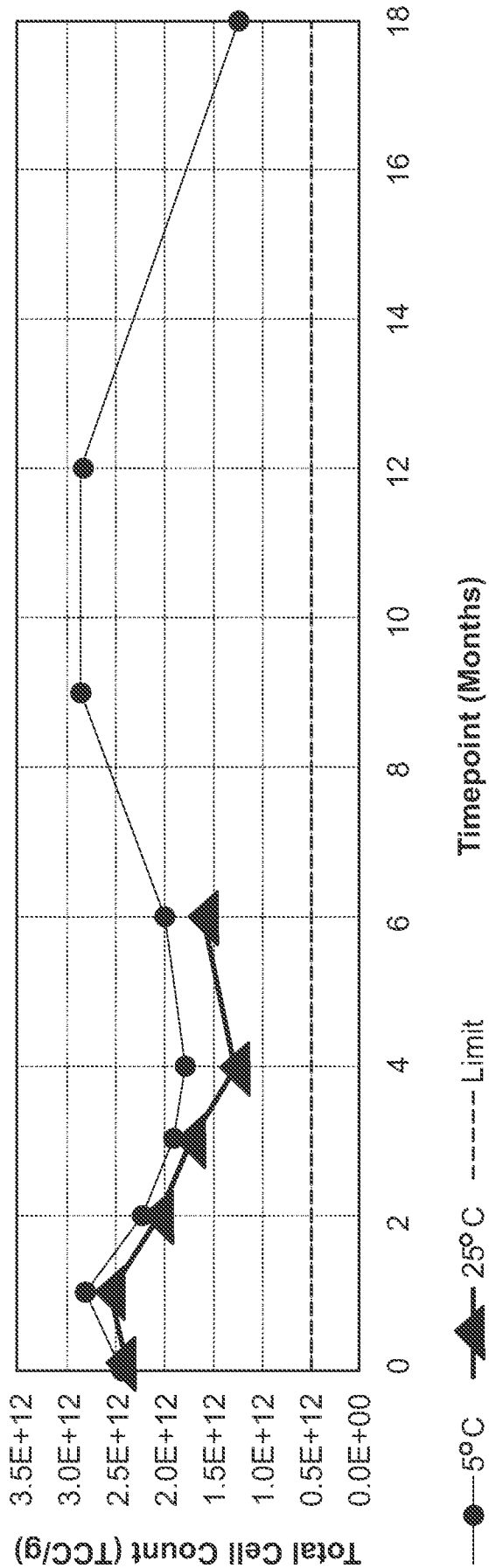

Total cell Count (TCC/g)
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
0.5E+12
0.0E+00
0
2
4
6
8
10
12
14
16
18
Timepoint (Months)
5°C
25°C
Limit

FIG. 9

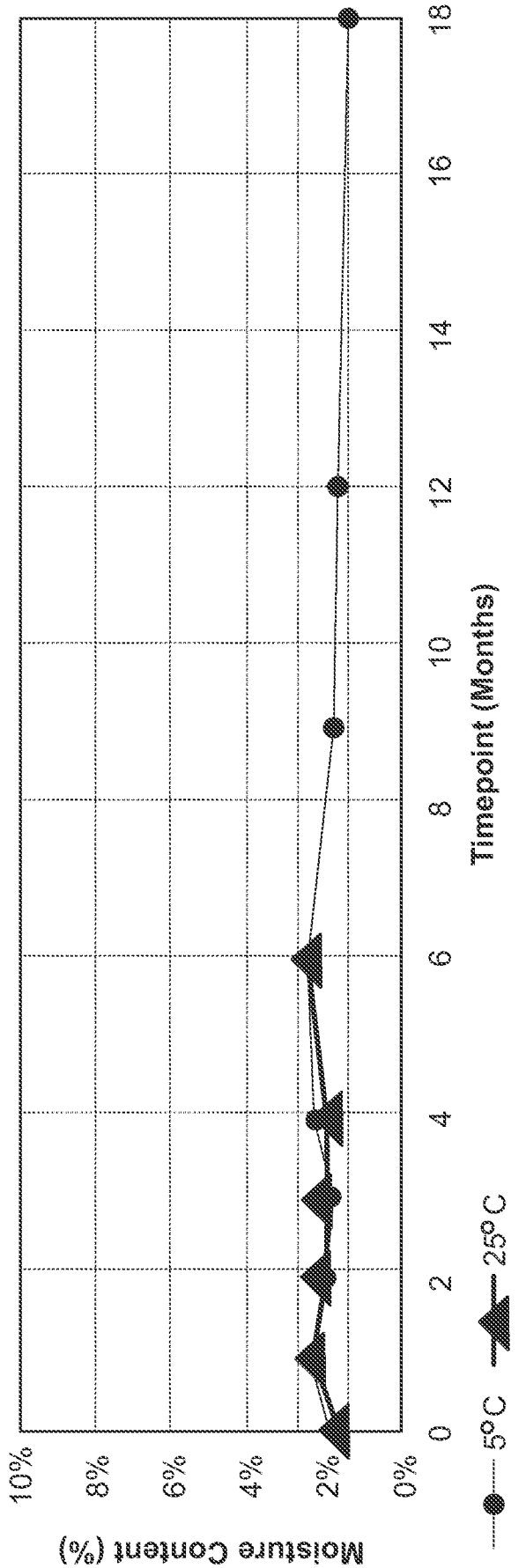

Moisture Content (%)
10%
8%
6%
4%
2%
0%
0
2
4
6
8
10
12
14
16
18
Timepoint (Months)
5°C
25°C

FIG. 10

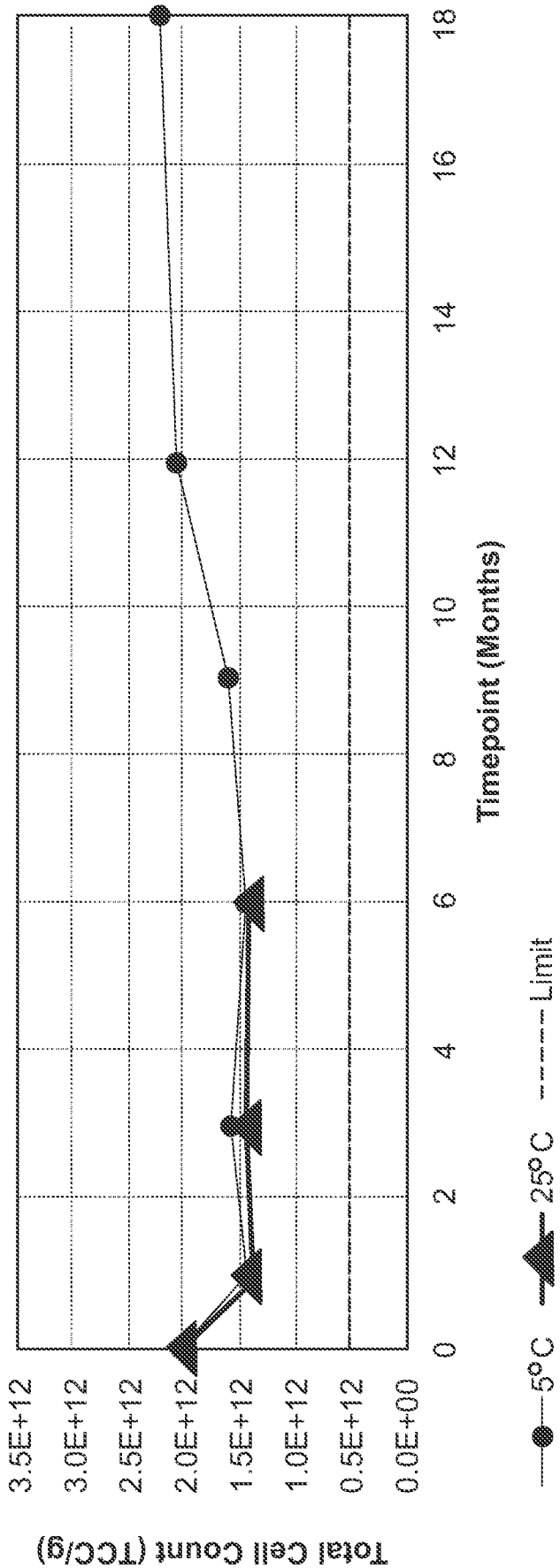

Total Cell Count (TCC/g)
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
0.5E+12
0.0E+00
0
2
4
6
8
10
12
14
16
18
Timepoint (Months)
5°C
25°C
Limit

FIG. 11

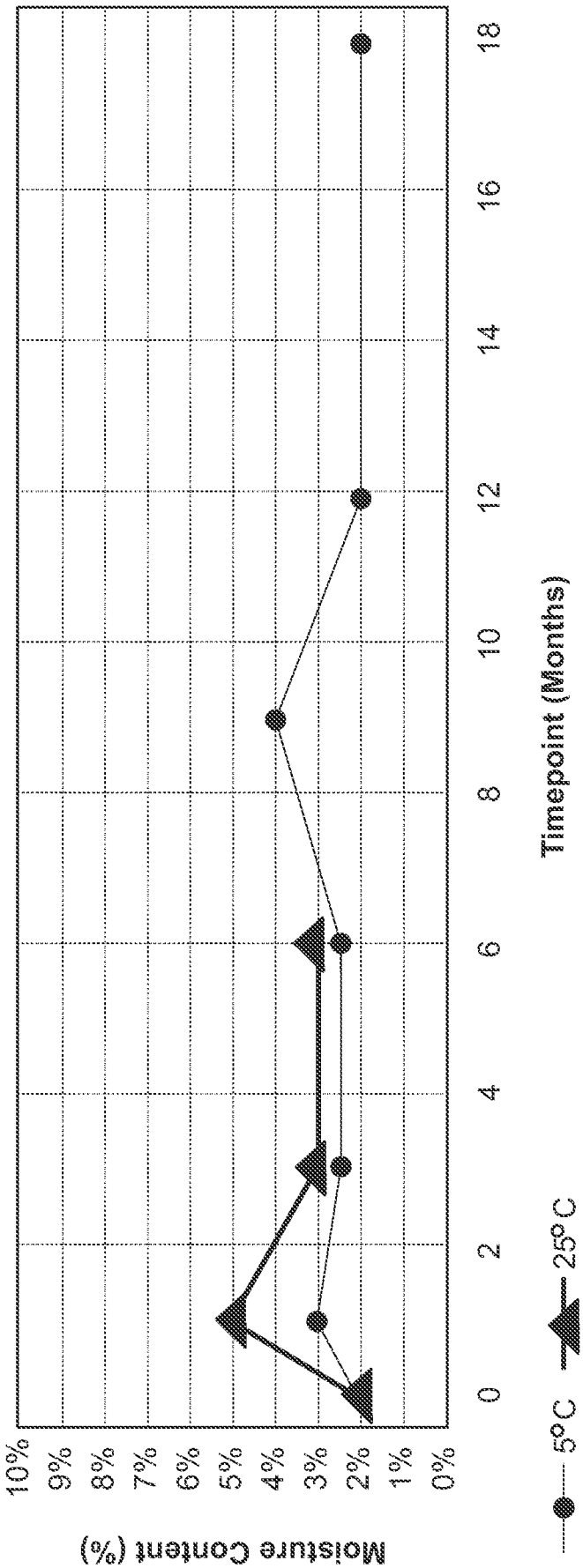

Moisture Content (%)
10%
9%
8%
7%
6%
5%
4%
3%
2%
1%
0%
0
2
4
6
8
10
12
14
16
18
Timepoint (Months)
5°C
25°C

FIG. 12

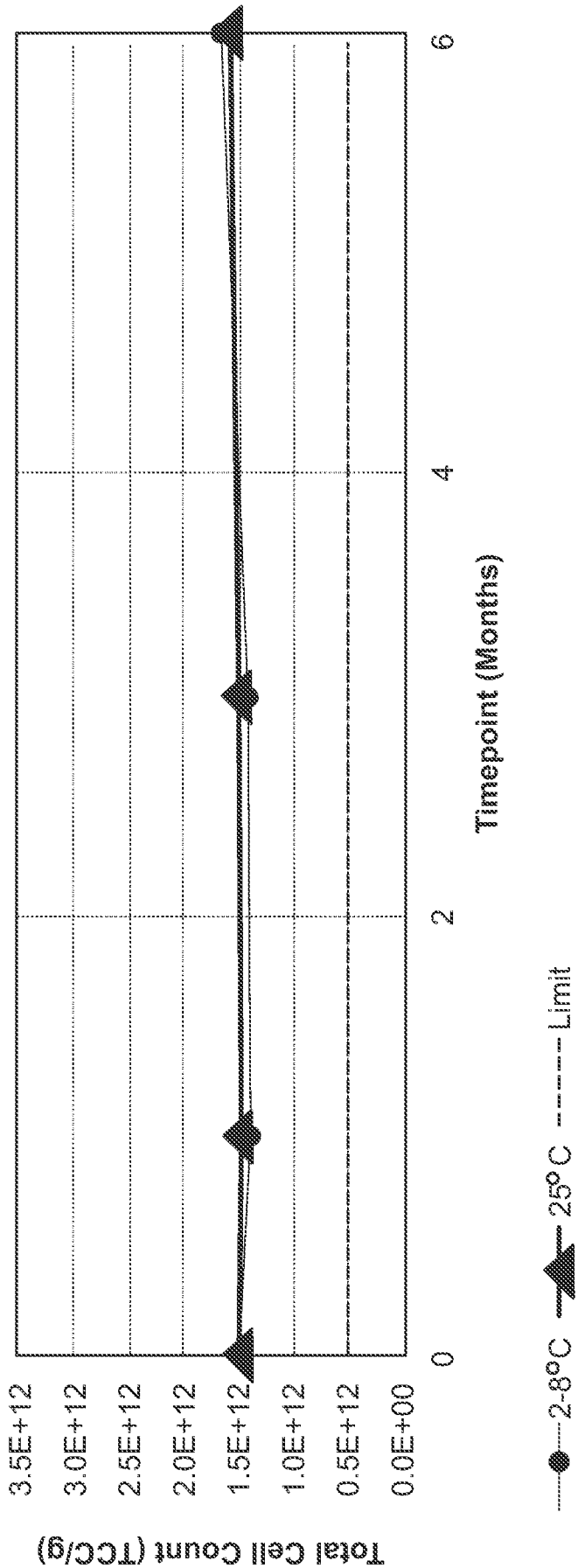

Total cell count (TCC/g)
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
0.5E+12
0.0E+00
0
2
4
6
Timepoint (Months)
2-8°C
25°C
Limit

FIG. 13

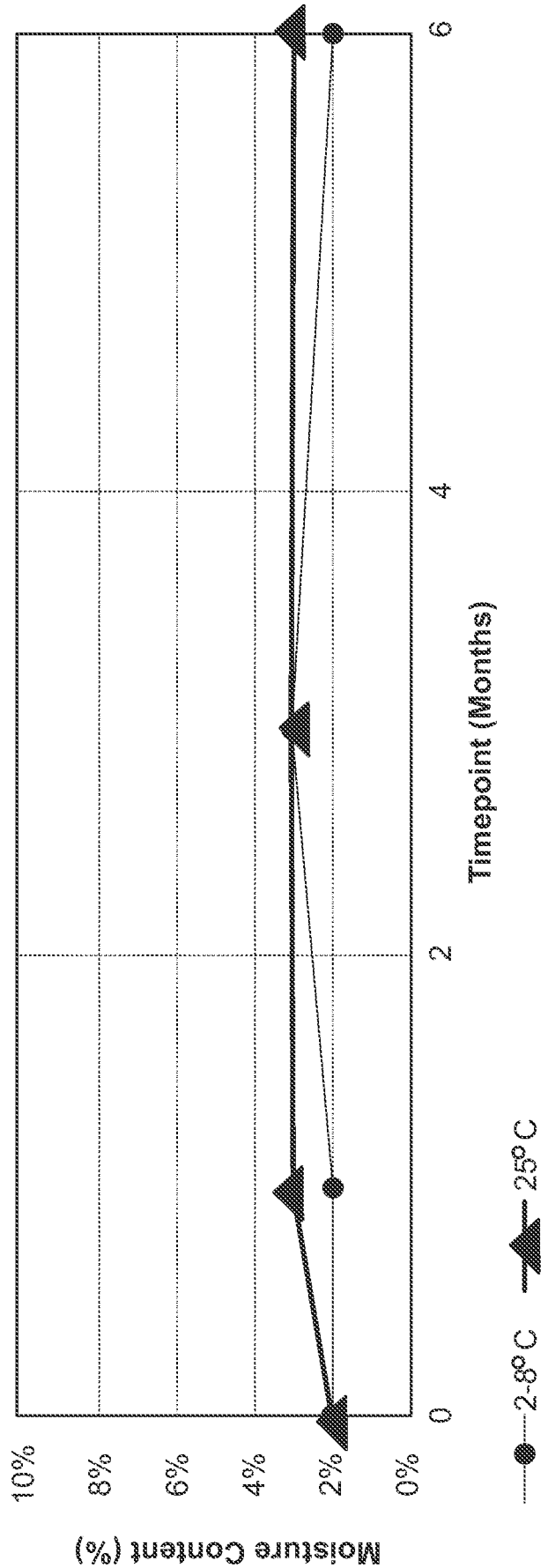


FIG. 14

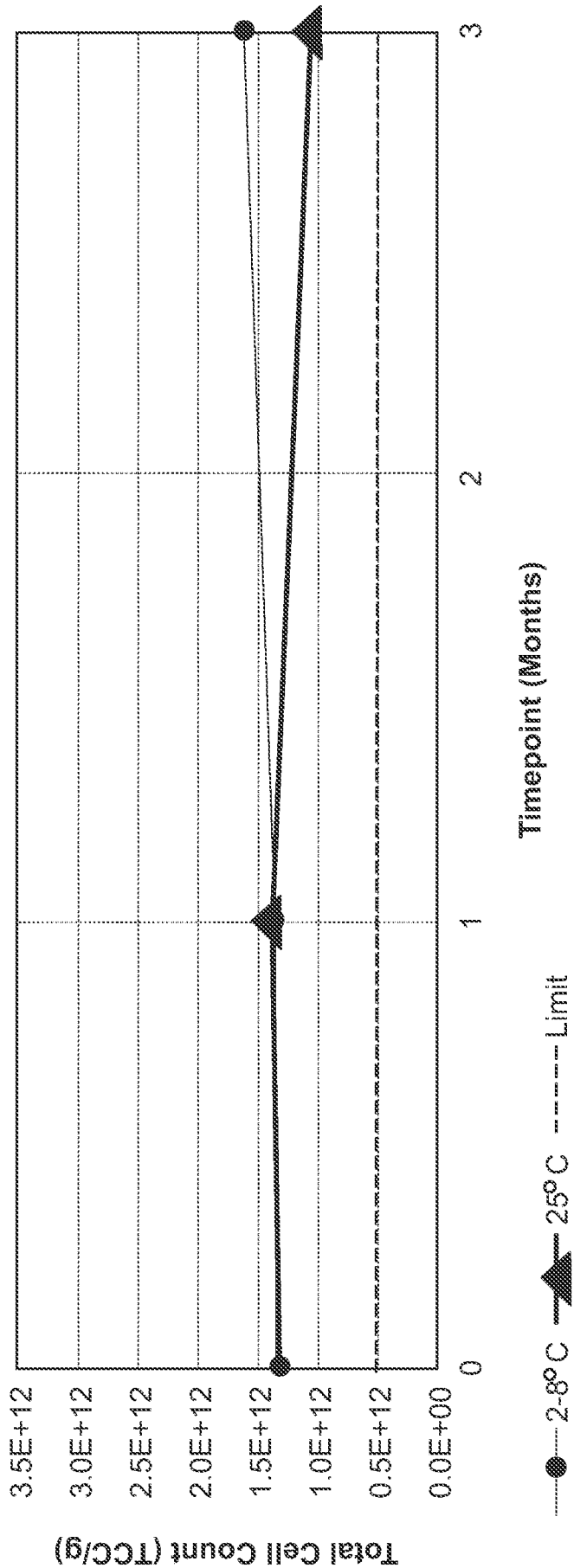

Total Cell Count (TCC/g)
3.5E+12
3.0E+12
2.5E+12
2.0E+12
1.5E+12
1.0E+12
0.5E+12
0.0E+00
0
1
2
3
Timepoint (Months)
2-8° C
25° C
Limit

FIG. 15

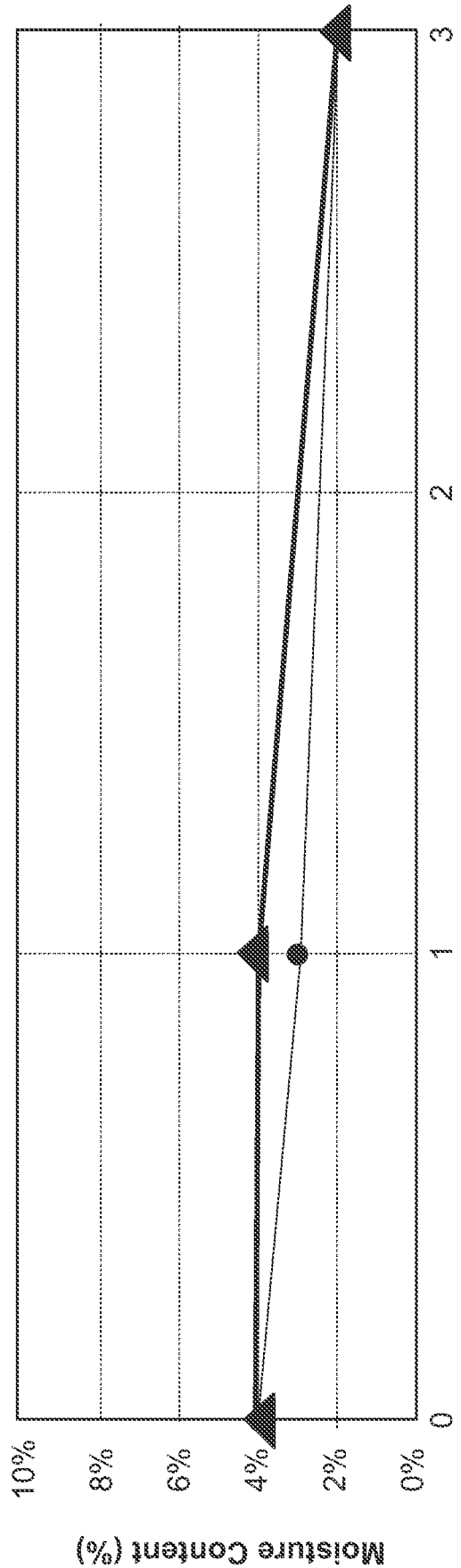


FIG. 16

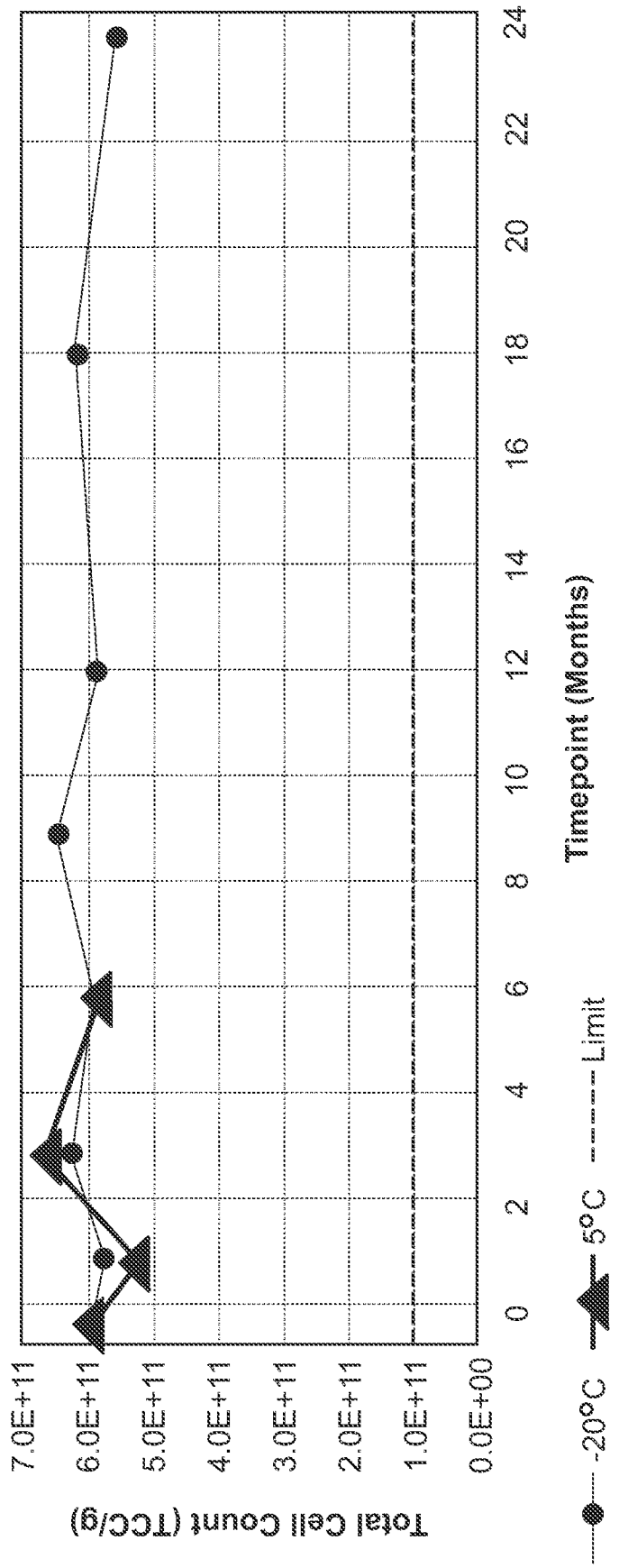

Total cell Count (TCC/g)
7.0E+11
6.0E+11
5.0E+11
4.0E+11
3.0E+11
2.0E+11
1.0E+11
0.0E+00
0
2
4
6
8
10
12
14
16
18
20
22
24
Timepoint (Months)
-20°C
5°C
Limit

FIG. 17

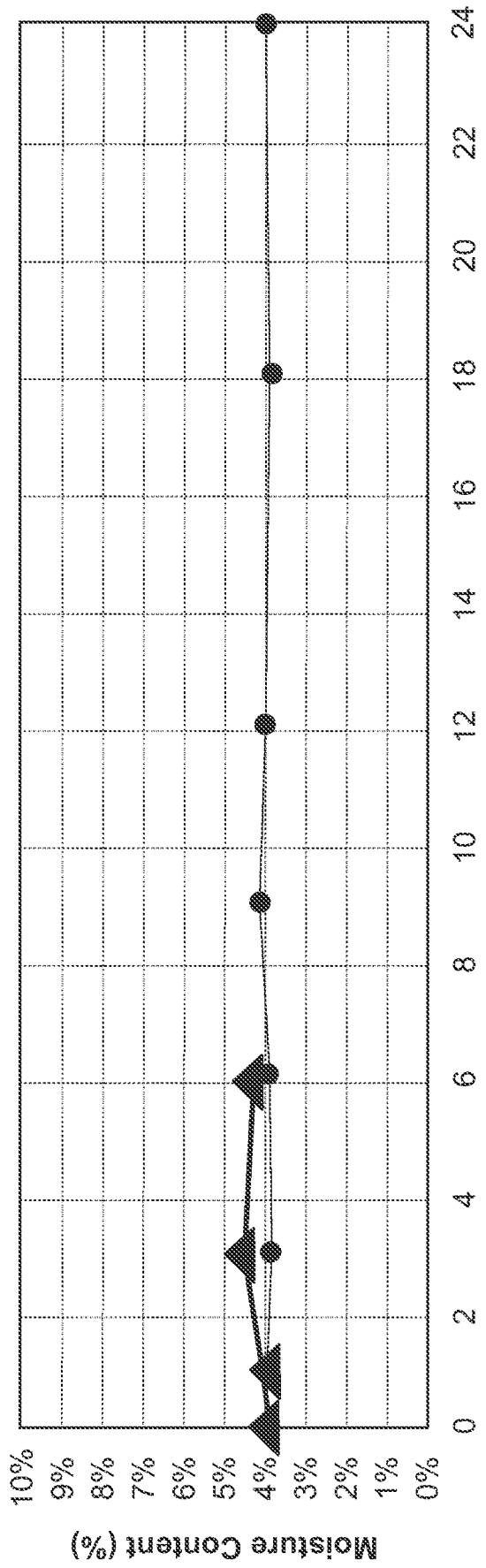

Moisture Content (%)
10%
9%
8%
7%
6%
5%
4%
3%
2%
1%
0%
0
2
4
6
8
10
12
14
16
18
20
22
24
Timepoint (Months)
-20°C
5°C

FIG. 18

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2022/023979

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K9/14 A61K9/19 A61K35/747
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2019/230183 A1 (HOKUKON CO LTD [JP]) 5 December 2019 (2019-12-05)	1-4,7,9, 20,23, 30-36
Y	paragraph [0042] paragraph [0063] claims 1-11	1-36

X	US 2020/179289 A1 (CARITE CHRISTOPHE [GB] ET AL) 11 June 2020 (2020-06-11)	1-4,9, 34-36
Y	example 3 paragraph [0086]	1-36

	-/--	

[x] Further documents are listed in the continuation of Box C.

[x] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance;; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the international search	Date of mailing of the international search report
12 July 2022	20/07/2022

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Sindel, Ulrike

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2022/023979

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2012/039853 A1 (CORVELEYN SAM [BE] ET AL) 16 February 2012 (2012-02-16)	1-4,6, 9-11,17, 20,23, 31-36
Y	claims 1-14 table 4a paragraph [0107] paragraph [0027] example 4	1-36
X	WO 2019/157003 A1 (EVELO BIOSCIENCES INC [US]) 15 August 2019 (2019-08-15)	3,20, 23-33
Y	table 1 paragraph [0120]	1-36
X	CN 110 251 474 A (UNIV BEIJING TECHNOLOGY & BUSINESS) 20 September 2019 (2019-09-20)	1-3,9, 20,23, 24,27, 30-36
Y	examples 4,5	1-36
X,P	WO 2021/252861 A1 (EVELO BIOSCIENCES INC [US]) 16 December 2021 (2021-12-16)	1-4,9, 20, 24-26, 30-33, 35,36
	claims 1-11, 60 example 1 paragraph [0527]	
Y	WO 2020/212961 A1 (PROBIOTICAL SPA [IT]) 22 October 2020 (2020-10-22) examples 1-5 page 11, line 26 - line 30	1-36

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2022/023979

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2019230183 A1	05-12-2019	CN 112088211 A	15-12-2020
		JP 7012840 B2	28-01-2022
		JP WO2019230183 A1	17-06-2021
		KR 20210005671 A	14-01-2021
		US 2021205378 A1	08-07-2021
		WO 2019230183 A1	05-12-2019
US 2020179289 A1	11-06-2020	AU 2018300358 A1	30-01-2020
		AU 2021201767 A1	15-04-2021
		CA 3068394 A1	17-01-2019
		CN 110892220 A	17-03-2020
		CN 112762661 A	07-05-2021
		DK 3652491 T3	05-07-2021
		EP 3652491 A1	20-05-2020
		EP 3978852 A1	06-04-2022
		ES 2878136 T3	18-11-2021
		GB 2564481 A	16-01-2019
		HR P20211227 T1	12-11-2021
		HU E055005 T2	28-10-2021
		IL 271979 A	30-06-2021
		IL 283604 A	01-02-2022
		JP 7049373 B2	06-04-2022
		JP 2020527688 A	10-09-2020
		JP 2022088502 A	14-06-2022
		KR 20200029497 A	18-03-2020
		LT 3652491 T	10-08-2021
		MD 3652491 T2	30-09-2021
		PL 3652491 T3	08-11-2021
		PT 3652491 T	15-07-2021
		SG 11202000223U A	27-02-2020
		SI 3652491 T1	30-09-2021
		TW 201934945 A	01-09-2019
		US 2020179289 A1	11-06-2020
		US 2022031621 A1	03-02-2022
		WO 2019012512 A1	17-01-2019
US 2012039853 A1	16-02-2012	AU 2010243906 A1	03-11-2011
		AU 2016201489 A1	24-03-2016
		CA 2760248 A1	04-11-2010
		CN 102414310 A	11-04-2012
		DK 2424972 T3	14-10-2013
		EP 2424972 A1	07-03-2012
		ES 2425385 T3	15-10-2013
		JP 5897459 B2	30-03-2016
		JP 6383717 B2	29-08-2018
		JP 2012525122 A	22-10-2012
		JP 2016105705 A	16-06-2016
		KR 20120022868 A	12-03-2012
		US 2012039853 A1	16-02-2012
		US 2017151292 A1	01-06-2017
		US 2020171105 A1	04-06-2020
		WO 2010124855 A1	04-11-2010
WO 2019157003 A1	15-08-2019	AU 2019217526 A1	13-08-2020
		BR 112020015639 A2	30-03-2021
		CA 3090166 A1	15-08-2019
		CN 112074283 A	11-12-2020
		CO 2020010956 A2	30-10-2020

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2022/023979

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		EP 3749340 A1	16-12-2020
		JP 2021512133 A	13-05-2021
		KR 20200118100 A	14-10-2020
		TW 201945015 A	01-12-2019
		US 2019350987 A1	21-11-2019
		US 2021330718 A1	28-10-2021
		WO 2019157003 A1	15-08-2019
CN 110251474 A	20-09-2019	NONE	
WO 2021252861 A1	16-12-2021	NONE	
WO 2020212961 A1	22-10-2020	CA 3136174 A1	22-10-2020
		EP 3956434 A1	23-02-2022
		JP 2022529449 A	22-06-2022
		KR 20220007617 A	18-01-2022
		US 2022195378 A1	23-06-2022
		WO 2020212961 A1	22-10-2020