WHAT IS CLAIMED IS:

1. A composition comprising:

(a) a therapeutically effective dose of purified, intact bacterially derived minicells comprising at least one anti-neoplastic agent, and

(b) an interferon type I agonist, an interferon type II agonist, or a combination of an interferon type I agonist and an interferon type II agonist.

2. The composition of claim 1, wherein element (b) of the composition comprises:

(i) a therapeutically effective dose of purified, intact bacterially derived minicells comprising an interferon type I agonist; or

(ii) a therapeutically effective dose of purified, intact bacterially derived minicells comprising an interferon type II agonist; or

(iii) a combination of:

(1) a therapeutically effective dose of purified, intact bacterially derived minicells comprising an interferon type I agonist; and

(2) a therapeutically effective dose of purified, intact bacterially derived minicells comprising an interferon type II agonist.

3. The composition of claim 1 or 2, wherein:

(a) the anti-neoplastic agent and the interferon type I agonist, the interferon type II agonist, or the combination of an interferon type I agonist and an interferon type II agonist, are packaged within two or more purified, intact bacterially derived minicells; or

(b) the anti-neoplastic agent and the interferon type I agonist, the interferon type II agonist, or the combination of an interferon type I agonist and an interferon type II agonist are packaged within three separate populations of purified, intact bacterially derived minicells.

4. The composition of any one of claims 1-3 comprising the anti-neoplastic agent, the interferon type I agonist, and the interferon type II agonist, wherein:

(a) the anti-neoplastic agent, the interferon type I agonist, and the interferon type II agonist are comprised within the same minicell;

(b) the anti-neoplastic agent and the interferon type I agonist are comprised within

a first minicell, and the interferon type II agonist is comprised within a second minicell;

(c) the anti-neoplastic agent and the interferon type II agonist are comprised within a first minicell, and the interferon type I agonist is comprised within a second minicell;

(d) the anti-neoplastic agent is comprised within a first minicell, and the interferon type I agonist and the interferon type II agonist are comprised within a second minicell; or

(e) the anti-neoplastic agent is comprised within a first minicell, the interferon type I agonist is comprised within a second minicell, and the interferon type II agonist is comprised within a third minicell.

5. The composition of any one of claims 1-4, wherein the composition does not comprise an interferon type I agonist.

6. The composition according to any one of claims 1-5, wherein:

(a) the anti-neoplastic agent is selected from the group consisting of a radionuclide, a chemotherapy drug, a functional nucleic acid, and a polynucleotide from which a functional nucleic acid can be transcribed; and/or

(b) the anti-neoplastic agent is a supertoxic chemotherapy drug; and/or

(c) the anti-neoplastic agent is a supertoxic chemotherapy drug selected from the group consisting of morpholinyl anthracycline, a maytansinoid, ducarmycin, auristatins, calicheamicins (DNA damaging agents), α-amanitin (RNA polymerase II inhibitor), centanamycin, pyrrolobenzodiazepine, streptonigtin, nitrogen mustards, nitrosorueas, alkane sulfonates, pyrimidine analogs, purine analogs, antimetabolites, folate analogs, anthracyclines, taxanes, vinca alkaloids, topoisomerase inhibitors, hormonal agents, and a combination thereof; and/or

(d) the anti-neoplastic agent is a supertoxic chemotherapy drug which is morpholinyl anthracycline which is selected from the group consisting of nemorubicin, PNU-159682, idarubicin, daunorubicin, caminomycin, andoxorubicin; and/or

(e) the anti-neoplastic agent is a supertoxic chemotherapy drug which is PNU-159682; and/or

(f) the anti-neoplastic agent is a functional nucleic acid selected from the group consisting of a siRNA, a miRNA, a shRNA, a lincRNA, an antisense RNA, and a ribozyme; and/or

(g) the anti-neoplastic agent is a functional nucleic acid selected from the group consisting of a siRNA, a miRNA, a shRNA, a lincRNA, an antisense RNA, and a ribozyme, wherein the functional nucleic acid inhibits a gene that promotes tumor cell proliferation, angiogenesis or resistance to chemotherapy and/or that inhibits apoptosis or cell cycle arrest, and optionally wherein (i) the siRNA inhibits ribonucleotide reductase M1 (RRM1) expression; (ii) the siRNA inhibits Polo like kinase 1 (Plk1) expression; or (iii) the miRNA is miRNA16a.

7. The composition according to any one of claims 1-6, wherein:

(a) the interferon type I agonist, the interferon type II agonist, or the combination of an interferon type I agonist and an interferon type II agonist is an oligonucleotide; and/or

(b) the interferon type I agonist, the interferon type II agonist, or the combination of an interferon type I agonist and an interferon type II agonist is an oligonucleotide and wherein the oligonucleotide comprises a sequence of at least about 40 nucleotides, at least about 50 nucleotides, or at least about 60 nucleotides; and/or

(c) the interferon type I agonist, the interferon type II agonist, or the combination of an interferon type I agonist and an interferon type II agonist is an oligonucleotide and wherein the oligonucleotide is a polynucleotide product of PNPase1, poly(I:C), poly-ICLC, imiquimod, imidazoquiolineresquimod, cGAMP or CpG-oligodeoxynucleotides.

8. The composition according to any one of claims 1-7, wherein the interferon type I agonist is selected from the group consisting of double stranded RNA (dsRNA), poly(dA:dT) DNAs, double stranded Z-DNA and B-DNA, DNAs (dsDNAs) longer than 36 bp and DNA-RNA hybrids, bacterial second messenger cyclic-di-GMP, TLR3, TLR4, TLR7, TLR8 and TLR9 agonists, STING Agonists, and a combination thereof.

9. The composition according to any one of claims 1-8, wherein:

(a) the interferon type II agonist is selected from the group consisting of C-glycosidic form of α-galactosylceramide (α-C-GalCer), α-galactosylceramide (α-GalCer), 12 carbon acyl form of galactosylceramide (β-GalCer), β-D-glucopyranosylceramide (β-GlcCer), l,2-Diacyl-3-0-galactosyl-sn-glycerol (BbGL-II), diacylglycerol containing glycolipids (Glc-DAG-s2), ganglioside (GD3), gangliotriaosylceramide (Gg3Cer), glycosylphosphatidylinositol (GPI), α-glucuronosylceramide (GSL-1 or GSL-4),

isoglobotrihexosylceramide (iGb3), lipophosphoglycan(LPG), lyosphosphatidylcholine (LPC), α-galactosylceramide analog (OCH), threitolceramide, and a combination thereof; and/or

(b) the interferon type II agonist is α-galactosylceramide (α-GalCer).

10. The composition according to any one of claims 1-9, further comprising:

(a) a bispecific ligand bound to the minicells comprising the anti-neoplastic agent; and/or

(b) a bispecific ligand bound to the minicells comprising the type I interferon agonist; and/or

(c) a bispecific ligand bound to the minicells comprising the type II interferon agonist.

11. The composition according to claim 10, wherein the bispecific ligand:

(a) comprises a first arm that carries specificity for a minicell surface structure and a second arm that carries specificity for a non-phagocytotic mammalian cell surface receptor; and/or

(b) comprises a first arm that carries specificity for a minicell surface structure and a second arm that carries specificity for a non-phagocytotic mammalian cell surface receptor and wherein the minicell surface structure is an O-polysaccharide component of a lipopolysaccharide on the minicell surface; and/or

(c) comprises a first arm that carries specificity for a minicell surface structure and a second arm that carries specificity for a non-phagocytotic mammalian cell surface receptor wherein the non-phagocytotic mammalian cell surface receptor is capable of activating receptor-mediated endocytosis of the minicell; and/or

(d) comprises a bispecific antibody or antibody fragment; and/or

(e) comprises a bispecific antibody or antibody fragment and wherein the antibody or antibody fragment comprises a first multivalent arm that carries specificity for a bacterially derived minicell surface structure and a second multivalent arm that carries specificity for a cancer cell surface receptor, wherein the cancer cell surface receptor is capable of activating receptor-mediated endocytosis of the minicell.

12. The composition of any one of claims 1-11, wherein the composition comprises fewer than about 1 contaminating parent bacterial cell per 10^7minicells, fewer than about 1 contaminating parent bacterial cell per 10^8minicells, fewer than about 1 contaminating parent bacterial cell per 10^9minicells, fewer than about 1 contaminating parent bacterial cell per 10^{10}minicells, or fewer than about 1 contaminating parent bacterial cell per 10^{11}minicells.

13. The composition of any one of claims 1-12, further comprising a pharmaceutically acceptable carrier.

14. The composition of any one of claims 1-13, wherein the minicells are approximately 400 nm in diameter.

15. The composition of any one of claims 1-14, wherein the composition is free of parent bacterial cell contamination removable through 200 nm filtration.

16. The composition of any one of claims 1-15, wherein the composition comprises the following amount of minicells or killed bacterial cells:

(a) at least about 10^9;
(b) at least about 1 x10^9;
(c) at least about 2 x 10^9;
(d) at least about 5 x 10^9;
(e) at least 8 x 10^9;
(f) no more than about 10^{11};
(g) no more than about 1 x 10^{11};
(h) no more than about 9 x 10^{10}; or
(i) no more than about 8 x 10^{10}.

17. The composition according to any one of claims 1-16 for use in a method of treating a subject in need, comprising administering to the subject an effective amount of the composition.

18. The composition of claim 17, wherein the subject is a human, a non-human primate, a dog, a cat, a cow, a sheep, a horse, a rabbit, a mouse, or a rat.

19. The composition of claim 17 or 18, wherein:

(a) the subject is suffering from a cancer; and/or

(b) the subject is suffering from a cancer and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, brain cancer, liver cancer, colon cancer, pancreatic cancer, and bladder cancer; and/or

(c) the subject is suffering from a cancer and wherein the cancer is selected from the group consisting of an acute lymphoblastic leukemia; acute myeloid leukemia; adrenocortical carcinoma; AIDS-related cancers; AIDS-related lymphoma; anal cancer; appendix cancer; astrocytomas; atypical teratoid/rhabdoid tumor; basal cell carcinoma; bladder cancer; brain stem glioma; brain tumor; breast cancer; bronchial tumors; Burkitt lymphoma; cancer of unknown primary site; carcinoid tumor; carcinoma of unknown primary site; central nervous system atypical teratoid/rhabdoid tumor; central nervous system embryonal tumors; cervical cancer; childhood cancers; chordoma; chronic lymphocytic leukemia; chronic myelogenous leukemia; chronic myeloproliferative disorders; colon cancer; colorectal cancer; craniopharyngioma; cutaneous T-cell lymphoma; endocrine pancreas islet cell tumors; endometrial cancer; ependymoblastoma; ependymoma; esophageal cancer; esthesioneuroblastoma; Ewing sarcoma; extracranial germ cell tumor; extragonadal germ cell tumor; extrahepatic bile duct cancer; gallbladder cancer; gastric (stomach) cancer; gastrointestinal carcinoid tumor; gastrointestinal stromal cell tumor; gastrointestinal stromal tumor (GIST); gestational trophoblastic tumor; glioma; hairy cell leukemia; head and neck cancer; heart cancer; Hodgkin lymphoma; hypopharyngeal cancer; intraocular melanoma; islet cell tumors; Kaposi sarcoma; kidney cancer; Langerhans cell histiocytosis; laryngeal cancer; lip cancer; liver cancer; malignant fibrous histiocytoma bone cancer; medulloblastoma; medulloepithelioma; melanoma; Merkel cell carcinoma; Merkel cell skin carcinoma; mesothelioma; metastatic squamous neck cancer with occult primary; mouth cancer; multiple endocrine neoplasia syndromes; multiple myeloma; multiple myeloma/plasma cell neoplasm; mycosis fungoides; myelodysplastic syndromes; myeloproliferative neoplasms; nasal cavity cancer; nasopharyngeal cancer; neuroblastoma; Non-Hodgkin lymphoma; nonmelanoma skin cancer; non-small cell lung cancer; oral cancer; oral cavity cancer; oropharyngeal cancer; osteosarcoma; other brain and spinal cord tumors; ovarian cancer; ovarian epithelial cancer; ovarian germ cell tumor; ovarian low malignant

potential tumor; pancreatic cancer; papillomatosis; paranasal sinus cancer; parathyroid cancer; pelvic cancer; penile cancer; pharyngeal cancer; pineal parenchymal tumors of intermediate differentiation; pineoblastoma; pituitary tumor; plasma cell neoplasm/multiple myeloma; pleuropulmonaryblastoma; primary central nervous system (CNS) lymphoma; primary hepatocellular liver cancer; prostate cancer; rectal cancer; renal cancer; renal cell (kidney) cancer; renal cell cancer; respiratory tract cancer; retinoblastoma; rhabdomyosarcoma; salivary gland cancer; Sezary syndrome; small cell lung cancer; small intestine cancer; soft tissue sarcoma; squamous cell carcinoma; squamous neck cancer; stomach (gastric) cancer; supratentorial primitive neuroectodermal tumors; T-cell lymphoma; testicular cancer; throat cancer; thymiccarcinoma; thymoma; thyroid cancer; transitional cell cancer; transitional cell cancer of the renal pelvis and ureter; trophoblastic tumor; ureter cancer; urethral cancer; uterine cancer; uterine sarcoma; vaginal cancer; vulvar cancer; Waldenstrommacroglobulinemia; and Wilm's tumor; and/or

(d) the subject is suffering from a brain cancer or tumor selected from the group consisting of brain stem glioma, central nervous system atypical teratoid/rhabdoid tumor, central nervous system embryonal tumors, astrocytomas, craniopharyngioma, ependymoblastoma, ependymoma, medulloblastoma, medulloepithelioma, pineal parenchymal tumors of intermediate differentiation, supratentorial primitive neuroectodermal tumors and pineoblastoma.

20. The composition of any one of claims 17-19, wherein the composition is administered:

(a) at least once a week over the course of several weeks; and/or

(b) at least once a week over several weeks to several months; and/or

(c) at least once a week for about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, about 19 or about 20 weeks or more; and/or

(d) about twice every week; and/or

(e) about twice a week for about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, about 19 or about 20 weeks or more.

CLAIMS

1. A composition comprising:

(a) a therapeutically effective dose of purified, intact bacterially derived minicells comprising at least one anti-neoplastic agent, wherein the anti-neoplastic agent comprises nemorubicin, PNU-159682, idarubicin, daunorubicin, caminomycin, and/or and

(b) an interferon type I agonist, an interferon type II agonist, or a combination of an interferon type I agonist and an interferon type II agonist,

wherein the interferon type I agonist is an oligonucleotide, wherein the oligonucleotide is double stranded DNA or DNA-RNA hybrids and comprises a sequence of at least about 40 nucleotides,

and

wherein the interferon type II agonist is selected from the group consisting of C-glycosidific form of α-galactosylceramide (α-C-GalCer), α-galactosylceramide (α-GalCer), 12 carbon acyl form of galactosylceramide (β-GalCer), β-D-glucopyranosylceramide (β-GlcCer), l,2-Diacyl-3-0-galactosyl-sn-glycerol (BbGL-II), diacylglycerol containing glycolipids (Glc-DAG-s2), ganglioside (GD3), gangliotriaosylceramide (Gg3Cer), glycosylphosphatidylinositol (GPI), α-glucuronosylceramide (GSL-1 or GSL-4), isoglobotrihexosylceramide (iGb3), lipophosphoglycan(LPG), lyosphosphatidylcholine (LPC), α-galactosylceramide analog (OCH), threitolceramide, and a combination thereof.

2. The composition of claim 1, wherein element (b) of the composition comprises:

(i) a therapeutically effective dose of purified, intact bacterially derived minicells comprising an interferon type I agonist; or

(ii) a therapeutically effective dose of purified, intact bacterially derived minicells comprising an interferon type II agonist; or

(iii) a combination of:

(1) a therapeutically effective dose of purified, intact bacterially derived minicells comprising an interferon type I agonist; and

(2) a therapeutically effective dose of purified, intact bacterially derived minicells comprising an interferon type II agonist.

3. The composition of claim 1, wherein:

(a) the anti-neoplastic agent and the interferon type I agonist, the interferon type II agonist, or the combination of an interferon type I agonist and an interferon type II agonist, are packaged within two or more purified, intact bacterially derived minicells; or

(b) the anti-neoplastic agent and the interferon type I agonist, the interferon type II agonist, or the combination of an interferon type I agonist and an interferon type II agonist are packaged within three separate populations of purified, intact bacterially derived minicells.

4. The composition of claim 1 comprising the anti-neoplastic agent, the interferon type I agonist, and the interferon type II agonist, wherein:

(a) the anti-neoplastic agent, the interferon type I agonist, and the interferon type II agonist are comprised within the same minicell;

(b) the anti-neoplastic agent and the interferon type I agonist are comprised within a first minicell, and the interferon type II agonist is comprised within a second minicell;

(c) the anti-neoplastic agent and the interferon type II agonist are comprised within a first minicell, and the interferon type I agonist is comprised within a second minicell;

(d) the anti-neoplastic agent is comprised within a first minicell, and the interferon type I agonist and the interferon type II agonist are comprised within a second minicell; or

(e) the anti-neoplastic agent is comprised within a first minicell, the interferon type I agonist is comprised within a second minicell, and the interferon type II agonist is comprised within a third minicell.

5. The composition of claim 1, wherein the composition does not comprise an interferon type I agonist.

6. The composition of claim 1, wherein the anti-neoplastic agent is PNU-159682.

7. The composition of claim 1, wherein:

(a) the oligonucleotide comprises a sequence of at least about 50 nucleotides or at least about 60 nucleotides.

8. The composition of claim 1, wherein the interferon type I agonist is an oligonucleotide selected from the group consisting of double stranded Z-DNA and B-DNA.

9. The composition of claim 1, wherein: the interferon type II agonist is α-galactosylceramide (α-GalCer).

10. The composition of claim 1, further comprising:

(a) a bispecific ligand bound to the minicells comprising the anti-neoplastic agent; and/or

(b) a bispecific ligand bound to the minicells comprising the type I interferon agonist; and/or

(c) a bispecific ligand bound to the minicells comprising the type II interferon agonist.

11. The composition according to claim 10, wherein the bispecific ligand:

(a) comprises a first arm that carries specificity for a minicell surface structure and a second arm that carries specificity for a non-phagocytotic mammalian cell surface receptor; and/or

(b) comprises a first arm that carries specificity for a minicell surface structure and a second arm that carries specificity for a non-phagocytotic mammalian cell surface receptor and wherein the minicell surface structure is an O-polysaccharide component of a lipopolysaccharide on the minicell surface; and/or

(c) comprises a first arm that carries specificity for a minicell surface structure and a second arm that carries specificity for a non-phagocytotic mammalian cell surface receptor wherein the non-phagocytotic mammalian cell surface receptor is capable of activating receptor-mediated endocytosis of the minicell; and/or

(d) comprises a bispecific antibody or antibody fragment; and/or

(e) comprises a bispecific antibody or antibody fragment and wherein the antibody or antibody fragment comprises a first multivalent arm that carries specificity for a bacterially

derived minicell surface structure and a second multivalent arm that carries specificity for a cancer cell surface receptor, wherein the cancer cell surface receptor is capable of activating receptor-mediated endocytosis of the minicell.

12. The composition of claim 1, wherein the composition comprises fewer than about 1 contaminating parent bacterial cell per 10^7minicells, fewer than about 1 contaminating parent bacterial cell per 10^8minicells, fewer than about 1 contaminating parent bacterial cell per 10^9minicells, fewer than about 1 contaminating parent bacterial cell per 10^{10}minicells, or fewer than about 1 contaminating parent bacterial cell per 10^{11}minicells.

13. The composition of claim 1, further comprising a pharmaceutically acceptable carrier.

14. The composition of claim 1, wherein the minicells are approximately 400 nm in diameter.

15. The composition of claim 1, wherein the composition is free of parent bacterial cell contamination removable through 200 nm filtration.

16. The composition of claim 1, wherein the composition comprises the following amount of minicells or killed bacterial cells:

(a) at least about 10^9;
(b) at least about 1 x10^9;
(c) at least about 2 x 10^9;
(d) at least about 5 x 10^9;
(e) at least 8 x 10^9;
(f) no more than about 10^{11};
(g) no more than about 1 x 10^{11};
(h) no more than about 9 x 10^{10}; or
(i) no more than about 8 x 10^{10}.