What is claimed is:

1. A method to improve the efficacy and/or reduce the side effects of the administration of a substituted hexitol derivative for treatment of GBM or medulloblastoma comprising the steps of:

(a) identifying at least one factor or parameter associated with the efficacy and/or occurrence of side effects of the administration of the substituted hexitol derivative for treatment of GBM or medulloblastoma; and

(b) modifying the factor or parameter to improve the efficacy and/or reduce the side effects of the administration of the substituted hexitol derivative for treatment of GBM or medulloblastoma.

2. The method of claim 1 wherein the substituted hexitol derivative is selected from the group consisting of galactitols, substituted galacitols, dulcitols, and substituted dulcitols.

3. The method of claim 2 wherein the substituted hexitol derivative is selected from the group consisting of dianhydrogalactitol, derivatives of dianhydrogalactitol, diacetyldianhydrogalactitol, derivatives of diacetyldianhydrogalactitol, dibromodulcitol, and derivatives of dibromodulcitol.

4. The method of claim 3 wherein the substituted hexitol derivative is dianhydrogalactitol.

5. The method of claim 1 wherein the method improves the efficacy and/or reduces the side effects of the administration of the substituted hexitol derivative for treatment of GBM.

6. The method of claim 5 wherein the substituted hexitol derivative is dianhydrogalactitol.

7. The method of claim 1 wherein the method improves the efficacy and/or reduces the side effects of the administration of the substituted hexitol derivative for treatment of medulloblastoma.

8. The method of claim 7 wherein the substituted hexitol derivative is dianhydrogalactitol.

9. The method of claim 1 wherein the factor or parameter is selected from the group consisting of:

(a) dose modification;
(b) route of administration;
(c) schedule of administration;
(d) indications for use;
(e) selection of disease stage;
(f) other indications;
(g) patient selection;
(h) patient/disease phenotype;
(i) patient/disease genotype;
(j) pre/post-treatment preparation;
(k) toxicity management;
(l) pharmacokinetic/pharmacodynamic monitoring;
(m) drug combinations;
(n) chemosensitization;
(o) chemopotentiation;
(p) post-treatment patient management;
(q) alternative medicine/therapeutic support;
(r) bulk drug product improvements;
(s) diluent systems;
(t) solvent systems;
(u) excipients;
(v) dosage forms;
(w) dosage kits and packaging;
(x) drug delivery systems;
(y) drug conjugate forms;
(z) compound analogs;
(aa) prodrugs;
(ab) multiple drug systems;

(ac) biotherapeutic enhancement;

(ad) biotherapeutic resistance modulation;

(ae) radiation therapy enhancement;

(af) novel mechanisms of action; and

(ag) selective target cell population therapeutics.

10. The method of claim 9 wherein the substituted hexitol derivative is dianhydrogalactitol.

11. The method of claim 1 wherein the improvement is made by dose modification and the dose modification is at least one dose modification selected from the group consisting of:

(i) continuous i.v. infusion for hours to days;

(ii) biweekly administration;

(iii) doses greater than 5 mg/m^2/day;

(iv) progressive escalation of dosing from 1 mg/m^2/day based on patient tolerance;

(v) use of caffeine to modulate metabolism;

(vi) use of isoniazid to modulate metabolism;

(vii) selected and intermittent boosting of dosage administration;

(viii) administration of single and multiple doses escalating from 5 mg/m^2/day via bolus;

(ix) oral dosages of below 30 mg/m^2;

(x) oral dosages of above 130 mg/m^2;

(xi) oral dosages up to 40 mg/m^2 for 3 days and then a nadir/recovery period of 18-21 days;

(xii) dosing at a lower level for an extended period;

(xiii) dosing at a higher level;

(xiv) dosing with a nadir/recovery period longer than 21 days;

(xv) dosing at a level to achieve a concentration of the substituted hexitol derivative in the cerebrospinal fluid (CSF) of equal to or greater than 5 μM;

(xvi) dosing at a level to achieve a cytotoxic concentration in the CSF; and

(xvii) the use of the substituted hexitol derivative as a single cytotoxic agent.

12. The method of claim 11 wherein the substituted hexitol derivative is dianhydrogalactitol.

13. The method of claim 1 wherein the improvement is made by route of administration and the route of administration is at least one route of administration selected from the group consisting of:

(i) topical administration;

(ii) oral administration;

(iii) slow release oral delivery;

(iv) intrathecal administration;

(v) intraarterial administration;

(vi) continuous infusion;

(vii) intermittent infusion;

(viii) intravenous administration;

(ix) administration through a longer infusion;

(x) administration through IV push; and

(xi) administration to maximize the concentration of the substituted hexitol derivative in the CSF.

14. The method of claim 13 wherein the substituted hexitol derivative is dianhydrogalactitol.

15. The method of claim 13 wherein the route of administration is intravenous administration and the intravenous administration is intravenous administration for 30 minutes.

16. The method of claim 1 wherein the improvement is made by schedule of administration and the schedule of administration is at least one schedule of administration selected from the group consisting of:

(i) daily administration;

(ii) weekly administration;

(iii) weekly administration for three weeks;

(iv) biweekly administration;

(v) biweekly administration for three weeks with a 1-2 week rest period;

(vi) intermittent boost dose administration; and

(vii) daily administration for one week for multiple weeks.

17. The method of claim 16 wherein the substituted hexitol derivative is dianhydrogalactitol.

18. The method of claim 1 wherein the improvement is made by selection of disease stage and wherein the selection of disease stage is at least one selection of disease stage selected from the group consisting of:

(i) use in an appropriate disease stage for GBM;

(ii) use in an appropriate disease stage for medulloblastoma;

(iii) use for newly diagnosed disease;

(iv) use for recurrent disease;

(v) use for resistant or refractory disease; and

(vi) use for childhood glioblastoma.

19. The method of claim 18 wherein the substituted hexitol derivative is dianhydrogalactitol.

20. The method of claim 1 wherein the improvement is made by patient selection and wherein the patient selection is at least one patient selection carried out by a criterion selected from the group consisting of:

(i) selecting patients with a disease condition characterized by a high level of a metabolic enzyme selected from the group consisting of histone deacetylase and ornithine decarboxylase;

(ii) selecting patients with a low or high susceptibility to a condition selected from the group consisting of thrombocytopenia and neutropenia;

(iii) selecting patients intolerant of GI toxicities;

(iv) selecting patients characterized by over- or under-expression of a gene selected from the group consisting of c-Jun, a GPCR, a signal transduction protein, VEGF, a prostate-specific gene, and a protein kinase.

(v) selecting patients characterized by carrying extra copies of the EGFR gene for GBM;

(vi) selecting patients characterized by mutations in at least one gene selected from the group consisting of TP53, PDGFRA, IDH1, and NF1 for GBM;

(vii) selecting patients characterized by methylation or lack of methylation of the promoter of the MGMT gene;

(viii) selecting patients characterized by one or more deletions of the distal part of chromosome 17, distal to the p53 gene for medulloblastoma; and

(ix) selecting patients characterized by a particular cytogenic subgroup selected from the group consisting of: (i) a gain of 6q or amplification of MYC or MYCN; (ii) gain of 17q or an i(17q) without gain of 6q or amplification of MYC or MYCN; and (iii) 6q and 17q balanced or 6q deletion for medulloblastoma;

(x) selecting patients characterized by the existence of an IDH1 mutation;

(xi) selecting patients characterized by the presence of IDH1 wild-type gene;

(xii) selecting patients characterized by the presence of 1p/19q co-deletion;

(xiii) selecting patients characterized by the absence of an 1p/19q co-deletion;

(xiv) selecting patients characterized by an unmethylated promoter region of MGMT (O^6-methylguanine methyltransferase);

(xv) selecting patients characterized by a methylated promoter region of MGMT;

(xvi) selecting patients characterized by a high expression of MGMT;

(xvii) selecting patients characterized by a low expression of MGMT; and

(xviii) selecting patients characterized by a mutation in EGFR.

21. The method of claim 20 wherein the substituted hexitol derivative is dianhydrogalactitol.

22. The method of claim 20 wherein the patient selection is selecting patients characterized by a mutation in EGFR and the mutation in EGFR is EGFR Variant III.

23. The method of claim 1 wherein the improvement is made by analysis of patient or disease phenotype and wherein the analysis of patient or disease phenotype is a method of analysis of patient or disease phenotype carried out by a method selected from the group consisting of:

(i) use of a diagnostic tool, a diagnostic technique, a diagnostic kit, or a diagnostic assay to confirm a patient's particular phenotype;

(ii) use of a method for measurement of a marker selected from the group consisting of histone deacetylase, ornithine decarboxylase, VEGF, a protein that is a gene product of jun, and a protein kinase;

(iii) surrogate compound dosing; and

(iv) low dose pre-testing for enzymatic status.

24. The method of claim 23 wherein the substituted hexitol derivative is dianhydrogalactitol.

25. The method of claim 1 wherein the improvement is made by analysis of patient or disease genotype and the analysis of patient or disease genotype is a method of analysis of patient or disease genotype carried out by a method selected from the group consisting of:

(i) use of a diagnostic tool, a diagnostic technique, a diagnostic kit, or a diagnostic assay to confirm a patient's particular genotype;

(ii) use of a gene chip;

(iii) use of gene expression analysis;

(iv) use of single nucleotide polymorphism (SNP) analysis;

(v) measurement of the level of a metabolite or a metabolic enzyme;

(vi) determination of mutation of PDGFRA gene;

(vii) determination of mutation of IDH1 gene;

(viii) determination of mutation of NF1 gene;

(ix) determination of copy number of the EGFR gene;

(x) determination of status of methylation of promoter of MGMT gene;

(xi) determination of cytogenic subgroup classification (for medulloblastoma);

(xii) determination of the existence of an IDH1 mutation;

(xiii) determination of the existence of IDH1 wild-type;

(xiv) determination of the existence of a 1p/19q co-deletion;

(xv) determination of the absence of a 1p/19q co-deletion;

(xvi) determination of the existence of an unmethylated promoter region of the MGMT gene;

(xvii) determination of the existence of a methylated promoter region of the MGMT gene;

(xviii) determination of the existence of high expression of MGMT; and

(xix) determination of the existence of low expression of MGMT.

26. The method of claim 25 wherein the substituted hexitol derivative is dianhydrogalactitol.

27. The method of claim 25 wherein the method determines the copy number of the EGFR gene.

28. The method of claim 25 wherein the method determines the methylation status of the promoter of the MGMT gene.

29. The method of claim 1 wherein the improvement is made by pre/post treatment preparation and the pre/post-treatment preparation is a method of pre/post treatment preparation selected from the group consisting of:

(i) the use of colchicine or an analog thereof;

(ii) the use of a uricosuric;

(iii) the use of uricase;

(iv) the non-oral use of nicotinamide;

(v) the use of a sustained-release form of nicotinamide;

(vi) the use of an inhibitor of poly-ADP ribose polymerase;

(vii) the use of caffeine;

(viii) the use of leucovorin rescue;

(ix) infection control; and

(x) the use of an anti-hypertensive agent.

30. The method of claim 29 wherein the substituted hexitol derivative is dianhydrogalactitol.

31. The method of claim 1 wherein the improvement is made by toxicity management and the toxicity management is a method of toxicity management selected from the group consisting of:

(i) the use of colchicine or an analog thereof;

(ii) the use of a uricosuric;

(iii) the use of uricase;

(iv) the non-oral use of nicotinamide;

(v) the use of a sustained-release form of nicotinamide;

(vi) the use of an inhibitor of poly-ADP ribose polymerase;

(vii) the use of caffeine;

(viii) the use of leucovorin rescue;

(ix) the use of sustained-release allopurinol;

(x) the non-oral use of allopurinol;

(xi) the use of bone marrow transplants;

(xii) the use of a blood cell stimulant;

(xiii) the use of blood or platelet infusions;

(xiv) the administration of an agent selected from the group consisting of filgrastim (Neupogen®), G-CSF, and GM-CSF;

(xv) the application of a pain management technique;

(xvi) the administration of an anti-inflammatory agent;

(xvii) the administration of fluids;

(xviii) the administration of a corticosteroid;

(xix) the administration of an insulin control medication;

(xx) the administration of an antipyretic;

(xxi) the administration of an anti-nausea treatment;

(xxii) the administration of an anti-diarrheal treatment;

(xxiii) the administration of N-acetylcysteine; and

(xxiv) the administration of an antihistamine.

32. The method of claim 31 wherein the substituted hexitol derivative is dianhydrogalactitol.

33. The method of claim 1 wherein the improvement is made by pharmacokinetic/pharmacodynamic monitoring and the pharmacokinetic/pharmacodynamic monitoring is a method selected from the group consisting of:

(i) multiple determinations of blood plasma levels; and

(ii) multiple determinations of at least one metabolite in blood or urine.

34. The method of claim 33 wherein the substituted hexitol derivative is dianhydrogalactitol.

35. The method of claim 1 wherein the improvement is made by drug combination and the drug combination is a drug combination selected from the group consisting of:

(i) use with topoisomerase inhibitors;

(ii) use with fraudulent nucleosides;

(iii) use with fraudulent nucleotides;

(iv) use with thymidylate synthetase inhibitors;

(v) use with signal transduction inhibitors;

(vi) use with cisplatin or platinum analogs;

(vii) use with monofunctional alkylating agents;
(viii) use with bifunctional alkylating agents;
(ix) use with anti-tubulin agents;
(x) use with antimetabolites;
(xi) use with berberine;
(xii) use with apigenin;
(xiii) use with amonafide;
(xiv) use with vinca alkaloids;
(xv) use with 5-fluorouracil;
(xvi) use with curcumin;
(xvii) use with NF-κB inhibitors;
(xviii) use with rosmarinic acid;
(xix) use with mitoguazone;
(xx) use with tetrandrine;
(xxi) use with VEGF inhibitors;
(xxii) use with cancer vaccines;
(xxiii) use with EGFR inhibitors;
(xxiv) use with tyrosine kinase inhibitors; and
(xxv) use with poly (ADP-ribose) polymerase (PARP) inhibitors.

36. The method of claim 35 wherein the substituted hexitol derivative is dianhydrogalactitol.

37. The method of claim 35 wherein the drug combination is use with EGFR inhibitors.

38. The method of claim 35 wherein the drug combination is use with tyrosine kinase inhibitors.

39. The method of claim 35 wherein the drug combination is use with PARP inhibitors.

40. The method of claim 1 wherein the improvement is made by chemosensitization and the chemosensitization comprises the use of a substituted

hexitol derivative as a chemosensitizer in combination with an agent selected from the group consisting of:

(i) topoisomerase inhibitors;
(ii) fraudulent nucleosides;
(iii) fraudulent nucleotides;
(iv) thymidylate synthetase inhibitors;
(v) signal transduction inhibitors;
(vi) cisplatin or platinum analogs;
(vii) alkylating agents;
(viii) anti-tubulin agents;
(ix) antimetabolites;
(x) berberine;
(xi) apigenin;
(xii) amonafide;
(xiii) vinca alkaloids;
(xiv) 5-fluorouracil;
(xv) curcumin;
(xvi) NF-κB inhibitors;
(xvii) rosmarinic acid;
(xviii) mitoguazone;
(xix) tetrandrine;
(xx) a tyrosine kinase inhibitor;
(xxi) an inhibitor of EGFR; and
(xxii) an inhibitor of PARP.

41. The method of claim 40 wherein the substituted hexitol derivative is dianhydrogalactitol.

42. The method of claim 1 wherein the improvement is made by chemopotentiation and the chemopotentiation comprises the use of a substituted hexitol derivative as a chemopotentiator in combination with an agent selected from the group consisting of:

(i) topoisomerase inhibitors;
(ii) fraudulent nucleosides;
(iii) fraudulent nucleotides;
(iv) thymidylate synthetase inhibitors;
(v) signal transduction inhibitors;
(vi) cisplatin or platinum analogs;
(vii) alkylating agents;
(viii) anti-tubulin agents;
(ix) antimetabolites;
(x) berberine;
(xi) apigenin;
(xii) amonafide;
(xiii) vinca alkaloids;
(xiv) 5-fluorouracil;
(xv) curcumin;
(xvi) NF-κB inhibitors;
(xvii) rosmarinic acid;
(xviii) mitoguazone;
(xix) tetrandrine;
(xx) a tyrosine kinase inhibitor;
(xxi) an inhibitor of EGFR; and
(xxii) an inhibitor of PARP.

43. The method of claim 42 wherein the substituted hexitol derivative is dianhydrogalactitol.

44. The method of claim 42 wherein the drug combination is use with an alkylating agent selected from the group consisting of BCNU, BCNU wafers (Gliadel), ACNU, CCNU, bendamustine (Treanda), lomustine, and temozolimide (Temodar).

45. The method of claim 42 wherein the drug combination is use with a monofunctional alkylating agent.

46. The method of claim 42 wherein the drug combination is use with a bifunctional alkylating agent.

47. The method of claim 42 wherein the drug combination is use with an alkylating agent that damages DNA at a different place than dianhydrogalactitol.

48. The method of claim 1 wherein the improvement is made by post-treatment management and the post-treatment management is a method selected from the group consisting of:

(i) a therapy associated with pain management;

(ii) administration of an anti-emetic;

(iii) an anti-nausea therapy;

(iv) administration of an anti-inflammatory agent;

(v) administration of an anti-pyretic agent; and

(vi) administration of an immune stimulant.

49. The method of claim 48 wherein the substituted hexitol derivative is dianhydrogalactitol.

50. The method of claim 1 wherein the improvement is made by alternative medicine/post-treatment support and the alternative medicine/post-treatment support is a method selected from the group consisting of:

(i) hypnosis;

(ii) acupuncture;

(iii) meditation;

(iv) a herbal medication created either synthetically or through extraction; and

(v) applied kinesiology.

51. The method of claim 50 wherein the substituted hexitol derivative is dianhydrogalactitol.

52. The method of claim 50 wherein the alternative medicine/post-treatment support is a herbal medication created either synthetically or through extraction and the herbal medication created either synthetically or through extraction is selected from the group consisting of:

(i) a NF-κB inhibitor;

(ii) a natural anti-inflammatory;

(iii) an immunostimulant;

(iv) an antimicrobial; and

(v) a flavonoid, isoflavone, or flavone.

53. The method of claim 1 wherein the improvement is made by a bulk drug product improvement and the bulk drug product improvement is a bulk drug product improvement selected from the group consisting of:

(i) salt formation;

(ii) preparation as a homogeneous crystal structure;

(iii) preparation as a pure isomer;

(iv) increased purity;

(v) preparation with lower residual solvent content; and

(vi) preparation with lower residual heavy metal content.

54. The method of claim 53 wherein the substituted hexitol derivative is dianhydrogalactitol.

55. The method of claim 1 wherein the improvement is made by use of a diluent and the diluent is selected from the group consisting of:

(i) an emulsion;

(ii) dimethylsulfoxide (DMSO);

(iii) N-methylformamide (NMF)

(iv) DMF;

(v) ethanol;

(vi) benzyl alcohol;

(vii) dextrose-containing water for injection;

(viii) Cremophor;

(ix) cyclodextrin; and

(x) PEG.

56. The method of claim 55 wherein the substituted hexitol derivative is dianhydrogalactitol.

57. The method of claim 1 wherein the improvement is made by use of a solvent system and the solvent system is selected from the group consisting of:

(i) an emulsion;

(ii) dimethylsulfoxide (DMSO);

(iii) N-methylformamide (NMF)

(iv) DMF;

(v) ethanol;

(vi) benzyl alcohol;

(vii) dextrose-containing water for injection;

(viii) Cremophor;

(ix) cyclodextrin; and

(x) PEG.

58. The method of claim 57 wherein the substituted hexitol derivative is dianhydrogalactitol.

59. The method of claim 1 wherein the improvement is made by use of an excipient and the excipient is an excipient selected from the group consisting of:

(i) mannitol;

(ii) albumin;

(iii) EDTA;

(iv) sodium bisulfite;

(v) benzyl alcohol;

(vi) a carbonate buffer; and

(g) a phosphate buffer.

60. The method of claim 59 wherein the substituted hexitol derivative is dianhydrogalactitol.

61. The method of claim 1 wherein the improvement is made by a dosage form and the dosage form is a dosage form selected from the group consisting of:

(i) tablets;

(ii) capsules;

(iii) topical gels;

(iv) topical creams;

(v) patches;

(vi) suppositories; and

(vii) lyophilized dosage fills.

62. The method of claim 61 wherein the substituted hexitol derivative is dianhydrogalactitol.

63. The method of claim 1 wherein the improvement is made by use of dosage kits and packaging and the dosage kits and packaging are selected from the group consisting of the use of amber vials to protect from light and the use of stoppers with specialized coatings to improve shelf-life stability.

64. The method of claim 63 wherein the substituted hexitol derivative is dianhydrogalactitol.

65. The method of claim 1 wherein the improvement is made by use of a drug delivery system and the drug delivery system is a drug delivery system selected from the group consisting of:

(i) nanocrystals;

(ii) bioerodible polymers;

(iii) liposomes;

(iv) slow release injectable gels; and

(v) microspheres.

66. The method of claim 65 wherein the substituted hexitol derivative is dianhydrogalactitol.

67. The method of claim 1 wherein the improvement is made by use of a drug conjugate form and the drug conjugate form is a drug conjugate form selected from the group consisting of:

(i) a polymer system;

(ii) polylactides;

(iii) polyglycolides;

(iv) amino acids;

(v) peptides; and

(vi) multivalent linkers.

68. The method of claim 67 wherein the substituted hexitol derivative is dianhydrogalactitol.

69. The method of claim 1 wherein the improvement is made by use of a prodrug system and the prodrug system is selected from the group consisting of:

(i) the use of enzyme sensitive esters;

(ii) the use of dimers;

(iii) the use of Schiff bases;

(iv) the use of pyridoxal complexes; and

(v) the use of caffeine complexes.

70. The method of claim 69 wherein the substituted hexitol derivative is dianhydrogalactitol.

71. The method of claim 1 wherein the improvement is made by use of a multiple drug system and the multiple drug system is selected from the group consisting of:

(i) use of multi-drug resistance inhibitors;

(ii) use of specific drug resistance inhibitors;

(iii) use of specific inhibitors of selective enzymes;

(iv) use of signal transduction inhibitors;

(v) use of repair inhibition; and

(vi) use of topoisomerase inhibitors with non-overlapping side effects.

72. The method of claim 71 wherein the substituted hexitol derivative is dianhydrogalactitol.

73. The method of claim 1 wherein the improvement is made by biotherapeutic enhancement and the biotherapeutic enhancement is performed by use in combination as sensitizers/potentiators with a therapeutic agent or technique that is selected from the group consisting of:

(i) cytokines;

(ii) lymphokines;

(iii) therapeutic antibodies;
(iv) antisense therapies;
(v) gene therapies;
(vi) ribozymes; and
(vii) RNA interference.

74. The method of claim 73 wherein the substituted hexitol derivative is dianhydrogalactitol.

75. The method of claim 1 wherein the improvement is made by use of biotherapeutic resistance modulation and the biotherapeutic resistance modulation is use against glioblastoma multiforme or medulloblastoma tumors resistant to a therapeutic agent or technique selected from the group consisting of:

(i) biological response modifiers;
(ii) cytokines;
(iii) lymphokines;
(iv) therapeutic antibodies;
(v) antisense therapies;
(vi) gene therapies;
(vii) ribozymes;
(viii) RNA interference; and
(ix) vaccines.

76. The method of claim 75 wherein the substituted hexitol derivative is dianhydrogalactitol.

77. The method of claim 1 wherein the improvement is made by radiation therapy enhancement and the radiation therapy enhancement is a radiation therapy enhancement agent or technique selected from the group consisting of:

(i) hypoxic cell sensitizers;
(ii) radiation sensitizers/protectors;
(iii) photosensitizers;
(iv) radiation repair inhibitors;
(v) thiol depleters;

(vi) vaso-targeted agents;
(vii) DNA repair inhibitors;
(viii) radioactive seeds;
(ix) radionuclides;
(x) radiolabeled antibodies; and
(xi) brachytherapy.

78. The method of claim 77 wherein the substituted hexitol derivative is dianhydrogalactitol.

79. The method of claim 1 wherein the improvement is by use of a novel mechanism of action and the novel mechanism of action is a therapeutic interaction with a target or mechanism selected from the group consisting of:

(i) inhibitors of poly-ADP ribose polymerase;
(ii) agents that affect vasculature or vasodilation;
(iii) oncogenic targeted agents;
(iv) signal transduction inhibitors;
(v) EGFR inhibition;
(vi) protein kinase C inhibition;
(vii) phospholipase C downregulation;
(viii) Jun downregulation;
(ix) histone genes;
(x) VEGF;
(xi) ornithine decarboxylase;
(xii) ubiquitin C;
(xiii) Jun D;
(xiv) v-Jun;
(xv) GPCRs;
(xvi) protein kinase A;
(xvii) protein kinases other than protein kinase A;
(xviii) prostate specific genes;
(xix) telomerase;

(xx) histone deacetylase; and

(xxi) tyrosine kinase inhibitors.

80. The method of claim 79 wherein the substituted hexitol derivative is dianhydrogalactitol.

81. The method of claim 1 wherein the improvement is made by use of selective target cell population therapeutics and the use of selective target cell population therapeutics is a use selected from the group consisting of:

(i) use against radiation sensitive cells;

(ii) use against radiation resistant cells; and

(iii) use against energy depleted cells.

82. The method of claim 71 wherein the substituted hexitol derivative is dianhydrogalactitol.

83. The method of claim 1 wherein the improvement is made by use of a substituted hexitol derivative together with ionizing radiation.

84. The method of claim 83 wherein the substituted hexitol derivative is dianhydrogalactitol.

85. A composition to improve the efficacy and/or reduce the side effects of suboptimally administered drug therapy employing a substituted hexitol derivative for the treatment of GBM or medulloblastoma comprising an alternative selected from the group consisting of:

(a) a therapeutically effective quantity of a modified substituted hexitol derivative or a derivative, analog, or prodrug of a substituted hexitol derivative or a modified substituted hexitol derivative, wherein the modified substituted hexitol derivative or the derivative, analog or prodrug of the substituted hexitol derivative or modified substituted hexitol derivative possesses increased therapeutic efficacy or reduced side effects for treatment of GBM or medulloblastoma as compared with an unmodified substituted hexitol derivative;

(b) a composition comprising:

(i) a therapeutically effective quantity of a substituted hexitol derivative, a modified substituted hexitol derivative, or a derivative, analog, or prodrug of a substituted hexitol derivative or a modified substituted hexitol derivative; and

(ii) at least one additional therapeutic agent, therapeutic agent subject to chemosensitization, therapeutic agent subject to chemopotentiation, diluent, excipient, solvent system, or drug delivery system, wherein the composition possesses increased therapeutic efficacy or reduced side effects for treatment of GBM or medulloblastoma as compared with an unmodified substituted hexitol derivative;

(c) a therapeutically effective quantity of a substituted hexitol derivative, a modified substituted hexitol derivative or a derivative, analog, or prodrug of a substituted hexitol derivative or a modified substituted hexitol derivative that is incorporated into a dosage form, wherein the substituted hexitol derivative, the modified substituted hexitol derivative or the derivative, analog, or prodrug of a substituted hexitol derivative or a modified substituted hexitol derivative incorporated into the dosage form possesses increased therapeutic efficacy or reduced side effects for treatment of GBM or medulloblastoma as compared with an unmodified substituted hexitol derivative;

(d) a therapeutically effective quantity of a substituted hexitol derivative, a modified substituted hexitol derivative or a derivative, analog, or prodrug of a substituted hexitol derivative or a modified substituted hexitol derivative that is incorporated into a dosage kit and packaging, wherein the substituted hexitol derivative, the modified substituted hexitol derivative or the derivative, analog, or prodrug of a substituted hexitol derivative or a modified substituted hexitol derivative incorporated into the dosage kit and packaging possesses increased therapeutic efficacy or reduced side effects for treatment of GBM or medulloblastoma as compared with an unmodified substituted hexitol derivative; and

(e) a therapeutically effective quantity of a substituted hexitol derivative, a modified substituted hexitol derivative or a derivative, analog, or prodrug of a substituted hexitol derivative or a modified substituted hexitol derivative that is subjected to a bulk drug product improvement, wherein substituted hexitol derivative, a modified substituted hexitol derivative or a derivative, analog, or prodrug of a substituted

hexitol derivative or a modified substituted hexitol derivative subjected to the bulk drug product improvement possesses increased therapeutic efficacy or reduced side effects for treatment of GBM or medulloblastoma as compared with an unmodified substituted hexitol derivative.

86. The composition of claim 85 wherein the unmodified substituted hexitol derivative is selected from the group consisting of dianhydrogalactitol, derivatives of dianhydrogalactitol, diacetyldianhydrogalactitol, derivatives of diacetyldianhydrogalactitol, dibromodulcitol, and derivatives of dibromodulcitol.

87. The composition of claim 86 wherein the unmodified substituted hexitol derivative is dianhydrogalactitol.

88. The composition of claim 85 wherein the composition comprises a drug combination comprising:

(a) a substituted hexitol derivative, and

(b) an additional therapeutic agent selected from the group consisting of:

(i) topoisomerase inhibitors;
(ii) fraudulent nucleosides;
(iii) fraudulent nucleotides;
(iv) thymidylate synthetase inhibitors;
(v) signal transduction inhibitors;
(vi) cisplatin or platinum analogs;
(vii) alkylating agents;
(viii) anti-tubulin agents;
(ix) antimetabolites;
(x) berberine;
(xi) apigenin;
(xii) amonafide;
(xiii) vinca alkaloids;
(xiv) 5-fluorouracil;
(xv) curcumin;

(xvi) NF-κB inhibitors;

(xvii) rosmarinic acid;

(xviii) mitoguazone;

(xix) tetrandrine;

(xx) tyrosine kinase inhibitors;

(xxi) epidermal growth factor inhibitors; and

(xxii) inhibitors of poly-ADP ribose polymerase (PARP).

89. The composition of claim 88 wherein the substituted hexitol derivative is dianhydrogalactitol.

90. The composition of claim 85 wherein the composition comprises:

(a) a substituted hexitol derivative; and

(b) a therapeutic agent subject to chemosensitization selected from the group consisting of:

(i) topoisomerase inhibitors;

(ii) fraudulent nucleosides;

(iii) fraudulent nucleotides;

(iv) thymidylate synthetase inhibitors;

(v) signal transduction inhibitors;

(vi) cisplatin or platinum analogs;

(vii) alkylating agents;

(viii) anti-tubulin agents;

(ix) antimetabolites;

(x) berberine;

(xi) apigenin;

(xii) amonafide;

(xiii) vinca alkaloids;

(xiv) 5-fluorouracil;

(xv) curcumin;

(xvi) NF-κB inhibitors;

(xvii) rosmarinic acid;

(xviii) mitoguazone; and

(xix) tetrandrine;

(xx) tyrosine kinase inhibitors;

(xxi) epidermal growth factor inhibitors; and

(xxii) inhibitors of poly-ADP ribose polymerase (PARP);

wherein the substituted hexitol derivative acts as a chemosensitizer.

91. The composition of claim 90 wherein the substituted hexitol derivative is dianhydrogalactitol.

92. The composition of claim 85 wherein the composition comprises:

(a) a substituted hexitol derivative; and

(b) a therapeutic agent subject to chemopotentiation selected from the group consisting of:

(i) topoisomerase inhibitors;

(ii) fraudulent nucleosides;

(iii) fraudulent nucleotides;

(iv) thymidylate synthetase inhibitors;

(v) signal transduction inhibitors;

(vi) cisplatin or platinum analogs;

(vii) alkylating agents;

(viii) anti-tubulin agents;

(ix) antimetabolites;

(x) berberine;

(xi) apigenin;

(xii) amonafide;

(xiii) vinca alkaloids;

(xiv) 5-fluorouracil;

(xv) curcumin;

(xvi) NF-κB inhibitors;

(xvii) rosmarinic acid;

(xviii) mitoguazone;

(xix) tetrandrine;

(xx) biotherapeutics;

(xxi) a tyrosine kinase inhibitor;

(xxii) an inhibitor of EGFR; and

(xxiii) an inhibitor of PARP;

wherein the substituted hexitol derivative acts as a chemopotentiator.

93. The composition of claim 92 wherein the substituted hexitol derivative is dianhydrogalactitol.

94. The composition of claim 85 wherein the substituted hexitol derivative is subjected to a bulk drug product improvement, wherein the bulk drug product improvement is selected from the group consisting of:

(i) salt formation;

(ii) preparation as a homogeneous crystal structure;

(iii) preparation as a pure isomer;

(iv) increased purity;

(v) preparation with lower residual solvent content; and

(vi) preparation with lower residual heavy metal content.

95. The composition of claim 94 wherein the substituted hexitol derivative is dianhydrogalactitol.

96. The composition of claim 85 wherein the composition comprises a substituted hexitol derivative and a diluent, wherein the diluent is selected from the group consisting of:

(i) an emulsion;

(ii) dimethylsulfoxide (DMSO);

(iii) N-methylformamide (NMF)

(iv) DMF;

(v) ethanol;

(vi) benzyl alcohol;

(vii) dextrose-containing water for injection;

(viii) Cremophor;

(ix) cyclodextrin; and

(x) PEG.

97. The composition of claim 96 wherein the substituted hexitol derivative is dianhydrogalactitol.

98. The composition of claim 85 wherein the composition comprises a substituted hexitol derivative and a solvent system, wherein the solvent system is selected from the group consisting of:

(i) an emulsion;

(ii) dimethylsulfoxide (DMSO);

(iii) N-methylformamide (NMF)

(iv) DMF;

(v) ethanol;

(vi) benzyl alcohol;

(vii) dextrose-containing water for injection;

(viii) Cremophor;

(ix) cyclodextrin; and

(x) PEG.

99. The composition of claim 98 wherein the substituted hexitol derivative is dianhydrogalactitol.

100. The composition of claim 85 wherein the composition comprises a substituted hexitol derivative and an excipient, wherein the excipient is selected from the group consisting of:

(i) mannitol;

(ii) albumin;

(iii) EDTA;

(iv) sodium bisulfite;

(v) benzyl alcohol;

(vi) a carbonate buffer; and

(vii) a phosphate buffer.

101. The composition of claim 100 wherein the substituted hexitol derivative is dianhydrogalactitol.

102. The composition of claim 85 wherein the substituted hexitol derivative is incorporated into a dosage form selected from the group consisting of:

(i) tablets;
(ii) capsules;
(iii) topical gels;
(iv) topical creams;
(v) patches;
(vi) suppositories; and
(vii) lyophilized dosage fills.

103. The composition of claim 102 wherein the substituted hexitol derivative is dianhydrogalactitol.

104. The composition of claim 85 wherein the substituted hexitol derivative is incorporated into a dosage kit and packaging selected from the group consisting of amber vials to protect from light and stoppers with specialized coatings to improve shelf-life stability.

105. The composition of claim 104 wherein the substituted hexitol derivative is dianhydrogalactitol

106. The composition of claim 85 wherein the composition comprises a substituted hexitol derivative and a drug delivery system selected from the group consisting of:

(i) nanocrystals;
(ii) bioerodible polymers;
(iii) liposomes;
(iv) slow release injectable gels; and
(v) microspheres.

107. The composition of claim 106 wherein the substituted hexitol derivative is dianhydrogalactitol.

108. The composition of claim 85 wherein the substituted hexitol derivative is present in the composition in a drug conjugate form selected from the group consisting of:

(i) a polymer system;

(ii) polylactides;

(iii) polyglycolides;

(iv) amino acids;

(v) peptides; and

(vi) multivalent linkers.

109. The composition of claim 108 wherein the substituted hexitol derivative is dianhydrogalactitol.

110. The composition of claim 85 wherein the therapeutic agent is a modified substituted hexitol derivative and the modification is selected from the group consisting of:

(i) alteration of side chains to increase or decrease lipophilicity;

(ii) addition of an additional chemical functionality to alter a property selected from the group consisting of reactivity, electron affinity, and binding capacity; and

(iii) alteration of salt form.

111. The composition of claim 110 wherein the modified substituted hexitol derivative is a modified dianhydrogalactitol.

112. The composition of claim 85 wherein the composition comprises a substituted hexitol derivative and at least one additional therapeutic agent to form a multiple drug system, wherein the at least one additional therapeutic agent is selected from the group consisting of:

(i) an inhibitor of multi-drug resistance;

(ii) a specific drug resistance inhibitor;

(iii) a specific inhibitor of a selective enzyme;

(iv) a signal transduction inhibitor;

(v) an inhibitor of a repair enzyme; and

(vi) a topoisomerase inhibitor with non-overlapping side effects.

113. The composition of claim 112 wherein the substituted hexitol derivative is dianhydrogalactitol.

114. A method of treating a malignancy selected from the group consisting of glioblastoma multiforme and medulloblastoma comprising the step of administering a therapeutically effective quantity of a substituted hexitol derivative to a patient suffering from the malignancy.

115. The method of claim 114 wherein the substituted hexitol derivative is selected from the group consisting of galactitols, substituted galacitols, dulcitols, and substituted dulcitols.

116. The method of claim 115 wherein the substituted hexitol derivative is selected from the group consisting of dianhydrogalactitol, derivatives of dianhydrogalactitol, diacetyldianhydrogalactitol, derivatives of diacetyldianhydrogalactitol, dibromodulcitol, and derivatives of dibromodulcitol.

117. The method of claim 116 wherein the substituted hexitol derivative is dianhydrogalactitol.

118. The method of claim 114 wherein the malignancy is glioblastoma multiforme.

119. The method of claim 114 wherein the malignancy is medulloblastoma.

120. The method of claim 117 wherein the therapeutically effective quantity of dianhydrogalactitol is a quantity of dianhydrogalactitol that results in a dosage of from about 1 mg/m^2 to about 40 mg/m^2.

121. The method of claim 120 wherein the therapeutically effective quantity of dianhydrogalactitol is a quantity of dianhydrogalactitol that results in a dosage of from about 5 mg/m^2 to about 25 mg/m^2.

122. The method of claim 114 wherein the substituted hexitol derivative is administered by a route selected from the group consisting of intravenous and oral.

123. The method of claim 122 wherein the substituted hexitol derivative is dianhydrogalactitol.

124. The method of claim 122 wherein the substituted hexitol derivative is administered intravenously.

125. The method of claim 114 further comprising the step of administering a therapeutically effective dose of ionizing radiation.

126. The method of claim 114 further comprising the step of administering a therapeutically effective quantity of temozolomide.

127. The method of claim 114 further comprising the step of administering a therapeutically effective quantity of bevacizumab.

128. The method of claim 114 further comprising the step of administering a therapeutically effective quantity of a corticosteroid.

129. The method of claim 114 further comprising the step of administering a therapeutically effective quantity of at least one chemotherapeutic agent selected from the group consisting of lomustine, cisplatin, carboplatin, vincristine, and cyclophosphamide.

130. The method of claim 117 wherein the dianhydrogalactitol substantially suppresses the growth of cancer stem cells (CSCs).

131. The method of claim 130 wherein the suppression of the growth of cancer stem cells is at least 50%.

132. The method of claim 131 where the suppression of the growth of cancer stem cells is at least 99%.

133. The method of claim 117 wherein the dianhydrogalactitol is effective in suppressing the growth of cancer cells possessing O^6-methylguanine-DNA methyltransferase (MGMT)-driven drug resistance.

134. The method of claim 117 wherein the dianhydrogalactitol is effective in suppressing the growth of cancer cells resistant to temozolomide.

135. The method of claim 114 wherein the method further comprises the administration of a therapeutically effective quantity of a tyrosine kinase inhibitor.

136. The method of claim 114 wherein the method further comprises the administration of a therapeutically effective quantity of an EGFR inhibitor.

137. The method of claim 136 wherein the EGFR inhibitor affects wild-type binding sites.

138. The method of claim 136 wherein the EGFR inhibitor affects mutated binding sites.

139. The method of claim 138 wherein the EGFR inhibitor affects EGFR Variant III.

CLAIMS

1. A method for manufacture of a medicament to improve the efficacy and/or reduce the side effects of the administration of a substituted hexitol derivative for treatment of GBM or medulloblastoma comprising the steps of:

(a) identifying at least one factor or parameter associated with the efficacy and/or occurrence of side effects of the administration of the substituted hexitol derivative for treatment of GBM or medulloblastoma; and

(b) modifying the factor or parameter to improve the efficacy and/or reduce the side effects of the administration of the substituted hexitol derivative for treatment of GBM or medulloblastoma for production of a medicament to treat GBM or medulloblastoma, wherein the substituted hexitol derivative is selected from the group consisting of dianhydrogalactitol, derivatives of dianhydrogalactitol, diacetyldianhydrogalactitol, derivatives of diacetyldianhydrogalactitol, dibromodulcitol, and derivatives of dibromodulcitol.

2. The method of claim 1 wherein the substituted hexitol derivative is dianhydrogalactitol.

3. The method of claim 1 wherein the factor or parameter is selected from the group consisting of:

(a) dose modification;
(b) route of administration;
(c) schedule of administration;
(d) indications for use;
(e) selection of disease stage;
(f) other indications;
(g) patient selection;
(h) patient/disease phenotype;
(i) patient/disease genotype;
(j) pre/post-treatment preparation

(k) toxicity management;

(l) pharmacokinetic/pharmacodynamic monitoring;

(m) drug combinations;

(n) chemosensitization;

(o) chemopotentiation;

(p) post-treatment patient management;

(q) alternative medicine/therapeutic support;

(r) bulk drug product improvements;

(s) diluent systems;

(t) solvent systems;

(u) excipients;

(v) dosage forms;

(w) dosage kits and packaging;

(x) drug delivery systems;

(y) drug conjugate forms;

(z) compound analogs;

(aa) prodrugs;

(ab) multiple drug systems;

(ac) biotherapeutic enhancement;

(ad) biotherapeutic resistance modulation;

(ae) radiation therapy enhancement;

(af) novel mechanisms of action; and

(ag) selective target cell population therapeutics.

4. The method of claim 1 wherein the improvement is made by patient selection and wherein the patient selection is at least one patient selection carried out by a criterion selected from the group consisting of:

(i) selecting patients with a disease condition characterized by a high level of a metabolic enzyme selected from the group consisting of histone deacetylase and ornithine decarboxylase;

(ii) selecting patients with a low or high susceptibility to a condition selected from the group consisting of thrombocytopenia and neutropenia;

(iii) selecting patients intolerant of GI toxicities;

(iv) selecting patients characterized by over- or under-expression of a gene selected from the group consisting of c-Jun, a GPCR, a signal transduction protein, VEGF, a prostate-specific gene, and a protein kinase.

(v) selecting patients characterized by carrying extra copies of the EGFR gene for GBM;

(vi) selecting patients characterized by mutations in at least one gene selected from the group consisting of TP53, PDGFRA, IDH1, and NF1 for GBM;

(vii) selecting patients characterized by methylation or lack of methylation of the promoter of the MGMT gene;

(viii) selecting patients characterized by one or more deletions of the distal part of chromosome 17, distal to the p53 gene for medulloblastoma; and

(ix) selecting patients characterized by a particular cytogenic subgroup selected from the group consisting of: (i) a gain of 6q or amplification of MYC or MYCN; (ii) gain of 17q or an i(17q) without gain of 6q or amplification of MYC or MYCN; and (iii) 6q and 17q balanced or 6q deletion for medulloblastoma;

(x) selecting patients characterized by the existence of an IDH1 mutation;

(xi) selecting patients characterized by the presence of IDH1 wild-type gene;

(xii) selecting patients characterized by the presence of 1p/19q co-deletion;

(xiii) selecting patients characterized by the absence of an 1p/19q co-deletion;

(xiv) selecting patients characterized by an unmethylated promoter region of MGMT (O^6-methylguanine methyltransferase);

(xv) selecting patients characterized by a methylated promoter region of MGMT;

(xvi) selecting patients characterized by a high expression of MGMT;

(xvii) selecting patients characterized by a low expression of MGMT; and

(xviii) selecting patients characterized by a mutation in EGFR.

5. The method of claim 1 wherein the improvement is made by analysis of patient or disease genotype and the analysis of patient or disease genotype is a method of analysis of patient or disease genotype carried out by a method selected from the group consisting of:

(i) use of a diagnostic tool, a diagnostic technique, a diagnostic kit, or a diagnostic assay to confirm a patient's particular genotype;

(ii) use of a gene chip;

(iii) use of gene expression analysis;

(iv) use of single nucleotide polymorphism (SNP) analysis;

(v) measurement of the level of a metabolite or a metabolic enzyme;

(vi) determination of mutation of PDGFRA gene;

(vii) determination of mutation of IDH1 gene;

(viii) determination of mutation of NF1 gene;

(ix) determination of copy number of the EGFR gene;

(x) determination of status of methylation of promoter of MGMT gene;

(xi) determination of cytogenic subgroup classification (for medulloblastoma);

(xii) determination of the existence of an IDH1 mutation;

(xiii) determination of the existence of IDH1 wild-type;

(xiv) determination of the existence of a 1p/19q co-deletion;

(xv) determination of the absence of a 1p/19q co-deletion;

(xvi) determination of the existence of an unmethylated promoter region of the MGMT gene;

(xvii) determination of the existence of a methylated promoter region of the MGMT gene;

(xviii) determination of the existence of high expression of MGMT; and

(xix) determination of the existence of low expression of MGMT.

6. A composition to improve the efficacy and/or reduce the side effects of suboptimally administered drug therapy employing a substituted hexitol derivative for the treatment of GBM or medulloblastoma comprising an alternative selected from the group consisting of:

(a) a therapeutically effective quantity of a modified substituted hexitol derivative or a derivative, analog, or prodrug of a substituted hexitol derivative or a modified substituted hexitol derivative, wherein the modified substituted hexitol derivative or the derivative, analog or prodrug of the substituted hexitol derivative or modified substituted hexitol derivative possesses increased therapeutic efficacy or reduced side effects for treatment of GBM or medulloblastoma as compared with an unmodified substituted hexitol derivative;

(b) a composition comprising:

(i) a therapeutically effective quantity of a substituted hexitol derivative, a modified substituted hexitol derivative, or a derivative, analog, or prodrug of a substituted hexitol derivative or a modified substituted hexitol derivative; and

(ii) at least one additional therapeutic agent, therapeutic agent subject to chemosensitization, therapeutic agent subject to chemopotentiation, diluent, excipient, solvent system, or drug delivery system, wherein the composition possesses increased therapeutic efficacy or reduced side effects for treatment of GBM or medulloblastoma as compared with an unmodified substituted hexitol derivative;

(c) a therapeutically effective quantity of a substituted hexitol derivative, a modified substituted hexitol derivative or a derivative, analog, or prodrug of a substituted hexitol derivative or a modified substituted hexitol derivative that is incorporated into a dosage form, wherein the substituted hexitol derivative, the modified substituted hexitol derivative or the derivative, analog, or prodrug of a substituted hexitol

derivative or a modified substituted hexitol derivative incorporated into the dosage form possesses increased therapeutic efficacy or reduced side effects for treatment of GBM or medulloblastoma as compared with an unmodified substituted hexitol derivative;

(d) a therapeutically effective quantity of a substituted hexitol derivative, a modified substituted hexitol derivative or a derivative, analog, or prodrug of a substituted hexitol derivative or a modified substituted hexitol derivative that is incorporated into a dosage kit and packaging, wherein the substituted hexitol derivative, the modified substituted hexitol derivative or the derivative, analog, or prodrug of a substituted hexitol derivative or a modified substituted hexitol derivative incorporated into the dosage kit and packaging possesses increased therapeutic efficacy or reduced side effects for treatment of GBM or medulloblastoma as compared with an unmodified substituted hexitol derivative; and

(e) a therapeutically effective quantity of a substituted hexitol derivative, a modified substituted hexitol derivative or a derivative, analog, or prodrug of a substituted hexitol derivative or a modified substituted hexitol derivative that is subjected to a bulk drug product improvement, wherein substituted hexitol derivative, a modified substituted hexitol derivative or a derivative, analog, or prodrug of a substituted hexitol derivative or a modified substituted hexitol derivative subjected to the bulk drug product improvement possesses increased therapeutic efficacy or reduced side effects for treatment of GBM or medulloblastoma as compared with an unmodified substituted hexitol derivative.

7. The composition of claim 6 wherein the unmodified substituted hexitol derivative is selected from the group consisting of dianhydrogalactitol, derivatives of dianhydrogalactitol, diacetyldianhydrogalactitol, derivatives of diacetyldianhydrogalactitol, dibromodulcitol, and derivatives of dibromodulcitol.

8. The composition of claim 7 wherein the unmodified substituted hexitol derivative is dianhydrogalactitol.

9. The composition of claim 6 wherein the composition comprises a drug combination comprising:

(a) a substituted hexitol derivative; and

(b) an additional therapeutic agent selected from the group consisting of:

(i) topoisomerase inhibitors;

(ii) fraudulent nucleosides;

(iii) fraudulent nucleotides;

(iv) thymidylate synthetase inhibitors;

(v) signal transduction inhibitors;

(vi) cisplatin or platinum analogs;

(vii) alkylating agents;

(viii) anti-tubulin agents;

(ix) antimetabolites;

(x) berberine;

(xi) apigenin;

(xii) amonafide;

(xiii) vinca alkaloids;

(xiv) 5-fluorouracil;

(xv) curcumin;

(xvi) NF-κB inhibitors;

(xvii) rosmarinic acid;

(xviii) mitoguazone;

(xix) tetrandrine;

(xx) tyrosine kinase inhibitors;

(xxi) epidermal growth factor inhibitors; and

(xxii) inhibitors of poly-ADP ribose polymerase (PARP).

10. The composition of claim 6 wherein the composition comprises:

(a) a substituted hexitol derivative; and

(b) a therapeutic agent subject to chemosensitization selected from the group consisting of:

(i) topoisomerase inhibitors;
(ii) fraudulent nucleosides;
(iii) fraudulent nucleotides;
(iv) thymidylate synthetase inhibitors;
(v) signal transduction inhibitors;
(vi) cisplatin or platinum analogs;
(vii) alkylating agents;
(viii) anti-tubulin agents;
(ix) antimetabolites;
(x) berberine;
(xi) apigenin;
(xii) amonafide;
(xiii) vinca alkaloids;
(xiv) 5-fluorouracil;
(xv) curcumin;
(xvi) NF-κB inhibitors;
(xvii) rosmarinic acid;
(xviii) mitoguazone; and
(xix) tetrandrine;
(xx) tyrosine kinase inhibitors;
(xxi) epidermal growth factor inhibitors; and
(xxii) inhibitors of poly-ADP ribose polymerase (PARP);

wherein the substituted hexitol derivative acts as a chemosensitizer.

11. The composition of claim 6 wherein the composition comprises:

(a) a substituted hexitol derivative; and

(b) a therapeutic agent subject to chemopotentiation selected from the group consisting of:

(i) topoisomerase inhibitors;

(ii) fraudulent nucleosides;
(iii) fraudulent nucleotides;
(iv) thymidylate synthetase inhibitors;
(v) signal transduction inhibitors;
(vi) cisplatin or platinum analogs;
(vii) alkylating agents;
(viii) anti-tubulin agents;
(ix) antimetabolites;
(x) berberine;
(xi) apigenin;
(xii) amonafide;
(xiii) vinca alkaloids;
(xiv) 5-fluorouracil;
(xv) curcumin;
(xvi) NF-κB inhibitors;
(xvii) rosmarinic acid;
(xviii) mitoguazone;
(xix) tetrandrine;
(xx) biotherapeutics;
(xxi) a tyrosine kinase inhibitor;
(xxii) an inhibitor of EGFR; and
(xxiii) an inhibitor of PARP;

wherein the substituted hexitol derivative acts as a chemopotentiator.

12. The composition of claim 6 wherein the substituted hexitol derivative is subjected to a bulk drug product improvement, wherein the bulk drug product improvement is selected from the group consisting of:

(i) salt formation;
(ii) preparation as a homogeneous crystal structure;
(iii) preparation as a pure isomer;
(iv) increased purity;

(v) preparation with lower residual solvent content; and

(vi) preparation with lower residual heavy metal content.

13. The composition of claim 6 wherein the composition comprises a substituted hexitol derivative and a diluent, wherein the diluent is selected from the group consisting of:

(i) an emulsion;

(ii) dimethylsulfoxide (DMSO);

(iii) N-methylformamide (NMF)

(iv) DMF;

(v) ethanol;

(vi) benzyl alcohol;

(vii) dextrose-containing water for injection;

(viii) Cremophor;

(ix) cyclodextrin; and

(x) PEG.

14. The composition of claim 6 wherein the composition comprises a substituted hexitol derivative and a solvent system, wherein the solvent system is selected from the group consisting of:

(i) an emulsion;

(ii) dimethylsulfoxide (DMSO);

(iii) N-methylformamide (NMF)

(iv) DMF;

(v) ethanol;

(vi) benzyl alcohol;

(vii) dextrose-containing water for injection;

(viii) Cremophor;

(ix) cyclodextrin; and

(x) PEG.

15. The composition of claim 6 wherein the composition comprises a substituted hexitol derivative and an excipient, wherein the excipient is selected from the group consisting of:

(i) mannitol;

(ii) albumin;

(iii) EDTA;

(iv) sodium bisulfite;

(v) benzyl alcohol;

(vi) a carbonate buffer; and

(vii) a phosphate buffer.

16. The composition of claim 6 wherein the substituted hexitol derivative is incorporated into a dosage form selected from the group consisting of:

(i) tablets;

(ii) capsules;

(iii) topical gels;

(iv) topical creams;

(v) patches;

(vi) suppositories; and

(vii) lyophilized dosage fills.

17. The composition of claim 6 wherein the composition comprises a substituted hexitol derivative and a drug delivery system selected from the group consisting of:

(i) nanocrystals;

(ii) bioerodible polymers;

(iii) liposomes;

(iv) slow release injectable gels; and

(v) microspheres.

18. The composition of claim 6 wherein the substituted hexitol derivative is present in the composition in a drug conjugate form selected from the group consisting of:

(i) a polymer system;

(ii) polylactides;

(iii) polyglycolides;

(iv) amino acids;

(v) peptides; and

(vi) multivalent linkers.

19. The composition of claim 6 wherein the therapeutic agent is a modified substituted hexitol derivative and the modification is selected from the group consisting of:

(i) alteration of side chains to increase or decrease lipophilicity;

(ii) addition of an additional chemical functionality to alter a property selected from the group consisting of reactivity, electron affinity, and binding capacity; and

(iii) alteration of salt form.

20. The composition of claim 6 wherein the composition comprises a substituted hexitol derivative and at least one additional therapeutic agent to form a multiple drug system, wherein the at least one additional therapeutic agent is selected from the group consisting of:

(i) an inhibitor of multi-drug resistance;

(ii) a specific drug resistance inhibitor;

(iii) a specific inhibitor of a selective enzyme;

(iv) a signal transduction inhibitor;

(v) an inhibitor of a repair enzyme; and

(vi) a topoisomerase inhibitor with non-overlapping side effects.

21. A method for the preparation of a medicament for treating a malignancy selected from the group consisting of glioblastoma multiforme and medulloblastoma wherein the medicament comprises a therapeutically effective quantity of a substituted hexitol derivative for administration to a patient suffering from the malignancy.

22. The method of claim 21 wherein the substituted hexitol derivative is selected from the group consisting of galactitols, substituted galacitols, dulcitols, and substituted dulcitols.

23. The method of claim 22 wherein the substituted hexitol derivative is selected from the group consisting of dianhydrogalactitol, derivatives of dianhydrogalactitol, diacetyldianhydrogalactitol, derivatives of diacetyldianhydrogalactitol, dibromodulcitol, and derivatives of dibromodulcitol.

24. The method of claim 23 wherein the substituted hexitol derivative is dianhydrogalactitol.

25. The method of claim 21 wherein the malignancy is glioblastoma multiforme.

26. The method of claim 21 wherein the malignancy is medulloblastoma.

27. The method of claim 24 wherein the therapeutically effective quantity of dianhydrogalactitol is a quantity of dianhydrogalactitol that results in a dosage of from about 1 mg/m^2 to about 40 mg/m^2.

28. The method of claim 27 wherein the therapeutically effective quantity of dianhydrogalactitol is a quantity of dianhydrogalactitol that results in a dosage of from about 5 mg/m^2 to about 25 mg/m^2.

29. The method of claim 21 wherein the substituted hexitol derivative is administered by a route selected from the group consisting of intravenous and oral.

30. The method of claim 29 wherein the substituted hexitol derivative is dianhydrogalactitol.

31. The method of claim 29 wherein the substituted hexitol derivative is administered intravenously.

32. The method of claim 21 wherein the medicament is to be administered together with a therapeutically effective dose of ionizing radiation.

33. The method of claim 21 wherein the medicament is to be administered together with a therapeutically effective quantity of temozolomide.

34. The method of claim 21 wherein the medicament is to be administered together with a therapeutically effective quantity of bevacizumab.

35. The method of claim 21 wherein the medicament is to be administered together with a therapeutically effective quantity of a corticosteroid.

36. The method of claim 21 wherein the medicament is to be administered together with at least one chemotherapeutic agent selected from the group consisting of lomustine, cisplatin, carboplatin, vincristine, and cyclophosphamide.

37. The method of claim 21 wherein the dianhydrogalactitol substantially suppresses the growth of cancer stem cells (CSCs).

38. The method of claim 37 wherein the suppression of the growth of cancer stem cells is at least 50%.

39. The method of claim 38 where the suppression of the growth of cancer stem cells is at least 99%.

40. The method of claim 24 wherein the dianhydrogalactitol is effective in suppressing the growth of cancer cells possessing O^6-methylguanine-DNA methyltransferase (MGMT)-driven drug resistance.

41. The method of claim 24 wherein the dianhydrogalactitol is effective in suppressing the growth of cancer cells resistant to temozolomide.

42. The method of claim 21 wherein the medicament is to be administered together with a therapeutically effective quantity of a tyrosine kinase inhibitor.

43. The method of claim 21 wherein the medicament is to be administered together with a therapeutically effective quantity of an EGFR inhibitor.

44. The method of claim 43 wherein the EGFR inhibitor affects wild-type binding sites.

45. The method of claim 43 wherein the EGFR inhibitor affects mutated binding sites.

46. The method of claim 43 wherein the EGFR inhibitor affects EGFR Variant III.