CLAIMS

1. A pharmaceutical composition, comprising:
a hydrophilic antineoplastic chemotherapeutic encapsulated in ceramide anionic liposomes, wherein the liposomes comprise at least one pegylated neutral lipid, wherein the total amount of pegylated neutral lipid is an amount in the range of 5-20 Molar percent, inclusive, and wherein at least half of the amount of included modified neutrallipid is N-Octanoyl-Sphingosine-1- succinyl(methoxy(polyethylene)glycol)750 (PEG(750) C8); at least one anionic lipid, wherein the total amount of anionic lipid is an amount in the range of 5-15 Molar percent, inclusive; one or more ceramides selected from C4 ceramide, C6 ceramide, C8 ceramide, C 1O ceramide, C 12 ceramide, C 14 ceramide, C 16 ceramide and C 18 ceramide, in an amount in the range of 1-40 Molar percent, inclusive; and cationic or neutral lipids, with the proviso that the resulting ceramide anionic liposomes have a net negative charge at physiological pH.

2. The pharmaceutical composition of claim 1, wherein the hydrophilic antineop1astic chemotherapeutic is an antineoplastic vinca alkyloid.

3. The pharmaceutical composition of claim 1 ~~2~~, wherein the hydrophilic antineoplastic chemotherapeutic is selected from the group consisting of: vinblastine, vincristine, vinglycinate, vinorelbine, vindesine, sorafenib, cladribine and a combination of any two or more thereof.

4. The pharmaceutical composition of claim 1, wherein the ceramide anionic liposomes comprise a 3-5.5:1-4:1:3 ratio of neutral lipid:pegylated neutral lipid:anionic lipid:C4-C18 ceramide.

5. The pharmaceutical composition of claim 4, wherein the neutral lipid is a mixture of DSPC and DOPE, wherein the pegylated neutral lipid is a mixture of PEG(2000)-DSPE and N-Octanoyl-Sphingosine-1- succinyl(methoxy(polyethylene)glycol)750, and wherein the anionic lipid is dihexadecyl phosphate.

6. The pharmaceutical composition of claim 1, wherein the hydrophilic antineoplastic chemotherapeutic is vinblastine.

~~7. The pharmaceutical composition of claim 1, wherein the liposomes comprise at least one pegylated neutral lipid, wherein the total amount of pegylated neutral lipid is an amount in the range of 5-20 Molar percent, inclusive, and wherein at least half of the amount of included modified neutrallipid is N-Octanoyl-Sphingosine-1-succinyl(methoxy(polyethylene)glycol)750 (PEG(750) C8); at least one anionic lipid, wherein the total amount of anionic lipid is an amount in the range of 5-15 Molar~~

~~percent, inclusive; one or more ceramides selected from C4 ceramide, C6 ceramide, C8 ceramide, C 1O ceramide, C 12 ceramide, C 14 ceramide, C 16 ceramide and C 18 ceramide, in an amount in the range of 1-40 Molar percent, inclusive; and cationic or neutral lipids, with the proviso that the resulting ceramide anionic liposomes have a net negative charge at physiological pH.~~

~~8~~7. Use of a pharmaceutical composition, comprising:
a hydrophilic antineoplastic chemotherapeutic encapsulated in ceramide anionic liposomes, wherein the liposomes comprise at least one pegylated neutral lipid, wherein the total amount of pegylated neutral lipid is an amount in the range of 5-20 Molar percent, inclusive, and wherein at least half of the amount of included modified neutrallipid is N-Octanoyl-Sphingosine-1- succinyl(methoxy(polyethylene)glycol)750 (PEG(750) C8); at least one anionic lipid, wherein the total amount of anionic lipid is an amount in the range of 5-15 Molar percent, inclusive; one or more ceramides selected from C4 ceramide, C6 ceramide, C8 ceramide, C 1O ceramide, C 12 ceramide, C 14 ceramide, C 16 ceramide and C 18 ceramide, in an amount in the range of 1-40 Molar percent, inclusive; and cationic or neutral lipids, with the proviso that the resulting ceramide anionic liposomes have a net negative charge at physiological pH, in the manufacture of a medicament for treating a subject in need thereof, wherein the subject has cancer or a neoplasm.

~~9~~8. The use of claim ~~8~~7, wherein the subject has~~, or is at risk of having,~~ cancer.

~~10~~9. The use of claim ~~8~~7, wherein an adjunct anti-cancer treatment is to be further administered.

~~11~~10. A method of producing a pharmaceutical composition, comprising: providing a lipid mixture comprising at least one pegylated neutral lipid, wherein the total amount of pegylated neutral lipid is an amount in the range of 5-20 Molar percent, inclusive, and wherein at least half of the amount of included pegylated neutral lipid is N-Octanoyl-Sphingosine-1-succinyl(methoxy(polyethylene)glycol)750 (PEG(750) C8); at least one anionic lipid, wherein the total amount of anionic lipid is an amount in the range of 5-15 Molar percent, inclusive; one or more ceramides selected from C4 ceramide, C6 ceramide, C8 ceramide, C10 ceramide, C 12 ceramide, C14 ceramide, C16 ceramide and C18 ceramide, in an amount in the range of 1– 40 Molar percent, inclusive; and cationic or neutral lipids,

with the proviso that the resulting lipid mixture has a net negative charge at physiological pH;

sonicating the lipid mixture in the presence of an amount of a hydrophilic antineoplastic chemotherapeutic at a temperature in the range of 55–75 degrees Celsius, inclusive, to produce a sonicated mixture; and

passing the sonicated mixture through a filter having pores of a desired size to produce liposomes having the desired size, ata temperature in the range of 67-75 degrees

Celsius, producing a population of ceramide anionic liposomes, wherein the population comprises greater than 10% of the amount of the hydrophilic antineoplastic chemotherapeutic.

~~12~~11. The method of claim ~~11~~10, wherein the population comprises greater than 25% of the amount of the hydrophilic antineoplastic chemotherapeutic.

~~13~~12. The method of claim ~~11~~10, wherein the population comprises 15-75% of the amount of the hydrophilic antineoplastic chemotherapeutic.

~~14~~13. The method of claim ~~11~~10, wherein the ceramide is C6 ceramide, C8 ceramide or a combination of C6 ceramide and C8 ceramide.

~~15~~14. The method of claim ~~11~~10, wherein the hydrophilic antineoplastic chemotherapeutic is a vinca alkyloid antineoplastic chemotherapeutic.

~~16~~15. The method of claim ~~11~~10, wherein the hydrophilic antineoplastic chemotherapeutic is selected from the group consisting of: vinblastine, vincristine, vinglycinate, vinorelbine, vindesine, sorafenib, cladribine and a combination of any two or more thereof.

~~17~~16. The method of claim ~~11~~10, wherein the hydrophilic antineoplastic chemotherapeutic is vinblastine.