hydrabamine, an amino acid (e.g., arginine and/or lysine), a mono- and/or poly-hydroxyalkylamine, and/or a salt thereof, e.g., $(HO)_nR^8NH_2$, $[(HO)_nR^8]_2NH$, $[(HO)_nR^8]_3N$, and/or a salt thereof wherein each R^8 is independently C_{1-8}alkyl (e.g., C_{1-6}-alkyl, e.g., C_{1-4}-alkyl, e.g., $-CH_2CH_3$, e.g., $-CH_3$) and n is 0 or C_{1-8}-alkylene (e.g., C_{1-6}-alkylene, e.g., C_{1-4}-alkylene, e.g., $–CH_2–CH_2–$, e.g., $–C(CH_2)_3–$, e.g., one R^8 is $–CH_3$ and another R^8 is $–(CH_2)_6–$) and each n is independently 1-8 (e.g., 1, 2, 3, 4 , 5, or 6), e.g., tris(hydroxymethyl)aminomethane (also known as tris base) and/or a salt thereof (e.g., tris(hydroxymethyl)aminomethane acetate (also known as tris acetate), meglumine, dimethylethanolamine, diethylamine, diethylethanolamine, and/or diethanolamine), e.g., any of the preceding wherein a conjugate acid of the amine and/or salt thereof has a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9,

~~d) a metal chloride salt (e.g., zinc chloride),~~

e) an acetate salt, e.g., a metal acetate salt (e.g., an alkali and/or alkaline acetate salt, e.g., an alkali acetate salt, e.g., sodium acetate and/or potassium acetate),

f) a hydroxide and/or alkoxide salt, e.g., a metal hydroxide and/or metal alkoxide salt (e.g., a quarternary ammonium hydroxide, e.g., ammonium hydroxide and/or choline hydroxide, lithium hydroxide, aluminum hydroxide, e.g., an alkali and/or alkaline hydroxide salt, e.g., sodium hydroxide, potassium hydroxide, calcium hydroxide, magnesium hydroxide, and/or magnesium ethoxide, e.g., sodium hydroxide), and/or

g) a carbonate and/or bicarbonate salt, e.g., a metal carbonate and/or metal bicarbonate salt (e.g., an alkali and/or alkaline carbonate salt, e.g., an alkali and/or alkaline bicarbonate salt, e.g., sodium bicarbonate),

~~h~~g) a borate salt, e.g., a metal borate salt (e.g., an alkali borate salt, e.g., sodium borate),

e.g., one or more of sodium citrate, Na_2HPO_4, tris(hydroxymethyl)aminomethane, and a tris(hydroxymethyl)aminomethane salt (e.g., tris acetate), e.g., one or more of sodium citrate, Na_2HPO_4, and tris(hydroxymethyl)aminomethane, e.g., one or more of sodium citrate and Na_2HPO_4, e.g., Na_2HPO_4, e.g., tris(hydroxymethyl)aminomethane.

1.4 Composition I, 1.1, or 1.2 wherein the pharmaceutically acceptable excipient comprises one or more bases, e.g., a base wherein upon dissolution of the composition in an aquous solution the composition has a pH between 7, 7.5, or 8 and 10.5, e.g., between about 7, 7.5, or 8 and 9.5, e.g., between about 7 or 7.5 and 8, e.g., between about 7.5 and 8.5, e.g., about 7.5, e.g., about 8.5, e.g., between about 8 and 8.5, e.g., about 8.2, e.g., a base wherein a conjugate acid of the base has a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9, e.g., wherein the one or more bases are one or more of:

a) a metal citrate salt (e.g., an alkali and/or alkaline citrate salt, e.g., an alkali citrate salt, e.g., sodium citrate and/or potassium citrate),

b) a metal phosphate salt (e.g., an alkali and/or alkaline phosphate salt, e.g., an alkali phosphate salt, e.g., sodium phosphate (e.g., NaH_2PO_4 and/or Na_2HPO_4) and/or potassium phosphate (e.g., KH_2PO_4 and/or K_2HPO_4), e.g., sodium phosphate (e.g., Na_2HPO_4)),

c) an amine and/or a salt thereof (e.g., morpholine, an amino acid (e.g., arginine), a mono- and/or poly-hydroxyalkylamine, and/or a salt thereof, e.g., $(HO)_nR^8NH_2$, $[(HO)_nR^8]_2NH$, $[(HO)_nR^8]_3N$, and/or a salt thereof wherein each R^8 is independently $C_{1\text{-}8}$alkyl (e.g., $C_{1\text{-}6}$-alkyl, e.g., $C_{1\text{-}4}$-alkyl, e.g., $-CH_2CH_3$, e.g., $-CH_3$) and n is 0 or $C_{1\text{-}8}$-alkylene (e.g., $C_{1\text{-}6}$-alkylene, e.g., $C_{1\text{-}4}$-alkylene, e.g., $–CH_2–CH_2–$, e.g., $–C(CH_2)_3–$, e.g., one R^8 is $–CH_3$ and another R^8 is $–(CH_2)_6–$) and each n is independently 1-8 (e.g., 1, 2, 3, 4 , 5, or 6), e.g., tris(hydroxymethyl)aminomethane (also known as tris base) and/or a

1000 mM, e.g. from about 1 to 2, 5, 10, 15, 20, 25, 40, 50 or 60 mM, e.g., from about 5, 10, 15, 20, 25, or 50 to 100, 200, 250, 300, 400, 500, or 1000 mM, e.g., about 2, 20, or 200 mM, e.g., about 5, 10, 50, 500, 500, or 1000 mM.

1.60 Composition 1.47-1.59 wherein the solvent, e.g., the sterile solution, comprises one or more pharmaceutically acceptable bases, e.g., a base wherein upon dissolution of the composition in the solvent, e.g, aqueous solution, the composition has a pH between 7, 7.5, or 8 and 10.5, e.g., between about 7, 7.5, or 8 and 9.5, e.g., between about 7 or 7.5 and 8, e.g., between about 7.5 and 8.5, e.g., about 7.5, e.g., about 8.5, e.g., between about 8 and 8.5, e.g., about 8.2, e.g., a base wherein a conjugate acid of the pharmaceutically acceptable base has a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9, e.g., wherein the one or more pharmaceutically acceptable bases are one or more of:

a) a C_{1-8}-alkyl mono-, di-, or tri- carboxylic acid salt, e.g., a citrate salt, e.g, a metal citrate salt (e.g., an alkali and/or alkaline citrate salt, e.g., an alkali citrate salt, e.g., sodium citrate and/or potassium citrate), e.g., a tartrate salt (e.g., a metal tartrate salt, an alkali tartrate, e.g., sodium tartrate), e.g., a succinate salt (e.g., a metal succinate salt, e.g., an alkali succinate, e.g., disodium succinate), and/or e.g., a lactate salt (e.g., a metal lactate salt, e.g., an alkali lactate, e.g., sodium lactate),

b) a phosphate salt, e.g., a metal phosphate salt (e.g., an alkali and/or alkaline phosphate salt, e.g., an alkali phosphate salt, e.g., sodium phosphate (e.g., NaH_2PO_4 and/or Na_2HPO_4) and/or potassium phosphate (e.g., KH_2PO_4 and/or K_2HPO_4)),

c) an amine and/or a salt thereof (e.g., morpholine, piperazine, benethamine, benzathine, trimethylglycine, hydrabamine, 4-(2-hydroxyethyl)morpholine, 1-(2-hydroxyethyl)-pyrrolidine, an amino acid (e.g., arginine and/or lysine), a mono- and/or poly-hydroxyalkylamine, and/or a salt thereof, e.g., $(HO)_nR^8NH_2$, $[(HO)_nR^8]_2NH$, $[(HO)_nR^8]_3N$, and/or a salt thereof wherein each R^8 is independently C_{1-8}alkyl (e.g., C_{1-6}-alkyl, e.g., C_{1-4}-alkyl, e.g., -

CH_2CH_3, e.g., $-CH_3$) and n is 0 or C_{1-8}-alkylene (e.g., C_{1-6}-alkylene, e.g., C_{1-4}-alkylene, e.g., $-CH_2-CH_2-$, e.g., $-C(CH_2)_3-$, e.g., one R^8 is $-CH_3$ and another R^8 is $-(CH_2)_6-$) and each n is independently 1-8 (e.g., 1, 2, 3, 4 , 5, or 6), e.g., tris(hydroxymethyl)aminomethane (also known as tris base) and/or a salt thereof (e.g., tris(hydroxymethyl)aminomethane acetate (also known as tris acetate), meglumine, dimethylethanolamine, diethylamine, diethylethanolamine, and/or diethanolamine), e.g., any of the preceding wherein a conjugate acid of the amine and/or salt thereof has a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9,

~~d) a metal chloride salt (e.g., zinc chloride),~~

~~e~~d) an acetate salt, e.g., a metal acetate salt (e.g., an alkali and/or alkaline acetate salt, e.g., an alkali acetate salt, e.g., sodium acetate and/or potassium acetate),

~~f~~e) a hydroxide and/or alkoxide salt, e.g., a metal hydroxide and/or alkoxide salt (.g., a quarternary ammonium hydroxide, e.g., ammonium hydroxide and/or choline hydroxide, lithium hydroxide, aluminum hydroxide, e.g., an alkali and/or alkaline hydroxide salt, e.g., sodium hydroxide, potassium hydroxide, calcium hydroxide, magnesium hydroxide, and/or magnesium ethoxide e.g., sodium hydroxide),

~~g~~f) a carbonate and/or bicarbonate salt, e.g., a metal carbonate and/or metal bicarbonate salt (e.g., an alkali and/or alkaline carbonate salt, e.g., an alkali and/or alkaline bicarbonate salt, e.g., sodium bicarbonate), and/or

~~h~~g) a metal borate salt (e.g., an alkali borate salt, e.g., sodium borate), e.g., one or more of sodium citrate, Na_2HPO_4, tris(hydroxymethyl)aminomethane, and a tris(hydroxymethyl)aminomethane salt (e.g., tris acetate), e.g., one or more of sodium citrate, Na_2HPO_4, and tris(hydroxymethyl)aminomethane, e.g., one or

Formula III

1.102 Composition 1.44-1.98 or 1.101 wherein the composition comprises at least a 1:2 molar ratio of Formula III to a cation of the base, e.g., at least about 1:2, 1:3, 1:4, or 1:5 to 1:6, 1:7, 1:8 to 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5 to 1:5, 1:6, 1:7, 1:8, 1:9, 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5, e.g., at least about 1:5, e.g. at least about 1:10.

1.103 Composition I or 1.1-1.102 wherein the composition is for injection, e.g., subcutaneously, intramuscularly, intravenously, or intrathecally, e.g., intramuscularly or intravenously, e.g., a bolus injected subcutaneously, intramuscularly, intravenously, or intrathecally.

1.104 Composition 1.103 wherein the composition is for injection intravenously, e.g., IV bolus and/or IV infusion, e.g., IV bolus followed by IV infusion, e.g., a loading bolus (e.g., 10 or 20 to 30, 50, 70, 75, 100, 140, 150, 200, 300 or 400 mg per day administered by a loading bolus dose, e.g., about 50 to 200 or 250 mg per day administered by a loading bolus dose, e.g., about 70 to 140 mg per day administered by a loading bolus dose, e.g., a concentration of the dissolved salt administered by a loading bolus dose of 1 to 4, 5, 8, 10, 15, 20, 30, or 50 mM per day, e.g., a concentration of the dissolved salt administered by a loading bolus dose of about 2 to 5, 10, 15, or 20 mM per day, e.g., a concentration of the dissolved salt administered by a loading bolus dose of about 4 to 8 or 9 mM per day) and then an IV infusion over 24 hours for 3 days (e.g., at a rate of 1, 2, 3, 5, 6, 7, 8, 10, 15, 20, 25, 30, or 50 mg/hr for 24 hours, e.g., at a rate of 3, 6, or 15 mg/hr).

1.105 Composition 1.1043 wherein the composition is for injection intramuscularly, e.g., IM bolus and/or IM infusion, e.g., IM bolus followed by IM infusion.

1.106 Composition 1.104 or 1.105 wherein the infusion, e.g., IV or IM, is administered over about 10 or 30 minutes to 72 hours, e.g., about 30 minutes to 24 hours, e.g, about 30 minutes to 12 hours, e.g., about 30 minutes to 8 hours, e.g., about 30 minutes to 6 hours, e.g., about 30 minutes to 4 hours, e.g., about 30 minutes to 2 hours, e.g., about 30 minutes to 1 hour, e.g., about 72 hours.

1.113 Composition 1.110 wherein the composition comprises between 20 and 500 mg 2-{[3,5-bis(trifluoromethyl)phenyl]carbamoyl}-4-chlorophenyl dihydrogen phosphate (Formula I), e.g., between about 25 and 450 mg, e.g., between about 30 and 400 mg, e.g., between about 35 and 350 mg, and meglumine, e.g., between 20 and 900 mg meglumine, e.g., between about 30 and 800, e.g., between about 60 and 500 mg, e.g, between about 70 and 400 mg.

1.114 Composition 1.110 wherein the composition comprises between 20 and 500 mg 2-{[3,5-bis(trifluoromethyl)phenyl]carbamoyl}-4-chlorophenyl dihydrogen phosphate (Formula I), e.g., between about 25 and 450 mg, e.g., between about 30 and 400 mg, e.g., between about 35 and 350 mg, and sodium citrate, e.g., between 30 and 1500 mg sodium citrate, e.g., between about 40 and 1200, e.g., between about 50 and 1000 mg, e.g, between about 80 and 600 mg, e.g., between about 100 and 500 mg.

1.115 Composition 1.110-1.11~~5~~4 wherein the composition is admixed with a solvent, e.g., sterile water for injection, a sterile solution comprising dextrose (e.g., dextrose injection 5%), a sterile solution comprising sodium chloride (e.g., 0.9% sodium chloride injection), a sterile solution comprising benzyl alcohol (e.g., bacteriostatic water for injection with benzyl alcohol or bacteriostatic sodium chloride for injection with benzyl alcohol), or Lactated Ringer's, e.g., wherein the composition is admixed with 1 mL to 100 mL, e.g., about 3 to 50 mL, e.g., about 3.5 to 35 mL.

1.116 Composition 1.110-1.115 wherein the composition is admixed with a sterile water for injection, e.g., wherein the composition is admixed with 1 mL to 100 mL, e.g., about 3 to 50 mL, e.g., about 3.5 to 35 mL.

1.117 Composition 1.110-1.115 wherein the composition is admixed with a sterile solution comprising sodium chloride (e.g., 0.9% sodium chloride injection), e.g., wherein the composition is admixed with 1 mL to 100 mL, e.g., about 3 to 50 mL, e.g., about 3.5 to 35 mL.

1.118 Composition 1 or 1.1-1.117 wherein the composition comprises one or more additional therapeutic agents, e.g., one or more additional therapeutic agents for cerebral edema, stroke, traumatic brain injury, glioma (e.g., glioblastoma),

of the preceding wherein a conjugate acid of the amine and/or salt thereof has a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9,

d) ~~a metal chloride salt (e.g., zinc chloride),~~

ed) an acetate salt, e.g., a metal acetate salt (e.g., an alkali and/or alkaline acetate salt, e.g., an alkali acetate salt, e.g., sodium acetate and/or potassium acetate),

~~f~~e) a hydroxide and/or alkoxide salt, e.g., a metal hydroxide and/or alkoxide salt (e.g., a quarternary ammonium hydroxide, e.g., ammonium hydroxide and/or choline hydroxide, lithium hydroxide, aluminum hydroxide, e.g., an alkali and/or alkaline hydroxide salt, e.g., sodium hydroxide, potassium hydroxide, calcium hydroxide, magnesium hydroxide, and/or magnesium ethoxide, e.g., sodium hydroxide),

gf) a carbonate and/or bicarbonate salt, e.g., a metal carbonate and/or metal bicarbonate salt (e.g., an alkali and/or alkaline carbonate salt, e.g., an alkali and/or alkaline bicarbonate salt, e.g., sodium bicarbonate), and/or

~~h~~g) a metal borate salt (e.g., an alkali borate salt, e.g., sodium borate), e.g., one or more of sodium citrate, Na_2HPO_4, tris(hydroxymethyl)aminomethane, and a tris(hydroxymethyl)aminomethane salt (e.g., tris acetate), e.g., one or more of sodium citrate, Na_2HPO_4, and tris(hydroxymethyl)aminomethane, e.g., one or more of sodium citrate and Na_2HPO_4, e.g., Na_2HPO_4, e.g., tris(hydroxymethyl)aminomethane.

1.5 Method 1.1-1.4 wherein upon dissolution of the composition in a solvent, e.g., the aqueous solution, the composition has a pH between 7, 7.5, or 8 and 10.5, e.g., between about 7, 7.5, or 8 and 9.5, e.g., between about 7 or 7.5 and 8, e.g., between about 7.5 and 8.5, e.g., about 7.5, e.g., about 8.5, e.g., between about 8 and 8.5, e.g., about 8.2, e.g., a base wherein a conjugate acid of the base has a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g.,

an alkali citrate salt, e.g., sodium citrate and/or potassium citrate), e.g., a tartrate salt (e.g., a metal tartrate salt, an alkali tartrate, e.g., sodium tartrate), e.g., a succinate salt (e.g., a metal succinate salt, e.g., an alkali succinate, e.g., disodium succinate), and/or e.g., a lactate salt (e.g., a metal lactate salt, e.g., an alkali lactate, e.g., sodium lactate),

b) a phosphate salt, e.g., a metal phosphate salt (e.g., an alkali and/or alkaline phosphate salt, e.g., an alkali phosphate salt, e.g., sodium phosphate (e.g., NaH_2PO_4 and/or Na_2HPO_4) and/or potassium phosphate (e.g., KH_2PO_4 and/or K_2HPO_4)),

~~a~~c) an amine and/or a salt thereof (e.g., morpholine, piperazine, benethamine, benzathine, trimethylglycine, hydrabamine, 4-(2-hydroxyethyl)morpholine, 1-(2-hydroxyethyl)-pyrrolidine, an amino acid (e.g., arginine and/or lysine), a mono- and/or poly-hydroxyalkylamine, and/or a salt thereof, e.g., $(HO)_nR^8NH_2$, $[(HO)_nR^8]_2NH$, $[(HO)_nR^8]_3N$, and/or a salt thereof wherein each R^8 is independently C_{1-8}alkyl (e.g., C_{1-6}-alkyl, e.g., C_{1-4}-alkyl, e.g., -CH_2CH_3, e.g., -CH_3) and n is 0 or C_{1-8}-alkylene (e.g., C_{1-6}-alkylene, e.g., C_{1-4}-alkylene, e.g., –CH_2–CH_2–, e.g., –$C(CH_2)_3$–, e.g., one R^8 is –CH_3 and another R^8 is –$(CH_2)_6$–) and each n is independently 1-8 (e.g., 1, 2, 3, 4 , 5, or 6), e.g., tris(hydroxymethyl)aminomethane (also known as tris base) and/or a salt thereof (e.g., tris(hydroxymethyl)aminomethane acetate (also known as tris acetate), meglumine, dimethylethanolamine, diethylamine, diethylethanolamine, and/or diethanolamine), e.g., any of the preceding wherein a conjugate acid of the amine and/or salt thereof has a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9,

~~b) a metal chloride salt (e.g., zinc chloride),~~

e~~d~~) an acetate salt, e.g., a metal acetate salt (e.g., an alkali and/or alkaline acetate salt, e.g., an alkali acetate salt, e.g., sodium acetate and/or potassium acetate),

~~d~~e) a hydroxide and/or alkoxide salt, e.g., a metal hydroxide and/or alkoxide salt (e.g., a quarternary ammonium hydroxide, e.g., ammonium hydroxide and/or choline hydroxide, lithium hydroxide, aluminum hydroxide, e.g., an alkali and/or alkaline hydroxide salt, e.g., sodium hydroxide, potassium hydroxide, calcium hydroxide, magnesium hydroxide, and/or magnesium ethoxide e.g., sodium hydroxide),

~~e~~f) a carbonate and/or bicarbonate salt, e.g., a metal carbonate and/or metal bicarbonate salt (e.g., an alkali and/or alkaline carbonate salt, e.g., an alkali and/or alkaline bicarbonate salt, e.g., sodium bicarbonate), and/or

~~f~~g) a metal borate salt (e.g., an alkali borate salt, e.g., sodium borate), e.g., one or more of sodium citrate, Na_2HPO_4, tris(hydroxymethyl)aminomethane, and a tris(hydroxymethyl)aminomethane salt (e.g., tris acetate), e.g., one or more of sodium citrate, Na_2HPO_4, and tris(hydroxymethyl)aminomethane, e.g., one or more of sodium citrate and Na_2HPO_4, e.g., Na_2HPO_4, e.g., tris(hydroxymethyl)aminomethane.

1.61 Method 1.47-1.60 wherein the solvent, e.g., the sterile solution, comprises a base, e.g., a base wherein upon dissolution of the composition in the solvent, e.g., the sterile solution, the composition has a pH between 7, 7.5, or 8 and 10.5, e.g., between about 7, 7.5, or 8 and 9.5, e.g., between about 7 or 7.5 and 8, e.g., between about 7.5 and 8.5, e.g., about 7.5, e.g., about 8.5, e.g., between about 8 and 8.5, e.g., about 8.2, e.g., a base with a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9, e.g., wherein the base is one or more of:

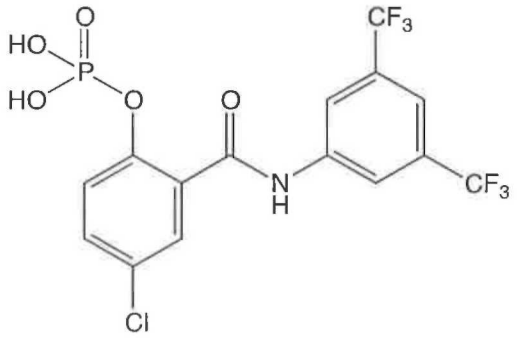
a) a metal citrate salt (e.g., an alkali and/or alkaline citrate salt, e.g., an alkali citrate salt, e.g., sodium citrate and/or potassium citrate),

b) a metal phosphate salt (e.g., an alkali and/or alkaline phosphate salt, e.g., an alkali phosphate salt, e.g., sodium phosphate (e.g., NaH_2PO_4 and/or Na_2HPO_4) and/or potassium phosphate (e.g., KH_2PO_4 and/or K_2HPO_4)),

meningitis, acute mountain sickness, infection, metabolic disorder, hypoxia, water intoxication, hepatic failure, hepatic encephalopathy, diabetic ketoacidosis, abscess, eclampsia, Creutzfeldt-Jakob disease, lupus cerebritis, optic nerve edema, hyponatremia, fluid retention, ovarian hyperstimulation syndrome, epilepsy, retinal ischemia or other diseases of the eye associated with abnormalities in intraocular pressure and/or tissue hydration, myocardial ischemia, myocardial ischemia/reperfusion injury, myocardial infarction, myocardial hypoxia, congestive heart failure, sepsis, neuromyelitis optica, or migraines.

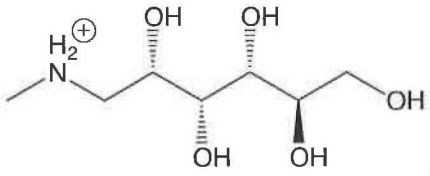
1.104 Method I or 1.1-1.103 further comprising admixing the composition with one or more additional therapeutic agents, e.g., one or more additional therapeutic agents for pulmonary edema, fibromyalgia, or multiple sclerosis.

[0062] In yet another embodiment, provided is a salt solution (Salt Solution I) comprising a solvent, e.g., an aqueous solution, and a salt formed from a compound of Formula I



Formula I

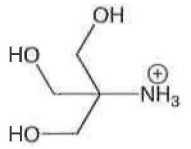
and an amine and/or a salt thereof (e.g., morpholine, piperazine, benethamine, benzathine, trimethylglycine, hydrabamine, 4-(2-hydroxyethyl)morpholine, 1-(2-hydroxyethyl)-pyrrolidine, an amino acid (e.g., arginine and/or lysine), a mono- and/or poly-hydroxyalkylamine, and/or a salt thereof, e.g., $(HO)_nR^8NH_2$, $[(HO)_nR^8]_2NH$, $[(HO)_nR^8]_3N$, and/or a salt thereof wherein each R^8 is independently C_{1-8}alkyl (e.g., C_{1-6}-alkyl, e.g., C_{1-4}-alkyl, e.g., $-CH_2CH_3$, e.g., $-CH_3$) and n is 0 or C_{1-8}-alkylene (e.g., C_{1-6}-alkylene, e.g., C_{1-4}-alkylene, e.g., $–CH_2–CH_2–$, e.g., $–C(CH_2)_3–$, e.g., one R^8 is $–CH_3$ and another R^8 is $–(CH_2)_6–$) and each n is independently 1-8 (e.g., 1, 2, 3, 4 , 5, or 6), e.g., tris(hydroxymethyl)aminomethane (also known as tris base) and/or a salt thereof (e.g., tris(hydroxymethyl)aminomethane acetate (also known as tris acetate), meglumine, dimethylethanolamine, diethylamine, diethylethanolamine, and/or diethanolamine), e.g., any of

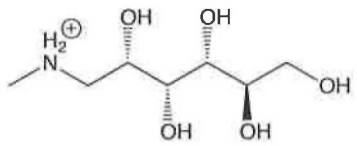


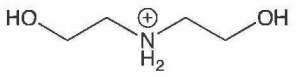
, e.g., at least about 1:2, 1:3, 1:4, or 1:5 to 1:6, 1:7, 1:8 to 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5 to 1:5, 1:6, 1:7, 1:8, 1:9, 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5, e.g., at least about 1:5, e.g. at least about 1:10.

1.13 Salt Solution I or 1.1-1.6 wherein the salt solution comprises at least a 1:2 molar ratio of Formula III to the protonated amine, e.g., at least about 1:2, 1:3, 1:4, or 1:5 to 1:6, 1:7, 1:8 to 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5 to 1:5, 1:6, 1:7, 1:8, 1:9, 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5, e.g., at least about 1:5, e.g. at least about 1:10.

1.14 Salt Solution 1.143 wherein the salt solution comprises at least a 1:2 molar ratio of Formula III to the protonated mono- and/or poly-hydroxyalkylamine, e.g., $(HO)_nR^8NH_3^+$, $[(HO)_nR^8]_2NH_2^+$, $[(HO)_nR^8]_3NH^+$, wherein each R^8 is independently C_{1-8}alkyl (e.g., C_{1-6}-alkyl, e.g., C_{1-4}-alkyl, e.g., $-CH_2CH_3$, e.g., $-CH_3$) and n is 0 or C_{1-8}-alkylene (e.g., C_{1-6}-alkylene, e.g., C_{1-4}-alkylene, e.g., $–CH_2–CH_2–$, e.g., $–C(CH_2)_3–$, e.g., one R^8 is $–CH_3$ and another R^8 is $–(CH_2)_6–$) and each n is independently 1-8 (e.g., 1, 2, 3, 4 , 5, or 6), e.g.,



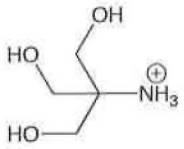
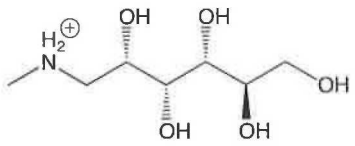
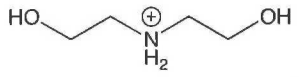
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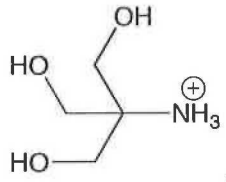
e.g., at least about 1:2, 1:3, 1:4, or 1:5 to 1:6, 1:7, 1:8 to 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5 to 1:5, 1:6, 1:7, 1:8, 1:9, 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5, e.g., at least about 1:5, e.g. at least about 1:10.

1.15 Salt Solution 1.143-1.154 wherein the salt solution comprises at least a 1:2 molar ratio of Formula III to $(HO)_nR^8NH_3^+$, $[(HO)_nR^8]_2NH_2^+$, $[(HO)_nR^8]_3NH^+$, wherein each R^8 is independently C_{1-8}alkyl (e.g., C_{1-6}-alkyl, e.g., C_{1-4}-alkyl, e.g., $-CH_2CH_3$, e.g., $-CH_3$) and n is 0 or C_{1-8}-alkylene (e.g., C_{1-6}-alkylene, e.g., C_{1-4}-alkylene, e.g., $–CH_2–CH_2–$, e.g., $–C(CH_2)_3–$, e.g., one R^8 is $–CH_3$ and another R^8 is $–(CH_2)_6–$) and each n is independently 1-8 (e.g., 1, 2, 3, 4 , 5, or 6), e.g.,

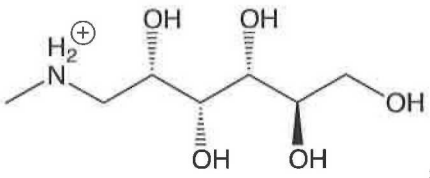


and/or


e.g., at least about 1:2, 1:3, 1:4, or 1:5 to 1:6, 1:7, 1:8 to 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5 to 1:5, 1:6, 1:7, 1:8, 1:9, 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5, e.g., at least about 1:5, e.g. at least about 1:10.

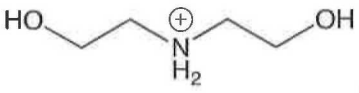
1.16 Salt Solution 1.143-1.165 wherein the salt solution comprises at least a 1:2 molar ratio of Formula III to


, e.g., at least about 1:2, 1:3, 1:4, or 1:5 to 1:6, 1:7, 1:8 to 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5 to 1:5, 1:6, 1:7, 1:8, 1:9, 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5, e.g., at least about 1:5, e.g. at least about 1:10.

1.17 Salt Solution 1.14-1.16 wherein the salt solution comprises at least a 1:2 molar ratio of Formula III to


, e.g., at least about 1:2, 1:3, 1:4, or 1:5 to 1:6, 1:7, 1:8 to 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5 to 1:5, 1:6, 1:7, 1:8, 1:9, 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5, e.g., at least about 1:5, e.g. at least about 1:10.

1.18 Salt Solution 1.14-1.16 wherein the salt solution comprises at least a 1:2 molar ratio of Formula III to


, e.g., at least about 1:2, 1:3, 1:4, or 1:5 to 1:6, 1:7, 1:8 to 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5 to 1:5, 1:6, 1:7, 1:8, 1:9, 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5, e.g., at least about 1:5, e.g. at least about 1:10.

1.19 Salt Solution I or 1.1-1.198 wherein the solvent is a sterile solution, e.g., sterile water for injection, a sterile solution comprising dextrose (e.g., dextrose injection 5%), a sterile solution comprising sodium chloride (e.g., 0.9% sodium chloride injection), a sterile solution comprising benzyl alcohol (e.g., bacteriostatic water for injection with benzyl alcohol or bacteriostatic sodium chloride for injection with benzyl alcohol), or Lactated Ringer's.

1.20 Salt Solution I or 1.1-1.2019 wherein the salt solution comprises 0.5 to 500 mL solvent, e.g., an aqueous solution, e.g., from about 1 or 2 mL to 500 mL, e.g., from about 1 or 2 mL to 5, 10, 25, 30, 35, 50, 75, 100, 150, 200, 300 or 500 mL, e.g., from about 1 or 2 mL to 5, 10, 25, 50, 75, 100, or 200 mL, e.g., from about 3.5 or 5 to 10, 25, 50, or 100 mL, e.g., about 3.5 or 35 mL.

1.21 Salt Solution I or 1.1-1.210 wherein the salt solution comprises 0.5 to 500 mL sterile solution, e.g., sterile water for injection, a sterile solution comprising dextrose (e.g., dextrose injection 5%), a sterile solution comprising sodium chloride (e.g., 0.9% sodium chloride injection), a sterile solution comprising benzyl alcohol (e.g., bacteriostatic water for injection with benzyl alcohol or bacteriostatic sodium chloride for injection with benzyl alcohol), or Lactated Ringer's, e.g., from about 1 or 2 mL to 500 mL, e.g., from about 1 or 2 mL to 5, 10, 25, 30, 35, 50, 75, 100, 150, 200, 300 or 500 mL, e.g., from about 1 or 2 mL to 5, 10, 25, 50, 75, 100, or 200 mL, e.g., from about 3.5 or 5 to 10, 25, 50, or 100 mL, e.g., about 3.5 or 35 mL.

1.22 Salt Solution I or 1.1-1.221 wherein the salt solution comprises sterile water for injection or a sterile solution comprising sodium chloride (e.g., 0.9% sodium chloride injection).

1.23 Salt Solution I or 1.1-1.232 wherein the salt solution comprises sterile water for injection.

1.24 Salt Solution 1.243 wherein the salt solution comprises 0.5 to 500 mL sterile water for injection, e.g., from about 1 or 2 mL to 500 mL, e.g., from about 1 or 2 mL to 5, 10, 25, 30, 35, 50, 75, 100, 150, 200, 300 or 500 mL, e.g., from about 1 or 2 mL to 5, 10, 25, 50, 75, 100, or 200 mL, e.g., from about 3.5 or 5 to 10, 25, 50, or 100 mL, e.g., about 3.5 or 35 mL.

1.25 Salt Solution I or 1.1-1.254 wherein the salt solution comprises a sterile solution comprising sodium chloride (e.g., 0.9% sodium chloride injection).

1.26 Salt Solution 1.265 wherein the salt solution comprises 0.5 to 500 mL of a sterile solution comprising sodium chloride (e.g., 0.9% sodium chloride injection), e.g., from about 1 or 2 mL to 500 mL, e.g., from about 1 or 2 mL to 5, 10, 25, 30, 35, 50, 75, 100, 150, 200, 300 or 500 mL, e.g., from about 1 or 2 mL to 5, 10, 25, 50, 75, 100, or 200 mL, e.g., from about 3.5 or 5 to 10, 25, 50, or 100 mL, e.g., about 3.5 or 35 mL.

1.27 Salt Solution I or 1.1-1.276 wherein the concentration of Formula II or Formula III, e.g., the concentration of Formula II, e.g, the concentration of Formula III is 0.01 or 0.02 or 0.05 or 0.1 or 0.5 or 1 or 2 to 250 mM, e.g., from about 0.01 or 0.1 or 0.5 to 1, 2, 5, 10, 15, 20, 25, 40, 50, 60, 75, 100, 125, 150, 175, 200, 250, or 1000 mM, e.g. from about 1 to 2, 5, 10, 15, 20, 25, 40, 50 or 60 mM, e.g., from about 5, 10, 15, 20, 25, or 50 to 100, 200, 250, 300, 400, 500, or 1000 mM, e.g., about 2, 20, or 200 mM, e.g., about 5, 10, 50, 500, 500, or 1000 mM.

1.28 Salt Solution I or 1.1-1.287 wherein the salt solution comprises one or more bulking agents, e.g., one or more of maltose, mannose, ribose, cyclodextrin, mannitol, lactose, sucrose, trehalose, sorbitol, glucose, raffinose, arginine, glycine, histidine, dextran (e.g., dextran 40), polyvinylpyrrolidone, polyethylene glycol, and polypropylene glycol, e.g., one or more of mannitol, glucose, sucrose, lactose, trehalose, and dextran (e.g., dextran 40).

1.29 Salt Solution I or 1.1-1.298 wherein the salt solution comprises 5 or 10 or 50 mg to 2 or 5 g of one or more bulking agents, e.g., from about 50 or 100 mg to 200, 300, 500, or 800 mg, or 1, 1.5, 2, 3, 4, or 5 g of one or more bulking agents.

1.30 Salt Solution I or 1.1-1.3029 wherein the salt solution comprises dextran (e.g., dextran 40).

1.31 Salt Solution 1.310 wherein the salt solution comprises 5 or 10 or 50 mg to 2 or 5 g dextran (e.g., dextran 40), e.g., from about 50 or 100 mg to 200, 300, 500, or 800 mg, or 1, 1.5, 2, 3, 4, or 5 g dextran (e.g., dextran 40).

1.32 Salt Solution I or 1.1-1.321 wherein the salt solution comprises one or more solubilizing agents, e.g., ethylenediamine tetraacetic acid (EDTA) or a salt thereof

(e.g., calcium disodium EDTA, disodium EDTA, sodium EDTA), alpha cyclodextrin, hydroxypropyl-β-cyclodextrin, polysorbate 80, tert-butanol, isopropanol, dichloromethane, ethanol, acetone, and glycerol; one or more collapse temperature modifiers which may shift the overall collapse temperature higher, e.g., one or more of dextran, Ficoll®, gelatin, and hydroxyethyl starch; one or more tonicity modifiers, e.g., one or more of sodium chloride, potassium chloride, sucrose, mannitol, and glucose; and one or more antimicrobial agents, e.g., one or more of benzyl alcohol, phenol, 2-phenoxyethanol, m-cresol, chlorobutanol, parabens (e.g., methyl paraben, ethyl paraben, propyl paraben), benzalkonium chloride, benzethonium chloride, myristyl gamma-picolinium salt (e.g., myristyl gamma-picolinium chloride), and organomercury compounds and salts (e.g., phenyl mercuric acetate, phenyl mercuric borate, phenyl mercuric nitrate, and thimerosal).

1.33 Salt Solution I or 1.1-1.~~33~~2 wherein the pH of the salt solution is between pH 7 and pH 10.5, e.g., between pH 7 and pH 9.5, e.g., between pH 7 and pH 8, e.g., between 7.5 and 8.5, e.g., 7.5, e.g., 8.5, e.g., 8.2.

1.34 Salt Solution I or 1.1-1.~~34~~3 wherein the salt solution is filtered to remove particles and microbes, e.g., filtered prior to injection.

1.35 Salt Solution I or 1.1-1.~~35~~4 wherein the salt solution is for injection, e.g., subcutaneously, intramuscularly, intravenously, or intrathecally, e.g., intramuscularly or intravenously, e.g., a bolus injected subcutaneously, intramuscularly, intravenously, or intrathecally.

1.36 Salt Solution 1.~~36~~5 wherein the salt solution is for injection intravenously, e.g., IV bolus and/or IV infusion, e.g., IV bolus followed by IV infusion, e.g., a loading bolus (e.g., 10 or 20 to 30, 50, 70, 75, 100, 140, 150, 200, 300 or 400 mg per day administered by a loading bolus dose, e.g., about 50 to 200 or 250 mg per day administered by a loading bolus dose, e.g., about 70 to 140 mg per day administered by a loading bolus dose, e.g., a concentration of the dissolved salt administered by a loading bolus dose of 1 to 4, 5, 8, 10, 15, 20, 30, or 50 mM per day, e.g., a concentration of the dissolved salt administered by a loading bolus dose of about 2 to 5, 10, 15, or 20 mM per day, e.g., a concentration of the

dissolved salt administered by a loading bolus dose of about 4 to 8 or 9 mM per day) and then an IV infusion over 24 hours for 3 days (e.g., at a rate of 1, 2, 3, 5, 6, 7, 8, 10, 15, 20, 25, 30, or 50 mg/hr for 24 hours, e.g., at a rate of 3, 6, or 15 mg/hr).

1.37 Salt Solution 1.365 wherein the salt solution is for injection intramuscularly, e.g., IM bolus and/or IM infusion, e.g., IM bolus followed by IM infusion.

1.38 Salt Solution 1.376 or 1.387 wherein the infusion, e.g., IV or IM, is administered over about 10 or 30 minutes to 72 hours, e.g., about 30 minutes to 24 hours, e.g, about 30 minutes to 12 hours, e.g., about 30 minutes to 8 hours, e.g., about 30 minutes to 6 hours, e.g., about 30 minutes to 4 hours, e.g., about 30 minutes to 2 hours, e.g., about 30 minutes to 1 hour, e.g., about 72 hours.

1.39 Salt Solution I or 1.1-1.398 wherein the salt solution comprises one or more additional therapeutic agents, e.g., one or more additional therapeutic agents for cerebral edema, stroke, traumatic brain injury, glioma (e.g., glioblastoma), meningitis, acute mountain sickness, infection, metabolic disorder, hypoxia, water intoxication, hepatic failure, hepatic encephalopathy, diabetic ketoacidosis, abscess, eclampsia, Creutzfeldt-Jakob disease, lupus cerebritis, optic nerve edema, hyponatremia, fluid retention, ovarian hyperstimulation syndrome, epilepsy, retinal ischemia or other diseases of the eye associated with abnormalities in intraocular pressure and/or tissue hydration, myocardial ischemia, myocardial ischemia/reperfusion injury, myocardial infarction, myocardial hypoxia, congestive heart failure, sepsis, neuromyelitis optica, or migraines.

1.40 Salt Solution I or 1.1-1.4039 wherein the salt solution comprises one or more additional therapeutic agents, e.g., one or more additional therapeutic agents for pulmonary edema, fibromyalgia, or multiple sclerosis.

1.41 Salt Solution I or 1.1-1.410 wherein the salt solution is stable for at least one week, at room temperature, e.g., for at least 1, 2, 4, 6, 8, or 12 months, e.g., the composition has < 20% N-[3,5-bis(trifluoromethyl)phenyl]-5-chloro-2-hydroxybenzamide, < 15% N-[3,5-bis(trifluoromethyl)phenyl]-5-chloro-2-hydroxybenzamide, < 10% N-[3,5-bis(trifluoromethyl)phenyl]-5-chloro-2-

hydroxybenzamide, < 5% N-[3,5-bis(trifluoromethyl)phenyl]-5-chloro-2-hydroxybenzamide, < 2% N-[3,5-bis(trifluoromethyl)phenyl]-5-chloro-2-hydroxybenzamide, 1% N-[3,5-bis(trifluoromethyl)phenyl]-5-chloro-2-hydroxybenzamide, or < 1% N-[3,5-bis(trifluoromethyl)phenyl]-5-chloro-2-hydroxybenzamide.

1.42 Salt Solution I or 1.1-1.421 wherein the salt solution comprises less than 10%, 15%, or 20% of N-[3,5-bis(trifluoromethyl)phenyl]-5-chloro-2-hydroxybenzamide, e.g., less than 5, 4, 3, or 2% of N-[3,5-bis(trifluoromethyl)phenyl]-5-chloro-2-hydroxybenzamide for at least one week, e.g., for at least 1, 2, 4, 6, 8, or 12 months.

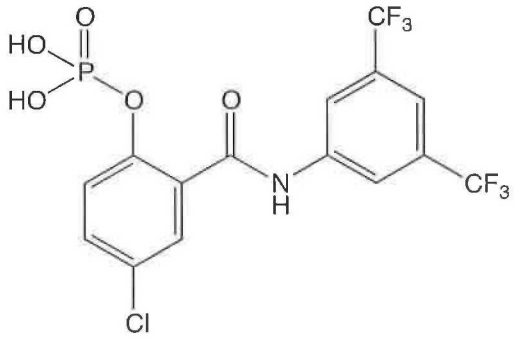
1.43 Salt Solution I or 1.1-1.432 wherein the salt solution is administered concurrently or sequentially, in either order, with one or more additional therapeutic agents, e.g., one or more additional therapeutic agents for cerebral edema, stroke, traumatic brain injury, glioma (e.g., glioblastoma), meningitis, acute mountain sickness, infection, metabolic disorder, hypoxia, water intoxication, hepatic failure, hepatic encephalopathy, diabetic ketoacidosis, abscess, eclampsia, Creutzfeldt-Jakob disease, lupus cerebritis, optic nerve edema, hyponatremia, fluid retention, ovarian hyperstimulation syndrome, epilepsy, retinal ischemia or other diseases of the eye associated with abnormalities in intraocular pressure and/or tissue hydration, myocardial ischemia, myocardial ischemia/reperfusion injury, myocardial infarction, myocardial hypoxia, congestive heart failure, sepsis, neuromyelitis optica, or migraines.

1.44 Salt Solution I or 1.1-1.443 wherein the salt solution is administered concurrently or sequentially, in either order, with one or more additional therapeutic agents, e.g., one or more additional therapeutic agents for pulmonary edema, fibromyalgia, or multiple sclerosis.

1.45 Salt Solution I or 1.1-1.454 wherein the salt solution is for use in any of the methods described herein, e.g., for use in Method A, e.g., Method A.1-A.58, for use in Method B, e.g., Method B.1-B.41, e.g., for use in Method C, e.g., C.1-C.8, e.g., for use in Method D, e.g., D.1-D.19, e.g., for use in Method E, e.g., E.1-E.59,

e.g., for use in Method F, e.g., F.1-F.5, e.g., for use in Method G, e.g., G.1-G.58, for use in Method H, e.g., H.1-H.9, *vida infra*.

[0064] In yet another embodiment, provided is a method (Method II) for making a salt solution, e.g., Salt Solution I, e.g., Salt Solution 1.1-1.46, comprising admixing a compound of Formula I



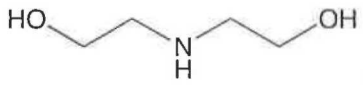
Formula I

and an amine and/or a salt thereof (e.g., morpholine, piperazine, benethamine, benzathine, trimethylglycine, hydrabamine, 4-(2-hydroxyethyl)morpholine, 1-(2-hydroxyethyl)-pyrrolidine, an amino acid (e.g., arginine and/or lysine), a mono- and/or poly-hydroxyalkylamine, and/or a salt thereof, e.g., $(HO)_nR^8NH_2$, $[(HO)_nR^8]_2NH$, $[(HO)_nR^8]_3N$ and/or a salt thereof wherein each R^8 is independently C_{1-8}alkyl (e.g., C_{1-6}-alkyl, e.g., C_{1-4}-alkyl, e.g., $-CH_2CH_3$, e.g., $-CH_3$) and n is 0 or C_{1-8}-alkylene (e.g., C_{1-6}-alkylene, e.g., C_{1-4}-alkylene, e.g., $–CH_2–CH_2–$, e.g., $–C(CH_2)_3–$, e.g., one R^8 is $–CH_3$ and another R^8 is $–(CH_2)_6–$) and each n is independently 1-8 (e.g., 1, 2, 3, 4 , 5, or 6), e.g., tris(hydroxymethyl)aminomethane (also known as tris base) and/or a salt thereof (e.g., tris(hydroxymethyl)aminomethane acetate (also known as tris acetate), meglumine, dimethylethanolamine, diethylamine, diethylethanolamine, and/or diethanolamine), e.g., any of the preceding wherein a conjugate acid of the amine and/or salt thereof has a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9, in a solvent, e.g., an aqueous solution,.

[0065] Further provided is Method II as follows:

2.1 Method II comprising admixing the compound of Formula I with a mono- and/or poly-hydroxyalkylamine and/or a salt thereof, e.g., $(HO)_nR^8NH_2$, $[(HO)_nR^8]_2NH$, and/or $[(HO)_nR^8]_3N$ and/or a salt thereof, wherein each R^8 is independently C_{1-8}alkyl (e.g., C_{1-6}-alkyl, e.g., C_{1-4}-alkyl, e.g., $-CH_2CH_3$, e.g., $-CH_3$) and n is 0 or C_{1-8}-alkylene (e.g., C_{1-6}-alkylene, e.g., C_{1-4}-alkylene, e.g., $–CH_2–CH_2–$, e.g., –

2.5 Method II or 2.1-2.4 comprising admixing the compound of Formula I with

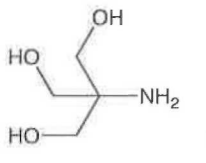


and/or a salt thereof.

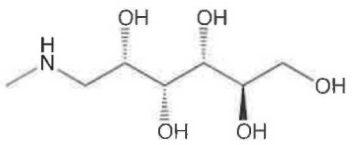
2.6 Method II or 2.1-2.5 wherein Formula I‡ and the amine and/or salt thereof are admixed in at least a 1:1 molar ratio.

2.7 Method II or 2.1-2.6 wherein Formula I‡ and the amine and/or salt thereof are admixed in at least a 1:2 molar ratio, e.g., at least about 1:2, 1:3, 1:4, or 1:5 to 1:6, 1:7, 1:8 to 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5 to 1:5, 1:6, 1:7, 1:8, 1:9, 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5, e.g., at least about 1:5, e.g. at least about 1:10.

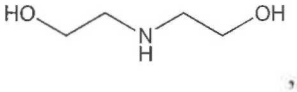
2.8 Method II or 2.1-2.7 wherein Formula I‡ and the mono- and/or poly-hydroxyalkylamine and/or salt thereof, e.g., $(HO)_nR^8NH_2$, $[(HO)_nR^8]_2NH$, and/or $[(HO)_nR^8]_3N$ and/or salt thereof and/or salt thereof (e.g., acetate, e.g., tris(hydroxymethyl)aminomethane acetate), wherein each R^8 is independently C_{1-8}alkyl (e.g., C_{1-6}-alkyl, e.g., C_{1-4}-alkyl, e.g., $-CH_2CH_3$, e.g., $-CH_3$) and n is 0 or C_{1-8}-alkylene (e.g., C_{1-6}-alkylene, e.g., C_{1-4}-alkylene, e.g., $–CH_2–CH_2–$, e.g., $–C(CH_2)_3–$, e.g., one R^8 is $–CH_3$ and another R^8 is $–(CH_2)_6–$) and each n is independently 1-8 (e.g., 1, 2, 3, 4 , 5, or 6), e.g.,



,



, and/or

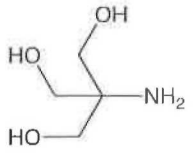


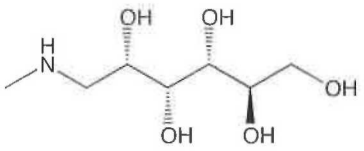
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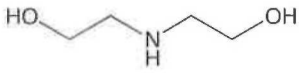
and/or a salt thereof, e.g., any of the preceding wherein a conjugate acid of the amine and/or salt thereof has a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9, are admixed in at least a 1:2 molar ratio, e.g., at least about 1:2, 1:3, 1:4, or 1:5 to 1:6, 1:7, 1:8 to 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5 to 1:5, 1:6, 1:7, 1:8, 1:9, 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5, e.g., at least about 1:5, e.g. at least about 1:10.

2.9 Method II or 2.1-2.8 wherein Formula I‡ and $(HO)_nR^8NH_2$, $[(HO)_nR^8]_2NH$, and/or $[(HO)_nR^8]_3N$ and/or salt thereof (e.g., acetate, e.g., tris(hydroxymethyl)aminomethane acetate), wherein each R^8 is independently C_{1-}

$_{8}$alkyl (e.g., C_{1-6}-alkyl, e.g., C_{1-4}-alkyl, e.g., $-CH_2CH_3$, e.g., $-CH_3$) and n is 0 or C_{1-8}-alkylene (e.g., C_{1-6}-alkylene, e.g., C_{1-4}-alkylene, e.g., $–CH_2–CH_2–$, e.g., $–C(CH_2)_3–$, e.g., one R^8 is $–CH_3$ and another R^8 is $–(CH_2)_6–$) and each n is independently 1-8 (e.g., 1, 2, 3, 4 , 5, or 6), e.g.,

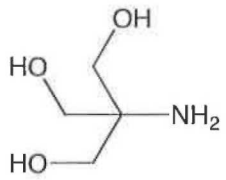


,


, and/or


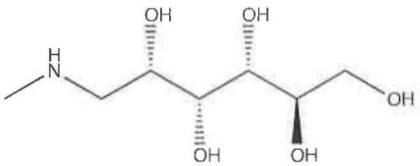
and/or a salt thereof are admixed in at least a 1:2 molar ratio, e.g., at least about 1:2, 1:3, 1:4, or 1:5 to 1:6, 1:7, 1:8 to 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5 to 1:5, 1:6, 1:7, 1:8, 1:9, 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5, e.g., at least about 1:5, e.g. at least about 1:10.

2.10 Method II or 2.1-2.9 wherein Formula II and



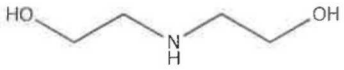
and/or a salt thereof are admixed in at least a 1:2 molar ratio, e.g., at least about 1:2, 1:3, 1:4, or 1:5 to 1:6, 1:7, 1:8 to 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5 to 1:5, 1:6, 1:7, 1:8, 1:9, 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5, e.g., at least about 1:5, e.g. at least about 1:10.

2.11 Method II or 2.1-2.10 wherein Formula II and



and/or a salt thereof are admixed in at least a 1:2 molar ratio, e.g., at least about 1:2, 1:3, 1:4, or 1:5 to 1:6, 1:7, 1:8 to 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5 to 1:5, 1:6, 1:7, 1:8, 1:9, 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5, e.g., at least about 1:5, e.g. at least about 1:10.

2.12 Method II or 2.1-2.11 wherein Formula II and



hydroxyethyl)morpholine, 1-(2-hydroxyethyl)-pyrrolidine, an amino acid (e.g., arginine and/or lysine), a mono- and/or poly-hydroxyalkylamine, and/or a salt thereof, e.g., $(HO)_nR^8NH_2$, $[(HO)_nR^8]_2NH$, $[(HO)_nR^8]_3N$, and/or a salt thereof wherein each R^8 is independently C_{1-8}alkyl (e.g., C_{1-6}-alkyl, e.g., C_{1-4}-alkyl, e.g., -CH_2CH_3, e.g., -CH_3) and n is 0 or C_{1-8}-alkylene (e.g., C_{1-6}-alkylene, e.g., C_{1-4}-alkylene, e.g., –CH_2–CH_2–, e.g., –$C(CH_2)_3$–, e.g., one R^8 is –CH_3 and another R^8 is –$(CH_2)_6$–) and each n is independently 1-8 (e.g., 1, 2, 3, 4 , 5, or 6), e.g., tris(hydroxymethyl)aminomethane (also known as tris base) and/or a salt thereof (e.g., tris(hydroxymethyl)aminomethane acetate (also known as tris acetate), meglumine, dimethylethanolamine, diethylamine, diethylethanolamine, and/or diethanolamine), e.g., any of the preceding wherein a conjugate acid of the amine and/or salt thereof has a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9 between 6 and 11, e.g., between 6.5 and 10, e.g., between 7 and 9,

~~d) a metal chloride salt (e.g., zinc chloride);~~

ed) an acetate salt, e.g., a metal acetate salt (e.g., an alkali and/or alkaline acetate salt, e.g., an alkali acetate salt, e.g., sodium acetate and/or potassium acetate),

fe) a hydroxide and/or alkoxide salt, e.g., a metal hydroxide and/or alkoxide salt (e.g., a quarternary ammonium hydroxide, e.g., ammonium hydroxide and/or choline hydroxide, lithium hydroxide, aluminum hydroxide, e.g., an alkali and/or alkaline hydroxide salt, e.g., sodium hydroxide, potassium hydroxide, calcium hydroxide, magnesium hydroxide, and/or magnesium ethoxide, e.g., sodium hydroxide),

gf) a carbonate and/or bicarbonate salt, e.g., a metal carbonate and/or metal bicarbonate salt (e.g., an alkali and/or alkaline carbonate salt,

e.g., an alkali and/or alkaline bicarbonate salt, e.g., sodium bicarbonate),

~~h~~g) a metal borate salt (e.g., an alkali borate salt, e.g., sodium borate), e.g., one or more of sodium citrate, Na_2HPO_4, tris(hydroxymethyl)aminomethane, and a tris(hydroxymethyl)aminomethane salt (e.g., tris acetate), e.g., one or more of sodium citrate, Na_2HPO_4, and tris(hydroxymethyl)aminomethane, e.g., one or more of sodium citrate and Na_2HPO_4, e.g., Na_2HPO_4, e.g., tris(hydroxymethyl)aminomethane.

1.5 Kit 1.2-1.4 wherein the one or more pharmaceutically acceptable excipients comprise one or more bases, e.g., a base wherein upon dissolution of the composition in a solvent, e.g., an aqueous solution, the solution has a pH between 7, 7.5, or 8 and 10.5, e.g., between about 7, 7.5, or 8 and 9.5, e.g., between about 7 or 7.5 and 8, e.g., between about 7.5 and 8.5, e.g., about 7.5, e.g., about 8.5, e.g., between about 8 and 8.5, e.g., about 8.2, e.g., a base wherein a conjugate acid of the base has a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9, e.g., wherein the one or more bases are one or more of:

a) a metal citrate salt (e.g., an alkali and/or alkaline citrate salt, e.g., an alkali citrate salt, e.g., sodium citrate and/or potassium citrate),

b) a metal phosphate salt (e.g., an alkali and/or alkaline phosphate salt, e.g., an alkali phosphate salt, e.g., sodium phosphate (e.g., NaH_2PO_4 and/or Na_2HPO_4) and/or potassium phosphate (e.g., KH_2PO_4 and/or K_2HPO_4)),

c) an amine and/or a salt thereof (e.g., morpholine, an amino acid (e.g., arginine), a mono- and/or poly-hydroxyalkylamine, and/or a salt thereof, e.g., $(HO)_nR^8NH_2$, $[(HO)_nR^8]_2NH$, $[(HO)_nR^8]_3N$, and/or a salt thereof wherein each R^8 is independently $C_{1\text{-}8}$alkyl (e.g., $C_{1\text{-}6}$-alkyl, e.g., $C_{1\text{-}4}$-alkyl, e.g., $-CH_2CH_3$, e.g., $-CH_3$) and n is 0 or $C_{1\text{-}8}$-alkylene (e.g., $C_{1\text{-}6}$-alkylene, e.g., $C_{1\text{-}4}$-alkylene, e.g., $–CH_2–CH_2–$, e.g., $–C(CH_2)_3–$, e.g., one R^8 is $–CH_3$ and another R^8 is $–(CH_2)_6–$) and each n is independently 1-8 (e.g., 1, 2, 3, 4 , 5, or 6), e.g.,

tris(hydroxymethyl)aminomethane salt (e.g., tris(hydroxymethyl)aminomethane acetate), e.g., 1 or 5 mg to 200 or 500 mg tris(hydroxymethyl)aminomethane acetate, e.g., from about 1 or 5 or 10 mg to 15, 20, 25, 30, 40, 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, 500, 1000, or 1500 mg, e.g., from about 15, 20, 30, 50, or 100 to 200, 250, 400, 450, 500, 600, 700, 800, 1000, or 1500 mg.

1.32 Kit 1.30 wherein the concentration of the tris(hydroxymethyl)aminomethane salt (e.g., tris(hydroxymethyl)aminomethane acetate) is 0.01 or 0.1 or 0.5 or 1 or 2 to 250 mM, e.g., from about 0.01 or 0.1 or 0.5 to 1, 2, 5, 10, 15, 20, 25, 40, 50, 60, 75, 100, 125, 150, 175, 200, 250, or 1000 mM, e.g. from about 1 to 2, 5, 10, 15, 20, 25, 40, 50 or 60 mM, e.g., from about 5 to 50 mM, e.g., from about 5, 10, 15, 20, 25, or 50 to 100, 200, 250, 300, 400, 500, or 1000 mM, e.g., about 2, 20, or 200 mM, e.g., about 5, 10, 50, 500, 500, or 1000 mM, e.g., from about 5, 10, 15, 20, 25, or 50 to 100, 200, 250, 300, 400, 500, or 1000 mM, e.g., about 2, 20, or 200 mM, e.g., about 5, 10, 50, 500, 500, or 1000 mM, e.g., wherein the concentration of the tris(hydroxymethyl)aminomethane salt (e.g., tris(hydroxymethyl)aminomethane acetate) is 2 or 3 to 5, 6, 8, 10, 15 or 20 equivalents of Formula II, e.g., about 2.5 or 5 to 10, e.g. about 2.5, e.g., about 5, e.g., wherein the concentration of the tris(hydroxymethyl)aminomethane salt (e.g., tris(hydroxymethyl)aminomethane acetate) is 2 or 3 to 5, 6, 8, 10, 15 or 20 equivalents of Formula III, e.g., about 5 to 10, e.g. about 5, e.g., about 10.

1.33 Kit 1.3-1.332 wherein the one or more bases comprise a base, e.g., an amine and/or a salt thereof, wherein a conjugate acid of the base has a pKa between 6, 7, 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9.

1.34 Kit 1.343 wherein the kit comprises 1 or 5 mg to 200 or 500 mg of the base, e.g., from about 1 or 5 or 10 mg to 15, 20, 25, 30, 40, 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, 500, 1000, or 1500 mg, e.g., from about 15, 20, 30, 50, or 100 to 200, 250, 400, 450, 500, 600, 700, 800, 1000, or 1500 mg.

1.35 Kit 1.34 wherein the concentration of the base is 0.01 or 0.1 or 0.5 or 1 or 2 to 250 mM, e.g., from about 0.01 or 0.1 or 0.5 to 1, 2, 5, 10, 15, 20, 25, 40, 50, 60, 75, 100, 125, 150, 175, 200, 250, or 1000 mM, e.g. from about 1 to 2, 5, 10, 15,

has a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9, is at least 1:2, e.g., at least about 1:2, 1:3, 1:4, or 1:5 to 1:6, 1:7, 1:8 to 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5 to 1:5, 1:6, 1:7, 1:8, 1:9, 1:10, 1:15, 1:20, or 1:30, e.g., at least about 1:2.5, e.g., at least about 1:5, e.g. at least about 1:10.

1.46 Kit 1.2-1.45 wherein the kit comprises one or more bulking agents which may provide an adequate structure to the lyophilized cake, e.g., one or more of mannitol, lactose, sucrose, trehalose, sorbitol, glucose, raffinose, arginine, glycine, histidine, dextran (e.g., dextran 40), polyvinylpyrrolidone, polyethylene glycol, and polypropylene glycol, e.g., one or more of mannitol, glucose, sucrose, lactose, trehalose, and dextran (e.g., dextran 40).

1.47 Kit 1.46 wherein the kit comprises 5 or 10 or 50 mg to 2 or 5 g of one or more bulking agents, e.g., from about 50 or 100 mg to 200, 300, 500, or 800 mg, or 1, 1.5, 2, 3, 4, or 5 g of one or more bulking agents.

1.48 Kit 1.2-1.247 wherein the kit comprises dextran (e.g., dextran 40).

1.49 Kit 1.48 wherein the kit comprises 5 or 10 or 50 mg to 2 or 5 g dextran (e.g., dextran 40), e.g., from about 50 or 100 mg to 200, 300, 500, or 800 mg, 1, 1.5, 2, 3, 4, or 5 g dextran (e.g., dextran 40).

1.50 Kit 1.2-1.49 wherein the composition comprises one or more solubilizing agents, e.g., ethylenediamine tetraacetic acid (EDTA) or a salt thereof (e.g., calcium disodium EDTA, disodium EDTA, sodium EDTA), alpha cyclodextrin, hydroxypropyl-β-cyclodextrin, polysorbate 80, tert-butanol, isopropanol, dichloromethane, ethanol, acetone, and glycerol; one or more collapse temperature modifiers which may shift the overall collapse temperature higher, e.g., one or more of dextran, Ficoll®, gelatin, and hydroxyethyl starch; one or more tonicity modifiers, e.g., one or more of sodium chloride, potassium chloride, sucrose, mannitol, glucose, and lactose; and one or more antimicrobial agents, e.g., one or more of benzyl alcohol, phenol, 2-phenoxyethanol, m-cresol, chlorobutanol, parabens (e.g., methyl paraben, ethyl paraben, propyl paraben), benzalkonium chloride, benzethonium chloride, myristyl gamma-picolinium salt (e.g., myristyl gamma-picolinium chloride), and organomercury compounds and

salts (e.g., phenyl mercuric acetate, phenyl mercuric borate, phenyl mercuric nitrate, and thimerosal).

1.51 Kit 1.2-1.50 wherein 2-{[3,5-bis(trifluoromethyl)phenyl]carbamoyl}-4-chlorophenyl dihydrogen phosphate and the one pharmaceutically acceptable excipients are in the same container or in one or more different containers.

1.52 Kit 1.51 wherein the one or more pharmaceutically acceptable excipients comprise one or more bases, e.g., a base wherein upon dissolution of the composition in a solvent, e.g., an aqueous solution, e.g., an aqueous solution, the solution has a pH between 7, 7.5, or 8 and 10.5, e.g., between about 7, 7.5, or 8 and 9.5, e.g., between about 7 or 7.5 and 8, e.g., between about 7.5 and 8.5, e.g., about 7.5, e.g., about 8.5, e.g., between about 8 and 8.5, e.g., about 8.2, e.g., a base wherein a conjugate acid of the base has a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9, e.g., wherein the one or more bases are one or more of:

a) a C_{1-8}-alkyl mono-, di-, or tri- carboxylic acid salt, e.g., a citrate salt, e.g, a metal citrate salt (e.g., an alkali and/or alkaline citrate salt, e.g., an alkali citrate salt, e.g., sodium citrate and/or potassium citrate), e.g., a tartrate salt (e.g., a metal tartrate salt, an alkali tartrate, e.g., sodium tartrate), e.g., a succinate salt (e.g., a metal succinate salt, e.g., an alkali succinate, e.g., disodium succinate), and/or e.g., a lactate salt (e.g., a metal lactate salt, e.g., an alkali lactate, e.g., sodium lactate),

b) a phosphate salt, e.g., a metal phosphate salt (e.g., an alkali and/or alkaline phosphate salt, e.g., an alkali phosphate salt, e.g., sodium phosphate (e.g., NaH_2PO_4 and/or Na_2HPO_4) and/or potassium phosphate (e.g., KH_2PO_4 and/or K_2HPO_4)),

c) an amine and/or a salt thereof (e.g., morpholine, piperazine, benethamine, benzathine, trimethylglycine, hydrabamine, 4-(2-hydroxyethyl)morpholine, 1-(2-hydroxyethyl)-pyrrolidine, an amino acid (e.g., arginine and/or lysine), a mono- and/or poly-hydroxyalkylamine, and/or a salt thereof, e.g., $(HO)_nR^8NH_2$, $[(HO)_nR^8]_2NH$, $[(HO)_nR^8]_3N$, and/or a salt thereof wherein each R^8 is

independently C_{1-8}alkyl (e.g., C_{1-6}-alkyl, e.g., C_{1-4}-alkyl, e.g., -CH_2CH_3, e.g., -CH_3) and n is 0 or C_{1-8}-alkylene (e.g., C_{1-6}-alkylene, e.g., C_{1-4}-alkylene, e.g., –CH_2–CH_2–, e.g., –$C(CH_2)_3$–, e.g., one R^8 is –CH_3 and another R^8 is –$(CH_2)_6$–) and each n is independently 1-8 (e.g., 1, 2, 3, 4 , 5, or 6), e.g., tris(hydroxymethyl)aminomethane (also known as tris base) and/or a salt thereof (e.g., tris(hydroxymethyl)aminomethane acetate (also known as tris acetate), meglumine, dimethylethanolamine, diethylamine, diethylethanolamine, and/or diethanolamine), e.g., any of the preceding wherein a conjugate acid of the amine and/or salt thereof has a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9,

~~d) a metal chloride salt (e.g., zinc chloride),~~

ed) an acetate salt, e.g,. a metal acetate salt (e.g., an alkali and/or alkaline acetate salt, e.g., an alkali acetate salt, e.g., sodium acetate and/or potassium acetate),

fe) a hydroxide and/or alkoxide salt, e.g., a metal hydroxide and/or alkoxdie salt (e.g., a quarternary ammonium hydroxide, e.g., ammonium hydroxide and/or choline hydroxide, lithium hydroxide, aluminum hydroxide, e.g., an alkali and/or alkaline hydroxide salt, e.g., sodium hydroxide, potassium hydroxide, calcium hydroxide, magnesium hydroxide, and/or magnesium ethoxide, e.g., sodium hydroxide),

gf) a carbonate and/or bicarbonate salt, e.g., a metal carbonate and/or metal bicarbonate salt (e.g., an alkali and/or alkaline carbonate salt, e.g., an alkali and/or alkaline bicarbonate salt, e.g., sodium bicarbonate), and/or

hg) a metal borate salt (e.g., an alkali borate salt, e.g., sodium borate), e.g., one or more of sodium citrate, Na_2HPO_4, tris(hydroxymethyl)aminomethane, and a tris(hydroxymethyl)aminomethane salt (e.g., tris acetate), e.g., one or more of sodium citrate, Na_2HPO_4, and tris(hydroxymethyl)aminomethane, e.g., one or

1.78 Kit 1.71-1.77 wherein the solvent, e.g., the sterile solution, comprises one or more bases, e.g., a base wherein upon dissolution of the composition in a solvent, e.g., an aqueous solution, the solution has a pH between 7, 7.5, or 8 and 10.5, e.g., between about 7, 7.5, or 8 and 9.5, e.g., between about 7 or 7.5 and 8, e.g., between about 7.5 and 8.5, e.g., about 7.5, e.g., about 8.5, e.g., between about 8 and 8.5, e.g., about 8.2, e.g., a base wherein a conjugate acid of the base has a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9, e.g., wherein the one or more bases are one or more of:

a) a C_{1-8}-alkyl mono-, di-, or tri- carboxylic acid salt, e.g., a citrate salt, e.g, a metal citrate salt (e.g., an alkali and/or alkaline citrate salt, e.g., an alkali citrate salt, e.g., sodium citrate and/or potassium citrate), e.g., a tartrate salt (e.g., a metal tartrate salt, an alkali tartrate, e.g., sodium tartrate), e.g., a succinate salt (e.g., a metal succinate salt, e.g., an alkali succinate, e.g., disodium succinate), and/or e.g., a lactate salt (e.g., a metal lactate salt, e.g., an alkali lactate, e.g., sodium lactate),

b) a phosphate salt, e.g., a metal phosphate salt (e.g., an alkali and/or alkaline phosphate salt, e.g., an alkali phosphate salt, e.g., sodium phosphate (e.g., NaH_2PO_4 and/or Na_2HPO_4) and/or potassium phosphate (e.g., KH_2PO_4 and/or K_2HPO_4)),

c) an amine and/or a salt thereof (e.g., morpholine, piperazine, benethamine, benzathine, trimethylglycine, hydrabamine, 4-(2-hydroxyethyl)morpholine, 1-(2-hydroxyethyl)-pyrrolidine, an amino acid (e.g., arginine and/or lysine), a mono- and/or poly-hydroxyalkylamine, and/or a salt thereof, e.g., $(HO)_nR^8NH_2$, $[(HO)_nR^8]_2NH$, $[(HO)_nR^8]_3N$, and/or a salt thereof wherein each R^8 is independently C_{1-8}alkyl (e.g., C_{1-6}-alkyl, e.g., C_{1-4}-alkyl, e.g., -CH_2CH_3, e.g., -CH_3) and n is 0 or C_{1-8}-alkylene (e.g., C_{1-6}-alkylene, e.g., C_{1-4}-alkylene, e.g., –CH_2–CH_2–, e.g., –$C(CH_2)_3$–, e.g., one R^8 is –CH_3 and another R^8 is –$(CH_2)_6$–) and each n is independently 1-8 (e.g., 1, 2, 3, 4 , 5, or 6), e.g., tris(hydroxymethyl)aminomethane (also

known as tris base) and/or a salt thereof (e.g., tris(hydroxymethyl)aminomethane acetate (also known as tris acetate), meglumine, dimethylethanolamine, diethylamine, diethylethanolamine, and/or diethanolamine), e.g., any of the preceding wherein a conjugate acid of the amine and/or salt thereof has a pKa between 6, 7 , 8, 9, or 10 and 11, e.g., between about 6, 7, 8, or 9 and 10, e.g., between about 7 and 9, e.g., between about 8 and 9,

~~d) a metal chloride salt (e.g., zinc chloride);~~

~~e~~d) an acetate salt, e.g., a metal acetate salt (e.g., an alkali and/or alkaline acetate salt, e.g., an alkali acetate salt, e.g., sodium acetate and/or potassium acetate),

~~f~~e) a hydroxide and/or alkoxide salt, e.g., a metal hydroxide and/or alkoxide salt (e.g., a quarternary ammonium hydroxide, e.g., ammonium hydroxide and/or choline hydroxide, lithium hydroxide, aluminum hydroxide, e.g., an alkali and/or alkaline hydroxide salt, e.g., sodium hydroxide, potassium hydroxide, calcium hydroxide, magnesium hydroxide, and/or magnesium ethoxide, e.g., sodium hydroxide),

~~g~~f) a carbonate and/or bicarbonate salt, e.g., a metal carbonate and/or metal bicarbonate salt (e.g., an alkali and/or alkaline carbonate salt, e.g., an alkali and/or alkaline bicarbonate salt, e.g., sodium bicarbonate), and/or

~~h~~g) a metal borate salt (e.g., an alkali borate salt, e.g., sodium borate),

e.g., one or more of sodium citrate, Na_2HPO_4, tris(hydroxymethyl)aminomethane, and a tris(hydroxymethyl)aminomethane salt (e.g., tris acetate), e.g., one or more of sodium citrate, Na_2HPO_4, and tris(hydroxymethyl)aminomethane, e.g., one or more of sodium citrate and Na_2HPO_4, e.g., Na_2HPO_4, e.g., tris(hydroxymethyl)aminomethane.

1.79 Kit 1.71-1.78 wherein the solvent, e.g., the sterile solution, comprises one or more pharmaceutically acceptable bases, e.g., one or more bases wherein upon dissolution of the composition in a solvent the solution has a pH between 7, 7.5,

1.83 Kit 1.~~1~~78-1.82 wherein the solvent, e.g. the sterile solution, comprises a metal citrate salt (e.g., sodium citrate).

1.84 Kit 1.83 wherein the solvent, e.g., the sterile solution, comprises 1 or 5 mg to 200 mg or 500 mg of the metal citrate salt (e.g., sodium citrate), e.g., from about 1 or 5 mg to 200 or 500 mg, e.g., from about 1 or 5 or 10 mg to 15, 20, 25, 30, 40, 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, 500, 1000, or 1500 mg, e.g., from about 15, 20, 30, 50, or 100 to 200, 250, 400, 450, 500, 600, 700, 800, 1000, or 1500 mg.

1.85 Kit 1.83 wherein the concentration of the metal citrate salt (e.g., sodium citrate) is from about 0.01 or 0.1 or 0.5 or 1 or 2 to 250 mM, e.g., from about 0.01 or 0.1 or 0.5 to 1, 2, 5, 10, 15, 20, 25, 40, 50, 60, 75, 100, 125, 150, 175, 200, 250, or 1000 mM, e.g. from about 1 to 2, 5, 10, 15, 20, 25, 40, 50 or 60 mM, e.g., from about 5 to 50 mM, e.g., from about 5, 10, 15, 20, 25, or 50 to 100, 200, 250, 300, 400, 500, or 1000 mM, e.g., about 2, 20, or 200 mM, e.g., about 5, 10, 50, 500, 500, or 1000 mM, e.g., from about 5, 10, 15, 20, 25, or 50 to 100, 200, 250, 300, 400, 500, or 1000 mM, e.g., about 2, 20, or 200 mM, e.g., about 5, 10, 50, 500, 500, or 1000 mM, e.g., wherein the concentration of the metal citrate salt (e.g., sodium citrate) is 2 or 3 to 5, 6, 8, 10, 15 or 20 equivalents of Formula II, e.g., about 2.5 or 5 to 10, e.g. about 2.5, e.g., about 5, e.g., wherein the concentration of the metal citrate salt (e.g., sodium citrate) is 2 or 3 to 5, 6, 8, 10, 15 or 20 equivalents of Formula III, e.g., about 5 to 10, e.g. about 5, e.g., about 10.

1.86 Kit 1.78-1.85 wherein the solvent, e.g., the sterile solution, comprises a metal phosphate salt (e.g., sodium phosphate, e.g., Na_2HPO_4).

1.87 Kit 1.86 wherein the solvent, e.g., the sterile solution, comprises 1 or 5 mg to 200 mg or 500 mg of the metal phosphate salt (e.g., sodium phosphate, e.g., Na_2HPO_4), e.g., from about 1 or 5 mg to 200 or 500 mg, e.g., from about 1 or 5 or 10 mg to 15, 20, 25, 30, 40, 50, 75, 100, 150, 200, 250, 300, 350, 400, 450, 500, 1000, or 1500 mg, e.g., from about 15, 20, 30, 50, or 100 to 200, 250, 400, 450, 500, 600, 700, 800, 1000, or 1500 mg.

1.88 Kit 1.86 wherein the concentration of the metal phosphate salt (e.g., sodium phosphate, e.g., Na_2HPO_4), is from 0.01 or 0.1 or 0.5 or 1 or 2 to 250 mM, e.g.,

administration of aspirin; administration of amantadine; intravenous thrombolysis (e.g. using rtPA); mechanical clot removal; angioplasty; and/or stents.

G.4 Method G.2 wherein the patient is at elevated risk of cerebral edema, e.g., due to head trauma, ischemic stroke, glioma, meningitis, acute mountain sickness, epileptic seizure, infection, metabolic disorder, water intoxication, hepatic failure, hepatic encephalopathy, or diabetic ketoacidosis.

G.5 Method G.2 wherein the patient has suffered a stroke, head injury, or spinal injury.

G.6 Method G.5 wherein the patient has suffered a stroke, head injury or spinal injury within 12 hours, e.g. within 6 hours, preferably within 3 hours of commencing treatment.

G.7 Method G.2 wherein the patient is at elevated risk of suffering a stroke, head injury or spinal injury, e.g., in combat or in an athletic competition.

G.8 Method G or G.1-AG.7 wherein the patient already has cerebral edema.

G.9 Method G or G.1-AG.8 wherein the condition to be treated or controlled is cerebral edema consequent to a stroke or a traumatic brain injury.

G.10 Method G or G.1- AG.9 wherein the condition to be treated or controlled is cerebral edema consequent to a middle cerebral artery stroke.

G.11 Method G or G.1-G.9 wherein the condition to be treated or controlled is cerebral edema consequent to closed head trauma.

G.12 Method G or G.1-G.4 wherein the condition to be treated or controlled is cerebral edema consequent to an epileptic seizure.

G.13 Method G or G.1-G.4 wherein the condition to be treated or controlled is cerebral edema consequent to an infection.

G.14 Method G or G.1-G.4 wherein the condition to be treated or controlled is cerebral edema consequent to a metabolic disorder.

G.15 Method G or G.1-G.4 wherein the condition to be treated or controlled is cerebral edema consequent to glioma.

G.16 Method G or G.1-G.4 wherein the condition to be treated or controlled is cerebral edema consequent to meningitis.

AQP4	581618	66311	11%	0.629	5.0
CD81	2910106	221240	8%		

[00105] As will be observed, the signal for the CD81 cells is ca. 5x higher than the signal for the APQ4 cells, because by 5.5 mins, most of the AQP4 cells have burst, while most of the CD81 cells remain intact. Inhibition of AQP4 would therefore be expected to provide a higher signal, more like the CD81 cells.

[00106] This assay is applied in a pilot screen of the MicroSource GenPlus 960 and the Maybridge Diversity™ 20k libraries (approximately 21,000 compounds tested, each compound at 10-20 μM).

[00107] From this assay, a specific chemical series is identified, phenylbenzamides, which represents 3 out of the top 234 hits.

[00108] Hits from the HTS are validated using the same assay using a different plating arrangement. In Figure 4, we show this validation assay used to examine 5-chloro-*N*-(3,5-dichlorophenyl)-2-hydroxybenzamide. Cells are seeded in a 96 well multiplate format with the plates edges omitted (lanes 1 and 24) and an entire column (n=16) is used to test the ability of a compound to block AQP4-mediated cell bursting upon H_2O shock. CHO cells expressing CD81 are seeded in lanes 2-3 as a control, and CHO cells expressing AQP4, in lanes 4-23. Cells are treated with 0.1% DMSO in 10% FBS, DMEM (even numbered columns) or 10 μM N-[3,5-bis(trifluoromethyl)phenyl]-5-chloro-2-hydroxybenzamide (odd number columns) in 0.1% DMSO, 10% FBS, DMEM for 30 minutes. The cells are shocked with H_2O for 5:30 minutes, then osmolality returned to 300 mOsm in the presence of 1 μM calcein-AM, as described above. The cells are incubated at 37°C for 30 minutes and the relative fluorescence measured (ex 495/em 535 nM) on a fluorescence multiplate reader. The data in Figure ~~7~~4 represents the average relative fluoresence units (RFU ± SEM, n=16).

EXAMPLE 5 – Water Toxicity Model for CE: Intracranial Pressure (ICP)

[00109] ICP is monitored using a Samba 420 Sensor, pressure transducer, with a Samba 202 control unit (Harvard Apparatus, Holliston, MA). This ICP monitoring system consists of a 0.42 mm silicon sensor element mounted on an optical fiber. A 20-gauge syringe needle is implanted through the cisterna magna to a depth of ~ 1 cm. The needle then acts as a guide for

purified as follows. 15 g is dissolved in 1.2 L of water with 120 mM of sodium hydroxide and extracted with 500 ml ethyl acetate to remove phenol and non acid impurities. The aqueous layer is acidified with concentrated HCl to pH 1.2 and extracted with ethyl acetate 1 L followed by 600 ml. The ethyl acetate layer is dried $MgSO_4$ and sodium sulphate, filtered, and evaporated to give about 13 g of 98% pure 2-((3,5-bis(trifluoromethyl)phenyl)carbamoyl)-4-chlorophenyl dihydrogen phosphate. NMR showed 1 mole of ethyl acetate trapped in solid. Ethyl acetate is removed by adding 100 ml of methanol and evaporating. 2-((3,5-bis(trifluoromethyl)phenyl)carbamoyl)-4-chlorophenyl dihydrogen phosphate is stable at RT for a week or more. Sample kept at RT. It is soluble at 5 mg/mL in 1% Na_2HPO_4 giving pH of about 7. Dissolved in 2% Na_2HPO_4 at 5 mg/mL gives pH of 7.4

[00130] 2-((3,5-bis(trifluoromethyl)phenyl)carbamoyl)-4-chlorophenyl hydrogen phosphate mono sodium salt ("mono sodium salt"), 2-((3,5-bis(trifluoromethyl)phenyl)carbamoyl)-4-chlorophenyl phosphate bis sodium salt ("bis sodium salt"), and 2-((3,5-bis(trifluoromethyl)phenyl)carbamoyl)-4-chlorophenyl phosphate bis ethanolamine salt ("bis ethanolamine salt") are made and freeze dried as in Example ~~7~~13. In all cases stability studies show hydrolysis in the solid state at about 1% per day. Solubilities are about 5 mg/mL for mono sodium salt and 10 mg/mL for both bis sodium and bis ethanolamine salt in water.

[00131] Final pH of solutions are about 7.5 for the bis ethanolamine salt, pH 8.5 for mono sodium salt, and pH 9.5 for bis sodium salt in water. In all cases solutions of these salts show less than 1% phenol over 12 hrs. Longer term their stability is the same as the solid samples (about 1% per day at RT). Hydrolysis rate is expected to be faster at higher pH.

[00132] 2-((3,5-bis(trifluoromethyl)phenyl)carbamoyl)-4-chlorophenyl ~~di~~hydrogen phosphate mono ethanolamine salt ("mono ethanolamine salt") is made as in Example ~~8~~14. Surprisingly, the mono ethanolamine salt only shows about 1% hydrolysis after 5 days at RT. Its solubility in water is about 5 mg/ml. Solubility is expected to be higher at higher pH.

EXAMPLE 16

Synthesis of ala and ala ala prodrugs of N-[3,5-bis(trifluoromethyl)phenyl]-5-chloro-2-hydroxybenzamide