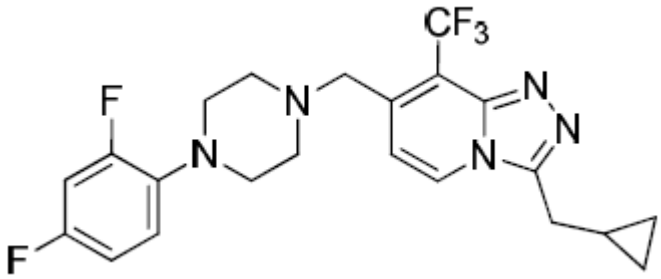
## CLAIMS

**1.** A combination comprising

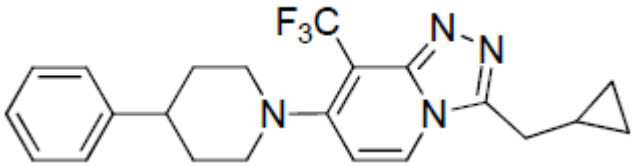
(a) a synaptic vesicle protein 2a ("SV2A") ligand selected from the group consisting of levetiracetam, brivaracetam and seletracetam; and

(b) a positive allosteric modulator of the metabotropic glutamatergic receptor subtype 2 selected from

1) a compound of Formula (I) selected from

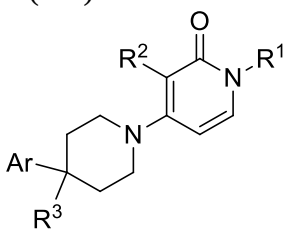



and



or a pharmaceutically acceptable salt or a solvate thereof;

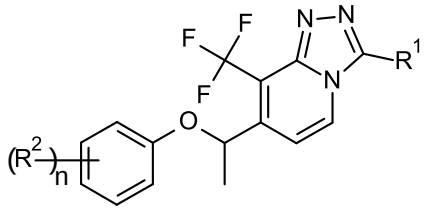
2) a compound of Formula (I-A)



(I-A)

or a stereochemically isomeric form thereof, wherein
$R^1$ is $C_{1-6}$alkyl; or $C_{1-3}$alkyl substituted with $C_{3-7}$cycloalkyl, phenyl, or phenyl substituted with halo, trifluoromethyl or trifluoromethoxy;
$R^2$ is halo, trifluoromethyl, $C_{1-3}$alkyl or cyclopropyl;
$R^3$ is hydrogen, fluoro, hydroxyl, hydroxy$C_{1-3}$alkyl, hydroxy$C_{1-3}$alkyloxy, fluoro$C_{1-3}$alkyl, fluoro$C_{1-3}$alkyloxy or cyano; and
Ar is unsubstituted phenyl; or phenyl substituted with n radicals $R^4$, wherein n is 1, 2 or 3;
$R^4$ is selected from the group consisting of hydrogen, halo, $C_{1-3}$alkyl, hydroxy$C_{1-3}$alkyl, polyhalo$C_{1-3}$alkyl, cyano, hydroxyl, amino, carboxyl, $C_{1-3}$alkyloxy$C_{1-3}$alkyl, $C_{1-3}$alkyloxy, polyhalo$C_{1-3}$alkyloxy, $C_{1-3}$alkylcarbonyl, mono- and di($C_{1-3}$alkyl)amino, and morpholinyl;
or a pharmaceutically acceptable salt or a solvate thereof; and

3) a compound of Formula (I-B)



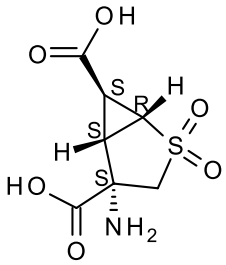
(I-B)

or a stereochemically isomeric form thereof, wherein

$R^1$ is selected from the group consisting of $C_{1-6}$alkyl, ($C_{3-8}$cycloalkyl)$C_{1-3}$alkyl, and ($C_{1-3}$alkyloxy)$C_{1-3}$alkyl;
each $R^2$ is independently selected from F, Cl, $C_{1-3}$alkyl, $C_{1-3}$alkyloxy, mono- or polyhalo$C_{1-3}$alkyl, and mono- or polyhalo$C_{1-3}$alkyloxy;
n is an integer selected from 1, 2, and 3;
or a pharmaceutically acceptable salt or a solvate thereof; or

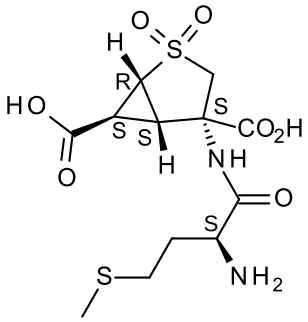
c) an orthosteric agonist of the metabotropic glutamatergic receptor subtype 2 selected from

1) LY-404039



or a salt or a solvate thereof; and

2) LY-2140023

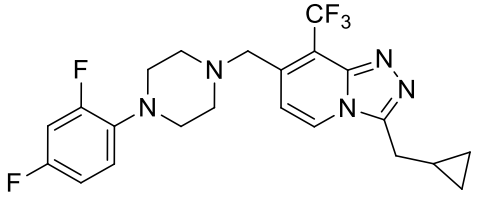


or a salt or a solvate thereof, in particular the monohydrate thereof.

**2.** The combination according to claim 1, wherein the SV2A ligand is levetiracetam or brivaracetam.

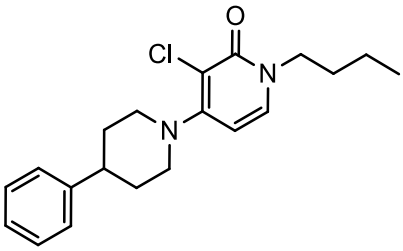
**3.** The combination according to claim 1 or 2, wherein the positive allosteric modulator of the metabotropic glutamatergic receptor subtype 2 is selected from

1) a compound of Formula (I) selected from

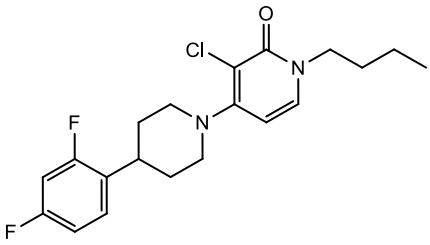


or a hydrochloride salt thereof;

2) a compound of Formula (I-A) selected from

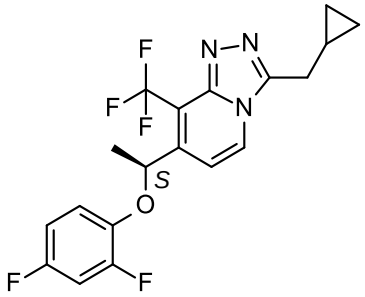


and



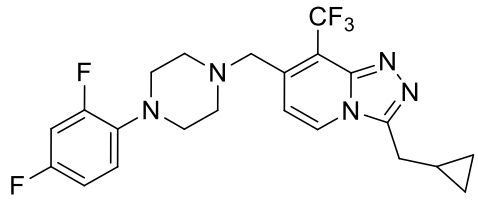
;

3) a compound of Formula (I-B) selected from



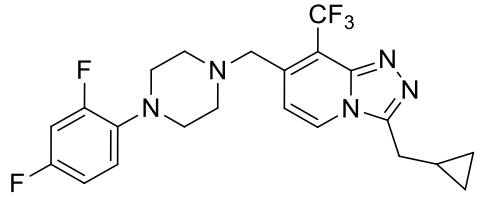
or a hydrochloride salt thereof.

**4.** The combination according to any one of claims 1 to 3, wherein the positive allosteric modulator of the metabotropic glutamatergic receptor subtype 2 is



or a hydrochloride salt thereof.

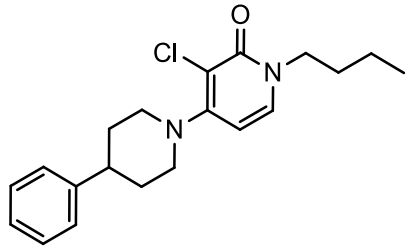
**5.** The combination according to any one of claims 1 to 4, wherein the positive allosteric modulator of the metabotropic glutamatergic receptor subtype 2 is



or a hydrochloride salt thereof;
and the SV2A ligand is levetiracetam.

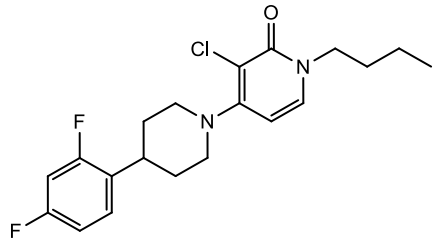
**6.** The combination according to claim 5, wherein levetiracetam and the positive allosteric modulator of the metabotropic glutamatergic receptor subtype 2 of Formula (I) are in a fixed-dose ratio of (a) levetiracetam : (b) compound of Formula (I) of between 1:3 to 3:1, calculated on the $ED_{50}$ values of the individual components.

**7.** The combination according to any one of claims 1 to 3, wherein the positive allosteric modulator of the metabotropic glutamatergic receptor subtype 2 is



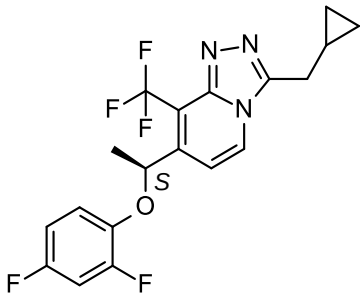
.

**8.** The combination according to any one of claims 1 to 3, wherein the positive allosteric modulator of the metabotropic glutamatergic receptor subtype 2 is



.

**9.** The combination according to any one of claims 1 to3, wherein the positive allosteric modulator of the metabotropic glutamatergic receptor subtype 2 is



or a hydrochloride salt thereof.

**10.** The combination according to claim 1 or 2, wherein the orthosteric agonist of the metabotropic glutamatergic receptor subtype 2 is LY-404039.

**11.** The combination according to claim 1 or 2, wherein the orthosteric agonist of the metabotropic glutamatergic receptor subtype 2 is LY-2140023.

**12.** A pharmaceutical composition comprising a combination as claimed in any one of claims 1 to 11, and a pharmaceutically acceptable carrier.

**13**. The pharmaceutical composition according to claim 12, formulated as a combined pharmaceutical composition.

**14**. The ~~pharmaceutical composition~~ combination according to any one of claims ~~12~~1 to 11, wherein each of the SV2A ligand and the positive allosteric modulator of the metabotropic glutamatergic receptor subtype 2 is formulated in separate pharmaceutical compositions.

**15.** A process for the preparation of the pharmaceutical composition according to claim 12 or 13, wherein the combination as claimed in any one of claims 1 to 11 is admixed with a pharmaceutical carrier.

**16.** A product comprising the combination of the SV2A ligand and a positive allosteric modulator of the metabotropic glutamatergic receptor subtype 2 or an orthosteric agonist of the metabotropic glutamatergic receptor subtype 2, as

defined in any one of claims 1 to 11, as a combined preparation for simultaneous, separate or sequential use in the treatment or prevention of epilepsy and related disorders; neuropathic pain; migraine or resistant headache; bipolar and related disorders.

**17.** A combination as defined in any one of claims 1 to 11, or a pharmaceutical composition as defined in any one of claims 12 to 14, for use as a medicament.

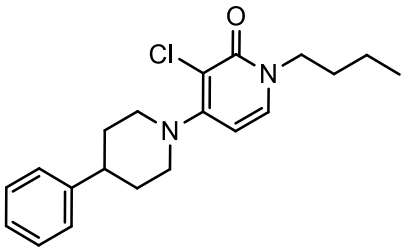
**18.** A combination as claimed in any one of claims 1 to 11, or a pharmaceutical composition as defined in any one of claims 12 to 14, for use in the prevention of epileptogenesis.

**19.** A combination as claimed in any one of claims 1 to 11, or a pharmaceutical composition as claimed in any one of claims 12 to 14, for use in the treatment or prevention of epilepsy and related disorders; neuropathic pain; migraine or resistant headache; and bipolar and related disorders.

**20**. The combination for use according to claim 19, in the treatment or prevention of epilepsy and related disorders.

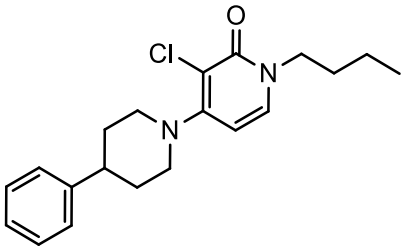
**21**. The combination for use according to claim 20, as a neuroprotectant.

**22.** Use of a positive allosteric modulator of a metabotropic glutamatergic receptor subtype 2 having the structure below



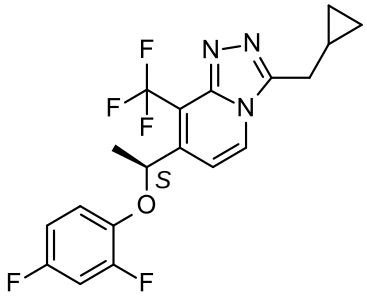

in the manufacture of a medicament that is to be administered in combination with a SV2A ligand selected from levetiracetam for treating epilepsy and related disorders; neuropathic pain; migraine or resistant headache; bipolar and related disorder~~generalised onset seizures~~.

**23.** Use of a positive allosteric modulator of a metabotropic glutamatergic receptor subtype 2 having the structure below



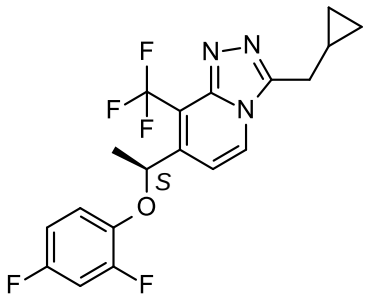

in the manufacture of a medicament that is to be administered in combination with a SV2A ligand selected from brivaracetam for treating epilepsy and related disorders; neuropathic pain; migraine or resistant headache; bipolar and related disorder~~generalised onset seizures~~.

**24.** Use of a positive allosteric modulator of a metabotropic glutamatergic receptor subtype 2 having the structure below



or a hydrochloride salt thereof, in the manufacture of a medicament that is to be administered in combination with a SV2A ligand selected from levetiracetam for treating epilepsy and related disorders; neuropathic pain; migraine or resistant headache; bipolar and related disorder~~generalised onset seizures~~.

**25.** Use of a positive allosteric modulator of a metabotropic glutamatergic receptor subtype 2 having the structure below



or a hydrochloride salt thereof, in the manufacture of a medicament that is to be administered in combination with a SV2A ligand selected from brivaracetam for treating epilepsy and related disorders; neuropathic pain; migraine or resistant headache; bipolar and related disorder~~generalised onset seizures~~.

**26.** The use according to any one of claims 22 to 25, wherein said medicament and said SV2A ligand are to be administered in separate formulations.

**27.** The use according to any one of claims 22 to 25, wherein said medicament and said SV2A ligand are to be administered in a combined formulation.

**28.** The use according to any one of claims 22 to 27, wherein said epilepsy and related disorders is selected from the group consisting of partial onset seizures with or without generalisation, generalised epilepsies and primary generalised tonic-clonic seizures.

**29.** The use according to any one of claims 22 to 27, wherein said bipolar and related disorder is selected from the group consisting of bipolar disorder type I, bipolar disorder type II and cyclothymic disorder.