and 24 mg and reports PK data including a half-life at steady state ranging from 4.81 to 6.50 hours.

[0006] There is a significant unmet need for safe and effective treatments for DEE and other seizure disorders. The compound and dosing methods described herein help satisfy this need and provide related advantages as well.

SUMMARY

[0007] Provided is a method of treating or preventing a 5-hydroxytryptamine $(HT)_{2C}$ receptor-associated disorder in a patient in need thereof, wherein the method comprises administering to the patient (R)-N-(2,2-difluoroethyl)-7-methyl-l,2,3,4,6,7-hexahydro-[l,4]diazepino[6,7,l-hi]indole-8-carboxamide (Compound 1), or a pharmaceutically acceptable salt thereof, wherein Compound 1, or a pharmaceutically acceptable salt thereof, is administered twice daily. In one aspect, the present disclosure refers to use of (*R*)-N-(2,2-difluoroethyl)-7-methyl-l,2,3,4,6,7-hexahydro-[l,4]diazepino[6,7,l-*hi*]indole-8- carboxamide (Compound 1), or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prevention of a 5-hydroxytryptamine $(HT)_{2C}$ receptor-associated disorder in a patient in need thereof, wherein Compound 1, or a pharmaceutically acceptable salt thereof, is to be administered twice daily.

[0008] Also provided is a method of treating or preventing epilepsy in a patient in need thereof, wherein the method comprises administering to the patient (*R*)-N-(2,2-difluoroethyl)-7-methyl-l,2,3,4,6,7-hexahydro-[l,4]diazepino[6,7,l-*hi*]indole-8-carboxamide (Compound 1), or a pharmaceutically acceptable salt thereof, wherein Compound 1, or a pharmaceutically acceptable salt thereof, is administered twice daily. In one aspect, the present disclosure refers to use of (*R*)-N-(2,2-difluoroethyl)-7-methyl-l,2,3,4,6,7- hexahydro-[l,4]diazepino[6,7,l-*hi*]indole-8-carboxamide (Compound 1), or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prevention of epilepsy in a patient in need thereof, wherein Compound 1, or a pharmaceutically acceptable salt thereof, is to be administered twice daily.

[0009] Also provided is a method of reducing severity of an epileptic seizure in a patient in need thereof, wherein the method comprises administering to the patient (*R*)-N-(2,2-difluoroethyl)-7-methyl-l,2,3,4,6,7-hexahydro-[l,4]diazepino[6,7,l-*hi*]indole-8-carboxamide (Compound 1), or a pharmaceutically acceptable salt thereof, wherein Compound 1, or a pharmaceutically acceptable salt thereof, is administered twice daily. In one aspect, the present disclosure refers to use of (*R*)-N-(2,2-difluoroethyl)-7-methyl- l,2,3,4,6,7-hexahydro-[l,4]diazepino[6,7,l-*hi*]indole-8-carboxamide (Compound 1), or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing severity of an epileptic seizure in a patient in need thereof, wherein Compound 1, or a pharmaceutically acceptable salt thereof, is to be administered twice daily.

[0010] Also provided is a method of reducing the frequency of epileptic seizures in a patient in need thereof, wherein the method comprises administering to the patient (*R*)-N-(2,2-difluoroethyl)-7-methyl-l,2,3,4,6,7-hexahydro-[l,4]diazepino[6,7,l-*hi*]indole-8-carboxamide (Compound 1), or a pharmaceutically acceptable salt thereof, wherein Compound 1, or a pharmaceutically acceptable salt thereof, is administered twice daily. In one aspect, the present disclosure refers to use of (*R*)-N-(2,2-difluoroethyl)-7-methyl- l,2,3,4,6,7-hexahydro-[l,4]diazepino[6,7,l-*hi*]indole-8-carboxamide (Compound 1), or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing the frequency of epileptic seizures in a patient in need thereof, wherein Compound 1, or a pharmaceutically acceptable salt thereof, is to be administered twice daily.

[0011] Also provided is a method of treating or preventing a seizure disorder in a patient in need thereof, wherein the method comprises administering to the patient (*R*)-N-(2,2-difluoroethyl)-7-methyl-l,2,3,4,6,7-hexahydro-[l,4]diazepino[6,7,l-*hi*]indole-8-carboxamide (Compound 1), or a pharmaceutically acceptable salt thereof, wherein Compound 1, or a pharmaceutically acceptable salt thereof, is administered twice daily. In one aspect, the present disclosure refers to use of (*R*)-N-(2,2-difluoroethyl)-7-methyl- l,2,3,4,6,7-hexahydro-[l,4]diazepino[6,7,l-*hi*]indole-8-carboxamide (Compound 1), or a pharmaceutically acceptable salt thereof, the manufacture of a medicament for the treatment or prevention of a seizure disorder in a patient in need thereof, wherein Compound 1, or a pharmaceutically acceptable salt thereof, is to be administered twice daily.

[0012] Also provided is a method of treating or preventing developmental and epileptic encephalopathy (DEE) in a patient in need thereof, wherein the method comprises administering to the patient (*R*)-N-(2,2-difluoroethyl)-7-methyl-l,2,3,4,6,7-hexahydro-[l,4]diazepino[6,7,l- *hi*]indole-8-carboxamide (Compound 1), or a pharmaceutically acceptable salt thereof, wherein Compound 1, or a pharmaceutically acceptable salt thereof, is administered twice daily. In one aspect, the present disclosure refers to use of (*R*)-N-(2,2-difluoroethyl)-7-methyl-l,2,3,4,6,7-hexahydro-[l,4]diazepino[6,7,l-*hi*]indole-8-carboxamide (Compound 1), or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prevention of developmental and epileptic encephalopathy (DEE) in a patient in need thereof, wherein Compound 1, or a pharmaceutically acceptable salt thereof, is to be administered twice daily.

[0013] Also provided is a method of treating or preventing a refractory epilepsy in a patient in need thereof, wherein the method comprises administering to the patient (*R*)-N-(2,2-difluoroethyl)-7-methyl-l,2,3,4,6,7-hexahydro-[l,4]diazepino[6,7,l-*hi*]indole-8-carboxamide (Compound 1), or a pharmaceutically acceptable salt thereof, wherein Compound 1, or a pharmaceutically acceptable salt thereof, is administered twice daily. In one aspect, the present disclosure refers to use of of (*R*)-N-(2,2-difluoroethyl)-7-methyl- l,2,3,4,6,7-hexahydro-[l,4]diazepino[6,7,l-*hi*]indole-8-carboxamide (Compound 1), or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prevention a refractory epilepsy in a patient in need thereof, wherein Compound 1, or a pharmaceutically acceptable salt thereof, is to be administered twice daily.

[0014] These and other aspects of the disclosure disclosed herein will be set forth in greater detail as the patent disclosure proceeds.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] FIG. 1 is a graph showing PK (pharmacokinetic) profiles of Compound 1 in plasma and CSF (cerebrospinal fluid) following TID administration of 6 mg/dose of Compound 1.

[0016] FIG. 2 is a graph showing PK profiles of Compound 1 in plasma and CSF following TID administration of 12 mg/dose of Compound 1.

[0017] FIG. 3 is a set of plots of Compound 1 concentration in CSF and plasma following TID administration of 6 mg/dose (subjects 101–110) or 12 mg/dose (subjects 201–210) of Compound 1.

[0018] FIG. 4 is a plot comparing C_{max} of Compound 1 in CSF and plasma for TID administration of Compound 1.

[0019] FIG. 5 is a plot comparing AUC_{tau} of Compound 1 in CSF and plasma for TID administration of Compound 1.

[0020] FIG. 6 is a table showing qEEG results following TID administration of 6 mg/dose of Compound 1.

[0021] FIG. 7 is a table showing qEEG results following TID administration of 12 mg/dose of Compound 1.

[0022] FIG. 8 is table showing PK characteristics for Compound 1 when administered with quinidine.