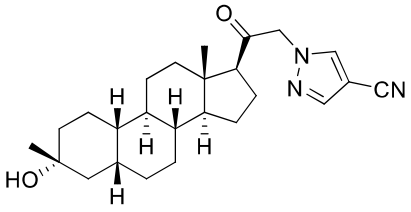
bioavailability. In order for Compound 1 to be administered orally as a therapeutic agent for CNS related disorders, especially in a solid dosage form, an acceptable bioavailability must be achieved.

SUMMARY

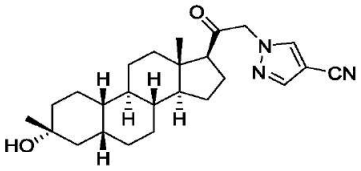
The disclosure provides methods of treating a CNS related disorder by administering a therapeutically effective amount of Compound 1 or 1-(2-((3R,5R,8R,9R,10S,13S,14S,17S)-3-hydroxy-3,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)-2-oxoethyl)-1H-pyrazole-4-carbonitrile, which has the formula



(Compound 1)

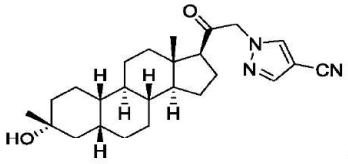
in a subject in need thereof. Compound 1 is also known as the compound SAGE-217.

In one aspect, the present disclosure refers to the use a compound in the manufacture of a medicament for the treatment of a CNS-related disorder in a patient, wherein the compound is a compound having the formula



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In another aspect, the present disclosure refers to an article of manufacture comprising: a therapeutically effective amount of a compound having the formula

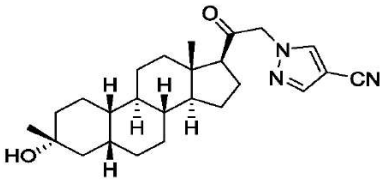


;

packaging material; and

a label affixed to the packaging material indicating that the therapeutically effective amount of the compound should be taken with food or a package insert contained within the packaging material indicating that the therapeutically effective amount of the compound should be taken with food.

In yet another aspect, the present disclosure refers to the use of a compound in the manufacture of a medicament for the treatment of a CNS-related disorder in a subject, wherein the compound is to be administered substantially contemporaneously with food, the compound having the formula:



,

wherein the administration results in an increase in the bioavailability of the compound compared to administration without food, wherein bioavailability is based on a comparison of AUC values.

In some examples, Compound 1 is administered without food or substantially contemporaneously with food. In some examples, Compound 1 is administered substantially contemporaneously with food.

In some examples, the method comprises a method of treating a CNS related disorder by administering a therapeutically effective amount of Compound 1 or a pharmaceutically acceptable salt thereof in a subject, wherein the therapeutically effective amount of Compound 1 is administered substantially contemporaneously with food.

In some examples, the therapeutically effective amount is in a solid dosage form. Examples of solid dosage forms include tablets, capsules, granules, powders, sachets, reconstitutable powders, dry powder inhalers and chewables.

In an example of the disclosure, the therapeutically effective amount of Compound 1 is administered substantially contemporaneously with food to increase the bioavailability of Compound 1, as compared to when Compound 1 is administered without food. The bioavailability of Compound 1 can be determined from plasma concentration-time curves, specifically the area under the curve (AUC). For example, bioavailability, or the increase thereof, can be determined by comparing the AUC_{0-t} (the AUC from the time of dosing to the last quantifiable concentration) for a formulation of Compound 1 administered with food, with the AUC_{0-t} for a formulation of Compound 1 without food.

In some examples, the therapeutically effective amount of Compound 1 (or a pharmaceutically acceptable salt thereof) is administered substantially contemporaneously with food to increase the bioavailability of Compound 1 for the treatment of a CNS related disorder, and the therapeutically effective amount of Compound 1 is in a solid dosage form such as a tablet or capsule. In some examples, the therapeutically effective amount of Compound 1 is administered substantially contemporaneously with food, and the bioavailability is increased by about 10% or greater; by about 20% or greater; by about 30% or greater; by about 40% or greater; by about 50% or greater; or by about 55% or greater when compared to the bioavailability when Compound 1 is administered without food.

In some examples, the therapeutically effective amount of Compound 1 is administered once daily substantially contemporaneously with food. In other examples, the therapeutically effective amount of Compound 1 is administered twice daily substantially contemporaneously with food. In

some examples, the therapeutically effective amount of Compound 1 is administered once daily as one capsule substantially contemporaneously with food. In some examples, the therapeutically effective amount of Compound 1 is administered once daily as two capsules substantially contemporaneously with food.

In some examples, the therapeutically effective amount of Compound 1 is about 20 mg to about 60 mg and is administered substantially contemporaneously with food. In other examples, the therapeutically effective amount of Compound 1 is about 25 mg to about 50 mg and is administered substantially contemporaneously with food. In other examples, the therapeutically effective amount of Compound 1 is about 25 mg to about 35 mg and is administered substantially contemporaneously with food. In other examples, the therapeutically effective amount of Compound 1 is about 30 mg, e.g., 30 mg and is administered substantially contemporaneously with food.

In an example of the disclosure, the therapeutically effective amount of Compound 1 is administered substantially contemporaneously with food, *e.g.*, within about 60 minutes before or after ingesting food. In some examples, the therapeutically effective amount of Compound 1 is administered substantially contemporaneously with food, *e.g.*, within about 45 minutes, within about 30 minutes, within about 15 minutes, or within about 5 minutes before or after ingesting food. In some examples, the food is a high fat meal, as defined herein, or the food is a regular meal, as discussed herein. In other examples, the food is at least 50 calories, at least 100 calories, at least 200 calories, or at least 300 calories.

The disclosure features, *inter alia*, a method comprising administering to a subject a therapeutically effective amount of Compound 1, as described below, to treat a CNS-related disorder, *e.g.* a mood disorder or a movement disorder. The disclosure features methods of treating a subject having a CNS-related disorder, *e.g.,* tremor, *e.g.,* essential tremor; depression, *e.g.,* postpartum depression; and anxiety disorder a composition described herein comprising Compound 1. In some examples, Compound 1 is administered substantially contemporeously with food or without food. In some examples of any of the foregoing, Compound 1 is administered substantially contemporeously with food. The disclosure also features, *inter alia*, such as a GABA related disease or disorder, *e.g.*, a mood disorder, a movement disorder, postpartum depression, major depressive disorder, essential tremor, or Parkinson's disease.

In some examples, the CNS related disorder is a depressive disorder such as major depressive disorder. In some examples, the subject has a mild depressive disorder, *e.g.*, mild major depressive disorder. In some examples, the subject has a moderate depressive disorder, *e.g.*, moderate major depressive disorder. In some examples, the subject has a severe depressive disorder, *e.g.*, severe major depressive disorder. In some examples, the subject has a very severe depressive disorder, *e.g.*, very severe major depressive disorder. In some examples, the baseline HAM-D total score of the subject (i.e., prior to treatement with Compound 1) is at least 24. In some examples, the baseline HAM-D total score of the subject is at least 18. In some examples, the baseline HAM-D total score of

the subject is between and including 14 and 18. In some examples, the baseline HAM-D total score of the subject is between and including 19 and 22. In some examples, the HAM-D total score of the subject before treatement with Compound 1 is greater than or equal to 23. In some examples, the baseline score is at least 10, 15, or 20. In some examples, the HAM-D total score of the subject after treatment with Compound 1 is about 0 to 10 (e.g., less than 10; 0 to 10, 0 to 6, 0 to 4, 0 to 3, 0 to 2, or 1.8). In some examples, the HAM-D total score after treatment with Compound 1 is less than 10, 7, 5, or 3. In some examples, the decrease in HAM-D total score is from a baseline score of about 20 to 30 (e.g., 22 to 28, 23 to 27, 24 to 27, 25 to 27, 26 to 27) to a HAM-D total score at about 0 to 10 (e.g., less than 10; 0 to 10, 0 to 6, 0 to 4, 0 to 3, 0 to 2, or 1.8) after treatment with Compound 1. In some examples, the decrease in the baseline HAM-D total score to HAM-D total score after treatment with Compound 1 is at least 1, 2, 3, 4, 5, 7, 10, 25, 40, 50, or 100 fold). In some examples, the percentage decrease in the baseline HAM-D total score to HAM-D total score after treatment with Compound 1 is at least 50% (e.g., 60%, 70%, 80%, or 90%). In some examples, the therapeutic effect is measured as a decrease in the HAM-D total score after treatment with Compound 1 relative to the baseline HAM-D total score (e.g., 12, 24, 48 hours after administration; or 24, 48, 72, 96 hours or more; or 1 day, 2 days, 14 days, or more) is at least 10, 15, or 20 points.

In some examples, the method of treating a depressive disorder, e.g., major depressive disorder provides a therapeutic effect (e.g., as measured by reduction in Hamilton Depression Score (HAM-D)) within 14, 10, 4, 3, 2, or 1 days, or 24, 20, 16, 12, 10, or 8 hours or less. In some examples, the method of treating the depressive disorder, e.g., major depressive disorder, provides a therapeutic effect (*e.g.*, as determined by a statistically significant reduction in HAM-D total score) within the first or second day of the treatment with Compound 1. In some examples, the method of treating the depressive disorder, e.g., major depressive disorder, provides a therapeutic effect (*e.g.*, as determined by a statistically significant reduction in HAM-D total score) within less than or equal to 14 days since the beginning of the treatment with Compound 1. In some examples, the method of treating the depressive disorder, e.g., major depressive disorder, provides a therapeutic effect (*e.g.*, as determined by a statistically significant reduction in HAM-D total score) within less than or equal to 21 days since the beginning of the treatment with Compound 1. In some examples, the method of treating the depressive disorder, e.g., major depressive disorder, provides a therapeutic effect (*e.g.*, as determined by a statistically significant reduction in HAM-D total score) within less than or equal to 28 days since the beginning of the treatment with Compound 1. In some examples, the therapeutic effect is a decrease from baseline in HAM-D total score after treatment with Compound 1 (e.g., treatment with Compound 1 once a day for 14 days). In some examples, the HAM-D total score of the subject before treatement with Compound 1 is at least 24. In some examples, the HAM-D total score of the subject before treatement with Compound 1 is at least 18. In some examples, the HAM-D total score of the subject before treatement with Compound 1 is between and including 14 and 18. In some

examples, the decrease in HAM-D total score after treating the subject with Compound 1 relative to the baseline HAM-D total score is at least 10. In some examples, the decrease in HAM-D total score after treating the subject with Compound 1 relative to the baseline HAM-D total score is at least 15 (*e.g.*, at least 17). In some examples, the HAM-D total score associated with treating the subject with Compound 1 is no more than a number ranging from 6 to 8. In some examples, the HAM-D total score associated with treating the subject with Compound 1 is no more than 7.

In some examples, the method provides therapeutic effect (e.g., as measured by reduction in Clinical Global Impression-Improvement Scale (CGI)) within 14, 10, 4, 3, 2, or 1 days, or 24, 20, 16, 12, 10, or 8 hours or less. In some examples, the CNS-disorder is a depressive disorder, *e.g.*, major depressive disorder. In some examples, the method of treating the depressive disorder, *e.g.*, major depressive disorder provides a therapeutic effect within the second day of the treatment period. In some examples, the therapeutic effect is a decrease from baseline in CGI score at the end of a treatment period (e.g., 14 days after administration).

In some examples, the method provides therapeutic effect (e.g., as measured by reduction in Montgomery-Asberg Depression Rating Scale (MADRS)) within 14, 10, 4, 3, 2, or 1 days, or 24, 20, 16, 12, 10, or 8 hours or less. In some examples, the CNS-disorder is a depressive disorder, *e.g.*, major depressive disorder. In some examples, the method of treating the depressive disorder, *e.g.*, major depressive disorder provides a therapeutic effect within the second day of the treatment period. In some examples, the therapeutic effect is a decrease from baseline in MADRS score at the end of a treatment period (e.g., 14 days after administration).

The disclosure features, *inter alia*, an article of manufacture comprising a therapeutically effective amount of a Compound 1, packaging material, and a label affixed to the packaging material indicating that the therapeutically effective amount of the compound should be taken with food, or a package insert contained within the packaging material indicating that the therapeutically effective amount of Compound 1 should be taken with food. In some examples, the therapeutically effective amount of Compound 1 is in a solid dosage form, such as a tablet or a capsule. In some examples, the label or package insert further indicates that the therapeutically effective amount of Compound 1 is administered once daily. In some examples, the label or package insert further indicates that the therapeutically effective amount of Compound 1 is about 20 mg to about 60 mg; is about 25 mg to about 50 mg; or is about 25 mg to about 35 mg; is about 30 mg, e.g., 30 mg. In some examples, the label or package insert further indicates that the therapeutically effective amount of Compound 1 should be taken with food that is a high fat meal or is a regular meal. In some examples, the label or package insert further indicates that the therapeutically effective amount of Compound 1 should be taken with food to increase the bioavailability of Compound 1. In some examples, the label or

package insert further indicates that the therapeutically effective amount of Compound 1 is for treating CNS related disorders.

In some examples, the method comprises a method of treating a CNS related disorder by administering a therapeutically effective amount of Compound 1, wherein the therapeutically effective amount of Compound 1 is about 30 mg, e.g., 30 mg, and is administered substantially contemporaneously with food.

In an example of the disclosure, provided is, *inter alia*, a method for effecting positive allosteric modulation of a $GABA_A$ receptor in a patient in need thereof, where the method comprises administering to the patient a therapeutically effective amount of a Compound 1 substantially contemporaneously with food. In some examples the therapeutically effective amount is in a solid dosage form, such as a tablet or a capsule. In some examples, the therapeutically effective amount of a Compound 1 is administered once daily. In some examples, the therapeutically effective amount of Compound 1 is about 20 mg to about 60 mg; is about 25 mg to about 50 mg; or is about 25 mg to about 35 mg; or is about 30 mg, e.g., 30 mg. In some examples, the therapeutically effective amount of Compound 1 is administered substantially contemporaneously with food, *e.g.*, within about 45 minutes, within about 30 minutes, within about 15 minutes, or within about 5 minutes before or after ingesting food. In some examples, the food is a high fat meal, as defined herein, or the food is a regular meal, as discussed herein. In other examples, the food is at least 50 calories, at least 100 calories, at least 200 calories, or at least 300 calories. In some examples, administering the therapeutically effective amount of Compound 1 contemporaneously with food increases the bioavailability of the compound compared to administration without food. In some examples, bioavailability is based on a comparison of AUC values. In some examples, the bioavailability is increased by about 10% or greater; by about 20% or greater; by about 30% or greater; by about 40% or greater; by about 50% or greater; or by about 55% or greater.

In an example of the disclosure, provided is, *inter alia*, a method of treating a CNS-related disorder, *e.g.*, a GABA related disease or disorder, *e.g.*, a mood disorder, a movement disorder, postpartum depression, major depressive disorder, essential tremor, or Parkinson's disease, in a subject, the method comprising administering to the subject a therapeutically effective amount of Compound 1 substantially contemporaneously with food, wherein the administration results in an increase in the bioavailability of Compound 1 compared to administration without food. In some examples, bioavailability is based on a comparison of AUC values. In some examples, bioavailability is based on the AUC_{0-t} value. In some examples, the bioavailability or AUC_{0-t} value for Compound 1 in a formulation is compared to the AUC_{0-t} value for Compound 1 in another formulation. In some examples, the formulation is Compound 1 in a capsule administered with food and the other formulation is Compound 1 in a capsule administered without food. In some examples, these AUC_{0-t} values are compared and the AUC_{0-t} value for the formulation of Compound 1 in a capsule administered with food is higher than the AUC_{0-t} value for the formulation of Compound 1 in a

capsule administered without food. In some examples, the AUC_{0-t} value for the formulation of Compound 1 in a capsule administered with food has a percent increase of at least 10% or greater when compared to the AUC_{0-t} value for the formulation of Compound 1 in a capsule administered without food. In other examples, this percent increase is at least 20% or greater; is at least 30% or greater; is at least 40% or greater; is at least 40% or greater; or is at least 55% or greater.

In some examples, the CNS related disorder is a depressive disorder, *e.g.*, major depressive disorder. In some examples, the method of treating the depressive disorder, *e.g.*, major depressive disorder provides a therapeutic effect (e.g., as measured by reduction in Hamilton Depression Score (HAM-D)) within 14, 10, 4, 3, 2, or 1 days, or 24, 20, 16, 12, 10, or 8 hours or less.

In some examples, the CNS related disorder is a depressive disorder such as major depressive disorder. In some examples, the subject has a mild depressive disorder, *e.g.*, mild major depressive disorder. In some examples, the subject has a moderate depressive disorder, *e.g.*, moderate major depressive disorder. In some examples, the subject has a severe depressive disorder, *e.g.*, severe major depressive disorder. In some examples, the subject has a very severe depressive disorder, *e.g.*, very severe major depressive disorder. In some examples, the baseline HAM-D total score of the subject is at least 24. In some examples, the baseline HAM-D total score of the subject is at least 18. In some examples, the baseline HAM-D total score of the subject is between and including 14 and 18. In some examples, the baseline HAM-D total score of the subject is between and including 19 and 22. In some examples, the HAM-D total score of the subject before treatement with Compound 1 is greater than or equal to 23. In some examples, the baseline score is at least 10, 15, or 20. In some examples, the HAM-D total score of the subject after treatment with Compound 1 is about 0 to 10 (e.g., less than 10; 0 to 10, 0 to 6, 0 to 4, 0 to 3, 0 to 2, or 1.8). In some examples, the HAM-D total score after treatment with Compound 1 is less than 10, 7, 5, or 3. In some examples, the decrease in HAM-D total score is from a baseline score of about 20 to 30 (e.g., 22 to 28, 23 to 27, 24 to 27, 25 to 27, 26 to 27) to a HAM-D total score at about 0 to 10 (e.g., less than 10; 0 to 10, 0 to 6, 0 to 4, 0 to 3, 0 to 2, or 1.8) after treatment with Compound 1. In some examples, the decrease in the baseline HAM-D total score to HAM-D total score after treatment with Compound 1 is at least 1, 2, 3, 4, 5, 7, 10, 25, 40, 50, or 100 fold). In some examples, the percentage decrease in the baseline HAM-D total score to HAM-D total score after treatment with Compound 1 is at least 50% (e.g., 60%, 70%, 80%, or 90%). In some examples, the therapeutic effect is measured as a decrease in the HAM-D total score after treatment with Compound 1 relative to the baseline HAM-D total score (e.g., 12, 24, 48 hours after administration; or 24, 48, 72, 96 hours or more; or 1 day, 2 days, 14 days, or more) is at least 10, 15, or 20 points.

In some examples, the method of treating a depressive disorder, e.g., major depressive disorder provides a therapeutic effect (e.g., as measured by reduction in Hamilton Depression Score (HAM-D)) within 14, 10, 4, 3, 2, or 1 days, or 24, 20, 16, 12, 10, or 8 hours or less. In some

examples, the method of treating the depressive disorder, e.g., major depressive disorder, provides a therapeutic effect (*e.g.*, as determined by a statistically significant reduction in HAM-D total score) within the first or second day of the treatment with Compound 1. In some examples, the method of treating the depressive disorder, e.g., major depressive disorder, provides a therapeutic effect (*e.g.*, as determined by a statistically significant reduction in HAM-D total score) within less than or equal to 14 days since the beginning of the treatment with Compound 1. In some examples, the method of treating the depressive disorder, e.g., major depressive disorder, provides a therapeutic effect (*e.g.*, as determined by a statistically significant reduction in HAM-D total score) within less than or equal to 21 days since the beginning of the treatment with Compound 1. In some examples, the method of treating the depressive disorder, e.g., major depressive disorder, provides a therapeutic effect (*e.g.*, as determined by a statistically significant reduction in HAM-D total score) within less than or equal to 28 days since the beginning of the treatment with Compound 1. In some examples, the therapeutic effect is a decrease from baseline in HAM-D total score after treatment with Compound 1 (e.g., treatment with Compound 1 once a day for 14 days). In some examples, the HAM-D total score of the subject before treatement with Compound 1 is at least 24. In some examples, the HAM-D total score of the subject before treatement with Compound 1 is at least 18. In some examples, the HAM-D total score of the subject before treatement with Compound 1 is between and including 14 and 18. In some examples, the decrease in HAM-D total score after treating the subject with Compound 1 relative to the baseline HAM-D total score is at least 10. In some examples, the decrease in HAM-D total score after treating the subject with Compound 1 relative to the baseline HAM-D total score is at least 15 (*e.g.*, at least 17). In some examples, the HAM-D total score associated with treating the subject with Compound 1 is no more than a number ranging from 6 to 8. In some examples, the HAM-D total score associated with treating the subject with Compound 1 is no more than 7.

In some examples, the method provides therapeutic effect (e.g., as measured by reduction in Clinical Global Impression-Improvement Scale (CGI)) within 14, 10, 4, 3, 2, or 1 days, or 24, 20, 16, 12, 10, or 8 hours or less. In some examples, the method of treating the depressive disorder, *e.g.*, major depressive disorder provides a therapeutic effect within the second day of the treatment period. In some examples, the therapeutic effect is a decrease from baseline in CGI score at the end of a treatment period (e.g., 14 days after administration).

In some examples, the method provides therapeutic effect (e.g., as measured by reduction in Montgomery-Asberg Depression Rating Scale (MADRS)) within 14, 10, 4, 3, 2, or 1 days, or 24, 20, 16, 12, 10, or 8 hours or less. In some examples, the method of treating the depressive disorder, *e.g.*, major depressive disorder provides a therapeutic effect within the second day of the treatment period. In some examples, the therapeutic effect is a decrease from baseline in MADRS score at the end of a treatment period (e.g., 14 days after administration).

In some examples of any of the foregoing, the subject is administered Compound 1, *e.g.*, about a 30 mg dose of Compound 1, *e.g.*, a 30 mg dose of Compound 1, once a day for less than 2 weeks. In some examples of any of the foregoing, the subject is administered Compound 1, *e.g.*, about a 30 mg dose of Compound 1, *e.g.*, a 30 mg dose of Compound 1, once a day for 1 day. In some examples of any of the foregoing, the subject is administered Compound 1, *e.g.*, about a 30 mg dose of Compound 1, *e.g.*, a 30 mg dose of Compound 1, once a day for 2 days. In some examples of any of the foregoing, the subject is administered Compound 1, *e.g.*, about a 30 mg dose of Compound 1, *e.g.*, a 30 mg dose of Compound 1, once a day for at least 14 days. In some examples, the subject is administered Compound 1, *e.g.*, about a 30 mg dose, *e.g.*, a 30 mg dose once a day for at least 28 days. In some examples, the subject is administered Compound 1, *e.g.*, about a 30 mg dose, *e.g.*, a 30 mg dose once a day for at least 6 months. In some examples, the subject is administered Compound 1, *e.g.*, about a 30 mg dose, *e.g.*, a 30 mg dose once a day for at least 1 year. In some examples, the subject is administered Compound 1, *e.g.*, about a 30 mg dose, *e.g.*, a 30 mg dose once a day for life. In some examples, the subject is administered Compound 1 at night. In some examples, the subject is administered Compound 1 no longer than 1 hour before the subject sleeps. In some examples, the subject is administered Compound 1 no longer than 15 minutes before the subject sleeps. In some examples, Compound 1 is administered chronically.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 depicts the mean (± standard deviation) Compound 1 plasma concentrations over time by dosing condition (Linear Scale).

FIG. 2 depicts the mean (± standard deviation) Compound 1 plasma concentrations over time by dosing condition (Semi-Logarithmic Scale).

FIG. 3A depicts an exemplary XRPD pattern of Form A.

FIG. 3B depicts an exemplary unit cell of Form A along the b axis.

FIG. 3C depicts exemplary TGA (upper) and DSC (lower) curves of Form A.

FIG. 3D depicts an overlay of exemplary VT-XRPD patterns of Form A at selected temperatures, along with an exemplary XRPD pattern of Form K.

FIG. 3E depicts an exemplary DVS isotherm of Form A at 25 °C.

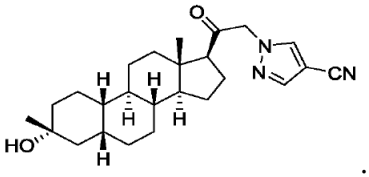
FIG. 3F depicts an exemplary XRPD patterns of Form A before and after an exemplary DVS measurement at 25 °C.

FIG. 4A depicts an exemplary XRPD pattern of Form C.

FIG. 4B depicts an exemplary unit cell of Form C along the b axis.

CLAIMS

1. Use of a compound in the manufacture of a medicament for the treatment of a CNS-related disorder in a patient, wherein the compound is a compound having the formula



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2. The use of claim 1, wherein the compound is to be administered without food or substantially contemporaneously with food.

3. The use of claim 1, wherein the medicament comprises about 20 mg to about 60 mg of the compound.

4. The use of claim 1, wherein the CNS-related disorder is a GABA related disease or disorder.

5. The use of claim 1, wherein the CNS-related disorder is a mood disorder.

6. The use of claim 1, wherein the CNS-related disorder is a movement disorder.

7. The use of claim 1, wherein the CNS-related disorder is postpartum depression.

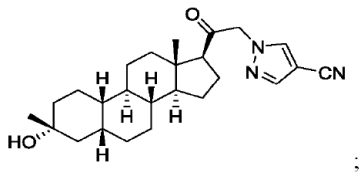
8. The use of claim 1, wherein the CNS-related disorder is major depressive disorder.

9. The use of claim 1, wherein the CNS-related disorder is essential tremor.

10. The use of claim 6, wherein the movement disorder is Parkinson's disease.

11. An article of manufacture comprising:

a therapeutically effective amount of a compound having the formula



;

packaging material; and

a label affixed to the packaging material indicating that the therapeutically effective amount of the compound should be taken with food or a package insert contained within the packaging material indicating that the therapeutically effective amount of the compound should be taken with food.

12. The article of manufacture of claim 11, wherein the therapeutically effective amount of the compound is in a solid dosage form.

13. The article of manufacture of claim 12, wherein the solid dosage form is a tablet or a capsule.

14. The article of manufacture of claim 11, wherein the label or package insert further indicates that the therapeutically effective amount of the compound is to be administered once daily.

15. The article of manufacture of claim 11, wherein the therapeutically effective amount of the compound is about 20 mg to about 60 mg.

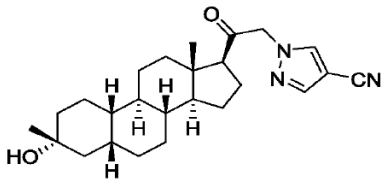
16. The article of manufacture of claim 11, wherein the therapeutically effective amount of the compound is about 25 mg to about 50 mg.

17. The article of manufacture of claim 11, wherein the food comprises a high fat meal.

18. The article of manufacture of claim 11, wherein the label further indicates that the therapeutically effective amount of the compound should be taken with food to increase bioavailability.

19. The article of manufacture of claim 11, wherein the label or the package insert further indicates that the therapeutically effective amount of the compound is for treating CNS related disorders.

20. Use of a compound in the manufacture of a medicament for the treatment of a CNS-related disorder in a subject, wherein the compound is to be administered substantially contemporaneously with food, the compound having the formula:



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wherein the administration results in an increase in the bioavailability of the compound compared to administration without food, wherein bioavailability is based on a comparison of AUC values.

21. The article of manufacture of claim 11, wherein the compound exists as Form C.