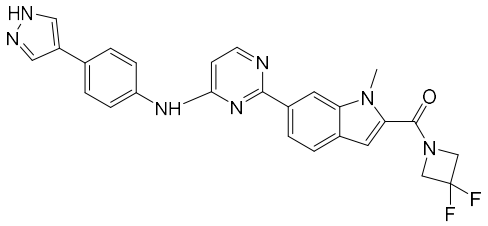
WHAT IS CLAIMED:

1. A pharmaceutical formulation for oral administration comprising:

(a) an active pharmaceutical ingredient (API) comprising a compound having a structure:

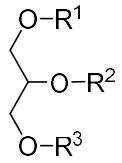


or a pharmaceutically acceptable salt thereof, and

(b) one or more selected from:

(i) a fatty acid component comprising saturated or unsaturated C_8-C_{24} fatty acids and/or a pharmaceutically acceptable salt thereof;

(ii) a first glyceride component comprising one or more glyceride compounds having a structure of Formula (I)



(I)

wherein:

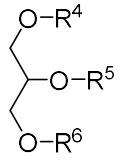
each R^1, R^2, and R^3 is independently hydrogen or -C(O)-R^A;

each R^A is independently C_7-C_{21} alkenyl comprising one or two double bonds,

provided that at least one of R^1, R^2, and R^3 is not hydrogen; and

(iii) a second glyceride component comprising:

one or more glyceride compounds having a structure of Formula (II)



(II)

wherein:

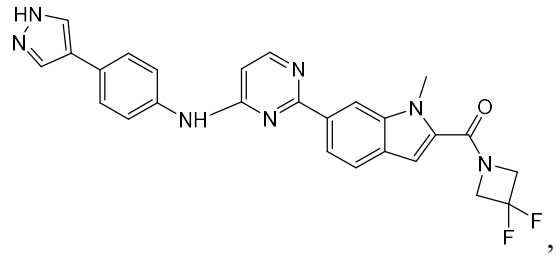
each R^4, R^5, and R^6 is independently hydrogen, or -C(O)-R^B;

each R^B is independently C_7-C_{21} alkyl,

provided that at least one of R^4, R^5, and R^6 is not hydrogen.

2. The pharmaceutical formulation of claim 1, wherein the pharmaceutical composition comprises one or more of:

   (a) the API comprises a HCl salt of

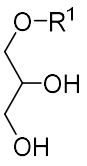
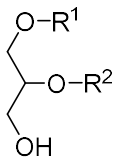
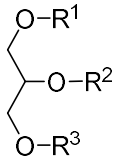


   (b) the fatty acid component comprises a saturated or unsaturated C_{12}-C_{18} fatty acid and/or a pharmaceutically acceptable salt thereof;

   (c) the fatty acid component comprises an oleic acid, sodium oleate, or a combination thereof; or

   (d) the first glyceride component comprises the one or more compounds having a structure of Formula (I) and each R^A is independently C_{13}-C_{21} alkenyl comprising one or two double bonds.

3. The pharmaceutical formulation of claim 1, wherein the first glyceride component comprises the one or more compounds having one of the following structures:

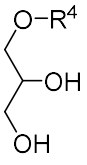
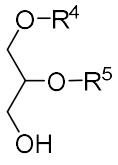
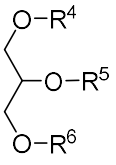
 (Ia),  (I-b), and  (I-c).

4. The pharmaceutical formulation of claim 3, wherein a ratio of the compound of Formula (I-a), the compound of Formula (I-b), and the compound of Formula (I-c) is about 32 to 52 : 40 to 55: 5 to 20.

5. The pharmaceutical formulation of claim 1, wherein

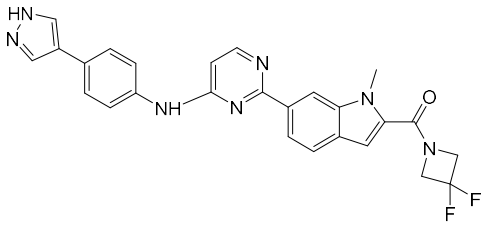
   (a) the second glyceride component comprises the one or more compounds having a structure of Formula (II) and each R^B is independently C_7-C_{17} alkyl; or

   (b) the second glyceride component comprises the one or more compounds having one of the following structures:

 (II-a),  (II-b), and  (II-c).

6. The pharmaceutical formulation of claim 1, wherein the API is formulated in a solid dispersion, in a solution, or as combination thereof.

7. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation comprises the compound having a structure of



or a pharmaceutically acceptable salt thereof in an amount of about 1 to 15 wt% of the pharmaceutical formulation, or about 1-10 wt % of the pharmaceutical formulation, or from about 2-8 wt % of the pharmaceutical formulation, or from about 5-7 wt % of the pharmaceutical formulation.

8. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation comprises one or more of:
   (a) the fatty acid component in an amount of about 15 to 50 wt% of the pharmaceutical formulation, or about 20 to 45 wt%, about 30 to 45 wt%, about 35 to 45 wt%, or about 35 to 40 wt%, based on the weight of the pharmaceutical formulation,
   (b) a fatty acid having saturated or unsaturated C_{12}-C_{18} fatty acid in an amount of 12 to 48 wt%, about 15 to 45 wt%, about 25 to 40 wt%, about 30 to 40 wt%, or about 35 to 40 wt%, based on the weight of the pharmaceutical formulation; and a sodium salt of a fatty acid having saturated or unsaturated C_{12}-C_{18} fatty acids in an amount of about 1 to 5 wt%, or about 2 to 4 wt%, or about 2 to 3 wt%, based on the weight of the pharmaceutical formulation. Or
   (c) the first glyceride component in an amount of about 30 to 50 wt% of the pharmaceutical formulation, or about 30 to 45 wt%, or about 32 to 40 wt%, or about 35 to 40 wt% of the pharmaceutical formulation;
   (d) the second glyceride component in an amount of about 10 to 35 wt%, or about 10 to 30 wt%, or about 10 to 20 wt%, or about 15 to 18 wt% based on the weight of the pharmaceutical formulation.

9. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation comprises:
   (a) Compound A, or a pharmaceutically acceptable salt in an amount of about 1-15 wt %;

(b) a fatty acid having saturated or unsaturated C_{12}-C_{18} fatty acid in an amount 12 to 48 wt%;

(c) a sodium salt of a fatty acid having saturated or unsaturated C_{12}-C_{18} fatty acids in an amount of about 1 to 5 wt%;

(d) the first glyceride component in an amount of about 30 to 50 wt%; and

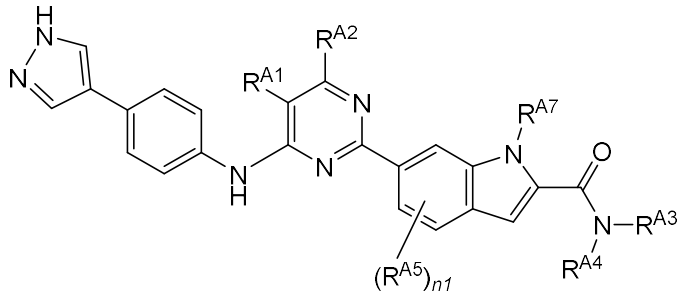
(e) the second glyceride component in an amount of about 10 to 35 wt%,

based on the weight of the pharmaceutical formulation.

10. Use of a pharmaceutical formulation comprising a therapeutically effective amount of a ROCK2 inhibitor in the manufacture of a medicament for the treatment of a neurodegenerative disease characterized by the degeneration of motor neurons, wherein the pharmaceutical formulation is to be administered to a patient in need thereof.

11. The use of claim 10, wherein the neurodegenerative disease is amyotrophic lateral sclerosis (ALS), primary lateral sclerosis (PLS), progressive muscular atrophy (PMA), progressive bulbar palsy, pseudobulbar palsy, or monomelic amyotrophy (MMA), and preferably the neurodegenerative disease is amyotrophic lateral sclerosis (ALS).

12. The use according to any one of claims 10 to 11, wherein the ROCK2 inhibitor has the structure of Formula (A-I):



(A-I)

or a pharmaceutically acceptable salt thereof, wherein:

R^{A1} is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, -OR^{A11}, -O-(C_1-C_6 alkyl)-OR^{A11}, -(C_1-C_6 alkyl)-OR^{A11}, -$NR^{A11}R^{A12}$, -O-(C_1-C_6 alkyl)-$NR^{A11}R^{A12}$, -(C_1-C_6 alkyl)-$NR^{A11}R^{A12}$, -NR^{A11}-(C_1-C_6 alkyl)-$NR^{A11}R^{A12}$, -NR^{A11}-(C_1-C_6 alkyl)-OR^{A11}, -(C_1-C_6 alkyl)$_x$-C(=O)R^{A11}, -O-(C_1-C_6 alkyl)$_{x1}$-C(=O)R^{A11}, -(C_1-C_6 alkyl)$_{x1}$-C(=O)OR^{A11}, -

C(=O)-R^{A11}, -C(=O)OR^{A11}, -(C_1-C_6 alkyl)$_{x1}$-C(=O)$NR^{A11}R^{A12}$, -NR^{A11}-(C_1-C_6 alkyl)$_{x1}$-C(=O)R^{A11}, and -NR^{A11}-(C_1-C_6 alkyl)$_{x1}$-C(=O)OR^{A11};

R^{A2} is selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, -OR^{A11}, -O-(C_1-C_6 alkyl)-OR^{A11}, -(C_1-C_6 alkyl)-OR^{A11}, -$NR^{A11}R^{A12}$, -O-(C_1-C_6 alkyl)-$NR^{A11}R^{A12}$, -(C_1-C_6 alkyl)-$NR^{A11}R^{A12}$, -NR^{A11}-(C_1-C_6 alkyl)-$NR^{A11}R^{A12}$, -NR^{A11}-(C_1-C_6 alkyl)-OR^{A11}, -(C_1-C_6 alkyl)$_{x1}$-C(=O)R^{A11}, -O-(C_1-C_6 alkyl)$_{x1}$-C(=O)R^{A11}, -(C_1-C_6 alkyl)$_{x1}$-C(=O)OR^{A11}, -C(=O)-R^{A11}, -C(=O)OR^{A11}, -(C_1-C_6 alkyl)$_{x1}$-C(=O)$NR^{A11}R^{A12}$, -NR^{A11}-(C_1-C_6 alkyl)$_{x1}$-C(=O)R^{A11}, and -NR^{A11}-(C_1-C_6 alkyl)$_{x1}$-C(=O)OR^{A11};

alternatively, R^{A1} and R^{A2} are taken together to form a 5- or 6-membered saturated or unsaturated fused ring which may contain from 0 to 2 ring heteroatoms selected from the group consisting of N, O, and S, and which is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of C_1-C_6 alkyl, halo, -CN, -OH, oxo, -O-(C_1-C_6 alkyl), -O-(C_1-C_6 alkyl)-OH, -O-(C_1-C_6 alkyl)-O-(C_1-C_6 alkyl), -$NR^{A11}R^{A12}$, -O-(C_1-C_6 alkyl)-$NR^{A11}R^{A12}$, C_1-C_3 perfluoro alkyl, -NR^{A11}-(C_1-C_6 alkyl)$NR^{A11}R^{A12}$, and -NR^{A11}-(C_1-C_6 alkyl)-OR^{A11};

R^{A3} and R^{A4} are each independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, 3- to 10-membered heterocyclyl, C_6-C_{10} aryl, 5- to 14-membered heteroaryl, C_{6-12} aralkyl, -(C_1-C_6 alkyl)-OR^{A11}, -(C_1-C_6 alkyl)-$NR^{A11}R^{A12}$, -(C_1-C_6 alkyl)$_{x1}$-C(=O)R^{A11}, -(C_1-C_6 alkyl)$_{x1}$-C(=O)OR^{A11}, and -(C_1-C_6 alkyl)$_{x1}$-C(=O)$NR^{A11}R^{A12}$;

alternatively R^{A3} and R^{A4} are taken together with the nitrogen to which they are attached to provide (i) a 4- to 6-membered heterocyclic ring having from 0 to 2 additional ring to heteroatoms selected from N, O and S, or (ii) a 5- to 10-membered hetero bicyclic ring system having from 0 to 3 additional ring heteroatoms selected from N, O and S; wherein the heterocyclic ring or the bicyclic ring system are unsubstituted or are substituted with from 1 to 4 substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, -OR^{A11}, oxo, -O-(C_1-C_6 alkyl)-OR^{A11}, -(C_1-C_6 alkyl)-OR^{A11}, -$NR^{A11}R^{A12}$, -O-(C_1-C_6 alkyl)-$NR^{A11}R^{A12}$, -(C_1-C_6 alkyl)-$NR^{A11}R^{A12}$, -NR^{A11}-(C_1-C_6 alkyl)-$NR^{A11}R^{A12}$, -NR^{A11}-(C_1-C_6 alkyl)-OR^{A11}, -(C_1-C_6 alkyl)$_{x1}$-C(=O)R^{A11}, -O-(C_1-C_6 alkyl)$_{x1}$-C(=O)R^{A11}, -(C_1-C_6 alkyl)$_{x1}$-C(=O)OR^{A11}, -C(=O)-R^{A11}, -C(=O)OR^{A11}, -(C_1-C_6 alkyl)$_{x1}$-C(=O)$NR^{A11}R^{A12}$, -NR^{A11}-(C_1-C_6 alkyl)$_{x1}$-C(=O)R^{A11}, and -NR^{A11}-(C_1-C_6 alkyl)$_{x1}$-C(=O)OR^{A11};

the dotted lines represent optional double bonds;

each R^{A5} is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, halo, -CN, C_1-C_3 perfluoro alkyl, oxo, -OR^{A11}, -O-(C_1-C_6 alkyl)-OR^{A11}, -(C_1-C_6 alkyl)-OR^{A11}, -$NR^{A11}R^{A12}$, -O-(C_1-C_6 alkyl)-$NR^{A11}R^{A12}$, -(C_1-C_6 alkyl)-$NR^{A11}R^{A12}$, -NR^{A11}-(C_1-C_6 alkyl)-$NR^{A11}R^{A12}$, -NR^{A11}-(C_1-C_6 alkyl)-OR^{A11}, -(C_1-C_6 alkyl)$_{x1}$-C(=O)R^{A11}, -O-(C_1-C_6 alkyl)$_{x1}$-C(=O)R^{A11}, -(C_1-C_6 alkyl)$_{x1}$-C(=O)OR^{A11}, -C(=O)-R^{A11}, -C(=O)OR^{A11}, -(C_1-C_6 alkyl)$_{x1}$-C(=O)$NR^{A11}R^{A12}$, -NR^{A11}-(C_1-C_6 alkyl)$_{x1}$-C(=O)R^{A11}, and -NR^{A11}-(C_1-C_6 alkyl)$_{x1}$-C(=O)OR^{A11};

n1 is 0 to 3;

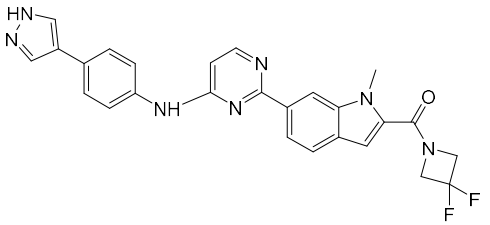
R^{A7} is independently selected from the group consisting of H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -(C_1-C_6 alkyl)-OR^{A11}, -(C_1-C_6 alkyl)-$NR^{A11}R^{A12}$, -(C_1-C_6 alkyl)$_{x1}$-C(=O)R^{A11}, -(C_1-C_6 alkyl)$_{x1}$-C(=O)OR^{A11}, and -(C_1-C_6 alkyl)$_{x1}$-C(=O)$NR^{A11}R^{A12}$;

each *x1* is independently selected from 0 and 1; and

each R^{A11} and R^{A12} are independently selected from the group consisting of H and C_1-C_6 alkyl;

or alternatively, R^{A11} and R^{A12} are taken together when both are attached to the same nitrogen to form a 4- to 7- membered heterocyclic ring having from 0 to 2 additional ring heteroatoms selected from the group consisting of N, O and S, and which heterocyclic ring is unsubstituted or is substituted with 1 to 3 substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -CN, -NH_2, C_1-C_3 perfluoro alkyl, -OH, -O-(C_1-C_6 alkyl), and -(C_1-C_6 alkyl)-OH.

13. The use of claim 12, wherein the ROCK2 inhibitor has the formula:



or a pharmaceutically acceptable salt thereof.

14. The use according to any one of claims 10 to 11, wherein the ROCK2 inhibitor is selected from Compound D, belumosudil (KD025), Zelasudil, Y-27632, Fasudil,

GSK429286A, RKI-1447, Azaindole 1 (TC-S 7001), Hydroxyfasudil, GSK269962A, Ripasudil, AT13148, RX007, and derivatives, isomers, hydrates, or pharmaceutically acceptable salts thereof.

15. Use of a pharmaceutical formulation according to any one of claims 1 to 9 in the manufacture of a medicament for the treatment of a neurodegenerative disease characterized by the degeneration of motor neurons, wherein the pharmaceutical formulation is to be orally administered to a patient in need thereof.

16. The use of claim 15, wherein the neurodegenerative disease is amyotrophic lateral sclerosis (ALS), primary lateral sclerosis (PLS), progressive muscular atrophy (PMA), progressive bulbar palsy, pseudobulbar palsy, or monomelic amyotrophy (MMA), and preferably the neurodegenerative disease is amyotrophic lateral sclerosis (ALS).