

LANIFIBRANOR FORMULATION

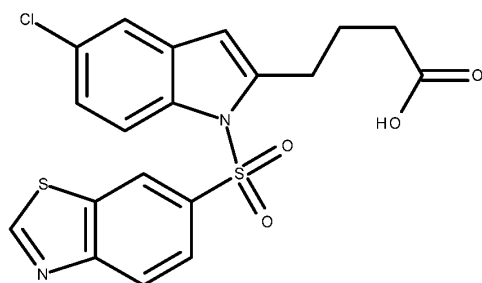
FIELD OF THE INVENTION

The present invention relates to a pharmaceutical composition comprising lanifibranor, and
5 to the use of said composition in therapy, notably for the treatment of liver fibrosis.

BACKGROUND OF THE INVENTION

Lanifibranor or 1-(6-benzothiazolylsulfonyl)-5-chloro-1H-indole-2-butanoic acid is a pan-PPAR agonist which is currently in clinical development for the treatment of patients with non-alcoholic steatohepatitis (NASH), for which there is currently no approved therapy.

10 Lanifibranor is described in example 117 of WO 2007/026097, where it is obtained as a pale-yellow powder having a melting point of 74-80°C, and has the following structure:



The daily dosage regimen of lanifibranor used in phase 2 clinical trial was either 800 mg or 1,200 mg, with two or three 400 mg tablets containing 44 wt% lanifibranor being
15 administered once-a-day depending on the regimen considered. It is contemplated to follow the same daily dosage regimen scheme during the upcoming phase 3 clinical trials but using pharmaceutical formulations containing a higher lanifibranor load. While it is desirable in theory to incorporate the higher amount possible of an active ingredient in a pharmaceutical formulation, there are challenges e.g. in terms of manufacturing process or acceptability (of
20 the size of a dosage form) by patients. In particular, it is not straightforward to incorporate a hydrophobic ingredient (which is the case of lanifibranor), *a fortiori* a high amount of hydrophobic ingredient, in a pharmaceutical formulation as this may be detrimental to bioavailability.

The present invention was made having the above problems in mind.

25 SUMMARY OF THE INVENTION

In one aspect, the present disclosure relates to a pharmaceutical composition comprising, based on the total weight of the composition:

about 55.0 wt% to about 75.0 wt% of lanifibranor; and

about 25.0 wt% to about 45.0 wt% of pharmaceutically acceptable excipients;

wherein lanifibranor has a particle size distribution such that $D50 \leq 30 \mu\text{m}$ and $D90 \leq 50 \mu\text{m}$.

In some embodiments, the pharmaceutically acceptable excipients include two or more of a binder, a disintegrant, a filler, a glidant, a lubricant, and a surfactant. In some embodiments,
5 the pharmaceutically acceptable excipients include a binder, a disintegrant, a filler, a glidant, a lubricant and a surfactant.

In some embodiments, the pharmaceutical composition is a solid dosage form, such as for example a capsule, a sachet, a lozenge, a powder, a pill or a tablet.

In some embodiments, the solid dosage form comprises from about 200 mg to about 1,200 mg of lanifibranor, such as for example 200 mg, 400 mg, 600 mg, 800 mg, 1,000 mg or
10 1,200 mg of lanifibranor.

In some embodiments, lanifibranor is present as a crystalline form.

In some embodiments, the pharmaceutical composition has a dissolution of at least 30% and not more than 60% after 15 minutes, and at least 80%, preferably at least 85%, after 45
15 minutes, as measured with a USP test-apparatus 1 (basket 10 mesh) at 100 rpm, in 1000 mL of a sodium phosphate buffer pH 6.8 thermostated at $37^\circ\text{C} \pm 0.5^\circ\text{C}$ and comprising from about 0.7% to 1.7% of tetradecyltrimethyl-ammonium bromide.

In another aspect, the present disclosure relates to a method of treating non-alcoholic fatty liver disease, which comprises administering to a subject in need thereof a pharmaceutical
20 composition as defined above.

In another aspect, the present disclosure relates to a method of treating a cirrhotic subject at risk of progressing from compensated stage to decompensated stage, which comprises administering to the subject a pharmaceutical composition as defined above.

Both the foregoing general description and the following detailed description are exemplary
25 and explanatory and are intended to provide further explanation of the invention defined in the appended claims.

DESCRIPTION OF THE FIGURES

Figure 1 shows the dissolution profile of a 600 mg lanifibranor tablet.

Figure 2 shows the dissolution profile of a 400 mg lanifibranor tablet.

30 DETAILED DESCRIPTION OF THE INVENTION

As used herein, the articles including "a" and "an", are understood to mean one or more of what is claimed or described.

As used herein, the terms "include", "includes" and "including" are meant to be non-limiting.

As used herein, the term "about xx" refers to a measurable value such as a parameter, an
35 amount, a temporal duration, and the like, is meant to encompass variations of $\pm 10\%$ or

less, preferably +/-5% or less, more preferably +/-1% or less, even more preferably +/-0.5% or less, more preferably +/-0.05% or less, and still more preferably +/-0.04% or less, +/-0.03% or less, +/-0.02% or less, +/-0.01% or less of and from the specified value, insofar such variations are appropriate to perform in the disclosed invention. However, it is to be understood that the value to which "about" refers is itself also specifically disclosed. In other words, the term "about xx" includes the value "xx".

It is to be understood that concentrations disclosed herein in weight percent (wt%) are based on a total weight of the pharmaceutical composition or formulations being made, unless otherwise indicated.

Embodiments described herein can be combined.

In one aspect, the present disclosure relates to a pharmaceutical composition comprising, based on the total weight of the composition:

about 55.0 wt% to about 75.0 wt% of lanifibranor; and

about 25.0 wt% to about 45.0 wt% of pharmaceutically acceptable excipients;

wherein lanifibranor has a particle size distribution such that $D_{50} \leq 30 \mu\text{m}$ and $D_{90} \leq 50 \mu\text{m}$.

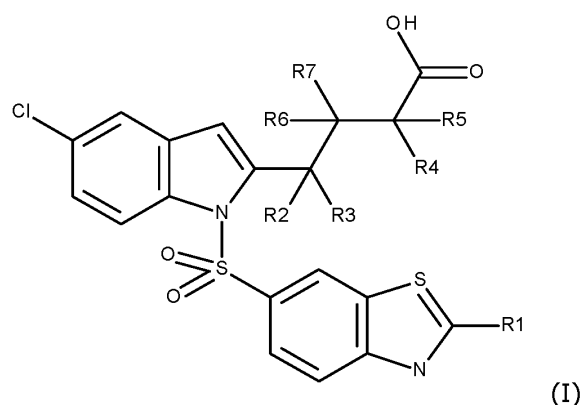
As used herein, D_{50} and D_{90} (which are also sometimes referred to as $D(v; 0.5)$, respectively $D(v; 0.9)$) are the points in the size distribution, up to which 50%, respectively 90% of the total volume of material in a sample is "contained". For example, $D_{90} \leq 50 \mu\text{m}$ means that 90% of the sample has a size of at most $50 \mu\text{m}$. D_{50} and D_{90} were measured with a laser diffraction/scattering particle size distribution analyzer (available e.g. from Malvern.).

In some embodiments, the particle size distribution of lanifibranor is such that it has a $D_{50} \leq 10 \mu\text{m}$ and a $D_{90} \leq 30 \mu\text{m}$, advantageously lanifibranor has a $D_{90} \leq 15 \mu\text{m}$.

In some embodiments, lanifibranor has a particle size distribution such that both its D_{90} and its D_{50} are $\leq 5 \mu\text{m}$, for example the values for both D_{90} and D_{50} are in the range of about 200 nm to about 2000 nm.

As used herein, "lanifibranor" refers to lanifibranor as referring under CAS No. 927961-18-0 (also called IVA337) or as described in example 117 of WO 2007/026097. In some embodiments, the term "lanifibranor" also includes deuterated derivatives of lanifibranor. In some embodiments, lanifibranor is in crystalline form. Examples of crystalline form of lanifibranor have been described in WO2023/194339, in WO2023/016319, in WO2022/122014, in WO2022/261410 or in WO2022/258060, all incorporated herein by reference.

In some embodiments, a deuterated derivative of lanifibranor is a compound of formula (I):



wherein at least one of the groups R1 to R7 is a deuterium (D) atom and the other groups R1 to R7 are hydrogen (H) atoms, as described in WO2020/021215. In some aspects, at least group R1 is D. In some aspects at least one of the groups R2 to R7 is D, notably at least one of the groups R2 and R3 and/or at least one of the groups R4 and R5 and/or at least one of the groups R6 and R7 is D. In a preferred aspect each of R2, R3, R4, R5, R6 and R7 is D. Preferred compounds of formula (I) include 4-(1-(2-deuterio-1,3-benzothiazol-6-yl)sulfonyl)-5-chloro-1H-indol-2-yl)butanoic acid and 4-[1-(1,3-benzothiazol-6-ylsulfonyl)-5-chloro-indol-2-yl]-2,2,3,3,4,4-hexadeuteriobutanoic acid.

In some embodiments, lanifibranor or a deuterated derivative thereof is in the form of one of its pharmaceutically acceptable salts or solvates. The term "solvate" is used herein to describe a molecular complex comprising lanifibranor or a deuterated derivative thereof and one or more pharmaceutically acceptable solvent molecules, for example, ethanol. The term "hydrate" is employed when said solvent is water. Pharmaceutically acceptable salts of lanifibranor or a deuterated derivative thereof include base addition salts thereof. Base addition salts may be prepared from inorganic and organic bases. Examples of inorganic bases include sodium hydroxide, potassium hydroxide, magnesium hydroxide and calcium hydroxide. Examples of organic bases include amines, amino alcohols, basic amino acids such as lysine or arginine, and quaternary ammonium compounds such as betaine or choline.

In some embodiments, lanifibranor represents from about 55.0 wt% to about 75.0 wt%, for example from about 55.0 wt% to about 70.0 wt%, for example from about 55.0 wt% to about 65.0 wt%, for example from about 55.0 wt% to about 60.0 wt%. In some embodiments, lanifibranor represents from about 56.0 wt% to about 75.0 wt%, for example from about 56.0 wt% to about 70.0 wt%, for example from about 56.0 wt% to about 65.0 wt%, for example from about 56.0 wt% to about 60.0 wt%. In some embodiments, lanifibranor represents from example from about 57.0 wt% to about 75.0 wt%, for example

from about 57.0 wt% to about 70.0 wt%, for example from about 57.0 wt% to about 65.0 wt%, for example from about 57.0 wt% to about 60.0 wt%. In some embodiments, lanifibranor represents about 55.0 wt%, about 55.1 wt%, about 55.2 wt%, about 55.3 wt%, about 55.4 wt%, about 55.5 wt%, about 55.6 wt%, about 55.7 wt%, about 55.8 wt%,
5 about 55.9 wt%, about 56.0 wt%, about 56.1 wt%, about 56.2wt%, about 56.3 wt%, about 56.4 wt%, about 56.5 wt%, about 56.6 wt%, about 56.7 wt%, about 56.8 wt%, about 56.9 wt%, about 57.0 wt%, about 57.1 wt%, about 57.2wt%, about 57.3 wt%, about 57.4 wt%, about 57.5 wt%, about 57.6 wt%, about 57.7 wt%, about 57.8 wt%, about 57.9 wt%, about 58.0 wt%, about 58.1 wt%, about 58.2wt%, about 58.3 wt%, about 58.4 wt%, about
10 58.5 wt%, about 58.6 wt%, about 58.7 wt%, about 58.8 wt%, about 58.9 wt%, about 59.0 wt%, about 59.1 wt%, about 59.2wt%, about 59.3 wt%, about 59.4 wt%, about 59.5 wt%, about 59.6 wt%, about 59.7 wt%, about 59.8 wt%, about 59.9 wt%, about 60.0 wt%, about 60.1 wt%, about 60.2wt%, about 60.3 wt%, about 60.4 wt%, about 60.5 wt%, about 60.6 wt%, about 60.7 wt%, about 60.8 wt%, about 60.9 wt%, about 61.0 wt%, about 61.1
15 wt%, about 61.2wt%, about 61.3 wt%, about 61.4 wt%, about 61.5 wt%, about 61.6 wt%, about 61.7 wt%, about 61.8 wt%, about 61.9 wt%, about 62.0 wt%, about 62.1 wt%, about 62.2wt%, about 62.3 wt%, about 62.4 wt%, about 62.5 wt%, about 62.6 wt%, about 62.7 wt%, about 62.8 wt%, about 62.9 wt%, about 63.0 wt%, about 63.1 wt%, about 63.2wt%, about 63.3 wt%, about 63.4 wt%, about 63.5 wt%, about 63.6 wt%, about 63.7
20 wt%, about 63.8 wt%, about 63.9 wt%, about 64.0 wt%, about 64.1 wt%, about 64.2wt%, about 64.3 wt%, about 64.4 wt%, about 64.5 wt%, about 64.6 wt%, about 64.7 wt%, about 64.8 wt%, about 64.9 wt%, about 65.0 wt%, about 65.1 wt%, about 65.2wt%, about 65.3 wt%, about 65.4 wt%, about 65.5 wt%, about 65.6 wt%, about 65.7 wt%, about 65.8 wt%, about 65.9 wt%, about 66.0 wt%, about 66.1 wt%, about 66.2wt%, about 66.3 wt%,
25 about 66.4 wt%, about 66.5 wt%, about 66.6 wt%, about 66.7 wt%, about 66.8 wt%, about 66.9 wt%, about 67.0 wt%, about 67.1 wt%, about 67.2wt%, about 67.3 wt%, about 67.4 wt%, about 67.5 wt%, about 67.6 wt%, about 67.7 wt%, about 67.8 wt%, about 67.9 wt%, about 68.0wt%, about 68.1 wt%, about 68.2wt%, about 68.3 wt%, about 68.4 wt%, about 68.5 wt%, about 68.6 wt%, about 68.7 wt%, about 68.8 wt%, about 68.9 wt%,
30 about 69.0 wt%, about 69.1 wt%, about 69.2wt%, about 69.3 wt%, about 69.4 wt%, about 69.5 wt%, about 69.6 wt%, about 69.7 wt%, about 69.8 wt%, about 69.9 wt%, about 70.0 wt%, about 70.1 wt%, about 70.2wt%, about 70.3 wt%, about 70.4 wt%, about 70.5 wt%, about 70.6 wt%, about 70.7 wt%, about 70.8 wt%, about 70.9 wt%, about 71.0 wt%, about 71.1 wt%, about 71.2wt%, about 71.3 wt%, about 71.4 wt%, about 71.5 wt%, about
35 71.6 wt%, about 71.7 wt%, about 71.8 wt%, about 71.9 wt%, about 72.0 wt%, about 72.1

wt%, about 72.2wt%, about 72.3 wt%, about 72.4 wt%, about 72.5 wt%, about 72.6 wt%,
about 72.7 wt%, about 72.8 wt%, about 72.9 wt%, about 73.0wt%, about 73.1 wt%, about
73.2wt%, about 73.3 wt%, about 73.4 wt%, about 73.5 wt%, about 73.6 wt%, about 73.7
wt%, about 73.8 wt%, about 73.9 wt%, about 74.0wt%, about 74.1 wt%, about 74.2wt%,
5 about 74.3 wt%, about 74.4 wt%, about 74.5 wt%, about 74.6 wt%, about 74.7 wt%,
about 74.8 wt%, about 74.9 wt%, about 75.0 wt%.

The inventors have surprisingly demonstrated that the specific distribution of lanifibranor (as
active ingredient) and pharmaceutically acceptable excipients allows obtaining an immediate
release pharmaceutical composition, which is stable and easy to tableting, has a good
10 dissolution profile and good general tolerability.

In some embodiments, the pharmaceutically acceptable excipients include two or more of a
binder, a disintegrant, a filler, a glidant, a lubricant, and a surfactant. In some embodiments,
the pharmaceutically acceptable excipients include a binder, a disintegrant, a filler, a glidant,
a lubricant and a surfactant.

15 *Fillers*

In some embodiments, the pharmaceutically acceptable excipients include a filler, and the
filler represents from about 10.0 wt% to about 35.0 wt%, for example from about 11.0 wt%
to about 35.0 wt%, for example from about 12.0 wt% to about 35.0 wt%, for example from
about 13.0 wt% to about 35.0 wt%, for example from about 14.0 wt% to about 35.0 wt%,
20 for example from about 15.0 wt% to about 35.0 wt%, for example from about 16.0 wt% to
about 35.0 wt%, for example from about 17.0 wt% to about 35.0 wt%, for example from
about 18.0 wt% to about 35.0 wt%, for example from about 19.0 wt% to about 35.0 wt%,
for example from about 20.0 wt% to about 35.0 wt%, for example from about 21.0 wt% to
about 35.0 wt%, for example from about 22.0 wt% to about 35.0 wt%, for example from
25 about 23.0 wt% to about 35.0 wt%, for example from about 24.0 wt% to about 35.0 wt%,
for example from about 25.0 wt% to about 35.0 wt%, for example from about 26.0 wt% to
about 35.0 wt%, for example from about 27.0 wt% to about 35.0 wt%, for example from
about 28.0 wt% to about 35.0 wt%, for example from about 29.0 wt% to about 35.0 wt%,
for example from about 30.0 wt% to about 35.0 wt%, for example from about 31.0 wt% to
30 about 35.0 wt%, for example from about 32.0 wt% to about 35.0 wt%, for example from
about 33.0 wt% to about 35.0 wt%, for example from about 34.0 wt% to about 35.0 wt%,
for example from about 10.0 wt% to about 34.0 wt%, for example from about 11.0 wt% to
about 34.0 wt%, for example from about 12.0 wt% to about 34.0 wt%, for example from
about 13.0 wt% to about 34.0 wt%, for example from about 14.0 wt% to about 34.0 wt%,
35 for example from about 15.0 wt% to about 34.0 wt%, for example from about 16.0 wt% to

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

about 11.0 wt% to about 12.0 wt%, for example from about 10.0 wt% to about 11.0 wt%, of the total weight of the composition.

In some embodiments, the filler represents about 10.0 wt%, about 10.1 wt%, about 10.2 wt%, about 10.3 wt%, about 10.4 wt%, about 10.5 wt%, about 10.6 wt%, about 10.7 wt%,
5 about 10.8 wt%, about 10.9 wt%, about 11.0 wt%, about 11.1 wt%, about 11.2 wt%, about 11.3 wt%, about 11.4 wt%, about 11.5 wt%, about 11.6 wt%, about 11.7 wt%, about 11.8 wt%, about 11.9 wt%, about 12.0 wt%, about 12.1 wt%, about 12.2 wt%, about 12.3 wt%, about 12.4 wt%, about 12.5 wt%, about 12.6 wt%, about 12.7 wt%, about 12.8 wt%, about 12.9 wt%, about 13.0 wt%, about 13.1 wt%, about 13.2 wt%,
10 about 13.3 wt%, about 13.4 wt%, about 13.5 wt%, about 13.6 wt%, about 13.7 wt%, about 13.8 wt%, about 13.9 wt%, about 14.0 wt%, about 14.1 wt%, about 14.2 wt%, about 14.3 wt%, about 14.4 wt%, about 14.5 wt%, about 14.6 wt%, about 14.7 wt%, about 14.8 wt%, about 14.9 wt%, about 15.0 wt%, about 15.1 wt%, about 15.2 wt%, about 15.3 wt%, about 15.4 wt%, about 15.5 wt%, about 15.6 wt%, about 15.7 wt%,
15 about 15.8 wt%, about 15.9 wt%, about 16.0 wt%, about 16.1 wt%, about 16.2 wt%, about 16.3 wt%, about 16.4 wt%, about 16.5 wt%, about 16.6 wt%, about 16.7 wt%, about 16.8 wt%, about 16.9 wt%, about 17.0 wt%, about 17.1 wt%, about 17.2 wt%, about 17.3 wt%, about 17.4 wt%, about 17.5 wt%, about 17.6 wt%, about 17.7 wt%, about 17.8 wt%, about 17.9 wt%, about 18.0 wt%, about 18.1 wt%, about 18.2 wt%,
20 about 18.3 wt%, about 18.4 wt%, about 18.5 wt%, about 18.6 wt%, about 18.7 wt%, about 18.8 wt%, about 18.9 wt%, about 19.0 wt%, about 19.1 wt%, about 19.2 wt%, about 19.3 wt%, about 19.4 wt%, about 19.5 wt%, about 19.6 wt%, about 19.7 wt%, about 19.8 wt%, about 19.9 wt%, about 20.0 wt%, about 20.1 wt%, about 20.2 wt%, about 20.3 wt%, about 20.4 wt%, about 20.5 wt%, about 20.6 wt%, about 20.7 wt%,
25 about 20.8 wt%, about 20.9 wt%, about 21.0 wt%, about 21.1 wt%, about 21.2 wt%, about 21.3 wt%, about 21.4 wt%, about 21.5 wt%, about 21.6 wt%, about 21.7 wt%, about 21.8 wt%, about 21.9 wt%, about 22.0 wt%, about 22.1 wt%, about 22.2 wt%, about 22.3 wt%, about 22.4 wt%, about 22.5 wt%, about 22.6 wt%, about 22.7 wt%, about 22.8 wt%, about 22.9 wt%, about 23.0 wt%, about 23.1 wt%, about 23.2 wt%,
30 about 23.3 wt%, about 23.4 wt%, about 23.5 wt%, about 23.6 wt%, about 23.7 wt%, about 23.8 wt%, about 23.9 wt%, about 24.0 wt%, about 24.1 wt%, about 24.2 wt%, about 24.3 wt%, about 24.4 wt%, about 24.5 wt%, about 24.6 wt%, about 24.7 wt%, about 24.8 wt%, about 24.9 wt%, about 25.0 wt%, about 25.1 wt%, about 25.2 wt%, about 25.3 wt%, about 25.4 wt%, about 25.5 wt%, about 25.6 wt%, about 25.7 wt%,
35 about 25.8 wt%, about 25.9 wt%, about 26.0 wt%, about 26.1 wt%, about 26.2 wt%,

about 26.3 wt%, about 26.4 wt%, about 26.5 wt%, about 26.6 wt%, about 26.7 wt%,
about 26.8 wt%, about 26.9 wt%, about 27.0 wt%, about 27.1 wt%, about 27.2 wt%,
about 27.3 wt%, about 27.4 wt%, about 27.5 wt%, about 27.6 wt%, about 27.7 wt%,
about 27.8 wt%, about 27.9 wt%, about 28.0 wt%, about 28.1 wt%, about 28.2 wt%,
5 about 28.3 wt%, about 28.4 wt%, about 28.5 wt%, about 28.6 wt%, about 28.7 wt%,
about 28.8 wt%, about 28.9 wt%, about 29.0 wt%, about 29.1 wt%, about 29.2 wt%,
about 29.3 wt%, about 29.4 wt%, about 29.5 wt%, about 29.6 wt%, about 29.7 wt%,
about 29.8 wt%, about 29.9 wt%, about 30.0 wt%, about 30.1 wt%, about 30.2 wt%,
about 30.3 wt%, about 30.4 wt%, about 30.5 wt%, about 30.6 wt%, about 30.7 wt%,
10 about 30.8 wt%, about 30.9 wt%, about 31.0 wt%, about 31.1 wt%, about 31.2 wt%,
about 31.3 wt%, about 31.4 wt%, about 31.5 wt%, about 31.6 wt%, about 31.7 wt%,
about 31.8 wt%, about 31.9 wt%, about 32.0 wt%, about 32.1 wt%, about 32.2 wt%,
about 32.3 wt%, about 32.4 wt%, about 32.5 wt%, about 32.6 wt%, about 32.7 wt%,
about 32.8 wt%, about 32.9 wt%, about 33.0 wt%, about 33.1 wt%, about 33.2 wt%,
15 about 33.3 wt%, about 33.4 wt%, about 33.5 wt%, about 33.6 wt%, about 33.7 wt%,
about 33.8 wt%, about 33.9 wt%, about 34.0 wt%, about 34.1 wt%, about 34.2 wt%,
about 34.3 wt%, about 34.4 wt%, about 34.5 wt%, about 34.6 wt%, about 34.7 wt%,
about 34.8 wt%, about 34.9 wt%, about 35.0 wt%. Examples of fillers include lactose
monohydrate, lactose anhydrous, modified starch, mannitol and mixtures thereof. In one
20 embodiment, the filler includes lactose monohydrate and/or lactose anhydrous.

Surfactants

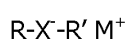
In some embodiments, the pharmaceutically acceptable excipients include a surfactant, and
the surfactant represents from about 1.0 wt% to about 5.0 wt%, for example from about 1.5
wt% to about 5.0 wt%, for example from about 2.0 wt% to about 5.0 wt%, for example
25 from about 2.5 wt% to about 5.0 wt%, for example from about 3.0 wt% to about 5.0 wt%,
for example from about 3.5 wt% to about 5.0 wt%, for example from about 4.0 wt% to
about 5.0 wt%, for example from about 4.5 wt% to about 5.0 wt%, from example from
about 1.0 wt% to about 4.5 wt%, for example from about 1.5 wt% to about 4.5 wt%, for
example from about 2.0 wt% to about 4.5 wt%, for example from about 2.5 wt% to about
30 4.5 wt%, for example from about 3.0 wt% to about 4.5 wt%, for example from about 3.5
wt% to about 4.5 wt%, for example from about 4.0 wt% to about 4.5 wt%, from example
from about 1.0 wt% to about 4.0 wt%, for example from about 1.5 wt% to about 4.0 wt%,
for example from about 2.0 wt% to about 4.0 wt%, for example from about 2.5 wt% to
about 4.0 wt%, for example from about 3.0 wt% to about 4.0 wt%, for example from about
35 3.5 wt% to about 4.0 wt%, from example from about 1.0 wt% to about 3.5 wt%, for

example from about 1.5 wt% to about 3.5 wt%, for example from about 2.0 wt% to about 3.5 wt%, for example from about 2.5 wt% to about 3.5 wt%, for example from about 3.0 wt% to about 3.5 wt%, for example from about 1.0 wt% to about 3.0 wt%, for example from about 1.5 wt% to about 3.0 wt%, for example from about 2.0 wt% to about 3.0 wt%,
5 for example from about 2.5 wt% to about 3.0 wt%, from example from about 1.0 wt% to about 2.5 wt%, for example from about 1.5 wt% to about 2.5 wt%, for example from about 2.0 wt% to about 2.5 wt%, from example from about 1.0 wt% to about 2.0 wt%, for example from about 1.5 wt% to about 2.0 wt%, for example from about 1.0 wt% to about 1.5 wt%, of the total weight of the composition.

10 In some embodiments, the surfactant represents about 1.0 wt%, about 1.1 wt%, about 1.2 wt%, about 1.3 wt%, about 1.4 wt%, about 1.5 wt%, about 1.6 wt%, about 1.7 wt%, about 1.8 wt%, about 1.9 wt%, about 2.0 wt%, about 2.1 wt%, about 2.2 wt%, about 2.3 wt%, about 2.4 wt%, about 2.5 wt%, about 2.51 wt%, about 2.52 wt%, about 2.53 wt%, about 2.54 wt%, about 2.55 wt%, about 2.56 wt%, about 2.57 wt%, about 2.58 wt%, about 2.59
15 wt%, about 2.6 wt%, about 2.61 wt%, about 2.62 wt%, about 2.63 wt%, about 2.64 wt%, about 2.65 wt%, about 2.66 wt%, about 2.67 wt%, about 2.68 wt%, about 2.69 wt%, about 2.7 wt%, about 2.71 wt%, about 2.72 wt%, about 2.73 wt%, about 2.74 wt%, about 2.75 wt%, about 2.76 wt%, about 2.77 wt%, about 2.78 wt%, about 2.79 wt%, about 2.8 wt%, about 2.9 wt%, about 3.0 wt%, about 3.1 wt%, about 3.2 wt%, about 3.3 wt%, about
20 3.4 wt%, about 3.5 wt%, about 3.6 wt%, about 3.7 wt%, about 3.8 wt%, about 3.9 wt%, about 4.0 wt%, about 4.1 wt%, about 4.2 wt%, about 4.3 wt%, about 4.4 wt%, about 4.5 wt%, about 4.6 wt%, about 4.7 wt%, about 4.8 wt%, about 4.9 wt%, about 5.0 wt%, of the total weight of the composition.

In some embodiments, the surfactant is selected from non-ionic surfactants, anionic surfactants, cationic surfactants, and mixtures thereof. In some embodiments, the surfactant
25 is selected from non-ionic surfactants, anionic surfactants, and mixtures thereof.

Examples of anionic surfactants include those having at least one hydrophobic chain containing between 4 and 20 carbon atoms. Exemplary surfactants may contain multiple hydrophobic chains, i.e. at least 2 separate linear or branched alkyl, or alkaryl (i.e. an alkyl
30 chain with an aromatic substituent such as a benzyl group) moieties as shown in the formula below:



wherein:

X represents any of the common polar hydrophilic groups known in anionic surfactants for example carboxylate, sulphate, sulphonate, ether sulphate, sulphosuccinate, glutamate, or phosphate;

R represents a linear or branched alkyl group, or an alkaryl group each having from 4 to 20 carbon atoms, preferably from 4 to 16 carbon atoms and more preferably from 4 to 12 carbon atoms;

R' can be either a hydrogen atom or R; and

M⁺ is a pharmaceutically acceptable cation as defined below.

In one embodiment, the anionic surfactant is selected from the group consisting of:

- 10 - an alkyl benzene sulfonate having the formula R-Ar-SO₃⁻M⁺ wherein R is a C₄-C₂₀ alkyl or alkenyl group, Ar is a phenyl group, and M⁺ is a pharmaceutically acceptable cation, for example selected from the group consisting of ammonium ion, a charged alkanolamine ion (such as a cationic triethanolamine), an alkali metal ion (such as sodium or potassium ions), and mixtures thereof. Examples of alkyl benzene sulfonates include sodium tridecyl benzene sulfonate, sodium dodecyl benzene sulfonate, and mixtures thereof;
- 15 - an alkyl sulfate having the formula R-OSO₃⁻M⁺, wherein R and M⁺ are each as defined above. Examples of alkyl sulfates include ammonium lauryl sulfate, ammonium laureth sulfate, triethylamine lauryl sulfate, triethylamine laureth sulfate, triethanolamine lauryl sulfate, triethanolamine laureth sulfate, monoethanolamine lauryl sulfate, monoethanolamine laureth sulfate, diethanolamine lauryl sulfate, diethanolamine laureth sulfate, lauric monoglyceride sodium sulfate, sodium lauryl sulfate, sodium laureth sulfate, potassium lauryl sulfate, potassium laureth sulfate, ammonium cocoyl sulfate, ammonium lauroyl sulfate, sodium cocoyl sulfate, sodium lauroyl sulfate, potassium cocoyl sulfate, potassium lauryl sulfate, triethanolamine lauryl sulfate, triethanolamine lauroyl sulfate, monoethanolamine cocoyl sulfate, monoethanolamine lauryl sulfate;
- 20 - an alkyl ether sulfate having the formula R-O(C₂H₄O)_ySO₃⁻M⁺, wherein R and M⁺ are each independently as defined above and y is an integer comprised between 1 and 10;
- an alkyl phosphate having the formula RO-P(=O)(OR')O⁻M⁺, wherein R, R' and M⁺ are each independently as defined above. Preferably the alkyl phosphate is a dialkyl phosphate;
- 25 - an alkyl isethionate having the formula R-O-C(=O)-C₂H₄-SO₃⁻M⁺, wherein R and M⁺ are each defined as above;
- an alkyl glutamate having the formula R-(C=O)-NH-(C₂H₄COOH)-COO⁻M⁺, wherein R and M⁺ are each defined as above;
- a sulfosuccinate, such as a dialkyl sulfosuccinate; examples of sulfosuccinates include 30 disodium N-octadecylsulfosuccinate, disodium lauryl sulfosuccinate, diammonium lauryl

sulfosuccinate, tetrasodium N-(1,2-dicarboxyethyl)-N-octadecylsulfosuccinate, diamyl sodium sulfosuccinate, dihexyl sodium sulfosuccinate, dioctyl sodium sulfosuccinate, and mixtures thereof.

In some embodiments, the anionic surfactant is selected from alkyl sulfates, sulfosuccinates, and mixtures thereof. In one embodiment, the anionic surfactant comprises sodium lauryl sulfate and/or dioctyl sodium sulfosuccinate (aka docusate sodium).

Examples of non-ionic surfactants include ethoxylated and/or propoxylated C₄-C₂₀ aliphatic alkyl ethers containing 5 to 60 EO or PO units. The aliphatic groups can be petrochemically derived but are preferably derived from vegetable oils such as coconut oil, palm oil, rapeseed oil etc. and include both saturated and unsaturated alkyl chains. Commercial examples of suitable alkyl ethoxylate ethers are those known with the trade name Genapol™. Other suitable non-ionic surfactants are the polyethylene glycol sorbitan esters containing 3 to 30 ethoxylate units such as sorbitan esters with lauric, oleic, myristic, stearic, and palmitic acids known under the tradenames Tween™ from Croda or Glycosperse™ from Lonza. Other suitable non-ionic surfactants are the ethoxylated polyglyceryl esters of C₈-C₂₀ fatty acids with 20-80 ethoxylate groups, such as glycerol-polyethylene glycol oxystearate commercialized by BASF under the trade name Cremophor™. Polyglyceryl esters are also suitable non-ionic surfactants, these esters comprise from 1 to 10 glycerin units and one or two C₄ to C₂₀ aliphatic alkyl groups. Examples are available under the Polyaldo™ trade name from Lonza.

Further suitable non-ionic surfactants are the N-alkyl-N-acyl glucamines (also referred to as glucamides) where the acyl groups are derived from C₈-C₂₀ fatty acids. Preferably the fatty acids are derived from plant materials such as coconut oil and palm oil. Examples of these surfactants include lauroyl/myristoyl methyl glucamide, Cocoyl methyl glucamide and capryloyl/caproyl methyl glucamide. Commercially these surfactants are available as Glucotain Flex™, Glucotain Care™ and Glucotain Clear™ respectively.

Other suitable non-ionic surfactants are the C₆-C₂₀ ethers or esters of mono-, di- or poly-saccharides. Suitable non-ionic surfactants are the sucrose esters with C₈-C₂₀ fatty acid, such as sucrose esters with lauric, oleic, palmitic or stearic acid, such as the Ryoto™ Sugar Esters commercialized by Mitsubishi-Kagaku Foods Corporation. Other saccharide surfactants include the Oramix™ range by Seppic, the Sepiclear™ range by Seppic such as Sepiclear™ G7 or the Sisterna™ range such as L70-C by Sisterna. Further suitable non-ionic surfactants are (C₆-C₁₆)alkyl glucosides, such as those sold under the Plantacare™ name by Cognis, e.g. C₁₂-C₁₆ fatty alcohol polyglycoside sold as Plantacare™1200UP.

In some embodiments, the non-ionic surfactant is selected from: sorbitan esters with lauric, oleic, myristic, stearic, or palmitic acid; sucrose esters with C₈-C₂₀ fatty acid; polyglyceryl esters comprising from 1 to 10 glycerin units and one or two C₄ to C₂₀ aliphatic alkyl groups; (C₆-C₁₆)alkyl glucosides; glucamides; and mixtures thereof.

5 *Binders*

In some embodiments, the pharmaceutically acceptable excipients include a binder, and the binder represents from about 1.0 wt% to about 10.0 wt%, for example from 1.5 wt% to about 10.0 wt%, for example from 2.0 wt% to about 10.0 wt%, for example from 2.5 wt% to about 10.0 wt%, for example from 3.0 wt% to about 10.0 wt%, for example from 3.5 wt%
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20 Avicel® PH102), polyvinylpyrrolidone and mixtures thereof. In one embodiment, the binder is hydroxypropyl methyl cellulose.

Lubricants

In some embodiments, the pharmaceutically acceptable excipients include a lubricant, and the lubricant represents from about 0.5 wt% to about 5.0 wt%, for example from about 1.0
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25 *Disintegrants*

In some embodiments, the pharmaceutically acceptable excipients include a disintegrant, and the disintegrant represents from about 1.0 wt% to about 8.0 wt%, for example from 1.5 wt% to about 8.0 wt%, for example from 2.0 wt% to about 8.0 wt%, for example from 2.5 wt% to about 8.0 wt%, for example from 3.0 wt% to about 8.0 wt%, for example from 3.5 wt% to about 8.0 wt%, for example from 4.0 wt% to about 8.0 wt%, for example from 4.5 wt% to about 8.0 wt%, for example from 5.0 wt% to about 8.0 wt%, for example from 5.5 wt% to about 8.0 wt%, for example from 6.0 wt% to about 8.0 wt%, for example from 6.5 wt% to about 8.0 wt%, for example from 7.0 wt% to about 8.0 wt%, for example from 7.5 wt% to about 8.0 wt%, for example from about 1.0 wt% to about 7.5 wt%, for example from 1.5 wt% to about 7.5 wt%, for example from 2.0 wt% to about 7.5 wt%, for example

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wt% to about 4.5 wt%, for example from 3.5 wt% to about 4.5 wt%, for example from 4.0
35 wt% to about 4.5 wt%, for example from about 1.0 wt% to about 4.0 wt%, for example

from 1.5 wt% to about 4.0 wt%, for example from 2.0 wt% to about 4.0 wt%, for example from 2.5 wt% to about 4.0 wt%, for example from about 3.0 wt% to about 4.0 wt%, for example from 3.5 wt% to about 4.0 wt%, for example from about 1.0 wt% to about 3.5 wt%, for example from 1.5 wt% to about 3.5 wt%, for example from 2.0 wt% to about 3.5 wt%, for example from 2.5 wt% to about 3.5 wt%, for example from 3.0 wt% to about 3.5 wt%, for example from about 1.0 wt% to about 3.0 wt%, for example from 1.5 wt% to about 3.0 wt%, for example from 2.0 wt% to about 3.0 wt%, for example from 2.5 wt% to about 3.0 wt%, for example from about 1.0 wt% to about 2.5 wt%, for example from 1.5 wt% to about 2.5 wt%, for example from 2.0 wt% to about 2.5 wt%, for example from about 1.0 wt% to about 2.0 wt%, for example from 1.5 wt% to about 2.0 wt%, for example from 1.0 wt% to about 1.5 wt %, of the total weight of the composition. In some embodiments, the binder represents about 1.0 wt%, about 1.1 wt%, about 1.2 wt%, about 1.3 wt%, about 1.4 wt%, about 1.5 wt%, about 1.6 wt%, about 1.7 wt%, about 1.8 wt%, about 1.9 wt%, about 2.0 wt%, about 2.1 wt%, about 2.2 wt%, about 2.3 wt%, about 2.4 wt%, about 2.5 wt%, about 2.6 wt%, about 2.7 wt%, about 2.8 wt%, about 2.9 wt%, about 3.0 wt%, about 3.1 wt%, about 3.2 wt%, about 3.3 wt%, about 3.4 wt%, about 3.5 wt%, about 3.6 wt%, about 3.7 wt%, about 3.8 wt%, about 3.9 wt%, about 4.0 wt%, about 4.1 wt%, about 4.11 wt%, about 4.12 wt%, about 4.13 wt%, about 4.14 wt%, about 4.15 wt%, about 4.16 wt%, about 4.17 wt%, about 4.18 wt%, about 4.19 wt%, about 4.2 wt%, about 4.21 wt%, about 4.22 wt%, about 4.23 wt%, about 4.24 wt%, about 4.25 wt%, about 4.26 wt%, about 4.27 wt%, about 4.28 wt%, about 4.29 wt%, about 4.3 wt%, about 4.31 wt%, about 4.32 wt%, about 4.33 wt%, about 4.34 wt%, about 4.35 wt%, about 4.36 wt%, about 4.37 wt%, about 4.38 wt%, about 4.39 wt%, about 4.4 wt%, about 4.41 wt%, about 4.42 wt%, about 4.43 wt%, about 4.44 wt%, about 4.45 wt%, about 4.46 wt%, about 4.47 wt%, about 4.48 wt%, about 4.49 wt%, about 4.5 wt%, about 4.6 wt%, about 4.7 wt%, about 4.8 wt%, about 4.9 wt%, about 5.0 wt%, about 5.1 wt%, about 5.2 wt%, about 5.3 wt%, about 5.31 wt%, about 5.32 wt%, about 5.33 wt%, about 5.34 wt%, about 5.35 wt%, about 5.36 wt%, about 5.37 wt%, about 5.38 wt%, about 5.39 wt%, about 4.4 wt%, about 4.41 wt%, about 4.42 wt%, about 4.43 wt%, about 4.44 wt%, about 4.45 wt%, about 4.46 wt%, about 4.47 wt%, about 4.48 wt%, about 4.49 wt%, about 5.4 wt%, about 5.5 wt%, about 5.6 wt%, about 5.7 wt%, about 5.8 wt%, about 5.9 wt%, about 6.0 wt%, about 6.1 wt%, about 6.2 wt%, about 6.3 wt%, about 6.4 wt%, about 6.5 wt%, about 6.6 wt%, about 6.7 wt%, about 6.8 wt%, about 6.9 wt%, about 7.0 wt%, about 7.1 wt%, about 7.2 wt%, about 7.3 wt%, about 7.4 wt%, about 7.5 wt%, about 7.6 wt%, about 7.7 wt%, about 7.8 wt%, about 7.9 wt%, about 8.0 wt %, of the total weight of the composition.

Examples of disintegrants include starch, modified starch, croscarmellose sodium, crospovidone, sodium starch glycolate, and mixtures thereof. In some embodiments, the disintegrant is sodium starch glycolate.

Glidants

5 In some embodiments, the pharmaceutically acceptable excipients include a glidant, and the
glidant represents from about 0.1 wt% to about 5.0 wt%, for example from about 0.2 wt%
to about 5.0 wt%, for example from about 0.3 wt% to about 5.0 wt%, for example from
about 0.4 wt% to about 5.0 wt%, for example from about 0.5 wt% to about 5.0 wt%, for
example from about 0.6 wt% to about 5.0 wt%, for example from about 0.7 wt% to about
10 5.0 wt%, for example from about 0.8 wt% to about 5.0 wt%, for example from about 0.9
wt% to about 5.0 wt%, for example from about 1.0 wt% to about 5.0 wt%, for example
from about 1.5 wt% to about 5.0 wt%, for example from about 2.0 wt% to about 5.0 wt%,
for example from about 2.5 wt% to about 5.0 wt%, for example from about 3.0 wt% to
about 5.0 wt%, for example from about 3.5 wt% to about 5.0 wt%, for example from about
15 4.0 wt% to about 5.0 wt%, for example from about 4.5 wt% to about 5.0 wt%, for example
from about 0.1 wt% to about 4.5 wt%, for example from about 0.2 wt% to about 4.5 wt%,
for example from about 0.3 wt% to about 4.5 wt%, for example from about 0.4 wt% to
about 4.5 wt%, for example from about 0.5 wt% to about 4.5 wt%, for example from about
0.6 wt% to about 4.5 wt%, for example from about 0.7 wt% to about 4.5 wt%, for example
20 from about 0.8 wt% to about 4.5 wt%, for example from about 0.9 wt% to about 4.5 wt%,
for example from about 1.0 wt% to about 4.5 wt%, for example from about 1.5 wt% to
about 4.5 wt%, for example from about 2.0 wt% to about 4.5 wt%, for example from about
2.5 wt% to about 4.5 wt%, for example from about 3.0 wt% to about 4.5 wt%, for example
from about 3.5 wt% to about 4.5 wt%, for example from about 4.0 wt% to about 4.5 wt%,
25 for example from about 0.1 wt% to about 4.0 wt%, for example from about 0.2 wt% to
about 4.0 wt%, for example from about 0.3 wt% to about 4.0 wt%, for example from about
0.4 wt% to about 4.0 wt%, for example from about 0.5 wt% to about 4.0 wt%, for example
from about 0.6 wt% to about 4.0 wt%, for example from about 0.7 wt% to about 4.0 wt%,
for example from about 0.8 wt% to about 4.0 wt%, for example from about 0.9 wt% to
30 about 4.0 wt%, for example from about 1.0 wt% to about 4.0 wt%, for example from about
1.5 wt% to about 4.0 wt%, for example from about 2.0 wt% to about 4.0 wt%, for example
from about 2.5 wt% to about 4.0 wt%, for example from about 3.0 wt% to about 4.0 wt%,
for example from about 3.5 wt% to about 4.0 wt%, for example from about 0.1 wt% to
about 3.5 wt%, for example from about 0.2 wt% to about 3.5 wt%, for example from about
35 0.3 wt% to about 3.5 wt%, for example from about 0.4 wt% to about 3.5 wt%, for example

[illegible]

from about 0.6 wt% to about 1.0 wt%, for example from about 0.7 wt% to about 1.0 wt%, for example from about 0.8 wt% to about 1.0 wt%, for example from about 0.9 wt% to about 1.0 wt%, for example from about 0.1 wt% to about 0.5 wt%, for example from about 0.2 wt% to about 0.5 wt%, for example from about 0.3 wt% to about 0.5 wt%, for example from about 0.4 wt% to about 0.5 wt%, of the total weight of the composition. In some embodiments, the glidant represents about 0.1 wt%, about 0.11 wt%, about 0.12 wt%, about 0.13 wt%, about 0.14 wt%, about 0.15 wt%, about 0.16 wt%, about 0.17 wt%, about 0.18 wt%, about 0.19 wt%, about 0.2 wt%, about 0.21 wt%, about 0.22 wt%, about 0.23 wt%, about 0.24 wt%, about 0.25 wt%, about 0.26 wt%, about 0.27 wt%, about 0.28 wt%, about 0.29 wt%, about 0.3 wt%, about 0.31 wt%, about 0.32 wt%, about 0.33 wt%, about 0.34 wt%, about 0.35 wt%, about 0.36 wt%, about 0.37 wt%, about 0.38 wt%, about 0.39 wt%, about 0.4 wt%, about 0.41 wt%, about 0.42 wt%, about 0.43 wt%, about 0.44 wt%, about 0.45 wt%, about 0.46 wt%, about 0.47 wt%, about 0.48 wt%, about 0.49 wt%, about 0.5 wt%, about 0.51 wt%, about 0.52 wt%, about 0.53 wt%, about 0.54 wt%, about 0.55 wt%, about 0.56 wt%, about 0.57 wt%, about 0.58 wt%, about 0.59 wt%, about 0.6 wt%, about 0.61 wt%, about 0.62 wt%, about 0.63 wt%, about 0.64 wt%, about 0.65 wt%, about 0.66 wt%, about 0.67 wt%, about 0.68 wt%, about 0.69 wt%, about 0.7 wt%, about 0.8 wt%, about 0.9 wt%, about 1.0 wt%, about 1.1 wt%, about 1.2 wt%, about 1.3 wt%, about 1.4 wt%, about 1.5 wt%, about 1.6 wt%, about 1.7 wt%, about 1.8 wt%, about 1.9 wt%, about 2.0 wt%, about 2.1 wt%, about 2.2 wt%, about 2.3 wt%, about 2.4 wt%, about 2.5 wt%, about 2.6 wt%, about 2.7 wt%, about 2.8 wt%, about 2.9 wt%, about 3.0 wt%, about 3.1 wt%, about 3.2 wt%, about 3.3 wt%, about 3.4 wt%, about 3.5 wt%, about 3.6 wt%, about 3.7 wt%, about 3.8 wt%, about 3.9 wt%, about 4.0 wt%, about 4.1 wt%, about 4.2 wt%, about 4.3 wt%, about 4.4 wt%, about 4.5 wt%, about 4.6 wt%, about 4.7 wt%, about 4.8 wt%, about 4.9 wt%, about 5.0 wt% of the total weight of the composition. Examples of glidants include ascorbyl palmitate, calcium palmitate, fumed silica (colloidal silicon dioxide), and mixtures thereof. In some embodiments, the glidant is colloidal silicon dioxide.

Other excipients

The pharmaceutical composition may optionally further comprise one or more additional excipients such as a colouring agent, a flavouring agent, a preservative and/or a sweetener. Examples of sweeteners include any natural or artificial sweetener, such as sucrose, xylitol, sodium saccharin, cyclamate, aspartame, and acesulfame. Examples of flavoring agents include Magnasweet[®], bubble gum flavor, and fruit flavors, and the like. Examples of preservatives include potassium sorbate, methylparaben, propylparaben, benzoic acid and its

salts, other esters of parahydroxybenzoic acid such as butylparaben, alcohols such as ethyl or benzyl alcohol, phenolic compounds such as phenol, or quaternary compounds such as benzalkonium chloride.

In some embodiments, the pharmaceutical composition comprises, based on the total weight
5 of the composition:

55.0 wt% to 75.0 wt% of lanifibranor; and
25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients.

In some embodiments, the pharmaceutical composition comprises, based on the total weight
of the composition:

10 55.0 wt% to 75.0 wt% of lanifibranor; and
25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients, wherein among the
pharmaceutically acceptable excipients, a surfactant represents from about 1.0 wt% to about
5.0 wt% of the total weight of the composition.

In some embodiments, the pharmaceutical composition comprises, based on the total weight
15 of the composition:

55.0 wt% to 75.0 wt% of lanifibranor; and
25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients, wherein among the
pharmaceutically acceptable excipients, a surfactant represents from about 1.0 wt% to about
3.0 wt% of the total weight of the composition.

20 In some embodiments, the pharmaceutical composition comprises, based on the total weight
of the composition:

55.0 wt% to 75.0 wt% of lanifibranor;
10.0 wt% to 35.0 wt% of filler, advantageously 15.0 wt% to 35.0 wt% of filler;
advantageously 20.0 wt% to 35.0 wt% of filler;
25 1.0 wt% to 5.0 wt% of surfactant, advantageously 1.0 wt% to 3.0 wt% of surfactant;
1.0 wt% to 10.0 wt% of binder, advantageously 2.0 wt% to 8.0 wt% of binder,
advantageously 3.0 wt% to 6.0 wt% of binder;
0.5 wt% to 5.0 wt% of lubricant, advantageously 0.5 wt% to 3.0 wt% of lubricant;
1.0 wt% to 8.0 wt% of disintegrant, advantageously 2.0 wt% to 6.0 wt% of disintegrant;
30 0.1 wt% to 5.0 wt% of glidant, advantageously 0.1 wt% to 2.0 wt% of glidant, and
optionally, one or more additional excipients as defined above,
the sum of all the above-mentioned ingredients being 100 wt%.

In some embodiments, the pharmaceutical composition consists essentially of, based on the
total weight of the composition:

35 55.0 wt% to 75.0 wt% of lanifibranor; and

25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients.

In some embodiments, the pharmaceutical composition consists essentially of, based on the total weight of the composition:

55.0 wt% to 75.0 wt% of lanifibranor; and

- 5 25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients, wherein among the pharmaceutically acceptable excipients, a surfactant represents from about 1.0 wt% to about 5.0 wt% of the total weight of the composition.

In some embodiments, the pharmaceutical composition consists essentially of, based on the total weight of the composition:

- 10 55.0 wt% to 75.0 wt% of lanifibranor; and

25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients, wherein among the pharmaceutically acceptable excipients, a surfactant represents from about 1.0 wt% to about 3.0 wt% of the total weight of the composition.

In some embodiments, the pharmaceutical composition consists essentially of, based on the total weight of the composition:

- 15 55.0 wt% to 75.0 wt% of lanifibranor;

10.0 wt% to 35.0 wt% of filler, advantageously 15.0 wt% to 35.0 wt% of filler; advantageously 20.0 wt% to 35.0 wt% of filler;

1.0 wt% to 5.0 wt% of surfactant, advantageously 1.0 wt% to 3.0 wt% of surfactant;

- 20 1.0 wt% to 10.0 wt% of binder, advantageously 2.0 wt% to 8.0 wt% of binder, advantageously 3.0 wt% to 6.0 wt% of binder;

0.5 wt% to 5.0 wt% of lubricant, advantageously 0.5 wt% to 3.0 wt% of lubricant;

1.0 wt% to 8.0 wt% of disintegrant, advantageously 2.0 wt% to 6.0 wt% of disintegrant;

0.1 wt% to 5.0 wt% of glidant, advantageously 0.1 wt% to 2.0 wt% of glidant, and

- 25 optionally, one or more additional excipients as defined above.

In some embodiments, the pharmaceutical composition consists of, based on the total weight of the composition:

55.0 wt% to 75.0 wt% of lanifibranor; and

25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients.

- 30 In some embodiments, the pharmaceutical composition consists of, based on the total weight of the composition:

55.0 wt% to 75.0 wt% of lanifibranor; and

25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients, wherein among the pharmaceutically acceptable excipients, a surfactant represents from about 1.0 wt% to about

- 35 5.0 wt% of the total weight of the composition.

In some embodiments, the pharmaceutical composition consists of, based on the total weight of the composition:

55.0 wt% to 75.0 wt% of lanifibranor; and

- 25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients, wherein among the
5 pharmaceutically acceptable excipients, a surfactant represents from about 1.0 wt% to about 3.0 wt% of the total weight of the composition.

In some embodiments, the pharmaceutical composition consists of, based on the total weight of the composition:

55.0 wt% to 75.0 wt% of lanifibranor;

- 10 10.0 wt% to 35.0 wt% of filler, advantageously 15.0 wt% to 35.0 wt% of filler; advantageously 20.0 wt% to 35.0 wt% of filler;

1.0 wt% to 5.0 wt% of surfactant, advantageously 1.0 wt% to 3.0 wt% of surfactant;

1.0 wt% to 10.0 wt% of binder, advantageously 2.0 wt% to 8.0 wt% of binder, advantageously 3.0 wt% to 6.0 wt% of binder;

- 15 0.5 wt% to 5.0 wt% of lubricant, advantageously 0.5 wt% to 3.0 wt% of lubricant; 1.0 wt% to 8.0 wt% of disintegrant, advantageously 2.0 wt% to 6.0 wt% of disintegrant; 0.1 wt% to 5.0 wt% of glidant, advantageously 0.1 wt% to 2.0 wt% of glidant and optionally, one or more additional excipients as defined above.

- In some embodiments, the pharmaceutical composition is a solid dosage form. Exemplary
20 solid dosage forms include tablets, capsules, stick-packs, sachets, lozenges, powders, pills, or granules. Preferred solid dosage forms include tablets, capsules and stick-packs, tablets being especially preferred.

- In some embodiments, the pharmaceutical composition comprises from 200 mg to 1,200 mg of lanifibranor. Exemplary pharmaceutical compositions comprise 200 mg, 400 mg, 600 mg,
25 800 mg, 1,000 mg or 1,200 mg of lanifibranor.

In any of the embodiments described above, lanifibranor can be present in the pharmaceutical composition as a crystalline form.

Dissolution profile

- When the pharmaceutical compositions of the invention are in the form of solid dosage
30 forms, said forms have a fast dissolution profile. Specifically, the solid pharmaceutical compositions of the invention have a dissolution profile in which within 15 minutes at least 30% and at most 60% of the composition is dissolved; and within 45 minutes at least 80%, advantageously at least 85%, of the composition is dissolved.

- Dissolution is preferably measured in a medium which is discriminating. Such a dissolution
35 medium will produce two very different dissolution curves for two products having very

different dissolution profiles in gastric juices; *i.e.*, the dissolution medium is predictive of *in vivo* dissolution of a composition. An exemplary dissolution medium is an aqueous medium containing from about 0.7% to about 1.7% of tetradecyltrimethyl-ammonium bromide (cetrimide). Specifically, the dissolution was measured with a USP test-apparatus 1 (basket
5 10 mesh) at 100 rpm, in 1000 mL of a sodium phosphate buffer pH 6.8 thermostated at $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$ and comprising from about 0.7% to about 1.7% of cetrimide. A person skilled in the art will be able to determine the appropriate cetrimide concentration by applying the Sink condition (*i.e.*, the ability of the dissolution medium to dissolve at least 3 times the amount of drug that is present in a dosage form).

10 In some embodiments, the pharmaceutical compositions of the invention have the following dissolution profile:

- from 30% to 60% released within 15 minutes after oral ingestion,
- at least 80%, advantageously at least 85% released within 45 minutes after oral ingestion,

15 as determined by USP test-apparatus 1 (basket 10 mesh) at 100 rpm, in 1000 mL of a sodium phosphate buffer pH 6.8 thermostated at $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$ and comprising from about 0.7% to about 1.7% of cetrimide.

Due to their fast dissolution profiles, the pharmaceutical compositions of the invention are stable immediate release pharmaceutical compositions. The term "immediate release" as
20 used herein, refers to any type of release of the active ingredient (lanifibranor) from the pharmaceutical composition of the present invention resulting in *in-vitro* release over a short period of time, *i.e.*, (less than one hour). Preferably, more than 85% of lanifibranor is released within 45 minutes after oral ingestion.

Advantageously, the pharmaceutical composition of the present invention releases from
25 about 30 to 60% of lanifibranor within 15 minutes after oral ingestion.

Advantageously, the pharmaceutical composition of the present invention releases at least 80%, preferably at least 85% of lanifibranor within 45 minutes after oral ingestion.

In some embodiments, the immediate release pharmaceutical compositions comprise, consist essentially of, or consist of, based on the total weight of the composition, from 55.0 wt% to
30 75.0 wt% of lanifibranor and from 25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients, wherein the immediate release pharmaceutical compositions have a lanifibranor dissolution profile with the following constraint:

- from 30% to 60% released within 15 minutes after oral ingestion,
- at least 80%, advantageously at least 85% released within 45 minutes after oral
35 ingestion.

In some embodiments, the immediate release pharmaceutical compositions comprise, consist essentially of, or consist of, based on the total weight of the composition, from 55.0 wt% to 75.0 wt% of lanifibranor and from 25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients; wherein lanifibranor has a particle size distribution such that $D_{50} \leq 30 \mu\text{m}$ and
5 $D_{90} \leq 50 \mu\text{m}$, preferably $D_{50} \leq 10 \mu\text{m}$ and $D_{90} \leq 30 \mu\text{m}$.

In some embodiments, the immediate release pharmaceutical compositions comprise, consist essentially of, or consist of, based on the total weight of the composition, from 55.0 wt% to 75.0 wt% of lanifibranor and from 25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients, wherein among the pharmaceutically acceptable excipients, a surfactant
10 represents from about 1.0 wt% to about 5.0 wt%, advantageously from about 1.0 wt% to about 3.0 wt% of the total weight of the immediate release pharmaceutical composition.

In some embodiments, the immediate release pharmaceutical compositions comprise, consist essentially of, or consist of, based on the total weight of the composition:

- from 55.0 wt% to 75.0 wt% of lanifibranor,
- 15 - from 10.0 wt% to 35.0 wt% of filler; advantageously 15.0 wt% to 35.0 wt% of filler, advantageously 20.0 wt% to 35.0 wt% of filler;
- from 1.0 wt% to 5.0 wt% of surfactant, advantageously 1.0 wt% to 3.0 wt% of surfactant;
- from 1.0 wt% to 10.0 wt% of binder, advantageously 2.0 wt% to 8.0 wt% of binder,
20 advantageously 3.0 wt% to 6.0 wt% of binder;
- from 0.5 wt% to 5.0 wt% of lubricant, advantageously 0.5 wt% to 3.0 wt% of lubricant;
- from 1.0 wt% to 8.0 wt% of disintegrant, advantageously 2.0 wt% to 6.0 wt% of disintegrant;
- 25 - from 0.1 wt% to 5.0 wt% of glidant, advantageously 0.1 wt% to 2.0 wt% of glidant; and
- optionally, one or more additional excipients as defined above.

In some embodiments, the immediate release pharmaceutical compositions comprise, consist essentially of, or consist of, based on the total weight of the composition, from 55.0 wt% to
30 75.0 wt% of lanifibranor and from 25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients, wherein:

- the immediate release pharmaceutical compositions have a lanifibranor dissolution profile with the following constraint:
 - o from 30% to 60% released within 15 minutes after oral ingestion,

- at least 80%, advantageously at least 85% released within 45 minutes after oral ingestion, and
 - lanifibranor has a particle size distribution such that $D_{50} \leq 30 \mu\text{m}$ and $D_{90} \leq 50 \mu\text{m}$, preferably $D_{50} \leq 10 \mu\text{m}$ and $D_{90} \leq 30 \mu\text{m}$.
- 5 In some embodiments, the immediate release pharmaceutical compositions comprise, consist essentially of, or consist of, based on the total weight of the composition, from 55.0 wt% to 75.0 wt% of lanifibranor and from 25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients, wherein:
- among the pharmaceutically acceptable excipients, a surfactant represents from
10 about 1.0 wt% to 5.0 wt%, advantageously from about 1.0 wt% to 3.0 wt% of the total weight of the immediate release pharmaceutical composition, and
 - the immediate release pharmaceutical compositions have a lanifibranor dissolution profile with the following constraint:
 - from about 30% to 60% released within 15 minutes after oral ingestion,
 - 15 ○ at least 80%, advantageously at least 85% released within 45 minutes after oral ingestion.

- In some embodiments, the immediate release pharmaceutical compositions comprise, consist essentially of, or consist of, based on the total weight of the composition, from 55.0 wt% to 75.0 wt% of lanifibranor and from 25.0 wt% to 45.0 wt% of pharmaceutically acceptable
- 20 excipients, wherein:
- among the pharmaceutically acceptable excipients, a surfactant represents from about 1.0 wt% to 5.0 wt%, advantageously from about 1.0 wt% to 3.0 wt% of the total weight of the immediate release pharmaceutical composition, and
 - the immediate release pharmaceutical compositions have a lanifibranor dissolution
25 profile with the following constraint:
 - from 30% to 60% released within 15 minutes after oral ingestion,
 - at least 80%, advantageously at least 85% released within 45 minutes after oral ingestion, and
 - lanifibranor has a particle size distribution such that $D_{50} \leq 30 \mu\text{m}$ and $D_{90} \leq 50 \mu\text{m}$,
30 preferably $D_{50} \leq 10 \mu\text{m}$ and $D_{90} \leq 30 \mu\text{m}$.

- In some embodiments, the immediate release pharmaceutical compositions comprise, consist essentially of, or consist of, based on the total weight of the composition:
- from 55.0 wt% to 75.0 wt% of lanifibranor,
 - from 10.0 wt% to 35.0 wt% of filler; advantageously 15.0 wt% to 35.0 wt% of filler,
 - 35 advantageously 20.0 wt% to 35.0 wt% of filler;

- from 1.0 wt% to 5.0 wt% of surfactant, advantageously 1.0 wt% to 3.0 wt% of surfactant;
- from 1.0 wt% to 10.0 wt% of binder, advantageously 2.0 wt% to 8.0 wt% of binder, advantageously 3.0 wt% to 6.0 wt% of binder;
- from 0.5 wt% to 5.0 wt% of lubricant, advantageously 0.5 wt% to 3.0 wt% of lubricant;
- 5 - from 1.0 wt% to 8.0 wt% of disintegrant, advantageously 2.0 wt% to 6.0 wt% of disintegrant;
- from 0.1 wt% to 5.0 wt% of glidant, advantageously 0.1 wt% to 2.0 wt% of glidant; and optionally, one or more additional excipients as defined above, wherein:
the immediate release pharmaceutical compositions have a lanifibranor dissolution profile
- 10 with the following constraint:
 - 30% to 60% released within 15 minutes after oral ingestion,
 - at least 80%, advantageously at least 85% released within 45 minutes after oral ingestion.

In some embodiments, the immediate release pharmaceutical compositions comprise, consist
15 essentially of, or consist of, based on the total weight of the composition:

- from 55.0 wt% to 75.0 wt% of lanifibranor,
- from 10.0 wt% to 35.0 wt% of filler; advantageously 15.0 wt% to 35.0 wt% of filler, advantageously 20.0 wt% to 35.0 wt% of filler;
- from 1.0 wt% to 5.0 wt% of surfactant, advantageously 1.0 wt% to 3.0 wt% of surfactant;
- 20 - from 1.0 wt% to 10.0 wt% of binder, advantageously 2.0 wt% to 8.0 wt% of binder, advantageously 3.0 wt% to 6.0 wt% of binder;
- from 0.5 wt% to 5.0 wt% of lubricant, advantageously 0.5 wt% to 3.0 wt% of lubricant;
- from 1.0 wt% to 8.0 wt% of disintegrant, advantageously 2.0 wt% to 6.0 wt% of disintegrant;
- 25 - from 0.1 wt% to 5.0 wt% of glidant, advantageously 0.1 wt% to 2.0 wt% of glidant; and optionally, one or more additional excipients as defined above, wherein:
 - the immediate release pharmaceutical compositions have a lanifibranor dissolution profile with the following constraint:
 - 30 ○ from 30% to 60% released within 15 minutes after oral ingestion,
 - at least 80%, advantageously at least 85% released within 45 minutes after oral ingestion, and
 - lanifibranor has a particle size distribution such that $D_{50} \leq 30 \mu\text{m}$ and $D_{90} \leq 50 \mu\text{m}$, preferably $D_{50} \leq 10 \mu\text{m}$ and $D_{90} \leq 30 \mu\text{m}$.

In some embodiments, the immediate release pharmaceutical compositions as described
35 above are in a solid dosage form. Advantageously, solid dosage forms include tablets,

capsules, stick-packs, sachets, lozenges, powders, pills, or granules. Preferred solid dosage forms include tablets, capsules and stick-packs, tablets being especially preferred.

In some embodiments, the immediate release pharmaceutical compositions as described above comprise from 200 mg to 1,200 mg of lanifibranor. Advantageously, pharmaceutical
5 compositions comprise 200 mg, 400 mg, 600 mg, 800 mg, 1,000 mg or 1,200 mg of lanifibranor.

In some embodiments, the immediate release pharmaceutical compositions as described above are for oral administration.

In another aspect of the invention, the present invention discloses an immediate release
10 tablet comprising, consisting essentially of, or consisting of, based on the total weight of the tablet, from 55.0 wt% to 75.0 wt% of lanifibranor and from 25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients.

In some embodiments, the immediate release tablet comprises, consists essentially of, or consists of, based on the total weight of the tablet, from 55.0 wt% to 75.0 wt% of
15 lanifibranor and from 25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients, wherein the immediate release tablet has a lanifibranor dissolution profile with the following constraint:

- from 30% to 60% released within 15 minutes after oral ingestion,
- at least 80%, advantageously at least 85% released within 45 minutes after oral
20 ingestion.

In some embodiments, the immediate release tablet comprises, consists essentially of, or consists of, based on the total weight of the tablet, from 55.0 wt% to 75.0 wt% of lanifibranor and from 25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients, wherein lanifibranor has a particle size distribution such that $D_{50} \leq 30 \mu\text{m}$ and $D_{90} \leq 50$
25 μm , preferably $D_{50} \leq 10 \mu\text{m}$ and $D_{90} \leq 30 \mu\text{m}$.

In some embodiments, the immediate release tablet comprises, consists essentially of, or consists of, based on the total weight of the tablet, from 55.0 wt% to 75.0 wt% of lanifibranor and from 25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients, wherein:

- 30 - the immediate release tablet has a lanifibranor dissolution profile with the following constraint:
 - o from 30% to 60% released within 15 minutes after oral ingestion,
 - o at least 80%, advantageously at least 85% released within 45 minutes after oral ingestion, and

- lanifibranor has a particle size distribution such that $D50 \leq 30 \mu\text{m}$ and $D90 \leq 50 \mu\text{m}$, preferably $D50 \leq 10 \mu\text{m}$ and $D90 \leq 30 \mu\text{m}$.

In some embodiments, the immediate release tablet comprises, consists essentially of, or consists of, based on the total weight of the tablet, from 55.0 wt% to 75.0 wt% of lanifibranor and from 25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients, wherein among the pharmaceutically acceptable excipients, a surfactant represents from 1.0 wt% to 5.0 wt%, advantageously from 1.0 wt% to 3.0 wt% of the total weight of the immediate release tablet.

In some embodiments, the immediate release tablet comprises, consists essentially of, or consists of, based on the total weight of the tablet:

- from 55.0 wt% to 75.0 wt% of lanifibranor,
- from 10.0 wt% to 35.0 wt% of filler; advantageously 15.0 wt% to 35.0 wt% of filler, advantageously 20.0 wt% to 35.0 wt% of filler;
- from 1.0 wt% to 5.0 wt% of surfactant, advantageously 1.0 wt% to 3.0 wt% of surfactant;
- from 1.0 wt% to 10.0 wt% of binder, advantageously 2.0 wt% to 8.0 wt% of binder, advantageously 3.0 wt% to 6.0 wt% of binder;
- from 0.5 wt% to 5.0 wt% of lubricant, advantageously 0.5 wt% to 3.0 wt% of lubricant;
- from 1.0 wt% to 8.0 wt% of disintegrant, advantageously 2.0 wt% to 6.0 wt% of disintegrant;
- from 0.1 wt% to 5.0 wt% of glidant, advantageously 0.1 wt% to 2.0 wt% of glidant; and optionally, one or more additional excipients as defined above.

In some embodiments, the immediate release tablet comprises, consists essentially of, or consists of, based on the total weight of the tablet, from 55.0 wt% to 75.0 wt% of lanifibranor and from 25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients, wherein:

- among the pharmaceutically acceptable excipients, a surfactant represents from 1.0 wt% to 5.0 wt%, advantageously from 1.0 wt% to 3.0 wt% of the total weight of the immediate release tablet, and
- the immediate release tablet has a lanifibranor dissolution profile with the following constraint:
 - o from 30% to 60% released within 15 minutes after oral ingestion,
 - o at least 80%, advantageously at least 85% released within 45 minutes after oral ingestion.

In some embodiments, the immediate release tablet comprises, consists essentially of, or consists of, based on the total weight of the tablet, from 55.0 wt% to 75.0 wt% of

lanifibranor and from 25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients, wherein:

- among the pharmaceutically acceptable excipients, a surfactant represents from 1.0 wt% to 5.0 wt%, advantageously from 1.0 wt% to 3.0 wt% of the total weight of the immediate release tablet, and
- the immediate release tablet has a lanifibranor dissolution profile with the following constraint:
 - o from 30% to 60% released within 15 minutes after oral ingestion,
 - o at least 80%, advantageously at least 85% released within 45 minutes after oral ingestion, and
- lanifibranor has a particle size distribution such that $D_{50} \leq 30 \mu\text{m}$ and $D_{90} \leq 50 \mu\text{m}$, preferably $D_{50} \leq 10 \mu\text{m}$ and $D_{90} \leq 30 \mu\text{m}$.

In some embodiments, the immediate release tablet comprises, consists essentially of, or consists of, based on the total weight of the tablet:

- from 55.0 wt% to 75.0 wt% of lanifibranor,
 - from 10.0 wt% to 35.0 wt% of filler; advantageously 15.0 wt% to 35.0 wt% of filler, advantageously 20.0 wt% to 35.0 wt% of filler;
 - from 1.0 wt% to 5.0 wt% of surfactant, advantageously 1.0 wt% to 3.0 wt% of surfactant;
 - from 1.0 wt% to 10.0 wt% of binder, advantageously 2.0 wt% to 8.0 wt% of binder, advantageously 3.0 wt% to 6.0 wt% of binder;
 - from 0.5 wt% to 5.0 wt% of lubricant, advantageously 0.5 wt% to 3.0 wt% of lubricant;
 - from 1.0 wt% to 8.0 wt% of disintegrant, advantageously 2.0 wt% to 6.0 wt% of disintegrant;
 - from 0.1 wt% to 5.0 wt% of glidant, advantageously 0.1 wt% to 2.0 wt% of glidant; and
- optionally, one or more additional excipients as defined above, wherein:
- the immediate release tablet has a lanifibranor dissolution profile with the following constraint:
- from 30% to 60% released within 15 minutes after oral ingestion,
 - at least 80%, advantageously at least 85% released within 45 minutes after oral ingestion.

In some embodiments, the immediate release tablets comprise, consist essentially of or contain, based on the total weight of the tablet:

- from about 55.0 wt% to 75.0 wt% of lanifibranor,
- from about 10.0 wt% to 35.0 wt% of filler; advantageously 15.0 wt% to 35.0 wt% of filler, advantageously 20.0 wt% to 35.0 wt% of filler;

- from about 1.0 wt% to 5.0 wt% of surfactant, advantageously 1.0 wt% to 3.0 wt% of surfactant;
- from about 1.0 wt% to 10.0 wt% of binder, advantageously 2.0 wt% to 8.0 wt% of binder, advantageously 3.0 wt% to 6.0 wt% of binder;
- 5 - from about 0.5 wt% to 5.0 wt% of lubricant, advantageously 0.5 wt% to 3.0 wt% of lubricant;
- from about 1.0 wt% to 8.0 wt% of disintegrant, advantageously 2.0 wt% to 6.0 wt% of disintegrant;
- from about 0.1 wt% to 5.0 wt% of glidant, advantageously 0.1 wt% to 2.0 wt% of glidant; and optionally, one or more additional excipients as defined above,

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wherein:

- the immediate release tablets have a lanifibranor dissolution profile with the following constraint:
 - o from about 30% to 60% released within 15 minutes after oral ingestion,
 - 15 o at least 80%, advantageously at least 85% released within 45 minutes after oral ingestion, and
- lanifibranor has a particle size distribution such that $D_{50} \leq 30 \mu\text{m}$ and $D_{90} \leq 50 \mu\text{m}$, preferably $D_{50} \leq 10 \mu\text{m}$ and $D_{90} \leq 30 \mu\text{m}$.

In some embodiments, the immediate release tablets as described above comprise from 200 mg to 1,200 mg of lanifibranor. Advantageously, immediate release tablets comprise 200 mg, 400 mg, 600 mg, 800 mg, 1,000 mg or 1,200 mg of lanifibranor.

In some embodiments, the immediate release tablets as described above are for oral administration.

Methods of using the lanifibranor compositions

- 25 The pharmaceutical compositions of the invention, the immediate release pharmaceutical compositions and the immediate release tablets as described above, are useful for treating fibrotic conditions such as non-alcoholic fatty liver disease (NAFLD), including non-alcoholic fatty liver and non-alcoholic steatohepatitis (NASH). The pharmaceutical compositions of the invention, the immediate release pharmaceutical compositions and the immediate release tablets as described above are also useful for treating a cirrhotic subject at risk of progressing from compensated stage to decompensated stage. The pharmaceutical compositions, the immediate release pharmaceutical compositions and the immediate release tablets of the invention as described above are also useful for treating a disease selected among cirrhosis, liver fibrosis, liver steatosis, fatty liver disease, acute decompensation, acute on chronic liver failure (ACLF), acute liver failure (ALF), decompensated cirrhosis,

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compensated cirrhosis, metabolic-associated fatty liver disease (MAFLD), metabolic-associated steatohepatitis (MASH), diabetes, and liver cirrhosis.

In one aspect, the present disclosure therefore relates to a pharmaceutical composition, an immediate release pharmaceutical composition, or an immediate release tablet as defined above for use in a method of treating NAFLD, including non-alcoholic fatty liver and non-alcoholic steatohepatitis (NASH). The present disclosure also relates to a pharmaceutical composition, an immediate release pharmaceutical composition or an immediate release tablet as defined above for use in a method of treating a cirrhotic subject at risk of progressing from compensated stage to decompensated stage. The present disclosure also relates to a pharmaceutical composition, an immediate release pharmaceutical composition or an immediate release tablet as defined above for use in a method of treating a disease selected among cirrhosis, liver fibrosis, liver steatosis, fatty liver disease, acute decompensation, acute on chronic liver failure (ACLF), acute liver failure (ALF), decompensated cirrhosis, compensated cirrhosis, metabolic-associated fatty liver disease (MAFLD), metabolic-associated steatohepatitis (MASH), diabetes, and liver cirrhosis.

In one aspect, the present disclosure relates to a method of treating non-alcoholic fatty liver disease (NAFLD), which comprises administering to a subject in need thereof a pharmaceutical composition, an immediate release pharmaceutical composition or an immediate release tablet as defined above. The present disclosure also relates to a method of treating a cirrhotic subject at risk of progressing from compensated stage to decompensated stage, which comprises administering to the subject a pharmaceutical composition, an immediate release pharmaceutical composition or an immediate release tablet as defined above.

The present disclosure also relates to a method of treating a disease selected among cirrhosis, liver fibrosis, liver steatosis, fatty liver disease, acute decompensation, acute on chronic liver failure (ACLF), acute liver failure (ALF), decompensated cirrhosis, compensated cirrhosis, metabolic-associated fatty liver disease (MAFLD), metabolic-associated steatohepatitis (MASH), diabetes, or liver cirrhosis, which comprises administering to a subject in need thereof a pharmaceutical composition, an immediate release pharmaceutical composition or an immediate release tablet as defined above.

As used herein, the term "subject" is used to mean an animal, preferably a mammal, including a human or non-human. The subject is for example a human or an animal liable to have a fibrotic condition or suffering from such a disease. The subject is advantageously a human being. The patient may be a child (human patient aged 18 years or under) or an adult (human patient over 18). In some embodiments, the subject is a non-human animal

including, but not limited to, dog, cat, guinea pig, rabbit, rat, mouse, horse, cattle, bear, cow, ape, monkey, orangutan, and chimpanzee, and so on. The terms patient and subject may be used interchangeably.

In some embodiments, a daily dosage of from 400 mg to 1,200 mg of lanifibranor is administered to the patient, such as for example 400 mg, 600 mg, 800 mg, 1,000 mg or 1,200 mg.

Method of making lanifibranor compositions

It is to be appreciated that while reference is made below to a process suitable for preparing tablets, other solid dosage forms can be prepared by appropriate techniques known to a person skilled in the art. Exemplary pharmaceutical compositions comprising a binder, a disintegrant, a filler, a glidant, a lubricant and a surfactant as excipients can be prepared by a process comprising:

- a) providing lanifibranor having a particle size distribution such that $D_{50} \leq 30 \mu\text{m}$ and $D_{90} \leq 50 \mu\text{m}$;
- b) providing a granulation solution consisting of an aqueous solution of a surfactant;
- c) preparing a blend of lanifibranor, a filler, a disintegrant and a binder;
- d) spraying the granulation solution (obtained in step b)) onto the resulting blend to obtain granulates (wet-granulation);
- e) preparing a blend of a filler and a glidant, then adding another portion of filler and a disintegrant to the blend;
- f) mixing the granulates obtained in step d) with the blend obtained in step e) and with a lubricant, then mixing the resulting blend;
- g) processing the blend obtained in step f) into the desired dosage form.

In some embodiments, the aqueous solution of a surfactant used in step c) comprises from about 80.0 wt% to about 90.0 wt% of (purified) water. In some embodiments, the surfactant makes up from about 10.0 wt% to about 20.0 wt% of the aqueous solution, and is a mixture of sodium lauryl sulfate (SLS) and dioctyl sodium sulfosuccinate (DOSS) in a weight ratio (SLS/DOSS) from about 2.5 to about 5.0.

In some embodiments, the binder is added last during the blending process of step c).

The wet-granulation of step d) is carried out by methods known in the art, for example in a high shear mixer. In some embodiments, the granulation time is from about 10 s to about 30 min, for example from about 30 s to about 15 min.

In some embodiments, the same filler is used twice in step e). In some embodiments different fillers are used in step e). In the latter embodiments, at least one the filler used is the same as the filler used in step c).

In some embodiments, the desired dosage form is a tablet, and the above-described method can further comprise a step of film-coating the tablet.

The invention is illustrated by the non-limiting examples below.

EXAMPLES

- 5 In the following examples, lanifibranor was provided in crystalline form characterized by XRPD, DSC and TGA as described in example 5. It was micronized before processing such that its particle size distribution was characterized by a $D50 \leq 10 \mu\text{m}$ and a $D90 \leq 30 \mu\text{m}$.

XRPD

- 10 Powder X-ray diffraction analysis was conducted using a Panalytical Empyrean S3 diffractometer equipped with a Cu radiation source (Cu wavelength = $1.5406 \text{ \AA}$). Analyses were performed in transmission mode (samples were placed between Kapton® and polypropylene foils), on the angular range $2\theta = 2 - 50^\circ$, with a step size of 0.026° and a time per step of 20.4 s.

DSC

- 15 DSC analysis was conducted on a Mettler Toledo DSC3+ calorimeter. Analyses were performed on a few milligrams of sample, in $40 \mu\text{L}$ sealed aluminum pans, punctured before analysis, under nitrogen flush at 50 mL/min . A temperature range between 20°C and 300°C was scanned at a 10°C/min rate.

TGA

- 20 TGA analysis was conducted on a Mettler Toledo TGA/DSC3+ thermogravimetric analyzer. Analyses were performed on a few milligrams of sample, in $100 \mu\text{L}$ sealed aluminum pans, punctured before analysis, under nitrogen flush at 50 mL/min . A temperature range between 25°C and 300°C was scanned at a 10°C/min rate.

Example 1: wettability tests

- 25 Blends and granulation solutions (GS) were prepared by combining the materials listed in Table 1.

Table 1

Material	Amount (wt%)			
	Blend 1	Blend 2	GS1	GS2
Lanifibranor	100.0	75.0	-	-
Lactose monohydrate	0.0	25.0	-	-
Distilled water	-	-	100.0	90.0
Anionic surfactant	-	-	0.0	10.0

A sample of each blend was spread on a flat surface by pressing lightly to make powder bed almost flat. Using a dropper, a drop of either GS1 or GS2 was gently placed onto the powder bed. If the drop stays on the powder, then the wettability of the blend is poor; if the drop spreads over the surface and penetrates the powder, then the wettability is good. The results are presented in Table 2.

Table 2

Tested combination	Observations
Blend 1 + GS 1	The drop is round and does not penetrate powder. Poor wettability
Blend 1 + GS2	The drop penetrates powder in a few seconds. Good wettability
Blend 2 + GS1	The drop is round and does not penetrate powder. Poor wettability
Blend 2 + GS2	The drop penetrates powder in a few seconds. Good wettability

These observations confirm that lanifibranor is hydrophobic since, with water alone (GS1), wettability is poor. When the granulation solution contains a surfactant, lanifibranor gets wet, whether or not lactose is present.

Example 2: lanifibranor formulations

The purpose of this example was to prepare lanifibranor tablets by combining the materials listed in Table 3, using the general method described above, i.e. the tablets were prepared using a spray granulation step. Care was taken during the manufacture of the tablets to comply with the respective required weight percentages of lanifibranor and excipients, i.e. 55-75 wt% lanifibranor and 25-45 wt% excipients.

Table 3

Material	Amount
Lanifibranor	600-800 g/kg
Hypromellose, USP	25-50 g/kg
Sodium starch glycolate	20-50 g/kg
Lactose monohydrate	200-340 g/kg
Sodium lauryl sulfate, NF	10-30 g/kg
Docusate Sodium, USP/EP	2-10 g/kg
Colloidal silica	3-10 g/kg
Magnesium stearate	5-15 g/kg

Example 3: stability study

600 mg lanifibranor tablets were prepared using the materials listed in Table 3 and the general method described above such that the content of lanifibranor in the tablets was 57

wt%. A stability study was performed on these tablets, packaged in HDPE bottle fitted with a PP cap with a silica gel cartridge. The results are shown in Table 4.

Table 4

Storage conditions	Initial	1 mo	3 mo	6 mo	12 mo	24 mo
25 ± 2 °C / 60 ± 5% RH	x	-	-	x	x	x
30 ± 2 °C / 70 ± 5% RH		x	x	x	x	x
40 ± 2 °C / 75 ± 5% RH		x	x	x+m	-	-

mo = months

- 5
- x = no change in drug product appearance, assay, impurity profile, disintegration time, resistance to crushing, loss on drying and dissolution
m = microbial contamination (< 100 CFU/g)

10

As can be seen from the above Table, no OOT (Out-Of-Trend) / OOS (Out-Of-Specification) was observed after 6 months of storage. Specifically, no significant change was observed in the drug product appearance, assay, impurity profile, disintegration time, resistance to crushing, loss on drying and dissolution after 6-month at 25°C/60% RH, 30°C/70% RH and 40°C/75% RH, and packed in HDPE Bottle with a dessicant closure.

15

As can be seen from the above Table, no OOT (Out-Of-Trend) / OOS (Out-Of-Specification) was observed after 24 months of storage. Specifically, no significant change was observed in the drug product appearance, assay, impurity profile, disintegration time, resistance to crushing, loss on drying and dissolution after 24-months at 25°C/60% RH and 30°C/70% RH.

Example 4: dissolution profile

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The dissolution profile of 600 mg lanifibranor tablets (used for the stability study) was measured with a USP test-apparatus 1 (basket 10 mesh) at 100 rpm, in 1000 mL of a sodium phosphate buffer pH 6.8 thermostated at 37°C ± 0.5°C and comprising 1.7% of tetradecyltrimethyl-ammonium bromide. The results are shown in Table 5.

Table 5

Time (min)	5	10	15	30	45	60	90
Dissolution (%) *	7	18	31	86	96	98	100

* mean of 6 measurements

Example 5: dissolution profile

- 5 400 mg lanifibranor tablets were prepared using the materials listed in Table 3 and the general method described above such that the content of lanifibranor in the tablets was 57 wt%. The dissolution profile of these tablets was measured with a USP test-apparatus 1 (basket 10 mesh) at 100 rpm, in 1000 mL of a sodium phosphate buffer pH 6.8 thermostated at 37°C ± 0.5°C and comprising 1.7% of tetradecyltrimethyl-ammonium
- 10 bromide. The results are shown in Table 6.

Table 6

Time (min)	5	10	15	30	45	60	90
Dissolution (%) *	12	26	42	90	100	101	101

* mean of 6 measurements

Example 6: crystallography

- 15 The active pharmaceutical ingredient (API), lanifibranor, present in the 600 mg tablets of example 3, was analysed by XRPD. It was found that its characteristics are the same as those of the starting API before processing into tablets. In particular, lanifibranor as analysed from the tablets:
- has a XRPD pattern comprising the peaks shown in Table 7 (the 2θ positions may show some variability, typically as much as ±0.2°, and the relative peak intensities may show inter-
- 20 apparatus variability).

Table 7

2θ position (°)	Relative intensity	2θ position (°)	Relative intensity
9.3	4.6%	28.2	20.5%
10.5	2.5%	28.6	3.3%
11.1	21.2%	28.7	1.7%
11.4	60.4%	29.0	1.0%
12.0	40.0%	29.2	3.0%
12.6	5.7%	29.4	3.1%
13.2	5.3%	30.0	23.2%
13.4	2.8%	30.3	9.6%

14.3	24.2%	30.5	8.1%
15.0	21.4%	30.7	5.5%
16.0	100.0%	31.7	4.5%
16.4	6.5%	32.1	8.9%
18.0	55.4%	32.3	13.6%
18.3	41.4%	32.7	5.5%
18.7	91.5%	32.9	9.1%
18.9	20.0%	33.2	14.0%
19.9	39.1%	33.3	9.9%
20.2	42.3%	33.6	1.8%
20.6	36.8%	34.4	4.3%
21.2	47.4%	34.5	3.4%
22.1	12.2%	34.8	8.0%
22.2	10.4%	35.0	9.6%
22.5	7.8%	35.4	1.5%
22.8	77.1%	36.2	14.6%
23.3	3.9%	36.3	11.2%
23.5	50.9%	36.5	1.5%
23.9	8.3%	37.0	10.0%
24.0	31.2%	37.2	7.3%
24.6	91.7%	38.0	1.7%
24.8	39.5%	38.1	1.0%
25.1	3.8%	38.4	3.9%
25.2	7.8%	38.5	8.7%
25.5	7.9%	38.6	5.2%
26.1	46.6%	39.1	1.5%
26.7	64.6%	39.4	1.8%
27.3	18.8%	39.8	4.3%
27.7	2.2%		

Example 7: preparation of scaled-up batch of coated tablets

- a) A granulation solution was prepared with 1125.0 g of sodium lauryl sulphate and 300.0 g of docusate sodium in 6750.0 g of water. It was stirred until complete dissolution.
- 5 b) Separately, a mixture of lanifibranor (30000.0 g), lactose monohydrate (12150 g), sodium starch glycolate (1500.0 g), hydroxypropyl methyl cellulose (2250.0 g) was prepared by blending.
- c) The granulation solution was sprayed onto the blend obtained in step b), and the resulting granulates were dried.
- 10 d) A blend of lactose spray dried monohydrate (3650.0 g), sodium starch glycolate (700.0 g) and colloidal silicon dioxide (240 g) was then prepared.
- e) The granulates obtained in step c), the blend obtained in step d) and magnesium stearate (500.0 g) were mixed together in a final blend.
- f) The blend obtained in step e) was processed into tablets using a tablet press equipped
- 15 with a metal check.

g) Finally, the tablets obtained in step f) were coated with Opadry™.

Example 8: Effect of surfactant on granulation and tableting performances

The pharmaceutical compositions according to the present invention as described in Table 8 were prepared and tested.

Table 8

Pharmaceutical composition	A (wt%)	B (wt%)
Lanifibranor	57.1	57.1
Hypromellose, USP	4.3	4.3
Sodium starch glycolate	4.3	4.3
Lactose monohydrate	31.6	32.2
Sodium lauryl sulfate, NF	1.0	0.5
Docusate Sodium, USP/EP	0.2	0.1
Colloidal silica	0.5	0.5
Magnesium stearate	1.0	1.0

For each pharmaceutical composition of Table 8, sodium lauryl sulphate and docusate sodium were mixed with water and stirred until complete dissolution to obtain a granulation solution. A mixture of lanifibranor, lactose monohydrate, sodium starch glycolate, hydroxypropyl methyl cellulose was separately prepared by blending. The granulation step was performed by spraying the granulation solution onto the blend. This step led to the formation of granulates which were then dried. A blend of lactose monohydrate, sodium starch glycolate and colloidal silicon dioxide was then prepared. The granulates, the blend and magnesium stearate were mixed together to obtain a final blend. Tablets were prepared from the final blend using a tablet press equipped with a metal check and coated with Opadry™.

Observations made during the preparation of the tablets are reported in Table 9.

Table 9

Pharmaceutical composition	Observations during the granulation step	Observations during the tableting step
A	The granulation step is possible.	Tablets are obtained
B	The granulation step is partial with large sticking of the powder on the wall of the granulator. A non negligible amount of	Tablets cannot be obtained.

	lanifibranor remains on the wall of the granulator.	
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These observations confirm that the variation of the amount of surfactant has an impact on the granulation step and on tableting. Indeed, even if the formation of granulates is possible, it nevertheless results that a non negligible amount of lanifibranor remains on the wall of the granulator, when the total amount of surfactant is less than 1.0%. Moreover, tablets cannot be obtained with an amount of surfactant below than 1.0 wt%. Thus, the amount of surfactants plays an important role for the success of the granulation and tableting.

Aspects of the present disclosure are further illustrated by reference to the following, non-limiting embodiments.

1. A pharmaceutical composition comprising, based on the total weight of the composition:
55.0 wt% to 75.0 wt% of lanifibranor; and
25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients;
wherein lanifibranor has a particle size distribution such that $D_{50} \leq 30 \mu\text{m}$ and $D_{90} \leq 50 \mu\text{m}$, preferably $D_{50} \leq 10 \mu\text{m}$ and $D_{90} \leq 30 \mu\text{m}$.
2. The pharmaceutical composition according to paragraph 1, wherein said pharmaceutical composition releases from 30 to 60% of lanifibranor within 15 minutes after oral ingestion.
3. The pharmaceutical composition according to any one of paragraphs 1 to 2, wherein said pharmaceutical composition releases at least 80% of lanifibranor within 45 minutes after oral ingestion.
4. A pharmaceutical composition according to any preceding paragraphs, wherein the pharmaceutically acceptable excipients include two or more of a binder, a colouring agent, a disintegrant, a filler, a glidant, a lubricant, a preservative, a surfactant, and a sweetener.
5. A pharmaceutical composition according to any preceding paragraphs, wherein the pharmaceutically acceptable excipients include a filler, and the filler represents from 10.0 wt% to 35.0 wt% of the total weight of the composition.
6. A pharmaceutical composition according to paragraph 5, wherein the filler is selected from lactose monohydrate, lactose anhydrous, starch, modified starch, mannitol and mixtures thereof.

7. A pharmaceutical composition according to any preceding paragraphs, wherein the pharmaceutically acceptable excipients include a surfactant, and the surfactant represents from 1.0 wt% to 5.0 wt% of the total weight of the composition.
8. A pharmaceutical composition according to paragraph 7, wherein the surfactant is selected from non-ionic surfactants, anionic surfactants, cationic surfactants, and mixtures thereof.
9. A pharmaceutical composition according to any preceding paragraphs, wherein the pharmaceutically acceptable excipients include a binder, and the binder represents from 1.0 wt% to 10.0 wt% of the total weight of the composition.
10. A pharmaceutical composition according to paragraph 9, wherein the binder is selected from cellulose, modified cellulose, microcrystalline cellulose, polyvinylpyrrolidone and mixtures thereof.
11. A pharmaceutical composition according to any preceding paragraphs, wherein the pharmaceutically acceptable excipients include a lubricant, and the lubricant represents from 0.5 wt% to 5.0 wt% of the total weight of the composition.
12. A pharmaceutical composition according to paragraph 11, wherein the lubricant is selected from talc, stearic acid, magnesium stearate, calcium stearate, sodium sterayl fumarate, silica gel and mixtures thereof.
13. A pharmaceutical composition according to any preceding paragraphs, wherein the pharmaceutically acceptable excipients include a disintegrant, and the disintegrant represents from 1.0 wt% to 8.0 wt% of the total weight of the composition.
14. A pharmaceutical composition according to paragraph 13, wherein the disintegrant is selected from starch, modified starch, croscarmellose sodium, crospovidone, sodium starch glycolate, and mixtures thereof.
15. A pharmaceutical composition according to any preceding paragraphs, wherein the pharmaceutically acceptable excipients include a glidant, and the glidant represents from 0.1 wt% to 5.0 wt% of the total weight of the composition.
16. A pharmaceutical composition according to any preceding paragraphs, which is a solid dosage form.
17. A pharmaceutical composition according to paragraph 16, which is a tablet, a capsule or a stick-pack, preferably a tablet.
18. A pharmaceutical composition according to paragraph 16 or 17, which comprises from 200 mg to 1,200 mg of lanifibranor.
19. A pharmaceutical composition according to any preceding paragraphs, wherein lanifibranor is in crystalline form.

20. A pharmaceutical composition as defined in any one of paragraphs 1 to 19, for use in a method of treating non-alcoholic fatty liver disease (NAFLD).
21. A pharmaceutical composition for use according to paragraph 20, wherein NAFLD includes non-alcoholic fatty liver and non-alcoholic steatohepatitis (NASH).
- 5 22. A pharmaceutical composition as defined in any one of paragraphs 1 to 19, for use in a method of treating a cirrhotic subject at risk of progressing from compensated stage to decompensated stage.
23. A pharmaceutical composition as defined in any one of paragraphs 1 to 19, for use in a method of treating cirrhosis, liver fibrosis, liver steatosis, fatty liver disease, acute
10 decompensation, acute on chronic liver failure (ACLF), acute liver failure (ALF), decompensated cirrhosis, compensated cirrhosis, metabolic-associated fatty liver disease (MAFLD), metabolic-associated steatohepatitis (MASH), diabetes, or liver cirrhosis.
24. A method of treating non-alcoholic fatty liver disease (NAFLD), which comprises administering to a subject in need thereof a pharmaceutical composition as defined in any
15 one of paragraphs 1 to 19.
25. A method according to paragraph 24, wherein NAFLD includes non-alcoholic fatty liver and non-alcoholic steatohepatitis (NASH).
26. A method of treating a cirrhotic subject at risk of progressing from compensated stage to decompensated stage, which comprises administering to the subject a
20 pharmaceutical composition as defined in any one of paragraphs 1 to 19.
27. A method of treating a disease selected among cirrhosis, liver fibrosis, liver steatosis, fatty liver disease, acute decompensation, acute on chronic liver failure (ACLF), acute liver failure (ALF), decompensated cirrhosis, compensated cirrhosis, metabolic-associated fatty liver disease (MAFLD), metabolic-associated steatohepatitis (MASH), diabetes, or liver
25 cirrhosis, which comprises administering to a subject in need thereof a pharmaceutical composition as defined in any one of paragraphs 1 to 19.
28. A method according to any one of paragraphs 24 to 27, wherein a daily dosage of from 400 mg to 1,200 mg of lanifibranor is administered to the subject.
29. A pharmaceutical composition as defined in any one of paragraphs 1 to 3,
30 comprising, based on the total weight of the composition:
55.0 wt% to 75.0 wt% of lanifibranor; and
25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients;
wherein lanifibranor has a particle size distribution such that $D_{50} \leq 30 \mu\text{m}$ and $D_{90} \leq 50 \mu\text{m}$, preferably $D_{50} \leq 10 \mu\text{m}$ and $D_{90} \leq 30 \mu\text{m}$, and

wherein among the pharmaceutically acceptable excipients, a surfactant represents from 1.0 wt% to 5.0 wt% of the total weight of the composition.

30. A stable immediate release pharmaceutical composition comprising, based on the total weight of the composition:

5 55.0 wt% to 75.0 wt% of lanifibranor; and

25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients;

wherein lanifibranor has a particle size distribution such that $D_{50} \leq 30 \mu\text{m}$ and $D_{90} \leq 50 \mu\text{m}$, preferably $D_{50} \leq 10 \mu\text{m}$ and $D_{90} \leq 30 \mu\text{m}$.

31. A stable immediate release pharmaceutical composition according to paragraph 30,
10 wherein said pharmaceutical composition releases from 30 to 60% of lanifibranor within 15 minutes after oral ingestion.

32. A stable immediate release pharmaceutical composition according to any one of paragraphs 30 to 31, wherein said pharmaceutical composition releases at least 80% of lanifibranor within 45 minutes after oral ingestion.

15 33. A stable immediate release pharmaceutical composition according to any one of paragraphs 30 to 32, wherein the pharmaceutically acceptable excipients include two or more of a binder, a colouring agent, a disintegrant, a filler, a glidant, a lubricant, a preservative, a surfactant, and a sweetener.

34. A stable immediate release pharmaceutical composition according to any one of
20 paragraphs 30 to 33, wherein the pharmaceutically acceptable excipients include a filler, and the filler represents from 10.0 wt% to 35.0 wt% of the total weight of the composition.

35. A stable immediate release pharmaceutical composition according to paragraph 34, wherein the filler is selected from lactose monohydrate, lactose anhydrous, starch, modified starch, mannitol and mixtures thereof.

25 36. A stable immediate release pharmaceutical composition according to any one of paragraphs 30 to 35, wherein the pharmaceutically acceptable excipients include a surfactant, and the surfactant represents from 1.0 wt% to 5.0 wt% of the total weight of the composition.

37. A stable immediate release pharmaceutical composition according to paragraph 36,
30 wherein the surfactant is selected from non-ionic surfactants, anionic surfactants, cationic surfactants, and mixtures thereof.

38. A stable immediate release pharmaceutical composition according to any one of paragraphs 30 to 37, wherein the pharmaceutically acceptable excipients include a binder, and the binder represents from 1.0 wt% to 10.0 wt% of the total weight of the composition.

39. A stable immediate release pharmaceutical composition according to paragraph 38, wherein the binder is selected from cellulose, modified cellulose, microcrystalline cellulose, polyvinylpyrrolidone and mixtures thereof.

40. A stable immediate release pharmaceutical composition according to any one of paragraphs 30 to 39, wherein the pharmaceutically acceptable excipients include a lubricant, and the lubricant represents from 0.5 wt% to 5.0 wt% of the total weight of the composition.

41. A stable immediate release pharmaceutical composition according to paragraph 40, wherein the lubricant is selected from talc, stearic acid, magnesium stearate, calcium stearate, sodium steryl fumarate, silica gel and mixtures thereof.

42. A stable immediate release pharmaceutical composition according to any one of paragraphs 30 to 41, wherein the pharmaceutically acceptable excipients include a disintegrant, and the disintegrant represents from 1.0 wt% to 8.0 wt% of the total weight of the composition.

43. A stable immediate release pharmaceutical composition according to paragraph 42, wherein the disintegrant is selected from starch, modified starch, croscarmellose sodium, crospovidone, sodium starch glycolate, and mixtures thereof.

44. A stable immediate release pharmaceutical composition according to any one of paragraphs 30 to 33, wherein the pharmaceutically acceptable excipients include a glidant, and the glidant represents from 0.1 wt% to 5.0 wt% of the total weight of the composition.

45. A stable immediate release pharmaceutical composition according to any one of paragraphs 30 to 44, which is a solid dosage form.

46. A stable immediate release pharmaceutical composition according to paragraph 45, which is a tablet, a capsule or a stick-pack, preferably a tablet.

47. A stable immediate release pharmaceutical composition according to paragraph 45 or 46, which comprises from 200 mg to 1,200 mg of lanifibranor.

48. A stable immediate release pharmaceutical composition according to any one of paragraphs 30 to 47, wherein lanifibranor is in crystalline form.

49. A stable immediate release tablet comprising, based on the total weight of the composition:

55.0 wt% to 75.0 wt% of lanifibranor; and

25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients;

wherein lanifibranor has a particle size distribution such that $D_{50} \leq 30 \mu\text{m}$ and $D_{90} \leq 50 \mu\text{m}$, preferably $D_{50} \leq 10 \mu\text{m}$ and $D_{90} \leq 30 \mu\text{m}$.

50. A stable immediate release tablet according to paragraph 49, wherein said tablet releases from 30 to 60% of lanifibranor within 15 minutes after oral ingestion.

51. A stable immediate release tablet according to any one of paragraphs 49 to 50, wherein said tablet releases at least 80% of lanifibranor within 45 minutes after oral
5 ingestion.

52. A stable immediate release tablet according to any one of paragraphs 49 to 51, wherein the pharmaceutically acceptable excipients include two or more of a binder, a colouring agent, a disintegrant, a filler, a glidant, a lubricant, a preservative, a surfactant, and a sweetener.

10 53. A stable immediate release tablet according to any one of paragraphs 49 to 52, wherein the pharmaceutically acceptable excipients include a filler, and the filler represents from 10.0 wt% to 35.0 wt% of the total weight of the composition.

54. A stable immediate release tablet according to paragraph 53, wherein the filler is selected from lactose monohydrate, lactose anhydrous, starch, modified starch, mannitol and
15 mixtures thereof.

55. A stable immediate release tablet according to any one of paragraphs 49 to 54, wherein the pharmaceutically acceptable excipients include a surfactant, and the surfactant represents from 1.0 wt% to 5.0 wt% of the total weight of the composition.

56. A stable immediate release tablet according to paragraph 55, wherein the surfactant
20 is selected from non-ionic surfactants, anionic surfactants, cationic surfactants, and mixtures thereof.

57. A stable immediate release tablet according to any one of paragraphs 49 to 56, wherein the pharmaceutically acceptable excipients include a binder, and the binder represents from 1.0 wt% to 10.0 wt% of the total weight of the composition.

25 58. A stable immediate release tablet according to paragraph 57, wherein the binder is selected from cellulose, modified cellulose, microcrystalline cellulose, polyvinylpyrrolidone and mixtures thereof.

59. A stable immediate release tablet according to any one of paragraphs 49 to 58, wherein the pharmaceutically acceptable excipients include a lubricant, and the lubricant
30 represents from 0.5 wt% to 5.0 wt% of the total weight of the composition.

60. A stable immediate release tablet according to paragraph 59, wherein the lubricant is selected from talc, stearic acid, magnesium stearate, calcium stearate, sodium sterayl fumarate, silica gel and mixtures thereof.

61. A stable immediate release tablet according to any one of paragraphs 49 to 60, wherein the pharmaceutically acceptable excipients include a disintegrant, and the disintegrant represents from 1.0 wt% to 8.0 wt% of the total weight of the composition.

5 62. A stable immediate release tablet according to paragraph 61, wherein the disintegrant is selected from starch, modified starch, croscarmellose sodium, crospovidone, sodium starch glycolate, and mixtures thereof.

63. A stable immediate release tablet according to any one of paragraphs 49 to 62, wherein the pharmaceutically acceptable excipients include a glidant, and the glidant represents from 0.1 wt% to 5.0 wt% of the total weight of the composition.

10 64. A stable immediate release pharmaceutical composition as defined in any one of paragraphs 30 to 48 or a stable immediate release tablet as defined in any one of paragraphs 49 to 63, for use in a method of treating non-alcoholic fatty liver disease (NAFLD).

15 65. A stable immediate release pharmaceutical composition as defined in any one of paragraphs 30 to 48 or a stable immediate release tablet as defined in any one of paragraphs 49 to 63, for use in a method of treating non-alcoholic fatty liver disease (NAFLD), wherein NAFLD includes non-alcoholic fatty liver and non-alcoholic steatohepatitis (NASH).

20 66. A stable immediate release pharmaceutical composition as defined in any one of paragraphs 30 to 48 or a stable immediate release tablet as defined in any one of paragraphs 49 to 63, for use in a method of treating a cirrhotic subject at risk of progressing from compensated stage to decompensated stage.

25 67. A stable immediate release pharmaceutical composition as defined in any one of paragraphs 30 to 48 or a stable immediate release tablet as defined in any one of paragraphs 49 to 63, for use in a method of treating cirrhosis, liver fibrosis, liver steatosis, fatty liver disease, acute decompensation, acute on chronic liver failure (ACLF), acute liver failure (ALF), decompensated cirrhosis, compensated cirrhosis, metabolic-associated fatty liver disease (MAFLD), metabolic-associated steatohepatitis (MASH), diabetes, or liver cirrhosis.

CLAIMS

1. A pharmaceutical composition comprising, based on the total weight of the composition:
 - 5 55.0 wt% to 75.0 wt% of lanifibranor; and
 - 25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients;wherein lanifibranor has a particle size distribution such that $D_{50} \leq 30 \mu\text{m}$ and $D_{90} \leq 50 \mu\text{m}$, preferably $D_{50} \leq 10 \mu\text{m}$ and $D_{90} \leq 30 \mu\text{m}$.
- 10 2. The pharmaceutical composition of claim 1, wherein said pharmaceutical composition releases from about 30 to 60% of lanifibranor within 15 minutes after oral ingestion.
3. The pharmaceutical composition of any one of claims 1 to 2, wherein said pharmaceutical composition releases at least 80% of lanifibranor within 45 minutes after oral
15 ingestion.
4. The pharmaceutical composition of any preceding claims, wherein the pharmaceutically acceptable excipients include two or more of a binder, a colouring agent, a disintegrant, a filler, a glidant, a lubricant, a preservative, a surfactant, and a sweetener.
20
5. The pharmaceutical composition of any preceding claims, wherein the pharmaceutically acceptable excipients include a filler, and the filler represents from 10.0 wt% to 35.0 wt% of the total weight of the composition.
- 25 6. The pharmaceutical composition of claim 5, wherein the filler is selected from lactose monohydrate, lactose anhydrous, starch, modified starch, mannitol and mixtures thereof.
7. The pharmaceutical composition of any preceding claims, wherein the pharmaceutically acceptable excipients include a surfactant, and the surfactant represents
30 from 1.0 wt% to 5.0 wt% of the total weight of the composition.
8. The pharmaceutical composition of claim 7, wherein the surfactant is selected from non-ionic surfactants, anionic surfactants, cationic surfactants, and mixtures thereof.

9. The pharmaceutical composition of any preceding claims, wherein the pharmaceutically acceptable excipients include a binder, and the binder represents from 1.0 wt% to 10.0 wt% of the total weight of the composition.

5 10. The pharmaceutical composition of claim 9, wherein the binder is selected from cellulose, modified cellulose, microcrystalline cellulose, polyvinylpyrrolidone and mixtures thereof.

11. The pharmaceutical composition of any preceding claims, wherein the
10 pharmaceutically acceptable excipients include a lubricant, and the lubricant represents from 0.5 wt% to 5.0 wt% of the total weight of the composition.

12. The pharmaceutical composition of claim 11, wherein the lubricant is selected from
15 talc, stearic acid, magnesium stearate, calcium stearate, sodium sterayl fumarate, silica gel and mixtures thereof.

13. The pharmaceutical composition of any preceding claims, wherein the
pharmaceutically acceptable excipients include a disintegrant, and the disintegrant
represents from 1.0 wt% to 8.0 wt% of the total weight of the composition.

20

14. The pharmaceutical composition of claim 13, wherein the disintegrant is selected
from starch, modified starch, croscarmellose sodium, crospovidone, sodium starch glycolate,
and mixtures thereof.

25 15. The pharmaceutical composition of any preceding claims, wherein the
pharmaceutically acceptable excipients include a glidant, and the glidant represents from 0.1
wt% to 5.0 wt% of the total weight of the composition.

16. A pharmaceutical composition as defined in any one of claims 1 to 15, comprising,
30 based on the total weight of the composition:

- from 55.0 wt% to 75.0 wt% of lanifibranor,
- from 10.0 wt% to 35.0 wt% of filler;
- from 1.0 wt% to 5.0 wt% of surfactant;
- from 1.0 wt% to 10.0 wt% of binder;
- 35 - from 0.5 wt% to 5.0 wt% of lubricant;

- from 1.0 wt% to 8.0 wt% of disintegrant;
- from 0.1 wt% to 5.0 wt% of glidant.

17. The pharmaceutical composition of any preceding claims, which is a solid dosage
5 form.

18. The pharmaceutical composition of claim 17, which is a tablet, a capsule or a stick-
pack, preferably a tablet.

10 19. The pharmaceutical composition of claim 17 or claim 18, which comprises from 200
mg to 1,200 mg of lanifibranor.

20. The pharmaceutical composition of any preceding claims, wherein lanifibranor is in
crystalline form.

15

21. The pharmaceutical composition as defined in any one of claims 1 to 20, for use in a
method of treating non-alcoholic fatty liver disease (NAFLD).

22. The pharmaceutical composition for use of claim 21, wherein NAFLD includes non-
20 alcoholic fatty liver and non-alcoholic steatohepatitis (NASH).

23. The pharmaceutical composition as defined in any one of claims 1 to 20, for use in a
method of treating a cirrhotic subject at risk of progressing from compensated stage to
decompensated stage.

25

24. The pharmaceutical composition as defined in any one of claims 1 to 20, for use in a
method of treating cirrhosis, liver fibrosis, liver steatosis, fatty liver disease, acute
decompensation, acute on chronic liver failure, acute liver failure, decompensated cirrhosis,
compensated cirrhosis, metabolic-associated fatty liver disease, metabolic-associated
30 steatohepatitis, diabetes, or liver cirrhosis.

25. A pharmaceutical composition as defined in any one of claims 1 to 3, comprising,
based on the total weight of the composition:

- 55.0 wt% to 75.0 wt% of lanifibranor; and
35 25.0 wt% to 45.0 wt% of pharmaceutically acceptable excipients;

wherein lanifibranor has a particle size distribution such that $D_{50} \leq 30 \mu\text{m}$ and $D_{90} \leq 50 \mu\text{m}$, preferably $D_{50} \leq 10 \mu\text{m}$ and $D_{90} \leq 30 \mu\text{m}$, and wherein among the pharmaceutically acceptable excipients, a surfactant represents from 1.0 wt% to 5.0 wt% of the total weight of the composition.

5

26. The pharmaceutical composition of claim 25, wherein the pharmaceutically acceptable excipients further include two or more of a binder, a colouring agent, a disintegrant, a filler, a glidant, a lubricant, a preservative, a surfactant, and a sweetener.

10 27. The pharmaceutical composition of claim 25 or claim 26, which is a solid dosage form.

28. The pharmaceutical composition of any one of claims 25 to 27, which is a tablet, a capsule or a stick-pack, preferably a tablet.

15

29. The pharmaceutical composition of any one of claims 25 to 28, which comprises from 200 mg to 1,200 mg of lanifibranor.

30 20 The pharmaceutical composition of any one of claims 25 to 29, wherein lanifibranor is in crystalline form.

31. The pharmaceutical composition as defined in any one of claims 25 to 30, for use in a method of treating non-alcoholic fatty liver disease (NAFLD).

25 32. The pharmaceutical composition for use of claim 31, wherein NAFLD includes non-alcoholic fatty liver and non-alcoholic steatohepatitis (NASH).

33. The pharmaceutical composition as defined in any one of claims 25 to 30, for use in a method of treating a cirrhotic subject at risk of progressing from compensated stage to
30 decompensated stage.

34. The pharmaceutical composition as defined in any one of claims 25 to 30, for use in a method of treating cirrhosis, liver fibrosis, liver steatosis, fatty liver disease, acute decompensation, acute on chronic liver failure, acute liver failure, decompensated cirrhosis,

compensated cirrhosis, metabolic-associated fatty liver disease, metabolic-associated steatohepatitis, diabetes, or liver cirrhosis.