

(I),

or a pharmaceutically acceptable salt thereof, wherein:

R^1, R^2, R^3, R^4, R^7, R^8, R^9, R^{10}, R^{13} and R^{14} are independently selected from the group consisting of hydrogen and methyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^5 and R^6 cannot be –OH;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^{11} and R^{12} cannot be –OH;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

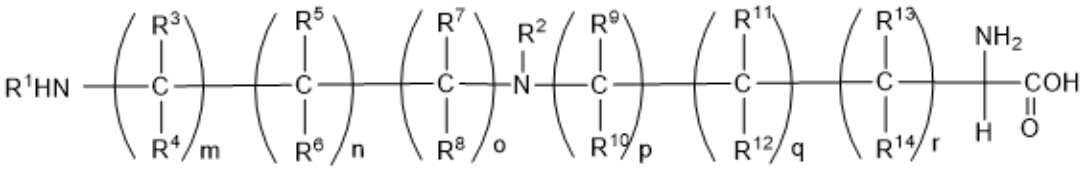
o is 0, 1, 2, 3 or 4;

p is 1, 2, 3 or 4;

q is 0, 1, 2, 3 or 4; and

r is 0, 1, 2, 3 or 4.

[0005b] In a further aspect, the present disclosure provides a use of a compound in the manufacture of a medicament for treating liver inflammation in a subject in need thereof wherein said compound is a compound according to Formula I,



(I),

or a pharmaceutically acceptable salt thereof, wherein:

R^1, R^2, R^3, R^4, R^7, R^8, R^9, R^{10}, R^{13} and R^{14} are independently selected from the group consisting of hydrogen and methyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^5 and R^6 cannot be –OH;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^{11} and R^{12} cannot be –OH;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

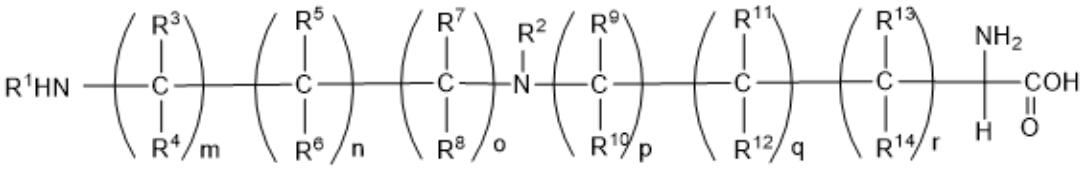
o is 0, 1, 2, 3 or 4;

p is 1, 2, 3 or 4;

q is 0, 1, 2, 3 or 4; and

r is 0, 1, 2, 3 or 4.

[0005c] In another aspect, the present disclosure provides a use of a compound in the manufacture of a medicament for treating hepatocellular ballooning in a subject in need thereof wherein said compound is a compound according to Formula I,



(I),

or a pharmaceutically acceptable salt thereof, wherein:

R^1, R^2, R^3, R^4, R^7, R^8, R^9, R^{10}, R^{13} and R^{14} are independently selected from the group consisting of hydrogen and methyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^5 and R^6 cannot be –OH;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^{11} and R^{12} cannot be –OH;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

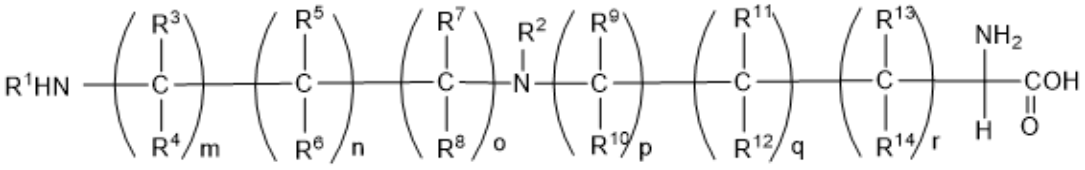
o is 0, 1, 2, 3 or 4;

p is 1, 2, 3 or 4;

q is 0, 1, 2, 3 or 4; and

r is 0, 1, 2, 3 or 4.

[0005d] In yet another aspect, the present disclosure provides a use of a compound in the manufacture of a medicament for treating liver fibrosis in a subject in need thereof, wherein said compound is a compound according to Formula I,



(I),

or a pharmaceutically acceptable salt thereof, wherein:

R^1, R^2, R^3, R^4, R^7, R^8, R^9, R^{10}, R^{13} and R^{14} are independently selected from the group consisting of hydrogen and methyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^5 and R^6 cannot be –OH;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^{11} and R^{12} cannot be –OH;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

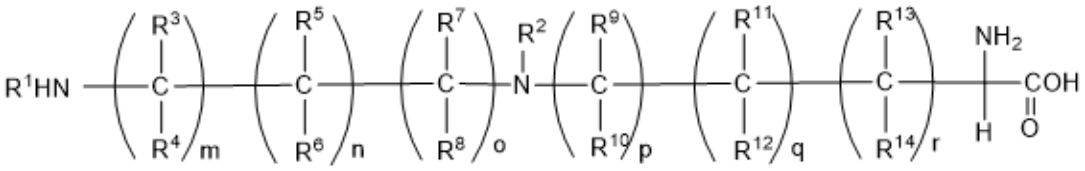
o is 0, 1, 2, 3 or 4;

p is 1, 2, 3 or 4;

q is 0, 1, 2, 3 or 4; and

r is 0, 1, 2, 3 or 4.

[0005e] In yet another aspect, the present disclosure provides a use of a compound in the manufacture of a medicament for treating steatosis in a subject in need thereof, wherein said compound is a compound according to Formula I,



(I),

or a pharmaceutically acceptable salt thereof, wherein:

R^1, R^2, R^3, R^4, R^7, R^8, R^9, R^{10}, R^{13} and R^{14} are independently selected from the group consisting of hydrogen and methyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^5 and R^6 cannot be –OH;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^{11} and R^{12} cannot be –OH;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

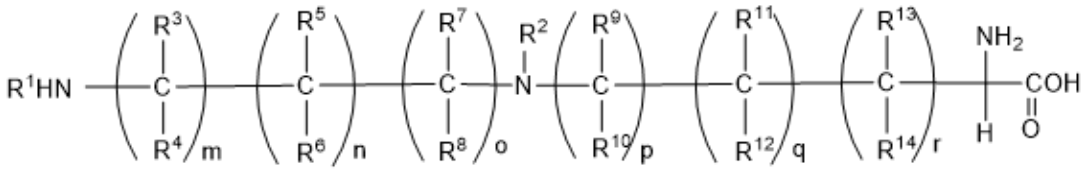
o is 0, 1, 2, 3 or 4;

p is 1, 2, 3 or 4;

q is 0, 1, 2, 3 or 4; and

r is 0, 1, 2, 3 or 4.

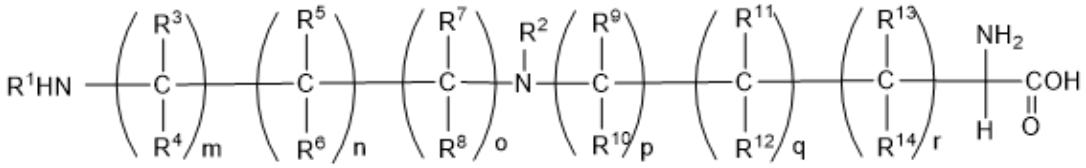
[0006] In one example, the disclosure features a method for treating non-alcoholic steatohepatitis (NASH), the method comprising administering to the subject in need thereof an effective amount of a compound according to Formula I,



CLAIMS

WHAT IS CLAIMED IS:

1. Use of a compound in the manufacture of a medicament for treating non-alcoholic steatohepatitis (NASH) in a subject in need thereof, wherein said compound is a compound according to Formula I,



(I),

or a pharmaceutically acceptable salt thereof, wherein:

R^1, R^2, R^3, R^4, R^7, R^8, R^9, R^{10}, R^{13} and R^{14} are independently selected from the group consisting of hydrogen and methyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^5 and R^6 cannot be –OH;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^{11} and R^{12} cannot be –OH;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

o is 0, 1, 2, 3 or 4;

p is 1, 2, 3 or 4;

q is 0, 1, 2, 3 or 4; and

r is 0, 1, 2, 3 or 4.

2. The use of claim 1, wherein:

(i) the subject has a NAFLD Activity Score (NAS) of ≥ 4; and/or

(ii) the compound of Formula I or a pharmaceutically acceptable salt thereof results in a NAFLD Activity Score (NAS) of < 4.

3. The use of claim 1 or claim 2, wherein the subject has non-cirrhotic NASH or cirrhotic NASH.

4. The use of claim 1 or claim 2, wherein:

(i) the subject has liver inflammation, wherein optionally:

(a) the liver inflammation is lobular inflammation; and/or

(b) the compound of Formula I, or a pharmaceutically acceptable salt thereof, results in a decrease in liver inflammation; and/or

(c) the compound of Formula I or a pharmaceutically acceptable salt thereof, results in a liver inflammation score of 0 or 1; and/or

(ii) the liver of the subject is characterized by hepatocellular ballooning, and wherein optionally the compound of Formula I or a pharmaceutically acceptable salt thereof results in a decrease in hepatocellular ballooning, optionally wherein the compound of Formula I or a pharmaceutically acceptable salt thereof results in a ballooning score of 0; and/or

(iii) the subject has elevated hepatic alanine aminotransferase (ALT) levels, wherein optionally wherein the compound of Formula I or a pharmaceutically acceptable salt thereof results in decreased hepatic alanine aminotransferase (ALT) levels; and/or

(iv) the subject has elevated hepatic aspartate aminotransferase (AST) levels, optionally wherein the compound of Formula I or a pharmaceutically acceptable salt thereof results in decreased hepatic aspartate aminotransferase (AST) levels; and/or

(v) the subject has liver fibrosis; optionally wherein

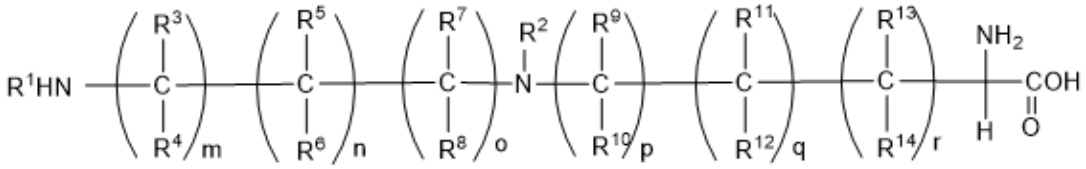
(a) the subject has stage 2, stage 3, or stage 4 liver fibrosis; and/or

(b) the compound of Formula I or a pharmaceutically acceptable salt thereof results in stabilization or reversal of liver fibrosis in the subject; and/or

(vi) the subject has a steatosis score of 1, 2, or 3, optionally wherein the compound of Formula I or a pharmaceutically acceptable salt thereof results in a decrease of steatosis in the subject; and/or

(vii) the compound of Formula I or a pharmaceutically acceptable salt thereof results in a decrease in liver hypertrophy in the subject.

5. Use of a compound in the manufacture of a medicament for treating liver inflammation in a subject in need thereof wherein said compound is a compound according to Formula I,



(I),

or a pharmaceutically acceptable salt thereof, wherein:

R^1, R^2, R^3, R^4, R^7, R^8, R^9, R^{10}, R^{13} and R^{14} are independently selected from the group consisting of hydrogen and methyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^5 and R^6 cannot be –OH;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^{11} and R^{12} cannot be –OH;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

o is 0, 1, 2, 3 or 4;

p is 1, 2, 3 or 4;

q is 0, 1, 2, 3 or 4; and

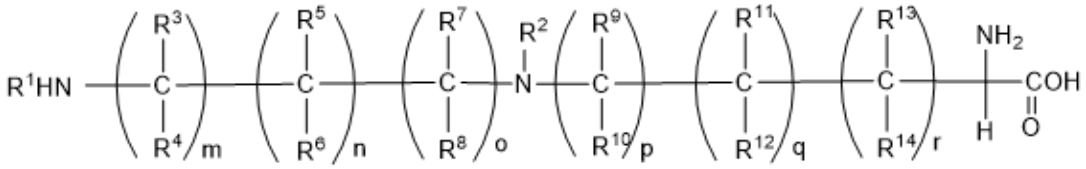
r is 0, 1, 2, 3 or 4.

6. The use of claim 5, wherein:

(i) said liver inflammation is lobular inflammation; and/or

(ii) the compound of Formula I or a pharmaceutically acceptable salt thereof results in a liver inflammation score of 0 or 1.

7. Use of a compound in the manufacture of a medicament for treating hepatocellular ballooning in a subject in need thereof wherein said compound is a compound according to Formula I,



(I),

or a pharmaceutically acceptable salt thereof, wherein:

R^1, R^2, R^3, R^4, R^7, R^8, R^9, R^{10}, R^{13} and R^{14} are independently selected from the group consisting of hydrogen and methyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^5 and R^6 cannot be –OH;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^{11} and R^{12} cannot be –OH;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

o is 0, 1, 2, 3 or 4;

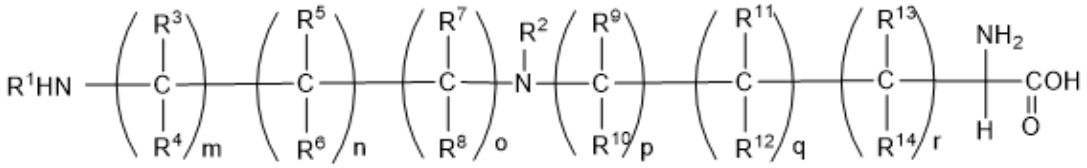
p is 1, 2, 3 or 4;

q is 0, 1, 2, 3 or 4; and

r is 0, 1, 2, 3 or 4.

8. The use of claim 7, wherein the compound of Formula I or a pharmaceutically acceptable salt thereof results in a ballooning score of 0.

9. Use of a compound in the manufacture of a medicament for treating liver fibrosis in a subject in need thereof, wherein said compound is a compound according to Formula I,



(I),

or a pharmaceutically acceptable salt thereof, wherein:

R^1, R^2, R^3, R^4, R^7, R^8, R^9, R^{10}, R^{13} and R^{14} are independently selected from the group consisting of hydrogen and methyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^5 and R^6 cannot be –OH;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^{11} and R^{12} cannot be –OH;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

o is 0, 1, 2, 3 or 4;

p is 1, 2, 3 or 4;

q is 0, 1, 2, 3 or 4; and

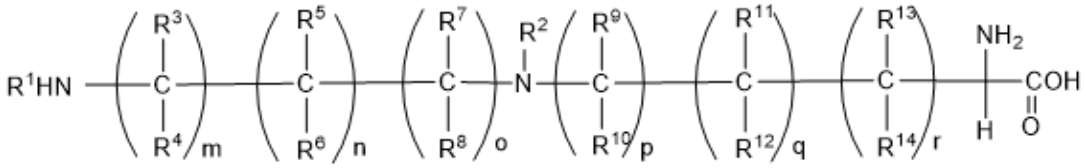
r is 0, 1, 2, 3 or 4.

10. The use of claim 9, wherein:

(i) the subject has (a) stage 2, stage 3, or stage 4 liver fibrosis or (b) cirrhosis; and/or

(ii) the compound of Formula I or a pharmaceutically acceptable salt thereof results in stabilization or reversal of liver fibrosis in the subject.

11. Use of a compound in the manufacture of a medicament for treating steatosis in a subject in need thereof, wherein said compound is a compound according to Formula I,



(I),

or a pharmaceutically acceptable salt thereof, wherein:

R^1, R^2, R^3, R^4, R^7, R^8, R^9, R^{10}, R^{13} and R^{14} are independently selected from the group consisting of hydrogen and methyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^5 and R^6 cannot be –OH;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, methyl and –OH, provided that both R^{11} and R^{12} cannot be –OH;

m is 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

o is 0, 1, 2, 3 or 4;

p is 1, 2, 3 or 4;

q is 0, 1, 2, 3 or 4; and

r is 0, 1, 2, 3 or 4.

12. The use of claim 11, wherein:

(i) the subject has a steatosis score of 1, 2, or 3; and/or

(ii) the compound of Formula I or a pharmaceutically acceptable salt thereof results in a decrease of steatosis in the subject.

13. The use of any one of claims 5-12, wherein the subject has non-alcoholic steatohepatitis (NASH).

14. The use of any one of the preceding claims, wherein:

(i) the subject is a human; and/or

(ii) the compound of Formula I, or a pharmaceutically acceptable salt thereof, is to be administered to the subject

(a) for a time period that is at least four, five, six, seven, eight, nine, ten, eleven, twelve, thirteen, fourteen, fifteen, or sixteen weeks;

(b) for a time period that is at least 4-6, 4-8, 4-10, 4-12, 4-14, or 4-16 weeks;

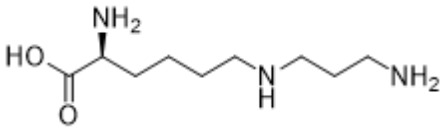
(c) at a dose of 2-1000, 10-1000 or 10-100 mg/kg per day;

(d) at a dose that is about 10 mg/kg or greater per day; or

(e) at a total daily dose that is 100-5000, 500-5000 or 600-3000 mg per day; and/or

(iii) the compound of Formula I is to be orally administered.

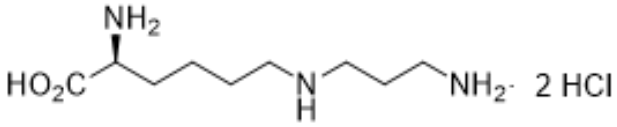
15. The use of any one of the preceding claims, wherein the compound is:
(i) (*S*)-2-amino-6-((3-aminopropyl)amino)hexanoic acid,



, or a pharmaceutically acceptable salt thereof,

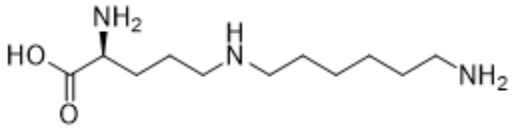
optionally wherein the compound is a hydrochloride salt of (S)-2-amino-6-((3-aminopropyl)amino)hexanoic acid,

optionally wherein the compound is (S)-2-amino-6-((3-aminopropyl)amino)hexanoic acid dihydrochloride,



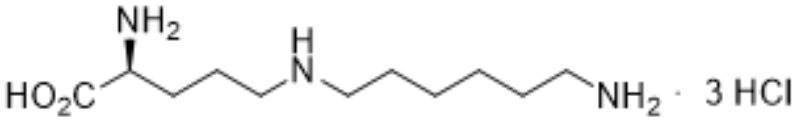
; or

(ii) (S)-2-amino-5-((6-aminohexyl)amino)pentanoic acid,



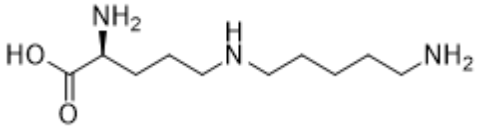
, or a pharmaceutically acceptable salt thereof, optionally wherein the compound is a hydrochloride salt of (*S*)-2-amino-5-((6-aminohexyl)amino)pentanoic acid,

optionally wherein the compound is (*S*)-2-amino-5-((6-aminohexyl)amino)pentanoic acid trihydrochloride,



; or

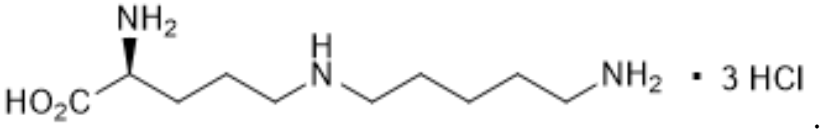
(iii) (S)-2-amino-5-((5-aminopentyl)amino)pentanoic acid,



, or a pharmaceutically acceptable salt thereof,

optionally wherein the compound is a hydrochloride salt of (S)-2-amino-5-((5-aminopentyl)amino)pentanoic acid,

optionally wherein the compound is (S)-2-amino-5-((5-aminopentyl)amino)pentanoic acid trihydrochloride,


NH2
HO2C
H
N
NH2
• 3 HCl