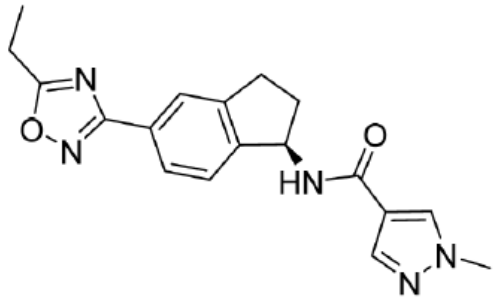
CLAIMS

What is claimed is:

1. Use of CK-274



CK-274,

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating non-obstructive hypertrophic cardiomyopathy (nHCM) in a patient in need thereof, wherein a therapeutically effective amount of CK-274, or a pharmaceutically acceptable salt thereof, is selected by titrating a daily dose of CK-274, or a pharmaceutically acceptable salt thereof, to be administered to the patient.

2. The use of claim 1, wherein the dose is titrated once during a course of treatment.

3. The use of claim 1, wherein the daily dose of CK-274, or a pharmaceutically acceptable salt thereof, is a first daily dose to be administered for a first time period, and

based on a component of a first echocardiogram for the patient acquired after the first time period, a second daily dose of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a second time period or administration of CK-274, or a pharmaceutically acceptable salt thereof, is to be terminated.

4. The use of claim 3, wherein the second daily dose of CK-274, or a pharmaceutically acceptable salt thereof, is to be selected based on the component of the first echocardiogram.

5. The use of claim 1, wherein the daily dose of CK-274, or a pharmaceutically acceptable salt thereof, is a first daily dose to be administered for a first time period; and

based a first echocardiogram comprising a biplane LVEF for the patient acquired after the first time period, a second daily dose of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a second time period or administration of CK-274, or a pharmaceutically acceptable salt thereof, is to be terminated, wherein:

CK-274, or a pharmaceutically acceptable salt thereof, to the patient is to be terminated if the biplane LVEF of the first echocardiogram is below a first predetermined biplane LVEF threshold;

the second daily dose of CK-274, or a pharmaceutically acceptable salt thereof, is the same as the first daily dose of CK-274, or a pharmaceutically acceptable salt thereof, if the biplane LVEF is at or above the first predetermined biplane LVEF threshold and below a second predetermined biplane LVEF threshold; and

the second daily dose of CK-274, or a pharmaceutically acceptable salt thereof, is greater than the first daily dose of CK-274, or a pharmaceutically acceptable salt thereof, if the biplane LVEF of the first echocardiogram is above the second predetermined biplane LVEF threshold.

6. The use of claim 5, wherein the first daily dose of CK-274, or a pharmaceutically acceptable salt thereof, is about 5 mg of CK-274 and the second daily dose of CK-274, or a pharmaceutically acceptable salt thereof, is about 5 mg or about 10 mg of CK-274.

7. The use of claim 1, wherein the daily dose of CK-274, or a pharmaceutically acceptable salt thereof, is a first daily dose ("Dose 1") to be administered for a first time period; and wherein:

(1) after the first time period, a first echocardiogram is conducted on the patient to determine the patient's biplane LVEF ("LVEF1"); and

(a) administration of CK-274, or a pharmaceutically acceptable salt thereof, is to be terminated if the patient's LVEF1 is <50%; or

(b) a second daily dose ("Dose 2") of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a second time period, if the patient's LVEF1 is ≥ 55%, wherein Dose 2 is greater than Dose 1; or

(c) the same dose as the dose administered for the first time period of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a second time period, if the patient's LVEF1 is ≥ 50% and < 55%; and optionally

(2) after the second time period, a second echocardiogram is conducted on the patient to determine the patient's biplane LVEF ("LVEF2"); and

(a) administration of CK-274, or a pharmaceutically acceptable salt thereof, is to be terminated, if the patient was receiving Dose 1 during the second time period and the patient's LVEF2 is <50%; or

(b) Dose 1 of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a third time period, if the patient was receiving Dose 2 during the second time period and the patient's LVEF2 is <50%; or

(c) a greater daily dose ("Dose 2") of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a third time period, if the patient was receiving Dose 1 during the second time period and the patient's LVEF2 is ≥ 55%; or

(d) a third daily dose ("Dose 3") of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a third time period, if the patient was receiving Dose 2 during the second time period and the patient's LVEF2 is ≥ 55%, wherein Dose 3 is greater than Dose 2; or

(e) the same dose as the dose administered during the second time period of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a third time period if the patient's LVEF2 is ≥ 50% and < 55%; and optionally

(3) after the third time period, a third echocardiogram is conducted on the patient to determine the patient's biplane LVEF ("LVEF3"); and

(a) administration of CK-274, or a pharmaceutically acceptable salt thereof, to the patient, is to be terminated if the patient was receiving Dose 1 during the third time period and the patient's LVEF3 is <50%; or

(b) Dose 1 of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a fourth time period, if the patient was receiving Dose 2 during the third time period and the patient's LVEF3 is <50%; or

(c) Dose 2 of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a fourth time period, if the patient was receiving Dose 3 during the third time period and the patient's LVEF3 is <50%; or

(d) Dose 2 of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a fourth time period, if the patient was receiving Dose 1 during the third time period and the patient's LVEF3 is ≥ 55%;

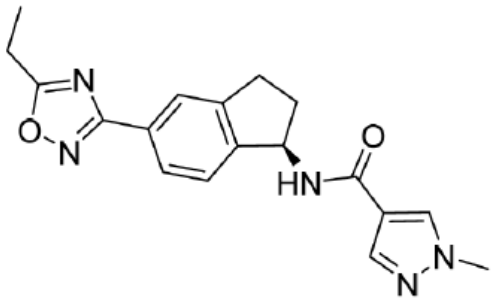
(e) Dose 3 of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a fourth time period, if the patient was receiving Dose 2 during the third time period and the patient's LVEF3 is ≥ 55%;

(f) a fourth daily dose ("Dose 4") of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a fourth time period, if the patient was receiving Dose 3 during the third time period and the patient's LVEF3 is ≥ 55%, wherein Dose 4 is greater than Dose 3; or

(4) the same dose as the one administered during the third time period of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a fourth time period if the patient's LVEF3 is ≥ 50% and < 55%.

8. The use of claim 7, wherein the first time period is about 2 weeks.

9. Use of CK-274



CK-274,

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating non-obstructive hypertrophic cardiomyopathy (nHCM) in a patient in need thereof.

10. The use of claim 9, wherein the patient has a resting left ventricular ejection fraction of at least 60% before CK-274 or a pharmaceutically acceptable salt thereof is to be administered.

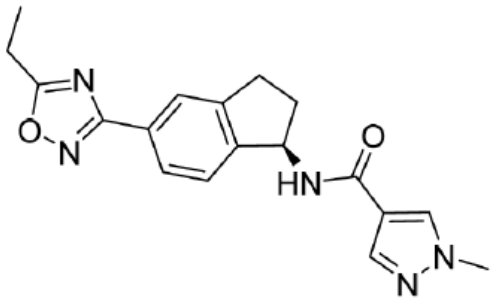
11. The use of claim 9, wherein the patient has a resting left ventricular ejection fraction of at least 60% and resting and post-Valsalva left ventricular outflow tract pressure gradients (LVOT-G) of less than 30 mmHg before CK-274 or a pharmaceutically acceptable salt thereof is to be administered.

12. The use of claim 9, wherein a therapeutically effective amount of CK-274, or a pharmaceutically acceptable salt thereof, is selected by titrating a daily dose of CK-274, or a pharmaceutically acceptable salt thereof, to be administered to the patient.

13. The use of claim 12, wherein the dose is titrated once during a course of treatment.

14. The use of claim 12, wherein the dose is titrated two or more times during a course of treatment.

15. Use of CK-274



CK-274,

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating HCM with mid-ventricular obstruction (MVO) in a patient in need thereof, wherein a therapeutically effective amount of CK-274, or a pharmaceutically acceptable salt thereof, is selected by titrating a daily dose of CK-274, or a pharmaceutically acceptable salt thereof, to be administered to the patient.

16. The use of claim 15, wherein the daily dose of CK-274, or a pharmaceutically acceptable salt thereof, is a first daily dose to be administered for a first time period; and:

based on a component of a first echocardiogram for the patient acquired after the first time period, a second daily dose of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a second time period or administration of CK-274, or a pharmaceutically acceptable salt thereof, is to be terminated.

17. The use of claim 1, wherein the administration of CK-274, or a pharmaceutically acceptable salt thereof, results in one or more of the following for the patient:

a) improvement in NYHA functional classification by one or more classes; and/or

b) decrease in mean NT-proBNP; and/or

c) decrease in cardiac troponin I.

18. The use of claim 1, wherein the daily dose of CK-274, or a pharmaceutically acceptable salt thereof, is a first daily dose ("Dose 1") to be administered for a first time period; and wherein:

(1) after the first time period, a first echocardiogram is conducted on the patient to determine the patient's biplane LVEF ("LVEF1"); and

(a) administration of CK-274, or a pharmaceutically acceptable salt thereof, is to be terminated, if the patient's LVEF1 is <50%; or

(b) a second daily dose ("Dose 2") of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a second time period, if the patient's LVEF1 is ≥ 60%, wherein Dose 2 is greater than Dose 1; or

(c) the same dose as the dose administered for the first time period of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a second time period, if the patient's LVEF1 is ≥ 50% and < 60%; and optionally

(2) after the second time period, a second echocardiogram is conducted on the patient to determine the patient's biplane LVEF ("LVEF2"); and

(f) administration of CK-274, or a pharmaceutically acceptable salt thereof, is to be terminated, if the patient was receiving Dose 1 during the second time period and the patient's LVEF2 is <50%; or

(g) Dose 1 of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a third time period, if the patient was receiving Dose 2 during the second time period and the patient's LVEF2 is <50%; or

(h) the second daily dose ("Dose 2") of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a third time period, if the patient was receiving Dose 1 during the second time period and the patient's LVEF2 is ≥ 60%; or

(i) a third daily dose ("Dose 3") of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a third time period, if the patient was receiving Dose 2 during the second time period and the patient's LVEF2 is ≥ 60%, wherein Dose 3 is greater than Dose 2; or

(j) the same dose as the dose administered during the second time period of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a third time period if the patient's LVEF2 is ≥ 50% and < 60%; and optionally

(3) after the third time period, a third echocardiogram is conducted on the patient to determine the patient's biplane LVEF ("LVEF3"); and

(a) administration of CK-274, or a pharmaceutically acceptable salt thereof, is to be terminated, if the patient was receiving Dose 1 during the third time period and the patient's LVEF3 is <50%; or

(g) Dose 1 of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a fourth time period, if the patient was receiving Dose 2 during the third time period and the patient's LVEF3 is <50%; or

(h) Dose 2 of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a fourth time period, if the patient was receiving Dose 3 during the third time period and the patient's LVEF3 is <50%; or

(i) Dose 2 of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a fourth time period, if the patient was receiving Dose 1 during the third time period and the patient's LVEF3 is ≥ 60%;

(j) Dose 3 of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a fourth time period, if the patient was receiving Dose 2 during the third time period and the patient's LVEF3 is ≥ 60%;

(k) a fourth daily dose ("Dose 4") of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a fourth time period, if the patient was receiving Dose 3 during the third time period and the patient's LVEF3 is ≥ 60%, wherein Dose 4 is greater than Dose 3; or

(4) the same dose as the one administered during the third time period of CK-274, or a pharmaceutically acceptable salt thereof, is to be administered for a fourth time period if the patient's LVEF3 is ≥ 50% and < 60%.

19. The use of claim 18, wherein the first time period is about 2 weeks.

20. The use of claim 1, wherein the CK-274 or pharmaceutically acceptable salt thereof comprises one or more of polymorphic Form I, Form II, Form III, Form IV, Form V, and Form VI of CK-274.