morbidity and mortality. Provided are new therapeutic agents and methods that remedy the long-felt need for improved treatment of HCM and related cardiac disorders.

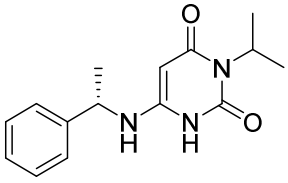
SUMMARY

[0004] In one example, provided is a method of treating hypertrophic cardiomyopathy (HCM). The method includes administering to a subject in need thereof a therapeutically effective amount of Compound 1, as described herein, where the pharmaceutically effective amount is a total daily dosage of about 2 mg to 50 mg, or about 5 mg to 30 mg.

[0005] In another example, provided herein is a method of treating myocardial diastolic dysfunction. The method includes administering to a subject in need thereof a therapeutically effective amount of Compound 1, as described herein, where the pharmaceutically effective amount is a total daily dosage of about 2 mg to 50 mg, or about 5 mg to 30 mg.

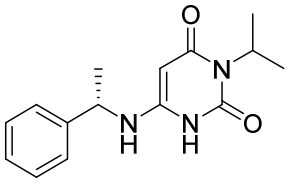
[0006] In another example, provided herein is a method of treating hypertrophic cardiomyopathy in an individual in need thereof comprising administering Compound 1 to the individual in an amount effective to achieve and maintain a blood plasma concentration of Compound 1 from 200 to 750 ng/mL. In some examples, the blood plasma concentration of Compound 1 is achieved and maintained at 350 to 700 ng/mL. In some examples, the effective amount to achieve and maintain the desired blood plasma concentration of Compound 1 is from 2 to 15 mg of Compound 1. In some examples, the effective amount to achieve and maintain the desired blood plasma concentration of Compound 1 is from 2.5 to 15 mg of Compound 1. In some examples, the effective amount to achieve and maintain the desired blood plasma concentration of Compound 1 is from 2 to 20 mg of Compound 1. In some examples, the effective amount to achieve and maintain the desired blood plasma concentration of Compound 1 is from 2.5 to 20 mg of Compound 1. In some examples, the daily dose of Compound 1 is adjusted after initial administration based on the determined blood plasma concentration. In some examples, the HCM is obstructive HCM (oHCM). In some examples, the HCM is non-obstructive HCM.

[0006a] In one aspect, the present disclosure refers to use of Compound 1, having the formula:



or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating symptomatic New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy (oHCM) in a subject in need thereof, wherein Compound 1 or a pharmaceutically acceptable salt thereof is to be administered in a therapeutically effective amount, which is a total daily dosage of 1 mg to 15 mg.

[0006b] In one aspect, the present disclosure refers to use of Compound 1, having the formula:



,

in the manufacture of a medicament for treating symptomatic New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy (oHCM) in a subject in need thereof, wherein Compound 1 is to be orally administered once daily in a therapeutically effective amount, which is from 1 mg to 15 mg.

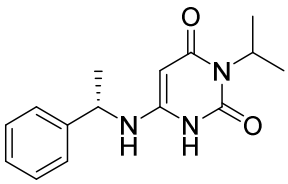
BRIEF DESCRIPTION OF THE DRAWINGS

[0007] **FIG. 1** shows the resting LVEF (%; 2DE) in a TTE analysis population.

[0008] **FIG. 2A** shows a change from baseline in resting LVEF (2DE) versus plasma concentrations of Compound 1 (MYK-461).

WHAT IS CLAIMED IS:

1. Use of Compound 1, having the formula:



or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating symptomatic New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy (oHCM) in a subject in need thereof, wherein Compound 1 or a pharmaceutically acceptable salt thereof is to be administered in a therapeutically effective amount, which is a total daily dosage of 1 mg to 15 mg.

2. The use of claim 1, wherein said therapeutically effective amount is a total daily dosage of 2.5 mg to 15 mg.

3. The use of claim 1, wherein said Compound 1 is to be administered orally.

4. The use of claim 1, wherein said Compound 1 is to be administered once daily.

5. The use of claim 1, wherein said Compound 1 is to be administered daily for at least twelve weeks.

6. The use of claim 1, wherein said subject has LVEF of 55% or higher, as measured prior to treatment.

7. The use of claim 1, wherein:

(a) Compound 1 or a pharmaceutically acceptable salt thereof is to be administered as a first dose administered once daily;

(b) a measurement of a first LVEF of the subject is obtained; and

(c) administration of Compound 1 or a pharmaceutically acceptable salt thereof is to be discontinued when the first LVEF is less than 50%.

8. The use of claim 7, wherein:

(d) a measurement of a second LVEF of the subject is obtained following discontinuation of administration; and

(e) administration of Compound 1 or a pharmaceutically acceptable salt thereof is to be resumed as a second dose administered once daily when the second LVEF is greater than or equal to 50%.

9. The use of claim 8, wherein the second dose is less than the first dose.

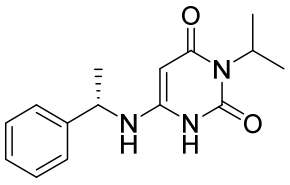
10. The use of claim 1, wherein the subject does not receive concomitant administration of a CYP2C19 inhibitor.

11. The use of claim 10, wherein the subject does not receive concomitant administration of a strong CYP3A4 inhibitor.

12. The use of claim 1, wherein the subject does not receive concomitant administration of a strong CYP3A4 inhibitor.

13. The use of claim 1, wherein Compound 1 is in free base form.

14. Use of Compound 1, having the formula:



,

in the manufacture of a medicament for treating symptomatic New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy (oHCM) in a subject in need thereof, wherein Compound 1 is to be orally administered once daily in a therapeutically effective amount, which is from 1 mg to 15 mg.

15. The use of claim 14, wherein the therapeutically effective amount is from 2.5 mg to 15 mg.

16. The use of claim 14, wherein said subject has a LVEF of 55% or higher, as measured prior to treatment.

17. The use of claim 14, wherein:

(a) Compound 1 is to be administered as a first dose administered once daily;

(b) a measurement of a first LVEF of the subject is obtained; and

(c) administration of Compound 1 is to be discontinued when the first LVEF is less than 50%.

18. The use of claim 17, wherein:

(d) a measurement of a second LVEF of the subject is obtained following discontinuation of administration; and

(e) administration of Compound 1 is to be resumed as a second dose administered once daily when the second LVEF is greater than or equal to 50%.

19. The use of claim 18, wherein the second dose is less than the first dose.

20. The use of claim 14, wherein the subject does not receive concomitant administration of a CYP2C19 inhibitor.

21. The use of claim 20, wherein the subject does not receive concomitant administration of a strong CYP3A4 inhibitor.

22. The use of claim 14, wherein the subject does not receive concomitant administration of a strong CYP3A4 inhibitor.