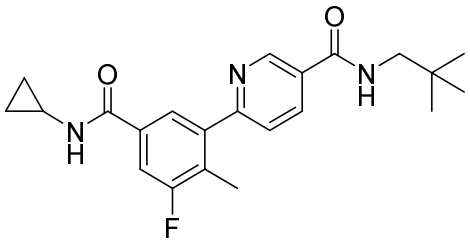
or a stereoisomer thereof, an isotopically-enriched compound thereof, a prodrug thereof, a solvate thereof, or a pharmaceutically acceptable salt thereof. The method includes the treatment of disorders associated with DUX4 gene expression, wherein the inhibition of p38 kinase with a p38 kinase inhibitor may reduce DUX4 expression levels and/or the expression of one or more downstream genes in cells of the subject.

[008a] In one aspect, the present disclosure refers to use of a p38 kinase inhibitor in the manufacture of a medicament for treating facioscapulohumeral muscular dystrophy (FSHD) in a subject in need thereof, wherein the p38 kinase inhibitor is characterized by Formula (V′):



(V′),

or a pharmaceutically acceptable salt thereof, wherein the compound of Formula V′ or the pharmaceutically acceptable salt thereof is to be orally administered at a dose of 15 mg two times per day.

[009] In another example, a method for treating facioscapulohumeral muscular dystrophy (FSHD) is provided. The method includes administering to a subject in need thereof, an effective amount of a p38 kinase inhibitor of Formula V′, or a stereoisomer thereof, an isotopically-enriched compound thereof, a prodrug thereof, a solvate thereof, or a pharmaceutically acceptable salt thereof.

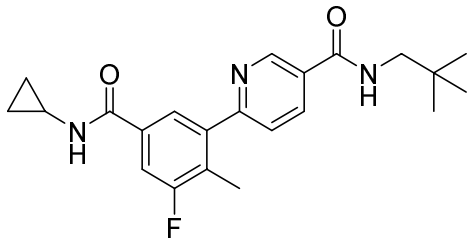
[0010] In one example, a method for treating a disorder responsive to p38 kinase inhibition is provided. The method includes administering to a subject in need thereof, an effective amount of a p38 kinase inhibitor selected from one or more of the following Formulae I′-XXIX′:

CLAIMS

What is claimed is:

1. Use of a p38 kinase inhibitor in the manufacture of a medicament for treating facioscapulohumeral muscular dystrophy (FSHD) in a subject in need thereof,

wherein the p38 kinase inhibitor is characterized by Formula (V′):



(V′),

or a pharmaceutically acceptable salt thereof, wherein the compound of Formula V′ or the pharmaceutically acceptable salt thereof is to be orally administered at a dose of 15 mg two times per day.

2. The use of claim 1, wherein the muscle cells are terminally differentiated muscle cells.

3. The use of claim 1, wherein the muscle cells comprise a dysregulated *D4Z4* array at chromosome 4q35.

4. The use of claim 1, wherein the facioscapuloumeral muscular dystrophy is FSHD type 1 (FSHD1).

5. The use of claim 4, wherein the muscle cells comprise a deletion of one or more macrosatellite *D4Z4* repeats in the subtelomeric region of chromosome 4q35.

6. The use of claim 5, wherein the muscle cell comprises less than 11 macrosatellite *D4Z4* repeats in the subtelomeric region of chromosome 4q35.

7. The use of claim 1, wherein the facioscapuloumeral muscular dystrophy is FSHD type 2 (FSHD2).

8. The use of claim 7, wherein the muscle cells comprise one or more mutations in a *Structural Maintenance Of Chromosomes Flexible Hinge Domain Containing 1 (SMCHD1) gene.*

9. The use of claim 1, wherein the muscle cells comprise at least one non-deleted 4qA allele.

10. The use of claim 1, wherein administration of the p38 kinase inhibitor causes a decrease in muscle degeneration in the subject.

11. The use of claim 1, wherein administration of the p38 kinase inhibitor causes a reduction in apoptosis of muscle cells in the subject.

12. The use of claim 1, wherein another p38 kinase inhibitor agent is to be further administered to the subject.