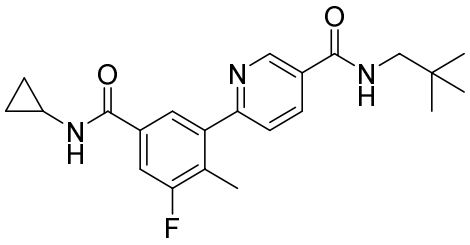
or a stereoisomer thereof, an isotopically-enriched compound thereof, a prodrug thereof, a solvate thereof, or a pharmaceutically acceptable salt thereof. The method includes the treatment of disorders associated with DUX4 gene expression, wherein the inhibition of p38 kinase with a p38 kinase inhibitor 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; ~~and wherein administration of the p38 kinase inhibitor reduces expression levels of a DUX4 polypeptide and/or a polypeptide encoded by a DUX4 downstream gene in muscle cells of the subject~~.

**[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.

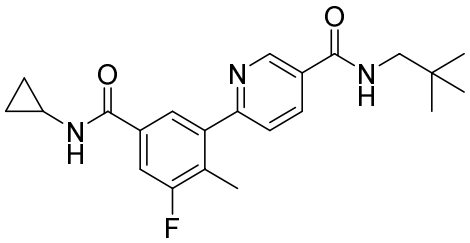
**[0010]** In one example, a method for treating a disorder responsive to p38 kinase inhibition is provided. The method includes administering to a subject in need thereof, an effective amount of a p38 kinase inhibitor selected from one or more of the following Formulae I′-XXIX′:

## 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~~; and~~

~~wherein administration of the p38 kinase inhibitor reduces expression levels of a DUX4 polypeptide and/or a polypeptide encoded by a DUX4 downstream gene in muscle cells of the subject~~.

~~2. The use of claim 1, wherein the DUX4 downstream gene is selected from the group consisting of: ZSCAN4, LEUTX, PRAMEF2, TRIM43, MBD3L2, KHDC1L, RFPL2, CCNA1, SLC34A2, TPRX1, PRAMEF20, TRIM49, PRAMEF4, PRAME6, PRAMEF15, and ZNF280A.~~

~~3.~~2. The use of claim 1, wherein the muscle cells are terminally differentiated muscle cells.

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

~~5.~~4. The use of claim 1, wherein the facioscapuloumeral muscular dystrophy is FSHD type 1 (FSHD1).

~~6.~~5. The use of claim ~~4~~5, wherein the muscle cells comprise a deletion of one or more macrosatellite *D4Z4* repeats in the subtelomeric region of chromosome 4q35.

~~7.~~6. The use of claim ~~5~~6, wherein the muscle cell comprises less than 11 macrosatellite *D4Z4* repeats in the subtelomeric region of chromosome 4q35.

~~8.~~7. The use of claim 1, wherein the facioscapuloumeral muscular dystrophy is FSHD type 2 (FSHD2).

~~9.~~8. The use of claim ~~7~~8, wherein the muscle cells comprise one or more mutations in a *Structural Maintenance Of Chromosomes Flexible Hinge Domain Containing 1 (SMCHD1) gene.*

~~10.~~9. The use of claim 1, wherein the muscle cells comprise at least one non-deleted 4qA allele.

~~11.~~10. The use of claim 1, wherein administration of the p38 kinase inhibitor causes a decrease in muscle degeneration in the subject.

~~12.~~11. The use of claim 1, wherein administration of the p38 kinase inhibitor causes a reduction in apoptosis of muscle cells in the subject.

~~13. The use of claim 1, wherein the compound of Formula V′ or the pharmaceutically acceptable salt thereof is to be administered at a dose of 7.5 mg or 15 mg.~~

~~14. The use of claim 1, wherein the compound of Formula V′ or the pharmaceutically acceptable salt thereof is to be administered at a dose of 7.5 mg.~~

~~15. The use of claim 13, wherein the compound of Formula V′ or the pharmaceutically acceptable salt thereof is to be administered at a dose of 15 mg.~~

~~16. The use of claim 13, wherein the compound of Formula V′ or the pharmaceutically acceptable salt thereof is to be administered two times per day.~~

~~17. The use of claim 1, wherein the compound or the pharmaceutically acceptable salt thereof is to be administered to the subject parenterally.~~

~~18. The use of claim 1, wherein the compound or the pharmaceutically acceptable salt thereof is to be administered to the subject orally.~~

~~19~~12. The use of claim 1, wherein another p38 kinase inhibitor agent is to be further administered to the subject.