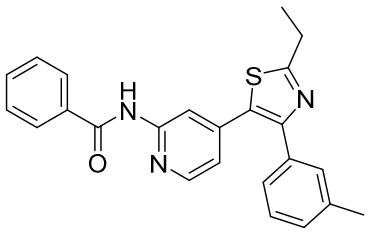
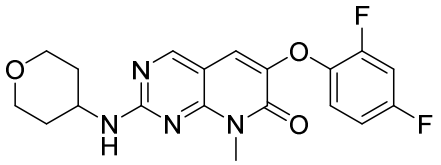
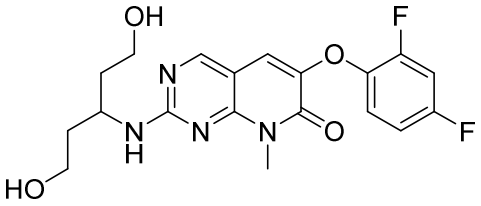
[0010a] In one example, the present disclosure refers to use of a p38 kinase inhibitor in the manufacture of a medicament for treating facioscapulohumeral muscular dystrophy (FSHD) in a subject in need thereof, wherein the p38 kinase inhibitor is selected from:



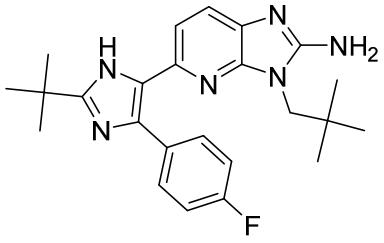
(I')



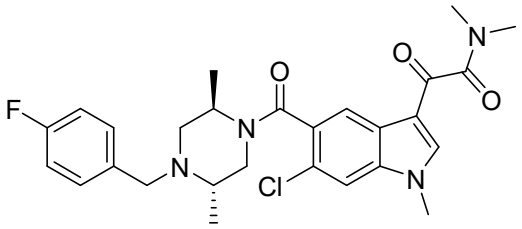
(IIIa')
"R1487"
,



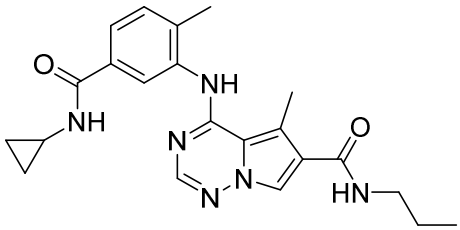
or "RO 4492257"



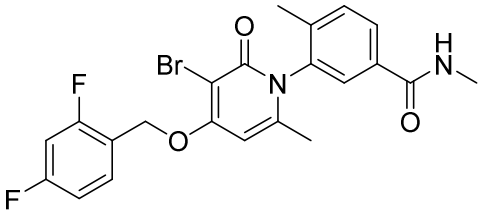
(VI')
"LY2228820" or "ralimetinib"
,

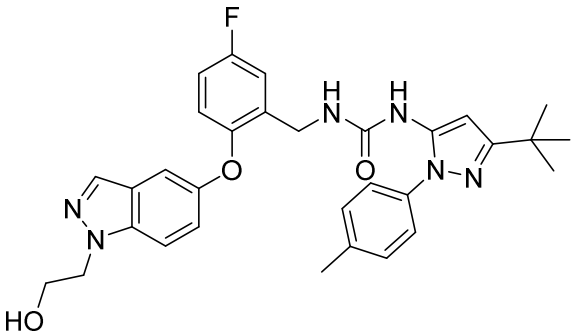


(VII')
"SCIO-469" or "talmapimod"

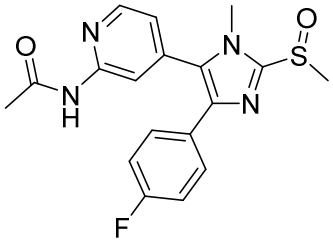


or
,

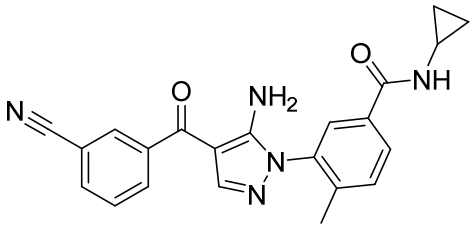




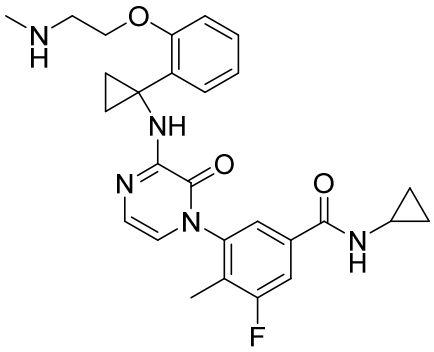
or "ARRY-614"
,



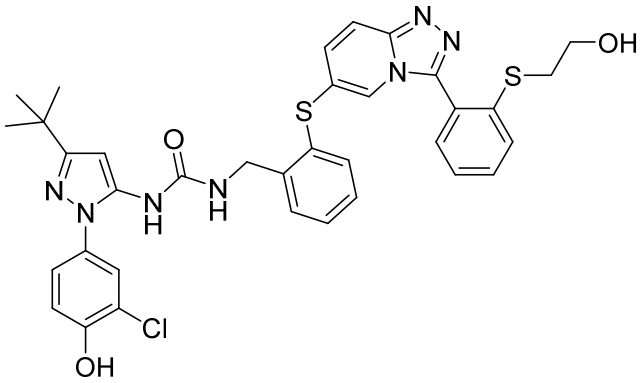
(XXVI')
"CBS-3595" or "ML-3595" ,



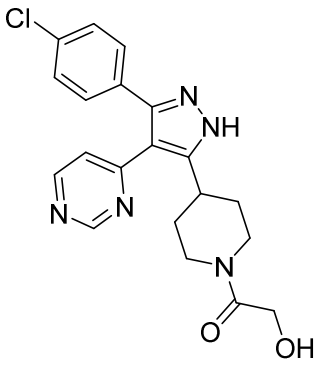
(XXVII')
"acumapimod" or "BCT-197" ,



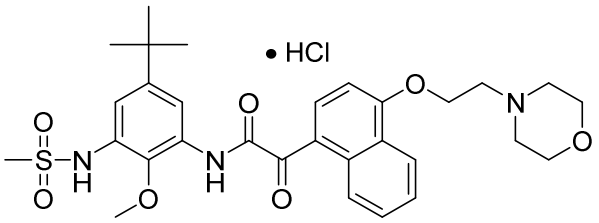
"AZD-7624" ,



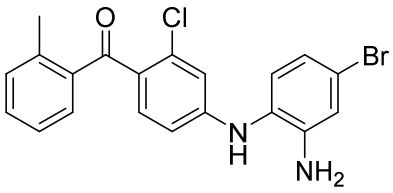
"PF-03715455" ,



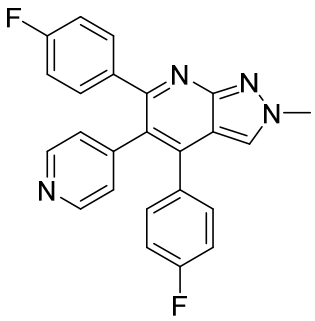
SC80036 ,



ITX-5061 ,



EO-1428 , and



UR-13870 ,

or a pharmaceutically acceptable salt thereof; 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.

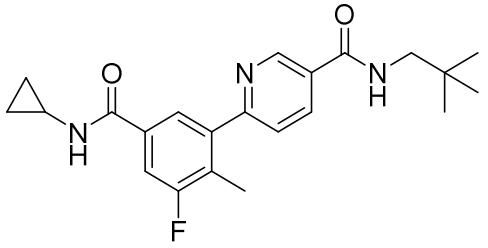
[0010b] In one example, the present disclosure refers to use of a p38 kinase inhibitor in the manufacture of a medicament for reducing expression levels of a DUX4 polypeptide and/or a polypeptide encoded by a DUX4 downstream gene in muscle cells in a subject in need thereof, wherein the p38 kinase inhibitor is selected from:

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

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

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

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

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

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

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

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

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

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