2-methylpyrimidin-4-yl)-6,6-dimethyl-1,4,5,6-tetrahydropyrrolo[3,4-c]pyrazol-3-amine, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

[0018a] One embodiment provides a use of a pharmaceutical composition comprising 5-{[(2S,5R)-2,5-Dimethyl-4-(tetrahydro-2H-pyran-4-ylmethyl)piperazin-1-yl]carbonyl}-N-(5-fluoro-2-methylpyrimidin-4-yl)-6,6-dimethyl-1,4,5,6-tetrahydropyrrolo[3,4-c]pyrazol-3-amine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating autoimmune or alloimmune disease selected from the group consisting of rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, optic neuritis, neuromyelitis optica, Sjögren's syndrome, psoriasis, systemic scleroderma, ankylosing spondylitis, autoimmune hepatitis, graft vs host disease, and organ transplant rejection.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] Figure 1 illustrates the body weight change in grams from day 17 to day 35 in a rheumatoid arthritis mouse model;

Figure 2 illustrates the percent change in body weight from baseline day 17 in a rheumatoid arthritis mouse model;

Figure 3 illustrates the body weight change in grams from study day 17 in a rheumatoid arthritis mouse model;

Figure 4 illustrates the clinical arthritis score for all paws in a rheumatoid arthritis mouse model;

Figure 5 illustrates the clinical arthritis score with AUC calculation for all paws in a rheumatoid arthritis mouse model; and

Figure 6 illustrates the percent incidence over time in a rheumatoid arthritis mouse model.

Figure 7 illustrates efficacy of compound A in reducing urine score in a MRL/lpr lupus model;

Figure 8 illustrates efficacy of compound A in reducing lymphadenopathy in a MRL/lpr lupus model;

Figure 9 illustrates efficacy of compound A in reducing splenomegaly in a MRL/lpr lupus model;

Figure 10 illustrates efficacy of compound A in treatment of increased spleen weight;

Figure 11 illustrates efficacy of compound A in a rat model of encephalitis;

Figure 12 illustrates clinical scores after administration of compound A in a rat uveitis model; and

Figure 13 illustrates histological scores of compound A in a rat uveitis model.

INCORPORATION BY REFERENCE

[0020] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference for the specific purposes identified herein.

DETAILED DESCRIPTION OF THE INVENTION

Certain Terminology

[0021] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in the art to which the claimed subject matterbelongs. It is to be understood that the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of any subject matter claimed. In this application, the use of the singular includes the plural unless specifically stated otherwise. It must be noted that, as used in the specification and the appended claims, the singular forms "a," "an" and "the" include plural referents unless the context clearly dictates otherwise. In

CLAIMS

1. Use of a pharmaceutical composition comprising 5-{[(2S,5R)-2,5-Dimethyl-4-(tetrahydro-2H-pyran-4-ylmethyl)piperazin-1-yl]carbonyl}-N-(5-fluoro-2-methylpyrimidin-4-yl)-6,6-dimethyl-1,4,5,6-tetrahydropyrrolo[3,4-c]pyrazol-3-amine, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating autoimmune or alloimmune disease selected from the group consisting of rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, optic neuritis, neuromyelitis optica, Sjögren's syndrome, psoriasis, systemic scleroderma, ankylosing spondylitis, autoimmune hepatitis, graft vs host disease, and organ transplant rejection.

2. The use of claim 1, wherein the autoimmune or alloimmune disease is rheumatoid arthritis.

3. The use of claim 2, wherein the rheumatoid arthritis is rheumatoid factor positive (seropositive) RA, rheumatoid factor negative (seronegative) RA, or juvenile RA.

4. The use of claim 1, wherein the autoimmune or alloimmune disease is multiple sclerosis.

5. The use of claim 4, wherein the multiple sclerosis is relapsing-remitting (RR) multiple sclerosis, secondary progressive (SP) multiple sclerosis, primary progressive (PP) multiple sclerosis, progressive relapsing multiple sclerosis, clinically isolated syndrome (CIS), or radiologically isolated syndrome (RIS).

6. The use of claim 1, wherein the autoimmune or alloimmune disease is inflammatory bowel disease.

7. The use of claim 6, wherein the inflammatory bowel disease is Crohn's disease, ulcerative colitis, collagenous colitis, lymphocytic colitis, diversion colitis, Behçet's disease, or indeterminate colitis.

8. The use of claim 1 or 7, wherein the autoimmune or alloimmune disease is Crohn's disease.

9. The use of claim 1 or 7, wherein the autoimmune or alloimmune disease is ulcerative colitis.

10. The use of claim 1, wherein the autoimmune or alloimmune disease is optic neuritis.

11. The use of claim 10, wherein the optic neuritis is papillitis neuritis or retrobulbar neuritis.

12. The use of claim 1, wherein the autoimmune or alloimmune disease is neuromyelitis optica.

13. The use of claim 1, wherein the autoimmune or alloimmune disease is Sjögren's syndrome.

14. The use of claim 1, wherein the autoimmune or alloimmune disease is psoriasis.

15. The use of claim 1, wherein the autoimmune or alloimmune disease is systemic scleroderma.

16. The use of claim 1, wherein the autoimmune or alloimmune disease is ankylosing spondylitis.

17. The use of claim 1, wherein the autoimmune or alloimmune disease is autoimmune hepatitis.

18. The use of claim 1, wherein the autoimmune or alloimmune disease is graft vs host disease.

19. The use of claim 18, wherein the graft vs host disease is acute graft vs host disease, or chronic graft vs host disease.

20. The use of claim 1, wherein the autoimmune or alloimmune disease is organ transplant rejection.