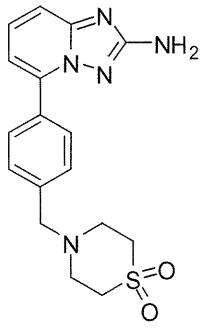
associated with hypersecretion of IL6 or interferons, in particular rheumatoid arthritis, by administering the compound as described herein according to Formula I.

[0024] Accordingly, in a first aspect as described herein, a compound as described herein is provided for use in medicine having a Formula I:

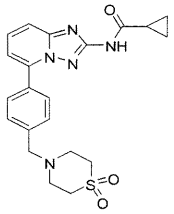


I

[0025] The compound according to Formula I, surprisingly, exhibits *in vivo* in human a very different profile from other animal species, which contrasts with *in vitro* predictions. Indeed, *in vivo* it has been demonstrated that in human, the apparent terminal half life of the compound according to Formula I is significantly longer than in the other animal species by at least 3 fold. This causes accumulation in human resulting in a maintained therapeutic effect over an extended period of time, thereby allowing once daily to once weekly dosing. Thus the compound according to Formula I may provide advantages including a low frequency dosage regimen and / or increased patient compliance. In particular, the impact of non adherence, if the patient misses a dose, might be reduced.

[0026] In a particular aspect, the compound according to Formula I is provided for use in the prophylaxis and / or treatment of inflammatory conditions, autoimmune diseases, proliferative diseases, allergy, transplant rejection, diseases involving impairment of cartilage turnover, congenital cartilage malformations, and/or diseases associated with hypersecretion of IL6 or interferons, in particular rheumatoid arthritis.

[0027] In a further aspect, the present disclosure provides pharmaceutical compositions comprising the compound of the invention according to Formula I, and a pharmaceutical carrier, excipient or diluent, which additionally comprises an additional therapeutic agent wherein the additional therapeutic agent is according to Formula II:



II

In a particular ~~example aspect~~, the pharmaceutical composition may additionally comprise further therapeutically active ingredients suitable for use in combination with the compound according to Formula I. In a more particular ~~exampleaspect~~, the further therapeutically active ingredient is a compound for the treatment of arthritis. In a most particular ~~example aspect~~, the further therapeutically active ingredient is a compound for the treatment of rheumatoid arthritis.

[0028] Moreover, the compound according to Formula I, useful in the pharmaceutical compositions and treatment methods disclosed herein, is pharmaceutically acceptable as prepared and used.

[0029] In a further aspect, there is provided use of a therapeutically effective amount of a compound as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for the prophylaxis and/or treatment of a mammal susceptible to or afflicted with a condition selected from inflammatory conditions, autoimmune diseases, proliferative diseases, uterine leiomyosarcoma, prostate cancer, polycythemia vera, essential thrombocytosis, myelofibrosis, acute myeloid leukaemia, acute lymphoblastic leukemia, multiple myeloma, psoriasis, restenosis, sclerodermitis, fibrosis, allergy, transplant rejection, diseases involving impairment of cartilage turnover, congenital cartilage malformations, ~~and/or~~ diseases associated with hypersecretion of IL6 or interferons, Castleman's disease, multiple myeloma, Kaposi's sarcoma, mesangial proliferative glomerulonephritis, systemic and cutaneous lupus erythematosis, lupus nephritis, dermatomyositis, Sjogren's syndrome, and/or rheumatoid arthritis, more particularly rheumatoid arthritis , wherein said compounds, JAK inhibitor and said pharmaceutical composition exhibit demonstrable activity *in vivo*. Also disclosed is a method of treating a mammal, in particular humans, susceptible to or afflicted with a condition selected from among those listed herein, and particularly inflammatory conditions, autoimmune diseases, proliferative diseases, allergy, transplant rejection, diseases involving impairment of cartilage turnover, congenital cartilage malformations, and/or diseases associated with hypersecretion of IL6 or interferons, more particularly rheumatoid arthritis, which method comprises administering a therapeutically effective amount of the pharmaceutical composition or compound of the invention according to Formula I as described herein.

[0030] The present disclosure also provides pharmaceutical compositions comprising the compound according to Formula I, and a suitable pharmaceutical carrier, excipient or diluent for use in medicine. In a particular aspect, the pharmaceutical composition is for use in the prophylaxis and/or treatment of inflammatory conditions, autoimmune diseases, proliferative diseases, allergy, transplant rejection, diseases involving impairment of cartilage turnover, congenital cartilage malformations, and/or diseases associated with hypersecretion of IL6 or interferons, in particular rheumatoid arthritis.

[0031] In additional examples ~~aspects~~, this present disclosure provides methods for synthesizing the compound according to Formula I, with representative synthetic protocols and pathways disclosed later on herein.

[0032] Other objects and advantages will become apparent to those skilled in the art from a consideration of the ensuing detailed description.

BRIEF DESCRIPTION OF THE DRAWINGS

[0033] **Figure 1:** Shows the rat CIA Clinical Score after treatment with the compounds disclosed herein.

[0034] **Figure 2:** Shows the evolution of ankle diameter in the rat CIA model after treatment with the compounds disclosed herein.

[0035] **Figure 3:** Shows the *in vitro* metabolic profile of the compound according to Formula II

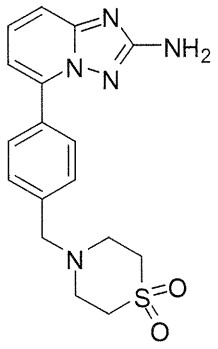
[0036] **Figure 4:** Shows the ratio of exposure (expressed as AUC) for Formula I:Formula II measured on administration of the compound according to Formula II.

[0037] **Figure 5:** Shows the values for the exposure levels of the disclosed compounds after administration of the compound according to Formula II expressed as a multiple of the IC_{50} value.

[0038] **Figure 6:** Shows the combined values for the exposure levels over a 24h period of the compounds according to Formula I and Formula II after administration of the compound according to Formula II expressed as a multiple of the IC_{50} value.

CLAIMS

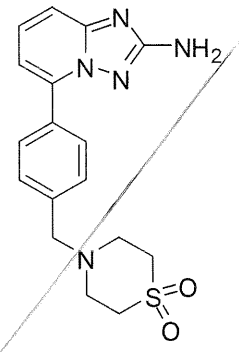
1. A compound according to Formula I:



I

or a pharmaceutically acceptable salt thereof, or a solvate or a pharmaceutically acceptable salt of a solvate, for use in medicine.

2. A compound according to Formula I:

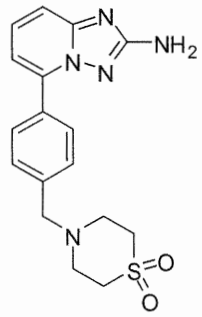


I

or a pharmaceutically acceptable salt thereof, or a solvate or a pharmaceutically acceptable salt of a solvate, for use in the treatment of inflammatory conditions, autoimmune diseases, proliferative diseases, allergy, transplant rejection, diseases involving impairment of cartilage turnover, congenital cartilage malformations, and/or diseases associated with hypersecretion of IL6 or interferons.

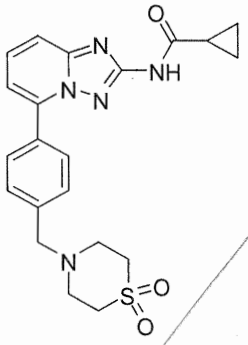
3. The compound according to claim 2 for use in the treatment of rheumatoid arthritis.
4. The compound according to claim 2 for use in the treatment of inflammatory bowel diseases.
5. The compound according to claim 2 for use in the treatment of psoriasis and/or psoriatic arthritis.
6. The compound for use according to any one of claims 1-5, in combination with another therapeutic agent.
7. The compound for use according to claim 6, wherein the further therapeutic agent is a rheumatoid arthritis treating agent.

~~8. A pharmaceutical composition, comprising a compound according to Formula I:~~



I

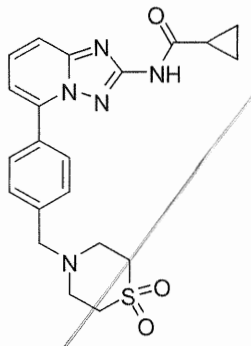
and a pharmaceutically acceptable carrier, excipient or diluent, which additionally comprises an additional therapeutic agent wherein the additional therapeutic agent is according to Formula II:



II

9. The pharmaceutical composition according to claim 8, wherein the ratio of Formula I/Formula II is from 1/5 to 1/20.
10. The pharmaceutical composition according to claim 8, wherein the ratio of Formula I/Formula II is from 1/5 to 1/10.
11. The pharmaceutical composition according to any one of claims 8-10, for use in medicine.
12. The pharmaceutical composition according to any one of claims 8-10, for use in the treatment of inflammatory conditions, autoimmune diseases, proliferative diseases, allergy, transplant rejection, diseases involving impairment of cartilage turnover, congenital cartilage malformations, and/or diseases associated with hypersecretion of IL6 or interferons.
13. The pharmaceutical composition according to any one of claims 8-10, for use in the treatment of rheumatoid arthritis.
14. The pharmaceutical composition according to any one of claims 8-10, for use in the treatment of inflammatory bowel diseases.
15. The pharmaceutical composition according to any one of claims 8-10, for use in the treatment of psoriasis and/or psoriatic arthritis.

16. Use of a therapeutically effective amount of a compound of claims 1-7, or the pharmaceutical composition of claims 8-10 in the manufacture of a medicament for the prophylaxis and/or treatment of a mammal susceptible to or afflicted with a condition selected from inflammatory conditions, autoimmune diseases, proliferative diseases, allergy, transplant rejection, diseases involving impairment of cartilage turnover, congenital cartilage malformations, and/or diseases associated with hypersecretion of IL6 or interferons, more particularly rheumatoid arthritis , wherein said compounds, JAK inhibitor and said pharmaceutical composition exhibit demonstrable activity *in vivo*.
17. The use according to claim 16, wherein the said compounds, JAK inhibitor and said pharmaceutical composition are to be administered in combination with one or more additional therapeutic agents.
18. The use according to claim 17, wherein said additional therapeutic agent is a rheumatoid arthritis treating agent.
19. The use according to claim 17, wherein the additional therapeutic agent is according to Formula II:

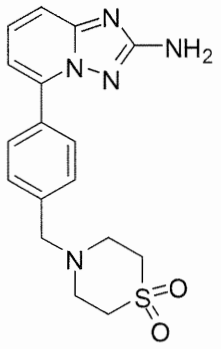


II

20. The use according to claim 19, wherein the ratio of Formula I/Formula II is from 1/5 to 1/20.
21. The use according to claim 19, wherein the ratio of Formula I/Formula II is from 1/5 to 1/10.
22. The use according to any of claims 16-21, wherein the mammal is a human.

CLAIMS

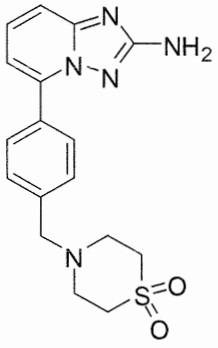
1. A compound according to Formula I:



I

or a pharmaceutically acceptable salt thereof, or a solvate or a pharmaceutically acceptable salt of a solvate, for use in medicine.

2. A compound according to Formula I:

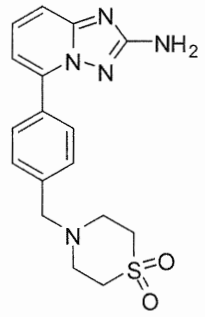


I

or a pharmaceutically acceptable salt thereof, or a solvate or a pharmaceutically acceptable salt of a solvate, for use in the treatment of inflammatory conditions, autoimmune diseases, proliferative diseases, allergy, transplant rejection, diseases involving impairment of cartilage turnover, congenital cartilage malformations, and/or diseases associated with hypersecretion of IL6 or interferons.

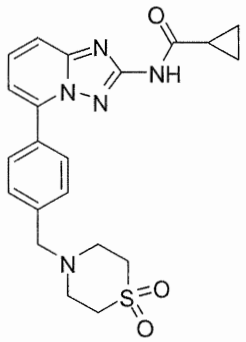
3. The compound according to claim 2 for use in the treatment of rheumatoid arthritis.
4. The compound according to claim 2 for use in the treatment of inflammatory bowel diseases.
5. The compound according to claim 2 for use in the treatment of Crohn's disease and/or colitis.
6. The compound according to claim 2 for use in the treatment of ankylosing spondylitis, psoriasis and/or psoriatic arthritis.
7. The compound for use according to any one of claims 1-6, in combination with another therapeutic agent.

8. The compound for use according to claim 7, wherein the further therapeutic agent is a rheumatoid arthritis treating agent.
9. A pharmaceutical composition, comprising a compound according to Formula I:



I

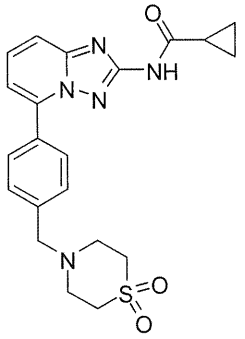
and a pharmaceutically acceptable carrier, excipient or diluent, which additionally comprises an additional therapeutic agent wherein the additional therapeutic agent is according to Formula II:



II

10. The pharmaceutical composition according to claim 9, wherein the ratio of Formula I/Formula II is from 1/5 to 1/20.
11. The pharmaceutical composition according to claim 9, wherein the ratio of Formula I/Formula II is from 1/5 to 1/10.
12. The pharmaceutical composition according to any one of claims 9-11, for use in medicine.
13. The pharmaceutical composition according to any one of claims 9-11, for use in the treatment of inflammatory conditions, autoimmune diseases, proliferative diseases, allergy, transplant rejection, diseases involving impairment of cartilage turnover, congenital cartilage malformations, and/or diseases associated with hypersecretion of IL6 or interferons.
14. The pharmaceutical composition according to any one of claims 9-11, for use in the treatment of rheumatoid arthritis.
15. The pharmaceutical composition according to any one of claims 9-11, for use in the treatment of inflammatory bowel diseases.

16. The pharmaceutical composition according to any one of claims 9-11, for use in the treatment of Crohn's disease and/or colitis.
17. The pharmaceutical composition according to any one of claims 9-11, for use in the treatment of ankylosing spondylitis, psoriasis and/or psoriatic arthritis.
18. Use of a therapeutically effective amount of a compound of claims 1-8, in the manufacture of a medicament for the prophylaxis and/or treatment of a mammal susceptible to or afflicted with a condition selected from inflammatory conditions, autoimmune diseases, uterine leiomyosarcoma, prostate cancer, polycythemia vera, essential thrombocytosis, myelofibrosis, acute myeloid leukaemia, acute lymphoblastic leukemia, multiple myeloma, psoriasis, restenosis, sclerodermitis, fibrosis, allergy, transplant rejection, diseases involving impairment of cartilage turnover, congenital cartilage malformations, Castleman's disease, multiple myeloma, Kaposi's sarcoma, mesangial proliferative glomerulonephritis, systemic and cutaneous lupus erythematosis, lupus nephritis, dermatomyositis, Sjogren's syndrome, and/or rheumatoid arthritis, more particularly rheumatoid arthritis , wherein said compounds, JAK inhibitor exhibit demonstrable activity *in vivo*.
19. The use according to claim 18, wherein the said compound, JAK inhibitor is to be administered in combination with one or more additional therapeutic agents.
20. The use according to claim 19, wherein said additional therapeutic agent is a rheumatoid arthritis treating agent.
21. The use according to claim 19, wherein the additional therapeutic agent is according to Formula II:



II

22. The use according to claim 21, wherein the ratio of Formula I/Formula II is from 1/5 to 1/20.
23. The use according to claim 21, wherein the ratio of Formula I/Formula II is from 1/5 to 1/10.
24. The use according to any of claims 18-23, wherein the mammal is a human.