SUMMARY

In one aspect, the present disclosure refers to use of a pharmaceutical dosage form comprising a therapeutically effective amount of (*R*)-2-(7-(4-cyclopentyl-3-(trifluoromethyl)benzyloxy)-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)acetic acid (Compound 1), or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating an individual with Crohn's Disease;

wherein said individual has moderately to severely active Crohn's Disease; and

wherein the individual has demonstrated an inadequate response to, loss of response to, or intolerance of to at least one agent for the treatment of Crohn's Disease chosen from glucocorticosteroids, immunosuppressants, and biologics; and

wherein the therapeutically effective amount is in an amount equivalent to 3 mg of Compound 1; and

wherein the Compound 1, or a pharmaceutically acceptable salt thereof, is to be administered orally; and

wherein the therapeutically effective amount of Compound 1, or a pharmaceutically acceptable salt thereof, is to be administered once daily to the individual.

Also provided is a method of treating an individual with moderately to severely active Crohn's Disease comprising: administering to the individual in need thereof a pharmaceutical dosage form comprising a therapeutically effective amount of (*R*)-2-(7-(4-cyclopentyl-3-(trifluoromethyl)benzyloxy)-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)acetic acid (Compound 1), or a pharmaceutically acceptable salt thereof.

In some examples, a compound that is (R)-2-(7-(4-cyclopentyl-3-(trifluoromethyl)benzyloxy)-1,2,3,4-tetrahydrocyclopenta[b]indol-3-yl)acetic acid (Compound 1), or a pharmaceutically acceptable salt thereof, is for use in a method of treatment of Crohn's Disease in an individual, wherein the method of use includes administering an induction dose of the compound to the individual for an induction phase, wherein the induction phase is at least 14 weeks long, and administering a maintenance dose of the compound to the individual for a maintenance phase. In some examples, the induction dose comprises an amount equivalent to 3 mg of Compound 1. In some examples, the maintenance dose comprises an amount equivalent to 2 mg of Compound 1. In some examples, the maintenance phase is at least 38 weeks. In some examples, the compound is administered at a frequency of once a day during both the induction phase and the maintenance phase. In some examples, the individual has moderately to severely active Crohn's Disease.

A phase 2 study demonstrated improved efficacy for 2 mg of Compound 1 over placebo in subjects with UC. However, a Phase 2 study with another selective S1P receptor modulator (amiselimod) did not result in improved efficacy over placebo in subjects with CD (*D'Haens G et al. Amiselimod, a selective S1P receptor modulator in Crohn's disease patients: A proof-of-concept study. J Crohn Colitis. 2019;13(Suppl):S055-S056*). Further, while UC and CD have overlapping features, there are differences in pathophysiology, disease location, and extent of disease that may dictate different doses for the treatment of UC and CD. Described herein is the elucidation of safe and efficacious dosing of Compound 1 for the treatment of CD.

These and other aspects of the disclosure disclosed herein will be set forth in greater detail as the patent disclosure proceeds.

CLAIMS

What is claimed is:

1. Use of a pharmaceutical dosage form comprising a therapeutically effective amount of (*R*)-2-(7-(4-cyclopentyl-3-(trifluoromethyl)benzyloxy)-1,2,3,4-tetrahydrocyclopenta[*b*]indol-3-yl)acetic acid (Compound 1), or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating an individual with Crohn's Disease;

wherein said individual has moderately to severely active Crohn's Disease;

and

wherein the individual has demonstrated an inadequate response to, loss of response to, or intolerance of to at least one agent for the treatment of Crohn's Disease chosen from glucocorticosteroids, immunosuppressants, and biologics;

and

wherein the therapeutically effective amount is in an amount equivalent to 3 mg of Compound 1;

and

wherein the Compound 1, or a pharmaceutically acceptable salt thereof, is to be administered orally;

and

wherein the therapeutically effective amount of Compound 1, or a pharmaceutically acceptable salt thereof, is to be administered once daily to the individual.

2. The use of claim 1, wherein the dosage form is to be administered under fasted conditions.

3. The use of claim 1, wherein the dosage form is to be administered under fed conditions.

4. The use of any one of the preceding claims, wherein the Compound 1, or a pharmaceutically acceptable salt thereof, is formulated as a capsule or tablet suitable for oral administration.

5. The use of any one of the preceding claims, wherein the Compound 1, or a pharmaceutically acceptable salt thereof, is an L-arginine salt of Compound 1.

6. The use of any one of the preceding claims, wherein the individual was previously administered at least one agent selected from: a TNFα antagonist, an integrin antagonist, and an immunosuppressive agent.

7. The use of any one of the preceding claims, wherein said individual has severely active Crohn's Disease.