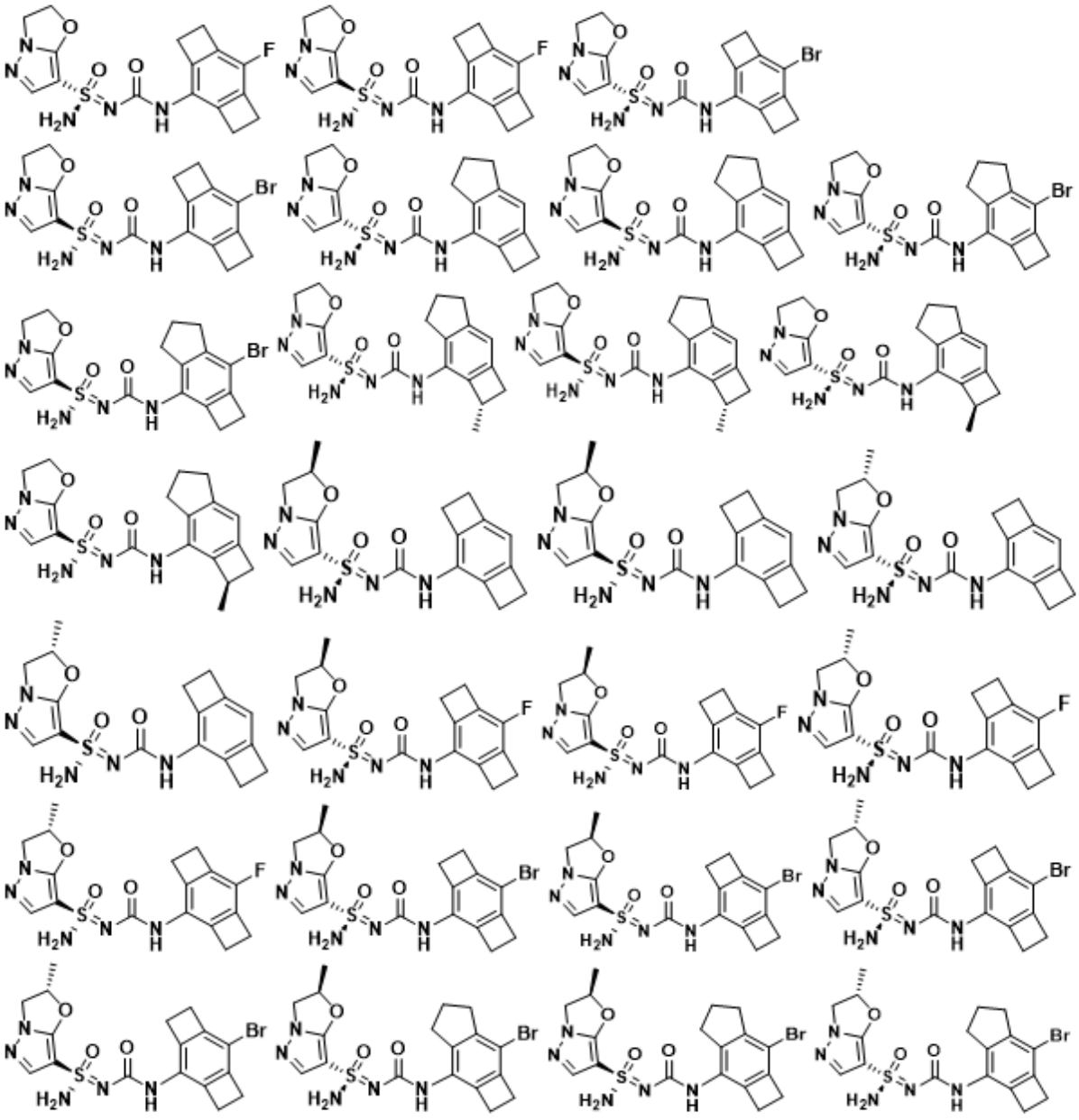
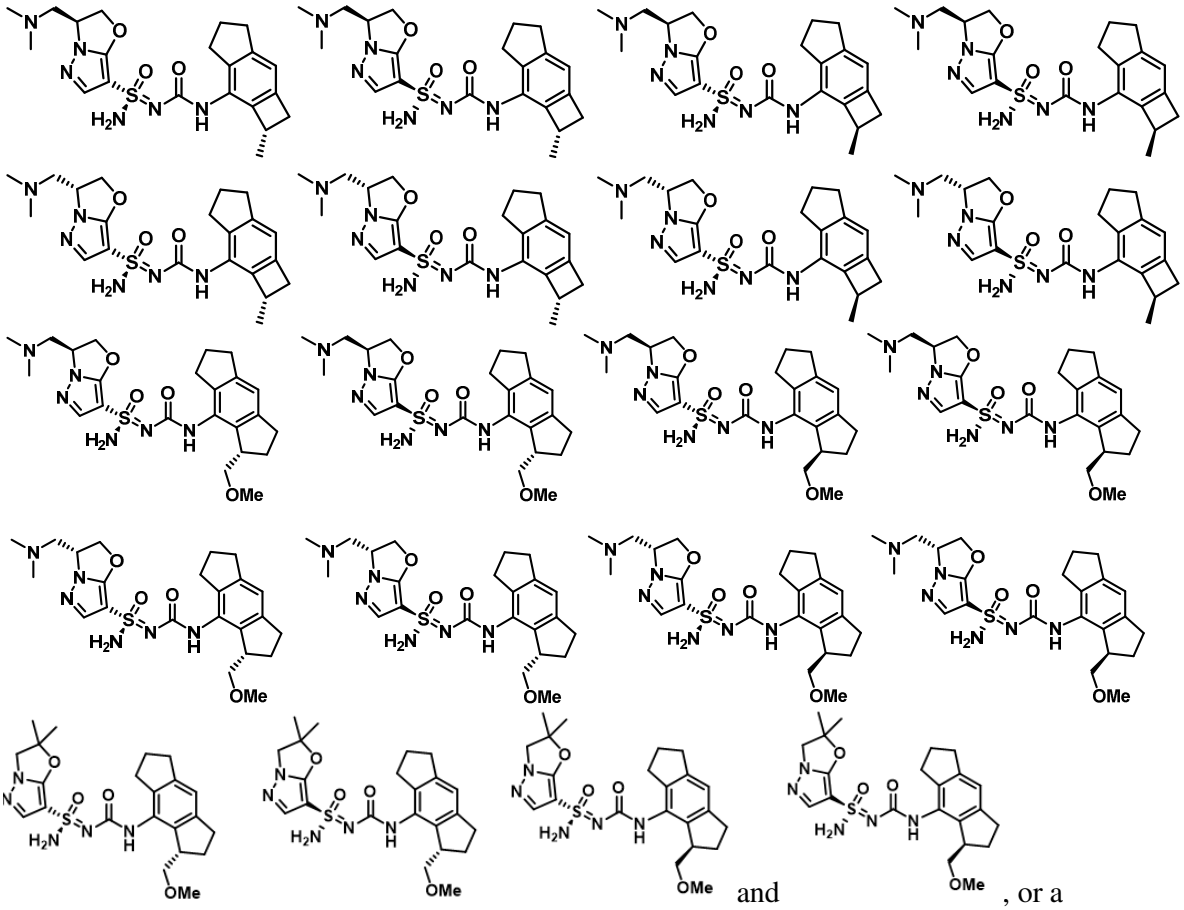
deposition of islet amyloid polypeptide in the pancreas activates NLRP3 and IL-1β signaling, resulting in cell death and inflammation.

[0011] There is a need to provide compounds and pharmaceutical compositions with improved pharmacological and/or physiological and/or physicochemical properties and/or those that provide a useful alternative to known compounds and pharmaceutical compositions.

BRIEF SUMMARY ~~OF THE INVENTION~~

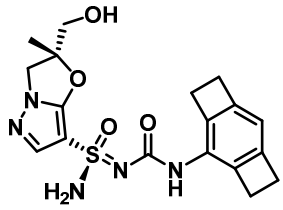
[0012] In some ~~aspects~~examples, provided herein is a compound selected from the group consisting of:





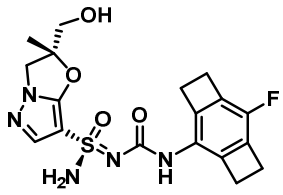
and , or a solvate, tautomer, or pharmaceutically acceptable salt thereof.

[0012a] In one aspect, the disclosure provides a compound, wherein the compound is:



, or a pharmaceutically acceptable salt thereof.

[0012b] In one aspect, the disclosure provides a compound, wherein the compound is:



, or a pharmaceutically acceptable salt thereof.

[0012c] In one aspect, the disclosure provides a pharmaceutical composition, comprising the compound as disclosed herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

[0012d] In one aspect, the disclosure provides a pharmaceutical composition, comprising the compound as disclosed herein, and a pharmaceutically acceptable excipient.

[0012e] In one aspect, the disclosure provides use of the compound as disclosed herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disorder in a subject in need thereof.

[0012f] In one aspect, the disclosure provides use of the compound as disclosed herein in the manufacture of a medicament for treating a disorder in a subject in need thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] **FIG. 1** is a graph plotting Percent Human PXR Activation @10 µM vs. IC90 in Human Whole Blood (µM) of two compounds of the present disclosure, Compounds 2 and 6, as compared to other sulfonimidamide (SIA) compounds.

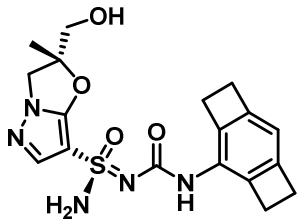
[0014] **FIG. 2** is a graph plotting % Rat Bioavailability vs. IC90 in Human Whole Blood (µM) of two compounds of the present disclosure, Compounds 2 and 6, as compared to other sulfonimidamide (SIA) compounds.

[0015] **FIG. 3** is a graph plotting Rat Half Life (h) vs. IC90 in Human Whole Blood (µM) of two compounds of the present disclosure, Compounds 2 and 6, as compared to other sulfonimidamide (SIA) compounds.

CLAIMS

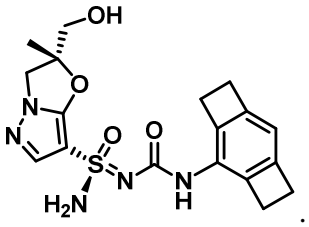
What is claimed is:

Claim 1. A compound, wherein the compound is:



, or a ~~solvate, tautomer, or~~ pharmaceutically acceptable salt thereof.

Claim 2. The compound of claim 1, wherein the compound is:



.

Claim 3. A pharmaceutical composition, comprising the compound of claim 1, or a ~~solvate, tautomer, or~~ pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

Claim 4. A pharmaceutical composition, comprising the compound of claim 2, and a pharmaceutically acceptable excipient.

Claim ~~4~~5. Use of the compound of claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for ~~A method of~~ treating a disorder in a subject in need thereof~~, comprising administering to the subject an effective amount of the compound of claim 1, or a solvate, tautomer, or pharmaceutically acceptable salt thereof~~.

Claim ~~5~~6. Use of the compound of claim 2 in the manufacture of a medicament for ~~A method of~~ treating a disorder in a subject in need thereof~~, comprising administering to the subject an effective amount of the pharmaceutical composition of claim 3~~.

~~Claim 6. The method of claim 4 or claim 5, wherein the disorder is responsive to inhibition of activation of the NLRP3 inflammasome.~~

Claim 7. The ~~method~~ use of ~~any one of claims 4 to~~claim 5 or claim 6, wherein the disorder is a disorder of the immune system, a disorder of the liver, a disorder of the lung, a disorder of the skin, a disorder of the cardiovascular system, a disorder of the renal system, a disorder of the gastrointestinal tract, a disorder of the respiratory system, a disorder of the endocrine system, a disorder of the central nervous system (CNS), an inflammatory disorder, an autoimmune disorder, or a cancer, tumor, or other malignancy.

Claim 8. The ~~method~~ use of any one of claims 5~~4~~ to 7, wherein the disorder is a bacterial infection, a viral infection, a fungal infection, inflammatory bowel disease, celiac disease, colitis, intestinal hyperplasia, cancer, metabolic syndrome, obesity, rheumatoid arthritis, liver disease, hepatic steatosis, fatty liver disease, liver fibrosis, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), lupus, lupus nephritis, cryopyrin-associated periodic syndromes (CAPS), myelodysplastic syndromes (MDS), gout, myeloproliferative neoplasms (MPN), atherosclerosis, Crohn's disease, or inflammatory bowel disease (IBD).

Claim 9. The use of any one of claims 5 to 8, wherein the subject is a human.

~~Claim 9. A compound of claim 1, or a solvate, tautomer, or pharmaceutically acceptable salt thereof, for use in the treatment of a disorder in a subject in need thereof.~~

~~Claim 10. The pharmaceutical composition of claim 3, for use in the treatment of a disorder in a subject in need thereof.~~

~~Claim 11. Use of a compound of claim 1, or a solvate, tautomer, or pharmaceutically acceptable salt thereof, in the treatment of a disorder in a subject in need thereof.~~

~~Claim 12. Use of the pharmaceutical composition of claim 3, in the treatment of a disorder in a subject in need thereof.~~

~~Claim 13. A compound of claim 1, or a solvate, tautomer, or pharmaceutically acceptable salt thereof, for use in the manufacture of a medicament for treatment of a disorder in a subject in need thereof.~~

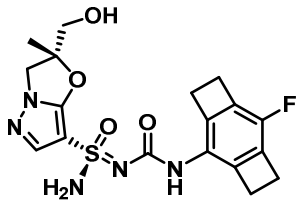
~~Claim 14. A pharmaceutical composition of claim 3, for use in the manufacture of a medicament for treatment of a disorder in a subject in need thereof.~~

~~Claim 15. The compound for use of claim 9, pharmaceutical composition for use of claim 10, use of a compound of claim 11, use of a pharmaceutical composition of claim 12, compound for use in the manufacture of a medicament of claim 13, or pharmaceutical composition for use in the manufacture of a medicament of claim 14, wherein the disorder is responsive to inhibition of activation of the NLRP3 inflammasome.~~

~~Claim 16. The compound for use of claim 9 or 15; pharmaceutical composition for use of claim 10 or 15; use of a compound of claim 11 or 15; use of a pharmaceutical composition of claim 12 or 15; compound for use in the manufacture of a medicament of claim 13 or 15; or pharmaceutical composition for use in the manufacture of a medicament of claim 14 or 15; wherein the disorder is a disorder of the immune system, a disorder of the liver, a disorder of the lung, a disorder of the skin, a disorder of the cardiovascular system, a disorder of the renal system, a disorder of the gastro-intestinal tract, a disorder of the respiratory system, a disorder of the endocrine system, a disorder of the central nervous system (CNS), an inflammatory disorder, an autoimmune disorder, or a cancer, tumor, or other malignancy.~~

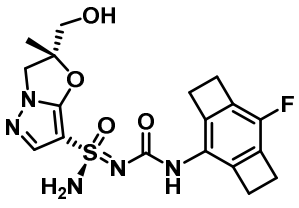
~~Claim 17. The compound for use of claim 9, 15, or 16; pharmaceutical composition for use of claim 10, 15, or 16; use of a compound of claim 11, 15, or 16; use of a pharmaceutical composition of claim 12, 15, or 16; compound for use in the manufacture of a medicament of claim 13, 15, or 16; or pharmaceutical composition for use in the manufacture of a medicament of claim 14, 15, or 16; wherein the disorder is a bacterial infection, a viral infection, a fungal infection, celiac disease, colitis, intestinal hyperplasia, cancer, metabolic syndrome, obesity, rheumatoid arthritis, liver disease, hepatic steatosis, fatty liver disease, liver fibrosis, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), lupus, lupus nephritis, cryopyrin-associated periodic syndromes (CAPS), myelodysplastic syndromes (MDS), gout, myeloproliferative neoplasms (MPN), atherosclerosis, Crohn's disease, or inflammatory bowel disease (IBD).~~

Claim 1<u>0</u>~~8~~. A compound, wherein the compound is:



, or a ~~solvate, tautomer, or~~ pharmaceutically acceptable salt thereof.

Claim ~~19~~11. The compound of claim ~~18~~10, wherein the compound is:



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Claim ~~20~~12. A pharmaceutical composition, comprising the compound of claim ~~18~~10, or a ~~solvate, tautomer, or~~ pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

Claim 13. A pharmaceutical composition, comprising the compound of claim 11, and a pharmaceutically acceptable excipient.

Claim ~~21~~14. Use of the compound of claim 10, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for ~~A method of~~ treating a disorder in a subject in need thereof~~, comprising administering to the subject an effective amount of the compound of claim 18, or a solvate, tautomer, or pharmaceutically acceptable salt thereof~~.

Claim ~~22~~15. Use of the compound of claim 11 in the manufacture of a medicament for ~~A method of~~ treating a disorder in a subject in need thereof~~, comprising administering to the subject an effective amount of the pharmaceutical composition of claim 20~~.

~~Claim 23. The method of claim 21 or 22, wherein the disorder is responsive to inhibition of activation of the NLRP3 inflammasome.~~

Claim ~~24~~16. The ~~method~~ use of ~~any one of claims 21 to 23~~claim 14 or 15, wherein the disorder is a disorder of the immune system, a disorder of the liver, a disorder of the lung, a disorder of the skin, a disorder of the cardiovascular system, a disorder of the renal system, a disorder of the gastrointestinal tract, a disorder of the respiratory system, a disorder of the endocrine system, a

disorder of the central nervous system (CNS), an inflammatory disorder, an autoimmune disorder, or a cancer, tumor, or other malignancy.

Claim ~~25~~17. The ~~method~~ use of any one of claims ~~21 to 24~~14 to 16, wherein the disorder is a bacterial infection, a viral infection, a fungal infection, inflammatory bowel disease, celiac disease, colitis, intestinal hyperplasia, cancer, metabolic syndrome, obesity, rheumatoid arthritis, liver disease, hepatic steatosis, fatty liver disease, liver fibrosis, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), lupus, lupus nephritis, cryopyrin-associated periodic syndromes (CAPS), myelodysplastic syndromes (MDS), gout, myeloproliferative neoplasms (MPN), atherosclerosis, Crohn's disease, or inflammatory bowel disease (IBD).

Claim 18. The use of any one of claims 14 to 17, wherein the subject is a human.

~~Claim 26. A compound of claim 18, or a solvate, tautomer, or pharmaceutically acceptable salt thereof, for use in the treatment of a disorder in a subject in need thereof.~~

~~Claim 27. The pharmaceutical composition of claim 20, for use in the treatment of a disorder in a subject in need thereof.~~

~~Claim 28. Use of a compound of claim 18, or a solvate, tautomer, or pharmaceutically acceptable salt thereof, in the treatment of a disorder in a subject in need thereof.~~

~~Claim 29. Use of the pharmaceutical composition of claim 20, in the treatment of a disorder in a subject in need thereof.~~

~~Claim 30. A compound of claim 18, or a solvate, tautomer, or pharmaceutically acceptable salt thereof, for use in the manufacture of a medicament for treatment of a disorder in a subject in need thereof.~~

~~Claim 31. A pharmaceutical composition of claim 20, for use in the manufacture of a medicament for treatment of a disorder in a subject in need thereof.~~

~~Claim 32. The compound for use of claim 26, pharmaceutical composition for use of claim 27, use of a compound of claim 28, use of a pharmaceutical composition of claim 29, compound for use in the manufacture of a medicament of claim 30, or pharmaceutical composition for use in~~

~~the manufacture of a medicament of claim 31, wherein the disorder is responsive to inhibition of activation of the NLRP3 inflammasome.~~

~~Claim 33. The compound for use of claim 26 or 32; pharmaceutical composition for use of claim 27 or 32; use of a compound of claim 28 or 32; use of a pharmaceutical composition of claim 29 or 32; compound for use in the manufacture of a medicament of claim 30 or 32; or pharmaceutical composition for use in the manufacture of a medicament of claim 31 or 32; wherein the disorder is a disorder of the immune system, a disorder of the liver, a disorder of the lung, a disorder of the skin, a disorder of the cardiovascular system, a disorder of the renal system, a disorder of the gastro-intestinal tract, a disorder of the respiratory system, a disorder of the endocrine system, a disorder of the central nervous system (CNS), an inflammatory disorder, an autoimmune disorder, or a cancer, tumor, or other malignancy.~~

~~Claim 34. The compound for use of claim 26, 32, or 33; pharmaceutical composition for use of claim 27, 32, or 33; use of a compound of claim 28, 32, or 33; use of a pharmaceutical composition of claim 29, 32, or 33; compound for use in the manufacture of a medicament of claim 30, 32, or 33; or pharmaceutical composition for use in the manufacture of a medicament of claim 31, 32, or 33; wherein the disorder is a bacterial infection, a viral infection, a fungal infection, celiac disease, colitis, intestinal hyperplasia, cancer, metabolic syndrome, obesity, rheumatoid arthritis, liver disease, hepatic steatosis, fatty liver disease, liver fibrosis, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), lupus, lupus nephritis, cryopyrin-associated periodic syndromes (CAPS), myelodysplastic syndromes (MDS), gout, myeloproliferative neoplasms (MPN), atherosclerosis, Crohn's disease, or inflammatory bowel disease (IBD).~~