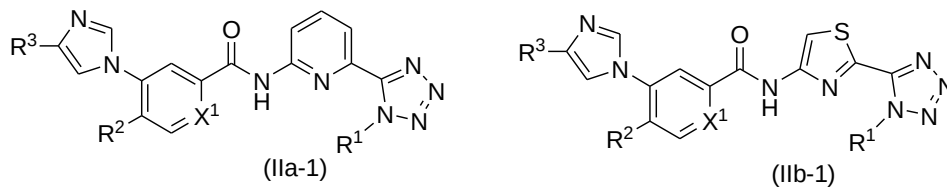


CLAIMS

WHAT IS CLAIMED:

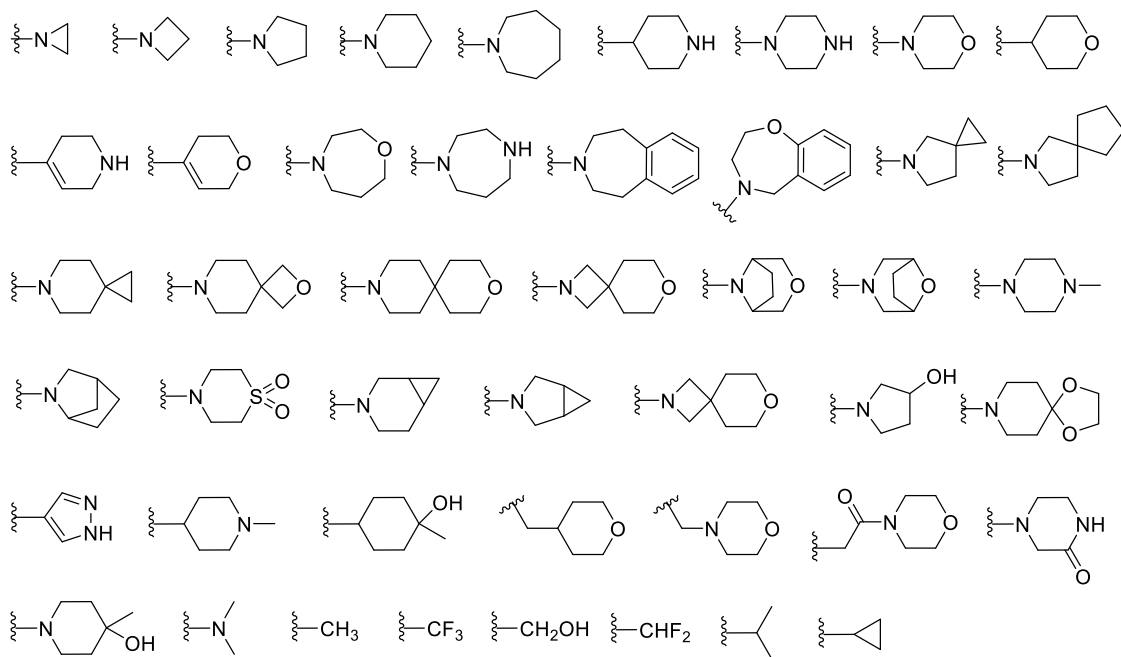
1. A compound selected from compounds of Formula (IIa-1) and Formula (IIb-1),



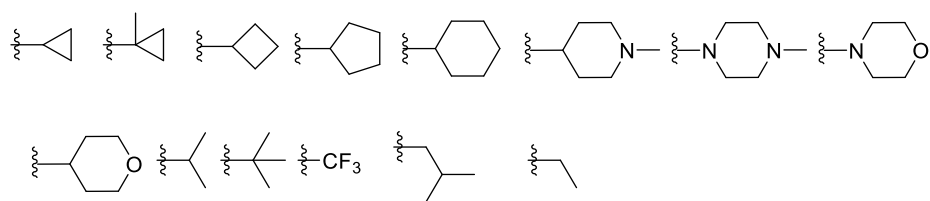
or a pharmaceutically acceptable salt thereof, wherein

X^1 is N or C(R⁵);

R^2 is selected from the groups below,



R^3 is selected from the groups below,



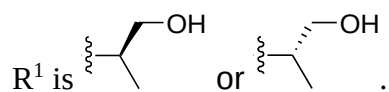
R^5 is selected from the group consisting of:

- 1) Hydrogen;
- 2) Halogen;
- 3) -C₁-C₈ alkyl;

4) $-C_3-C_8$ cycloalkyl; and

5) $-C_1-C_8$ alkoxy;

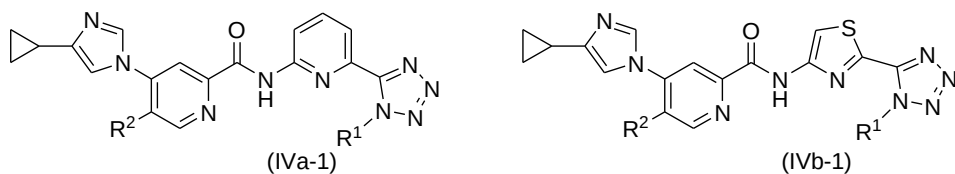
and



5

2. The compound of claim 1, which is selected from

(a) compounds of Formula (IVa-1) and Formula (IVb-1):



or a pharmaceutically acceptable salt thereof,

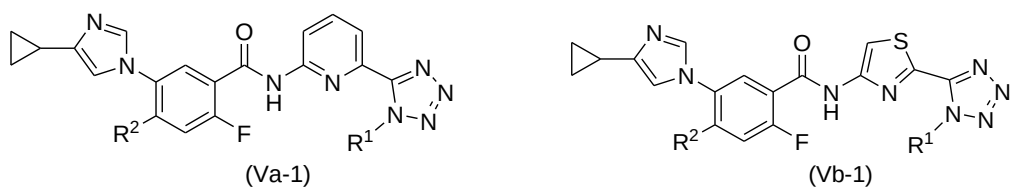
10 wherein R¹ and R² are delineated for each compound in Table 1,

Table 1

Entry	R ¹	R ²	Entry	R ¹	R ²
5		Me	55		
6		Me	56		
15		CF ₃	65		
16		CF ₃	66		
25			75		
26			76		
35			85		
36			86		
45			95		
46			96		

15

3. The compound of claim 1, which is selected from compounds of Formula (Va-1) or Formula (Vb-1), or a pharmaceutically acceptable salt thereof:



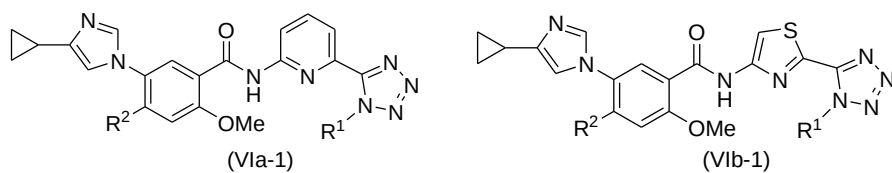
5 wherein R¹ and R² are delineated for each compound in Table 3,

Table 3

Entry	R ¹	R ²	Entry	R ¹	R ²
205		Me	255		
206		Me	256		
215		CF ₃	265		
216		CF ₃	266		
225			275		
226			276		
235			285		
236			286		
245			295		
246			296		

10 4. The compound of claim 1, which is selected

(a) compounds of Formula (VIa-1) or Formula (VIb-1)



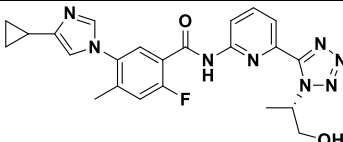
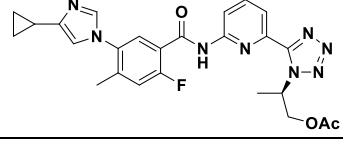
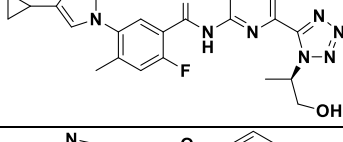
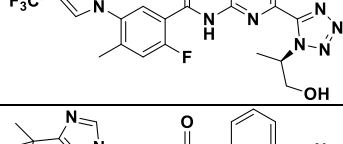
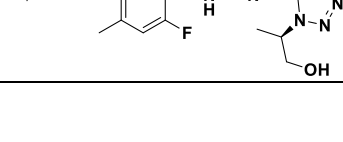
or a pharmaceutically acceptable salt thereof:

wherein R¹ and R² are delineated for each compound in Table 5,

Table 5

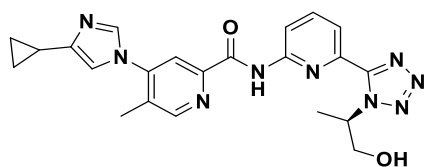
Entry	R ¹	R ²	Entry	R ¹	R ²
405		Me	455		
406		Me	456		
415		CF ₃	465		
416		CF ₃	466		
425			475		
426			476		
435			485		
436			486		
445			495		
446			496		

5. A compound selected from the compounds set forth below or a pharmaceutically acceptable salt thereof:

Compound	Structure
5a	
6a	
7a	
28a	
30a	

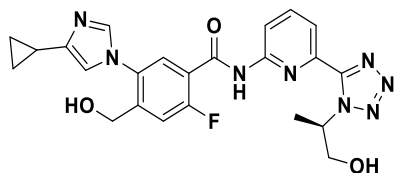
32a	
33a	
49a	
51a	
53a	
55a	
58a	
61a	

6. The compound of claim 5 having the structure



5 or a pharmaceutically acceptable salt thereof.

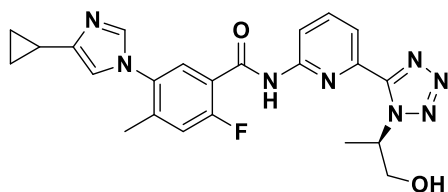
7. The compound of claim 5 having the structure



or a pharmaceutically acceptable salt thereof.

8. The compound of claim 5 having the structure

5



or a pharmaceutically acceptable salt thereof.

10 9. A pharmaceutical composition comprising the compound according to any one of claims 1-8 and a pharmaceutically acceptable carrier or excipient.

10. Use of a compound according to any one of claims 1-8 for the preparation of pharmaceutical compositions for the treatment of an ASK-1 mediated disease or condition
15 selected from the group consisting of an autoimmune disorder, a neurodegenerative disorder, an inflammatory disease, chronic kidney disease, renal disease, cardiovascular disease, a metabolic disease, or an acute or chronic liver disease.

11. The use according to claim 10, wherein the ASK-1 mediated disease or condition is a
20 chronic liver disease is selected from the group consisting of primary biliary cirrhosis (PBC), cerebrotendinous xanthomatosis (CTX), primary sclerosing cholangitis (PSC), drug induced cholestasis, intrahepatic cholestasis of pregnancy, parenteral nutrition associated cholestasis (PNAC), bacterial overgrowth or sepsis associated cholestasis, autoimmune hepatitis, chronic viral hepatitis, alcoholic liver disease, nonalcoholic fatty liver disease (NAFLD),
25 nonalcoholic steatohepatitis (NASH), liver transplant associated graft versus host disease, living donor transplant liver regeneration, congenital hepatic fibrosis, choledocholithiasis, granulomatous liver disease, intra- or extrahepatic malignancy, Sjogren's syndrome,

Sarcoidosis, Wilson's disease, Gaucher's disease, hemochromatosis, or alpha 1-antitrypsin deficiency.

- 5 12. The use according to claim 10, wherein the ASK-1 mediated disease or condition is a renal disease is selected from the group consisting of diabetic nephropathy, focal segmental glomerulosclerosis (FSGS), hypertensive nephrosclerosis, chronic glomerulonephritis, chronic transplant glomerulopathy, chronic interstitial nephritis, kidney fibrosis and polycystic kidney disease.
- 10 13. The use according to claim 10, wherein the ASK-1 mediated disease or condition is a cardiovascular disease is selected from the group consisting of atherosclerosis, arteriosclerosis, reperfusion/ischemia in stroke, cardiac hypertrophy, respiratory diseases, heart attacks, myocardial ischemia.
- 15 14. The use according to claim 10, wherein the ASK-1 mediated disease or condition is a metabolic disease is selected from the group consisting of insulin resistance, Type I and Type II diabetes, and obesity.
- 20 15. The use according to claim 10, wherein the ASK-1 mediated disease or condition is a chronic kidney disease is selected from the group consisting of polycystic kidney disease, pyelonephritis, kidney fibrosis and glomerulonephritis.
- 25 16. Use of a compound according to any one of claims 1-8 for the preparation of pharmaceutical compositions for the treatment of a disease selected from the group consisting of, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Graves' disease, autoimmune gastritis, diabetes, autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis, myasthenia gravis, multiple sclerosis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, psoriasis, Sjogren's syndrome, organ hypoxia, vascular hyperplasia, , hepatic ischemia, congestive
- 30 heart failure, pathologic immune responses such as that caused by T cell activation, thrombin-induced platelet aggregation, osteoporosis, osteoarthritis and multiple myeloma-related bone disorder, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis (ALS), epilepsy, seizures, Huntington's disease, polyglutamine diseases, traumatic brain injury, ischemic and hemorrhaging stroke, cerebral ischemias or neurodegenerative disease,

including apoptosis-driven neurodegenerative disease, caused by traumatic injury, acute hypoxia, ischemia or glutamate neurotoxicity.