

[0012] Available courses of treatment are scarce, as there are currently no options on the market proven to have an effect on long-term patient survival or symptomatology. There remains a need for treatment of fibrotic diseases.

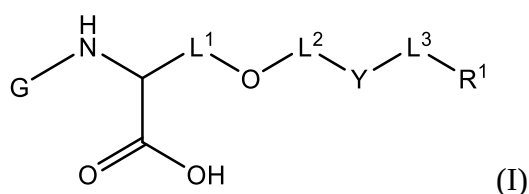
[0013] The $\alpha\beta6$ integrin is expressed in epithelial cells, and binds to the latency-associated peptide of transforming growth factor- $\beta1$ (TGF $\beta1$) and mediates TGF $\beta1$ activation. Its expression level is significantly increased after injury to lung and cholangiocytes, and plays a critical *in vivo* role in tissue fibrosis. Increased levels are also associated with increased mortality in IPF and NSIP patients.

[0014] Primary sclerosing cholangitis (PSC) involves bile duct inflammation, and fibrosis that obliterates the bile ducts. The resulting impediment to the flow of bile to the intestines can lead to cirrhosis of the liver and subsequent complications such as liver failure and liver cancer. Expression of $\alpha\beta6$ is elevated in liver and bile duct of PSC patients.

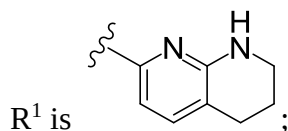
[0015] The present disclosure provides for $\alpha\beta6$ integrin inhibitors that may be useful for treatment of fibrosis.

SUMMARY

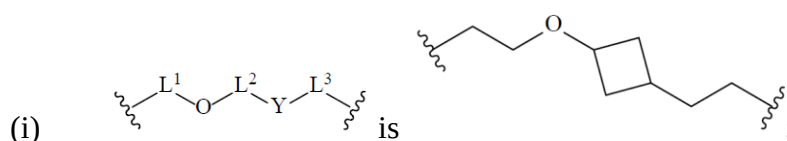
[0015a] In an aspect of the present disclosure, there is provided a compound of formula (I):



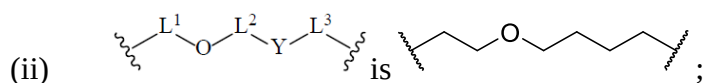
or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, wherein:



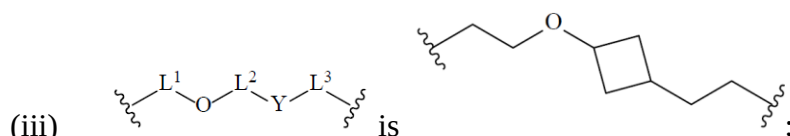
G is $\text{C}(\text{O})\text{R}^2$;



R^2 is tetrahydropyranyl, wherein the tetrahydropyranyl is substituted by 1, 2, or 3 independently selected R^{2c} substituents; and
each R^{2c} is independently R^4 ; or



R^2 is phenyl, wherein the phenyl is substituted by 1, 2, or 3 independently selected R^{2d} substituents; and
each R^{2d} is independently R^4 ; or



R^2 is pyridyl, wherein the pyridyl is substituted by 1, 2, or 3 independently selected R^{2e} substituents; and
each R^{2e} is independently R^4 ;

each R^4 is independently halogen, CN, NO₂, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C(NH)(OR⁵), C(O)R⁵, C(O)NR⁶R⁷, C(O)OR⁵, P(O)(OR⁵)(OR⁶), NR⁶R⁷, NR⁵C(O)R⁶, NR⁵C(O)NR⁶R⁷, NR⁵C(O)OR⁶, NR⁵S(O)R⁶, NR⁵S(O)₂R⁶, OR⁵, OC(O)R⁵, SR⁵, S(O)R⁵, S(O)NR⁶R⁷, S(O)₂R⁵, S(O)₂NR⁶R⁷, or C₃-C₈ cycloalkyl, wherein each C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, and C₃-C₈ cycloalkyl of R^4 is optionally and independently substituted by 1, 2, or 3 independently selected R^{4a} substituents;

each R^{4a} is independently halogen;

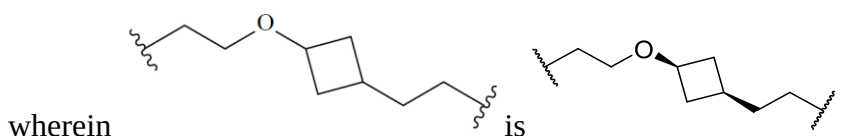
each R^5 is independently hydrogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, or C₃-C₆ cycloalkyl, wherein each C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, and C₃-C₆ cycloalkyl of R^5 is optionally and independently substituted by 1 or more independently selected R^{5a} substituents;

each R^{5a} is independently halogen, CN, C₁-C₆ alkyl, or =O, wherein each C₁-C₆ alkyl is optionally and independently substituted by 1 or more substituents independently selected from the group consisting of halogen, OH, and =O;

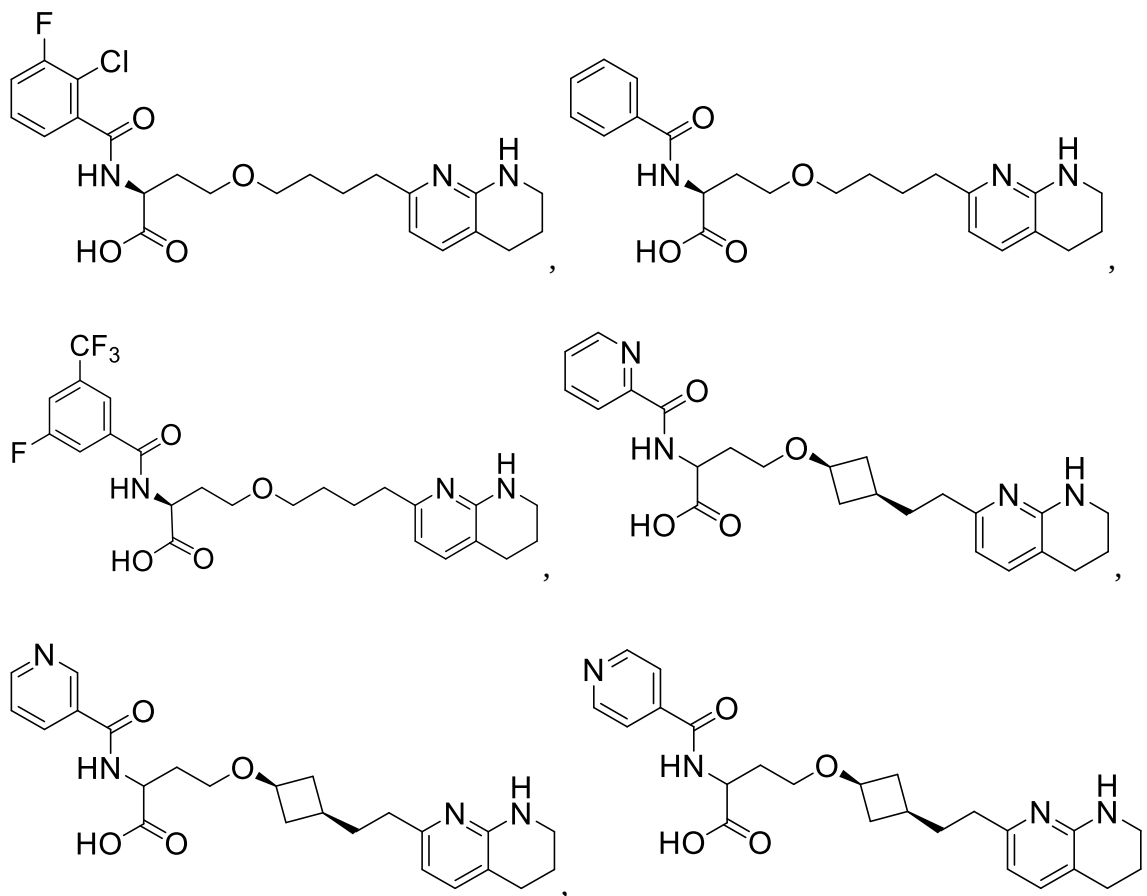
each R^6 is independently hydrogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, or C₃-C₆ cycloalkyl, wherein each C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, and C₃-C₆ cycloalkyl

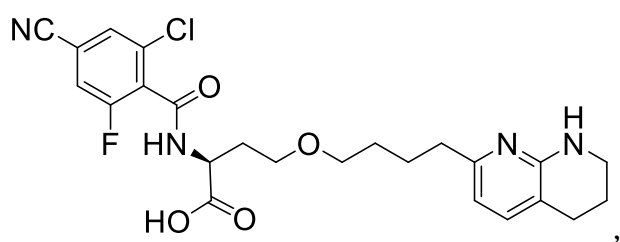
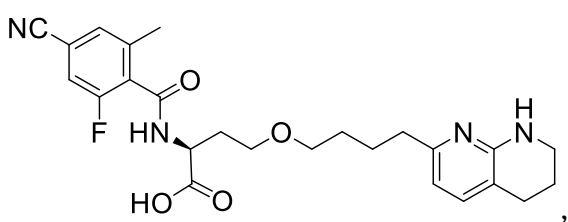
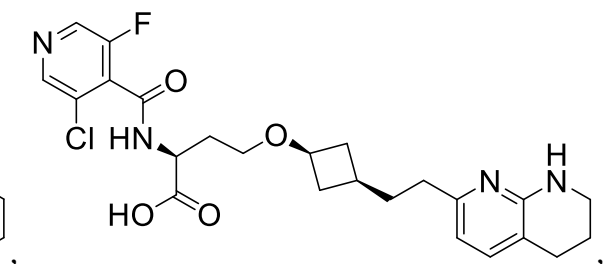
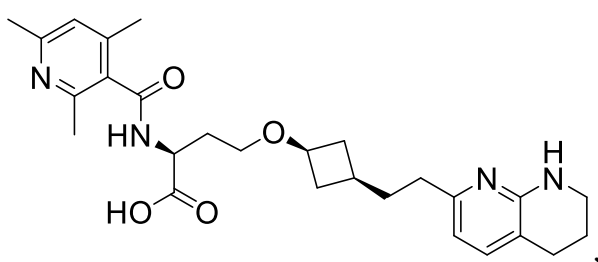
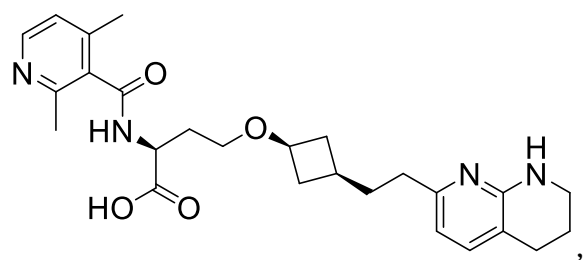
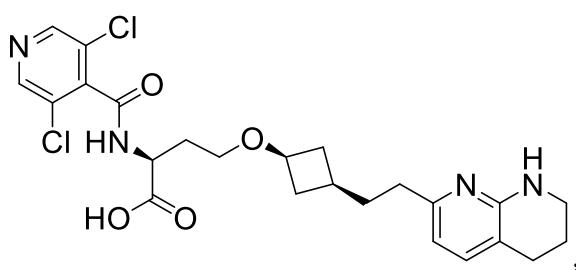
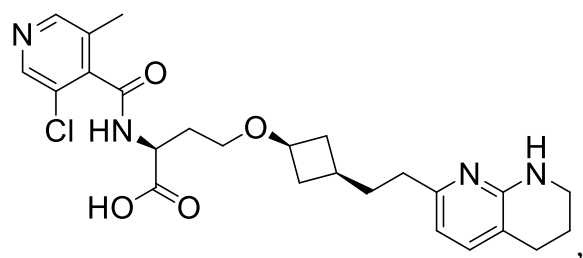
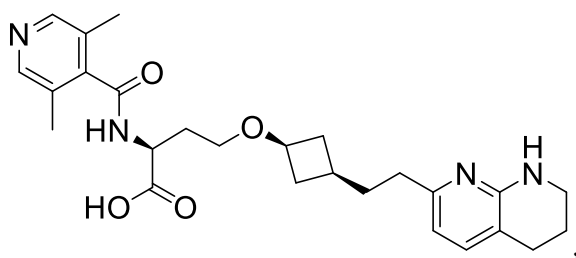
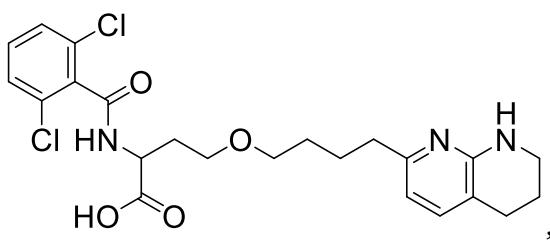
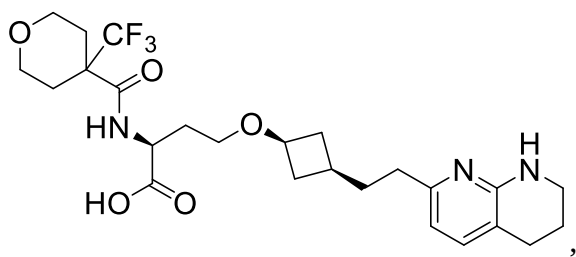
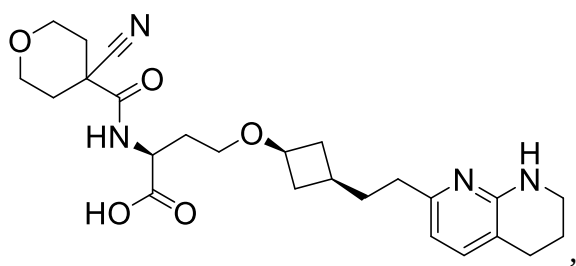
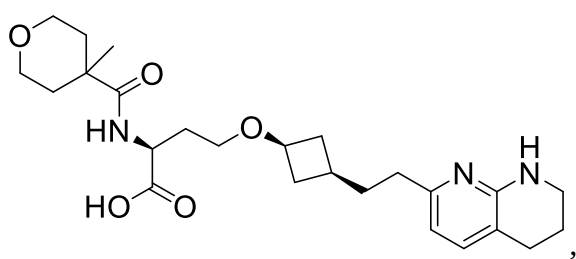
of R^6 is optionally and independently substituted by 1 or more substituents independently selected from the group consisting of halogen, CN, C_1 - C_6 alkyl, and =O, and further wherein each C_1 - C_6 alkyl substituent is optionally and independently substituted by 1 or more substituents independently selected from the group consisting of halogen, OH, and =O; and

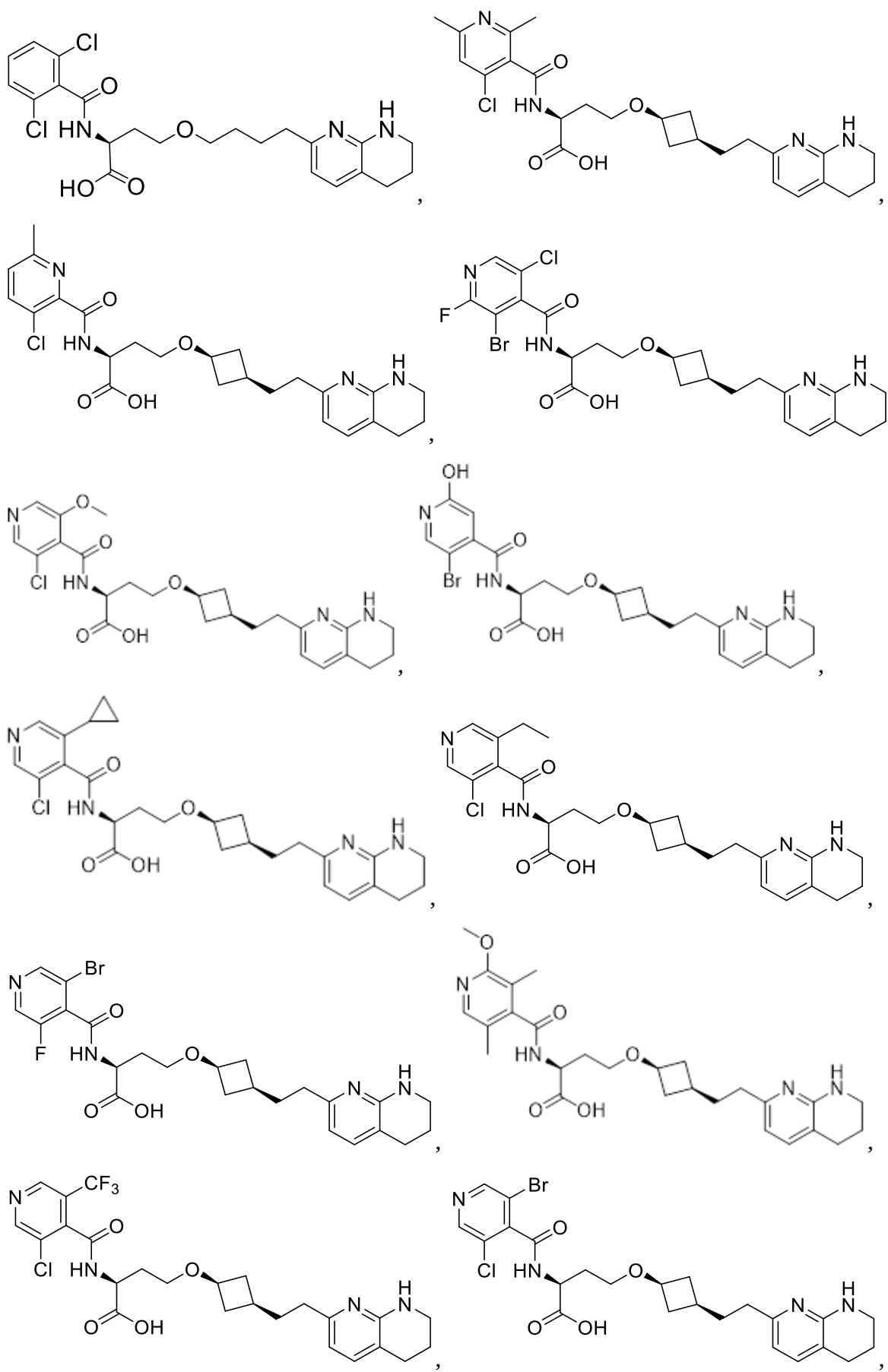
each R^7 is independently hydrogen, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, or C_3 - C_6 cycloalkyl, wherein each C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, and C_3 - C_6 cycloalkyl of R^7 is optionally and independently substituted by 1 or more substituents independently selected from the group consisting of halogen, CN, C_1 - C_6 alkyl, and =O, and further wherein each C_1 - C_6 alkyl substituent is optionally and independently substituted by 1 or more substituents independently selected from the group consisting of halogen, OH, and =O;

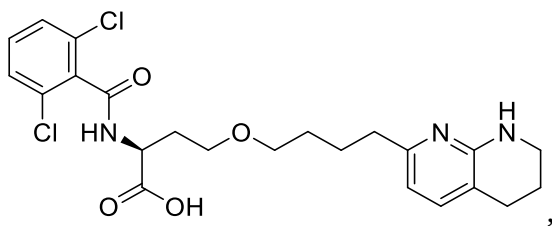
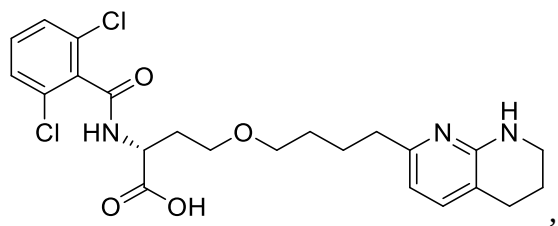
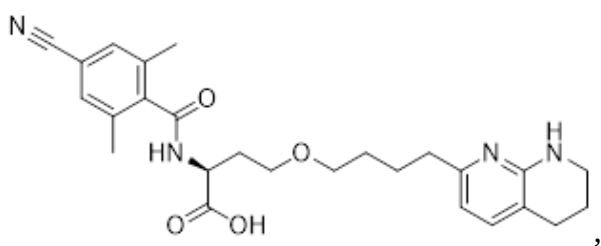
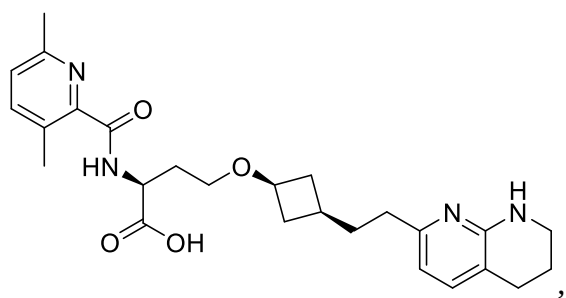
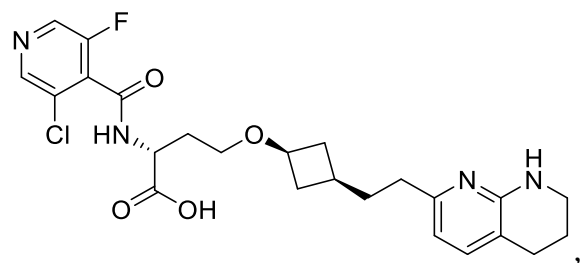
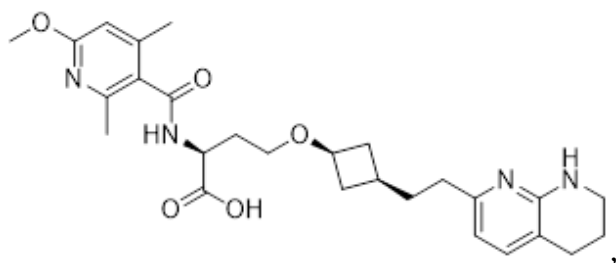
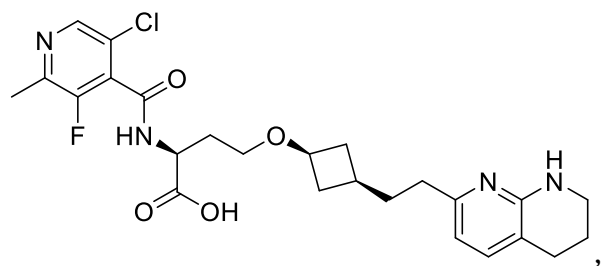
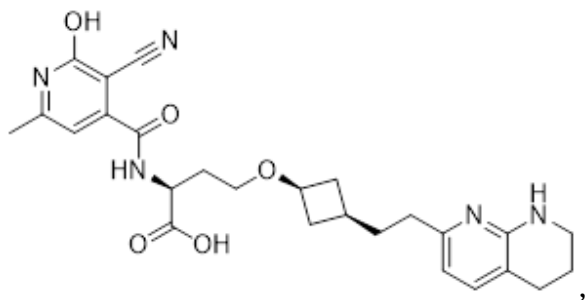
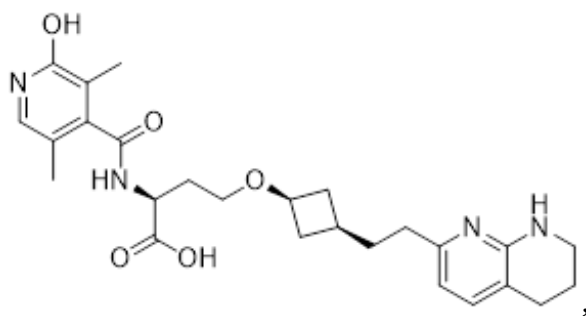
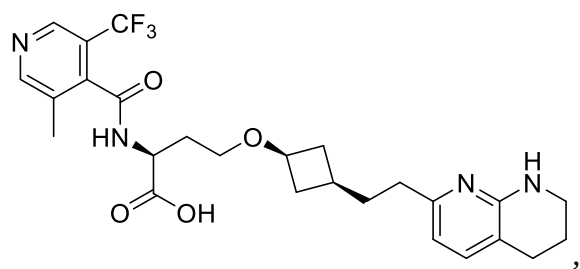
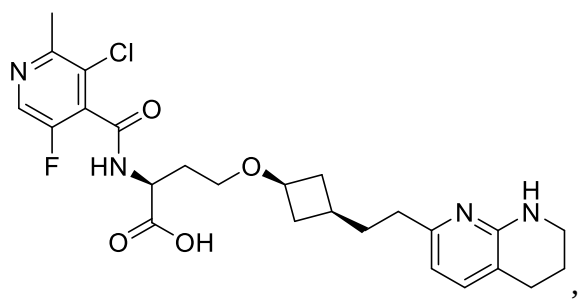
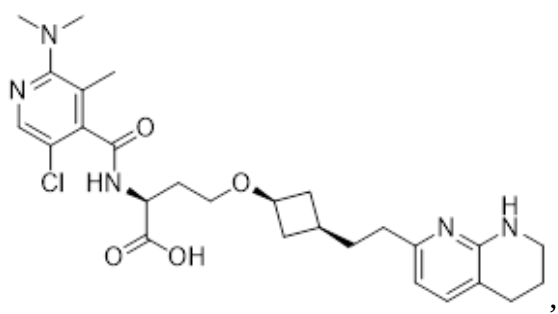


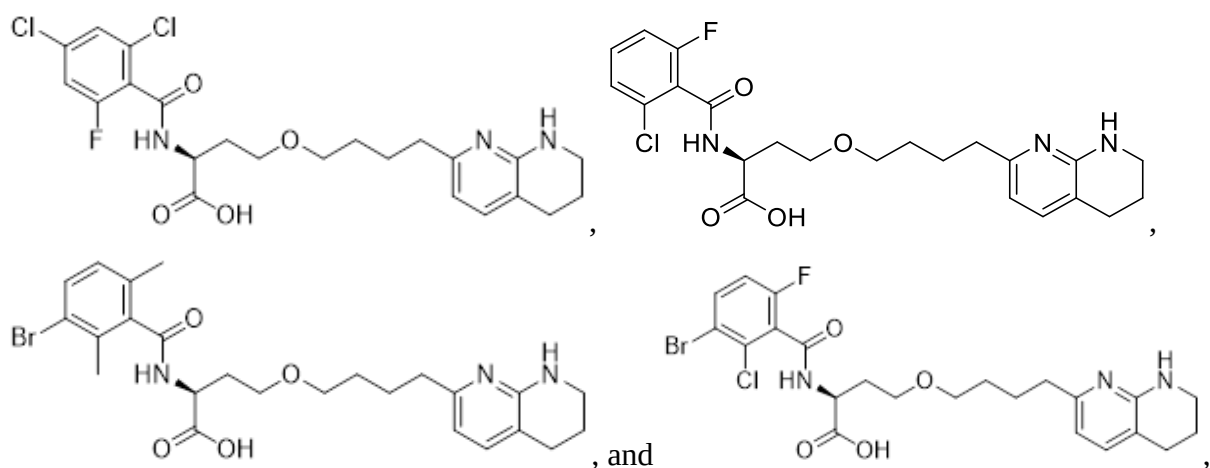
[0015b] In another aspect of the present disclosure, there is provided a compound selected from the group consisting of:











or a pharmaceutically acceptable salt or tautomer thereof.

[0015c] In a further aspect of the present disclosure, there is provided a compound selected from the group consisting of:

N-(2-chloro-3-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine; N-(2-chloro-3-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine; N-(2-chloro-3-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine; N-benzoyl-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine; N-benzoyl-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine; N-benzoyl-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine; N-(3-fluoro-5-(trifluoromethyl)benzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine; N-(3-fluoro-5-(trifluoromethyl)benzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine; N-(3-fluoro-5-(trifluoromethyl)benzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine; N-picolinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine; N-picolinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine; N-picolinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-nicotinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-nicotinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-nicotinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-isonicotinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-isonicotinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-isonicotinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(4-methyltetrahydro-2H-pyran-4-carbonyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(4-methyltetrahydro-2H-pyran-4-carbonyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(4-methyltetrahydro-2H-pyran-4-carbonyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(4-cyanotetrahydro-2H-pyran-4-carbonyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(4-cyanotetrahydro-2H-pyran-4-carbonyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(4-cyanotetrahydro-2H-pyran-4-carbonyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-N-(4-(trifluoromethyl)tetrahydro-2H-pyran-4-carbonyl)homoserine;

O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-N-(4-(trifluoromethyl)tetrahydro-2H-pyran-4-carbonyl)-L-homoserine;

O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-N-(4-(trifluoromethyl)tetrahydro-2H-pyran-4-carbonyl)-D-homoserine;

N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;

N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;

N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;

N-(3,5-dimethylisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3,5-dimethylisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3,5-dimethylisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-chloro-5-methylisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-chloro-5-methylisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-chloro-5-methylisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3,5-dichloroisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3,5-dichloroisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3,5-dichloroisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(2,4-dimethylnicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(2,4-dimethylnicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(2,4-dimethylnicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-N-(2,4,6-trimethylnicotinoyl)homoserine;

O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-N-(2,4,6-trimethylnicotinoyl)-L-homoserine;

O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-N-(2,4,6-trimethylnicotinoyl)-D-homoserine;

N-(3-chloro-5-fluoroisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(3-chloro-5-fluoroisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(3-chloro-5-fluoroisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(2-fluoro-4-isocyano-6-methylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;
 N-(2-fluoro-4-isocyano-6-methylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
 N-(2-fluoro-4-isocyano-6-methylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;
 N-(2-chloro-6-fluoro-4-isocyanobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;
 N-(2-chloro-6-fluoro-4-isocyanobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
 N-(2-chloro-6-fluoro-4-isocyanobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;
 N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;
 N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
 N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;
 N-(4-chloro-2,6-dimethylnicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(4-chloro-2,6-dimethylnicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(4-chloro-2,6-dimethylnicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(3-chloro-6-methylpicolinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(3-chloro-6-methylpicolinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-chloro-6-methylpicolinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-bromo-5-chloro-2-fluoroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-bromo-5-chloro-2-fluoroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-bromo-5-chloro-2-fluoroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-chloro-5-methoxyisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-chloro-5-methoxyisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-chloro-5-methoxyisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(5-bromo-2-hydroxyisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(5-bromo-2-hydroxyisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(5-bromo-2-hydroxyisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-chloro-5-cyclopropylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-chloro-5-cyclopropylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-chloro-5-cyclopropylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-chloro-5-ethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-chloro-5-ethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-chloro-5-ethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-bromo-5-fluoroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-bromo-5-fluoroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-bromo-5-fluoroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(2-methoxy-3,5-dimethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(2-methoxy-3,5-dimethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(2-methoxy-3,5-dimethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-chloro-5-(trifluoromethyl)isonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-chloro-5-(trifluoromethyl)isonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-chloro-5-(trifluoromethyl)isonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-bromo-5-chloroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-bromo-5-chloroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-bromo-5-chloroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(5-chloro-2-(dimethylamino)-3-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(5-chloro-2-(dimethylamino)-3-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(5-chloro-2-(dimethylamino)-3-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-chloro-5-fluoro-2-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-chloro-5-fluoro-2-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-chloro-5-fluoro-2-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-methyl-5-(trifluoromethyl)isonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-methyl-5-(trifluoromethyl)isonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-methyl-5-(trifluoromethyl)isonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(2-hydroxy-3,5-dimethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(2-hydroxy-3,5-dimethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(2-hydroxy-3,5-dimethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-cyano-2-hydroxy-6-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-cyano-2-hydroxy-6-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-cyano-2-hydroxy-6-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(5-chloro-3-fluoro-2-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(5-chloro-3-fluoro-2-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(5-chloro-3-fluoro-2-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(6-methoxy-2,4-dimethylnicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(6-methoxy-2,4-dimethylnicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(6-methoxy-2,4-dimethylnicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-chloro-5-fluoroisonicotinoyl)-O-((1r,3S)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-chloro-5-fluoroisonicotinoyl)-O-((1r,3S)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-chloro-5-fluoroisonicotinoyl)-O-((1r,3S)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3,6-dimethylpicolinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3,6-dimethylpicolinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3,6-dimethylpicolinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(4-cyano-2,6-dimethylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;

N-(4-cyano-2,6-dimethylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;

N-(4-cyano-2,6-dimethylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;

N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;

N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;

N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;

N-(2,4-dichloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;

N-(2,4-dichloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;

N-(2,4-dichloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;

N-(2-chloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;

N-(2-chloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
N-(2-chloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;
N-(3-bromo-2,6-dimethylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;
N-(3-bromo-2,6-dimethylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
N-(3-bromo-2,6-dimethylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;
N-(3-bromo-2-chloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;
N-(3-bromo-2-chloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine; and
N-(3-bromo-2-chloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine,

or a pharmaceutically acceptable salt or tautomer thereof.

[0015d] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a pharmaceutically acceptable carrier or excipient and a compound disclosed herein, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof.

[0015e] In a further aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, in the manufacture of a medicament for treating a fibrotic disease or fibrotic condition in an individual in need thereof.

[0015f] In another aspect of the present disclosure, there is provided a kit comprising a compound disclosed herein, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof.

[0015g] In a further aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, in the manufacture of a medicament for inhibiting $\alpha v \beta_6$ integrin activity in an individual in need thereof.

[0015h] In another aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, in the manufacture of a medicament for inhibiting transforming growth factor beta activation in a cell.

[0015i] In a further aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, in the manufacture of a medicament for modulating the activity of at least one integrin comprising an α_v subunit in an individual in need thereof.

[0015j] In another aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, in the manufacture of a medicament for modulating transforming growth factor beta activation in a cell.

[0015k] In a further aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, in the manufacture of a medicament for treating an individual having one or more tissues in need of therapy, wherein when compared to a healthy state of the one or more tissues, the one or more tissues have at least one elevated level of:

- (a) transforming growth factor beta activation; or
- (b) transforming growth factor beta expression; or
- (c) both transforming growth factor beta activation and transforming growth factor beta expression; or
- (d) $\alpha_v\beta_1$ integrin activity; or
- (e) $\alpha_v\beta_1$ integrin expression; or
- (f) both $\alpha_v\beta_1$ integrin activity and $\alpha_v\beta_1$ integrin expression; or
- (g) $\alpha_v\beta_6$ integrin activity; or
- (h) $\alpha_v\beta_6$ integrin expression; or
- (i) both $\alpha_v\beta_6$ integrin activity and $\alpha_v\beta_6$ integrin expression.

[0015l] In another aspect of the present disclosure, there is provided a use of a pharmaceutical composition disclosed herein in the manufacture of a medicament for modulating transforming growth factor beta activation in a cell.

[0015m] In a further aspect of the present disclosure, there is provided a compound selected from the group consisting of:

N-(4-methyltetrahydro-2H-pyran-4-carbonyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-N-(4-(trifluoromethyl)tetrahydro-2H-pyran-4-carbonyl)-L-homoserine;
 N-(3-chloro-5-fluoroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(4-chloro-2,6-dimethylnicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(3-bromo-5-chloroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(2-hydroxy-3,5-dimethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(5-chloro-3-fluoro-2-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(3-chloro-5-fluoroisonicotinoyl)-O-((1r,3S)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(2-chloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine; and
 N-(3-bromo-2,6-dimethylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine,
 or a pharmaceutically acceptable salt or tautomer thereof.

[0015n] In another aspect of the present disclosure, there is provided a compound which is N-(4-methyltetrahydro-2H-pyran-4-carbonyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.

[0015o] In a further aspect of the present disclosure, there is provided a compound which is O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-N-(4-(trifluoromethyl)tetrahydro-2H-pyran-4-carbonyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.

[0015p] In another aspect of the present disclosure, there is provided a compound which is N-(3-chloro-5-fluoroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.

[0015q] In a further aspect of the present disclosure, there is provided a compound which is N-(4-chloro-2,6-dimethylnicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.

[0015r] In another aspect of the present disclosure, there is provided a compound which is N-(3-bromo-5-chloroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.

[0015s] In a further aspect of the present disclosure, there is provided a compound which is N-(2-hydroxy-3,5-dimethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.

[0015t] In another aspect of the present disclosure, there is provided a compound which is N-(5-chloro-3-fluoro-2-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.

[0015u] In a further aspect of the present disclosure, there is provided a compound which is N-(3-chloro-5-fluoroisonicotinoyl)-O-((1r,3S)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.

[0015v] In another aspect of the present disclosure, there is provided a compound which is N-(2-chloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.

[0015w] In a further aspect of the present disclosure, there is provided a compound which is N-(3-bromo-2,6-dimethylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.

[0015x] In another aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, in the manufacture of a medicament for inhibiting $\alpha v \beta_1$ integrin activity in an individual in need thereof.

[0015y] In a further aspect of the present disclosure, there is provided a compound disclosed herein or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, or a composition disclosed herein, for use in therapy.

[0016] Disclosed are amino acid compounds that are $\alpha\text{v}\beta 6$ integrin inhibitors, compositions containing these compounds and methods for treating diseases mediated by $\alpha\text{v}\beta 6$ integrin such as a fibrotic disease.

[0017] In one example, provided is a compound of formula (I), or any variation thereof, or a salt thereof (*e.g.*, a pharmaceutically acceptable salt thereof), as detailed herein.

[0018] Further provided is a pharmaceutical composition comprising a compound of formula (I), or any variation thereof detailed herein, or a salt thereof (*e.g.*, a pharmaceutically acceptable salt thereof), and a pharmaceutically acceptable carrier or excipient.

[0019] In another example, provided is a method of treating a fibrotic disease or condition in an individual (such as a human) in need thereof comprising administering to the individual a therapeutically effective amount of a compound of formula (I), or any variation thereof detailed herein, or a pharmaceutically acceptable salt thereof. In some examples, the fibrotic disease or condition is pulmonary, liver, renal, cardiac, dermal, or gastrointestinal fibrosis. In other examples the fibrotic disease or condition is idiopathic pulmonary fibrosis, interstitial lung disease, radiation-induced pulmonary fibrosis, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), alcoholic liver disease induced

fibrosis, Alport syndrome, primary sclerosing cholangitis, primarily biliary cholangitis (also known as primary biliary cirrhosis), systemic sclerosis associated interstitial lung disease, scleroderma (also known as systemic sclerosis), diabetic nephropathy, diabetic kidney disease, focal segmental glomerulosclerosis, chronic kidney disease, and Crohn's Disease.

[0020] In another example, provided is a method of delaying the onset and/or development of a fibrotic disease or condition in an individual (such as a human) who is at risk for developing a fibrotic disease or condition comprising administering to the individual a therapeutically effective amount of a compound of formula (I), or any variation thereof detailed herein, or a pharmaceutically acceptable salt thereof. In some examples, the disease or condition is pulmonary, liver, renal, cardiac, dermal, or gastrointestinal fibrosis. In other examples the fibrotic disease or condition is idiopathic pulmonary fibrosis, interstitial lung disease, radiation-induced pulmonary fibrosis, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), alcoholic liver disease induced fibrosis, Alport syndrome, primary sclerosing cholangitis, primarily biliary cholangitis (also known as primary biliary cirrhosis), systemic sclerosis associated interstitial lung disease, scleroderma (also known as systemic sclerosis), diabetic nephropathy, diabetic kidney disease, focal segmental glomerulosclerosis, chronic kidney disease, and Crohn's Disease.

[0021] Also provided is a compound of formula (I), or any variation thereof detailed herein, or a pharmaceutical composition thereof, for the treatment of a fibrotic disease.

[0022] Also provided is use of a compound of formula (I), or any variation thereof detailed herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a fibrotic disease.

[0023] Further provided is a kit comprising a compound of formula (I), or any variation thereof detailed herein, or a pharmaceutically acceptable salt thereof. In some examples, the kit comprises instructions for use according to a method described herein, such as a method of treating a fibrotic disease in an individual.

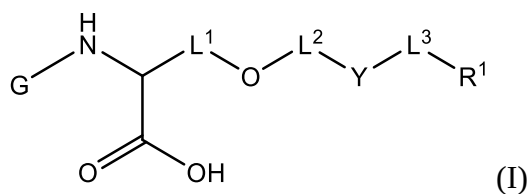
[0024] In another example, provided is a method of making a compound of formula (I) or any variation thereof. Also provided are compound intermediates useful in synthesis of a compound of formula (I), or any variation thereof.

[0025] It is understood that examples and variations described herein also include "consisting" and/or "consisting essentially of" examples and variations.

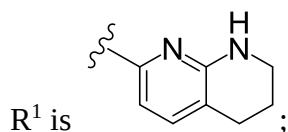
CLAIMS

What is claimed is:

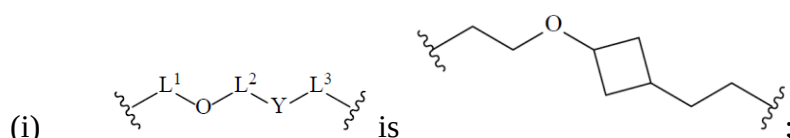
1. A compound of formula (I):



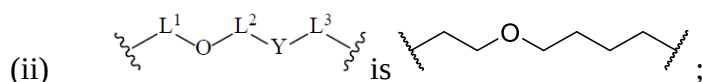
or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, wherein:



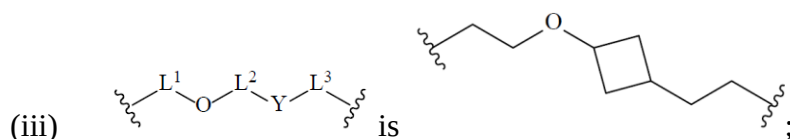
G is $\text{C}(\text{O})\text{R}^2$;



R^2 is tetrahydropyranyl, wherein the tetrahydropyranyl is substituted by 1, 2, or 3 independently selected R^{2c} substituents; and
each R^{2c} is independently R^4 ; or



R^2 is phenyl, wherein the phenyl is substituted by 1, 2, or 3 independently selected R^{2d} substituents; and
each R^{2d} is independently R^4 ; or



R^2 is pyridyl, wherein the pyridyl is substituted by 1, 2, or 3 independently selected R^{2e} substituents; and
each R^{2e} is independently R^4 ;

each R^4 is independently halogen, CN, NO_2 , C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, $\text{C}(\text{NH})(\text{OR}^5)$, $\text{C}(\text{O})\text{R}^5$, $\text{C}(\text{O})\text{NR}^6\text{R}^7$, $\text{C}(\text{O})\text{OR}^5$, $\text{P}(\text{O})(\text{OR}^5)(\text{OR}^6)$, NR^6R^7 ,

NR⁵C(O)R⁶, NR⁵C(O)NR⁶R⁷, NR⁵C(O)OR⁶, NR⁵S(O)R⁶, NR⁵S(O)₂R⁶, OR⁵, OC(O)R⁵, SR⁵, S(O)R⁵, S(O)NR⁶R⁷, S(O)₂R⁵, S(O)₂NR⁶R⁷, or C₃-C₈ cycloalkyl, wherein each C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, and C₃-C₈ cycloalkyl of R⁴ is optionally and independently substituted by 1, 2, or 3 independently selected R^{4a} substituents;

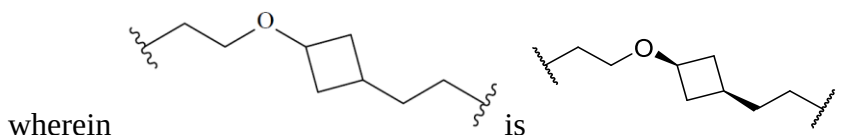
each R^{4a} is independently halogen;

each R⁵ is independently hydrogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, or C₃-C₆ cycloalkyl, wherein each C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, and C₃-C₆ cycloalkyl of R⁵ is optionally and independently substituted by 1 or more independently selected R^{5a} substituents;

each R^{5a} is independently halogen, CN, C₁-C₆ alkyl, or =O, wherein each C₁-C₆ alkyl is optionally and independently substituted by 1 or more substituents independently selected from the group consisting of halogen, OH, and =O;

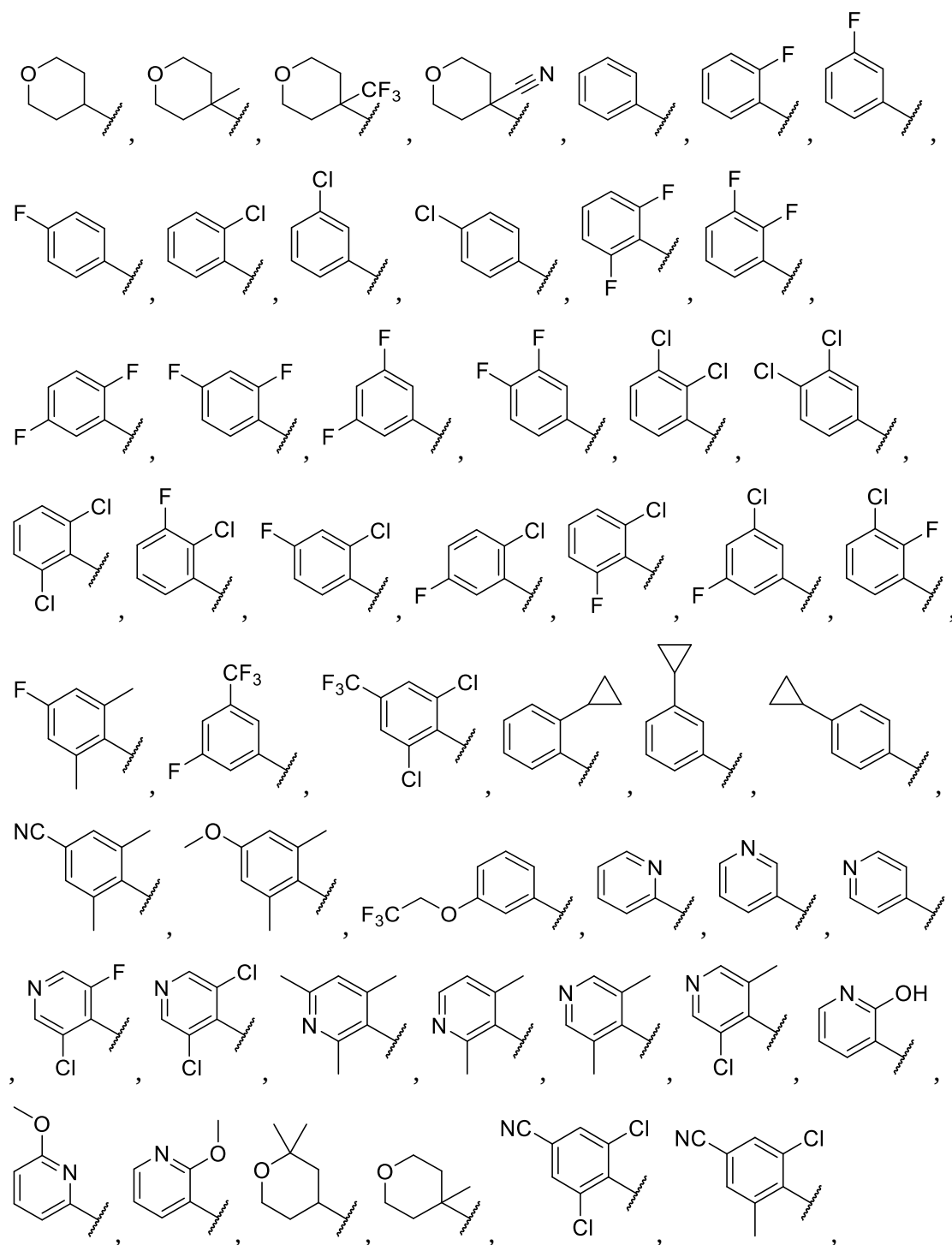
each R⁶ is independently hydrogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, or C₃-C₆ cycloalkyl, wherein each C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, and C₃-C₆ cycloalkyl of R⁶ is optionally and independently substituted by 1 or more substituents independently selected from the group consisting of halogen, CN, C₁-C₆ alkyl, and =O, and further wherein each C₁-C₆ alkyl substituent is optionally and independently substituted by 1 or more substituents independently selected from the group consisting of halogen, OH, and =O; and

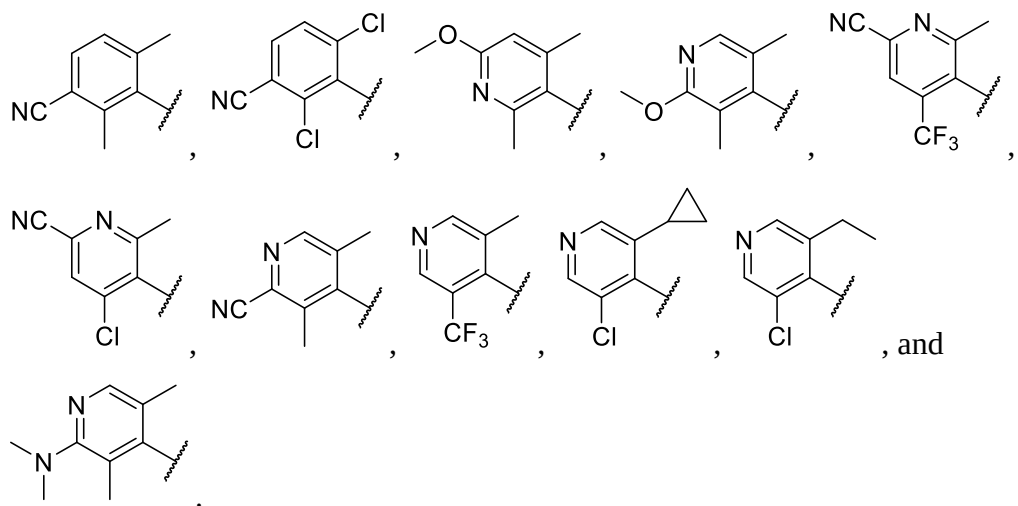
each R⁷ is independently hydrogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, or C₃-C₆ cycloalkyl, wherein each C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, and C₃-C₆ cycloalkyl of R⁷ is optionally and independently substituted by 1 or more substituents independently selected from the group consisting of halogen, CN, C₁-C₆ alkyl, and =O, and further wherein each C₁-C₆ alkyl substituent is optionally and independently substituted by 1 or more substituents independently selected from the group consisting of halogen, OH, and =O;



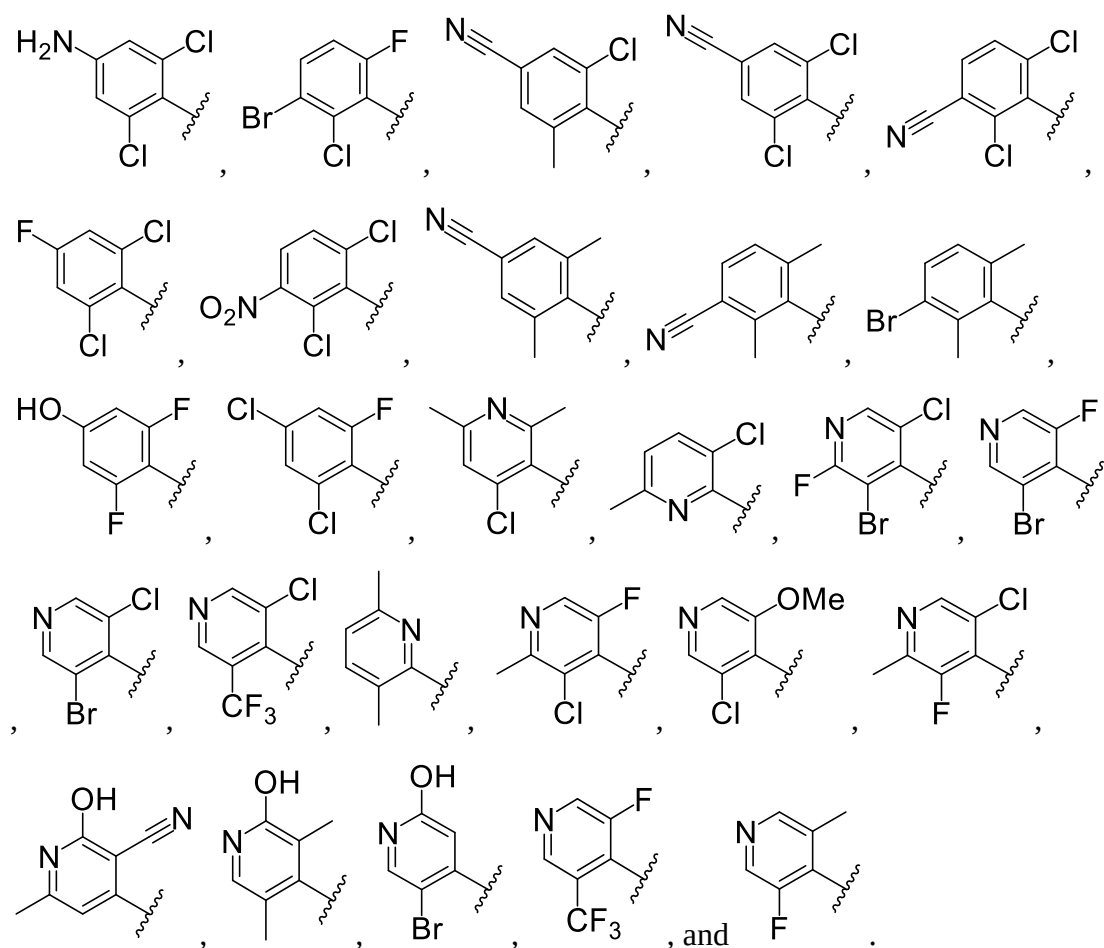
2. The compound of claim 1, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, wherein R^2 is tetrahydropyranyl, wherein the tetrahydropyranyl is substituted by 1, 2, or 3 independently selected R^{2c} substituents.
3. The compound of claim 2, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, wherein each R^{2c} is independently C_1 - C_6 alkyl, wherein each C_1 - C_6 alkyl is independently substituted by 3 independently selected R^{4a} substituents.
4. The compound of claim 3, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, wherein each R^{4a} is independently F, Cl, Br, or I.
5. The compound of claim 2, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, wherein R^2 is tetrahydropyran-4-yl, wherein the tetrahydropyran-4-yl is substituted by 1 R^{2c} substituent.
6. The compound of claim 1, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, wherein R^2 is phenyl, wherein the phenyl is substituted by 2 independently selected R^{2d} substituents.
7. The compound of claim 6, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, wherein each R^{2d} is independently halogen.
8. The compound of claim 1, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, wherein R^2 is pyridyl, wherein the pyridyl is substituted by 2 or 3 independently selected R^{2e} substituents.
9. The compound of claim 8, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, wherein each R^{2e} is independently halogen or C_1 - C_6 alkyl.
10. The compound of claim 9, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, wherein at least 1 R^{2e} substituent is halogen.
11. The compound of claim 8, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, wherein at least 2 R^{2e} substituents are independently selected halogen substituents.

12. The compound of claim 8, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, wherein R² is pyrid-4-yl, wherein the pyrid-4-yl is substituted by 2 or 3 independently selected R^{2e} substituents.
13. The compound of claim 1, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, wherein R² is selected from the group consisting of:

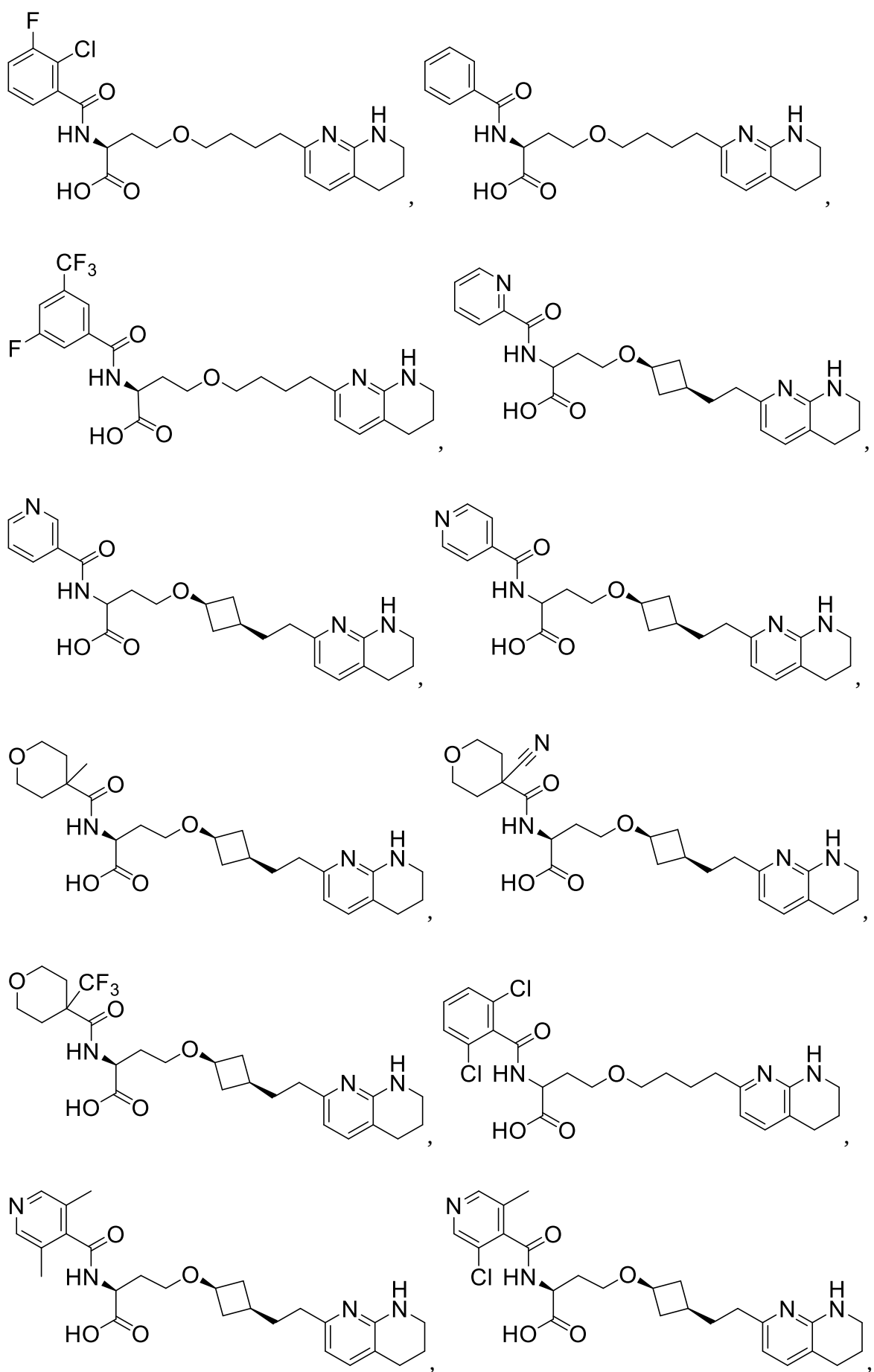


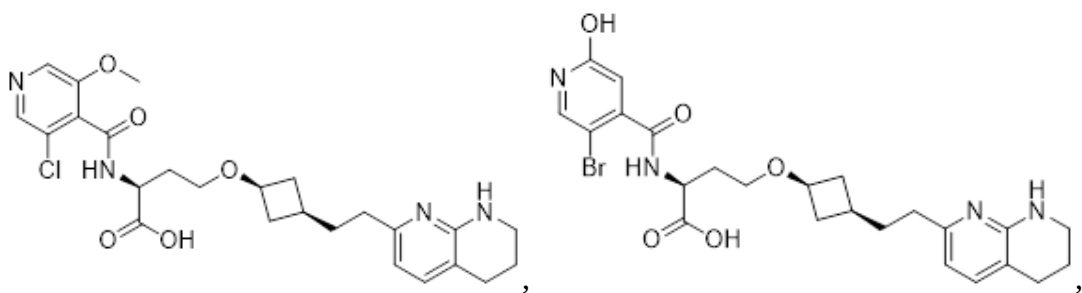
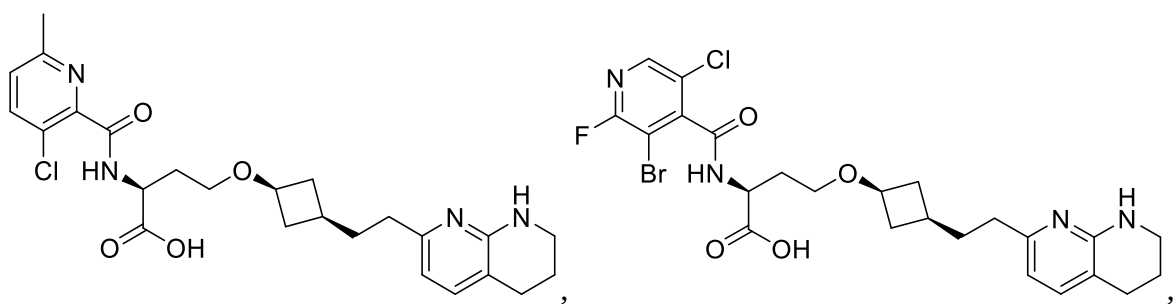
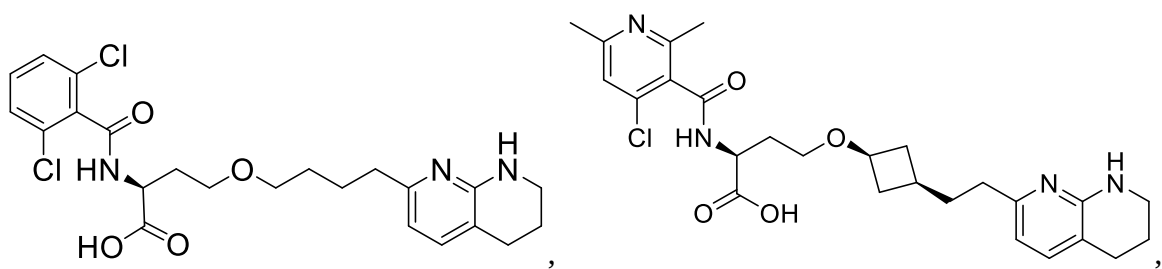
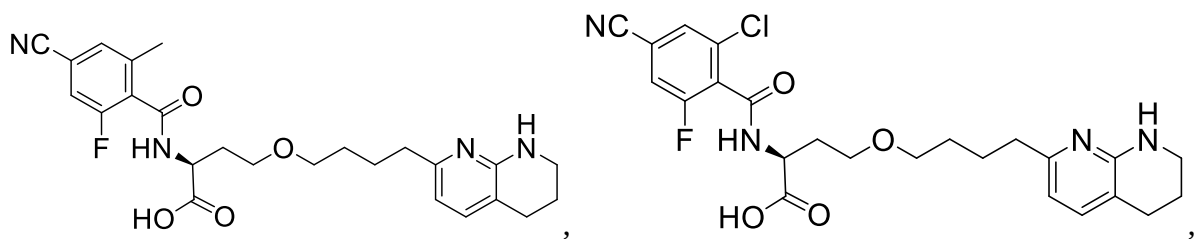
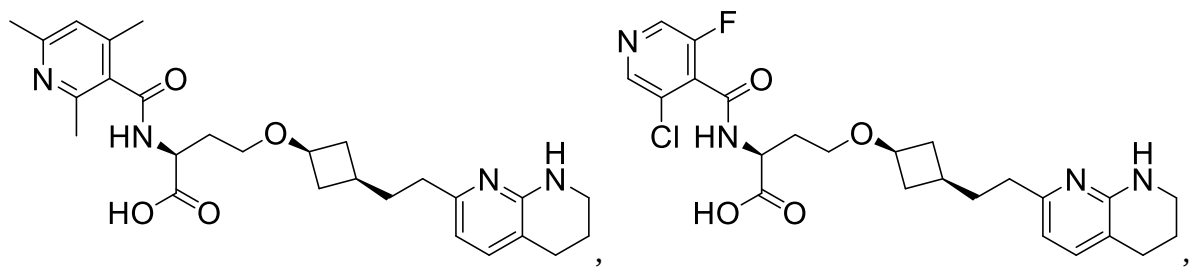
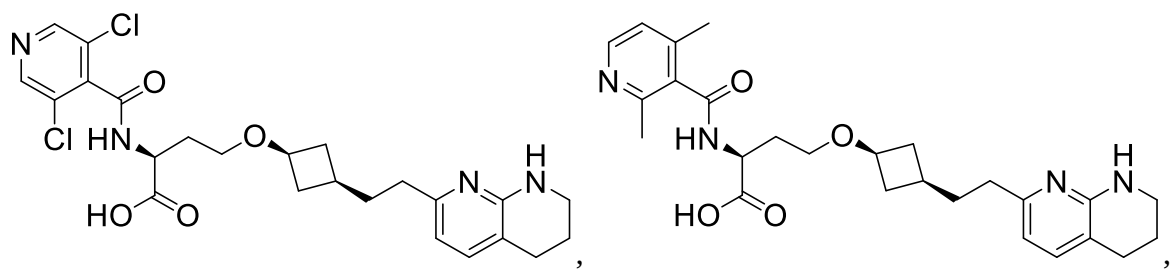


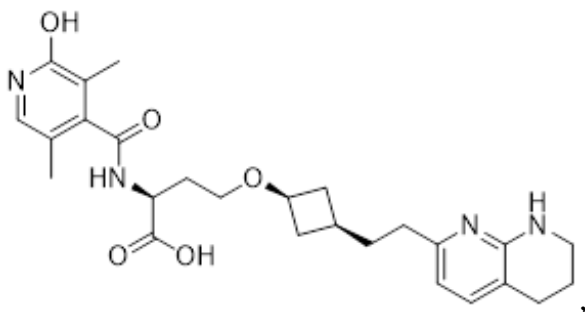
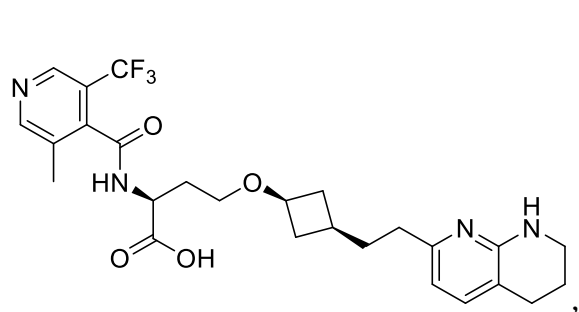
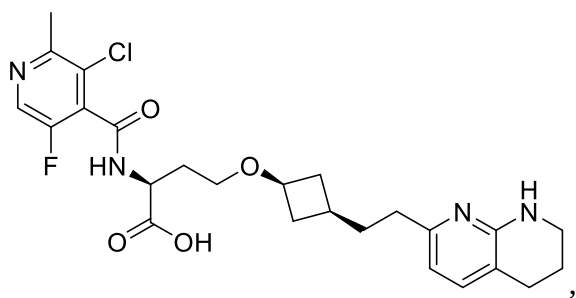
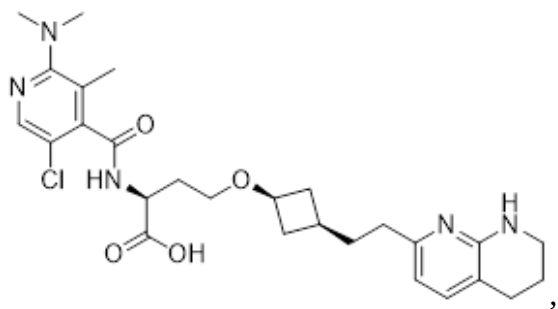
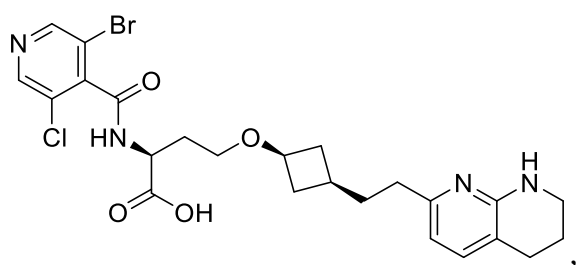
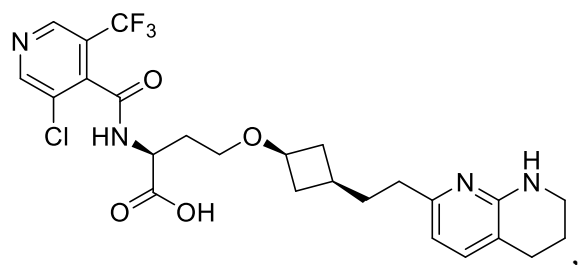
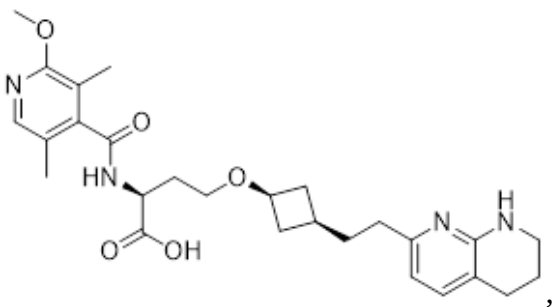
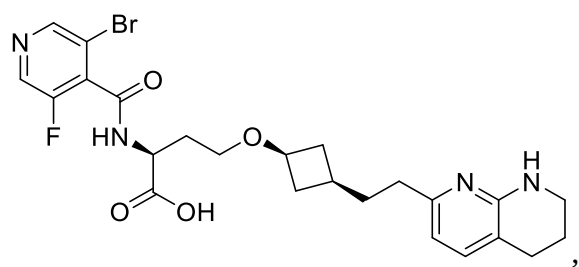
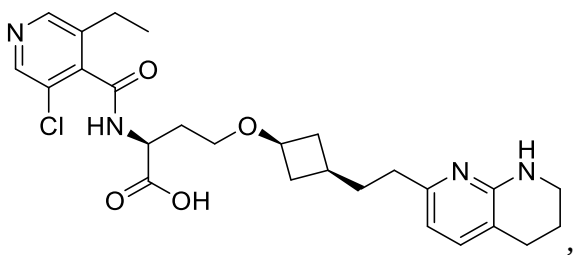
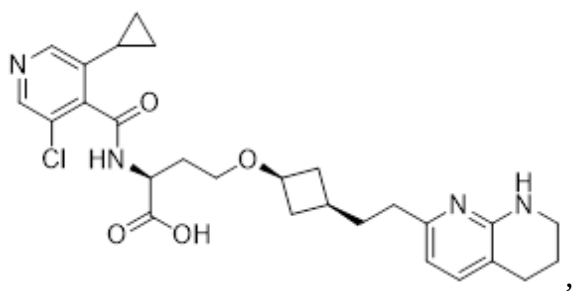
14. The compound of claim 1, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, wherein R^2 is selected from the group consisting of:

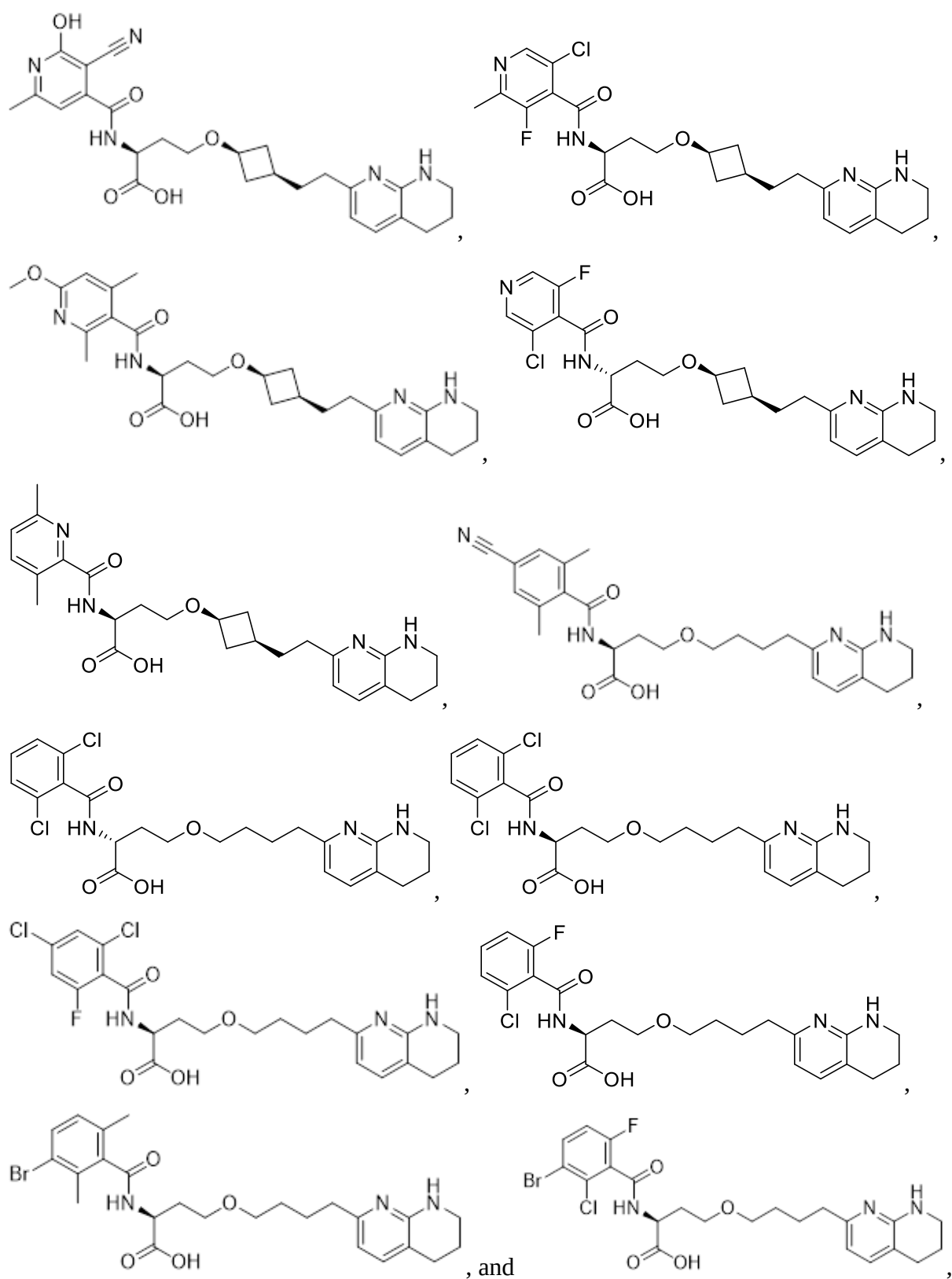


15. A compound selected from the group consisting of:









or a pharmaceutically acceptable salt or tautomer thereof.

16. A compound selected from the group consisting of:

N-(2-chloro-3-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine; N-(2-chloro-3-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
 N-(2-chloro-3-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;
 N-benzoyl-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;
 N-benzoyl-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
 N-benzoyl-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;
 N-(3-fluoro-5-(trifluoromethyl)benzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;
 N-(3-fluoro-5-(trifluoromethyl)benzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
 N-(3-fluoro-5-(trifluoromethyl)benzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;
 N-picolinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-picolinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-picolinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-nicotinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-nicotinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-nicotinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-isonicotinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-isonicotinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-isonicotinoyl-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(4-methyltetrahydro-2H-pyran-4-carbonyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(4-methyltetrahydro-2H-pyran-4-carbonyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(4-methyltetrahydro-2H-pyran-4-carbonyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(4-cyanotetrahydro-2H-pyran-4-carbonyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(4-cyanotetrahydro-2H-pyran-4-carbonyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(4-cyanotetrahydro-2H-pyran-4-carbonyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-N-(4-(trifluoromethyl)tetrahydro-2H-pyran-4-carbonyl)homoserine;
 O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-N-(4-(trifluoromethyl)tetrahydro-2H-pyran-4-carbonyl)-L-homoserine;
 O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-N-(4-(trifluoromethyl)tetrahydro-2H-pyran-4-carbonyl)-D-homoserine;
 N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;
 N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
 N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;
 N-(3,5-dimethylisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(3,5-dimethylisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(3,5-dimethylisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(3-chloro-5-methylisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(3-chloro-5-methylisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-chloro-5-methylisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(3,5-dichloroisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(3,5-dichloroisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(3,5-dichloroisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(2,4-dimethylnicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(2,4-dimethylnicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(2,4-dimethylnicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-N-(2,4,6-trimethylnicotinoyl)homoserine;
 O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-N-(2,4,6-trimethylnicotinoyl)-L-homoserine;
 O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-N-(2,4,6-trimethylnicotinoyl)-D-homoserine;
 N-(3-chloro-5-fluoroisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(3-chloro-5-fluoroisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(3-chloro-5-fluoroisonicotinoyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(2-fluoro-4-isocyano-6-methylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;
 N-(2-fluoro-4-isocyano-6-methylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
 N-(2-fluoro-4-isocyano-6-methylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;

N-(2-chloro-6-fluoro-4-isocyanobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;
 N-(2-chloro-6-fluoro-4-isocyanobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
 N-(2-chloro-6-fluoro-4-isocyanobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;
 N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;
 N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
 N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;
 N-(4-chloro-2,6-dimethylnicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(4-chloro-2,6-dimethylnicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(4-chloro-2,6-dimethylnicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(3-chloro-6-methylpicolinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(3-chloro-6-methylpicolinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(3-chloro-6-methylpicolinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(3-bromo-5-chloro-2-fluoroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(3-bromo-5-chloro-2-fluoroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(3-bromo-5-chloro-2-fluoroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(3-chloro-5-methoxyisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(3-chloro-5-methoxyisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-chloro-5-methoxyisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(5-bromo-2-hydroxyisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(5-bromo-2-hydroxyisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(5-bromo-2-hydroxyisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-chloro-5-cyclopropylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-chloro-5-cyclopropylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-chloro-5-cyclopropylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-chloro-5-ethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-chloro-5-ethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-chloro-5-ethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-bromo-5-fluoroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-bromo-5-fluoroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-bromo-5-fluoroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(2-methoxy-3,5-dimethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(2-methoxy-3,5-dimethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(2-methoxy-3,5-dimethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-chloro-5-(trifluoromethyl)isonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-chloro-5-(trifluoromethyl)isonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-chloro-5-(trifluoromethyl)isonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-bromo-5-chloroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-bromo-5-chloroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-bromo-5-chloroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(5-chloro-2-(dimethylamino)-3-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(5-chloro-2-(dimethylamino)-3-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(5-chloro-2-(dimethylamino)-3-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-chloro-5-fluoro-2-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-chloro-5-fluoro-2-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-chloro-5-fluoro-2-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(3-methyl-5-(trifluoromethyl)isonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(3-methyl-5-(trifluoromethyl)isonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3-methyl-5-(trifluoromethyl)isonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;

N-(2-hydroxy-3,5-dimethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;

N-(2-hydroxy-3,5-dimethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(2-hydroxy-3,5-dimethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(3-cyano-2-hydroxy-6-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(3-cyano-2-hydroxy-6-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(3-cyano-2-hydroxy-6-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(5-chloro-3-fluoro-2-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(5-chloro-3-fluoro-2-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(5-chloro-3-fluoro-2-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(6-methoxy-2,4-dimethylnicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(6-methoxy-2,4-dimethylnicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(6-methoxy-2,4-dimethylnicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(3-chloro-5-fluoroisonicotinoyl)-O-((1r,3S)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(3-chloro-5-fluoroisonicotinoyl)-O-((1r,3S)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
 N-(3-chloro-5-fluoroisonicotinoyl)-O-((1r,3S)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(3,6-dimethylpicolinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)homoserine;
 N-(3,6-dimethylpicolinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;

N-(3,6-dimethylpicolinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
 N-(4-cyano-2,6-dimethylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;
 N-(4-cyano-2,6-dimethylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
 N-(4-cyano-2,6-dimethylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;
 N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;
 N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
 N-(2,6-dichlorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;
 N-(2,4-dichloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;
 N-(2,4-dichloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
 N-(2,4-dichloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;
 N-(2-chloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;
 N-(2-chloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
 N-(2-chloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;
 N-(3-bromo-2,6-dimethylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;
 N-(3-bromo-2,6-dimethylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine;
 N-(3-bromo-2,6-dimethylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine;
 N-(3-bromo-2-chloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)homoserine;

N-(3-bromo-2-chloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine; and

N-(3-bromo-2-chloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-D-homoserine,

or a pharmaceutically acceptable salt or tautomer thereof.

17. A pharmaceutical composition comprising a pharmaceutically acceptable carrier or excipient and a compound of any one of claims 1 to 16, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof.
18. Use of a compound of any one of claims 1 to 16, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, in the manufacture of a medicament for treating a fibrotic disease or fibrotic condition in an individual in need thereof.
19. A kit comprising a compound of any one of claims 1 to 16, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof.
20. Use of a compound of any one of claims 1 to 16, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, in the manufacture of a medicament for inhibiting $\alpha_v\beta_6$ integrin activity in an individual in need thereof.
21. Use of a compound of any one of claims 1 to 16, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, in the manufacture of a medicament for inhibiting transforming growth factor beta activation in a cell.
22. Use of a compound of any one of claims 1 to 16, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, in the manufacture of a medicament for modulating the activity of at least one integrin comprising an α_v subunit in an individual in need thereof.
23. Use of a compound of any one of claims 1 to 16, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, in the manufacture of a medicament for modulating transforming growth factor beta activation in a cell.
24. Use of a compound of any one of claims 1 to 16, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, in the manufacture of a medicament for treating an individual having one or more tissues in need of therapy, wherein when

compared to a healthy state of the one or more tissues, the one or more tissues have at least one elevated level of:

- (a) transforming growth factor beta activation; or
- (b) transforming growth factor beta expression; or
- (c) both transforming growth factor beta activation and transforming growth factor beta expression; or
- (d) $\alpha_v\beta_1$ integrin activity; or
- (e) $\alpha_v\beta_1$ integrin expression; or
- (f) both $\alpha_v\beta_1$ integrin activity and $\alpha_v\beta_1$ integrin expression; or
- (g) $\alpha_v\beta_6$ integrin activity; or
- (h) $\alpha_v\beta_6$ integrin expression; or
- (i) both $\alpha_v\beta_6$ integrin activity and $\alpha_v\beta_6$ integrin expression.

25. The use according to claim 24, wherein an individual having one or more tissues in need of therapy is to be selectively treated with the compound; wherein when compared to a healthy state of the one or more tissues, the one or more tissues have an elevated level of:

- (d) $\alpha_v\beta_1$ integrin activity; or
- (e) $\alpha_v\beta_1$ integrin expression; or
- (f) both $\alpha_v\beta_1$ integrin activity and $\alpha_v\beta_1$ integrin expression.

26. The use according to claim 24, wherein an individual having one or more tissues in need of therapy is to be selectively treated with the compound; wherein when compared to a healthy state of the one or more tissues, the one or more tissues have an elevated level of:

- (g) $\alpha_v\beta_6$ integrin activity; or
- (h) $\alpha_v\beta_6$ integrin expression; or
- (i) both $\alpha_v\beta_6$ integrin activity and $\alpha_v\beta_6$ integrin expression.

27. The use according to claim 24, wherein an individual having one or more tissues in need of therapy is to be selectively treated with the compound; wherein when

compared to a healthy state of the one or more tissues, the one or more tissues have at least one elevated level of:

- (d) $\alpha_v\beta_1$ integrin activity; or
- (e) $\alpha_v\beta_1$ integrin expression; or
- (f) both $\alpha_v\beta_1$ integrin activity and $\alpha_v\beta_1$ integrin expression; or
- (g) $\alpha_v\beta_6$ integrin activity; or
- (h) $\alpha_v\beta_6$ integrin expression; or
- (i) both $\alpha_v\beta_6$ integrin activity and $\alpha_v\beta_6$ integrin expression.

28. The use according to claim 24, wherein an individual having one or more tissues in need of therapy is to be selectively treated with the compound; wherein when compared to a healthy state of the one or more tissues, the one or more tissues have at least one elevated level of:

- (d) $\alpha_v\beta_1$ integrin activity; or
 - (e) $\alpha_v\beta_1$ integrin expression; or
 - (f) both $\alpha_v\beta_1$ integrin activity and $\alpha_v\beta_1$ integrin expression;
- and further wherein the one or more tissues have at least one elevated level of:
- (g) $\alpha_v\beta_6$ integrin activity; or
 - (h) $\alpha_v\beta_6$ integrin expression; or
 - (i) both $\alpha_v\beta_6$ integrin activity and $\alpha_v\beta_6$ integrin expression.

29. The use according to claim 24, wherein the one or more tissues in the individual are made of one or more fibroblasts.
30. The use according to claim 24, wherein the one or more tissues in the individual are made of one or more epithelial cells.
31. Use of a pharmaceutical composition of claim 17 in the manufacture of a medicament for modulating transforming growth factor beta activation in a cell.
32. The pharmaceutical composition of claim 17, wherein the pharmaceutical composition further comprises one or more additional active agents.
33. The use of claim 18, wherein the fibrotic disease or fibrotic condition is selected from the group consisting of alcoholic liver disease induced fibrosis, Alport syndrome,

cardiac fibrosis, chronic kidney disease, cirrhosis, Crohn's disease, diabetic kidney disease, diabetic nephropathy, dermal fibrosis, focal segmental glomerulosclerosis, gastrointestinal fibrosis, interstitial lung disease, liver fibrosis, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, primarily biliary cholangitis, primary sclerosing cholangitis, pulmonary fibrosis, renal fibrosis, scleroderma, and systemic sclerosis associated interstitial lung disease.

34. The use of claim 18, wherein the fibrotic disease or fibrotic condition is selected from the group consisting of alcoholic liver disease induced fibrosis, alcoholic steatosis induced liver fibrosis, cirrhosis, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, and primary sclerosing cholangitis.
35. A compound selected from the group consisting of:
N-(4-methyltetrahydro-2H-pyran-4-carbonyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-N-(4-(trifluoromethyl)tetrahydro-2H-pyran-4-carbonyl)-L-homoserine;
N-(3-chloro-5-fluoroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
N-(4-chloro-2,6-dimethylnicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
N-(3-bromo-5-chloroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
N-(2-hydroxy-3,5-dimethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
N-(5-chloro-3-fluoro-2-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine;
N-(3-chloro-5-fluoroisonicotinoyl)-O-((1r,3S)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine;
N-(2-chloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine; and
N-(3-bromo-2,6-dimethylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine,
or a pharmaceutically acceptable salt or tautomer thereof.

36. A compound which is N-(4-methyltetrahydro-2H-pyran-4-carbonyl)-O-(cis-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.
37. A compound which is O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-N-(4-(trifluoromethyl)tetrahydro-2H-pyran-4-carbonyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.
38. A compound which is N-(3-chloro-5-fluoroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.
39. A compound which is N-(4-chloro-2,6-dimethylnicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.
40. A compound which is N-(3-bromo-5-chloroisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.
41. A compound which is N-(2-hydroxy-3,5-dimethylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.
42. A compound which is N-(5-chloro-3-fluoro-2-methylisonicotinoyl)-O-((1r,3R)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.
43. A compound which is N-(3-chloro-5-fluoroisonicotinoyl)-O-((1r,3S)-3-(2-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)ethyl)cyclobutyl)-D-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.
44. A compound which is N-(2-chloro-6-fluorobenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.

45. A compound which is N-(3-bromo-2,6-dimethylbenzoyl)-O-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)butyl)-L-homoserine, or a pharmaceutically acceptable salt or tautomer thereof.
46. Use of a compound of claim 1, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, in the manufacture of a medicament for inhibiting $\alpha\text{v}\beta_1$ integrin activity in an individual in need thereof.
47. The use of claim 33, wherein the fibrotic disease or fibrotic condition is idiopathic pulmonary fibrosis or radiation-induced pulmonary fibrosis.
48. A compound of claim 1, or a pharmaceutically acceptable salt, stereoisomer, or tautomer thereof, or a composition of claim 17, for use in therapy.