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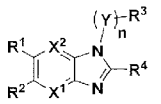
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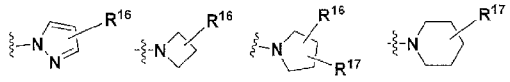
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(54) Title: 2-AMINO-BENZIMIDAZOLE DERIVATIVES AND THEIR USE AS 5-LIPOXYGENASE AND/OR PROSTAGLANDIN E SYNTHASE INHIBITORS


I


Ia

(57) Abstract: The present invention relates to benzimidazole derivatives having the general formula I, wherein n is 0 or 1; X^1 and X^2 are independently, at each occurrence, CR^5 or N; Y is C_1-C_6 alkylene, wherein alkylene is optionally substituted with one to two C_1-C_3 alkyl groups; R^1 is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkoxy, $-NH_2$, $-NHR^6$, $-NR^7R^8$ and $-NH-(R^9)_n-R^{10}$, n being 0 or 1; R^2 is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, $-NH_2$, $-NHR^6$, $-NR^7R^8$ and $-NH-(R^9)_n-R^{10}$; R^3 is selected from the group consisting of hydrogen, hydroxyl, OR^{11}, $-NR^7R^8$, C_1-C_6 alkoxy, C_1-C_6 alkyl, C_3-C_{10} cycloalkyl, C_1-C_3 haloalkyl, $-C(O)NHR^{11}$, aryl, heteroaryl and heterocyclyl, wherein each of said cycloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups; and R^4 is selected from the group consisting of $-NH_2$, $-N(R^{12})(V)_pR^{13}$, $-NH(V)_p-OR^{14}$, $-NHC(O)R^{15}$, and groups of formula Ia shown below, and their use in the treatment of diseases, in particular inflammatory diseases, cancer, stroke and/or Alzheimer's disease.

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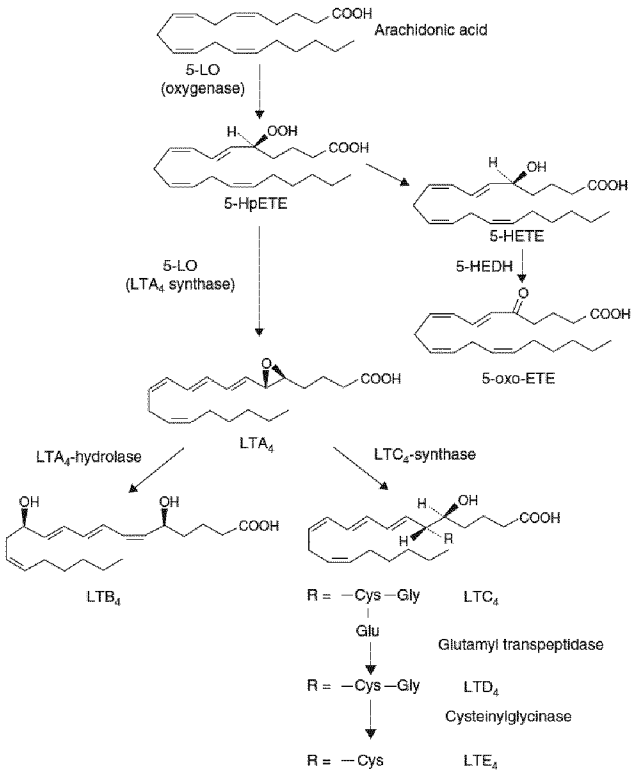
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2-AMINO-BENZIMIDAZOLE DERIVATIVES AND THEIR USE AS 5-LIPOXYGENASE AND/OR PROSTAGLANDIN E SYNTHASE INHIBITORS

Background of the invention

The present invention relates to small molecule compounds and their use in the treatment of diseases, in particular inflammatory diseases, cancer, stroke and/or Alzheimer's disease.

The arachidonate5-lipoxygenase (5-LOX, 5-LO, 5-lipoxygenase or Alox5) pathway has been shown to play an important role in the pathophysiology of many inflammatory diseases such as asthma, chronic obstructive pulmonary syndrome (COPD), allergic rhinitis, atherosclerosis, atopic dermatitis and pain by controlling the production of key inflammatory mediators. It has been also reported to be involved in cancer and Alzheimer's disease.
The 5-LOX enzyme is required in the production of LTB4 (leukotriene B4), a primary chemo-attractant and activator for leukocytes. LTB4 is primarily produced in neutrophils and macrophages where the enzyme LTA4 hydrolase converts LTA4 to LTB4. 5-LOX is also involved in the synthesis of LTC4, D4, and E4 (cysteinylleukotrienes; cys-LTs), which are strong bronchoconstrictors and proinflammatory mediators. Cys-LTs are also made from LTA4, a 5-LOX metabolite of arachidonic acid (AA). Another enzyme, LTC4 synthase, present in several cells, including eosinophils, basophils, and mast cells, conjugates LTA4 to glutathione to yield LTC4. LTC4 is further metabolized into LTD4 and LTE4. 5-LOX activity also results in the production of bioactive metabolites 5-hydroxyeicosatetraenoic acid (HETE) and 5-oxo-6,8,11,14-eicosatetraenoic acid (5-oxoETE). 5-oxoETE has been shown to induce tissue eosinophilia; thus, it may play a role in asthma and other diseases.



The clinical importance of the leukotriene pathway in inflammatory airway diseases has been demonstrated by the efficacy of various agents in the treatment of asthma and allergic rhinitis. Cys-LT receptor 1 antagonists (e.g., montelukast, zafirlukast, and pranlukast) have shown efficacy in asthma and allergic rhinitis, and the 5-LOX inhibitor zileuton has been shown to be efficacious in the treatment of asthma. 5-LOX inhibitors, which block both Cys-LTs and LTB4 production, have the potential for enhanced efficacy in asthma and allergic rhinitis compared to leukotriene receptor antagonists. 5-LOX inhibitors will block the proinflammatory activity of LTB4 and Cys-LTs as well as other leukotriene such as 5-HETE, and 5-oxo-ETE. Meta-analysis of several clinical trials suggest a better forced expiratory volume in 1 (FEV1) efficacy of zileuton versus the Cys-LT receptor antagonists in patients with severe asthma.

The only marketed 5-LOX inhibitor is zileuton, a redox hydroxyurea compound that chelates a critical active site iron moiety in the 5-LOX enzyme. Its efficacy and medical acceptance have been compromised by an inconvenient dosing regimen (i.e., four times daily), a suboptimal pharmacokinetic and pharmacodynamic profile, and a potential for hepatotoxicity. In addition, efforts to develop non-redox 5-LOX inhibitors have failed due to insufficient efficacy in human. Unmet medical needs therefore exist for more potent, better tolerated,non-

hepatotoxic 5-LOX inhibitors that could maximize thebenefits of inhibiting the leukotriene pathway and provide superior efficacy than obtained with zileuton and Cys-LT receptor antagonists.

Prostaglandin E synthase (PGES) is an enzyme involved in eicosanoid and glutathione metabolism, catalyzing the reaction from prostaglandin H_2 to prostaglandin E. It requires glutathione as an essential cofactor for its activity. It has been implicated in osteoarthritis, rheumatoid arthritis, atherosclerosis, and inflammatory pain.

Furthermore, inflammation-induced microsomal prostaglandin E synthase-1 (mPGES) is the terminal enzyme that synthesize prostaglandin E2 (PGE_2) downstream of cyclooxygenase-2 (COX-2). mPGES-1 is up-regulated in response to various pro-inflammatory stimuli with a concomitant increased expression of COX-2. Increase in the coordinate expression of COX-2 and mPGES-1 is reversed by glucocorticoid. The inhibition of PGES provides a rational for exploring mPGES-1 inhibition as a potential novel therapy for the above mentioned diseases. According to data of mPGES-1 knockout (KO) mice, these were less sensitive to inflammatory and neuropathic pain in rodent arthritis models, therefore, mPGES-1 has emerged as a potential target for the development of drugs for treatment of inflammation, pain, cancer, atherosclerosis, and stroke.

Herein are disclosed compounds with anti-inflammatory activity and anti-5-LOX activity and/or anti-PGES-activity.

It was an object of the present invention to identify compounds that interact and interfere with the 5-LOX-pathway and/or the PGES-pathway, in particular compounds having an inhibitory effect against arachidonate 5-lipoxygenase and/or prostaglandin E synthase.

It was also an object of the present invention to identify compounds with an anti-inflammatory activity.

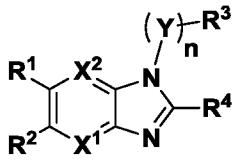
It was furthermore an object of the present invention to identify compounds effective against inflammatory disease, in particular asthma, atherosclerosis, pain, COPD, allergic rhinitis,

inflammation post infection, arthritis, dermatitis, pain, allergies, such as hay fever, autoimmune diseases, such as lupus erythematosus, inflammatory bowel diseases, such as Crohn's disease, celiac disease, acne, and against other diseases associated with a pathology of the 5-LOX-pathway and/or the PGES-pathway or diseases with an implication of the 5-LOX-pathway and/or the PGES-pathway, such as cancer and/or Alzheimer's disease and/or stroke.

1. Expert Opin. Ther. Patents **(2010)** 20**(3), 335-375**
2. Eur Respir J 2012; 40: 724.741
3. CurrOpin Allergy ClinImmunol. 2010 February ; 10(1): 60–66
4. Biochemical Pharmacology 70 (2005) 327–333
5. Int J ClinPract, April 2007, 61, 4, 663–676

Description of the Invention

In one aspect, the present invention relates to a compound having the general formula I:



Formula I

wherein

n is 0 or 1;

X^1 and X^2 are independently, at each occurrence, CR^5 or N;

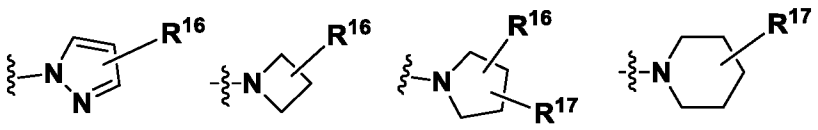
Y is C_1-C_6 alkylene, wherein alkylene is optionally substituted with one to two C_1-C_3 alkyl groups;

R^1 is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkoxy, $-NH_2$, $-NHR^6$, $-NR^7R^8$ and $-NH-(R^9)_n-R^{10}$, n being 0 or 1;

R^2 is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl,$-NH_2$, $-NHR^6$, $-NR^7R^8$ and $-NH-(R^9)_n-R^{10}$ group, n being 0 or 1;

R^3 is selected from the group consisting of hydrogen, hydroxyl, OR^{11}, $-NR^7R^8$, C_1-C_6 alkoxy, C_1-C_6 alkyl, C_3-C_{10}cycloalkyl, C_1-C_3 haloalkyl,$-C(O)NHR^{11}$, aryl, heteroaryl and heterocyclyl group, wherein each of said cycloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^4 is selected from the group consisting of $-NH_2$, $-N(R^{12})(V)_pR^{13}$, $-NH(V)_p-OR^{14}$, $-NHC(O)R^{15}$, and groups of formula Ia shown below,



Formula Ia

wherein,
p is 0 or 1,
V is C_1-C_6 alkylene, wherein alkylene is optionally substituted with one to three C_1-C_3 alkyl, C_3-C_6 cycloalkyl or phenyl groups, or wherein a carbon atom of said alkylene forms part of a C_3-C_6 cycloalkyl group;

R^5 is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl and C_1-C_6 alkoxy group;

R^6 is selected from the group consisting of C_1-C_6 alkyl, C_3-C_{10}cycloalkyl, C_1-C_6 haloalkyl, aryl, heteroaryl and heterocyclyl group, wherein each of said alkyl, cycloalkyl, haloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

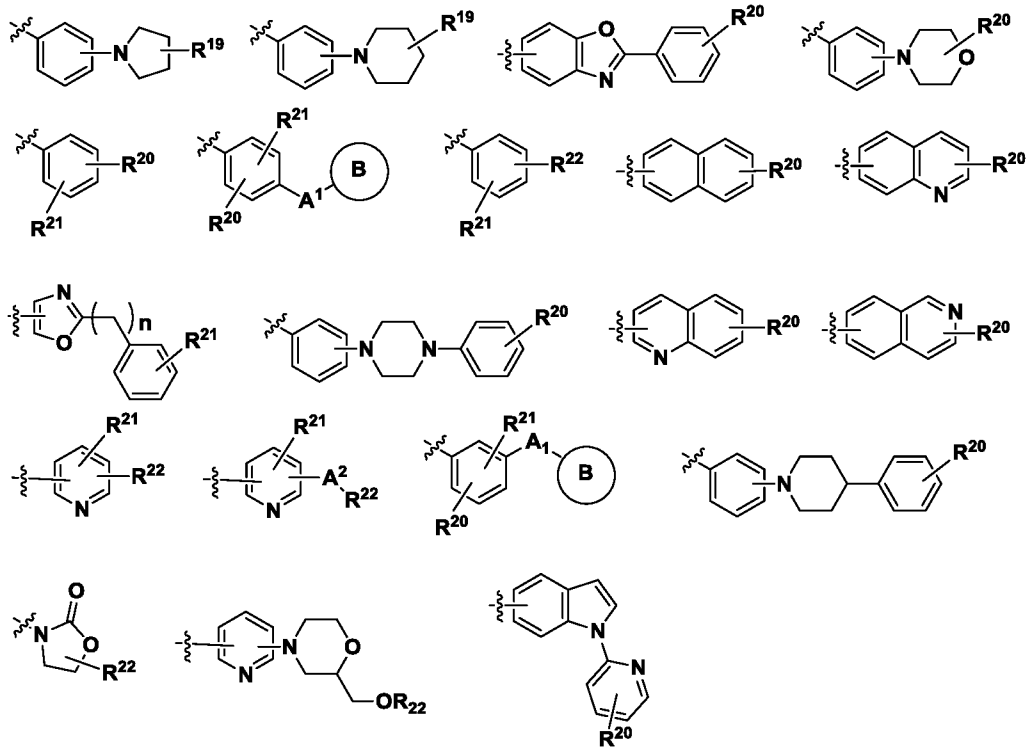
R^7 and R^8 are independently, at each occurrence, C_1-C_6 alkyl or heterocyclyl; or
R^7 and R^8 are connected to each other to make a four, five or six membered heterocyclyl or heteroaryl group, wherein each of said heterocyclyl and heteroaryl is optionally and independently substituted with one to four R^a groups;

R^9 is C_1-C_4 alkylene, wherein said alkylene is optionally substituted with one to three C_1-C_3 alkyl groups;
R^{10} is selected from the group consisting of hydroxyl, -OR^{11}, -CN, -C(O)OR^{18}, -C(O)NH_2, -C(NH)NH_2, aryl, heteroaryl and heterocyclyl group wherein each of said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{11} is independently, at each occurrence, selected from the group consisting of aryl, e.g. phenyl or benzyl, heteroaryl and heterocyclyl group wherein each of said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{12} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_4 alkyl-hydroxyl and C_1-C_4 alkyl-alkoxy;

R^{13} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_3-C_{10} cycloalkyl, C_1-C_4 alkyl-hydroxyl, -OH, -C(O)NH_2, -C(O)OR^{18}, -CN, C_1-C_3 haloalkyl and heterocyclyl, and groups of formula Ib shown below,



Formula Ib

wherein,

n is 0 or 1;

A^1 is -O-, -CH_2O-, -OCH_2-, -S-, -SO_2-, -SO_2NH-, -C(O)-, -C(O)NH-, -C(O)N(R^7)-, -CH(OH)-, -CH(OR^7)-, -NH-, -N(CH_3)- or -N(CH_2COOR^7)-;

A^2 is –O- or NH-;

B is selected from the group consisting of aryl, e.g. phenyl or benzyl, heteroaryl and heterocyclyl group wherein each of said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{14} is selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl, wherein each of said alkyl and aryl is optionally and independently substituted with one to four halogen or C_1-C_3 haloalkoxy groups;

R^{15} is aryl, wherein aryl is optionally substituted with one to four halogen groups;

R^{16} is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl and hydroxyl ;

R^{17} is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, -C(O)R^{11}, -C(O)NHR^{11}, -OR^{11} and aryl , wherein each of said alkyl and aryl is optionally and independently substituted with one to four R^a groups;

R^{18} is hydrogen or C_1-C_6 alkyl;

R^{19} is selected from the group consisting of hydrogen, -OR^{22} and -CH_2OR^{22};

R^{20} is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, –C(O)R^a and C_1-C_6 haloalkoxy;

R^{21} is selected from the group consisting of hydrogen, halogen and C_1-C_6 alkyl group;

R^{22} is selected from the group consisting of C_1-C_6 haloalkyl, aryl, e.g. phenyl or benzyl, and heteroaryl, wherein each of said haloalkyl, aryl and heteroaryl is optionally and independently substituted with one to four R^a groups;

R^a is independently, at each occurrence, selected from the group consisting of hydrogen, halogen, C_1-C_3 alkyl, C_3-C_{10} cycloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_6 haloalkoxy, hydroxyl, C_1-C_3 alkylhydroxyl, –CH_2OR^c, –OCH_2R^c, -OR^c, -CN, NO_2, -N$R^b$$R^c$, -C(O)N$R^b$$R^c$, -C(NH)$NH_2$, -C(O)$R^c$, -C(O)O$R^c$, sulfonyl, sulfoxide, heterocyclyl, heteroaryl and aryl, e.g. phenyl, benzyl, wherein each of said alkyl, haloalkyl, haloalkoxy, alkoxy, cycloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four C_1-C_3 alkyl, C_1-C_4 alkoxy, halogen, C_1-C_3 haloalkyl, -CN, -C(O)NH_2, -COOH, -CO_2Et and heteroaryl;

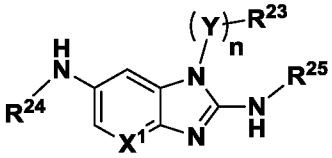
R^b and R^c are independently, at each occurrence, selected from the group consisting of hydrogen, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_1-C_6 alkyl-O-alkyl, C_2-C_{10} alkenyl, C_1-C_4 alkoxy, C_1-C_3 alkylhydroxyl, C_3-C_{10} cycloalkenyl, C_2-C_{10} alkynyl, C_1-C_6 haloalkyl, aryl, e.g. phenyl

or benzyl, heteroaryl, and heterocyclyl wherein each of said alkyl, cycloalkyl, alkyl-O-alkyl, alkenyl, alkoxy, cycloalkenyl, alkynyl, haloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four C_1-C_3 alkyl, C_1-C_4 alkoxy, halogen, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, hydroxyl, -C(O)NH_2, -COOH, -COOMe, -COOEt, -CN, -NO_2, -NH_2; or

R^b and R^c are connected to each other to make a four, five or six membered saturated or unsaturated cyclic or heterocyclic ring;

and pharmaceutically acceptable salts thereof.

In a further aspect, the present invention relates to a compound having the general formula II:



Formula II

wherein

n is 0 or 1;

X^1 is CR^5 or N;

Y is C_1-C_6 alkylene, wherein alkylene is optionally substituted with one to two C_1-C_3 alkyl groups;

R^5 is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl and C_1-C_6 alkoxy group;

R^{23} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_3 haloalkyl, aryl, heteroaryl and heterocyclyl group, wherein each of said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{24} is selected from the group consisting of hydrogen, C_3-C_{10}cycloalkyl, aryl, heteroaryl and heterocyclyl group, wherein each of said cycloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{25} is selected from the group consisting of hydrogen, $-(V)_pR^{26}$ and $-(V)_p-OR^{14}$;

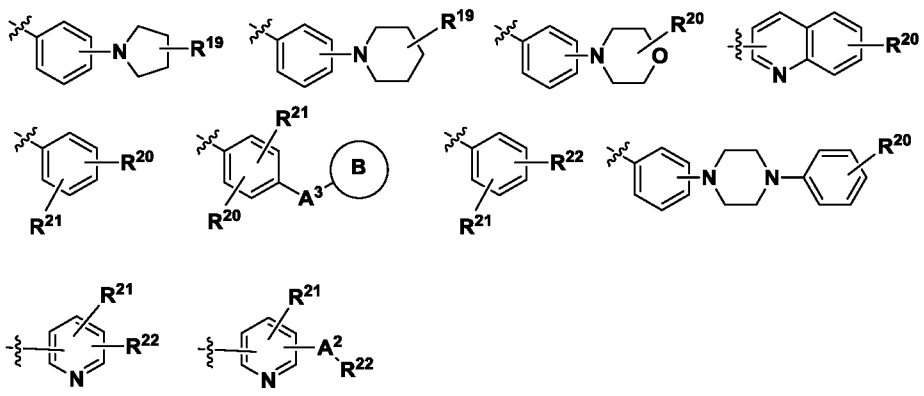
wherein,

p is 0 or 1,

V is C_1-C_6 alkylene, wherein alkylene is optionally substituted with one to three C_1-C_3 alkyl or phenyl groups, or wherein a carbon atom of said alkylene forms part of a C_3-C_6 cycloalkyl group;

R^{14} is selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl, wherein each of said alkyl and aryl is optionally and independently substituted with one to four halogen or C_1-C_3 haloalkoxy groups;

R^{26} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, -CN and C_1-C_3 haloalkyl, and groups of formula IIa shown below,



Formula IIa

wherein,

A^2 is -O- or NH-;

A^3 is -O-, $-CH_2O-$, $-OCH_2-$, or –NH-;

B is selected from the group consisting of aryl, e.g. phenyl or benzyl, heteroaryl and heterocyclyl group wherein each of said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{19} is selected from the group consisting of hydrogen, $-OR^{22}$ and $-CH_2OR^{22}$;

R^{20} is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy and C_1-C_6 haloalkoxy;

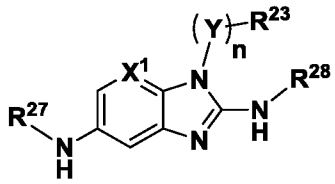
R^{21} is selected from the group consisting of hydrogen, halogen and C_1-C_6 alkyl;

R^{22} is selected from the group consisting of aryl, e.g. phenyl or benzyl, and heteroaryl, wherein each of said aryl and heteroaryl is optionally and independently substituted with one to four R^a groups;

R^a is independently, at each occurrence, selected from the group consisting of hydrogen, halogen, C_1-C_3 alkyl, C_3-C_{10} cycloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_6 haloalkoxy, hydroxyl, C_1-C_3 alkylhydroxyl, $–CH_2OR^c$, $–OCH_2R^c$, $-OR^c$, -CN, NO_2, $-NR^bR^c$, $-C(O)NR^bR^c$, $-C(NH)NH_2$, $-C(O)R^c$, $-C(O)OR^c$, sulfonyl, sulfoxide, heterocyclyl, heteroaryl and aryl, e.g. phenyl, benzyl, wherein each of said alkyl, haloalkyl, haloalkoxy, alkoxy, cycloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four C_1-C_3 alkyl, C_1-C_4 alkoxy, halogen, C_1-C_3 haloalkyl, -CN, $-C(O)NH_2$, -COOH, $-CO_2Et$ and heteroaryl;

R^b and R^c are independently, at each occurence, selected from the group consisting of hydrogen, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_1-C_6 alkyl-O-alkyl, C_2-C_{10} alkenyl, C_1-C_4 alkoxy, C_1-C_3 alkylhydroxyl, C_3-C_{10} cycloalkenyl, C_2-C_{10} alkynyl, C_1-C_6 haloalkyl, aryl, e.g. phenyl or benzyl, heteroaryl, and heterocyclyl wherein each of said alkyl, alkyl-O-alkyl, alkenyl, alkoxy, cycloalkenyl, alkynyl, haloalkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four C_1-C_3 alkyl, C_1-C_4 alkoxy, halogen, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, hydroxyl, $-C(O)NH_2$, -COOH, -COOMe, -COOEt, -CN, $-NO_2$, $-NH_2$; or
R^b and R^c are connected to each other to make a four, five or six membered saturated or unsaturated cyclic or heterocyclic ring;
and pharmaceutically acceptable salts thereof.

In a further aspect, the present invention relates to a compound having the general formula III:



Formula III

wherein

n is 0 or 1;

X^1 is CR^5 or N;

Y is C_1-C_6 alkylene, wherein alkylene is optionally substituted with one to two C_1-C_3 alkyl groups;

R^5 is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl and C_1-C_6 alkoxy group;

R^{23} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, aryl, heteroaryl and heterocyclyl group, wherein each of said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{27} is selected from the group consisting of hydrogen, $-R^6$, and $-R^9-R^{10}$;

wherein,

R^6 is selected from the group consisting of C_1-C_6 alkyl, C_3-C_{10}cycloalkyl, C_1-C_6 haloalkyl, aryl, heteroaryl and heterocyclyl group, wherein said alkyl, cycloalkyl, haloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^9 is C_1-C_4 alkylene, wherein said alkylene is optionally substituted with one to three C_1-C_3 alkyl groups;

R^{10} is selected from the group consisting of hydroxyl, $-OR^{11}$, $-C(O)OR^{18}$, $-C(O)NH_2$, aryl, heteroaryl and heterocyclyl group wherein each of said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

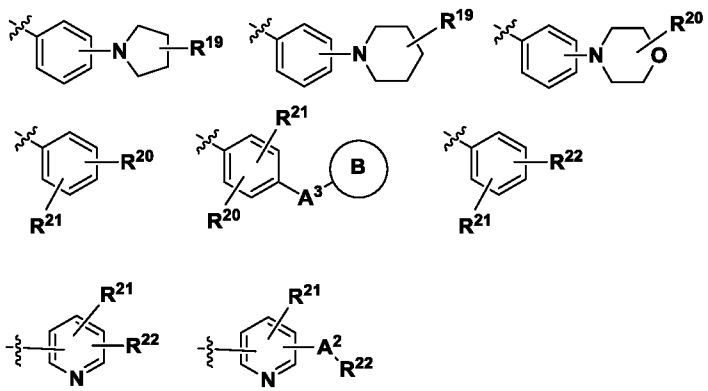
R^{11} is independently, at each occurrence selected from the group consisting of aryl, e.g. phenyl or benzyl, heteroaryl and heterocyclyl group wherein said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;
R^{18} is hydrogen or C_1-C_6 alkyl;

R^{28} is selected from the group consisting of hydrogen, -$(V)_pR^{29}$ and -$(V)_p$-OR^{14} group;

wherein,
p is 0 or 1,
V is C_1-C_6 alkylene, wherein alkylene is optionally substituted with one to three C_1-C_6 alkyl or phenyl groups;

R^{14} is selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl, wherein each of said alkyl and aryl is optionally and independently substituted with one to four halogen or C_1-C_3 haloalkoxy groups;

R^{29} is selected from the group consisting of hydrogen, C_1-C_6 alkyl and C_1-C_3 haloalkyl, and groups of formula IIIa shown below,



Formula IIIa

wherein,
A^2 is -O- or NH-;
A^3 is -O-, -CH_2O-, -OCH_2-, or –NH-;

B is selected from the group consisting of aryl, e.g. phenyl or benzyl, heteroaryl and heterocyclyl group wherein each of said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{19} is selected from the group consisting of hydrogen, $-OR^{22}$ and $-CH_2OR^{22}$;

R^{20} is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy and C_1-C_6 haloalkoxy;

R^{21} is selected from the group consisting of hydrogen, halogen and C_1-C_6 alkyl;

R^{22} is selected from the group consisting of aryl, e.g. phenyl or benzyl, and heteroaryl, wherein said aryl and heteroaryl is optionally and independently substituted with one to four R^a groups;

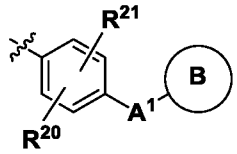
R^a is independently, at each occurrence, selected from the group consisting of hydrogen, halogen, C_1-C_3 alkyl, C_3-C_{10} cycloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_6 haloalkoxy, hydroxyl, C_1-C_3 alkylhydroxyl, $–CH_2OR^c$, $–OCH_2R^c$, $-OR^c$, -CN, NO_2, $-NR^bR^c$, $-C(O)NR^bR^c$, $-C(NH)NH_2$, $-C(O)R^c$, $-C(O)OR^c$, sulfonyl, sulfoxide, heterocyclyl, heteroaryl and aryl, e.g. phenyl, benzyl, wherein each of said alkyl, haloalkyl, haloalkoxy, alkoxy, cycloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four C_1-C_3 alkyl, C_1-C_4 alkoxy, halogen, C_1-C_3 haloalkyl, -CN, $-C(O)NH_2$, -COOH, $-CO_2Et$ and heteroaryl;

R^b and R^c are independently, at each occurrence, selected from the group consisting of hydrogen, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_1-C_6 alkyl-O-alkyl, C_2-C_{10} alkenyl, C_1-C_4 alkoxy, C_1-C_3 alkylhydroxyl, C_3-C_{10} cycloalkenyl, C_2-C_{10} alkynyl, C_1-C_6 haloalkyl, alkyl-O-alkyl, alkenyl, alkoxy, cycloalkenyl, alkynyl, haloalkyl, aryl, e.g. phenyl or benzyl, heteroaryl, and heterocyclyl wherein each of said alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four C_1-C_3 alkyl, C_1-C_4 alkoxy, halogen, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, hydroxyl, $-C(O)NH_2$,
-COOH, -COOMe , -COOEt, -CN, $-NO_2$, $-NH_2$; or

R^b and R^c are connected to each other to make a four, five or six membered saturated or unsaturated cyclic or heterocyclic ring;
and pharmaceutically acceptable salts thereof.

In one embodiment, the compound according to the present invention has one of the formulae 1- 556, as shown in tables 1-6 and/or example 7 and/or table 7, or a pharmaceutically acceptable salt thereof, preferably having one of the formulae 1-12, 14-16, 19-21, 24, 28-34, 36-40, 44, 48, 51-54, 56-68, 70, 71, 73-77, 79-81, 84, 86-173, 175-192, 194-234, 236-241, 243, 244, 246-261, 263-278, 280-321, 323-354, 356-385, 387- 428, 430-440, 442-446, 449-463, 465-471, 473-487, 489-492, 495-496, 499, 501, 503, 505, 507, 509, 512-514, 525, 529-544, 546-556 as indicated in Tables 1 and 7, or formula 14 as indicated in Tables 2 and 7, or one of the formulae 53, 54, 86, 90, 91, 95, 99, 103, 226 as indicated in Tables 5 - 7; or one of the formulae 14, 17, 24, 29, 30, 32, 33, 38, 43-46, 48, 49, 51-60, 62, 65-70, 73, 74, 79-81, 84, 86-88, 90-107, 109-113, 116, 118-132, 134-138, 140, 145, 147-150, 152, 153, 155, 160-162, 164-166, 168, 169, 172, 175-177, 179, 180, 184-187, 190-197, 199, 200, 202-220, 223, 224, 226, 227, 229-231, 233-236, 238-255, 257-262, 264, 265, 267-302, 304-306, 313, 316, 322-333, 335, 340, 342, 346, 347, 349, 350, 352, 353, 357-359, 361, 365-369, 372-375, 377-380, 382-384, 387, 389-393, 395-403, 405-407, 410, 412-415, 419-428, 430-432, 434-437, 440, 442, 445-453, 455, 457-458, 460-461, 463-482, 486-487, 489-496, 499, 501-553, 556 as indicated in Tables 3 and 7, or one of the formulae, 11, 12, 14, 24, 30, 32, 48, 52-54, 62, 65, 77, 79-81, 86-88, 92, 94, 97, 98, 101-103, 106, 109-111, 113, 119, 120, 122, 123, 125, 130, 136-138, 145, 147, 149, 155, 165, 166, 176, 177, 184, 193, 195, 199, 204, 211, 226, 227, 229, 231, 233, 234, 238, 239, 243, 249, 251, 253, 256, 268-271, 275, 277, 279, 281, 284, 288, 289, 296, 306, 311, 324, 328, 336, 341, 345, 350, 351, 358, 360, 362, 367-369, 373, 374, 378, 381, 392, 412-415, 430, 431, 433, 447-450, 461, 464-466, 468-471, 473-477, 479, 481, 482, 486, 487, 489-496, 498, 499, 501-506, 508, 509, 512-514, 516-519, 525-538, 540-547, 550, 553-554 as indicated in Tables 4 and 7; or having the formula 211 as indicated in Figure 1 and Table 7; or a pharmaceutically acceptable salt thereof.

In one embodiment of the compound having the formula I, R^4 is $-N(R^{12})(V)_pR^{13}$, R^{12} is H, V is C_1-alkylene, p is 1, R^{13} is



and B is heteroaryl which is optionally substituted with one to four R^a groups.

In one embodiment of the compound having formula I, R^1 is $-NH_2$ or $-NHR^6$, R^6 is heteroaryl or heterocyclyl wherein each of said heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups.

In a further aspect, the present invention relates to a compound, as defined above, or a pharmaceutically acceptable salt thereof, for use in the treatment of a disease associated with the 5LOX-pathway and/or the prostaglandin E synthase (PGES) pathway, said disease being selected from inflammatory diseases, e.g. asthma, atherosclerosis, pain, or COPD, cancer, stroke and Alzheimer's disease.

In one embodiment, said compound has an inhibitory activity on an enzyme involved in an inflammatory pathway or several inflammatory pathways, e.g. the arachidonate 5-lipoxygenese pathway and/or the prostaglandin E synthase pathway, preferably on arachidonate 5-lipoxygenase (5-lipoxygenase, 5-LO, 5-LOX, Alox5), at a concentration of said compound between 0.001-50μM, particularly preferably having an IC_{50} on arachidonate 5-lipoxygenase of less than 1μM and/or having an EC_{50} of less than 10μM on the production of leukotriene B4 (LTB4) in rat basophilic leucocyte cells (RBL) and/or rat whole blood (RWB), and/or having a 40-70 % inhibitory activity, preferably a>70 % inhibitory activity on the production of prostaglandin E2 in HeLaS3 cells, stimulated with TNF-α, at a concentration of 10μM of said compound.

The present invention also relates to a composition comprising a compound or a pharmaceutically acceptable salt thereof, as defined above and a pharmaceutically acceptable carrier.

The present invention also relates to such composition for use in the treatment of a disease associated with the 5LOX-pathway and/or the prostaglandin E synthase (PGES) pathway, said

disease being selected from inflammatory diseases, e.g. asthma, atherosclerosis, pain, or COPD, cancer, stroke and Alzheimer's disease.

In one embodiment, said inflammatory disease is one or several of asthma, allergic rhinitis, dermatitis, chronic obstructive pulmonary disease (COPD), inflammation post infection, arthritis, atherosclerosis, allergies, such as hay fever, autoimmune diseases, such as lupus erythematosus, inflammatory bowel diseases, such as Crohn's disease, celiac disease, acne, or pain, e.g. inflammatory and/or neuropathic pain.

In one embodiment, said treatment comprises administering a suitable amount of a compound as defined in any of claims 1-6 , or of a composition as defined in claim 9 , to a patient in need thereof, suffering from an inflammatory disease, and/or of cancer, and/or of stroke, and/or of Alzheimer's disease.

The present invention also relates to a method of treatment of a disease associated with the 5-LOX-pathway and/or the prostaglandin E synthase (PGES) pathway, said disease being selected from inflammatory diseases, cancer and Alzheimer's disease, said method comprising the application of a suitable amount of a compound as defined above or of a composition as defined above, to a patient in need thereof, suffering from a disease associated with the 5-LOX-pathway and/or the prostaglandin E synthase (PGES) pathway.

In one embodiment, said inflammatory disease is selected from asthma, allergic rhinitis, dermatitis, chronic obstructive pulmonary disease (COPD), inflammation post infection, arthritis, atherosclerosis, allergies, such as hay fever, autoimmune diseases, such as lupus erythematosus, inflammatory bowel diseases, such as Crohn's disease, celiac disease, acne, and pain, e.g. inflammatory and/or neuropathic pain.

In one embodiment, said suitable amount is an amount in the range of 0.01mg/kg body weight to 1g/kg body weight of said patient.

The present invention also relates to a compound that competitively inhibits the specific binding of a compound as defined above to arachidonate 5-lipoxygenase (5-lipoxygenase, 5-LO, 5-LOX, Alox5) or to prostaglandin E synthase (PGES). Such competitively inhibiting

compoundis herein also sometimes referred to as "competitive compound" or "competitively inhibiting compound".

The present invention also relates to a method of treatment of an inflammatory disease, in particular asthma, atherosclerosis, pain, chronic obstructive pulmonary disease (COPD), inflammation post infection, allergic rhinitis, arthritis, pain, e.g. inflammatory or neuropathic pain, allergies, such as hay fever, autoimmune diseases, such as lupus erythematosus, inflammatory bowel diseases, such as Crohn's disease, celiac disease, acne, and/or dermatitis, or a method of treatment of cancer/and or of Alzheimer's disease, said method comprising the application of a suitable amount of a competitively inhibiting compound as defined above, to a patient in need thereof.

In one embodiment, said patient is a patient suffering from an inflammatory disease and/or from cancer and/or from stroke and/or from Alzheimer's disease.

In one aspect, the present invention also relates to the use of a compound according to the present invention or of a composition according to the present invention for the manufacture of a medicament for the treatment of a disease associated with the 5LOX-pathway or the prostaglandin E synthase (PGES) pathway said disease being selected from inflammatory diseases, e. g. asthma, atherosclerosis, pain or COPD, cancer, stroke and Alzheimer's disease, wherein preferably, said inflammatory disease, in particular, is selected from asthma, atherosclerosis, pain, chronic obstructive pulmonary disease (COPD), inflammation post infection, allergic rhinitis, arthritis, pain, e. g. inflammatory or neuropathic pain, allergies, such as hay fever, autoimmune diseases, such as lupus erythematosus, inflammatory bowel diseases, such as Crohn's disease, celiac disease, acne, and / or dermatitis, wherein said treatment comprises the application of a suitable amount of a compound or a composition according to the present invention or composition according to the present invention, as defined above, to a patient in need thereof. The compound and the composition according to the present invention is either a compound according to the formula I, II or III, in particular, a compound according to any of claims 1 – 6, or it is a compound that is a competitive compound or competitively inhibiting compound, as defined further above.

The term "substituted" as used herein, for example as in "optionally substituted", is meant to indicate that a hydrogen atom attached to a member atom within a group is ("optionally") replaced by a group, such as halogen including fluorine, chlorine, bromine, C_1-C_{10} alkyl, C_1-C_3haloalkyl, C_3-C_7cycloalkyl, oxo, -OH, -OR^{23}, -$OC(O)R^{23}$, -CN, NO_2, -$N(R^{23})_2$, -$N(R^{23})C(O)R^{23}$, -$R^{23}N(R^{23})C(O)R^{23}$, -$C(O)R^{23}$, -$R^{23}C(O)R^{23}$, -$C(O)OR^{23}$, -$R^{23}C(O)OR^{23}$, -$C(O)N(R^{23})_2$, -$R^{23}C(O)N(R^{23})_2$, -$S(O)R^{23}$, -$S(O)_2R^{23}$, -$S(O)_2N(R^{23})_2$, phenyl, benzyl, aryl, heteroaryl or heterocyclyl, any of which itself is "optionally substituted"; it should be noted that the term "substituted" as used herein may also refer to several such substitutions in the same moiety.

R^{23} is, at each occurence, independently selected from the group consisting of hydrogen, halogen, C_1-C_{10} alkyl, C_1-C_3 haloalkyl, C_3-C_7 cycloalkyl, hydroxyl, oxo, -OR^{24}, -$C(O)OR^{24}$, -$C(O)R^{24}$, -$C(O)N(R^{24})_2$, -CN, -NO_2, -NH_2, -$N(R^{24})_2$, -OR^{24}HetA, -$OR^{24}N(R^{24})_2$, -$C(O)N(R^{24})$HetA, -C(O)HetA, -$C(O)N(R^{24})R^{24}S(O)_2R^{24}$; -$S(O)_2N(R^{24})_2$, -$S(O)_2R^{24}$, -$N(R^{24})C(O)R^{24}SR^{24}$, -$N(R^{24})R^{24}S(O)_2R^{24}$, or -$N(R^{24})S(O)_2R^{24}$, aryl, e.g. phenyl, benzyl, heteroaryl, and heterocyclyl, any of which is optionally substituted.

R^{24} is, at each occurrence, independently selected from the group consisting of hydrogen, C_1-C_8 alkyl optionally substituted with at least one hydroxyl or halogen; C_3-C_7cycloalkyl, aryl, e.g. phenyl, benzyl, and heterocycyl, any of which is optionally substituted.

In one embodiment, the present invention also relates to pharmaceutically acceptable salts of the compounds according to the present invention, and to such pharmaceutically acceptable salts for use in the treatment of an inflammatory disease and/or of cancer and/or of stroke and/or of Alzheimer's disease.

The term "alkyl" refers to a monovalent straight or branched chain, saturated aliphatic hydrocarbon radical having a number of carbon atoms in the specified range any of which is optionally substituted. Thus, for example, "C_1-C_6 alkyl" refers to any of the hexyl alkyl and pentyl alkyl isomers as well as n-, iso-, sec-, and t-butyl, n- and isopropyl, ethyl and methyl , any of which is optionally substituted.

The term "alkoxy" means a group having the formula –O-alkyl, in which an alkyl group, as defined above, is attached to the parent molecule via an oxygen atom. The alkyl portion of an

alkoxy group can have 1 to 20 carbon atoms (*i.e.*, C_1-C_{20}alkoxy), 1 to 12 carbon atoms (*i.e.*, C_1-C_{12}alkoxy), or 1 to 6 carbon atoms (*i.e.*, C_1-C_6alkoxy). Examples of suitable alkoxygroups include, but are not limited to, methoxy (-O-CH_3 or OMe), ethoxy (-OCH_2CH_3 or –OEt), t-butoxy (-O-$C(CH_3)_3$ or -OtBu) and the like. Such alkoxy group may itself be substituted once or several times.

The term "alkenyl" refers to a monovalent straight or branched chain aliphatic hydrocarbon radical containing one carbon-carbon double bond and having a number of carbon atoms in the specified range (and being optionally substituted). Thus, for example, "C_2-C_6alkenyl" refers to all of the hexenyl and pentenyl isomers as well as 1-butenyl, 2-butenyl, 3-butenyl, isobutenyl, 1-propenyl, 2-propenyl, and ethenyl (or vinyl).

The term "alkynyl" refers to a monovalent straight or branched chain aliphatic hydrocarbon radical containing one carbon-carbon triple bond and having a number of carbon atoms in the specified range. Thus, for example, "C_2-C_6alkynyl" refers to all of the hexynyl and pentynyl isomers as well as 1-butynyl, 2-butynyl, 3-butynyl, 1-propynyl, 2-propynyl, and ethynyl.

The term "alkylene" refers to a saturated, branched or straight chain or cyclic hydrocarbon radical having two monovalent radical centers derived by the removal of two hydrogen atoms from the same or two different carbon atoms, 1 to 10 carbon atoms, or 1 to 6 carbon atoms. Typical alkylene radicals include, but are not limited to, methylene (-CH_2-), 1,1-ethyl (-$CH(CH_3)$-), 1,2-ethyl (-CH_2CH_2-), 1,1-propyl (-$CH(CH_2CH_3)$-), 1,2-propyl (-$CH_2CH(CH_3)$-), 1,3-propyl (-$CH_2CH_2CH_2$-), 1,4-butyl (-$CH_2CH_2CH_2CH_2$-), and the like.

The term "alkenylene" refers to an unsaturated, branched or straight chain or cyclic hydrocarbon radical having two monovalent radical centers derived by the removal of two hydrogen atoms from the same or two different carbon atoms of parent alkene. For example, an alkenylene group can have 1 to 20 carbon atoms, 1 to 10 carbon atoms, or 1 to 6 carbon atoms. Typical alkenylene radicals include, but are not limited to, 1,2-ethenyl (-CH=CH-).

The term "alkynylene" refers to an unsaturated, branched or straight chain or cyclic hydrocarbon radical having two monovalent radical centers derived by the removal of two hydrogen atoms from the same or two different carbon atoms of parent alkyne. For example,

an alkynylene group can have 1 to 20 carbon atoms, 1 to 10 carbon atoms or 1 to 6 carbon atoms. Typical alkynylene radicals include, but are not limited to, acetylene (-C≡C-), propargyl (-CH_2C≡C-), and 4-pentynyl (-$CH_2CH_2CH_2$C≡CH-).

The term "cycloalkyl", alone or in combination with any other term, refers to a group, such as optionally substituted or non-substituted cyclic hydrocarbon, having from three to eight carbon atoms, unless otherwise defined. Thus, for example, "C_3-C_8cycloalkyl" refers to cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl.

The term "haloalkyl" refers to an alkyl group, as defined herein that is substituted with at least one halogen. Examples of straight or branched chained "haloalkyl" groups useful in the present invention include, but are not limited to, methyl, ethyl, propyl, isopropyl, *n*-butyl, and *t*-butyl substituted independently with one or more halogens. The term "haloalkyl" should be interpreted to include such substituents such as -CHF_2, –CF_3, -CH_2-CH_2-F, -CH_2-CF_3, and the like.

The term "heteroalkyl" refers to an alkyl group where one or more carbon atoms have been replaced with a heteroatom, such as, O, N, or S. For example, if the carbon atom of alkyl group which is attached to the parent molecule is replaced with a heteroatom (*e.g.*, O, N, or S) the resulting heteroalkyl groups are, respectively, an alkoxy group (*e.g.*, -OCH_3, etc.), an amine (*e.g.*, -$NHCH_3$, -$N(CH_3)_2$, etc.), or thioalkyl group (*e.g.*, -SCH_3, etc.). If a non-terminal carbon atom of the alkyl group which is not attached to the parent molecule is replaced with a heteroatom (*e.g.*, O, N, or S) and the resulting heteroalkyl groups are, respectively, an alkyl ether (*e.g.*, -CH_2CH_2-O-CH_3, etc.), alkyl amine (*e.g.*, -CH_2NHCH_3, -$CH_2N(CH_3)_2$, etc.), or thioalkyl ether (e.g., -CH_2-S-CH_3).

The term "halogen" refers to fluorine, chlorine, bromine, or iodine.

The term "aryl" refers to (i) optionally substituted phenyl, (ii) optionally substituted 9- or 10 membered bicyclic, fused carbocyclic ring systems in which at least one ring is aromatic, and (iii) optionally substituted 11- to 14-membered tricyclic, fused carbocyclic ring systems in which at least one ring is aromatic. Suitable aryls include, for example, phenyl, biphenyl, naphthyl, tetrahydronaphthyl (tetralinyl), indenyl, anthracenyl, and fluorenyl.

The term "phenyl" as used herein is meant to indicate that optionally substituted or non-substituted phenyl group.

The term "benzyl" as used herein is meant to indicate that optionally substituted or non-substituted benzyl group.

The term "heteroaryl" (herein sometimes also abbreviated as "HetA") refers to (i) optionally substituted 5- and 6-membered heteroaromatic rings and (ii) optionally substituted 9- and 10-membered bicyclic, fused ring systems in which at least one ring is aromatic, wherein the heteroaromatic ring or the bicyclic, fused ring system contains from 1 to 4 heteroatoms independently selected from N, O, and S, where each N is optionally in the form of an oxide and each S in a ring which is not aromatic is optionally S(O) or $S(O)_2$. Suitable 5- and 6-membered heteroaromatic rings include, for example, pyridyl, pyrrolyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, thienyl, furanyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, isooxazolyl, oxadiazolyl, thiazolyl, isothiazolyl, and thiadiazolyl. Suitable 9-and 10-membered heterobicyclic, fused ring systems include, for example, benzofuranyl, indolyl, indazolyl, naphthyridinyl, isobenzofuranyl, benzopiperidinyl, benzisoxazolyl, benzoxazolyl, chromenyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, isoindolyl, benzodioxolyl, benzofuranyl, imidazo[1,2-a]pyridinyl, benzotriazolyl, dihydroindolyl, dihydroisoindolyl, indazolyl, indolinyl, isoindolinyl, quinoxalinyl, quinazolinyl, 2,3-dihydrobenzofuranyl, and 2,3-dihydrobenzo-1,4-dioxinyl.

The term "heterocyclyl" refers to (i) optionally substituted 4- to 8-membered, saturated and unsaturated but non-aromatic monocyclic rings containing at least one carbon atom and from 1 to 4 heteroatoms, (ii) optionally substituted bicyclic ring systems containing from 1 to 6 heteroatoms, and (iii) optionally substituted tricyclic ring systems, wherein each ring in (ii) or (iii) is independent of fused to, or bridged with the other ring or rings and each ring is saturated or unsaturated but nonaromatic, and wherein each heteroatom in (i), (ii), and (iii) is independently selected from N, O, and S, wherein each N is optionally in the form of an oxide and each S is optionally oxidized to S(O) or $S(O)_2$. Suitable 4- to 8-membered saturated heterocyclyls include, for example, azetidinyl, piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isoxazolidinyl, pyrrolidinyl, imidazolidinyl,

piperazinyl, tetrahydrofuranyl, tetrahydrothienyl, pyrazolidinyl, hexahydropyrimidinyl, thiazinanyl, thiazepanyl, azepanyl, diazepanyl, tetrahydropyranyl, tetrahydrothiopyranyl, dioxanyl, and azacyclooctyl. Suitable unsaturated heterocyclic rings include those corresponding to the saturated heterocyclic rings listed in the above sentence in which a single bond is replaced with a double bond. It is understood that the specific rings and ring systems suitable for use in the present invention are not limited to those listed in this and the preceding paragraphs. These rings and ring systems are merely representative.

In one embodiment, said compound has an inhibitory activity on an enzyme involved in an inflammatory pathway(s), preferably an arachidonate 5-lipoxygenase (5-lipoxygenase, 5-LO, 5-LOX, Alox 5), at a concentration of said compound between 0.001-50 μM, particularly preferably having an IC_{50} on arachidonate 5-lipoxygenase of less than 1 μM and/or having an EC_{50} of less than 10 μM on the production of leukotriene B4 (LTB4) in rat basophilic leukocyte cells (RBL) or rat whole blood (RWB).

The term "5-LOX-Pathway" is meant to refer to the pathway starting from arachidonic acid to LTA4, LTB4, LTC4, LTD4, LTE4 and 5-oxoETE (5-oxo-6,8,11,14-eicosatetraenoic acid). The 5-LOX-pathway involves one or several of the enzymes arachidonate-5-lipoxygenase (5-LOX), LTA4-hydrolase, LTC4-synthase, glutamyltranspeptidase, and 5-hydroxy-6,8,11,14-eicosatetraenoic acid dehydrogenase. In this 5-LOX-pathway one or several enzymes may malfunction and lead to a pathology which, in many instances, manifests itself in a disease or disease state. Such malfunctioning of an enzyme may be a deviation of activity as compared to the normal healthy state (which is not affected by such pathology). Such deviation may be an excess activity of the respective enzyme, or it may be an activity that is below the normal activity of such enzyme in a healthy individual. A "disease associated with the 5-LOX-pathway" may be a disease wherein one or several of the above mentioned enzymes show an excess activity. Preferably, it is the 5-lipoxygenase (5-LOX), which shows a deviant activity, preferably an excess activity in comparison to a healthy, non-pathological state. In one embodiment, the 5-lipoxygenase (5-LOX) is the only enzyme of the 5-LOX-pathway showing a decreased activity. In another embodiment, other enzyme(s) alone or in addition to the 5-lipoxygenase show decreased or increased activity as well. A person skilled in the art knows how to determine whether or not one or several enzymes of the 5-LOX-pathway show a deviant activity. For example this can be easily determined by measurement of one or several

leukotrienes which are reaction products of the respective reactions within the 5-LOX-pathway. Measurement of these leukotrienes, for example one or several of LTA4, LTB4, LTC4, LTD4, LTE4, 5-HpETE, 5-HETE and 5-oxo-ETE, may be performed in an appropriate body fluid of a patient, such as blood, nasal secretions, bronchial secretions, urine, semen, spinal fluid, lymph, interstitial fluid, mucosal fluid, fluid extracted from cells or a cell homogenate, vaginal fluid, tears, synovial fluid, sweat, pus, pleural fluid, peritoneal fluid, pericardial fluid, mucus, chyle, breast milk, cerebrospinal fluid, serum, and amniotic fluid. Measurement of such leukotrienes may be done by various means, such as chromatography alone or coupled with mass spectrometry, for example as published by Knapp et al. (N. Engl. J. Med. 1989; 320:1037-1043), Knapp, Prostaglandins 1990; 39:407-423; and Reilly et al. J. Clin. Pathol. 1988; 41:1163-1167; reverse phase-HPLC (Antonelli et al.) Intensive Care Med. 1989; 15(5):296-301, HPLC, as published by Otila et al. Acta Derm. Venereol. 1986; 66(5):381-385, ELISA-Technology, as for example commercially available in the form of a kit for leukotrienes from Oxford Biomedical Research or from Assay Designs Inc., or from Cayman (cat no. 520111), as for example published by Chu et al., American Journal of Pathology, 2011, Volume 178, No. 4, pp. 1762-1769, or by Tardif et al. Circ. Cardiovasc. Imaging, 2010, 298-307. Hence, methodology for determining the levels of leukotrienes and other reaction products/intermediates of the 5-LOX-pathway are available to someone skilled in the art, and hence, a person skilled in the art can easily determine whether or not a disease is associated with the 5-LOX-pathway by determining whether or not the activity of one or several of the enzymes from the 5-LOX-pathway show a deviant activity when compared to the normal/healthy state.

The term “PGES-pathway” is meant to refer to a pathway involving the production of prostaglandin E. The PGES-pathway involves one or several enzymes, including cyclooxygenase-2 (COX-2) and prostaglandin E synthase (PGES). In this PGES-pathway, one or several enzymes may malfunction and lead to a pathology which, in many instances, manifests itself in a disease or disease state. Such malfunctioning of an enzyme may be a deviation of activity as compared to the normal healthy state (which is not effected by such pathology). Such deviation may be an excess activity of the respective enzyme, or it may be an activity that is below the normal activity of such enzyme in a healthy individual. A “disease associated with the PGES-pathway” may be a disease wherein one or several of the above-mentioned enzyme show a deviant activity. Preferably it is the prostaglandin E

synthase (PGES) which shows a deviant activity, preferably an excess activity in comparison to a healthy-non-pathological state.

In a preferred embodiment, such a "disease associated with the 5-LOX-pathway" or "a disease associated with the PGES-pathway" is a disease selected from inflammatory diseases, cancer, stroke and Alzheimer's disease. In a preferred embodiment, such disease is associated with an increased level of one or several reaction products or intermediates from the 5-LOX-pathway, such as the above mentioned leukotrienes or 5-HpETE, 5-HETE or 5-oxo-ETE, or one or several reaction products or intermediates from the PGES-pathway. In one embodiment, the inflammatory disease is a disease selected from inflammatory diseases of the respiratory system, such as asthma, allergic rhinitis, chronic obstructive pulmonary disease (COPD), sinusitis, bronchitis, hay fever, inflammatory diseases of the skin, such as dermatitis, psoriasis, acne, inflammatory bowel diseases, such as Crohn's disease, celiac disease, colitis ulcerosa, autoimmune diseases, such as lupus erythematosus arthritis, in particular rheumatoid arthritis, inflammatory diseases of the vascular system, such as atherosclerosis, vasculitis, Wegener granulomatosis, inflammation post infection and pain, e.g. inflammatory or neuropathic pain.

The 5-lipoxygenase pathway has been implicated in various diseases, and 5-lipoxygenase-products/intermediates have been measured for various diseases, as exemplified for atherosclerosis in Tardif et al. Circ. Cardiovasc. Imaging, 2010; 3: 298-307; for Alzheimer's disease in Chu et al. Am. J. Cathol. 2011 April; 178(4); 1762-1769; for cancer in Lim et al. J. Neurooncol. 2010, May; 97(3); 339-346; for asthma in Berger et al. Int. J. Clin. Pract., April 2007, 61, 4, 663-676; for COPD in Cazzola et al. European Respiratory Journal 2012; 40(3); 724-741, for allergic rhinitis in Knapp N. Engl. J. Med. 1990; 323; 1745-1748, for atopic dermatitis in Woodmansee et al. Ann. Allergy Asthma Immunol. 1999; 83:548-552, for Urticaria in Spector et al. J. Allergy Clinc. Immunol. 1998; 101(4)572, for chronic nasal polyposis/sinusitis in Ravikumar, J. Allergy Clin. Immunol. 2005; 115(2) Supplemental S201; A 801, for arthritis, in Lewis et al., N. Engl. J. Med. 1990; 323:645-655, for pain in Noguchi et al. Biol. Pharm. Bull. 2011;34(8):1163-1169, for autoimmune diseases in J. Rheumatol. 1995 (March); 22(3):462-468, for Crohn's disease in Lewis et al. N. Engl. J. Med. 1990; 323:645-655, for acne in Zouboulis, Dermatoendocrinology 2009 May/June; 1(3):188-192.

In one aspect, the present invention relates to compounds for use in the treatment of a disease associated with the 5-LOX-pathway and/or prostaglandin E synthase (PGES), e.g. an inflammatory disease or cancer or Alzheimer's disease, said compound having one of the formulae 1-415, as shown in Tables 1-6 and/or Example 7 and Table 7, preferably having one of the formulae 1-12, 14-16, 19-21, 24, 28-34, 36-40, 44, 48, 51-54, 56-68, 70, 71, 73-77, 79-81, 84, 86-173, 175-192, 194-234, 236-241, 243, 244, 246-261, 263-278, 280-321, 323-354, 356-385, 387-428, 430-440, 442-446, 449-463, 465-471, 473-487, 489-492, 495-496, 499, 501, 503, 505, 507, 509, 512-514, 525, 529-544, 546-556 as indicated in Tables 1 and 7 or formula 14 as indicated in Tables 2 and 7, or one of the formulae 53, 54, 86, 90, 91, 95, 99, 103, 226 as indicated in Tables 5 - 7; or one of the formulae 14, 17, 24, 29, 30, 32, 33, 38, 43-46, 48, 49, 51-60, 62, 65-70, 73, 74, 79-81, 84, 86-88, 90-107, 109-113, 116, 118-132, 134-138, 140, 145, 147-150, 152, 153, 155, 160-162, 164-166, 168, 169, 172, 175-177, 179, 180, 184-187, 190-197, 199, 200, 202-220, 223, 224, 226, 227, 229-231, 233-236, 238-255, 257-262, 264, 265, 267-302, 304-306, 313, 316, 322-333, 335, 340, 342, 346, 347, 349, 350, 352, 353, 357-359, 361, 365-369, 372-375, 377-380, 382-384, 387, 389-393, 395-403, 405-407, 410, 412-415, 419-428, 430-432, 434-437, 440, 442, 445-453, 455, 457-458, 460-461, 463-482, 486-487, 489-496, 499, 501-553, 556 as indicated in Tables 3 and 7, or one of the formulae 11, 12, 14, 24, 30, 32, 48, 52-54, 62, 65, 77, 79-81, 86-88, 92, 94, 97, 98, 101-103, 106, 109-111, 113, 119, 120, 122, 123, 125, 130, 136-138, 145, 147, 149, 155, 165, 166, 176, 177, 184, 193, 195, 199, 204, 211, 226, 227, 229, 231, 233, 234, 238, 239, 243, 249, 251, 253, 256, 268-271, 275, 277, 279, 281, 284, 288, 289, 296, 306, 311, 324, 328, 336, 341, 345, 350, 351, 358, 360, 362, 367-369, 373, 374, 378, 381, 392, 412-415, 430, 431, 433, 447-450, 461, 464-466, 468-471, 473-477, 479, 481, 482, 486, 487, 489-496, 498, 499, 501-506, 508, 509, 512-514, 516-519, 525-538, 540-547, 550, 553-554 as indicated in Tables 4 and 7; or the formula 211 as indicated in Figure 1 and Table 7; or a pharmaceutically acceptable salt thereof.

Preferably, the compounds as defined above have an inhibitory activity on an enzyme involved in an inflammatory pathway(s) e.g. the arachidonate 5-lipoxygenase pathway and/or the prostaglandin E synthase (PGES) pathway, preferably on arachidonate 5-lipoxygenase (5-lipoxygenase, 5-LO, 5-LOX, Alox5), at a concentration of said compound between 0.001-50μM, particularly preferably having an IC_{50} on arachidonate 5-lipoxygenase of less than 1μM and/or having an EC_{50} of less than 10 μM on the production of leukotriene B4 (LTB4) in

rat basophilic leukocyte cells (RBL) or rat whole blood (RWB), and/or having a 40-70 % inhibitory activity, preferably > 70 % inhibitory activity on the production of prostaglandin E2 in HeLa S3 cells stimulated with TNF-alpha, at a concentration of 10 μM of said compound.

In one aspect the present invention relates to a composition comprising a compound according to the present invention and a pharmaceutically acceptable carrier, for use in the treatment of a disease associated with the 5-LOX-pathway and/or the PGES-pathway, said disease being selected from inflammatory disease, e.g. asthma or COPD, cancer, stroke and Alzheimer's disease.

In one embodiment, said inflammatory disease is asthma or allergic rhinitis or dermatitis or chronic obstructive pulmonary disease (COPD) or inflammation post infection or arthritis or atherosclerosis or pain. e.g. inflammatory and/or neuropathic pain.

In one embodiment, said treatment comprises administering a suitable amount of a compound or of a composition as defined above to a patient in need thereof, suffering from a disease associated with the 5-LOX-pathway and/or the PGES-pathway, said disease being selected from inflammatory disease, cancer, stroke and Alzheimer's disease.

In a further aspect the present invention relates to a method of treatment of a disease associated with the 5-LOX-pathway and/or the PGES-pathway, said disease being selected from an inflammatory disease, cancer, stroke and Alzheimer's disease, said method comprising the application of a suitable amount of a compound or composition as defined above to a patient in need thereof. In one embodiment said inflammatory disease is asthma or allergic rhinitis or dermatitis or chronic obstructive pulmonary disease (COPD) or inflammation post infection or arthritis or atherosclerosis or pain, e.g. inflammatory and/or neuropathic pain.

In one embodiment, said suitable amount is an amount in the range of 0.01 mg/kg body weight to 1 g/kg body weight of said patient.

The present invention also relates to the use of a compound or composition according to the present invention, as defined above, for the manufacture of an medicament for the treatment of a disease associated with the 5-LOX-pathway / or the PGES-pathway, said disease being selected from an inflammatory disease, cancer, stroke and Alzheimer's disease, said treatment comprising the application of a suitable amount of a compound or a composition as defined above to a patient in need thereof. The inflammatory disease and the suitable amount is as defined further above.

In a further aspect the present invention relates to compound that competitively inhibits the specific binding of a compound according to the present invention as defined above to arachidonate 5-lipoxygenase (5-lipoxygenase, 5-LO, 5-LOX, Alox5) and/or the prostaglandin E synthase (PGES).

In yet a further aspect the present invention relates to method of treatment of a disease associated with the 5-LOX-pathway and/or the PGES-pathway, said disease being selected from an inflammatory disease, in particular asthma, atherosclerosis, pain, COPD, inflammation post infection, allergic rhinitis and/or atopic dermatitis or cancer or stroke or Alzheimer's disease, said method comprising the application of a suitable amount of a compound as just defined, i.e. a compound that competitively inhibits the specific binding of a compound according to the present invention to arachidonate 5-lipoxygenase or to prostaglandin E synthase, to a patient in need thereof.

Such compound that competitively inhibits the specific binding of a compound according to the present invention to 5-LOX or to PGES, is herein also sometimes referred to as a "competitively inhibitory compound".

In one embodiment, such patient is a patient suffering from an inflammatory disease, preferably as defined further above.

The present invention also relates to the use of a competitively inhibitory compound for the manufacturer of a medicament for the treatment of a disease associated with the 5-LOX-pathway or the PGES-pathway, said disease being selected from an inflammatory disease, in particular, asthma, atherosclerosis, pain or COPD, inflammation post-infection, allergic

rhinitis and/or arthritis, or cancer or stroke or Alzheimer's disease, said treatment comprising the application of a suitable amount of a compound that competitively inhibits the specific binding as defined above, to a patient in need thereof.

The terms "IC_{50}" and "EC_{50}" refer to the half-maximal inhibitory concentration and the half-maximal effective concentration, respectively, of a compound with respect to a given activity, for example an inhibition of an enzyme through a compound, or the production of a substance stimulated by a compound. One example of an IC_{50} is the half-maximum inhibitory concentration of a compound on the activity of arachidonate 5-lipoxygenase. One example for an EC_{50}-value is the half maximum effective concentration of a compound on the production and/or secretion of leukotriene B4 (LTB4) in a cell or whole blood, for example a rat basophilic leukocyte cell (RBL) or rat whole blood (RWB).

Pharmaceutical compositions

Pharmaceutically acceptable salts

Examples of pharmaceutically acceptable addition salts include, without limitation, the non-toxic inorganic and organic acid addition salts such as the acetate derived from acetic acid, the aconate derived from aconitic acid, the ascorbate derived from ascorbic acid, the benzenesulfonate derived from benzensulfonic acid, the benzoate derived from benzoic acid, the cinnamate derived from cinnamic acid, the citrate derived from citric acid, the embonate derived from embonic acid, the enanthate derived from enanthic acid, the formate derived from formic acid, the fumarate derived from fumaric acid, the glutamate derived from glutamic acid, the glycolate derived from glycolic acid, the hydrochloride derived from hydrochloric acid, the hydrobromide derived from hydrobromic acid, the lactate derived from lactic acid, the maleate derived from maleic acid, the malonate derived from malonic acid, the mandelate derived from mandelic acid, the methanesulfonate derived from methane sulphonicacid, the naphthalene-2-sulphonate derived from naphthalene-2-sulphonic acid, the nitrate derived from nitric acid, the oxalate derived from oxalic acid, the perchlorate derived from perchloric acid, the phosphate derived from phosphoric acid, the phthalate derived from phthalic acid, the salicylate derived from salicylic acid, the sorbate derived from sorbic acid, the stearate derived from stearic acid, the succinate derived from succinic acid, the sulphate

derived from sulphuric acid, the tartrate derived from tartaric acid, the toluene-p-sulphonate derived from p-toluene sulphonic acid, and the like. Such salts may be formed by procedures well known and described in the art.

Other acids which may not be considered pharmaceutically acceptable, may be useful in the preparation of salts useful as intermediates in obtaining a chemical compound of the invention and its pharmaceutically acceptable acid addition salt, for use in the treatment of an inflammatory disease.

In another embodiment, the compounds of the invention are used in their respective free base form, for use in the treatment of an inflammatory disease, according to the present invention.

Metal salts of a chemical compound of the invention include alkali metal salts, such as the sodium salt of a chemical compound of the invention containing a carboxy group.

The chemical compounds of the invention may be provided in unsolvated or solvated forms together with a pharmaceutically acceptable solvent(s) such as water, ethanol, and the like. Solvated forms may also include hydrated forms such as the monohydrate, the dihydrate, the hemihydrate, the trihydrate, the tetrahydrate, and the like. In general, solvated forms are considered equivalent to unsolvated forms for the purposes of this invention.

Administration and Formulation

The production of medicaments containing the compounds of the invention, its active metabolites or isomers and salts according to the invention and their application can be performed according to well-known pharmaceutical methods.

While the compounds of the invention, useable according to the invention for use in therapy, may be administered in the form of the raw chemical compound, it is preferred to introduce the active ingredient, optionally in the form of a physiologically acceptable salt in a pharmaceutical composition together with one or more adjuvants, excipients, carriers, buffers, diluents, and/or other customary pharmaceutical auxiliaries. Such salts of the compounds of the invention may be anhydrous or solvated.

In a preferred embodiment, the invention provides medicaments comprising a compound useable according to the invention, or a pharmaceutically acceptable salt or derivative thereof, together with one or more pharmaceutically acceptable carriers therefor, and, optionally, other therapeutic and/or prophylactic ingredients. The carrier(s) must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not harmful to the recipient thereof.

A medicament of the invention may be those suitable for oral, rectal, bronchial, nasal, topical, buccal, sub-lingual, transdermal, vaginal or parenteral (including cutaneous, subcutaneous, intramuscular, intraperitoneal, intravenous, intra-arterial, intracerebral, intraocular injection or infusion) administration, or those in a form suitable for administration by inhalation or insufflation, including powders and liquid aerosol administration, or by sustained release systems. Suitable examples of sustained release systems include semipermeable matrices of solid hydrophobic polymers containing the compound of the invention, which matrices may be in form of shaped articles, e.g. films or microcapsules.

The compounds useable according to the invention, together with a conventional adjuvant, carrier, or diluent, may thus be placed into the form of medicament and unit dosages thereof. Such forms include solids, and in particular tablets, filled capsules, powder and pellet forms, and liquids, in particular aqueous or non-aqueous solutions, suspensions, emulsions, elixirs, and capsules filled with the same, all for oral use, suppositories for rectal administration, and sterile injectable solutions for parenteral use. Such medicament and unit dosage forms thereof may comprise conventional ingredients in conventional proportions, with or without additional active compounds or principles, and such unit dosage forms may contain any suitable effective amount of the active ingredient commensurate with the intended daily dosage range to be employed.

The compounds useable according to the invention can be administered in a wide variety of oral and parenteral dosage forms. It will be obvious to those skilled in the art that the following dosage forms may comprise, as the active component, either a compound(s) useable according to the invention or a pharmaceutically acceptable salt of a compound(s) useable according to the invention.

For preparing a medicament from a compound useable according to the invention, pharmaceutically acceptable carriers can be either solid or liquid. Solid form preparations include powders, tablets, pills, capsules, cachets, suppositories, and dispersible granules. A solid carrier can be one or more substances which may also act as diluents, flavouring agents, solubilizers, lubricants, suspending agents, binders, preservatives, tablet disintegrating agents, or an encapsulating material.

In powders, the carrier is a finely divided solid which is in a mixture with the finely divided active component. In tablets, the active component is mixed with the carrier having the necessary binding capacity in suitable proportions and compacted in the shape and size desired. Suitable carriers are magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, a low melting wax, cocoa butter, and the like. The term "preparation" is intended to include the formulation of the active compound with encapsulating material as carrier providing a capsule in which the active component, with or without carriers, is surrounded by a carrier, which is thus in association with it. Similarly, cachets and lozenges are included. Tablets, powders, capsules, pills, cachets, and lozenges can be used as solid forms suitable for oral administration.

For preparing suppositories, a low melting wax, such as a mixture of fatty acid glyceride or cocoa butter, is first melted and the active component is dispersed homogeneously therein, as by stirring. The molten homogenous mixture is then poured into convenient sized moulds, allowed to cool, and thereby to solidify. Compositions suitable for vaginal administration may be presented as pessaries, tampons, creams, gels, pastes, foams or sprays containing in addition to the active ingredient such carriers as are known in the art to be appropriate. Liquid preparations include solutions, suspensions, and emulsions, for example, water or water-propylene glycol solutions. For example, parenteral injection liquid preparations can be formulated as solutions in aqueous polyethylene glycol solution.

The chemical compounds according to the present invention may thus be formulated for parenteral administration (e.g. by injection, for example bolus injection or continuous infusion) and may be presented in unit dose form in ampoules, pre-filled syringes, small volume infusion or in multi-dose containers with an added preservative. The compositions

may take such forms as suspensions, solutions, or emulsions in oily or aqueous vehicles, and may contain formulation agents such as suspending, stabilising and/or dispersing agents. Alternatively, the active ingredient may be in powder form, obtained by aseptic isolation of sterile solid or by lyophilization from solution, for constitution with a suitable vehicle, e.g. sterile, pyrogen-free water, before use.

Aqueous solutions suitable for oral use can be prepared by dissolving the active component in water and adding suitable colorants, flavours, stabilising and thickening agents, as desired. Aqueous suspensions suitable for oral use can be made by dispersing the finely divided active component in water with viscous material, such as natural or synthetic gums, resins, methylcellulose, sodium carboxymethylcellulose, or other well-known suspending agents.

Also included are solid form preparations which are intended to be converted, shortly before use, to liquid form preparations for oral administration. Such liquid forms include solutions, suspensions, and emulsions. These preparations may contain, in addition to the active component, colorants, flavours, stabilisers, buffers, artificial and natural sweeteners, dispersants, thickeners, solubilizing agents, and the like.

In one embodiment of the present invention, the medicament is applied topically or systemically or via a combination of the two routes.

For administration, the compounds of the present invention may, in one embodiment, be administered in a formulation containing 0,001% to 70% per weight of the compound, preferably between 0,01% to 70% per weight of the compound, even more preferred between 0,1% and 70% per weight of the compound. In one embodiment, a suitable amount of compound administered is in the range of 0.01 mg/kg body weight to 1 g/kg body weight.

Compositions suitable for administration also include lozenges comprising the active agent in a flavoured base, usually sucrose and acacia or tragacanth; pastilles comprising the active ingredient in an inert base such as gelatin and glycerol or sucrose and acacia; and mouthwashes comprising the active ingredient in a suitable liquid carrier.

Solutions or suspensions are applied directly to the nasal cavity by conventional means, for example with a dropper, pipette or spray. The compositions may be provided in single or multi-dose form. In the latter case of a dropper or pipette, this may be achieved by the patient administering an appropriate, predetermined volume of the solution or suspension. In the case of a spray, this may be achieved for example by means of a metering atomising spray pump.

Administration to the respiratory tract may also be achieved by means of an aerosol formulation in which the active ingredient is provided in a pressurised pack with a suitable propellant such as a chlorofluorocarbon (CFC) for example dichlorodifluoromethane, trichlorofluoromethane, or dichlorotetrafluoroethane, carbon dioxide, or other suitable gas. The aerosol may conveniently also contain a surfactant such as lecithin. The dose of drug may be controlled by provision of a metered valve.

Alternatively the active ingredients may be provided in the form of a dry powder, for example a powder mix of the compound in a suitable powder base such as lactose, starch, starch derivatives such as hydroxypropylmethyl cellulose and polyvinylpyrrolidone (PVP). Conveniently the powder carrier will form a gel in the nasal cavity. The powder composition may be presented in unit dose form for example in capsules or cartridges of, e.g., gelatin, or blister packs from which the powder may be administered by means of an inhaler.

In compositions intended for administration to the respiratory tract, including intranasal compositions, the compound will generally have a small particle size for example of the order of 5 microns or less. Such a particle size may be obtained by means known in the art, for example by micronization.

When desired, compositions adapted to give sustained release of the active ingredient may be employed.

The pharmaceutical preparations are preferably in unit dosage forms. In such form, the preparation is subdivided into unit doses containing appropriate quantities of the active component. The unit dosage form can be a packaged preparation, the package containing discrete quantities of preparation, such as packaged tablets, capsules, and powders in vials or ampoules. Also, the unit dosage form can be a capsule, tablet, cachet, or lozenge itself, or it

can be the appropriate number of any of these in packaged form. Tablets or capsules for oral administration and liquids for intravenous administration and continuous infusion are preferred compositions.

Further details on techniques for formulation and administration may be found in the latest edition of Remington's Pharmaceutical Sciences (Maack Publishing Co. Easton, Pa.) and Remington: The science and practice of pharmacy", Lippincott Williams and Wilkins.
Appropriate formulations and ways of manufacturing them are, for example also disclosed in "Arzneiformenlehre, Paul Heinz List, EinLehrbuchfürPharmazeuten, WissenschaftlicheVerlagsgesellschaft Stuttgart, 4. Auflage, 1985", or "The theory and practice of industrial pharmacy" by Lachman et al., Varghese Publishing House, 1987", or "Modern Pharmaceutics", edited by James Swarbrick, 2. Edition".

Figures and Tables

Reference is now made to the tables and figures, wherein

Figure 1 illustrates the anti-inflammatory effect of compound 211 in OVA-induced airway inflammation model in Brown Norway Rats

Table 1 summarizes 5-LOX IC_{50} inhibitory activities (uM) as measured by fluorescence wherein the compound number refers to the compounds listed in Example 7;

Table 2 summarizes 5-LOX IC_{50} inhibitory activities (uM) as detected by ELISA wherein the compound number refers to the compounds listed in Example 7;

Table 3 summarizes LTB4 secretion assay (EC_{50}, uM) in RBL (rat basophilic leukemia) cells wherein the compound number refers to the compounds listed in Example 7;

Table 4 summarizes LTB4 secretion assay (EC_{50}, uM) in RWB (rat whole blood) wherein the compound number refers to the compounds listed in Example 7;

Table 5 summarizes PGE_2 % inhibition at 10 uM as measured by HTRF (Homogeneous Time Resolved Fluorescence) wherein the compound number refers to the compounds listed in Example 7;

Table 6 summarizes COX-2 (Cyclooxygenase 2) % inhibition at 10 uM as measured by EIA (Enzyme Immunoassay) wherein the compound number refers to the compounds listed in Example 7 and Table 7;

Table 7 summarizes compounds 1 – 556 the synthesis of which is described in Example 7.

Examples

The invention is now further described by reference to the following examples which are intended to illustrate, not to limit the scope of the invention.

Example 1: Activity of compounds against 5-LOX enzyme

The activity of compounds against 5-LOX were determined by measuring LTB_4 (leukotriene B4) levels and/or by a fluorescence method. Both approaches are outlined in more detail below;

LTB_4 Measurement by ELISA:

Human 5-lipoxygenase (5-LOX) (Cayman, Cat#60402) produced in insect cells was pre-incubated with compoundsfor 5min at RT in incubation buffer (50mM Tris-Cl, pH 7.4, 2mM $CaCl_2$, 0.1mM ATP, 2% DMSO). Compounds were tested in dose reponse from 0.5nM to 10uM.The enzymatic reaction was started by adding arachidonic acid to a final concentration of 3uM. After 5min of incubation at 25℃, the reaction was stopped by adding H_2O_2 to a final concentration of 1mM. LTB_4 levels were quantified using a LTB_4 EIA kit (Cayman, Cat# 520111) as instructed.

Fluorescence Method:

Besides the above method for quantifying LTB4 levels, a fluorescence assay measuring 5-hydroperoxyeicosatetraenoic acid (5- HPETE) was introduced for high-throughput screening in a 384 well microplate format (Pufahl et al., 2007) Development of a Fluorescence-based enzyme assayof human 5-lipoxygenase. ANALYTICALBIOCHEMISTRY 364, 204–212). For nonspecific ester cleavage of the acetate groups in H_2DCFDA(2',7'-dichlorodihydrofluorescein diacetate), the insect cell lysate expressing human 5-LOX (Cayman Cat# 60402) was incubated with H_2DCFDA (50mM Tris-Cl, pH 7.5, 2mM CaCl2, 20uM H_2DCFDA, 600mU 5-LOX per reaction) for 5 minutes. The compound, in a dose response manner(0.5nM to 10uM),and enzyme mixture was pre-incubated for 5 minutes, and the enzymatic reaction was initiated by addition of ATP and arachidonic acid to a final concentration of 100uM and 3uM, respectively. After 5 minutes of incubation, fluorescence

was measured using Spectramax M5 (Molecular Device, Ex/Em=485nm/530nm). All steps were carried out at room temperature.

Example 2: LTB4 secretion assay in RBL(rat basophilic leukemia cells)

Rat basophilic leukemia (RBL) cells (ATCC, Cat# CRL-2256) were maintained in EMEM (ATCC, Cat# 30-2003) supplemented with 15% FBS. The day before RBL assay, cells were seeded at a concentration of 2 X 10^4 cells per well in 96-well plates. The media was replaced with 100ul of EMEM supplemented with 0.5% FBS and compounds in dose response(5nM to 100uM) were added. .After 15min of pre-incubation at 37℃, arachidonic acid and calcium ionophore (A23187) were added to give a final concentration of 2.5uM and 5uM, respectively. After a further 10min incubation at 37℃, culture supernatant was transferred and quantification of LTB4 was done with a Leukotriene B4 EIA kit (Cayman, Cat# 520111) as instructed.

Example 3: LTB4 secretion assay in RWB(rat whole blood)

Rat blood was drawn from caudal vena cava from male Sprague Dawley rat (6-9 weeks old) in vacuette coated with sodium heparin (Greiner bio-one, Cat# 455051). The blood was pooled and diluted with RPMI (WelGENE, Cat# LM 011-05) to 1:1. The diluted blood was aliquoted into 96 well plate (200ul per well) and compounds were added in dose response to a desired concentrationranging from 2.5nM to 50uM.. After 15min of pre-incubation at 37℃, calcium ionophore (A23187) was added to the final concentration of 10uM. After 10min of further incubation at 37℃, the LTB4 production was stopped by diluting the reaction mixture with ice cold PBS (1:4dilutions). Cells were removed by centrifugation at 1000Xg, 4℃ for 10min, and the supernatant was transferred and then the quantification of LTB4 was done with Leukotriene B4 EIA kit (Cayman, Cat# 520111) as instructed.

Example 4: Inflammation efficacy in OVA-induced airway inflammation model in Brown Norway Rats

The objective of this study is to determine the efficacy of compounds in the lungs of ovalbumin (OVA) induced in Brown Norway rats. As with most models of induced allergic asthma, animals are systemically sensitized to specific antigens and then, after a period of time, challenged with the same allergen administered via the airway. Ovalbumin had been used as the standard allergen to sensitize and challenge animals in this study.

Thirty (30) male Brown Norway rats were randomized into 5 groups on the basis of body weight. For sensitization, 1% OVA in PBS solution was mixed with alum solution (with volume ratio of 1:9). All rats in groups 1 - 5 were sensitized by i.p injection (1 mL/rat) of 1% OVA-alum sensitization solution on day 1, 2 and 3. At day 21, rats in groups 1 - 5 were challenged with 1% OVA in PBS solution with aerosolizing dosing system for 20 min.

Test compounds were administered by p.o. from days 19-21 of the study as per schedule below:

Group 1: sensitized-vehicle,

Group 2: reference drug dexamethasone, 0.3 mg/kg, p.o., Day 19-21, BID,

Group 3: compound 211, 25 mg/kg, p.o., Day 19-21, BID,

Group 4: compound 211, 50 mg/kg, p.o., Day 19-21, BID,

Group 5: compound 211, 100 mg/kg, p.o., Day 19-21, BID,

On day 22, bronchoalveolar lavage and lung tissues were harvested. Total cell number and differential cell counts in BALF, leukotriene B4 (LTB4) in BALF and lung tissue, histopathology of lung by H&E staining will be evaluated.

The results are shown in figure 1. Treatment of rats using compound 211 significantly reduced the increase of inflammatory cells including total cell and eosinophils, reduced LTB4 in BALF and Lung, and significantly reduced inflammation cell infiltration. These data indicate that compound 211 shows antiinflammatory activity in OVA-induced asthma.

Example 5: PGE_2 inhibition assay

Human epitheloid cervix carcinoma HeLa S3 cells ($2X10^6$cells/ml) were seeded with modified F-12K buffer medium pH 7.4 in tissue culture plate and incubated for overnight at 37℃ and 5% CO_2. Then medium was changed into new medium contained 10uM testing compounds or 0.1% DMSO and incubated overnight. After incubation, cells were stimulated with 30nM TNF- α (Tumor necrosis factor- α) for 16h. For determination of PGE_2, the supernatant was measured by PGE_2 HTRF (Homogeneous Time Resolved Fluorescence) assay kit. Inhibition of PGE_2 by compounds is calculated as a percentage of activity in the presence of drug versus the activity in the stimulator TNF-α.

Example 6: COX-2 inhibition assay

Human recombinant cyclooxygenase-2 expressed in insect Sf21 cells was used. The testing compounds and reference compound (Rofecoxib) were dissolved in DMSO (Sigma, USA) and tested at 10uM. Test samples were pre-incubated with 0.11 U enzyme in 100 mM modified Tris-HCl buffer pH 7.7 for 15 minutes at 37° C. The reactions were initiated by addition of 0.3 μM arachidonic acid for another 5-minute incubation period, then terminated by further addition of 1 N HCl. An aliquot was then combined with the EIA kit for spectrophotometric determination of the quantity of PGE_2 formed. Inhibition % was determined by compared with relative amounts of PGE_2 induced by arachidonic acid. The results show that the compounds according to the present, as exemplified by compounds (cpds.) 90 and 95, do not have an inhibitory effect on cyclooxygenase-2 (COX-2), thus lending support to the fact that their inhibitory action on the PGES-pathway occurs at the level of "PGES".

Example 7: Preparation of Compounds

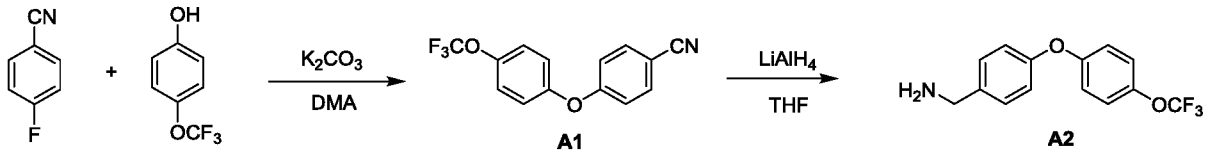
The synthesis of compounds described herein may be accomplished using means described in the chemical literature, using the methods described herein, or by a combination thereof.

Compounds described herein may be synthesized using standard synthetic techniques known to those of skill in the art or using methods known in the art in combination with methods described herein. In addition, solvents, temperatures and other reaction conditions presented herein may vary according to those of skill in the art. The starting material used for the synthesis of the compounds described herein may be synthesized or can be obtained from commercial sources, such as, but not limited to, Aldrich Chemical Co. (Milwaukee, Wis.), or

Sigma Chemical Co. (St. Louis, Mo.). The compounds described herein, and other related compounds having different substituents can be synthesized using techniques and materials described herein as well as those that are known to those of skill in the art. General methods for the preparation of compound as disclosed herein may be derived from known reactions in the field, and the reactions may be modified by the use of appropriate reagents and conditions, as would be recognized by the skilled person, for the introduction of the various moieties found in the formulae as provided herein. As a guide the synthetic method of Schemes may be utilized to prepare a compound described herein.

The compounds (scaffold I, II and III; see **Tables 1-7**) underwent derivatization according to the methods outlined below (**Schemes 1-37**), and the synthesized compounds as well as relevant NMR characterization data are shown in Table 7. Resulting derivatives were examined for inhibitory activity (IC_{50}, EC_{50}, *in vivo*) using the assays described above (Examples 1, 2, 3, 4, 5 and 6), and the results are summarized in **Tables 1, 2, 3, 4, 5 and 6 and Figure 1**.

Scheme 1. General synthesis 1 of an amine compound



General procedure for the synthesis of A1

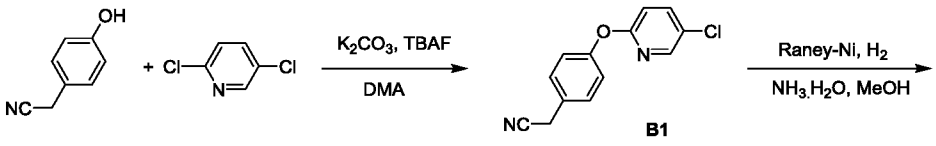
To a stirred solution of 4-fluorobenzonitrile (5.00 g, 41.3 mmol) and 4-trifluoromethoxy-phenol (8.10 g, 45.5 mmol) in DMA (30 mL) was added K_2CO_3 (6.30 g, 45.6 mmol). The resulting mixture was stirred at 120 °C for 16 hours. The mixture was cooled to 50 °C and 100 mL water was added dropwise under good stirring. The mixture was extracted with EtOAc (100 mL x 2), the combined organic phase was washed with water (100 mL) and brine (100 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford **A1**.

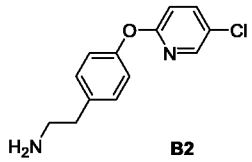
General procedure for the synthesis of A2

To a stirred solution of **A1** (3.00 g, 10.7 mmol) in anhydrous THF (30 mL) at 0 °C was added $LiAlH_4$ (1.63 g, 43.0 mmol) in portions, the reaction mixture was stirred at 0 °C for 3 hours, the resulting mixture was stirred at 50 °C for another 16 hours. The mixture was quenched

with water (1.6 mL) dropwise at 0 °C, then followed NaOH (10%, 3.2 mL) dropwise and water (1.6 mL) to the mixture. The mixture was filtered, the filter cake was washed with EtOAc (30 mL) and the filtrate was concentrated under reduced pressure to afford **A2**.

Scheme 2. General synthesis 2 of an amine compound





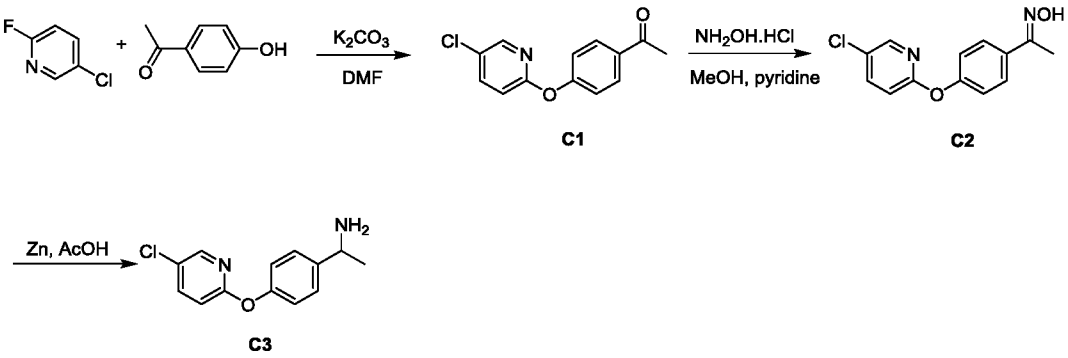
General procedure for the synthesis of B1

To a stirred solution of 2-(4-hydroxyphenyl)acetonitrile (10.0 g, 75.2 mmol) in DMA (120 mL) were added 2,5-dichloro pyridine (12.2 g, 82.7 mmol), K_2CO_3 (15.6g, 113 mmol) and TBAF (589 mg, 2.26 mmol), then the mixture was stirred at 115 °C for 16 hours. The reaction mixture was poured into water (600 mL) with vigorous stirring for 1 hour. The precipitate was collected by filtration, dried in air for 2 hours and purified by Combi Flash (PE: EtOAc = 5 : 1 to 2 : 1) to afford **B1**.

General procedure for the synthesis of B2

To a stirred solution of **B1** (500 mg, 2.04 mmol) in MeOH (15 mL) were added Raney-Ni (400 mg) and $NH_3.H_2O$ (0.5 mL, 28%). The reaction solution was stirred at 15 °C under H_2 atmosphere (45 psi) for 6 hours. Then the solution was filtered through a pad of Celite. The filtrate was concentrated and diluted with DCM (30 mL), then dried over anhydrous Na_2SO_4, evaporated to afford **B2**.

Scheme 3. General synthesis 3 of an amine compound



General procedure for the synthesis of C1

A mixture of 4'-hydroxyacetophenone (5.00 g, 36.7 mmol), 5-chloro-2-fluoropyridine (5.79 g, 44.0 mmol) and K_2CO_3 (10.1 g, 73.4 mmol) in DMF (150 mL) was stirred at 100 °C for 6 hours. After cooling to room temperature, the reaction mixture was diluted with EtOAc (200 mL), then filtered and the filtrate was washed with brine (150 mL ×3), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford a residue. The residue was washed with PE/ EtOAc = 20/1(40 mL) to afford **C1**.

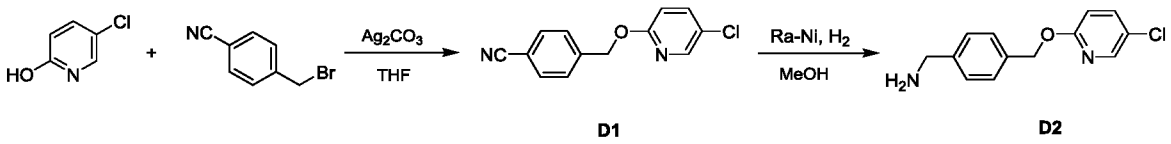
General procedure for the synthesis of C2

A mixture of **C2** (4.50 g, 18.2 mmol) and $NH_2OH.HCl$ (1.26 g, 18.2 mmol) in MeOH/pyridine (25 mL/25 mL) was stirred at 8-10 °C for 16 hours. The resulting mixture was concentrated under reduced pressure, acidified with HCl (2 M, 120 mL), extracted with DCM (50 mL x 4), the combined organic layer was washed with water (200 mL x 3), brine (200 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford **C2**.

General procedure for the synthesis of C3

A mixture of **C2** (4.70 g, 17.9 mmol) and Zn powder (11.6 g, 179 mmol) in AcOH (120 mL) was stirred at 65-75 °C for 28 hours. After cooling to room temperature, the reaction mixture was filtered, washed with EtOAc (10 mL x 3) and the combined filtrate was concentrated under reduced pressure to afford a residue. The residue was diluted with saturated $NaHCO_3$ (150 mL), extracted with EtOAc (100 mL x3), the combined organic layer was washed with brine (200 mL x 2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford **C3**.

Scheme 4. General synthesis 4 of an amine compound



D1 D2

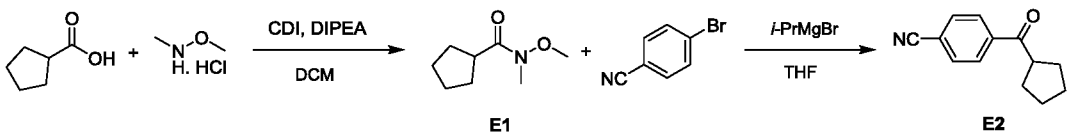
General procedure for the synthesis of D1

To a stirred mixture of 5-chloro-2-hydroxypyridine (15.0 g, 76.5 mmol) in anhydrous THF (200 mL) were added 4-cyanobenzyl bromide (8.26 g, 63.8 mmol) and Ag_2CO_3 (10.5 g, 38.3 mmol). The resulting mixture was refluxed for 16 hours. The mixture was cooled to room temperature and filtered. The filter cake was washed with THF (100 mL). The combined filtrate was concentrated under reduced pressure to afford a residue, which was purified by combi flash (PE/EtOAc=92/8 to 70/30) to afford **D1**.

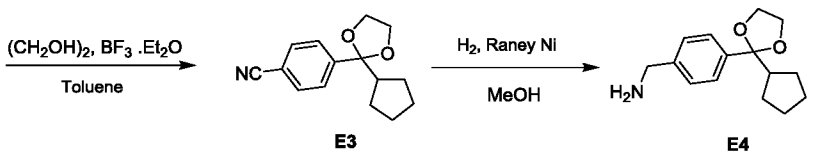
General procedure for the synthesis of D2

To a stirred solution of **D1** (5.00 g, 2.04 mmol) in MeOH (100 mL) were added Raney-Ni (1.00 g) and $NH_3.H_2O$ (0.5 mL, 28%) under N_2 atmosphere. The suspension was degassed under vacuum and purged with H_2 for three times. The solution was stirred at 12 °C under H_2 (45 psi) atmosphere for 2 hours. The mixture was filtered through a pad of celite, and the pad was washed with MeOH (200 mL). The filtrate was concentrated under reduced pressure to afford **D2**.

Scheme 5. General synthesis 5 of an amine compound



E1 E2



E3 E4

General procedure for the synthesis of E1

To a stirred solution of cyclopentanecarboxylic acid (5.00 g, 44.2 mmol) in anhydrous DCM

(100 mL) was added CDI (8.10 g, 57.5 mmol) in portions at 28 °C. The reaction solution was stirred at 28 °C for 0.5 hour. Then DIEA (8.00 g, 61.9 mmol) and *N,O*-dimethyl hydroxylamine hydrochloride (5.13 g, 61.9 mmol) were added. The reaction solution was stirred at 28 °C for 16 hours. The reaction solution was diluted with saturated $NaHCO_3$ (50 mL) and separated. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by Combi Flash (PE: EtOAc= 5: 1 to 2: 1) to afford **E1**.

General procedure for the synthesis of E2

To a stirred solution of 4-bromobenzonitrile (1.40 g, 7.69 mmol) in anhydrous THF (15 mL) was added *i*-PrMgBr (19.2 mL, 19.2 mmol, 1 M in THF) dropwise at -30 °C under N_2 atmosphere. Then the mixture was stirred at -30 °C under N_2 atmosphere for 30 minutes. A solution of **E1** (1.00 g, 6.37 mmol) in anhydrous THF (5 mL) was added dropwise at -30 °C. The reaction solution was allowed to warm to 30 °C and stirred at 30 °C for 16 hours. The reaction solution was quenched by saturated NH_4Cl solution (15 mL) at 0 °C. The organic phase was separated, concentrated under reduced pressure. The residue was purified by Combi Flash (PE: EtOAc= 10: 1) to afford **E2**.

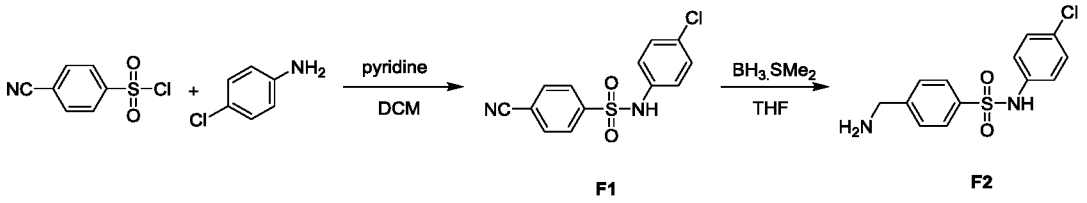
General procedure for the synthesis of E3

A mixture of **E2** (250 mg, 1.26 mmol), $BF_3.Et_2O$ (0.5 mL), ethylene glycol (1 mL) in toluene (50 mL) was refluxed with azeotropic removal of water for 48 hours. The reaction solution was cooled to room temperature and diluted with saturated Na_2CO_3 (30 mL). The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by prep-TLC (PE: EtOAc= 5: 1) to afford **E3**.

General procedure for the synthesis of E4

To a stirred solution of **E3** (100 mg, 0.410 mmol) in MeOH (5 mL) were added Raney-Ni (100 mg) and ammonia water (0.5 mL, 28%). The reaction solution was stirred at 25 °C under H_2 atmosphere (45 psi) for 2 hours. Then the solution was filtered through a pad of Celite. The filtrate was concentrated under reduced pressure to afford **E4**.

Scheme 6. General synthesis 6 of an amine compound



F1 F2

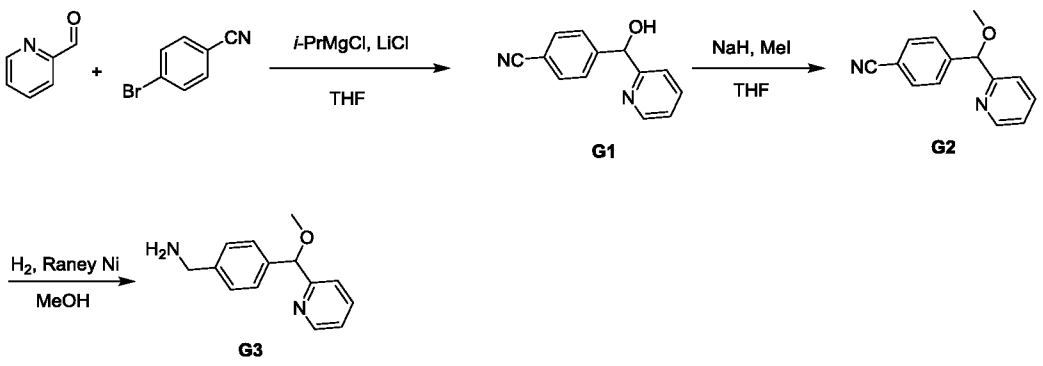
General procedure for the synthesis of F1

To a stirred solution of 4-chloroaniline (634 mg, 4.96 mmol) and pyridine (1.17 g, 14.9 mmol) in DCM (10 mL) was added a solution of 4-cyanobenzenesulfonyl chloride (1.00 g, 4.96 mmol) in DCM (5 mL) under ice bath, then the mixture was stirred under N_2 atmosphere at 25 °C for 12 hours. The mixture was poured into water (30 mL), extracted with DCM (10 mL × 3). The combined extracts was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford a residue, which was purified by flash column chromatography (eluent: DCM) to afford **F1**.

General procedure for the synthesis of F2

To a stirred solution of **F2** (500 mg, 1.71 mmol) in anhydrous THF (2.5 mL) was added BH_3/Me_2S (1.35 mL, 13.5 mmol, 10M) under ice bath, the mixture was stirred under N_2 atmosphere at 25 °C for 12 hours. MeOH (5 mL) was added dropwise carefully to quench the reaction, then the mixture was diluted with water (50 mL), adjusted pH 8 by saturated Na_2CO_3, extracted with EtOAc (30 mL × 3). The combined extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford a residue, which was purified by Combi Flash (eluent: PE/EtOAc=1/1 to EtOAc) to afford **F2**.

Scheme 7. General synthesis 7 of an amine compound



G1 G2 G3

General procedure for the synthesis of G1

To a stirred solution of 4-bromobenzonitrile (1.00 g, 5.50 mmol), LiCl (252 mg, 6.00 mmol) in anhydrous THF (10 mL) was added i-PrMgCl (3 mL, 6.0 mmol, 2 M in THF) dropwise at -15 °C under N_2 atmosphere. Then the mixture was stirred at -15 °C under N_2 atmosphere for 2 hours. Then picolinaldehyde (640 mg, 6.00 mmol) was added dropwise at -15 °C. The reaction solution was allowed to warm to 30 °C. TLC showed the reaction was complete. The reaction solution was quenched by saturated NH_4Cl solution (10 mL) at 0 °C. The organic layer was separated and concentrated under reduced pressure. The residue was purified by Combi Flash (PE: EtOAc= 5: 1 to 2: 1) to afford **G1**.

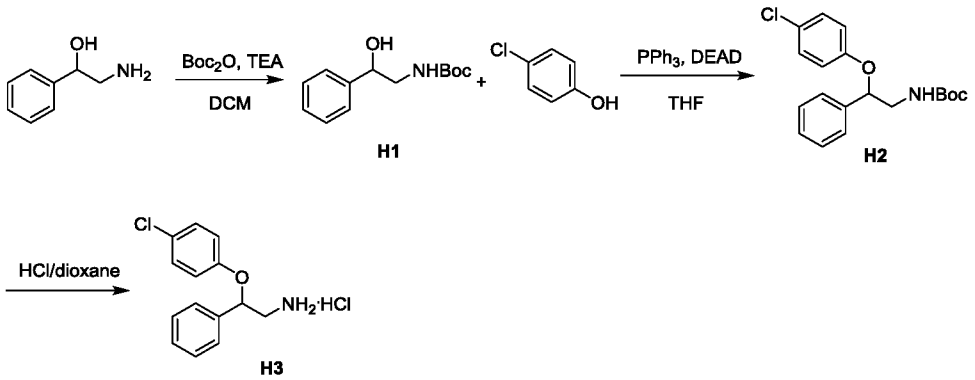
General procedure for the synthesis of G2

To a stirred solution of **G2** (400 mg, 1.90 mmol) in anhydrous THF (6 mL) was added NaH (298 mg, 2.10 mmol, 60% dispersion in mineral oil) at 0 °C, then the mixture was stirred at 0 °C for 15 minutes. Afterwards, MeI (298 mg, 2.10 mmol) was added to the mixture at 0 °C. The mixture was stirred under N_2 atmosphere at 25 °C for 1 hour. The reaction mixture was poured into water (10 mL), extracted with EtOAc (10 mL x 3). The combined organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by Combi Flash (PE: EtOAc = 5: 1 to 1: 1) to afford **G2**.

General procedure for the synthesis of G3

To a stirred solution of **G2** (1.50 g, 6.70 mmol) in MeOH (40 mL) were added Raney-Ni (2.0 g) and concentrated ammonia water (4 mL, 28%). The reaction solution was stirred at 25 °C under H_2 atmosphere (45 psi) for 3 hours. Then the solution was filtered through a pad of Celite. The filtrate was concentrated under reduced pressure to afford 1.53 g of residue, which was purified by silica gel column chromatography (DCM: MeOH = 10: 1) to afford **G3**.

Scheme 8. General synthesis 8 of an amine compound



General procedure for the synthesis of H1

To a stirred solution of 2-amino-1-phenylethanol (5.00 g, 36.4 mmol) and TEA (5.51 g, 54.6 mmol) in DCM (100 mL) was added Boc_2O (9.54 g, 43.7 mmol), then the resulting mixture was stirred at 27-28 °C for 2 hours. The reaction mixture was concentrated under reduced pressure to remove most of DCM. The residue was diluted with EtOAc (100 mL), then washed with 1% HCl solution (50 mL), brine (50 mL x2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was washed with PE/EtOAc (50 mL/5 mL) to afford **H1**.

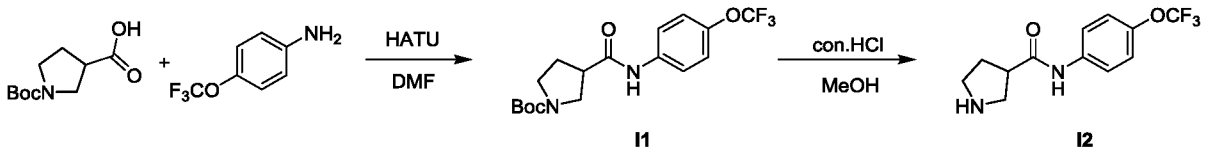
General procedure for the synthesis of H2

To a stirred solution of **H1** (4.00 g, 16.9 mmol), 4-chlorophenol (4.33 g, 33.7 mmol) and PPh_3 (6.63 g, 25.3 mmol) in anhydrous THF (150 mL) was added dropwise a solution of DEAD (4.40 g, 25.3 mmol) in THF (50 mL) at 0-5 °C. The resulting mixture was stirred at 26-30 °C for 16 hours. The reaction mixture was diluted with EtOAc (500 mL), then washed with brine (300 mL x3), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (PE/EtOAc = 20/1 to 5/1), diluted with MTBE (100 mL), then washed with 12 M NaOH solution (50 mL x3), brine (50 mL x3), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford **H2**.

General procedure for the synthesis of H3

A mixture of **H2** (2.00 g, 5.75 mmol) in HCl/dioxane (30 mL, 4.0 M) was stirred at 27 °C for 20 minutes. The reaction mixture was concentrated under reduced pressure to afford **H3**.

Scheme 9. General synthesis 9 of an amine compound



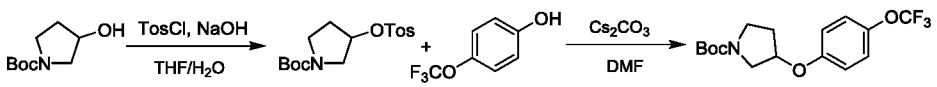
General procedure for the synthesis of I1

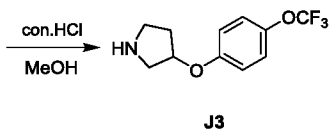
To a stirred solution of 1-Boc-pyrrolidine-3-carboxylic acid (5.00 g, 23.3 mmol) and 4-(trifluoromethoxy)aniline (3.91 g, 22.1 mmol) in anhydrous DMF (50 mL) was added DIPEA (9.0 g, 69.8 mmol). Then HATU (13.2 g, 34.7 mmol) was added portionwise at 0 °C. The reaction mixture was stirred at 25 °C for 4 hours. The mixture was quenched with water (100 mL), extracted with EtOAc (100 mL x 2). The combined organic phase was washed with saturated $NaHCO_3$ (100 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford **I1**.

General procedure for the synthesis of I2

To a stirred solution of **I1** (6.00 g, 16.0 mmol) in DCM (120 mL) was added TFA (40 mL) dropwise at 0 °C. After the addition, the mixture was stirred at 25 °C for 12 hours. The mixture was concentrated under reduced pressure and the residue was diluted with 100 mL water. Solid K_2CO_3 was added to adjust pH 10 and extracted with EtOAc (200 mL x 2). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford **I2**.

Scheme 10. General synthesis 10 of an amine compound





General procedure for the synthesis of J1

To a stirred solution of *tert*-butyl-3-hydroxypyrrolidine-1-carboxylate (10.0 g, 53.4 mmol) in THF (50 mL) was dropwise added aqueous NaOH (5.30 g/134 mmol in 5 mL water) under ice

bath (below 10 °C), then TosCl (13.2 g, 68.4 mmol) was added by portions below 10 °C. Then the mixture was warmed at 30 °C for 12 hours. THF was concentrated under reduced pressure to afford a residue, the residue was diluted with water (100 mL), extracted with EtOAc (50 mL x 3). The combined extract was washed with water (50 mL x 2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford a **J1**.

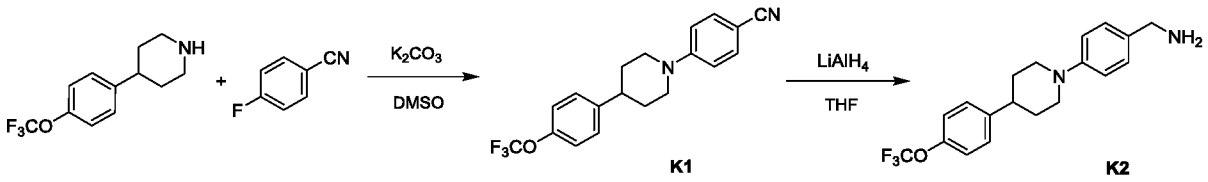
General procedure for the synthesis of J2

A mixture of compound **2** (5.00 g, 14.6 mmol), 4-(trifluoromethoxy)phenol (2.73 g, 15.3 mmol) and Cs_2CO_3 (9.50 g, 29.2 mmol) in DMF (25 mL) was stirred at 80-90 °C for 2 hours. The mixture was diluted with water (150 mL), extracted with EtOAc (50 mL x 4). The combined extract was dried over anhydrous Na_2SO_4 and concentrated to afford a crude, which was purified by flash column chromatography (eluent: EtOAc/PE=1/100 to 1/5) to afford **J2**

General procedure for the synthesis of J3

To a stirred solution of **J2** (3.80 g, 10.9 mmol) in MeOH (20 mL) was added aq.HCl (5 mL, 12M) at 10 °C, the mixture was stirred at 10 °C for 2 hours. The mixture was concentrated under reduced pressure to afford a residue. The residue was diluted with water (50 mL), adjusted pH = 9 by aqueous NaOH (2M), extracted with EtOAc (30 mL x 3). The combined extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford **J3**.

Scheme 11. General synthesis 11 of an amine compound



General procedure for the synthesis of K1

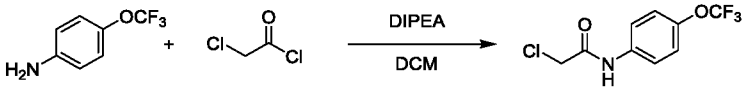
To a stirred solution of 4-(4-(trifluoromethoxy)phenyl)piperidine (86.0 g, 0.351 mol) in DMSO (1 L) was added K_2CO_3 (121 g, 0.878 mol) and 4-fluorobenzonitrile (63.8 g, 0.527 mol) at 18 °C. The reaction mixture was heated to 120 °C for 16 hours under N_2. After cooling to room temperature, the mixture was concentrated to about 400 mL over high vacuum. H_2O (2 L) was poured into the mixture and the resulting precipitate was collected by filtration. The crude product was triturated with H_2O (1.5 L), dried over high vacuum, then triturated with

EtOAc/PE (800 mL / 4 L), dried over high vacuum to afford **K1**.

General procedure for the synthesis of K2

To a stirred solution of **K1** (60.0 g, 0.173 mol) in anhydrous THF (1.0 L) was added $LiAlH_4$ (32.9 g, 0.865 mol) at 0 °C. The reaction mixture was heated to reflux for 3 hours under N_2. After cooling to room temperature, the mixture was quenched carefully with H_2O (33 mL), 10% NaOH solution (33 mL), H_2O (100 mL) in turn. The mixture was filtered, the filter cake was washed with THF (300 mL), and the filtrate was concentrated under high vacuum to afford **K2**.

Scheme 12. General synthesis of an alkyl halide

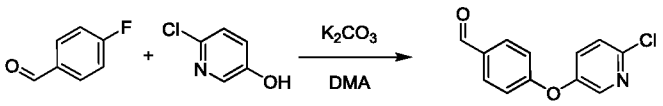


L1

General procedure for the synthesis of L1

To a stirred solution of 4-(trifluoromethoxy)aniline (2.00 g, 17.7 mmol), DIPEA (2.51 g, 19.3 mmol) in DCM (80 mL) was added a solution of chloroacetyl chloride (2.00 g, 17.7 mmol) in DCM (8 mL) dropwise at 0 °C. The reaction mixture was stirred at 0 °C for 0.5 hour and poured into water (50 mL). The mixture was separated and the organic layer was washed with water (20 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by recrystallization from PE/EtOAc (1/1) to afford **L1**.

Scheme 13. General synthesis 1 of an aryl aldehyde



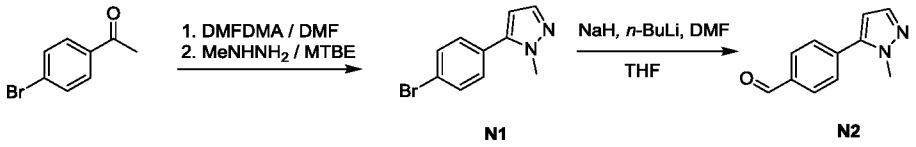
M1

General procedure for the synthesis of M1

To a stirred solution of 2-chloro-5-hydroxypyridine (3.00 g, 23.3 mmol) in anhydrous DMA (40 mL) were added 4-fluoro benzaldehyde (2.88 g, 23.3 mmol) and K_2CO_3 (6.40 g, 46.6 mmol). The resulting mixture was heated to 130 °C for 16 hours. Water (30 mL) was poured into the mixture, then extracted with EtOAc (40 mL×3). The combined organic phase was

washed with brine (40 mL×2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford crude product. The residue was purified by Combi-flash (PE: EtOAc= 20:1 to 15:1) to afford **M1**.

Scheme 14. General synthesis 2 of an aryl aldehyde



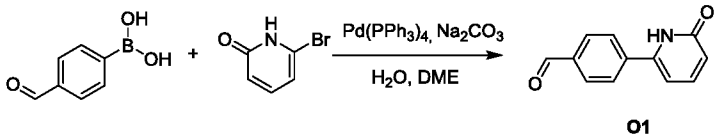
General procedure for the synthesis of N1

To a stirred solution of 1-(4-bromophenyl)ethan-1-one (30.0 g, 150 mmol) in DMF (18 mL) was added DMFDMA (43.5 mL, 300 mmol), the resulting mixture was stirred at 110 °C for 4 hours. After cooling to room temperature, MTBE (150 mL) was added to the mixture, then $MeNHNH_2$ (78.9 g, 600 mmol) was added into above mixture, the resulting mixture was stirred at 25 °C for 17 hours. The mixture was diluted with EtOAc (100 mL), filtered and the filter cake was washed with EtOAc (150 mL). The combined organic layer was washed with water (200 mL×3) and brine (200 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford a residue. The residue was purified by flash column chromatography (eluted: PE/EtOAc=8/1 to 4/1) to afford **N1**.

General procedure for the synthesis of N2

To a stirred solution of **N1** (1.20 g, 5.10 mmol) in anhydrous THF (10 mL) was added NaH (240 mg, 6.00 mmol, 60% dispersion in mineral oil), the resulting mixture was stirred at 0 °C for 1 hour, then *n*-BuLi (2.3 mL, 5.75 mmol, 2.5 M in hexane) was added into above mixture at -70 °C and stirred at -70 °C for 1 hour, freshly distilled DMF (1.85 g, 25.3 mmol) was added into above mixture and stirred at -70 °C for 1 hour, then the reaction mixture was allowed to warm to 0 °C. TLC showed the reaction was completed. The reaction was quenched with water (30 mL) at 0 °C, extracted with EtOAc (30 mL×3). The combined organic phase washed with brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford a residue. The residue was purified by flash column chromatography (eluted: PE/EtOAc=2/1) to afford **N2**.

Scheme 15. General synthesis 3 of an aryl aldehyde

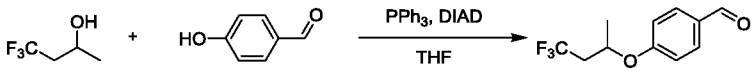


O1

General procedure for the synthesis of O1

To a stirred solution of 2-bromo-6-hydroxypyridine (100 mg, 0.57 mmol) and 4-formylphenylboronic acid (72 mg, 0.48 mmol) in DME (2 mL) were added $Pd(PPh_3)_4$ (55 mg, 0.05 mmol) and Na_2CO_3 solution (0.63 mL, 2M). The mixture was stirred under N_2 atmosphere maintaining gentle reflux for 16 hours. The mixture was diluted with water (10 mL) extracted with EtOAc (20 mL×3). The combined extracts were washed with brine (20 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford a crude, which was purified by combi flash (eluent: EtOAc) to afford **O1**.

Scheme 16. General synthesis 4 of an aryl aldehyde

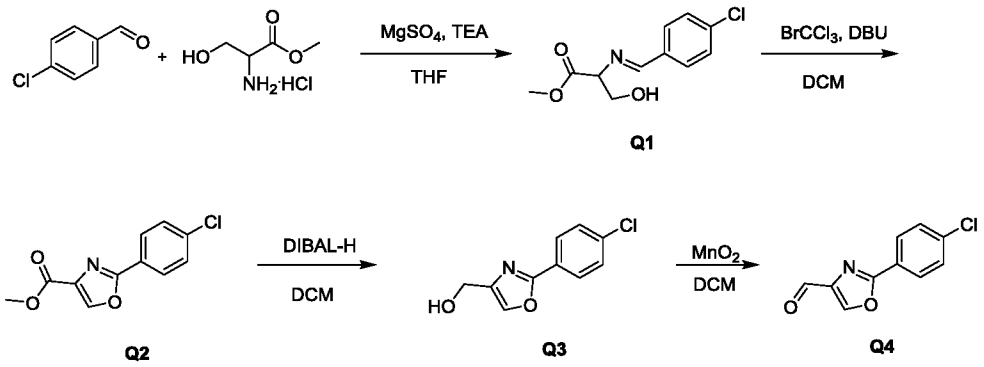


P1

General procedure for the synthesis of P1

To a stirred solution of 4,4,4-trifluoro-2-butanol (450 mg, 3.51 mmol) in anhydrous THF (10 mL) were added 4-hydroxybenzaldehyde (390 mg, 3.19 mmol), PPh_3 (1.26 g, 4.28 mmol) and DIAD (967 mg, 4.78 mmol). Then the mixture was stirred at 27-30°C for 16 hours. Then the mixture was diluted with water (50 mL), extracted with EtOAc (30 mL×2). The combined extracts were washed with brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford crude residue which was purified by Combi Flash (PE/EtOAc=10/1) to afford **P1**.

Scheme 17. General synthesis 5 of an aryl aldehyde



General procedure for the synthesis of Q1

To a stirred solution of DL-serine methyl ester hydrochloride (11.1 g, 71.4 mmol), $MgSO_4$ (8.64 g, 71.4 mmol) in anhydrous THF (350 mL) were added 4-chloro-benzaldehyde (10.0 g, 71.4 mmol) and TEA (14.4 g, 143 mmol), then the mixture was stirred at 25-30 °C for 12 hours. The resulting mixture was filtered, washed with MTBE (100 mL x 2). The combined filtrate was concentrated under reduced pressure to afford a crude **Q1**.

General procedure for the synthesis of Q2

To a stirred solution of **Q1** (13.8 g, crude) in anhydrous DCM (220 mL) were added $BrCCl_3$ (16.4 mL, 166 mmol) and DBU (25 mL, 166 mmol) at 0 °C. The resulting mixture was stirred at 0 °C for 2 hours and then at 25-30 °C for 10 hours. The mixture was concentrated under reduced pressure to dryness. The residue was dissolved in EtOAc (250 mL), washed with water (140 mL x 2), brine (80 mL) in turn, dried over anhydrous Na_2SO_4 and concentrated to afford a residue. The residue was washed with EtOAc (20 mL) to afford **Q2**.

General procedure for the synthesis of Q3

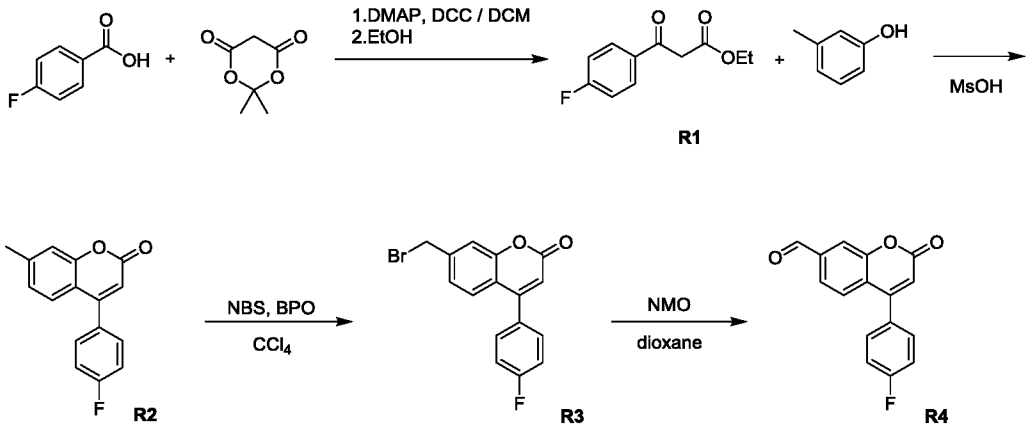
To a stirred solution of **Q2** (3.46 g, 14.6 mmol) in anhydrous DCM (65 mL) was added DIBAL-H (16.1 mL, 16.1 mmol, 1M in toluene) at -78 °C under N_2 atmosphere. The resulting mixture was stirred at 0 °C for 4 hours. The reaction was quenched with saturated NH_4Cl (25 mL) at 0 °C. Then the mixture was warmed to room temperature, adjusted pH 2 by HCl (1M). The mixture was extracted with DCM (50 mL x 3), the combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford a residue. The residue was washed with DCM (15 mL) to afford **Q3**.

General procedure for the synthesis of Q4

A mixture of **Q3** (1.49 g, 7.13 mmol) and MnO_2 (6.20 g, 71.3 mmol) in DCM (65 mL) was

stirred under N_2 atmosphere at 25-30 °C for 18 hours. The mixture was filtered and the filter cake was washed with DCM (10 mL x 2), the filtrate was concentrated under reduced pressure to dryness to afford **Q4**.

Scheme 18. General synthesis 6 of an aryl aldehyde



General procedure for the synthesis of R1

To a stirred solution of 4-fluorobenzoic acid (50.0 g, 357 mmol), 2,2-dimethyl-1,3-dioxane-4,6-dione (61.7 g, 428 mmol) and DMAP (65.5 g, 536 mmol) in DCM (1.5 L) was added DCC (97.5 g, 464 mmol) dropwised at 0 °C and stirred at 0 °C for 30 minutes, then stirred at 25 °C for 17 hours. The mixture was filtered, the filtrate was washed with aqueous HCl (1 M, 800 mL×3), washed with brine (800 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford a residue. The residue was dissolve in EtOH (600 mL) and stirred at 100 °C for 17 hours. The excessive EtOH was removed under reduced pressure to afford a residue, which was purified by flash column chromatography (eluted: PE/EtOAc = 20/1) to afford **R1**.

General procedure for the synthesis of R2

A mixture of **R1** (7.50 g, 35.7 mmol) and m-cresol (3.86 g, 35.7 mmol) in MsOH (9.5 mL) was stirred at 40 °C for 17 hours. After cooling to room temperature, the reaction mixture was poured into cooling EtOH (-30 °C, 60 mL) and stirred at -30 °C for 1 hour. The precipitate was filtered. The solid was dissolved in EtOAc (50 mL) and then washed with saturated $NaHCO_3$ (50 mL × 2), brine (50 mL), dried over Na_2SO_4 and concentrated under reduced pressure to afford **R2**.

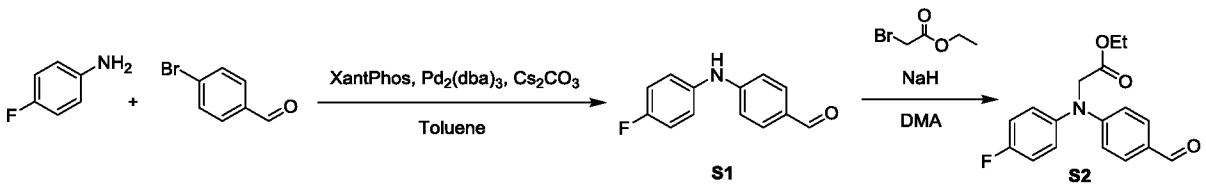
General procedure for the synthesis of R3

To a stirred solution of **R2** (1.00 g, 3.94 mmol) in CCl_4 (30 mL) were added NBS (842 mg, 4.73 mmol) and BPO (195 mg, 0.806 mmol), the resulting mixture was stirred at reflux for 48 hours. Then the mixture was filtered, the filtrate was concentrated under reduced pressure to afford a residue, which was purified by flash column chromatography (PE/EtOAc = 30/1) to afford **R3**.

General procedure for the synthesis of R4

To a stirred solution of **R4** (1.00 g, 3.00 mmol) in dioxane (15 mL) was added NMO (882 mg, 7.53 mmol) and the resulting mixture was stirred at reflux for 6 hours. After cooling to room temperature, the mixture was diluted with water (50 mL), extracted with EtOAc (30 mL × 3). The combined organic layer was washed with brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford a residue, which was purified flash column chromatography (PE/EtOAc = 20/1) to afford **R4**.

Scheme 19. General synthesis 7 of an aryl aldehyde



General procedure for the synthesis of S1

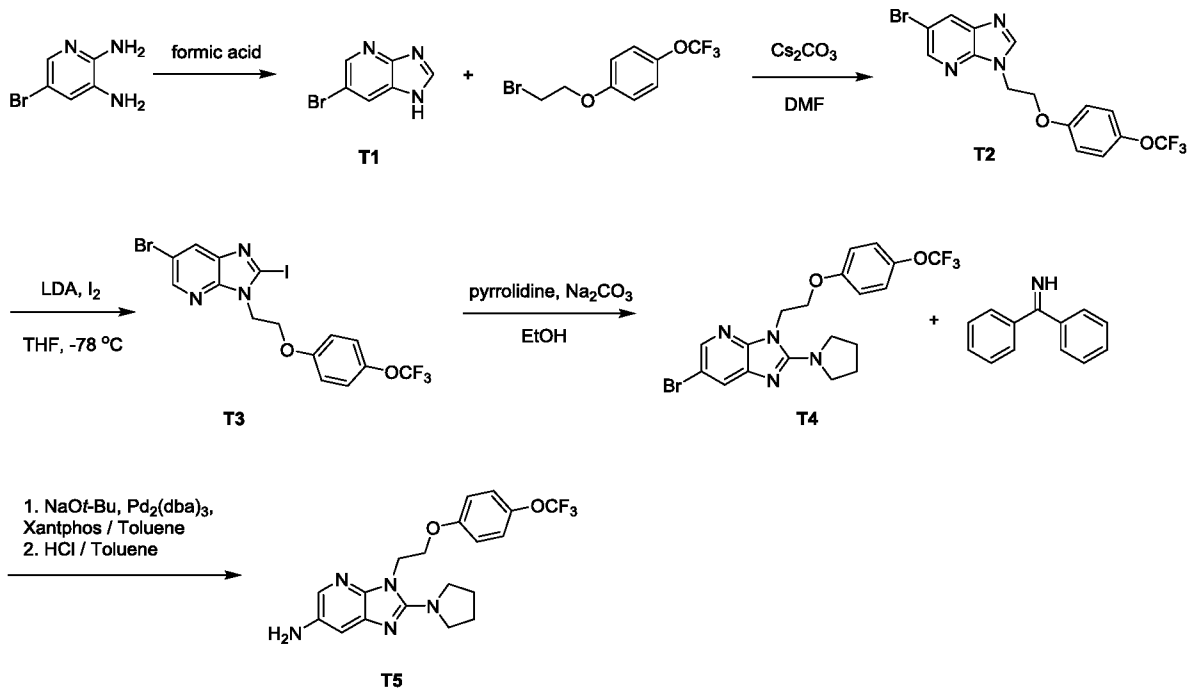
To a stirred solution of 4-fluoro aniline (360 mg, 3.24 mmol), 4-Bromobenzaldehyde (500 mg, 2.70 mmol), XantPhos (60 mg, 0.108 mmol) and $Pd_2(dba)_3$ (25 mg, 0.027 mmol) in anhydrous toluene (15 mL) was added Cs_2CO_3 (1.32 g, 4.05 mmol) under N_2 atmosphere. The reaction mixture was purged under N_2 atmosphere for 3 times, then heated to reflux (oil bath 120 ^oC) under N_2 atmosphere for 16 hours. 40 mL water was poured into the mixture, then extracted with EtOAc (20 mL×2), the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give crude product. The residue was purified by Combi-flash (PE: EtOAc= 20:1 to 9:1) to afford **S1**.

General procedure for the synthesis of S2

To a stirred solution of **S1** (200 mg, 0.929 mmol) in anhydrous DMA (20 mL) was added NaH

(74 mg, 1.86 mmol, 60% dispersion in mineral oil) at 0 °C for 0.5 hour, then ethyl bromoacetate (186 mg, 1.12 mmol) was added, after 1 hour, the resulting mixture was stirred at 60 °C for another 16 hours. The mixture was quenched with water (20 mL), then extracted with EtOAc (30 mL×2). The combined organic phase was washed with brine (20 mL×2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford **S2**.

Scheme 20. General synthesis of an imidazopyridine derivative



General procedure for the synthesis of T1

A mixture of 5-bromopyridine-2, 3-diamine (5.00 g, 26.6 mmol) in formic acid (80 mL) was heated to 110 °C for 16 hours. The reaction solution was concentrated under reduced pressure. The residue was partitioned between 2 N NaOH (200 mL) and DCM (100 mL). The organic phase was separated and the aqueous layer was cooled to 0 °C for 1 hour. The precipitate was collected by filtration, dried over high vacuum to afford **T1**.

General procedure for the synthesis of T2

To a stirred solution of **T1** (200 mg, 1.01 mmol) in DMF (4 mL) were added 1-(2-bromoethoxy)-4-(trifluoromethoxy)benzene (432 mg, 1.52 mmol) and Cs_2CO_3 (823 mg, 2.53 mmol) and stirred at 50 °C for 16 hours. The reaction mixture was poured into water (200 mL) and extracted with EtOAc (20 mL x 3). The combined organic layer was washed with water

(10 mL x 3), brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by Combi Flash (PE: EtOAc= 1:1) to afford **T2**.

General procedure for the synthesis of T3

To a stirred solution of diisopropylamine (0.125 mL, 0.894 mmol) in anhydrous THF (1.5 mL) was added *n*-BuLi (0.37 mL, 2.5 M in hexane) dropwise at -78 °C. The solution was stirred at -78 °C for 30 minutes. Then a solution of **T2** (200 mg, 0.447 mmol) in anhydrous THF (0.5 mL) was added dropwise at -78 °C and the solution was stirred at -78 °C for 0.5 hours. Then a solution of iodine (226 mg, 0.894 mmol) in anhydrous THF (0.5 mL) was added dropwise. The reaction solution was stirred at -78 °C for 1.5 hours and warmed to room temperature. The reaction mixture was quenched by saturated $Na_2S_2O_3$ (1.5 mL) and diluted with EtOAc (20 mL). The organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was recrystallized from PE/EtOAc (3 mL/ 3 mL) to afford **T3**.

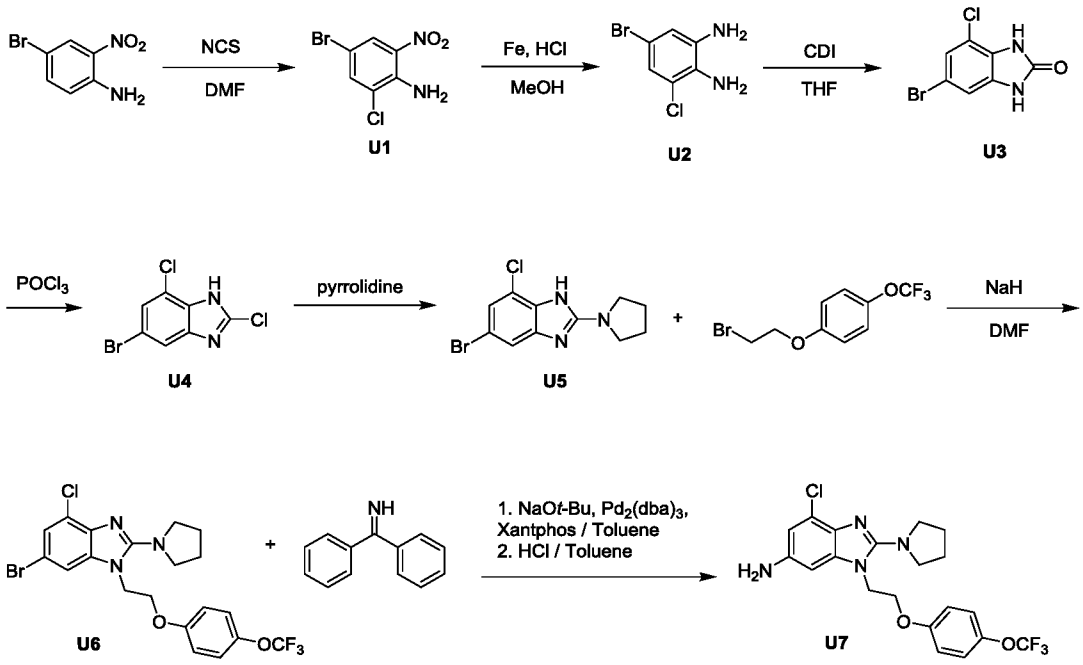
General procedure for the synthesis of T4

A mixture of **T3** (70 mg, 0.133 mmol), pyrrolidine (13 μg, 0.159 mmol) and Na_2CO_3 (21 mg, 0.200 mmol) in EtOH (1 mL) was stirred at 80 °C for 16 hours. The reaction mixture was diluted with EtOAc (20 mL), washed with brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by prep-TLC (PE: EtOAc= 1:1) to afford **T4**.

General procedure for the synthesis of T5

To a stirred solution of XantPhos (5 mg, 0.00847 mmol), $Pd_2(dba)_3$ (8 mg, 0.00847 mmol) and NaO*t*-Bu (20 mg, 0.211 mmol) in anhydrous toluene (1 mL) were added **T4** (40 mg, 0.0847 mmol) and benzophenone imine (18 mg, 0.101 mmol). The reaction mixture was stirred at 120 °C under N_2 for 1.5 hours. HCl (1 mL, 4 N) was added to the reaction mixture and the mixture was stirred at 16 °C for 5 minutes. The aqueous layer was basified with NaOH (4 mL, 2 N) and extracted with EtOAc (10 mL x 2). The combined extract was washed with brine (10 mL), dried over anhydrous Na_2SO_4, evaporated under reduced pressure. The resulting oil was purified by prep-TLC (DCM/MeOH, 15/1) to afford **T5**.

Scheme 21. General synthesis of a N^4 substituted benzimidazole derivative



General procedure for the synthesis of U1

A mixture of 4-bromo-2-nitroaniline (10.0 g, 0.046 mol) and NCS (6.15 g, 0.046 mol) in DMF (100 mL) was stirred at 120°C for 16 hours. The mixture was poured into water (100 mL), the precipitate was filtered, washed with water (50 mL) and dried under reduced pressure to afford **U1**.

General procedure for the synthesis of U2

To a stirred solution of **U1** in MeOH (100 mL) were added concentrated HCl (9 mL, 108 mmol, 12M) and iron powder (10.0 g, 179 mmol). The reaction mixture was stirred at 8-16 °C for 16 hours. After reaction was completed, the mixture was filtered. The filtrate was neutralized to pH 8 with $NaHCO_3$ aqueous solution and filtered. The filtrate was extracted with EtOAc (100 mL×2). The combined extracts were washed with brine (200 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford **U2**.

General procedure for the synthesis of U3

A mixture of **U2** (7.2 g, 32.5 mmol) and CDI (6.32 g, 39.0 mmol) in anhydrous THF (100 mL) was refluxed for 16 hours. After cooling to room temperature, the white precipitate was collected by filtration and dried under reduced pressure to afford **U3**.

General procedure for the synthesis of U4

A mixture of **U3** (4.90 g, 19.8 mmol) in $POCl_3$ (30 mL) was refluxed for 16 hours. After the

mixture was cooled to room temperature, the mixture was poured into water (100 mL) under stirring. The white precipitate was collected by filtration, washed with water (50 mL) and dried under reduced pressure to afford **U4**.

General procedure for the synthesis of U5

A mixture of **U4** (2.10 g, 7.90 mmol) in pyrrolidine (20 mL) was refluxed for 16 hours. The mixture was diluted with water (50 mL) and extracted with EtOAc (50 mL×2). The combined extracts were washed with brine (100 mL), dried over anhydrous Na_2SO_4 and concentrated under reduce pressure to afford crude residue which was purified by flash column chromatography (PE/EtOAc=5/1-2/1) to afford **U5**.

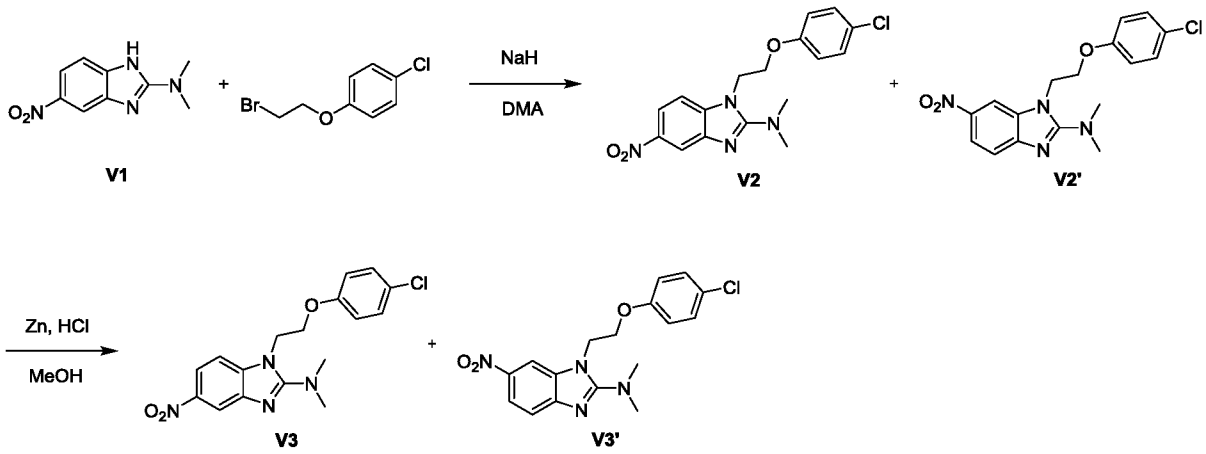
General procedure for the synthesis of U6

To a stirred solution of **U5** (850 mg, 2.83 mmol) in anhydrous DMF (10 mL) was added NaH (170 mg, 4.24 mmol, 60% in mineral oil) at 0°C. The mixture was stirred at 0°C for 30 minutes, added a solution of 1-(2-bromoethoxy)-4-(trifluoromethoxy)benzene (1.61 g, 5.66 mmol) in anhydrous DMF (5 mL) and stirred at 60°C for 16 hours. The mixture was quenched with water (50 mL), extracted with EtOAc (50 mL×2). The combined extracts were washed with brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated under reduce pressure to afford crude residue which was purified by Combi Flash to afford **U6**.

General procedure for the synthesis of U7

To a stirred solution of **U6** (680 mg, 1.35 mmol), benzophenone imine (488 mg, 2.69 mmol), $Pd_2(dba)_3$ (124 mg, 0.135 mmol) and XantPhos (156 mg, 0.270 mmol) in anhydrous toluene (10 mL) was added NaO*t*-Bu (324 mg, 3.38 mmol) under N_2 atmosphere. The reaction mixture was purged in N_2 atmosphere for three times. The mixture was heated to 80-100°C for 16 hours. The mixture was concentrated, dissolved in MeOH (2 mL), added HCl (3 M, 2 mL) and stirred at 20-25°C for 2 hours. Then the mixture was neutralized to pH 8 with $NaHCO_3$ aqueous solution and extracted with EtOAc (30 mL x 2), the combined extracts were washed with brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford crude residue, which was purified by prep-HPLC (0.05% HCl) to afford **U7**.

Scheme 22. General synthesis 1 of a N^1 substituted benzimidazole derivative



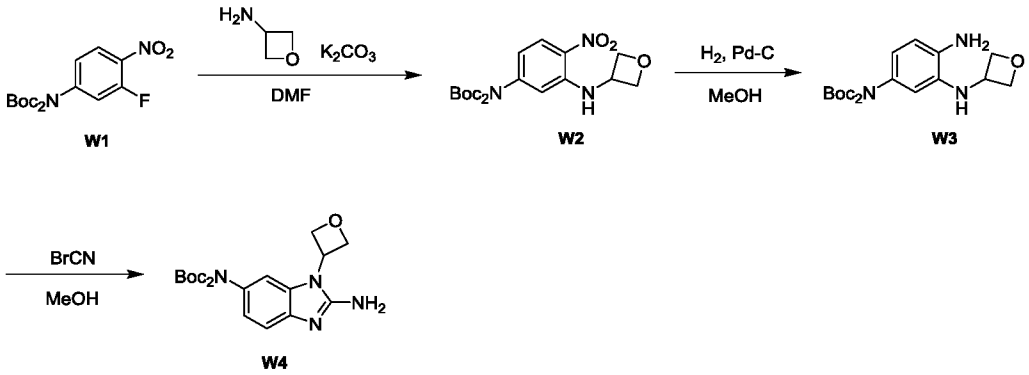
General procedure for the synthesis of V2

To a stirred solution of compound **2** (538 mg, 2.61 mmol) in DMA (10 mL) was added NaH (125mg, 3.13 mmol, 60% dispersion in mineral oil) portionwise. The mixture was stirred at 0 °C under N_2 atmosphere for 5 minutes. Then a solution of 1-(2-bromoethoxy)-4-chlorobenzene (908 mg, 3.90 mmol) in DMA (8 mL) was added to the mixture and the solution was stirred at 60 °C under N_2 for 24 hours. The mixture was diluted with water (80 mL) and extracted with EtOAc (40 mL×3), the combined extracts were washed with water (20 mL x 2), brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford the crude product, which was recrystallized from EtOAc (5 mL) to afford a mixture of **V2** and **V2`**.

General procedure for the synthesis of V3

To a stirred solution of a mixture of **V2** and **V2`** (100 mg, 0.302 mmol) in MeOH were added Zn powder (98.2 mg , 1.51 mmol) and NH_4Cl (326 mg, 6004 mmol) at 19 °C. The mixture was stirred at 45 °C for 16 hours. The reaction solution was diluted with EtOAc (10 mL) and filtered. The filtrate was concentrated under reduced pressure. The resulting oil was purified by prep-TLC (DCM/MeOH, 20/1) to afford **V3**.

Scheme 23. General synthesis 2 of a N^1 substituted benzimidazole derivative



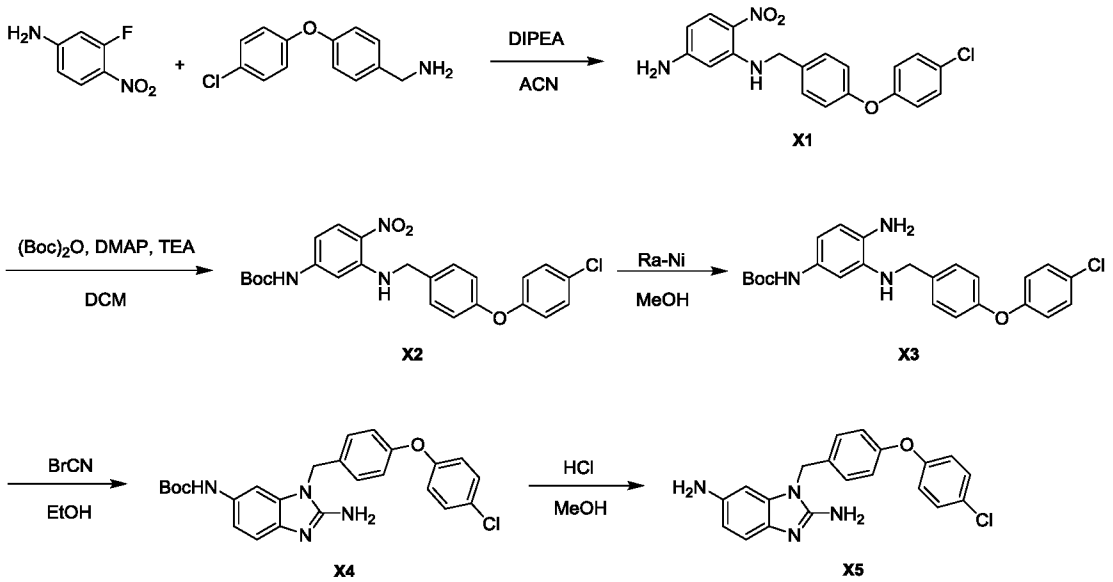
General procedure for the synthesis of W2

A mixture of compound **W1** (300 mg, 0.843 mmol), oxetan-3-amine (74 mg, 1.0 mmol), K_2CO_3 (175 mg, 1.26 mmol) in DMF (3 mL) was stirred at 10 °C for 16 hours. The reaction solution was diluted with water (15 mL) and extracted with EtOAc (20 mL x 2). The combined extract was washed with water (10 mL x 2), brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford **W2**.

General procedure for the synthesis of W4

To a stirred solution of **W2** (500 mg, 1.22 mmol) in MeOH (20 mL) was added Pd/C (50 mg, 5%, 60% wet) in N_2 atmosphere. The suspension was degassed under vacuum and purged with H_2 several times. The mixture was stirred under H_2 atmosphere (1 atm) for 1.5 hours. The reaction mixture was filtered through a pad of Celite. To the filtrate (**W3** in MeOH) was added BrCN (261 mg, 2.44 mmol). The reaction solution was stirred at 10 °C for 16 hours. The reaction solution was concentrated under reduced pressure. The residue was diluted with water (30 mL) and EtOAc (30 mL). Then solid Na_2CO_3 was added with stirring until aqueous layer was basified to pH 9. The organic layer was separated and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford **W4**.

Scheme 24. General synthesis 3 of a N^1 substituted benzimidazole derivative



General procedure for the synthesis of X1

A mixture of 3-fluoro-4-nitroaniline (1.00 g, 6.40 mmol), (4-(4-chlorophenoxy)phenyl) methanamine (1.79 g, 7.28 mmol), and DIPEA (1.65 g, 12.8 mmol) in ACN (15 mL) was refluxed 16 hours. The mixture was cooled to room temperature and diluted with water (40 mL). The mixture was extracted with EtOAc (40 mL x 2). The combined extracts was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford 3.42 g of crude residue, which was purified by Combi Flash to afford **X1**.

General procedure for the synthesis of X2

To a stirred solution of **X1** (1.50 g, 4.06 mmol), di-tert-butyl dicarbonate (1.15 g, 5.27 mmol) in DCM (20 mL) were added DMAP (248 mg, 2.03 mmol) and TEA (413 mg, 4.06 mmol). The mixture was stirred at 20 °C for 16 hours. The mixture was diluted with water (50 mL) and extracted with EtOAc (40 mL×2). The combined extracts were washed with brine (100 mL×2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford 3.00 g of crude residue, which was purified by Combi flash (PE/EtOAc =25/1 to 20/1 to 15/1) to afford **X2**.

General procedure for the synthesis of X3

To a stirred solution of **X2** (100 mg, 0.213 mmol) in MeOH (5 mL) was added Raney-Ni (20 mg) under Ar. The suspension was degassed under vacuum and purged with H_2 for three times. The solution was stirred at 28 °C under H_2 (50 psi) for 16 hours. The mixture was filtered through a pad of celite, and the pad was washed with MeOH (200 mL). The filtrate

was concentrated under reduced pressure to afford **X3**.

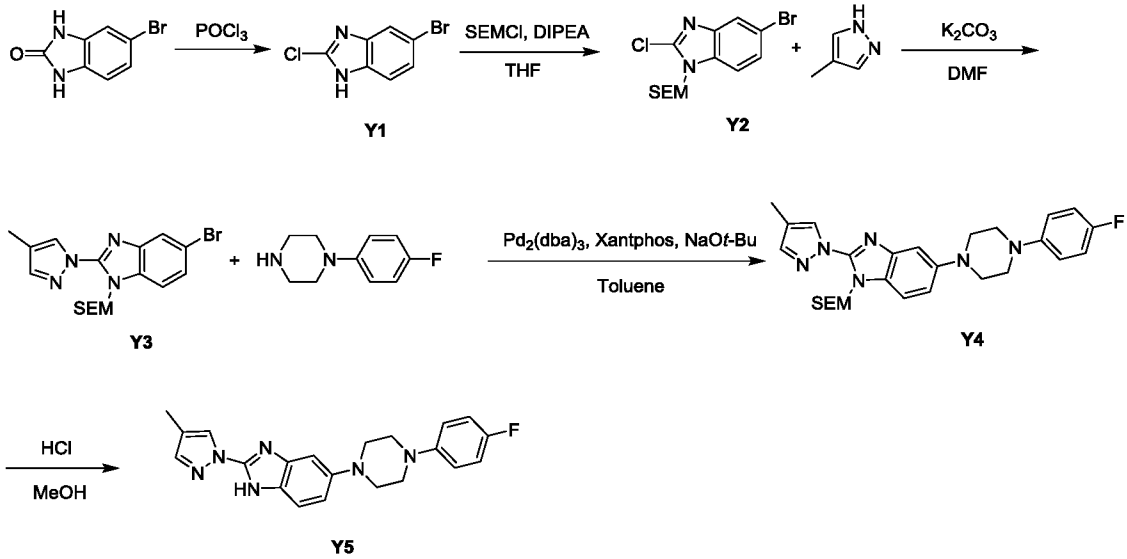
General procedure for the synthesis of X4

A mixture of **X3** (80 mg, 182 mmol), cyanogen bromide (29 mg, 0.273 mmol) in EtOH (4 mL) was stirred at 25 °C for 16 hours. The mixture was basified to pH 9 with Na_2CO_3 aqueous solution, diluted with water (20 mL) and extracted with EtOAc (20 mL x 2). The combined extracts was washed with brine (40 mL x 2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford **X4**.

General procedure for the synthesis of X5

To a stirred solution of **X4** (80 mg, 0.172 mmol) in MeOH (2 mL) was added HCl solution of MeOH (4M, 2 mL). The resulting solution was stirred at 25 °C for 2 hours. The mixture was diluted with water (20 mL), basified to pH 9 with Na_2CO_3 aqueous solution and extracted with EtOAc (20 mL x 2). The combined extracts was washed with brine (40 mL x 2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford crude residue, which was purified by prep-HPLC (0.01% $NH_3.H_2O$) to afford **X5**.

Scheme 25. General synthesis 1 of a N^2 substituted benzimidazole derivative



General procedure for the synthesis of Y1

A mixture of 5-bromo-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (5.00 g, 23.5 mmol) and $POCl_3$ (80 mL) was refluxed for 16 hours. After cooled to room temperature, the mixture was poured into water (300 mL) and NaOH aqueous solution (5 M, 80 mL) was added. The

precipitate was filtered and washed with water. The filtrate was dried over high vacuum to afford **Y1**.

General procedure for the synthesis of Y2

To a stirred solution of **Y1** (500 mg, 2.16 mmol) and DIPEA (558 mg, 4.32 mmol) in THF (5 mL) was added SEMCl (540 mg, 3.24 mmol) at 0°C and the resulting mixture was stirred at 35°C for 16 hours. The mixture was diluted with water (50 mL), extracted with EtOAc (50 mL×2). The combined extracts were washed with brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated under reduce pressure to afford a residue. The residue was purified by flash column chromatography to afford **Y2**.

General procedure for the synthesis of Y3

A mixture of **Y2** (480 mg, 1.33 mmol), 4-methyl-1*H*-pyrazole (109 mg, 1.33 mmol) and K_2CO_3 (275 mg, 1.99 mmol) in DMF (5 mL) was stirred at 100°C for 16 hours. The mixture was diluted with water (50 mL), extracted with EtOAc (50 mL×2). The combined extracts were washed with brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated under reduce pressure to afford a residue. The residue was purified by flash column chromatography to afford **Y3**.

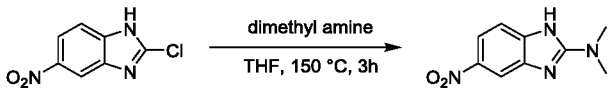
General procedure for the synthesis of Y4

A mixture of **Y3** (500 mg, 1.23 mmol), 1-(4-fluorophenyl)piperazine (243 mg, 1.35 mmol), NaO*t*-Bu (236 mg, 2.45 mmol), $Pd_2(dba)_3$ (112 mg, 0.123 mmol) and Xantphos (71 mg, 0.12 mmol) in toluene (5 mL) was stirred at 120°C for 16 hours. The mixture was diluted with water (50 mL), extracted with EtOAc (50 mL×2). The combined extracts were washed with brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated under reduce pressure to afford a residue. The residue was purified by flash column chromatography to afford **Y4**.

General procedure for the synthesis of Y5

A mixture of **Y4** (160 mg, 0.316 mmol) and conc.HCl (2 mL) in MeOH (6 mL) was stirred at 32°C for 16 hours. The mixture was diluted with water (50 mL), neutralized with NaOH aqueous solution and extracted with EtOAc (50 mL×2). The combined extracts were washed with brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated under reduce pressure to afford **Y5**.

Scheme 26. General synthesis 2 of a N^2 substituted benzimidazole derivative

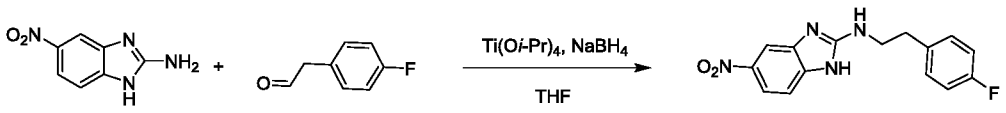


Z1

General procedure for the synthesis of Z1

To a stirred solution of dimethyl amine in THF (18 mL, 2 N) was added 2-chloro-5-nitro-1*H*-benzo[*d*]imidazole (1.80 g, 9.1 mmol) at 20 °C. The reaction solution was stirred at 150 °C in a sealed tube for 3 hours. The reaction solution was poured into water (20 mL) and extracted with EtOAc (10 mL x 3). The combined organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford **Z1**.

Scheme 27. General coupling reaction 1 of a benzimidazole N^2 amine

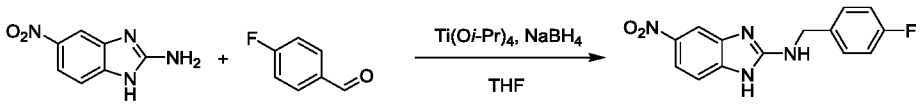


AA1

General procedure for the synthesis of AA1

A mixture of 5-nitro-1*H*-benzo[*d*]imidazol-2-amine (200 mg, 1.12 mmol), (4-fluoro-phenyl)-acetaldehyde (388 mg, 2.80 mmol) and Ti(O*i*-Pr)$_4$ (637 mg, 2.24 mmol) in anhydrous THF (5 mL) was stirred at 60°C for 30 minutes, then cooled to 20 °C and kept at this temperature for 30 minutes under stirring. Then $NaBH_4$ (213 mg, 5.60 mmol) was added into the mixture at 0°C and stirred at 20°C for 3 hours, then at 60 °C for 16 hours. The mixture was cooled and quenched with aqueous $NH_3.H_2O$ (2M, 10 mL). The precipitate was filtered and washed with THF (20 mL). The filtrate was diluted with water (20 mL) and extracted with EtOAc (20 mL×2). The combined extracts were washed with brine (50 mL×2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford crude product, which was purified by prep-HPLC (0.01% $NH_3.H_2O$) to afford **AA1**.

Scheme 28. General coupling reaction 2 of a benzimidazole N^2 amine

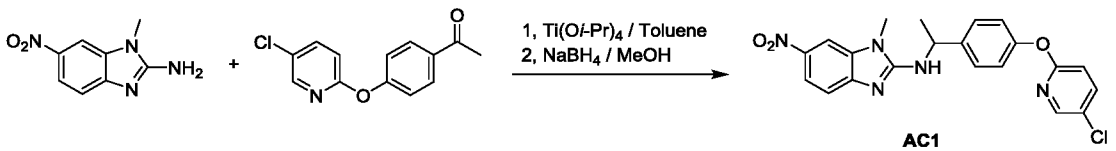


AB1

General procedure for the synthesis of AB1

A mixture of 5-nitro-1*H*-benzo[*d*]imidazol-2-amine (1.00 g, 5.60 mmol), 4-fluorobenzaldehyde (2.78 g, 22.4 mmol) and Ti(O*i*-Pr)$_4$ (3.18 g, 11.2 mmol) in THF (6 mL) was stirred at 60°C for 30 minutes, the mixture was cooled to 20 °C and kept at this temperature for 30 minutes. Then $NaBH_4$ (851 mg, 22.4 mmol) was added into the mixture at 0°C and stirred at 20°C for 3 hours and at 60 °C for 16 hours. The mixture was cooled to 20°C and quenched with aqueous $NH_3.H_2O$ (2M, 15 mL). The precipitate was filtered, washed with THF (50 mL). The filtrate was diluted with water (50 mL) and extracted with EtOAc (50 mL×2). The combined extracts were washed with brine (100 mL×2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford crude product, which was purified by prep-HPLC (0.01% $NH_3.H_2O$) to afford **AB1**.

Scheme 29. General coupling reaction 3 of a benzimidazole N^2 amine

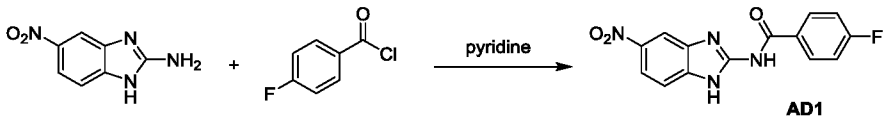


AC1

General procedure for the synthesis of AC1

To a stirred solution of 1-methyl-6-nitro-1*H*-benzo[*d*]imidazol-2-amine (900 mg, 3.63 mmol) and acetophenone (700 mg, 3.64 mmol) in anhydrous toluene (150 mL) was added Ti(O*i*-Pr)$_4$ (3.13 g, 10.9 mmol). The resulting mixture was stirred under reflux under N_2 atmosphere for 24 hours. After cooling to room temperature, $NaBH_4$ (290 mg, 7.26 mmol) was added to the mixture followed by MeOH (5 mL). The resulting mixture was stirred at 12 °C for 2 hours. The mixture was diluted with EtOAc (200 mL), washed with brine (200 mL) and water (200 mL x 2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford crude product, which was purified by flash column chromatography (eluted with PE/EtOAc = 50/1 to 5/1) to afford **AC1**.

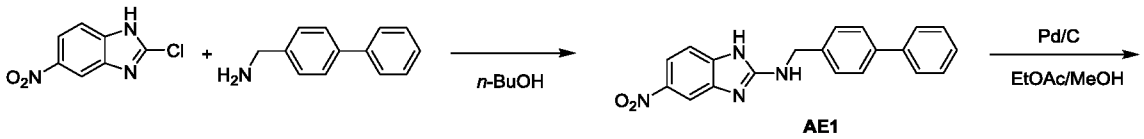
Scheme 30. General coupling reaction 4 of a benzimidazole N^2 amine

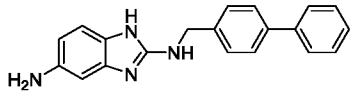


General procedure for the synthesis of AD1

A mixture of 5-nitro-1*H*-benzo[*d*]imidazol-2-amine (3.00 g, 16.8 mmol) and 4-fluorobenzoyl chloride (8.10 g, 53.6 mmol) in pyridine (30 mL) was stirred at 20°C for 10 minutes. The mixture was diluted with water (150 mL) and filtered. The filter cake was washed with water (100 mL) and dried over high vacuum to afford a crude residue which was purified by flash column chromatography to afford **AD1**.

Scheme 31. General coupling reaction 5 of a benzimidazole N^2 amine





General procedure for the synthesis of AE1

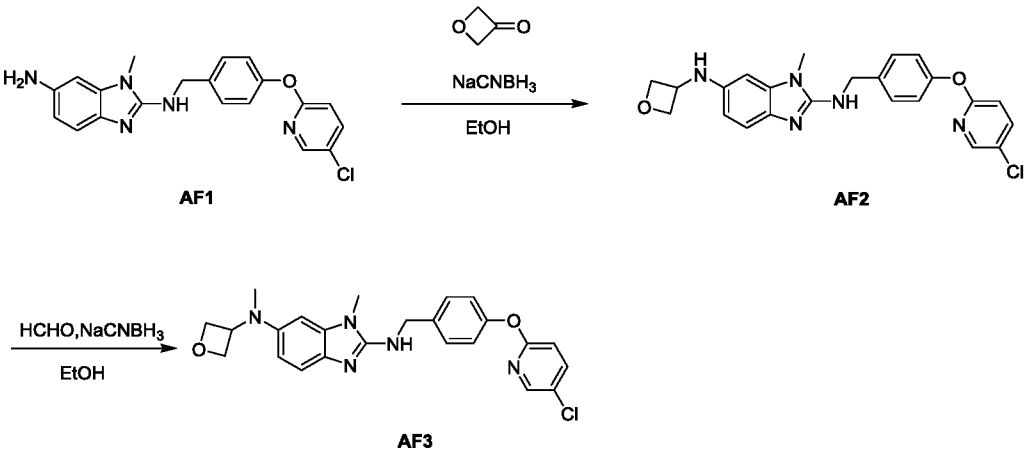
A mixture of 2-chloro-5-nitro-1*H*-benzo[*d*]imidazole (500 mg, 2.53 mmol), 4-phenylbenzylamine (696 mg, 3.80 mmol) in *n*-BuOH (8 mL) was refluxed for 36 hours. After reaction was complete, the mixture was diluted with water (50 mL) and extracted with EtOAc (50 mL×2). The combined extracts were washed with brine (100 mL×2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford crude residue, which was purified by combi flash (PE/EtOAc=3/1 to 2/1 to 1/1) to afford **AE1**.

General procedure for the synthesis of AE2

To a stirred solution of **AE1** (150 mg, 0.436 mmol) in EtOAc/MeOH (8 mL/2 mL) was added Pd/C (30 mg, 10%) under N_2. The suspension was degassed under vacuum and purged with H_2 for three times. The solution was stirred at 22 °C under H_2 balloon for 16 hours. The

mixture was filtered through a pad of celite and washed with EtOAc (30 mL). The filtrate was concentrated under reduced pressure to afford crude residue which was purified by washing with EtOAc/MeOH (5 mL/1 mL) to afford **AE2**.

Scheme 32. General coupling reaction 1 of a benzimidazole N^6 amine



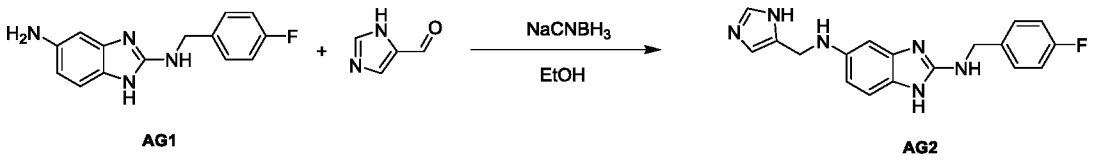
General procedure for the synthesis of AF2

A mixture of **A1** (200 mg, 0.488 mmol), AcOH (0.3 mL) and 3-oxetanone (42 mg, 0.59 mmol) in absolute EtOH (3 mL) was stirred at 18-22 °C for 16 hours. Then to the reaction mixture was added $NaBH_3CN$ (92 mg, 1.5 mmol), the resulting mixture was stirred at 18-20 °C for 4 hours. The reaction mixture was diluted with EtOAc (50 mL), then washed with water (40 mL) and brine (40 mL x3), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by prep-HPLC (0.01% $NH_3.H_2O$ as additive) to afford **AF2**.

General procedure for the synthesis of AF3

A mixture of **AF2** (100 mg, 0.229 mmol) and formaldehyde (86 mg, 1.15 mmol, 40% aqueous solution in water) in EtOH (5 mL) was added AcOH (adjusted to pH 4 of reaction mixture). The resulting mixture was stirred at 10 °C for 16 hours. $NaBH_3CN$ (72 mg, 1.15 mmol) was added to the mixture and the reaction mixture was stirred at 10 °C for 4 hours. The mixture was diluted with water (20 mL) and extracted with EtOAc (20 mL x 2), the combined extracts were washed with brine (40 mL x 2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford a residue, which was purified by prep-HPLC (0.01% $NH_3.H_2O$) to afford **AF3**.

Scheme 33. General coupling reaction 2 of a benzimidazole N^6 amine

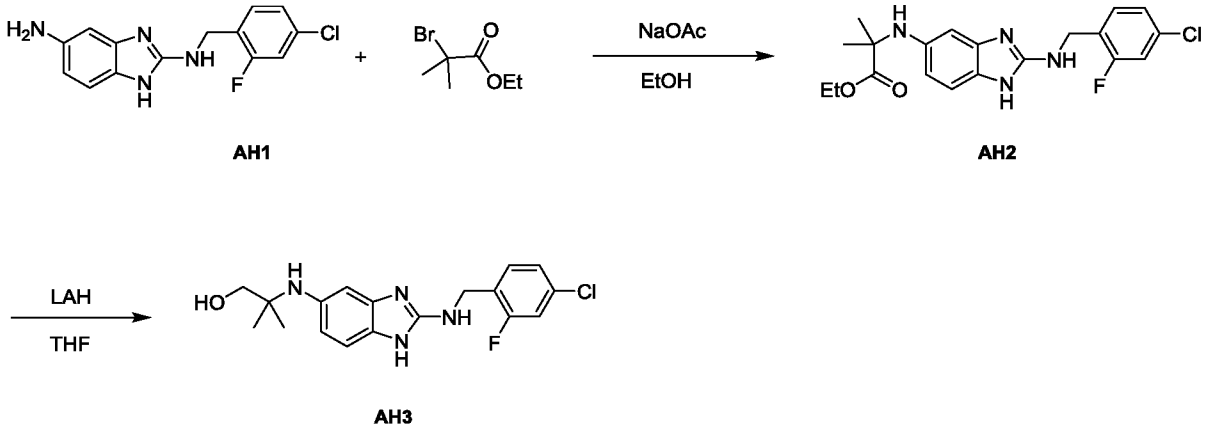


AG1 AG2

General procedure for the synthesis of AG2

To a stirred solution of **AG1** (150 mg, 0.583 mmol), 1*H*-imidazole-5-carbaldehyde (39 mg, 0.416 mmol) in EtOH (3 mL) was added AcOH (adjusted to pH 4 of reaction mixture). The resulting mixture was stirred at 20°C for 16 hours. Then $NaBH_3CN$ (73 mg, 1.17 mmol) was added and the mixture was stirred at 20°C for 16 hours. The mixture was neutralized with Na_2CO_3, diluted with water (20 mL) and extracted with EtOAc (20 mL×2). The combined extracts were washed with brine (40 mL×2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford crude residue, which was purified by prep-HPLC (0.01% $NH_3.H_2O$) to afford **AG2**.

Scheme 34. General coupling reaction 3 of a benzimidazole N^6 amine



AH1 AH2 AH3

General procedure for the synthesis of AH2

To a stirred solution of **AH1** (200 mg, 0.69 mmol) and ethyl 2-bromoisobutyrate (537 mg, 2.75 mmol) in EtOH (10 mL) was added NaOAc (226 mg, 2.75 mmol). The mixture was refluxed under N_2 for 16 hours. The mixture was diluted with water (10 mL) and extracted with EtOAc (10 mL×2). The combined extracts were washed with brine (10 mL×2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure afford a crude **AH2**.

General procedure for the synthesis of AH3

To a stirred solution of compound **AH2** (200 mg, crude) in anhydrous THF (5 mL) was added $LiAlH_4$ (75 mg, 1.98 mmol) at 0°C. After stirred at 0°C for 2 hours, the mixture was allowed to stir at 25°C under N_2 for 16 hours. The mixture was quenched with NaOH aqueous solution (5 M, 0.2 mL) and filtered. The filtrate was diluted with water (10 mL) and extracted with EtOAc (10 mL×2), the combined extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford crude product, which was purified by prep-TLC (MeOH : DCM = 1 : 10) to afford **AH3**.

Scheme 35. General synthesis of a N^6 substituted benzimidazole derivative



General procedure for the synthesis of AI2

A mixture of **AI1** (1.00 g, 4.05 mmol), 5-fluoro-2-nitroaniline (631 mg, 4.05 mmol) and DIPEA (1.55 g, 12.2 mmol) in ACN (10 mL) was heated to reflux for 12 hours. The mixture was concentrated under reduced pressure to afford a residue, which was purified by silica gel column (eluent: EtOAc/PE= 1/10 to DCM to DCM/EtOAc= 1/1) to afford **AI2**.

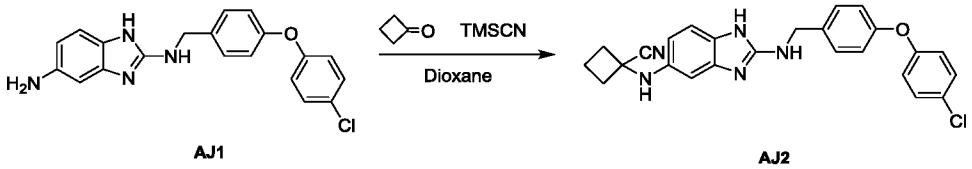
General procedure for the synthesis of AI3

A mixture of compound **AI2** (1.30 g, 3.39 mmol) and Pd-C (200 mg, 10%) in MeOH (30 mL) was stirred at 10 °C under H_2 (1 atm) for 2 hours. The mixture was filtered, the filtrate was concentrated under reduced pressure to afford a crude **AI3**.

General procedure for the synthesis of AI4

To a stirred solution of compound **AI3** (100 mg, 0.283 mmol) in MeOH (5 mL) was added BrCN (31 mg, in 0.5 mL ACN) with ice bath, the mixture was stirred at 10 °C for 1 hour. The reaction solution was purified by prep-HPLC (0.01% HCl) to afford **AI4**.

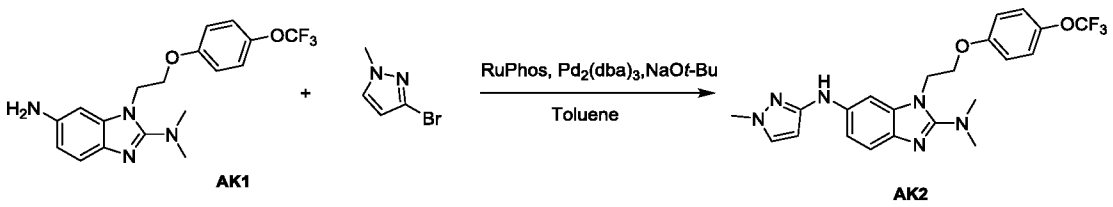
Scheme 36. General coupling reaction 4 of a benzimidazole N^6 amine



General procedure for the synthesis of AJ2

To a stirred solution of **AJ1** (100 mg, 0.274 mmol) in anhydrous dioxane (3 mL) were added cyclobutanone (23 mg, 0.329 mmol) and TMSCN (38 mg, 0.384 mmol), the resulting mixture was stirred at 50 °C under N_2 atmosphere for 16 hours. The mixture was diluted with water (15 mL) and extracted with EtOAc (15 mL x 2), the combined extracts were washed with brine (30 mL x 2), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford 90 mg of crude residue, which was purified by prep-HPLC (0.05% HCl) to afford **AJ2**.

Scheme 37. General coupling reaction 5 of a benzimidazole N^6 amine



General procedure for the synthesis of AK2

To a stirred solution of **AK1** (100 mg, 0.244 mmol) in anhydrous toluene (5 mL) were added RuPhos (12 mg, 0.0244 mmol), $Pd_2(dba)_3$ (23 mg, 0.0244 mmol), 3-bromo-1-methyl-1*H*-pyrazole (47 mg, 0.293 mmol) and NaO*t*-Bu (58 mg, 0.610 mmol). The mixture was stirred at 110 °C under N_2 for 16 hours. The reaction was diluted with brine (5 mL) and filtered. The filtrate was extracted with EtOAc (5 mL x 3). The combined extract was washed with brine (5 mL), dried over Na_2SO_4, evaporated under reduced pressure. The resulting oil was purified by prep-HPLC (0.01% $NH_3 \cdot H_2O$ as additive) to afford **AK2**.

Using the above procedures, compounds 1-556 as shown in **Table 7** (further below) were synthesized.

Table 1. 5-LO activity by fluorescence method

# cpds	5-LO (IC_{50}, uM)	# cpds	5-LO (IC_{50}, uM)	# cpds	5-LO (IC_{50}, uM)
1	+++	35	++	69	++
2	+++	36	+++	70	+++
3	+++	37	+++	71	+++
4	+++	38	+++	72	+
5	+++	39	+++	73	+++
6	+++	40	+++	74	+++
7	+++	41	++	75	+++
8	+++	42	++	76	+++
9	+++	43	++	77	+++
10	+++	44	+++	78	+
11	+++	45	+	79	+++
12	+++	46	+	80	+++
13	++	47	+	81	+++
14	+++	48	+++	82	+
15	+++	49	+	83	++
16	+++	50	++	84	+++
17	++	51	+++	85	++
18	++	52	+++	86	+++
19	+++	53	+++	87	+++
20	+++	54	+++	88	+++
21	+++	55	++	89	+++
22	+	56	+++	90	+++
23	++	57	+++	91	+++
24	+++	58	+++	92	+++
25	+	59	+++	93	+++
26	++	60	+++	94	+++
27	++	61	+++	95	+++
28	+++	62	+++	96	+++
29	+++	63	+++	97	+++
30	+++	64	+++	98	+++
31	+++	65	+++	99	+++
32	+++	66	+++	100	+++
33	+++	67	+++	101	+++
34	+++	68	+++	102	+++

Activity range: +++ indicates < 1 uM, ++ indicates between 1-10uM, + indicates >10 uM

Table 1 continued

# cpds	5-LO (IC_{50}, uM)	# cpds	5-LO (IC_{50}, uM)	# cpds	5-LO (IC_{50}, uM)
103	+++	137	+++	171	+++
104	+++	138	+++	172	+++
105	+++	139	+++	173	+++
106	+++	140	+++	174	++
107	+++	141	+++	175	+++
108	+++	142	+++	176	+++
109	+++	143	+++	177	+++
110	+++	144	+++	178	+++
111	+++	145	+++	179	+++
112	+++	146	+++	180	+++
113	+++	147	+++	181	+++
114	+++	148	+++	182	+++
115	+++	149	+++	183	+++
116	+++	150	+++	184	+++
117	+++	151	+++	185	+++
118	+++	152	+++	186	+++
119	+++	153	+++	187	+++
120	+++	154	+++	188	+++
121	+++	155	+++	189	+++
122	+++	156	+++	190	+++
123	+++	157	+++	191	+++
124	+++	158	+++	192	+++
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126	+++	160	+++	194	+++
127	+++	161	+++	195	+++
128	+++	162	+++	196	+++
129	+++	163	+++	197	+++
130	+++	164	+++	198	+++
131	+++	165	+++	199	+++
132	+++	166	+++	200	+++
133	+++	167	+++	201	+++
134	+++	168	+++	202	+++
135	+++	169	+++	203	+++
136	+++	170	+++	204	+++

Activity range: +++ indicates < 1 uM, ++ indicates between 1-10uM, + indicates >10 uM

Table 1 continued

# cpds	5-LO (IC_{50}, uM)	# cpds	5-LO (IC_{50}, uM)	# cpds	5-LO (IC_{50}, uM)
205	+++	239	+++	273	+++
206	+++	240	+++	274	+++
207	+++	241	+++	275	+++
208	+++	242	++	276	+++
209	+++	243	+++	277	+++
210	+++	244	+++	278	+++
211	+++	245	+	279	++
212	+++	246	+++	280	+++
213	+++	247	+++	281	+++
214	+++	248	+++	282	+++
215	+++	249	+++	283	+++
216	+++	250	+++	284	+++
217	+++	251	+++	285	+++
218	+++	252	+++	286	+++
219	+++	253	+++	287	+++
220	+++	254	+++	288	+++
221	+++	255	+++	289	+++
222	+++	256	+++	290	+++
223	+++	257	+++	291	+++
224	+++	258	+++	292	+++
225	+++	259	+++	293	+++
226	+++	260	+++	294	+++
227	+++	261	+++	295	+++
228	+++	262	+	296	+++
229	+++	263	+++	297	+++
230	+++	264	+++	298	+++
231	+++	265	+++	299	+++
232	+++	266	+++	300	+++
233	+++	267	+++	301	+++
234	+++	268	+++	302	+++
235	+	269	+++	303	+++
236	+++	270	+++	304	+++
237	+++	271	+++	305	+++
238	+++	272	+++	306	+++

Activity range: +++ indicates < 1 uM, ++ indicates between 1-10uM, + indicates >10 uM

Table 1 continued

# cpds	5-LO (IC_{50}, uM)	# cpds	5-LO (IC_{50}, uM)	# cpds	5-LO (IC_{50}, uM)
307	+++	341	+++	375	+++
308	+++	342	+++	376	+++
309	+++	343	+++	377	+++
310	+++	344	+++	378	+++
311	+++	345	+++	379	+++
312	+++	346	+++	380	+++
313	+++	347	+++	381	+++
314	+++	348	+++	382	+++
315	+++	349	+++	383	+++
316	+++	350	+++	384	+++
317	+++	351	+++	385	+++
318	+++	352	+++	386	++
319	+++	353	+++	387	+++
320	+++	354	+++	388	+++
321	+++	355	++	389	+++
322	+	356	+++	390	+++
323	+++	357	+++	391	+++
324	+++	358	+++	392	+++
325	+++	359	+++	393	+++
326	+++	360	+++	394	+++
327	+++	361	+++	395	+++
328	+++	362	+++	396	+++
329	+++	363	+++	397	+++
330	+++	364	+++	398	+++
331	+++	365	+++	399	+++
332	+++	366	+++	400	+++
333	+++	367	+++	401	+++
334	+++	368	+++	402	+++
335	+++	369	+++	403	+++
336	+++	370	+++	404	+++
337	+++	371	+++	405	+++
338	+++	372	+++	406	+++
339	+++	373	+++	407	+++
340	+++	374	+++	408	+++

Activity range: +++ indicates < 1 uM, ++ indicates between 1-10uM, + indicates >10 uM

Table 1 continued

# cpds	5-LO (IC_{50}, uM)	# cpds	5-LO (IC_{50}, uM)	# cpds	5-LO (IC_{50}, uM)
409	+++	443	+++	477	+++
410	+++	444	+++	478	+++
411	+++	445	+++	479	+++
412	+++	446	+++	480	+++
413	+++	447	++	481	+++
414	+++	448	++	482	+++
415	+++	449	+++	483	+++
416	+++	450	+++	484	+++
417	+++	451	+++	485	+++
418	+++	452	+++	486	+++
419	+++	453	+++	487	+++
420	+++	454	+++	488	++
421	+++	455	+++	489	+++
422	+++	456	+++	490	+++
423	+++	457	+++	491	+++
424	+++	458	+++	492	+++
425	+++	459	+++	493	++
426	+++	460	+++	494	++
427	+++	461	+++	495	+++
428	+++	462	+++	496	+++
429	+	463	+++	497	++
430	+++	464	++	498	+
431	+++	465	+++	499	+++
432	+++	466	+++	500	++
433	+++	467	+++	501	+++
434	+++	468	+++	502	++
435	+++	469	+++	503	+++
436	+++	470	+++	504	++
437	+++	471	+++	505	+++
438	+++	472	++	506	+
439	+++	473	+++	507	+++
440	+++	474	+++	508	++
441	+	475	+++	509	+++
442	+++	476	+++	510	+

Activity range: +++ indicates < 1 uM, ++ indicates between 1-10uM, + indicates >10 uM

Table 1 continued

# cpds	5-LO (IC_{50}, uM)	# cpds	5-LO (IC_{50}, uM)	# cpds	5-LO (IC_{50}, uM)
511	+	527	+	543	+++
512	+++	528	+	544	+++
513	+++	529	+++	545	++
514	+++	530	+++	546	+++
515	+	531	+++	547	+++
516	+	532	+++	548	+++
517	++	533	+++	549	+++
518	+	534	+++	550	+++
519	+	535	+++	551	+++
520	+	536	+++	552	+++
521	++	537	+++	553	+++
522	+	538	+++	554	+++
523	+	539	+++	555	+++
524	+	540	+++	556	+++
525	+++	541	+++		
526	++	542	+++		

Activity range: +++ indicates < 1 uM, ++ indicates between 1-10uM, + indicates >10 uM

Table 2. 5-LO activity by ELISA method

# cpds	5LO (IC_{50}, uM)
14	+++
48	++
49	++

Activity range: +++ indicates < 1 uM, ++ indicates between 1-20 uM, + indicates > 20 uM

Table 3. LTB4 secretion assay in RBL

# cpds	RBL (EC_{50}, uM)	# cpds	RBL (EC_{50}, uM)	# cpds	RBL (EC_{50}, uM)
14	+++	57	+++	91	+++
17	+++	58	+++	92	+++
24	+++	59	+++	93	+++
26	+	60	+++	94	+++
27	+	61	++	95	+++
28	++	62	+++	96	+++
29	+++	63	++	97	+++
30	+++	64	+	98	+++
31	+	65	+++	99	+++
32	+++	66	+++	100	+++
33	+++	67	+++	101	+++
34	++	68	+++	102	+++
35	+	69	+++	103	+++
36	++	70	+++	104	+++
37	+	71	++	105	+++
38	+++	72	+	106	+++
39	++	73	+++	107	+++
40	++	74	+++	108	+
41	++	75	++	109	+++
42	++	76	+	110	+++
43	+++	77	++	111	+++
44	+++	78	++	112	+++
45	+++	79	+++	113	+++
46	+++	80	+++	114	++
47	+	81	+++	115	+
48	+++	82	++	116	+++
49	+++	83	+	117	++
50	++	84	+++	118	+++
51	+++	85	+	119	+++
52	+++	86	+++	120	+++
53	+++	87	+++	121	+++
54	+++	88	+++	122	+++
55	+++	89	+	123	+++
56	+++	90	+++	124	+++

Activity range: +++ indicates <10uM, ++ indicates between 10-20uM, + indicates > 20 uM

Table 3 continued

# cpds	RBL (EC_{50}, uM)	# cpds	RBL (EC_{50}, uM)	# cpds	RBL (EC_{50}, uM)
125	+++	159	+	193	+++
126	+++	160	+++	194	+++
127	+++	161	+++	195	+++
128	+++	162	+++	196	+++
129	+++	163	+	197	+++
130	+++	164	+++	198	++
131	+++	165	+++	199	+++
132	+++	166	+++	200	+++
133	++	167	+	201	+
134	+++	168	+++	202	+++
135	+++	169	+++	203	+++
136	+++	170	++	204	+++
137	+++	171	+	205	+++
138	+++	172	+++	206	+++
139	+	173	+	207	+++
140	+++	174	+	208	+++
141	+	175	+++	209	+++
142	++	176	+++	210	+++
143	++	177	+++	211	+++
144	++	178	++	212	+++
145	+++	179	+++	213	+++
146	++	180	+++	214	+++
147	+++	181	+	215	+++
148	+++	182	++	216	+++
149	+++	183	+	217	+++
150	+++	184	+++	218	+++
151	+	185	+++	219	+++
152	+++	186	+++	220	+++
153	+++	187	+++	221	+
154	+	188	+	222	++
155	+++	189	+	223	+++
156	++	190	+++	224	+++
157	+	191	+++	225	+
158	+	192	+++	226	+++

Activity range: +++ indicates <10uM, ++ indicates between 10-20uM, + indicates > 20 uM

Table 3 continued

# cpds	RBL (EC_{50}, uM)	# cpds	RBL (EC_{50}, uM)	# cpds	RBL (EC_{50}, uM)
227	+++	261	+++	295	+++
228	+	262	+++	296	+++
229	+++	263	++	297	+++
230	+++	264	+++	298	+++
231	+++	265	+++	299	+++
232	+	266	++	300	+++
233	+++	267	+++	301	+++
234	+++	268	+++	302	+++
235	+++	269	+++	303	+
236	+++	270	+++	304	+++
237	+	271	+++	305	+++
238	+++	272	+++	306	+++
239	+++	273	+++	307	++
240	+++	274	+++	308	+
241	+++	275	+++	309	+
242	+++	276	+++	310	+
243	+++	277	+++	311	+
244	+++	278	+++	312	+
245	+++	279	+++	313	+++
246	+++	280	+++	314	++
247	+++	281	+++	315	++
248	+++	282	+++	316	+++
249	+++	283	+++	317	+
250	+++	284	+++	318	+
251	+++	285	+++	319	+
252	+++	286	+++	320	+
253	+++	287	+++	321	++
254	+++	288	+++	322	+++
255	+++	289	+++	323	+++
256	++	290	+++	324	+++
257	+++	291	+++	325	+++
258	+++	292	+++	326	+++
259	+++	293	+++	327	+++
260	+++	294	+++	328	+++

Activity range: +++ indicates <10uM, ++ indicates between 10-20uM, + indicates > 20 uM

Table 3 continued

# cpds	RBL (EC_{50}, uM)	# cpds	RBL (EC_{50}, uM)	# cpds	RBL (EC_{50}, uM)
329	+++	363	+	397	+++
330	+++	364	+	398	+++
331	+++	365	+++	399	+++
332	+++	366	+++	400	+++
333	+++	367	+++	401	+++
334	++	368	+++	402	+++
335	+++	369	+++	403	+++
336	++	370	++	404	+
337	++	371	++	405	+++
338	+	372	+++	406	+++
339	++	373	+++	407	+++
340	+++	374	+++	408	+
341	++	375	+++	409	+
342	+++	376	+	410	+++
343	+	377	+++	411	+
344	+	378	+++	412	+++
345	+	379	+++	413	+++
346	+++	380	+++	414	+++
347	+++	381	+	415	+++
348	+	382	+++	416	++
349	+++	383	+++	417	+
350	+++	384	+++	418	+
351	++	385	++	419	+++
352	+++	386	+	420	+++
353	+++	387	+++	421	+++
354	+	388	++	422	+++
355	+	389	+++	423	+++
356	++	390	+++	424	+++
357	+++	391	+++	425	+++
358	+++	392	+++	426	+++
359	+++	393	+++	427	+++
360	++	394	++	428	+++
361	+++	395	+++	429	++
362	++	396	+++	430	+++

Activity range: +++ indicates <10uM, ++ indicates between 10-20uM, + indicates > 20 uM

Table 3 continued

# cpds	RBL (EC_{50}, uM)	# cpds	RBL (EC_{50}, uM)	# cpds	RBL (EC_{50}, uM)
431	+++	465	+++	499	+++
432	+++	466	+++	500	++
433	++	467	+++	501	+++
434	+++	468	+++	502	+++
435	+++	469	+++	503	+++
436	+++	470	+++	504	+++
437	+++	471	+++	505	+++
438	++	472	+++	506	+++
439	++	473	+++	507	+++
440	+++	474	+++	508	+++
441	+	475	+++	509	+++
442	+++	476	+++	510	+++
443	+	477	+++	511	+++
444	++	478	+++	512	+++
445	+++	479	+++	513	+++
446	+++	480	+++	514	+++
447	+++	481	+++	515	+++
448	+++	482	+++	516	+++
449	+++	483	+	517	+++
450	+++	484	+	518	+++
451	+++	485	++	519	+++
452	+++	486	+++	520	+++
453	+++	487	+++	521	+++
454	++	488	+	522	+++
455	+++	489	+++	523	+++
456	+	490	+++	524	+++
457	+++	491	+++	525	+++
458	+++	492	+++	526	+++
459	++	493	+++	527	+++
460	+++	494	+++	528	+++
461	+++	495	+++	529	+++
462	+	496	+++	530	+++
463	+++	497	+	531	+++
464	+++	498	+	532	+++

Activity range: +++ indicates <10uM, ++ indicates between 10-20uM, + indicates > 20 uM

Table 3 continued

# cpds	RBL (EC_{50}, uM)	# cpds	RBL (EC_{50}, uM)	# cpds	RBL (EC_{50}, uM)
533	+++	541	+++	549	+++
534	+++	542	+++	550	+++
535	+++	543	+++	551	+++
536	+++	544	+++	552	+++
537	+++	545	+++	553	+++
538	+++	546	+++	554	++
539	+++	547	+++	555	++
540	+++	548	+++	556	+++

Activity range: +++ indicates <10uM, ++ indicates between 10-20uM, + indicates > 20 uM

Table 4. LTB4 secretion assay in Rat whole blood (RWB)

# cpds	RWB (EC_{50}, uM)	# cpds	RWB (EC_{50}, uM)	# cpds	RWB (EC_{50}, uM)
1	+	57	+	108	+
3	+	58	+	109	+++
4	+	59	+	110	+++
5	++	62	+++	111	+++
6	+	65	+++	112	++
7	+	66	+	113	+++
8	+	67	+	114	+
9	++	68	+	116	++
10	++	70	+	118	+
11	+++	73	++	119	+++
12	+++	74	++	120	+++
13	+	75	+	121	+
14	+++	77	+++	122	+++
15	+	79	+++	123	+++
16	+	80	+++	125	+++
17	+	81	+++	126	+
20	+	86	+++	127	+
21	+	87	+++	128	+
22	+	88	+++	129	+
23	++	90	++	130	+++
24	+++	91	++	132	+
30	+++	92	+++	135	++
32	+++	93	+	136	+++
38	+	94	+++	137	+++
43	+	97	+++	138	+++
44	+	98	+++	145	+++
48	+++	99	+	147	+++
49	++	101	+++	148	+
51	++	102	+++	149	+++
52	+++	103	+++	150	+
53	+++	104	+	152	++
54	+++	105	+	154	+
55	+	106	+++	155	+++
56	++	107	+	160	+

Activity range: +++ indicates <10uM, ++ indicates between 10-20uM, + indicates > 20 uM

Table 4 continued

# cpds	RWB (EC_{50}, uM)	# cpds	RWB (EC_{50}, uM)	# cpds	RWB (EC_{50}, uM)
161	++	253	+++	345	+++
164	+	256	+++	350	+++
165	+++	268	+++	351	+++
166	+++	269	+++	357	++
172	++	270	+++	358	+++
175	+	271	+++	360	+++
176	+++	273	++	362	+++
177	+++	275	+++	364	+
184	+++	277	+++	367	+++
190	+	279	+++	368	+++
191	+	281	+++	369	+++
193	+++	284	+++	371	++
195	+++	288	+++	373	+++
196	++	289	+++	374	+++
197	+	291	++	378	+++
199	+++	294	+	381	+++
202	+	296	+++	383	+
203	+	298	+	392	+++
204	+++	300	++	394	+
211	+++	302	++	409	+
219	+	303	+	412	+++
226	+++	305	+	413	+++
227	+++	306	+++	414	+++
229	+++	307	+	415	+++
231	+++	309	+	417	+
233	+++	311	+++	418	+
234	+++	315	+	430	+++
238	+++	324	+++	431	+++
239	+++	328	+++	433	+++
241	+	336	+++	447	+++
243	+++	337	++	448	+++
245	++	341	+++	449	+++
249	+++	343	++	450	+++
251	+++	344	++	459	++

Activity range: +++ indicates <10uM, ++ indicates between 10-20uM, + indicates > 20 uM

Table 4 continued

# cpds	RWB (EC_{50}, uM)	# cpds	RWB (EC_{50}, uM)	# cpds	RWB (EC_{50}, uM)
461	+++	496	+++	528	+++
464	+++	497	+	529	+++
465	+++	498	+++	530	+++
466	+++	499	+++	531	+++
468	+++	501	+++	532	+++
469	+++	502	+++	533	+++
470	+++	503	+++	534	+++
471	+++	504	+++	535	+++
473	+++	505	+++	536	+++
474	+++	506	+++	537	+++
475	+++	507	++	538	+++
476	+++	508	+++	540	+++
477	+++	509	+++	541	+++
479	+++	512	+++	542	+++
481	+++	513	+++	543	+++
482	+++	514	+++	544	+++
486	+++	516	+++	545	+++
487	+++	517	+++	546	+++
489	+++	518	+++	547	+++
490	+++	519	+++	550	+++
491	+++	523	++	552	++
492	+++	524	++	553	+++
493	+++	525	+++	554	+++
494	+++	526	+++	555	++
495	+++	527	+++		

Activity range: +++ indicates <10uM, ++ indicates between 10-20uM, + indicates > 20 uM

Table 5. PGE_2 inhibition assay

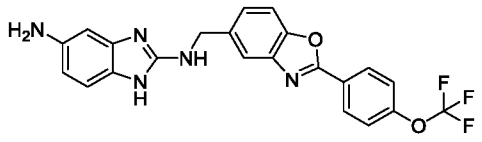
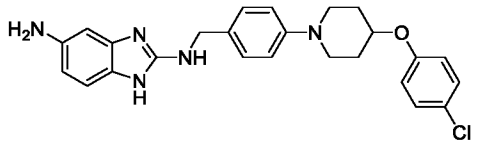
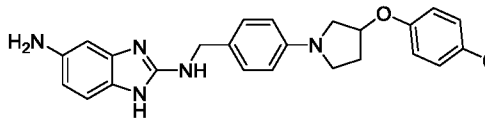
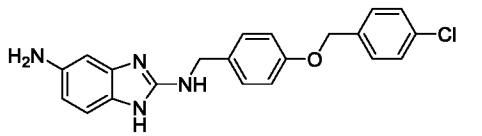
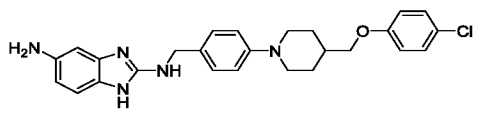
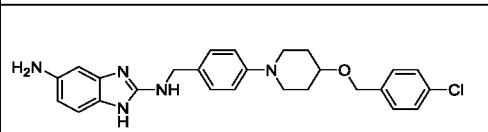
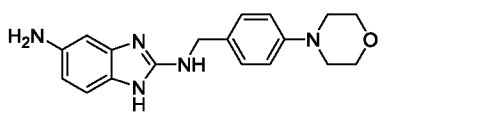
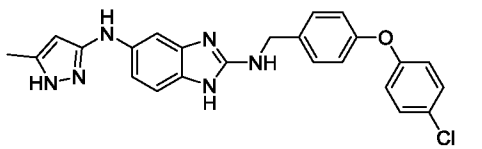
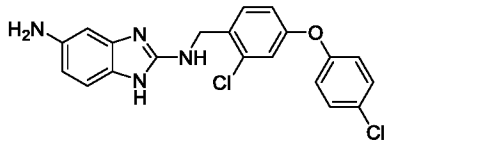
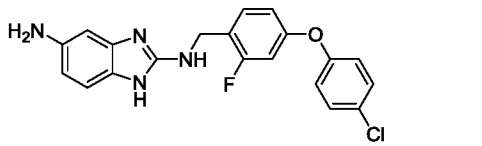
# cpds	Inhibition (%, 10 uM)	# cpds	Inhibition (%, 10 uM)	# cpds	Inhibition (%, 10 uM)
44	++	90	+++	103	+++
53	+++	91	+++	195	+
54	+++	95	+++	211	++
86	+++	99	+++	226	+++

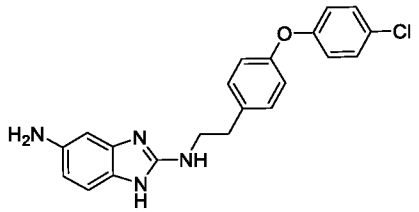
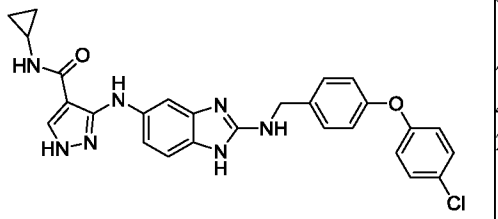
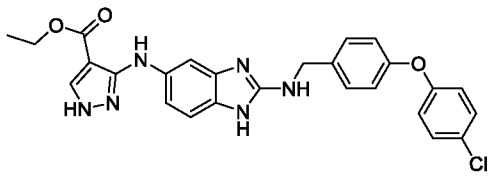
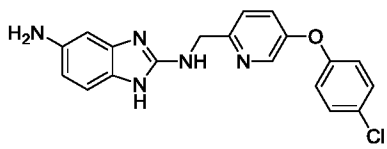
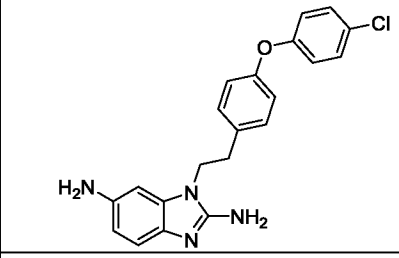
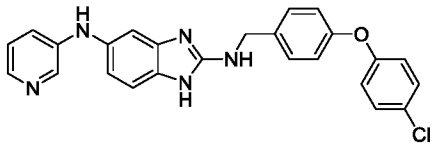
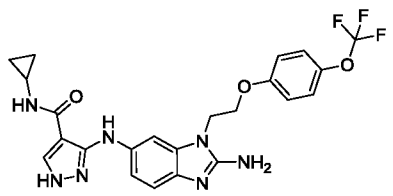
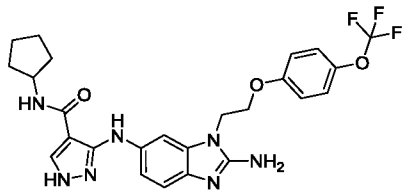
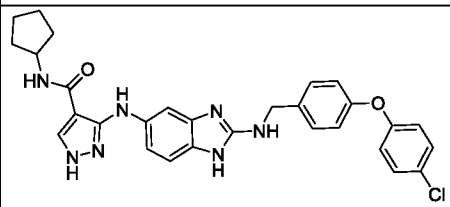
Activity range: +++ indicates > 70 %, ++ indicates between 40-70 %, + indicates < 40 %

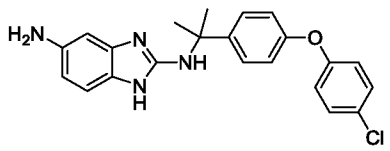
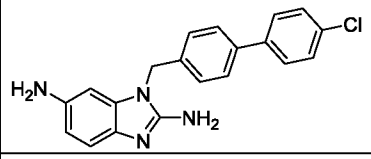
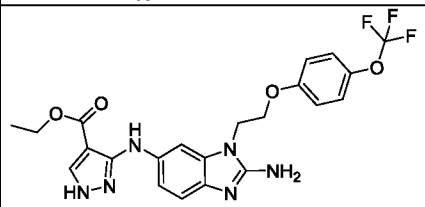
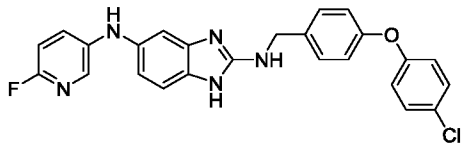
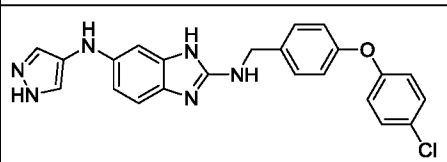
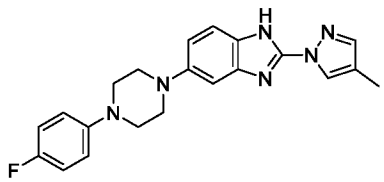
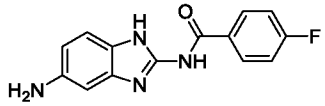
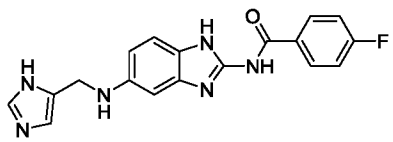
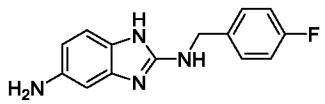
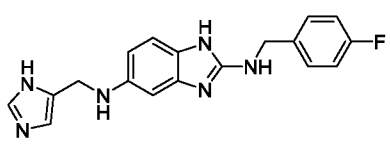
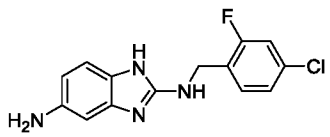
Table 6. COX-2 inhibition assay

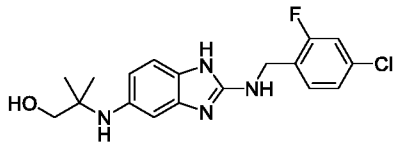
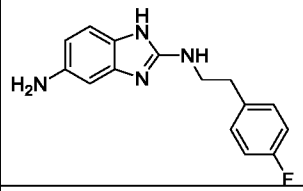
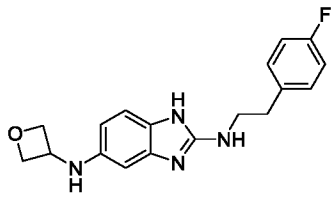
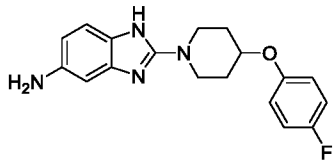
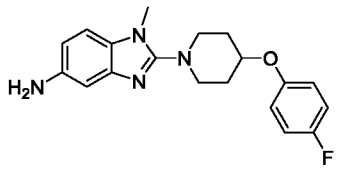
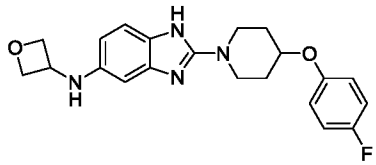
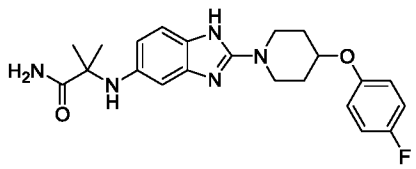
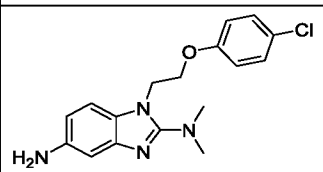
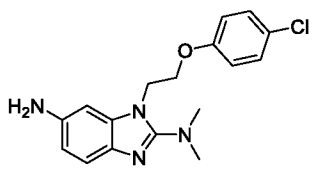
# cpds	Inhibition (%, 10 uM)	# cpds	Inhibition (%, 10 uM)
90	NA	95	NA

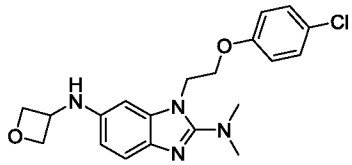
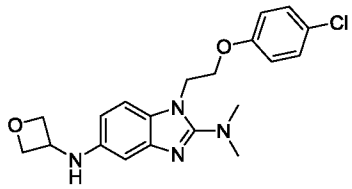
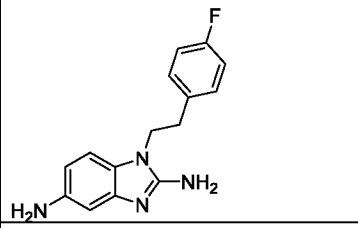
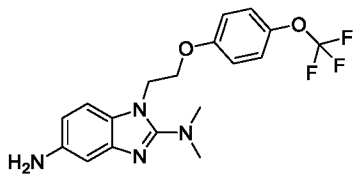
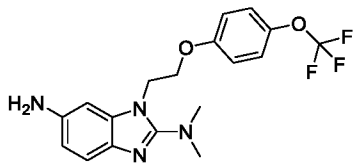
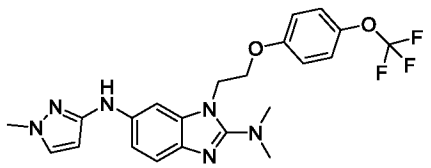
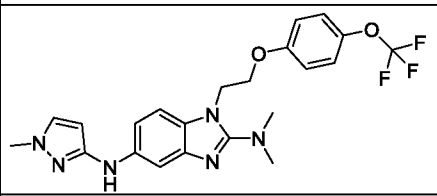
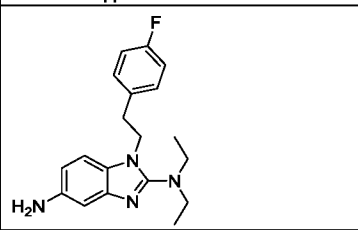
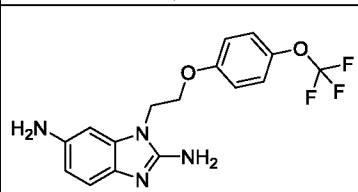
NA : not active (< 1 %)

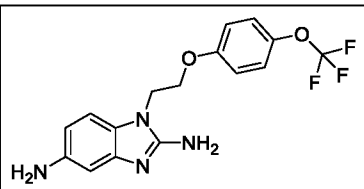
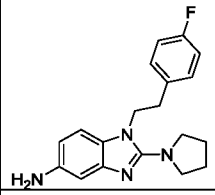
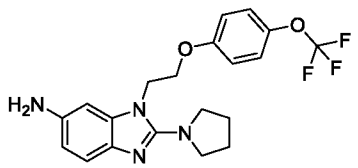
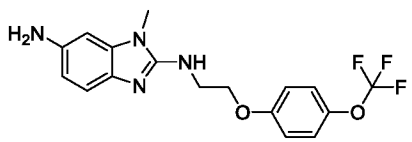
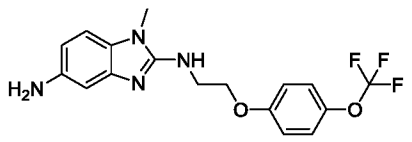
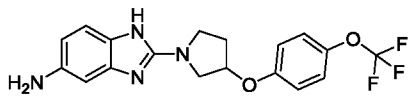
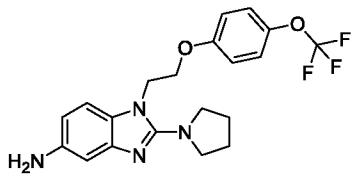
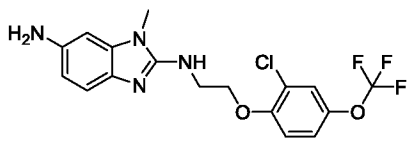
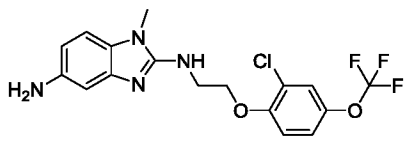
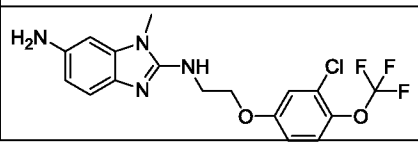
No.	Structure	NMR Characterization
1		Pale violet solid; 1H NMR (400 MHz, Acetone-*d6*); δ 9.77 (brs, 1H), 8.34 – 8.36 (m, 2H), 7.85 (s, 1H), 7.52 – 7.64 (m, 4H), 6.89 (s, 1H), 6.57 (s, 1H), 6.30 – 6.34 (m, 2H), 4.75 (s, 2H), 4.03 (brs, 2H); LCMS (electrospray) m/z 440 [M+H]+.
2		Green solid; 1H NMR (400 MHz, MeOH-*d4*); δ 7.22 – 7.27 (m, 4H), 6.90 – 6.99 (m, 5H), 6.69 (d, *J* = 1.6 Hz, 1H), 6.48 (dd, *J* = 8.0, 1.6 Hz, 1H), 4.43 (s, 2H), 3.43 – 3.50 (m, 3H), 3.03 – 3.09 (m, 2H), 2.06 – 2.10 (m, 2H), 1.81 – 1.87 (m, 2H); LCMS (electrospray) m/z 448 [M+H]+.
3		Pale brown solid; 1H NMR (400 MHz, MeOH-*d4*); δ 7.25 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 6.97-6.99 (m, 1H), 6.90-6.92 (m, 3H), 6.69 (m, 1H), 6.57 (d, *J* = 8.4 Hz, 2H), 6.50-6.52 (m, 1H), 4.58 (s, 2H, NH), 4.40 (s, 2H), 3.64-3.68 (m, 1H), 3.37-3.51 (m, 4H), 2.27-2.34 (m, 2H); LCMS (electrospray) m/z 434, 436 [M+H]+.
4		1H NMR (400 MHz, Acetone-*d6*); δ 7.49 (dd, *J* = 8.4 2.4 Hz, 2H), 7.41 (dd, *J* = 8.4 2.4 Hz, 2H), 7.33 (t, *J* = 9.2 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 1H), 6.91 (t, *J* = 9.2 Hz, 2H), 6.60 (d, *J* = 34.0 Hz, 1H), 6.40 (dd, *J* = 34.0 8.0 Hz, 1H), 5.08 (d, *J* = 8.0 Hz, 2H), 4.56 (d, *J* = 8.8 Hz, 2H); LCMS (electrospray) m/z 378 [M+H]+.
5		Gray solid; 1H NMR (400 MHz, Methanol-*d4*); δ 7.27 (d, *J* = 8.8 Hz, 2H), 7.22-7.25 (m, 2H), 6.94-7.00 (m, 3H), 6.89-6.91 (m, 2H), 6.70 (d, *J* = 2.0 Hz, 1H), 6.52 (dd, *J* = 8.2, 2.2 Hz, 1H), 4.44 (s, 2H), 3.85 (d, *J* = 6.0 Hz, 2H), 3.69-3.72 (m, 2H), 3.60-3.62 (m, 1H), 2.68-2.74 (m, 2H), 1.92-1.95 (m, 2H), 1.50-1.54 (m, 2H); LCMS (electrospray) m/z 462 [M+H]+.
6		Pale yellow solid; 1H NMR (400 MHz, MeOH-*d4*); δ 7.33 (s, 4H), 7.25 (d, *J* = 8.8 Hz, 2H), 6.95 - 7.01 (m, 3H), 6.70 (d, *J* = 2.4 Hz, 1H), 6.54 (dd, *J* = 8.4, 2.4 Hz, 1H), 4.56 (s, 2H), 4.44 (s, 2H), 3.58 - 3.59 (m, 1H), 3.48 - 3.51 (m, 2H), 2.88 - 2.94 (m, 2H), 1.91 - 2.05 (m, 2H), 1.28 - 1.74 (m, 2H); LCMS (electrospray) m/z 461 [M+H]+.
7		1H NMR (400 MHz, DMSO-*d6*); δ 7.22 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.65 (brs, 1H, NH), 6.39 (d, *J* = 1.6 Hz, 1H), 6.18 (dd, *J* = 8.0 1.6 Hz, 1H), 4.32 (d, *J* = 2.0 Hz, 2H), 3.67 – 3.70 (m, 4H), 3.01 – 3.05 (m, 4H); LCMS (electrospray) m/z 323 [M+H]+.
8		Dark green solid; 1H NMR (400 MHz, Acetone-*d6*); δ 9.81 (s, 1H, NH), 7.44-7.50 (m, 3H), 7.37 (d, *J* = 6.8 Hz, 2H), 7.05 (s, 1H, NH), 6.91-7.00 (m, 5H), 6.83 (d, *J* = 8.4 Hz, 1H), 6.15-6.25 (m, 1H), 4.63 (s, 2H), 2.21 (s, 3H); LCMS (electrospray) m/z 445 [M+H]+.
9		Dark yellow solid; 1H NMR (400 MHz, Acetone-*d6*); δ 7.60 (d, *J* = 8.4 Hz, 1H), 7.40-7.43 (m, 2H), 7.02-7.07 (m, 3H), 6.94-6.96 (m,1H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.58-6.59 (m, 1H), 6.35-6.38 (m, 1H), 4.70 (s, 2H); LCMS (electrospray) m/z 400 [M+H]+.
10		Dark yellow solid; 1H NMR (400 MHz, Acetone-*d6*); δ 7.53-7.59 (m, 1H), 7.39-7.43 (m, 2H), 7.17 (s, 1H, NH), 7.03-7.07 (m, 2H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.72-6.81 (m, 2H), 6.58 (d, *J* = 2.4 Hz, 1H), 6.35 (dd, *J* = 8.2, 2.4 Hz, 1H), 4.65 (s, 2H); LCMS (electrospray) m/z 383 [M+H]+.

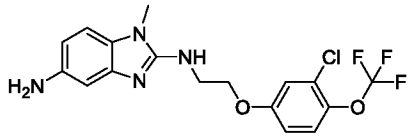
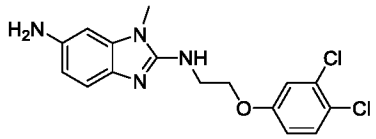
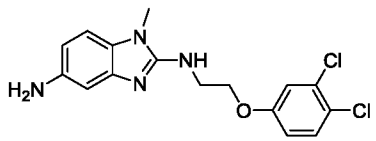
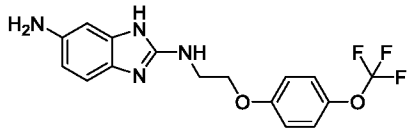
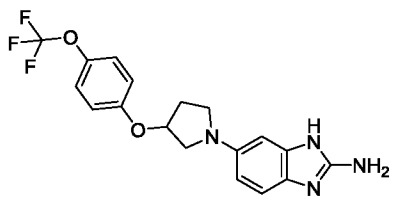
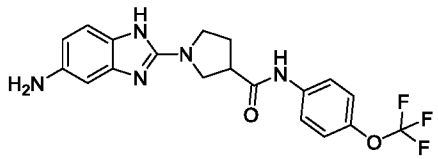
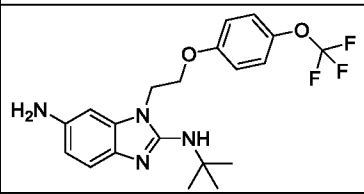
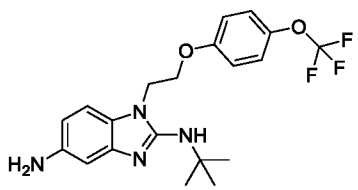
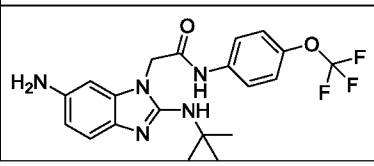
11		Pale brown solid; 1H NMR (400 MHz, MeOH-*d*4); δ 7.25-7.29 (m, 4H), 7.00-7.08 (m, 2H), 6.80-6.90 (m, 4H), 6.68 (m, 1H), 6.58-6.60 (m, 2H), 3.60 (t, *J* = 6.0 Hz, 2H), 2.96 (t, *J* = 6.0 Hz, 2H); LCMS (electrospray) m/z 379, 381 [M+H]+.
12		Yellow solid; 1H NMR (400 MHz, DMSO-*d*6); δ 8.87 (s, 1H), 8.10 (s, 1H), 7.99 – 8.00 (m, 1H), 7.62 (s, 1H), 7.20 – 7.43 (m, 5H), 7.09 – 7.12 (m, 1H), 6.96 – 7.02 (m, 5H), 6.84 – 6.86 (m, 1H), 4.47 (d, *J* = 4.4 Hz, 2H), 2.71 – 2.76 (m, 1H), 0.66 – 0.70 (m, 2H), 0.47 – 0.51 (m, 2H); LCMS (electrospray) m/z 514 [M+H]+.
13		Pale yellow solid; 1H NMR (400 MHz, Acetone-*d*6); δ 8.07 (s, 1H), 7.98 (s, 1H), 7.75 (s, 1H), 7.44 – 7.48 (m, 2H), 7.33 – 7.37 (m, 2H), 7.08 – 7.10 (m, 2H), 6.93 – 7.01 (m, 4H), 6.60 – 6.78 (m, 2H), 4.65 (s, 2H), 4.26 (q, *J* = 7.2 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 3H); LCMS (electrospray) m/z 503 [M+H]+.
14		Pale yellow solid; 1H NMR (400 MHz, MeOH-*d*4); δ 8.27 - 8.28 (m, 1H), 7.45 - 7.48 (m, 1H), 7.40 - 7.42 (m, 2H), 7.35 - 7.39 (m, 1H), 7.03 - 7.04 (m, 1H), 7.01 - 7.02 (m, 1H), 6.98 - 7.00 (m, 1H), 6.70 (d, *J* = 2.0 Hz, 1H), 6.52 (dd, *J* = 8.4, 2.0 Hz, 1H), 4.65 (s, 2H); LCMS (electrospray) m/z 365 [M+H]+.
15		Pale yellow solid; 1H NMR (400 MHz, MeOH-*d*4); δ 7.31 - 7.33 (m, 1H), 7.28 - 7.29 (m, 1H), 7.12 (d, *J* = 8.4 Hz, 2H), 7.05 - 7.09 (m, 1H), 6.99 - 7.01 (m, 1H), 6.88 - 6.90 (m, 1H), 6.85 -6.86 (m, 1H), 6.83 - 6.84 (m, 1H), 6.55 - 6.57 (m, 1H), 6.50 - 6.51 (m, 1H), 4.15 (t, *J* = 7.2 Hz, 2H), 3.02 (t, *J* = 7.2 Hz, 2H); LCMS (electrospray) m/z 378 [M+H] +.
16		Brown solid; 1H NMR (400 MHz, Acetone-*d*6); δ 8.27 (s, 1H), 7.90 (s, 1H), 7.46 (d, *J* = 7.6 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.23 – 7.28 (m, 2H), 7.07 – 7.14 (m, 3H), 6.97 – 6.99 (m, 4H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.57 (brs, 1H), 4.66 (s, 2H);
17		1H NMR (400 MHz, Acetone-*d*6); δ 9.21 (s, 1H, NH), 8.09 (s, 1H), 7.83 (s, 1H), 7.40 (s, 1H, NH), 7.15 – 7.24 (m, 4H), 7.05 – 7.09 (m, 2H), 6.41 (brs, 2H, NH2), 4.52 (t, *J* = 2.8 Hz, 2H), 4.42 (t, *J* = 2.8 Hz, 2H), 2.82 – 2.86 (m, 1H), 0.71 – 0.74 (m, 2H), 0.51 – 0.55 (m, 2H); LCMS (electrospray) m/z 502 [M+H]+.
18		1H NMR (400 MHz, Acetone-*d*6); δ 9.16 (s, 1H, NH), 8.11 (s, 1H), 7.74 (s, 1H), 7.22 (d, *J* = 8.8 Hz, 2H), 7.06 – 7.16 (m, 4H), 5.55 (brs, 2H, NH2), .4.46 (t, *J* = 2.8 Hz, 2H), 4.39 (t, *J* = 2.8 Hz, 2H), 4.32 – 4.37 (m, 1H), 1.94 – 2.20 (m, 4H), 1.60 – 1.71 (m, 1H), 1.52 – 1.59 (m, 3H); LCMS (electrospray) m/z 530 [M+H]+.
19		Pale green solid; 1H NMR (400 MHz, Acetone-*d*6); δ 9.13 (s, 1H, NH), 8.10 (m, 1H); 7.84 (s, 1H, NH), 7.49 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.10-7.15 (m, 3H), 6.96-7.02 (m, 4H), 4.68 (s, 2H), 4.32-4.36 (m, 1H), 1.96-1.99 (m, 2H), 1.68-1.72 (m, 2H), 1.50-1.61 (m, 4H); LCMS (electrospray) m/z 542, 544 [M+H]+.

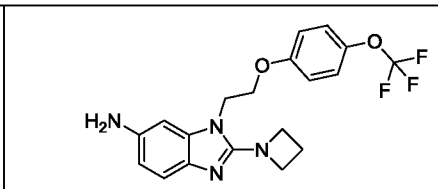
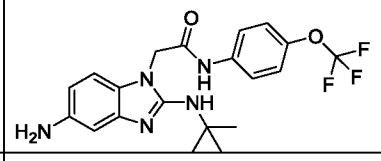
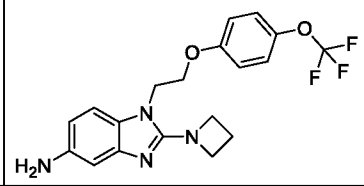
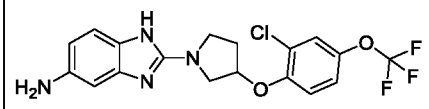
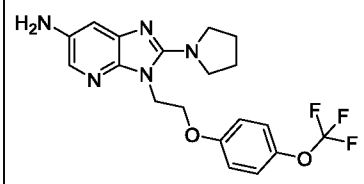
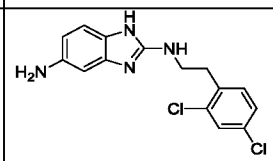
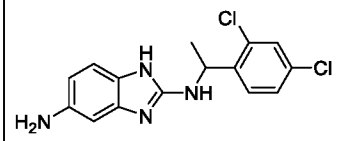
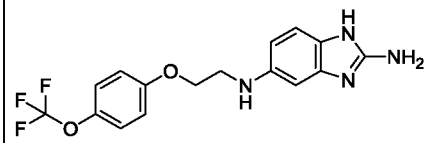
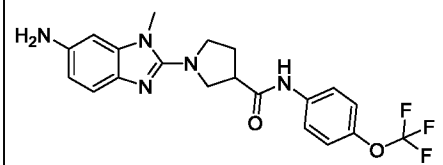
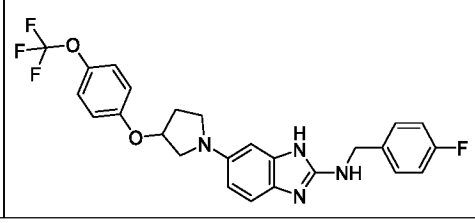
20		Dark beige solid; 1H NMR (400 MHz, Acetone-*d*6); δ 7.65 (s, 1H, NH), 7.56 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 6.97-7.02 (m, 4H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.55 (s, 1H), 6.39 (d, *J* = 7.6 Hz, 1H), 1.82 (s, 6H); LCMS (electrospray) m/z 393 [M+H]+.
21		1H NMR (400 MHz, DMSO-*d*6); δ 7.67 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.24 (t, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.29 (s, 1H), 6.27 (d, *J* = 8.0 Hz, 1H), 6.11 (s, 2H); LCMS (electrospray) m/z 348 [M+H]+.
22		1H NMR (400 MHz, Acetone-*d*6); δ 8.15 (s, 1H), 8.02 (s, 1H), 7.78 (s, 1H, NH), 7.21 (d, *J* = 8.8 Hz, 2H), 7.12 – 7.17 (m, 2H), 7.06 (d, *J* = 8.8 Hz, 2H), 5.85 (brs, 2H, NH2), 4.74 – 4.48 (m, 2H), 4.38 – 4.30 (m, 2H), 4.28 – 4.35 (m, 2H), 1.32 – 1.37 (m, 3H); LCMS (electrospray) m/z 491 [M+H]+.
23		Pale green solid; 1H NMR (400 MHz, Acetone-*d*6); δ 10.00 (s, 1H, NH), 7.81 (s, 1H), 7.47-7.49 (m, 3H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.14-7.18 (m, 1H), 7.11 (s, 1H, NH), 7.02-7.06 (m, 1H), 6.94-7.02 (m, 4H), 6.84 (d, *J* = 6.8 Hz, 1H), 6.76 (d, *J* = 6.8 Hz, 1H), 6.41 (s, 1H, NH), 4.66 (s, 2H); LCMS (electrospray) m/z 460 [M+H]+.
24		Pale green solid; 1H NMR (400 MHz, Acetone-*d*6); δ 7.45-7.50 (m, 3H), 7.37 (d, *J* = 7.2 Hz, 2H), 6.98-7.00 (m, 4H), 6.78 (s, 1H), 6.55 (d, *J* = 8.4 Hz, 1H), 6.30-6.35 (m, 2H), 4.63 (s, 2H); LCMS (electrospray) m/z 431 [M+H]+.
25		white solid; mp > 220 °C; 1H NMR (DMSO-*d*6, 400 MHz); δ 12.74 (1H, brs), 8.30 (1H, s), 7.74 (1H, d, *J* = 3.6 Hz), 7.44 (0.6H, d, *J* = 8.8 Hz), 7.31 (0.4H, d, *J* = 8.4 Hz), 6.91-7.18 (6H, m), 3.20-3.30 (8H, m), 2.14 (3H, s); LCMS: 99.3%, MS (ESI); m/z 377.0[M+ H]+.
26		brown solid; 1H NMR (DMSO-*d*6, 400 MHz); δ 12.02 (1H, brs), 8.07-8.44 (2H, m), 7.28 (2H, t, *J* = 8.8 Hz), 7.09 (1H, d, *J* = 8.4 Hz), 6.63 (1H, d, *J* = 1.6 Hz), 6.57 (1H, dd, *J* = 8.4, 2.0 Hz); LCMS: 100%, MS (ESI); m/z 271.0 [M+H]+.`
27		yellow amorphous; mp >142.9 °C, decomposed; 1H NMR (DMSO-*d*6, 400 MHz); δ 4.06-4.22 (2H, m), 5.62-5.80 (1H, m), 6.57 (1H, dd, *J* = 8.4, 2.0 Hz), 6.83 (0.3H, s), 6.98 (0.7H, s), 7.13 (1H, d, *J* = 8.4 Hz), 7.28 (2H, t, *J* = 8.8 Hz), 7.50-7.62 (1H, m), 8.12-8.24 (2H, m), 12.02 (3H, brs); LCMS: 100%, MS (ESI); m/z 351.0 [M+H]+.
28		gray powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 4.42 (2H, d, *J* = 5.6 Hz), 4.43 (2H, brs), 6.19 (1H, d, *J* = 8.0 Hz), 6.41 (1H, d, *J* = 1.6 Hz), 6.68-6.86 (2H, m), 7.08-7.20 (2H, m), 7.36-7.47 (2H, m), 10.38 (1H, brs); LCMS: 99.9%, MS (ESI); m/z 256.9 [M+H]+.
29		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 4.07 (2H, s), 4.42 (2H, d, *J* = 6.0 Hz), 5.08 (1H, brs), 6.29 (1H, d, *J* = 7.2 Hz), 6.46 (1H, d, *J* = 1.6 Hz), 6.78-6.93 (3H, m), 7.08-7.17 (2H, m), 7.35-7.45 (2H, m), 7.54 (1H, s), 10.42 (1H, brs), 11.82 (1H, brs); LCMS: 98.4%, MS (ESI); m/z 337.0 [M+H]+.
30		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.95 (1H, brs), 7.50-7.43 (2H, m), 7.28 (1H, dd, *J* = 8.4, 2.0 Hz), 6.93 (1H, d, *J* = 8.0 Hz), 6.52 (1H, s), 6.35 (1H, dd, *J* = 8.4, 2.0 Hz), 4.55 (2H, s); LCMS: 99.0%, MS (ESI); m/z 291.1 [M+H]+.

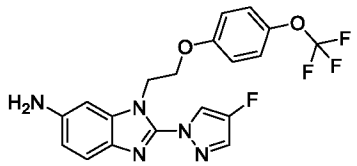
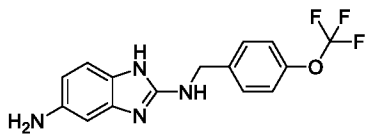
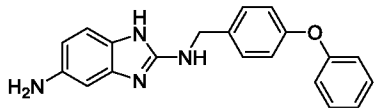
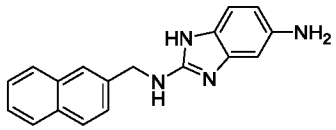
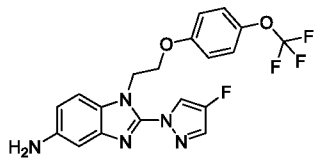
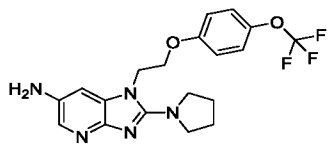
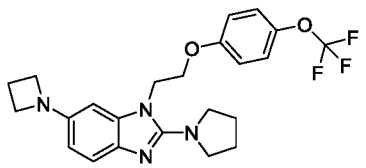
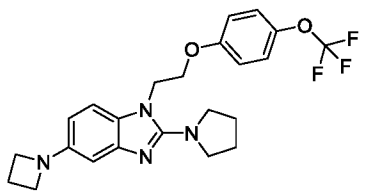
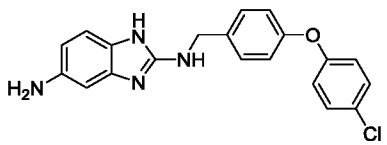
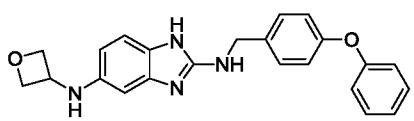
31		pale powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.14 (1H, brs), 7.49-7.40 (2H, m), 7.29-7.25 (1H, m), 7.18-7.01 (2H, m), 6.90-6.75 (1H, m), 5.40 (1H, brs), 4.56 (2H, d, *J* = 4.8 Hz), 3.26 (2H, s, overlapped with water peak, confirmed after adding D2O), 1.19 (6H, s); LCMS: 96.5%, MS (ESI); m/z 363.2 [M+H]+.
32		white powder; hydroscopic; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.45 (1H, brs), 7.35 (2H, dd, *J* = 8.0, 6.0 Hz), 7.13 (2H, t, *J* = 8.8 Hz), 7.01 (1H, d, *J* = 8.0 Hz), 6.57 (1H, s), 6.43 (1H, d, *J* = 7.6 Hz), 3.49 (2H, t, *J* = 7.2 Hz, overlapped with H2O peak), 2.85 (2H, t, *J* = 7.2 Hz); LCMS: 96.1%, MS (ESI); m/z 271.2 [M+H]+.
33		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.32-7.25 (2H, m), 7.22-7.18 (2H, m), 6.88 (1H, d, *J* = 8.4 Hz), 6.39 (1H, brs), 6.27 (1H, d, *J* = 2.0 Hz), 6.14 (1H, dd, *J* = 8.4, 2.0 Hz), 5.71 (1H, d, *J* = 6.8 Hz), 4.81 (2H, t, *J* = 6.0 Hz), 4.50-4.40 (1H, m), 4.38 (2H, t, *J* = 6.0 Hz), 3.50-3.45 (2H, m), 2.85 (2H, t, *J* = 7.2 Hz); LCMS: 99.5%, MS (ESI); m/z 327.2 [M+H]+.
34		brown amorphous; mp = 193.3-205°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.17-7.07 (2H, m), 7.06-6.98 (2H, m), 6.92 (1H, d, *J* = 8.4 Hz), 6.51 (1H, s), 6.33 (1H, dd, *J* = 8.4, 1.6 Hz), 4.62–4.50 (1H, m), 3.86–3.70 (2H, m), 3.46-3.40 (2H, m), 2.08-1.95 (2H, m), 1.74-1.59 (2H, m); LCMS: 100%, MS (ESI); m/z 327.2[M+ H]+.
35		brown gum; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.43 (1H, d, *J* = 8.8 Hz), 7.19-7.09 (2H, m), 7.09-6.96 (3H, m), 6.89 (1H, dd, *J* = 8.8, 1.6 Hz), 4.72-4.57 (1H, m), 3.75-3.65 (2H, m), 3.67 (3H, s), 3.49-3.40 (2H, m), 2.18-2.05 (2H, m), 1.90-1.77 (2H, m); LCMS: 100%, MS (ESI); m/z 341.2[M+ H]+.
36		off-white amorphous; 1H NMR (DMSO- *d*6, 400 MHz); δ 10.99 (1H, brs), 7.06-7.16 (2H, m), 6.98-7.05 (2H, m), 6.94 (1H, brs), 6.29 (1H, s), 6.20 (1H, d, *J* = 8.0 Hz), 5.78 (1H, brs), 4.82 (2H, t, *J* = 6.0 Hz), 4.54 (1H, brs), 4.43-4.50 (1H, m), 4.33-4.43 (2H, m), 3.79 (2H, d, m), 3.37-3.43 (2H, m), 1.98 (2H, m), 1.63 (2H, m); LCMS: 98.4%, MS (ESI); m/z 383.2[M+ H]+.
37		light green powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.25 (1H, brs), 7.19-7.08 (2H, m), 7.08-6.92 (4H, m), 6.51-6.36 (2H, m), 5.44 (1H, brs), 4.60-4.52 (1H, m), 3.87-3.75 (2H, m), 3.43-3.41 (2H, m, overlapped with H2O peak), 2.10-2.00 (2H, m), 1.78-1.60 (2H, m), 1.35 (6H, s); LCMS: 100%, MS (ESI); m/z 412.1 [M+H]+.
38		brown powder; 1H NMR (DMSO-*d*6); δ 7.80 (1H, d, *J* = 8.4 Hz), 7.56 (1H, s), 7.41-7.25 (3H, m), 6.89 (2H, d, *J* = 8.8 Hz), 4.72 (2H, t, *J* = 4.8 Hz), 4.37 (2H, t, *J* = 4.8 Hz), 3.34 (6H, s); LCMS: 99.4%, MS (ESI); m/z 330.9 [M+ H]+.
39		brown powder; 1H NMR (DMSO-*d*6); δ 7.34-7.24 (2H, m), 7.07 (1H, d, *J* = 8.0 Hz), 6.98-6.89 (2H, m), 6.66 (1H, d, *J* = 2.0 Hz), 6.41 (1H, dd, *J* = 8.0, 2.0 Hz), 4.80 (2H, brs), 4.30 (4H, s), 2.81 (6H, s); LCMS: 99.8%, MS (ESI); m/z 330.9 [M+ H]+.

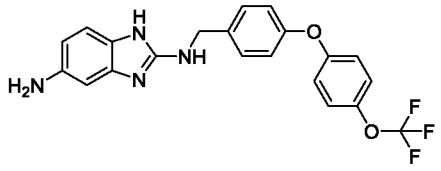
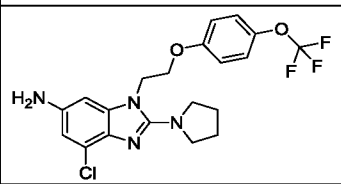
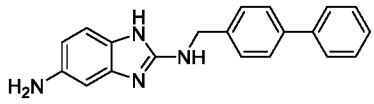
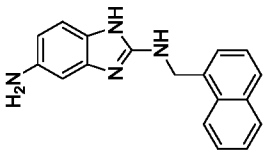
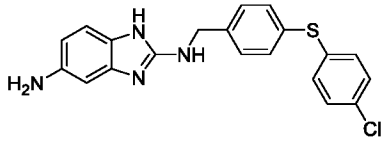
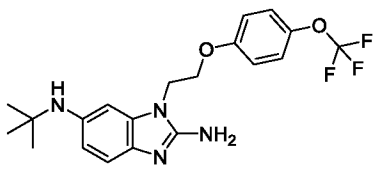
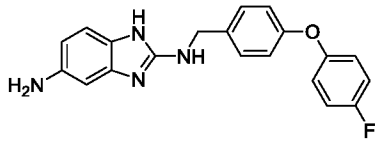
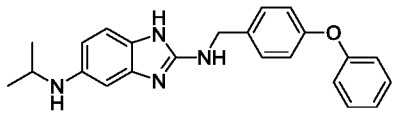
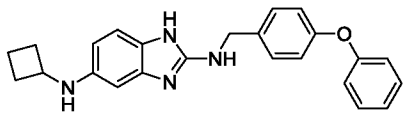
40		green powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.39-7.25 (2H, m), 7.13 (1H, d, *J* = 8.4 Hz), 6.99-6.85 (2H, m), 6.46 (1H, d, *J* = 2.0 Hz), 6.37 (1H, dd, *J* = 8.4, 2.0 Hz), 6.08 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.62-4.47 (1H, m), 4.45-4.36 (2H, m), 4.35-4.25 (4H, m), 2.81 (6H, s); LCMS: 99.8%, MS (ESI); m/z 386.9 [M+ H]+.
41		brown amorphous; 1H NMR (CDCl3, 400 MHz); δ 7.24-7.18 (2H, m), 7.14 (1H, d, *J* = 8.8 Hz), 6.80-6.72 (2H, m), 6.66 (1H, d, *J* = 2.4 Hz), 6.49 (1H, dd, *J* = 8.4 Hz, 2.0 Hz), 5.02 (2H, t, *J* = 6.4 Hz), 4.68-4.57(1H, m), 4.53 (2H, d, *J* = 6.0 Hz), 4.42-4.32 (2H, m), 4.30-4.21 (2H, m), 4.06 (1H, brs), 2.98 (6H, s); LCMS: 99.6 %, MS (ESI); m/z 387.0 [M+ H]+.
42		white solid; mp = 178.2-179.6°C; 1H NMR (DMSO–*d*6, 400 MHz); δ 8.95 (2H, brs), 7.44 (1H, d, *J* = 8.8 Hz), 7.39 (1H, s), 7.35-7.45 (2H, m), 7.10-7.25 (3H, m), 4.37 (2H, t, *J* = 7.2 Hz), 2.99 (2H, t, *J* = 7.2 Hz); LCMS: 99.2%, MS (ESI); m/z 271.0 [M+H]+.
43		white powder; mp = 60.8-61.6°C; 1H NMR (DMSO-*d*6); δ 7.26 (2H, d, *J* = 8.4 Hz), 7.14 (1H, d, *J* = 8.4 Hz), 6.97 (2H, d, *J* = 9.2 Hz), 6.59 (1H, d, *J* = 1.6 Hz), 6.41 (1H, dd, *J* = 8.4, 2.0 Hz), 4.61 (2H, brs), 4.32 (4H, s), 2.85 (6H, s); LCMS: 99.6%, MS (ESI); m/z 380.9 [M+ H]+.
44		white powder; mp > 133°C; 1H NMR (DMSO-*d*6); δ 7.27 (2H, d, *J* = 8.4 Hz), 7.14-6.94 (3H, m), 6.66 (1H, s), 6.41 (1H, d, *J* = 8.0 Hz), 4.77 (2H, brs), 4.25-4.35 (4H, m), 2.80 (6H, s); LCMS: 97.9 %, MS (ESI); m/z 381.0 [M+ H]+.
45		white powder: 1H NMR (DMSO-*d*6, 400 MHz); δ 8.23 (1H, s), 7.62 (1H, d, *J* = 2.0 Hz), 7.47 (1H, d, *J* = 2.0 Hz), 7.26 (2H, d, *J* = 8.8 Hz), 7.19 (1H, d, *J* = 8.4 Hz), 7.00-7.08 (2H, m), 6.97 (1H, dd, *J* = 8.4, 2.0 Hz), 5.76 (1H, d, *J* = 2.0 Hz), 4.37 (4H, dd, *J* = 8.0 Hz, 4.0 Hz), 3.68 (3H, s), 2.84 (6H, s); LCMS: 98.7%, MS (ESI); m/z 460.8 [M+ H]+.
46		white powder: 1H NMR (DMSO-*d*6, 400 MHz); δ 8.11 (1H, s), 7.56 (1H, d, *J* = 2.0 Hz), 7.45 (1H, d, *J* = 2.0 Hz), 7.22-7.33 (3H, m), 6.91-7.03 (3H, m), 5.70 (1H, d, *J* = 2.0 Hz), 4.36 (4H, s), 3.72 (3H, s), 2.88 (6H, s); LCMS: 100%, MS (ESI); m/z 461.0 [M+ H]+.
47		yellow gum; 1H NMR (CDCl3, 400 MHz); δ 7.10 (1H, s), 6.95-7.07 (5H, m), 6.63 (1H, dd, *J* = 8.4, 2.0 Hz), 4.18 (2H, t, *J* = 7.6 Hz), 3.25-3.40 (4H, m), 3.06 (2H, t, *J* = 7.6 Hz), 1.14 (6H, t, *J* = 7.2 Hz); LCMS: 95.7%, MS (ESI); m/z 327.2[M+ H]+.
48		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.26(2H, d, *J* = 8.8 Hz), 6.99 (2H, d, *J* = 8.8 Hz), 6.81 (1H, d, *J* = 8.4 Hz), 6.48 (1H, d, *J* = 1.6 Hz), 6.26 (1H, dd, *J* = 8.4, 2.0 Hz), 5.98 (2H, brs), 4.55 (2H, brs), 4.22 – 4.24 (2H, m), 4.18 (2H, t, *J* = 5.2 Hz); LCMS: 100%, MS (ESI); m/z 353.1 [M+H]+.

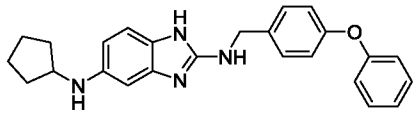
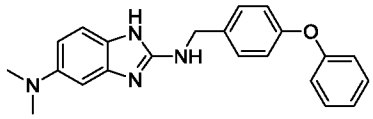
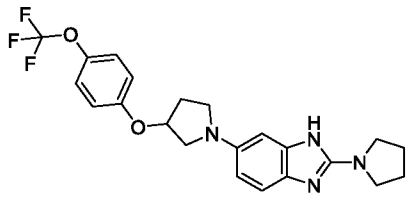
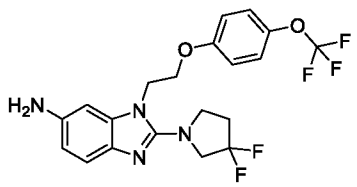
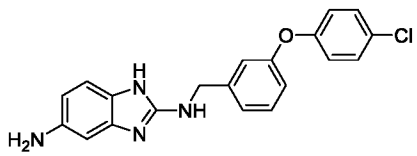
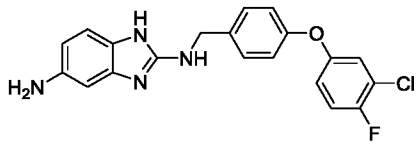
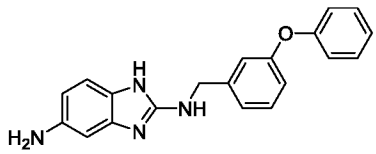
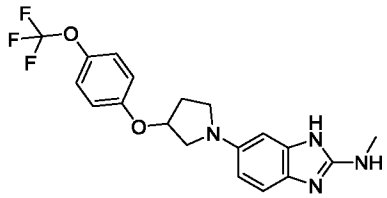
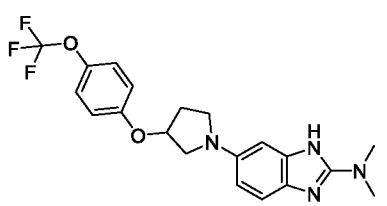
49		white powder: 1H NMR (DMSO-*d*6, 400 MHz); δ 7.26 (1H, d, *J* = 8.8 Hz), 6.96 (2H, d, *J* = 9.2 Hz), 6.86 (1H, d, *J* = 8.0 Hz), 6.41 (1H, d, *J* = 1.6 Hz), 6.21 (1H, dd, *J* = 8.4, 2.0 Hz), 6.17 (2H, brs), 4.39 (2H, brs), 4.22-4.29 (2H, m), 4.11-4.22 (2H, m); LCMS: 100%, MS (ESI); m/z 352.9 [M+H]+.
50		yellow gum: 1H NMR (CDCl3, 400 MHz); δ 7.06 (2H, dd, *J* = 8.4, 4.2 Hz), 7.00 (2H, t, *J* = 7.2 Hz), 6.95-6.85 (2H, m), 6.49 (1H, dd, *J* = 8.4, 6.4 Hz), 4.19 (2H, t, *J* = 7.2 Hz), 3.52 (4H, t, *J* = 6.8 Hz), 3.00 (2H, t, *J* = 7.2 Hz), 1.95-2.05 (4H, m); LCMS: 97.4%, MS (ESI); m/z 324.9[M+ H]+.
51		yellow powder: 1H NMR (CDCl3, 400 MHz); δ 7.31 (1H, d, *J* = 8.0 Hz), 7.13 (2H, d, *J* = 8.8 Hz), 6.83 (2H, dd, *J* = 6.8, 2.0 Hz), 6.60 (1H, d, *J* = 1.6 Hz), 6.57 (1H, d, *J* = 8.0 Hz), 4.39 (2H, t, *J* = 6.0 Hz), 4.25 (2H, t, *J* = 6.8 Hz), 3.59 (4H, t, *J* = 6.8 Hz), 1.99 (4H, m); LCMS: 98.3%, MS (ESI); m/z 407.1[M+ H]+.
52		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.28 (2H, d, *J* = 9.2 Hz), 7.08 (2H, d, *J* = 9.6 Hz), 6.89 (1H, d, *J* = 8.0 Hz), 6.58 (1H, t, *J* = 5.6 Hz), 6.35 (1H, d, *J* = 1.6 Hz), 6.27 (1H, dd, *J* = 8.4, 2.0 Hz), 4.55 (2H, brs), 4.19 (2H, t, *J* = 5.6 Hz), 3.52-3.68 (2H, m), 3.36 (3H, s); LCMS: 100%, MS (ESI); m/z 336.9 [M+H]+.
53		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.28 (2H, d, *J* = 8.8 Hz), 7.09 (2H, d, *J* = 9.2 Hz), 6.79 (1H, d, *J* = 8.4 Hz), 6.68 (1H, t, *J* = 5.6 Hz), 6.48 (1H, d, *J* = 1.6 Hz), 6.24 (1H, dd, *J* = 8.0, 1.6 Hz), 4.41 (2H, brs), 4.19 (2H, t, *J* = 5.6 Hz), 3.65-3.70 (2H, m), 3.38 (3H, s); LCMS: 100%, MS (ESI); m/z 367.1 [M+H]+.
54		pale green powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.72 (1H, brs), 7.30 (2H, d, *J* = 8.4 Hz), 7.06 (2H, d, *J* = 8.8 Hz), 6.82 (1H, d, *J* = 8.0 Hz), 6.45 (1H, s), 6.21 (1H, d, *J* = 8.0 Hz), 5.16 (1H, s), 4.50 (2H, brs), 3.65-3.85 (1H, m), 3.45-3.65 (3H, m), 2.23-2.40 (1H, m), 2.08-2.23 (1H, m); LCMS: 97.3%, MS (ESI); m/z 378.9 [M+H]+.
55		yellow powder: 1H NMR (CDCl3, 400 MHz); δ 7.12 (2H, d, *J* = 8.4 Hz), 7.00 (1H, d, *J* = 8.0 Hz), 6.88 (1H, d, *J* = 2.0 Hz), 6.82 (2H, dd, *J* = 6.8, 2.4 Hz), 6.50 (1H, dd, *J* = 8.4, 2.0 Hz), 4.41 (2H, t, *J* = 6.0 Hz), 4.24 (2H, t, *J* = 6.4 Hz), 3.63 (4H, t, *J* = 6.8 Hz), 2.00 (4H, m); LCMS: 98.5%, MS (ESI); m/z 407.2[M+ H]+.
56		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.56 (1H, d, *J* = 2.8 Hz) 7.36-7.43 (1H, m), 7.30-7.36 (1H, m), 6.91 (1H, d, *J* = 8.4 Hz), 6.55 (1H, t, *J* = 5.6 Hz), 6.36 (1H, d, *J* = 1.6 Hz), 6.28 (1H, dd, *J* = 8.4, 2.0 Hz), 4.54 (2H, brs), 4.31 (2H, t, *J* = 6.0 Hz), 3.44-3.68 (2H, m), 3.36 (3H, s); LCMS: 100%, MS (ESI); m/z 400.9 [M+H]+.
57		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.56 (1H, d, *J* = 2.0 Hz), 7.39 (1H, d, *J* = 9.2 Hz), 7.29-7.36 (1H, m), 6.79 (1H, d, *J* = 8.4 Hz), 6.67 (1H, t, *J* = 5.6 Hz), 6.49 (1H, d, *J* = 2.0 Hz), 6.24 (1H, dd, *J* = 8.0, 1.6 Hz), 4.41 (2H, brs), 4.30 (2H, t, *J* = 6.0 Hz), 3.67-3.72 (2H, m), 3.38 (3H, s); LCMS: 100%, MS (ESI); m/z 401.0 [M+H]+.
58		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.47 (1H, d, *J* = 8.4 Hz), 7.41 (1H, d, *J* = 3.2 Hz), 7.08 (1H, dd, *J* = 8.8, 2.8 Hz), 6.91 (1H, d, *J* = 8.4 Hz), 6.57 (1H, t, *J* = 5.2 Hz), 6.36 (1H, d, *J* = 2.0 Hz), 6.28 (1H, dd, *J* = 8.4, 2.0 Hz), 4.54 (2H, brs), 4.24 (2H, t, *J* = 5.6 Hz), 3.60-

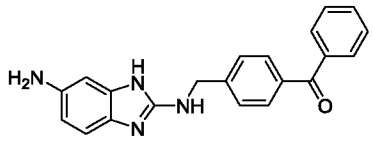
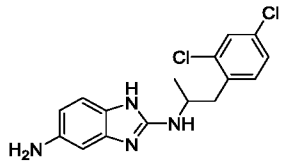
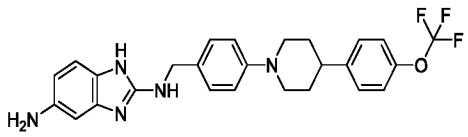
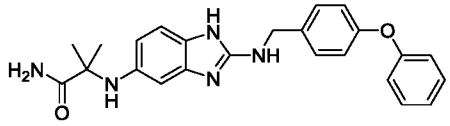
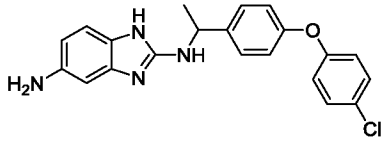
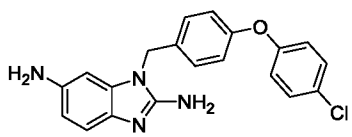
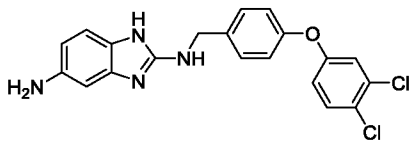
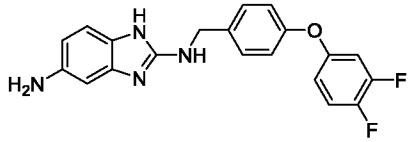
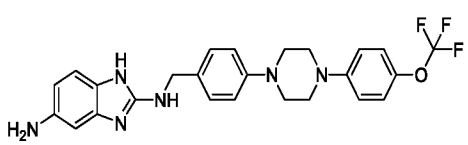
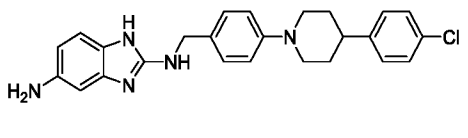
		3.66 (2H, m), 3.36 (3H, s); LCMS: 99.6%, MS (ESI); m/z 400.9 [M+H]+.
59		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.36 - 7.47 (2H, m) 7.05 (1H, dd, *J* = 9.2, 2.8 Hz), 6.77 (1H, d, *J* = 8.0 Hz), 6.66 (1H, t, *J* = 5.2 Hz), 6.48 (1H, d, *J* = 1.6 Hz), 6.22 (1H, dd, *J* = 8.0, 1.6 Hz), 4.43 (2H, brs), 4.21 (2H, t, *J* = 6.0 Hz), 3.62-3.69 (2H, m), 3.37 (3H, s); LCMS: 95.5%, MS (ESI); m/z 400.9 [M+H]+.
60		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.51 (1H, d, *J* = 9.2 Hz), 7.37 (1H, d, *J* = 2.8 Hz), 7.01 (1H, dd, *J* = 8.8, 2.8 Hz), 6.91 (1H, d, *J* = 8.4 Hz), 6.57 (1H, t, *J* = 5.2 Hz), 6.36 (1H, d, *J* = 2.0 Hz), 6.28 (1H, dd, *J* = 8.0, 1.6 Hz), 4.57 (2H, brs), 4.21 (2H, t, *J* = 6.0 Hz), 3.58-3.66 (2H, m), 3.36 (3H, s); LCMS: 99.7%, MS (ESI); m/z 350.9 [M+H]+.
61		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.48 (1H, d, *J* = 8.8 Hz), 7.39 (1H, d, *J* = 2.8 Hz), 7.01 (1H, dd, *J* = 8.8, 3.2 Hz), 6.79 (1H, d, *J* = 8.0 Hz), 6.69 (1H, t, *J* = 5.2 Hz), 6.50 (1H, d, *J* = 2.0 Hz), 6.24 (1H, dd, *J* = 8.0, 2.0 Hz), 4.46 (2H, brs), 4.21 (2H, t, *J* = 6.0 Hz), 3.63-3.68 (2H, m), 3.38 (3H, s); LCMS: 100%, MS (ESI); m/z 350.9 [M+H]+.
62		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.36 (1H, brs), 7.28 (1H, d, *J* = 8.8 Hz), 7.07 (1H, d, *J* = 9.2 Hz), 6.78-6.83 (1H, m), 6.40-6.44 (2H, m.), 6.18-6.22 (1H, m.), 4.42 (2H, brs), 4.14 (2H, t, *J* = 5.6 Hz), 3.59-3.61 (2H, m); LCMS: 100%, MS (ESI); m/z 353.1 [M+H]+.
63		dark powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 12.17 (2H, brs), 8.23 (2H, brs), 7.30 (2H, d, *J* = 8.8 Hz), 7.17 (2H, d, *J* = 8.4 Hz), 7.06 (2H, d, *J* = 9.2 Hz), 6.45-6.55 (2H, m), 5.10-5.20 (1H, m), 3.55-3.75 (1H, m), 3.25-3.48 (3H, m), 2.28-2.49 (1H, m), 2.11-2.25 (1H, m); LCMS: 93.4%, MS (ESI); m/z 379.1 [M+H]+.
64		white gum; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.50 (1H, brs), 7.74 (1H, d, *J* = 8.8 Hz), 7.32 (2H, d, *J* = 8.8 Hz), 6.91 (2H, d, *J* = 8.4 Hz), 6.52 (1H, s), 6.30-6.34 (1H, m), 3.70-3.80 (1H, m), 3.50-3.70 (2H, m), 3.39-3.50 (2H, overlap with water peak), 2.20-2.33 (2H, m); LCMS: 99.7%, MS (ESI); m/z 406.1[M+ H]+.
65		white powder; 1H NMR (DMSO-*d*6); δ 7.28 (2H, d, *J* = 8.8 Hz), 6.95-7.02 (2H, m), 6.92 (1H, d, *J* = 8.4 Hz), 6.49 (1H, d, *J* = 2.0 Hz), 6.29 (1H, dd, *J* = 8.0, 2.0 Hz), 5.51 (1H, brs), 4.67 (2H, brs), 4.27 (2H, t, *J* = 5.2 Hz), 4.18 (2H, t, *J* = 5.2 Hz), 1.42 (9H, s); LCMS: 99.8%, MS (ESI); m/z 409.2 [M+ H]+.
66		off-white powder; 1H NMR (DMSO-*d*6); δ 7.27 (2H, d, *J* = 8.8 Hz), 6.95 (2H, d, *J* = 8.8 Hz), 6.88 (1H, d, *J* = 8.0 Hz), 6.50 (1H, d, *J* = 2.0 Hz), 6.24 (1H, dd, *J* = 8.0, 2.0 Hz), 5.58 (1H, brs), 4.40 (2H, brs), 4.28 (2H, t, *J* = 5.2 Hz), 4.16 (2H, t, *J* = 5.2 Hz), 1.43 (9H, s); LCMS: 99.5%, MS (ESI); m/z 409.3 [M+ H]+.
67		off-white powder; 1H NMR (DMSO-*d*6); δ 10.57 (1H, brs), 7.73 (2H, d, *J* = 9.2 Hz), 7.34 (2H, d, *J* = 8.8 Hz), 6.93 (1H, d, *J* = 8.0 Hz), 6.22-6.33 (2H, m), 5.67-5.79 (1H, m), 4.74 (2H, s), 4.63 (2H, brs), 1.42 (9H, s); LCMS: 99.3%, MS (ESI); m/z 422.2 [M+ H]+.

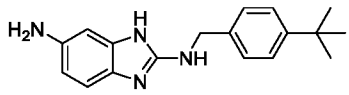
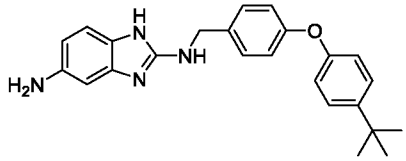
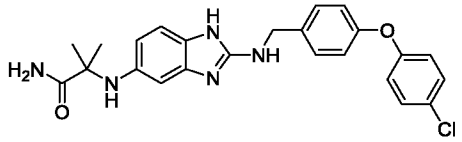
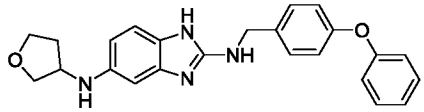
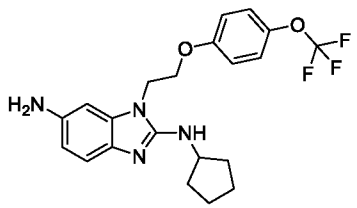
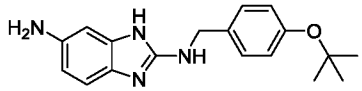
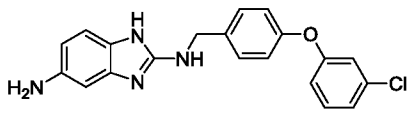
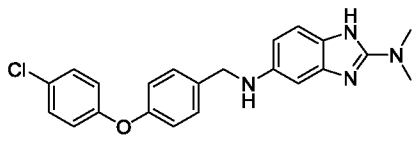
68		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.28(2H, d, *J* = 8.8 Hz), 7.02-7.06 (2H, m), 6.98 (1H, d, *J* = 8.4 Hz), 6.60 (1H, d, *J* = 2.0 Hz), 6.37 (1H, dd, *J* = 8.0, 2.0 Hz), 4.80 (2H, brs), 4.26 (2H, t, *J* = 4.8 Hz), 4.19 (2H, t, *J* = 5.2 Hz), 4.08 (4H, t, *J* = 7.2 Hz), 2.28-2.34 (2H, m); LCMS: 95.7%, MS (ESI); m/z 393.3[M+ H]+.
69		off-white powder; 1H NMR (DMSO-*d*6); δ 10.50 (1H, brs), 7.71 (2H, d, *J* = 8.8 Hz), 7.34 (2H, d, *J* = 8.8 Hz), 6.70 (1H, d, *J* = 8.0 Hz), 6.51 (1H, s), 6.19 (1H, d, *J* = 8.0 Hz), 5.84 (1H, s), 4.74 (2H, s), 4.42 (2H, brs), 1.43 (9H, s); LCMS: 92.7%, MS (ESI); m/z 422.0 [M+ H]+.
70		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.26 (2H, d, *J* = 8.4 Hz), 7.02 (1H, d, *J* = 8.4 Hz), 6.95-7.05 (2H, m), 6.52 (1H, d, *J* = 2.0 Hz), 6.32 (1H, dd, *J* = 8.0, 2.0 Hz), 4.53 (2H, brs), 4.25 (2H, t, *J* = 4.2 Hz), 4.20 (2H, t, *J* = 4.8 Hz), 4.10 (4H, t, *J* = 7.6 Hz), 2.28-2.33 (2H, m); LCMS: 95.9%, MS (ESI); m/z 393.2[M+ H]+.
71		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.75 (1H, brs), 7.59 (2H, d, *J* = 2.4 Hz), 7.33-7.42 (2H, m), 6.77-6.83 (1H, m), 6.44 (1H, s), 6.17-6.24 (1H, m), 5.25-5.30 (1H, m), 4.45 (2H, brs), 3.70-3.82 (1H, m), 3.50-3.62 (3H, m), 2.28-2.38 (1H, m), 2.16-2.22 (1H, m); LCMS: 95.9%, MS (ESI); m/z 413.3 [M+H]+.
72		off-white powder; 1H NMR (DMSO-*d*6); δ 7.38 (1H, d, *J* = 2.4 Hz), 7.25 (2H, d, *J* = 8.8 Hz), 6.91-6.99 (2H, m), 6.80 (1H, d, *J* = 2.0 Hz), 4.67 (2H, brs), 4.48 (2H, t, *J* = 5.6 Hz), 4.32 (2H, t, *J* = 5.6 Hz), 3.51-3.63 (4H, m), 1.85-1.94 (4H,m); LCMS: 97.6%, MS (ESI); m/z 408.3 [M+ H]+.
73		grey powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.20 (1H, brs), 7.59 (1H, s), 7.30-7.40 (2H, m), 6.68-6.89 (1H, m), 6.10-6.48 (3H, m), 4.43 (2H, brs), 3.43-3.52 (2H, m), 2.99 (2H, t, *J* = 7.2 Hz); LCMS: 99.5%, MS (ESI); m/z 321.1[M+ H]+.
74		grey powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.13-10.34 (1H, m), 7.49-7.61 (2H, m), 7.38 (1H, d, *J* = 8.4 Hz), 6.83-7.10 (1H, m), 6.80 (1H, dd, *J* = 8.4, 2.8 Hz), 6.31-6.43 (1H, m), 6.10-6.24 (1H, m), 5.08-5.25 (1H, m), 4.25-4.55 (2H, m), 1.40 (3H, d, *J* = 6.8 Hz); LCMS: 100%, MS (ESI); m/z 321.2[M+ H]+.
75		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.27 (1H, brs.), 7.28 (2H, d, *J* = 8.4 Hz), 7.05 (2H, d, *J* = 9.2 Hz), 6.84 (1H, d, *J* = 8.0 Hz), 6.45 (1H, s), 6.27 (1H, d, *J* = 7.6 Hz), 5.77 (2H, brs.), 5.06 (1H, brs), 4.13 (2H, t, *J* = 5.6 Hz), 3.38 (2H, t, *J* = 5.6 Hz); LCMS: 100%, MS (ESI); m/z 353.3 [M+H]+.
76		yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.58 (1H, brs), 7.76 (2H, d, *J* = 8.8 Hz), 7.34 (2H, d, *J* = 8.4 Hz), 7.09 (1H, d, *J* = 8.4 Hz), 6.61 (1H, s), 6.54 (1H, d, *J* = 8.4 Hz), 3.78-3.95 (5H, m), 3.68 (3H, s), 2.27-2.40 (1H, m), 2.11-2.25 (1H, m); LCMS: 93.9%, MS (ESI); m/z 420.0[M+ H]+.
77		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 12.5 (2H, brs), 9.23 (1H, brs), 7.29-7.49 (2H, m), 7.31 (2H, d, *J* = 8.8 Hz), 7.18-7.21 (3H, m), 7.08 (2H, d, *J* = 9.6 Hz), 6.50-6.52 (2H, m), 5.20-5.21 (1H, m), 4.60 (2H, d, *J* = 6.0 Hz), 3.67-3.72 (1H, m), 3.30-3.42 (3H, overlap with H2O peak), 2.33-2.38 (1H, m), 1.90-2.23 (1H, m); LCMS: 98.1%, MS (ESI); m/z 487.3[M+ H]+.

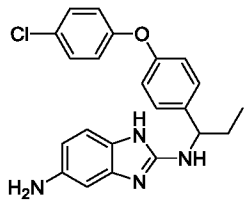
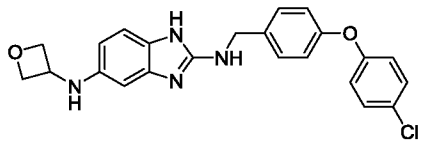
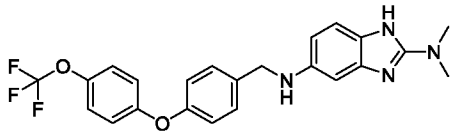
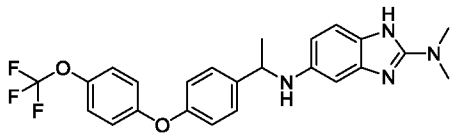
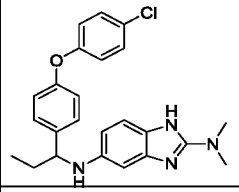
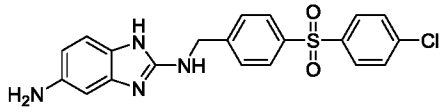
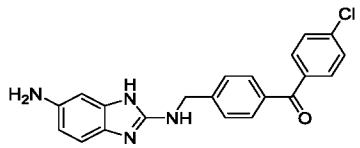
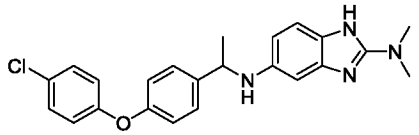
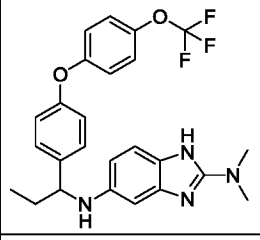
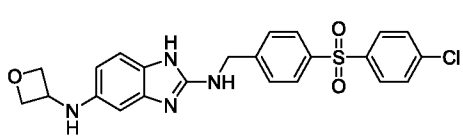
78		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.56 (1H, d, *J* = 4.4 Hz), 7.98 (1H, d, *J* = 4.0 Hz), 7.30 (1H, d, *J* = 8.4 Hz), 7.24 (2H, d, *J* = 8.4 Hz), 6.85-6.95 (2H, m), 6.79 (1H, d, *J* = 2.0 Hz), 6.55-6.60 (1H, m), 5.17 (2H, brs), 4.68 (2H, t, *J* = 5.2 Hz), 4.30 (2H, t, *J* = 5.2 Hz); LCMS: 95.6%, MS (ESI); m/z 422.2 [M+H]+.
79		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.46 (2H, d, *J* = 8.8 Hz), 7.29 (2H, d, *J* = 8.0 Hz), 6.88 (1H, brs), 6.77 (1H, d, *J* = 8.4 Hz), 6.40 (1H, d, *J* = 1.6 Hz), 6.17 (1H, dd, *J* = 8.4, 2.4, Hz), 4.45 (2H, d, *J* = 6.0 Hz); LCMS: 95.7 %, MS (ESI); m/z 323.1[M+ H]+.
80		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 9.72 (1H, t, *J* = 6.0 Hz), 7.49 (2H, d, *J* = 8.4 Hz), 7.35-7.45 (4H, m), 7.10-7.20 (2H, m), 6.95-7.09 (4H, m), 4.65 (2H, d, *J* = 6.0 Hz); LCMS: 100%, MS (ESI); m/z 331.2[M+ H]+.
81		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.35 (1H, brs), 8.09-8.18 (1H, m), 7.90-7.99 (1H, m), 7.82 (1H, d, *J* = 8.0 Hz), 7.49-7.59 (3H, m), 7.46 (1H, t, *J* = 8.0 Hz), 6.66-6.91 (2H, m), 6.41 (1H, s), 6.10-6.20 (1H, m), 4.91 (2H, d, *J* = 4.4 Hz), 4.43 (2H, brs); LCMS: 96.0 %, MS (ESI); m/z 289.1[M+ H]+.
82		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.60 (1H, d, *J* = 4.8 Hz), 7.99 (1H, d, *J* = 4.4 Hz), 7.38 (1H, d, *J* = 8.4 Hz), 7.15-7.28 (2H, m), 6.80-6.93 (2H, m), 6.70-6.80 (1H, m), 6.63-6.75 (1H, m), 4.91 (2H, brs), 4.78 (2H, t, *J* = 5.2 Hz), 4.29 (2H, t, *J* = 5.2 Hz); LCMS: 99.1%, MS (ESI); m/z 422.2 [M+H]+.
83		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.54 (1H, d, *J* = 2.4 Hz), 7.27 (2H, d, *J* = 8.4 Hz), 6.96-7.04 (3H, m), 4.78 (2H, brs), 4.38 (2H, t, *J* = 5.2 Hz), 4.26-4.34 (2H, m), 3.46-3.58 (4H, m), 1.85-1.95 (4H, m); LCMS: 97.7%, MS (ESI); m/z 408.0[M+ H]+.
84		white powder; 1H NMR (CDCl3, 400 MHz); δ 7.65 (1H, d, *J* = 8.4 Hz), 7.14 (2H, d, *J* = 8.8 Hz), 6.75-6.90 (2H, m), 6.39 (1H, d, *J* = 8.4 Hz), 6.21 (1H, s), 4.55-4.65 (2H, m), 4.29 (1H, t, *J* = 4.2 Hz), 3.95-4.05 (4H, m), 3.85-3.95 (4H, m), 2.35-2.45 (2H, m), 2.05-2.20 (4H, m); LCMS: 92%, MS (ESI); m/z 447.1[M+ H]+.
85		white powder; 1H NMR (CDCl3, 400 MHz); δ 7.12 (1H, d, *J* = 8.4 Hz), 7.08 (1H, d, *J* = 8.4 Hz), 6.81 (1H, d, *J* = 2.4 Hz), 6.75 (2H, d, *J* = 9.2 Hz), 6.31 (1H, dd, *J* = 8.8, 2.0 Hz), 4.55-4.65 (2H, m), 4.25-4.35 (2H, m), 3.90-4.00 (4H, m), 3.80-3.90 (4H, m), 2.35-2.45 (2H, m), 2.05-2.15 (4H, m); H NMR and NOE confirmed the structure; LCMS: 96.3%, MS (ESI); m/z 447.3[M+ H]+.
86		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.40-7.45 (4H, m), 6.95-7.05 (4H, m), 6.90-6.98 (1H, brs), 6.81 (1H, d, *J* = 8.4 Hz), 6.43 (1H, s), 6.21 (1H, dd, *J* = 8.0, 2.0 Hz), 4.44 (2H, d, *J* = 4.8 Hz); LCMS: 99.5 %, MS (ESI); m/z 365.1[M+ H]+.
87		pale yellow powder; hydroscopic; 1H NMR (DMSO-*d*6, 400 MHz); δ 12.60 (2H, brs), 9.24-9.38 (1H, m), 7.46 (2H, d, *J* = 8.8 Hz), 7.39 (2H, t, *J* = 7.6 Hz), 7.02 (2H, t, *J* = 8.4 Hz), 6.97-7.08 (4H, m), 6.74 (1H, s), 6.66 (1H, d, *J* = 8.4 Hz), 4.60 (2H, d, *J* = 6.4 Hz), 3.83-4.00 (2H, m), 3.71-3.82 (2H, m), 3.42-3.53 (1H, m); LCMS: 100%, MS (ESI); m/z 387.0[M+ H]+.

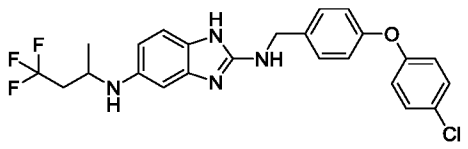
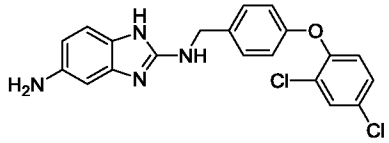
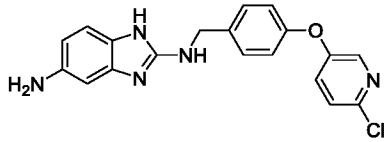
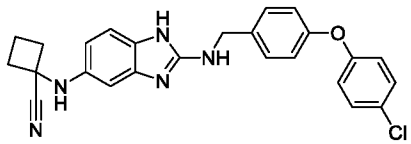
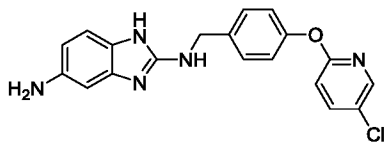
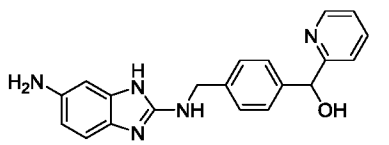
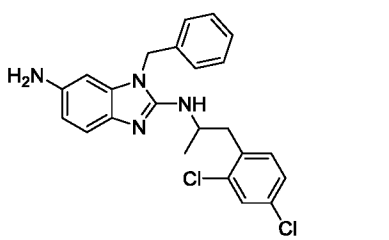
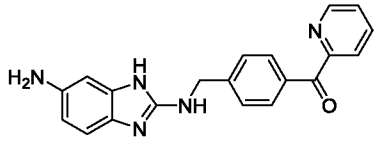
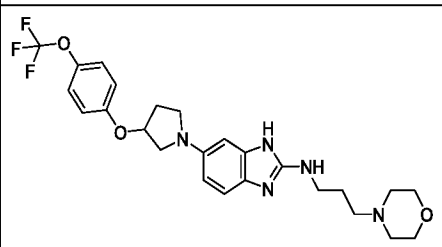
88		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.42 (2H, d, *J* = 8.8 Hz), 7.37 (2H, d, *J* = 8.0 Hz), 7.00-7.10 (4H, m), 6.90-7.00 (1H, brs), 6.82 (1H, d, *J* = 8.0 Hz), 6.44 (1H, d, *J* = 2.0 Hz), 6.20-6.25 (1H, m), 4.45 (2H, d, *J* = 5.2 Hz); LCMS: 99.5 %, MS (ESI); m/z 415.0[M+ H]+.
89		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.26 (2H, d, *J* = 8.8 Hz), 7.11 (1H, s), 6.90-7.00 (2H, m), 6.88 (1H, s), 4.61 (2H, t, *J* = 4.8 Hz), 4.35 (2H, t, *J* = 4.8 Hz), 3.74-3.76 (4H, m), 1.96-1.99 (4H, m); LCMS: 100 %, MS (ESI); m/z 441.2[M+ H]+.
90		grey powder; mp > 200°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.58-7.65 (4H, m), 7.41-7.48 (4H, m), 7.34 (1H, t, *J* = 7.6 Hz), 6.75-6.85 (2H, m), 6.41 (1H, d, *J* = 2.0 Hz), 6.18 (1H, d, *J* = 6.8 Hz), 4.30-4.65 (4H, m); LCMS: 99.1%, MS (ESI); m/z 315.1[M+H]+
91		white powder; mp > 107.8°C; 1H NMR (DMSO- *d*6, 400 MHz); δ 8.15 (1H, d, *J* = 7.6 Hz), 7.94 (1H, d, *J* = 2.4 Hz), 7.83 (1H, d, *J* = 8.0 Hz), 7.50-7.61 (3H, m), 7.44-7.48 (1H, m), 6.80 (1H, d, *J* = 8.0 Hz), 6.79 (1H, brs), 6.43 (1H, d, *J* = 2.0 Hz), 6.20 (1H, d, *J* = 6.8 Hz), 4.92 (2H, d, *J* = 5.6 Hz), 4.41 (2H, brs); LCMS: 99.3%, MS (ESI); m/z 289.1[M+H]+.
92		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.56 (1H, brs), 7.36-7.42 (6H, m), 7.24-7.26 (2H, m), 6.86 (1H, d, *J* = 8.4 Hz), 6.46 (1H, d, *J* = 2.0 Hz), 6.29 (1H, dd, *J* = 8.4, 2.0 Hz), 4.50 (2H, s); LCMS: 95.5 %, MS (ESI); m/z 381.1[M+ H]+.
93		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.26 (2H, d, *J* = 8.8 Hz), 6.92-7.01 (2H, m), 6.88 (1H, d, *J* = 8.4 Hz), 6.69 (1H, d, *J* = 2.0 Hz), 6.49 (1H, dd, *J* = 8.0, 2.0 Hz), 6.12 (2H, brs), 4.29 (2H, t, *J* = 5.2 Hz), 4.17-4.25 (2H, m), 4.04 (1H, brs), 1.17 (9H, s); LCMS: 100%, MS (ESI); m/z 409.1[M+ H]+.
94		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.37 (2H, d, *J* = 8.8 Hz), 7.16 - 7.24 (2H, m), 6.96 - 7.05 (2H, m), 6.94 (2H, d, *J* = 8.4 Hz), 6.70-6.79 (2H, m), 6.41 (1H, d, *J* = 2.0 Hz), 6.19 (1H, dd, *J* = 8.0, 1.6 Hz), 4.41 (2H, d, *J* = 6.0 Hz); LCMS: 99.2%, MS (ESI); m/z 349.2[M+H]+.
95		mp > 137.5 °C; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.30-10.40 (1H, m), 7.35-7.45 (4H, m), 7.12 (1H, t, *J* = 7.6 Hz), 6.95-7.05 (4H, m), 6.70-6.90 (2H, m), 6.39 (1H, s), 6.20-6.30 (1H, m), 4.40-4.70 (3H, m), 3.45-3.50 (1H, m), 1.10 (6H, d, *J* = 6.4 Hz); LCMS: 99.4%, MS (ESI); m/z 373.2[M+ H]+.
96		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.30-10.45 (1H, m), 7.35-7.45 (4H, m), 7.12 (1H, t, *J* = 7.2 Hz), 6.95-7.05 (4H, m), 6.60-6.90 (2H, m), 6.32 (1H, d, *J* = 2.0 Hz), 6.15-6.25 (1H, m), 5.16 (1H, brs), 4.42 (2H, d, *J* = 6.0 Hz), 3.65-3.80 (1H, m), 2.25-2.35 (2H, m), 1.65-1.85 (4H, m); LCMS: 98.8%, MS (ESI); m/z 385.3[M+ H]+.

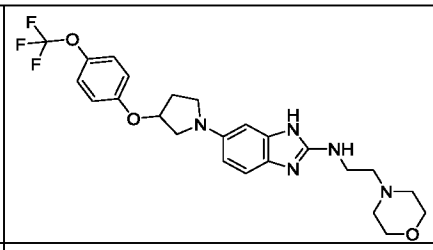
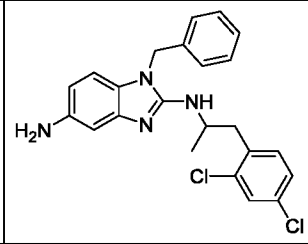
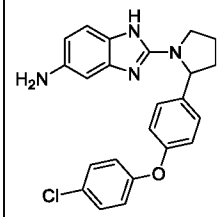
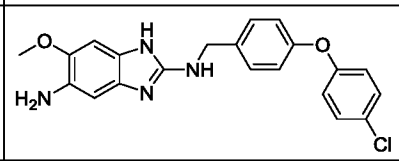
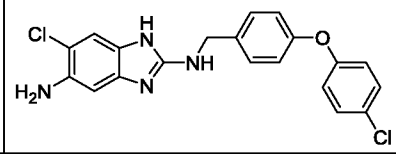
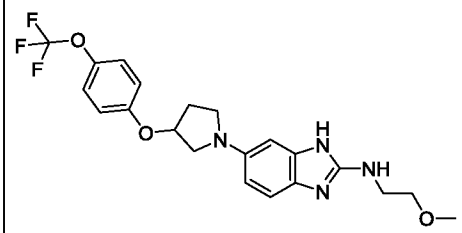
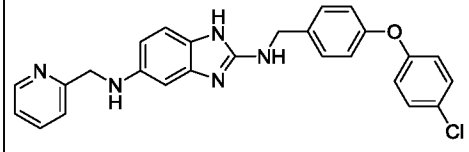
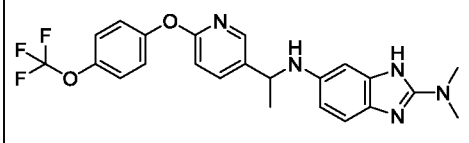
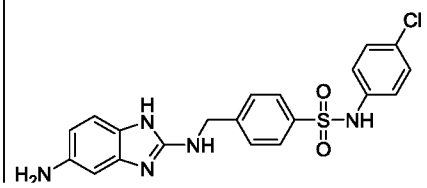
97		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.30-10.40 (1H, m), 7.30-7.40 (4H, m), 7.12 (1H, t, *J* = 7.6 Hz), 6.95-7.00 (4H, m), 6.60-6.90 (2H, m), 6.39 (1H, s), 6.15-6.30 (1H, m), 4.70-4.85 (1H, m), 4.40-4.50 (2H, m), 3.60-3.65 (1H, m), 1.75-1.95 (2H, m), 1.60-1.70 (2H, m), 1.45-1.55 (2H, m), 1.35-1.45 (2H, m); LCMS: 100%, MS (ESI); m/z 399.2[M+ H]+.
98		white solid; mp = 116.8-118.7°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.45 (1H, brs), 7.30-7.45 (4H, m), 7.12 (1H, t, *J* = 7.2 Hz), 6.75-7.05 (6H, m), 6.60 (1H, s), 6.40-6.50 (1H, m), 4.45 (2H, d, *J* = 6.0 Hz), 2.79 (6H, s); LCMS: 99.2%, MS (ESI); m/z 359.2[M+ H]+.
99		yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.70 (1H, brs), 7.29 (2H, d, *J* = 8.8 Hz), 7.00-7.08 (2H, m), 6.95-7.00 (1H, m), 6.42-6.48 (1H, m), 6.19-6.24 (1H, m), 5.12-5.19 (1H, m), 3.61-3.68 (1H, m), 3.30-3.40 (5H, m), 3.24-3.26 (2H, m), 2.32-2.35 (1H, m), 2.10-2.19 (1H, m), 1.90-1.95 (4H, m); LCMS: 95.2%, MS (ESI); m/z 433.2[M+ H]+.
100		yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.27 (2H, d, *J* = 4.2 Hz), 6.95-7.10 (3H, m), 6.66 (1H, d, *J* = 2.0 Hz), 6.35-6.45 (1H, m), 4.78 (2H, brs), 4.33 (4H, s), 3.83 (2H, t, *J* = 14.0 Hz), 3.64 (2H, *J* = 7.6 Hz), 2.40-2.55 (2H, M); LCMS: 95.3%, MS (ESI); m/z 443.2 [M+H]+.
101		grey powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.30-7.40 (3H, m), 7.17 (1H, d, *J* = 7.6 Hz), 7.00-7.10 (2H, m), 6.92-7.01 (2H, m), 6.89 (1H, dd, *J* = 8.0, 2.0 Hz), 6.81 (1H, d, *J* = 8.0 Hz), 6.43 (1H, d, *J* = 1.6 Hz), 6.23 (1H, dd, *J* = 8.0, 2.0 Hz), 4.46 (2H, s); LCMS: 99.5 %, MS (ESI); m/z 365.1[M + H]+.
102		white powder; mp = 58.4-66.6°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.37-7.46 (3H, m), 7.22 (1H, dd, *J* = 6.4, 3.2 Hz), 6.96-7.03 (3H, m), 6.70-6.80 (2H, m), 6.41 (1H, d, *J* = 2.0 Hz), 6.19 (1H, d, *J* = 7.6 Hz), 4.30-4.55 (4H, m); LCMS: 95.7%, MS (ESI); m/z 383.1[M+H]+.
103		pale green powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.30-7.40 (3H, m), 7.10-7.20 (2H, m), 7.04 (1H, s), 6.98 (2H, dd, *J* = 8.8, 1.2 Hz), 6.71-6.82 (3H, m), 6.41 (1H, d, *J* = 1.6 Hz), 6.20 (1H, d, *J* = 8.0 Hz), 4.44 (2H, d, *J* = 6.4 Hz); LCMS: 97.3 %, MS (ESI); m/z 331.2[M+ H]+.
104		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.44 (1H, brs), 7.30 (2H, d, *J* = 8.8 Hz), 7.06 (2H, d, *J* = 8.8 Hz), 6.90-6.99 (1H, m), 6.37-6.45 (1H, m), 6.07-6.28 (2H, m), 5.14-5.16 (1H, m), 3.62-3.67 (1H, m), 3.30-3.42 (3H, overlapped with H2O peak), 2.1 (3H, d, *J* = 4.0 Hz), 2.31-2.35 (1H, m), 2.14-2.17 (1H, m); LCMS: 96.2%, MS (ESI); m/z 393.1[M+ H]+.
105		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.30 (2H, d, *J* = 8.8 Hz), 7.06 (2H, d, *J* = 9.2 Hz), 6.98 (1H, d, *J* = 8.4 Hz), 6.43 (1H, s), 6.25 (1H, d, *J* = 8.4 Hz), 5.14-5.17 (1H, m), 3.62-3.68 (1H, m), 3.30-3.42 (3H, overlap with H2O peak), 2.99 (6H, s), 2.32-2.38 (1H, m), 2.14-2.17 (1H, m); LCMS: 100%, MS (ESI); m/z 407.1[M+ H]+.

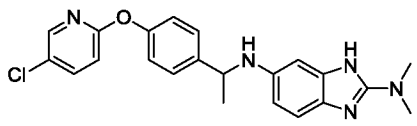
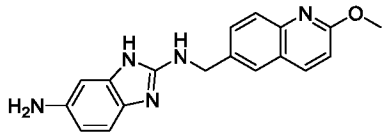
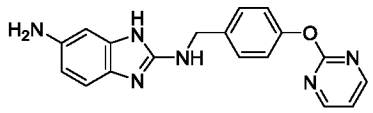
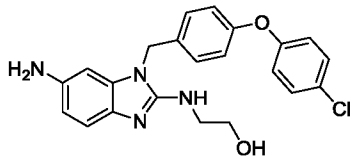
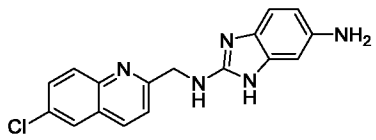
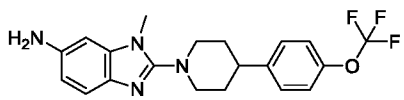
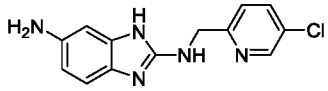
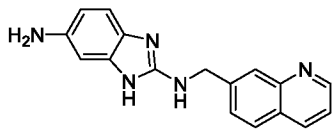
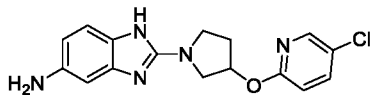
106		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.35-10.49 (1H, brs), 7.64-7.73 (5H, m), 7.51-7.58 (4H, m), 6.78-7.01 (2H, m), 6.42 (1H, s), 6.18-6.22 (1H, m), 4.54-4.58 (2H, m), 4.42-4.45 (2H, m); LCMS: 99.1%, MS (ESI); m/z 343.1[M+ H]+.
107		white powder; mp > 200.9°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 9.51 (1H, d, *J* = 8.8 Hz), 7.54-7.66 (2H, m), 7.33-7.51 (3H, m), 7.12-7.22 (1H, m), 4.15-4.29 (1H, m), 3.00-3.15 (2H, m), 1.29 (3H, d, *J* = 6.8 Hz); LCMS: 100 %, MS (ESI); m/z 334.9[M+ H]+.
108		yellow solid; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.41 (2H, d, *J* = 8.8 Hz), 7.29 (2H, d, *J* = 8.0 Hz), 7.23 (2H, d, *J* = 8.0 Hz), 6.94 (2H, d, *J* = 8.4 Hz), 6.80 (1H, d, *J* = 8.0 Hz), 6.64 (1H, brs), 6.42 (1H, d, *J* = 2.0 Hz), 6.19 (1H, d, *J* = 7.2 Hz), 4.34 (2H, d, *J* = 6.0 Hz), 4.04 (2H, d, *J* = 12.4 Hz), 2.68-2.75 (3H, m), 1.80-1.91 (2H, m), 1.65-1.80 (2H, m); LCMS: 98.0 %, MS (ESI); m/z 482.1[M+ H]+.
109		white powder; mp > 173°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.40 (1H, brs), 7.30-7.40 (4H, m), 7.18 (1H, s), 7.11 (1H, t, *J* = 7.2 Hz), 6.90-7.00 (5H, m), 6.70-6.85 (2H, m), 6.39 (1H, d, *J* = 2.0 Hz), 6.24 (1H, d, *J* = 7.6 Hz), 5.00 (1H, brs), 4.42 (2H, d, *J* = 6.0 Hz), 1.31 (6H, s); LCMS: 100%, MS (ESI); m/z 416.1[M+ H]+.
110		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.03 - 10.31 (1H, m), 7.30-7.55 (4H, m), 6.91-7.07 (4H, m), 6.60-6.88 (2H, m), 6.39 (1H, brs), 6.05-6.15 (1H, m) ,4.80-4.90 (1H, m), 4.40 (2H, brs), 1.44 (3H, d, *J* = 6.8 Hz); LCMS: 100%, MS (ESI); m/z 379.0[M+H]+.
111		white solid; mp = 156.4-158.5°C; 1H NMR (DMSO–*d*6, 400 MHz); δ 7.40 (1H, d, *J* = 8.8 Hz), 7.21 (1H, d, *J* = 8.4 Hz), 6.95 - 7.04 (4H, m), 6.83 (1H, d, *J* = 8.4 Hz), 6.31 (1H, d, *J* = 2.0 Hz), 6.26 (1H, dd, *J* = 8.0, 2.0 Hz), 6.08 (2H, brs), 5.10 (2H, s), 4.47 (2H, brs); LCMS: 99.8%, MS (ESI); m/z 365.1 [M+H]+.
112		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.60 (1H, d, *J* = 8.8 Hz), 7.44 (2H, d, *J* = 8.4 Hz), 7.40 (1H, brs), 7.23 (1H, d, *J* = 3.2 Hz), 7.07 (2H, d, *J* = 8.8 Hz), 6.96 (1H, dd, *J* = 8.8, 2.8 Hz), 6.85 (1H, d, *J* = 8.4 Hz), 6.46 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.0, 2.0 Hz), 4.48 (2H, s); LCMS: 97.6%, MS (ESI); m/z 399.1[M+ H]+.
113		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.65 (1H, brs), 7.32-7.50 (3H, m), 7.08-7.20 (1H, m), 7.02 (2H, d, *J* = 8.4 Hz), 6.88 (1H, d, *J* = 8.4 Hz), 6.74-6.84 (1H, m), 6.48 (1H, d, *J* = 2.0 Hz), 6.29 (1H, dd, *J* = 8.0, 2.0 Hz), 4.48 (2H, s); LCMS: 98.7%, MS (ESI); m/z 367.1[M+ H]+.
114		white powder; mp > 220°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.30 (1H, brs), 7.15-7.35 (4H, m), 7.06 (2H, d, *J* = 9.6 Hz), 6.95 (1H, d, *J* = 8.8 Hz), 6.78 (1H, d, *J* = 7.2 Hz), 6.50-6.70 (1H, m), 6.41 (1H, s), 6.15-6.25 (1H, m), 4.25-4.55 (4H, m), 3.25-3.40 (4H, m), 3.15-3.25 (4H, m); LCMS: 98.8%, MS (ESI); m/z 483.2[M+ H]+.
115		white powder; mp > 220°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.30 (1H, brs), 7.30-7.55 (4H, m), 7.22 (2H, d, *J* = 8.4 Hz), 6.92 (2H, d, *J* = 8.4 Hz), 6.79 (1H, d, *J* = 8.0 Hz), 6.50-6.75 (1H, m), 6.41 (1H, d, *J* = 2.0 Hz), 6.15-6.25 (1H, m), 4.25-4.50 (2H, brs), 4.33 (2H, *J* = 6.0 Hz) 3.60-3.80 (2H, m), 2.60-2.75 (3H, m), 1.80-1.95 (2H, m), 1.65-1.80

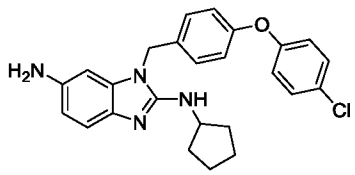
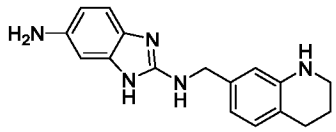
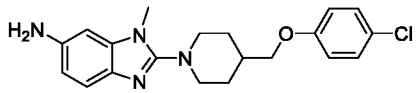
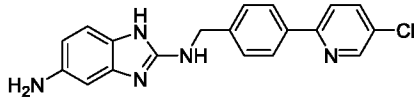
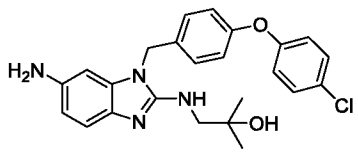
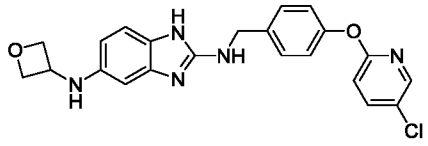
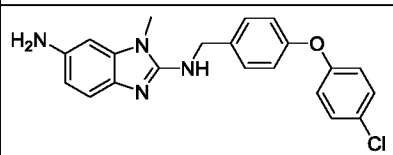
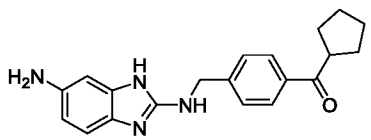
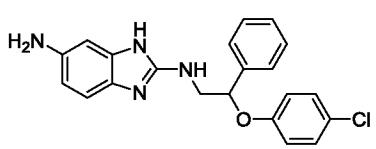
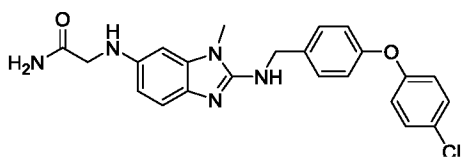
		(2H, m); LCMS: 98.7%, MS (ESI); m/z 432.1[M+ H]+.
116		pale yellow powder; mp > 130.8°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.34 (2H, d, *J* = 8.4 Hz), 7.28 (2H, d, *J* = 8.4 Hz), 7.02 (1H, brs), 6.75-6.85 (1H, m), 6.44 (1H, s), 6.22 (1H, d, *J* = 8.0 Hz), 4.43 (2H, s), 1.25 (9H, s); LCMS: 99.6%, MS (ESI); m/z 295.0[M+H]+.
117		off-white powder; mp > 207.2°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 9.78 (1H, t, *J* = 6.0 Hz), 7.42-7.49 (4H, m), 7.36-7.42 (2H, m), 7.19 (1H, dd, *J* = 8.4, 2.0 Hz), 7.00 (2H, d, *J* = 8.8 Hz), 6.88-6.96 (2H, m), 4.66 (2H, d, *J* = 6.0 Hz), 1.27 (9H, s); LCMS: 98.5%, MS (ESI); m/z 387.1[M+ H]+.
118		pale green powder; mp > 113.2°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.56 (0.4H, brs), 10.40 (0.4H, brs), 7.35-7.50 (4H, m), 7.19-7.25 (1H, m), 6.90-7.05 (5H, m), 6.75-6.95 (2H, m), 6.39 (1H, s), 6.15-6.35 (1H, m), 4.97 (0.5H, brs), 5.07 (0.5H, brs), 4.38-4.49 (2H, m), 1.31 (6H, d, *J* = 3.6 Hz); LCMS: 99.5%, MS (ESI); m/z 450.0[M+ H]+.
119		white powder; mp > 54.3°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.35-10.65 (1H, m), 7.30-7.60 (5H, m), 7.10-7.20 (1H, m), 6.90-7.10 (4H, m), 6.75-6.90 (1H, m), 6.40 (1H, s), 6.15-6.30 (1H, m), 5.00-5.25 (1H, m), 4.40-4.60 (2H, m), 3.85-4.05 (2H, m), 3.75-3.85 (1H, m), 3.60-3.75 (1H, m), 3.45-3.60 (1H, m), 2.05-2.25 (1H, m), 1.65-1.80 (1H, m); LCMS: 97.3%, MS (ESI); m/z 401.1[M+ H]+.
120		white powder; mp = 200.7-201.3°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.27 (2H, d, *J* = 8.8 Hz), 6.92-7.05 (2H, m), 6.87 (1H, d, *J* = 8.0 Hz), 6.48 (1H, s), 6.26 (2H, dd, *J* = 8.4, 2.4 Hz), 6.01 (1H, d, *J* = 6.8 Hz), 4.53 (2H, brs), 4.20-4.30 (2H, m), 4.13-4.20 (2H, m), 4.05-4.13 (1H, m), 1.85-2.05 (2H, m), 1.60-1.75 (2H, m), 1.45-1.60 (4H, m); LCMS: 98.6%, MS (ESI); m/z 421.1 [M+H]+.
121		white powder; mp > 59.7°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.26 (2H, d, *J* = 8.4 Hz), 6.90 (2H, d, *J* = 8.4 Hz), 6.79 (1 , d, *J* = 8.4 Hz), 6.69 (1H, brs), 6.42 (1H, d, *J* = 2.0 Hz), 6.19 (1H, dd, *J* = 8.0, 2.0 Hz), 4.39 (2H, d, *J* = 6.0 Hz), 1.26 (9H, s); LCMS: 99.5%, MS (ESI); m/z 311.1[M+H]+.
122		off-white powder; mp > 160.8°C; 1H NMR (DMSO-*d*6); δ 9.73 (1H, t, *J* = 6.4 Hz), 7.52 (2H, d, *J* = 8.4 Hz), 7.35-7.46 (3H, m), 7.19 (1H, dd, *J* = 8.0, 2.0 Hz), 7.14 (1H, d, *J* = 8.4 Hz), 7.10 (2H, d, *J* = 8.8 Hz), 7.02 (1H, t, *J* = 2.4 Hz), 6.95 (1H, dd, *J* = 8.4, 2.4 Hz), 4.67 (2H, d, *J* = 6.0 Hz); LCMS: 100%, MS (ESI); m/z 365.0[M+ H]+.
123		yellow powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 7.35-7.47 (4H, m), 6.95-7.05 (4H, m), 6.91 (1H, d, *J* = 8.0 Hz), 6.40 (1H, s), 6.34 (1H, d, *J* = 8.4 Hz), 5.79 (1H, brs), 4.22 (2H, s), 2.98 (6H, s); LCMS: 98.7%, MS (ESI); m/z 393.1 [M + H]+.

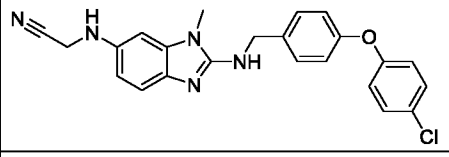
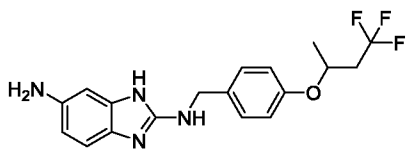
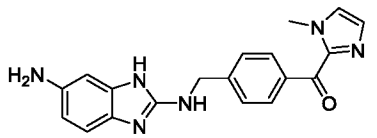
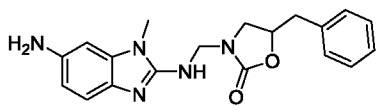
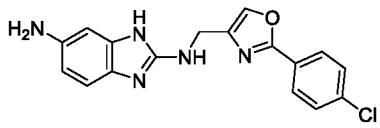
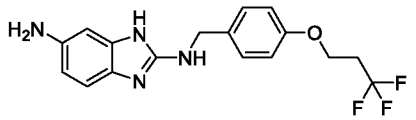
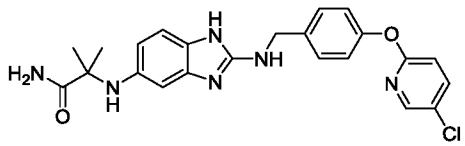
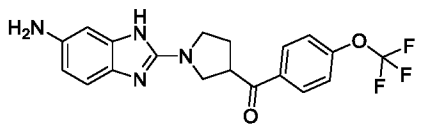
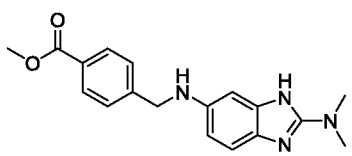
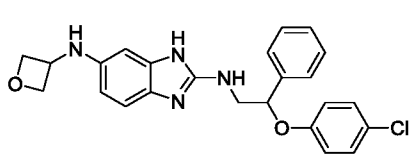
124		gray powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 10.14 (1H, brs), 7.30-7.40 (4H, m), 6.90-7.00 (4H, m), 6.55-6.87 (2H, m), 6.37 (1H, s), 6.14 (1H, d, *J* = 8.4 Hz), 4.20-4.70 (3H, m), 1.60-1.80 (2H, m), 0.87 (3H, t, *J* = 7.2 Hz); LCMS: 100%, MS (ESI); m/z 393.0[M+ H]+.
125		pale yellow powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 10.40 (1H, brs), 7.36 - 7.45 (4H, m), 6.95 - 7.06 (4H, m), 6.75-6.80 (2H, m), 6.26 (1H, s), 6.13 (1H, d, *J* = 7.6 Hz), 5.69 (1H, brs), 4.81 (2H, t, *J* = 6.0 Hz), 4.31 - 4.50 (5H, m); LCMS: 99.1%, MS (ESI); m/z 421.1 [M+H]+.
126		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 13.14 (2H, brs), 7.78 (2H, d, *J* = 8.8 Hz), 7.39 (2H, d, *J* = 8.4 Hz), 7.30 (1H, d, *J* = 8.8 Hz), 6.90-7.10 (6H, m), 4.42 (2H, s), 3.21 (6H, s); LCMS: 100 %, MS (ESI); m/z 443.1[M+ H]+.
127		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 13.20 (2H, brs), 7.50 (2H, d, *J* = 8.8 Hz), 7.38 (2H, d, *J* = 8.4 Hz), 7.29 (1H, d, *J* = 8.8 Hz), 7.16 (1H, brs), 6.80-7.10 (5H, m), 4.71 (1H, d, *J* = 5.6 Hz), 3.20 (6H, s), 1.66 (3H, d, *J* = 6.0 Hz); LCMS: 100 %, MS (ESI); m/z 457.1[M + H]+.
128		pale green powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 12.66 (2H, brs), 7.36-7.47 (4H, m), 7.13 (1H, d, *J* = 7.6 Hz), 6.90-7.00 (4H, m), 6.60-6.85 (2H, m), 4.25-4.35 (1H, m), 3.15 (6H, s), 1.70-2.00 (2H, m), 0.87 (3H, t, *J* = 7.2 Hz); LCMS: 99.39%, MS (ESI); m/z 421.1 [M+H]+.
129		gray powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.35-10.50 (1H, m), 7.80-7.98 (4H, m), 7.66 (2H, d, *J* = 8.8 Hz), 7.57 (2H, d, *J* = 8.4 Hz), 6.75-7.00 (1H, m), 6.70-6.80 (1H, m), 6.39 (1H, s), 6.10-6.25 (1H, m), 4.45-4.55 (2H, m), 4.25-4.45 (2H, m); LCMS: 98.0%, MS (ESI); m/z 413.0 [M+H]+.
130		white powder; 1H NMR (DMSO-*d*6); δ 9.92 (1H, t, *J* = 6.0 Hz), 7.69-7.83 (4H, m), 7.58-7.69 (4H, m), 7.39-7.51 (2H, m), 7.18 (1H, d, *J* = 8.8 Hz), 4.83 (2H, d, *J* = 6.0 Hz); LCMS: 100%, MS (ESI); m/z 377.0 [M+H]+.
131		pale green powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 12.91 (2H, brs), 7.41-7.47 (4H, m), 7.22 (1H, d, *J* = 8.4 Hz), 6.86-6.99 (6H, m), 4.50-4.70 (1H, m), 3.17 (6H, s), 1.58 (3H, d, *J* = 5.2 Hz); LCMS: 99.7 %, MS (ESI); m/z 407.0[M+ H]+.
132		pale green powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 12.76 (2H, brs), 7.43 (2H, d, *J* = 8.8 Hz), 7.38 (2H, d, *J* = 8.8 Hz), 7.16 (1H, d, *J* = 7.2 Hz), 7.02-7.08 (2H, m), 7.00 (2H, d, *J* = 8.8 Hz), 6.60-6.85 (2H, m), 4.30-4.40 (1H, m), 3.16 (6H, s), 1.75-2.10 (2H, m), 0.87 (3H, t, *J* = 7.2 Hz); LCMS: 99.6 %, MS (ESI); m/z 471.1[M+ H]+.
133		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.52 (1H, brs), 7.85-7.99 (4H, m), 7.61-7.70 (2H, m), 7.56 (2H, d, *J* = 8.4 Hz), 6.96 (1H, brs), 6.84 (1H, d, *J* = 8.0 Hz), 6.23 (1H, s), 6.12 (1H, dd, *J* = 8.4, 2.0 Hz), 5.70 (1H, brs), 4.80 (2H, t, *J* = 6.0 Hz), 4.52 (2H, d, *J* = 6.0 Hz), 4.38-4.45 (1H, m), 4.30-4.38 (2H, m); LCMS: 95.3%, MS (ESI); m/z 469.0 [M+H]+.

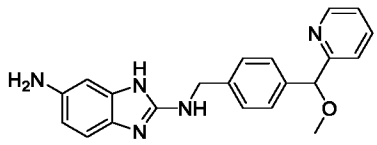
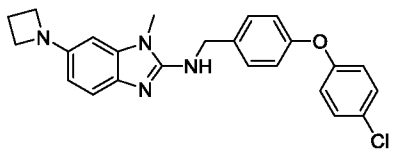
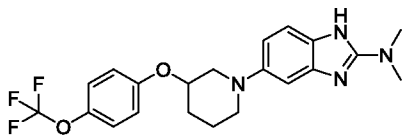
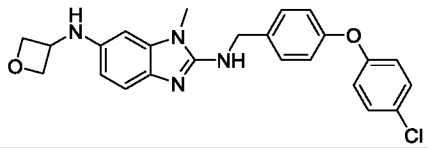
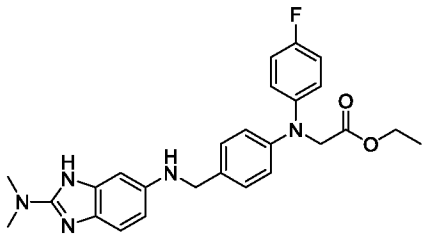
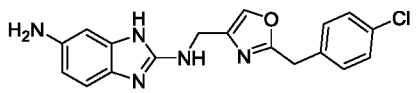
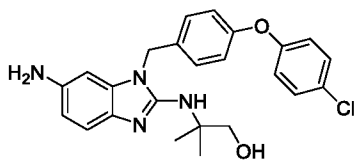
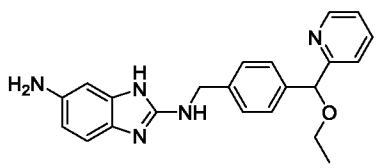
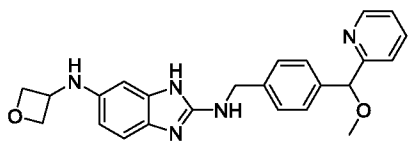
134		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.24 - 10.59 (1H, m), 7.34-7.44 (4H, m), 6.94-7.09 (4H, m), 6.85-6.88 (2H, m), 6.42 (1H, d, *J* = 2.0 Hz), 6.20-6.25 (1H, m), 4.83 (1H, brs), 4.44 (2H, d, *J* = 6.4 Hz), 3.63-3.67 (1H, m), 2.51-2.53 (1H, m), 2.26-2.30 (1H, m), 1.21 (3H, d, *J* = 6.0 Hz); LCMS: 98.0%, MS (ESI); m/z 375.1[M+H]+.
135		pale green powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.76 (1H, d, *J* = 2.8 Hz), 7.30-7.45 (4H, m), 7.05 (1H, d, *J* = 8.8 Hz), 6.97 (2H, d, *J* = 8.4 Hz), 6.85 (1H, d, *J* = 8.4 Hz), 6.46 (1H, d, *J* = 2.0 Hz), 6.26 (1H, dd, *J* = 8.4, 2.0 Hz), 4.46 (2H, s); LCMS: 98.2 %, MS (ESI); m/z 398.9[M + H]+.
136		pale green powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.19 (1H, d, *J* = 2.4 Hz), 7.41-7.52 (4H, m), 7.07 (2H, d, *J* = 8.8 Hz), 6.75-6.85 (2H, m), 6.42 (1H, d, *J* = 1.6 Hz), 6.20 (1H, dd, *J* = 8.4, 2.0 Hz), 4.45 (2H, d, *J* = 5.6 Hz); LCMS: 97.8 %, MS (ESI); m/z 366.0[M + H]+.
137		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.47-10.63 (1H, m), 7.40 (4H, d, *J* = 8.8 Hz), 6.86-7.04 (6H, m), 6.40-6.45 (1H, m), 6.18-6.32 (1H, m), 5.91-6.08 (1H, m), 4.42-4.48 (2H, m), 2.59-2.72 (2H, m), 2.27-2.40 (2H, m), 1.98-2.15 (2H, m); LCMS: 92.6%, MS (ESI); m/z 444.2[M+H]+.
138		white powder; 1H NMR (DMSO-*d*6); δ 9.78 (1H, t, *J* = 6.0 Hz), 8.17 (1H, d, *J* = 2.4 Hz), 7.96 (1H, dd, *J* = 8.8, 2.4 Hz), 7.51 (2H, d, *J* = 8.4 Hz), 7.37-7.45 (2H, m), 7.08-7.20 (4H, m), 4.69 (2H, d, *J* = 6.0 Hz); LCMS: 99.6%, MS (ESI); m/z 365.9[M+ H]+.
139		white powder; 1H NMR (DMSO-*d*6); δ 8.41 (1H, d, *J* = 4.8 Hz), 7.71-7.78 (1H, m), 7.53 (1H, d, *J* = 8.0 Hz), 7.29-7.35 (2H, m), 7.23-7.28 (2H, m), 7.16-7.22 (1H, m), 6.70-6.82 (2H, m), 6.40 (1H, s), 6.18 (1H, dd, *J* = 8.4, 2.0 Hz), 6.04 (1H, brs), 5.66 (1H, s), 4.38 (2H, d, *J* = 5.6 Hz); LCMS: 98.3%, MS (ESI); m/z 346.0 [M+H]+.
140		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.52 (1H, d, *J* = 2.0 Hz), 7.33 (1H, d, *J* = 8.0 Hz), 7.20-7.30 (4H, m), 7.03 (2H, d, *J* = 6.8 Hz), 6.86 (1H, d, *J* = 8.8 Hz), 6.31 (1H, d, *J* = 8.4 Hz), 6.15-6.27 (2H, m), 5.00-5.20 (2H, m), 4.46 (2H, brs), 4.10-4.25 (1H, m), 2.87-3.08 (2H, m), 1.22 (3H, d, *J* = 6.4 Hz); LCMS: 100 %, MS (ESI); m/z 425.1[M+ H]+.
141		pale yellow powder; 1H NMR (DMSO-*d*6); δ 8.70 (1H, d, *J* = 4.0 Hz), 8.01-8.10 (1H, m), 7.96 (1H, d, *J* = 8.0 Hz), 7.91 (2H, d, *J* = 8.4 Hz), 7.61-7.68 (1H, m), 7.50 (2H, d, *J* = 8.4 Hz), 7.04 (brs), 6.77-6.84 (1H, m), 6.43 (1H, d, *J* = 2.0 Hz), 6.21 (1H, dd, *J* = 8.0, 2.0 Hz), 4.55 (2H, s); LCMS: 89.4%, MS (ESI); m/z 344.1 [M+H]+.
142		white amorphous; hydroscopic; 1H NMR (DMSO-*d*6, 400 MHz); δ 12.52 (2H, brs), 10.73 (1H, brs), 8.87 (1H, t, *J* = 6.0 Hz), 7.29 (2H, d, *J* = 8.4 Hz), 7.11-7.22 (1H, m), 7.05 (2H, d, *J* = 9.2 Hz), 6.41-6.59 (2H, m), 5.10-5.22 (1H, m), 3.89-4.00 (2H, m), 3.71-3.81 (2H, m), 3.61-3.70 (3H, m), 3.50-3.60 (4H, m), 3.11-3.24 (4H, m), 2.92-3.10 (2H, m), 2.50-2.60 (2H, m), 2.11-2.21 (1H, m), 1.95-2.08 (1H, m); LCMS: 99.5 %, MS (ESI); m/z 506.3[M+ H]+.

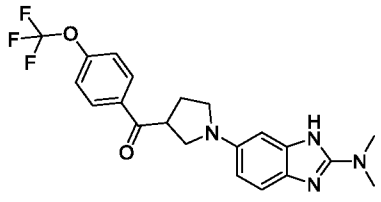
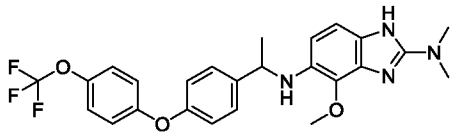
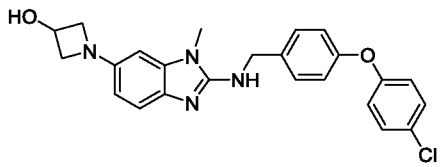
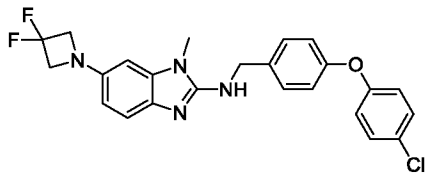
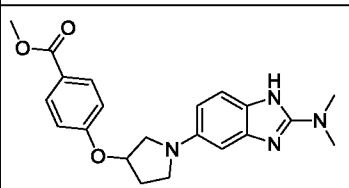
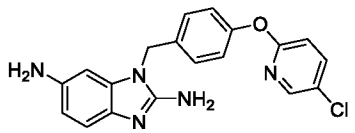
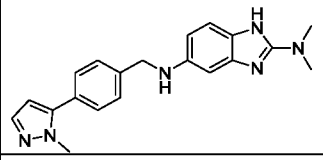
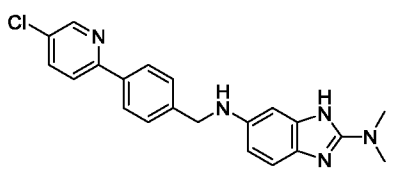
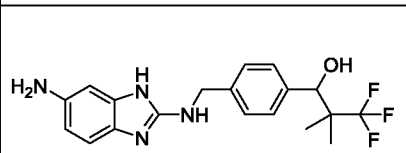
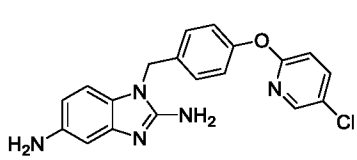
143		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.30-10.43 (1H, m), 7.29 (2H, d, *J* = 8.8 Hz), 7.04 (2H, d, *J* = 9.2 Hz), 6.86-6.99 (1H, m), 6.34-6.45 (1H, m), 5.95-6.25 (2H, m), 5.10-5.20 (1H, m), 3.60-3.69 (1H, m), 3.47-3.58 (4H, m), 3.30-3.37 (2H, m), 3.20-3.29 (2H, m), 2.53-2.61 (2H, m), 2.43-2.49 (2H, m), 2.28-2.40 (5H, m), 2.05-2.17 (1H, m); LCMS: 100 %, MS (ESI); m/z 492.1[M+ H]+.
144		pale-yellow amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.53 (1H, d, *J* = 2.0 Hz), 7.33 (1H, d, *J* = 8.0 Hz), 7.15-7.28 (4H, m), 7.04 (2H, d, *J* = 7.6 Hz), 6.64 (1H, d, *J* = 8.0 Hz), 6.37-6.50 (2H, m), 6.05-6.15 (2H, m), 5.00-5.20 (2H, m), 4.40 (2H, brs), 4.15-4.29 (1H, m), 2.88-3.04 (2H, m), 1.23 (3H, d, *J* = 6.8 Hz); LCMS: 98.1 %, MS (ESI); m/z 425.1[M+ H]+.
145		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.62 (1H, brs), 7.35-7.45 (2H, m), 7.25 (1H, d, *J* = 8.8 Hz), 6.90-7.10 (4H, m), 6.78 (1H, d, *J* = 8.4 Hz), 6.40 (1H, s), 6.19 (1H, d, *J* = 6.4 Hz), 5.07 (1H, d, *J* = 8.0 Hz), 4.45 (2H, brs), 3.65-3.75 (1H, m), 3.40-3.55 (1H, m), 2.30-2.40 (1H, m), 1.75-2.00 (3H, m); LCMS: 97.0%, MS (ESI); m/z 405.1[M+ H]+.
146		gray powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.20-10.40 (1H, m), 7.30-7.45 (4H, m), 6.90-7.10 (4H, m), 6.60-6.75 (2H, m), 6.45-6.55 (1H, m), 4.41 (2H, d, *J* = 6.0 Hz), 4.00-4.30 (2H, m), 3.70 (3H, s); LCMS: 99.5%, MS (ESI); m/z 394.9[M+ H]+.
147		off-white solid; mp = 191.4 C - 193.5 C; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.35-10.60 (1H, m), 7.35-7.45 (4H, m), 6.90-7.05 (6H, m), 6.63 (1H, s), 4.52-4.70 (2H, m), 4.40-4.45 (2H, m); LCMS: 100%, MS (ESI); m/z 399.0 [M+ H]+.
148		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.15-10.35 (1H, m), 7.28 (2H, d, *J* = 8.8 Hz), 7.04 (2H, d, *J* = 9.2 Hz), 6.86-6.98 (1H, m), 6.32-6.44 (1H, m), 6.12-6.26 (1H, m), 5.08-5.18 (1H, m), 3.60-3.70 (3H, m), 3.51-3.59 (2H, m), 3.36-3.41 (2H, m), 3.30-3.35 (1H, m), 3.21-3.29 (4H, m), 2.27-2.36 (1H, m), 2.05-2.18 (1H, m); LCMS: 100%, MS (ESI); m/z 437.2[M+ H]+.
149		pink amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.29-10.47 (1H, m), 8.51 (1H, d, *J* = 4.0 Hz), 7.70 (1H, t, *J* = 8.0 Hz), 7.29-7.47 (5H, m), 7.22 (1H, t, *J* = 6.0 Hz), 6.92-7.06 (4H, m), 6.65-6.90 (2H, m), 6.34 (1H, s), 6.15 - 6.31 (1H, m), 5.60-5.86 (1H, m), 4.41 (2H, t, *J* = 6.8 Hz), 4.30 (2H, d, *J* = 5.6 Hz); LCMS: 99.5%, MS (ESI); m/z 456.1 [M+H]+.
150		pale-yellow amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.60-10.85 (1H, m), 8.15 (1H, d, *J* = 2.0 Hz), 7.87 (1H, dd, *J* = 8.4, 2.4 Hz), 7.38 (2H, d, *J* = 8.4 Hz), 7.22 (2H, d, *J* = 9.2 Hz), 7.01 (1H, d, *J* = 8.8 Hz), 6.75-6.94 (1H, m), 6.18-6.40 (2H, m), 5.46-5.69 (1H, m), 4.41-4.55 (1H, m), 2.90-2.95 (6H, m), 1.42 (3H, d, *J* = 6.4 Hz); LCMS: 97.6 %, MS (ESI); m/z 458.1[M+ H]+.
151		grey powder; mp > 200°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 9.56 (1H, s), 6.83 (2H, d, *J* = 8.4 Hz), 6.61 (2H, d, *J* = 8.4 Hz), 6.39 (2H, d, *J* = 8.8 Hz), 6.21 (2H, d, *J* = 8.8 Hz), 5.97 (1H, brs), 5.90 (1H, d, *J* = 8.0 Hz), 5.53 (1H, d, *J* = 2.0 Hz), 5.32 (1H, d, *J* = 8.0 Hz), 3.62 (4H, d, *J* = 6.0 Hz); LCMS: 97.1 %, MS (ESI); m/z 428.1[M+ H]+.

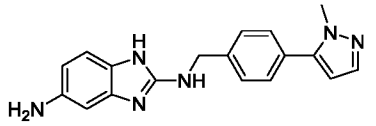
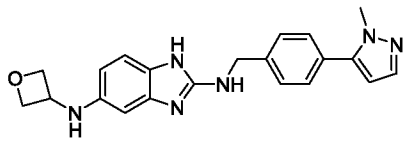
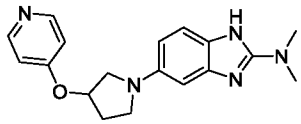
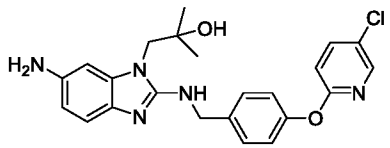
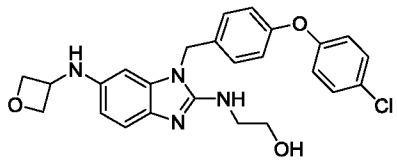
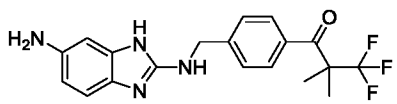
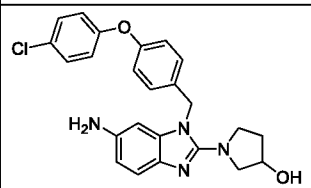
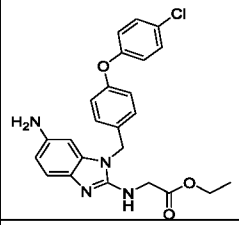
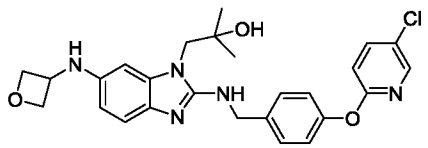
152		pale yellow amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.60-10.85 (1H, m), 8.19 (1H, s), 7.93 (1H, dd, *J* =8.8, 2.4 Hz), 7.42 (2H, d, *J* = 8.8 Hz), 7.00-7.10 (3H, m), 6.75-6.90 (1H, m), 6.19-6.36 (2H, m), 5.46-5.67 (1H, m), 4.36-4.50 (1H, m), 2.90-2.95 (6H, m), 1.42 (3H, d, *J* = 5.2 Hz); LCMS: 99.2 %, MS (ESI); m/z 408.1[M+ H]+.
153		off-white powder; 1H NMR (DMSO-*d*6); δ 8.12-8.23 (1H, m), 7.79 (1H, s), 7.71-7.77 (1H, m), 7.64-7.71 (1H, m), 6.98 (1H, d, *J* = 8.8 Hz), 6.89 (1H, brs), 6.79 (1H, d, *J* = 8.0 Hz), 6.42 (1H, d, *J* = 2.0 Hz), 6.19 (1H, dd, *J* = 8.0 Hz, 2.0 Hz), 4.59 (2H, d, *J* = 5.6 Hz), 3.96 (3H, s); LCMS: 93%, MS (ESI); m/z 319.9[M+ H]+.
154		grey amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.33-10.54 (1H, m), 8.60 (1H, d, *J* = 4.8 Hz), 7.40 (2H, d, *J* = 8.4 Hz), 7.22 (1H, t, *J* = 4.8 Hz), 7.10 (2H, d, *J* = 8.4 Hz), 6.70-6.94 (2H, m), 6.36-6.45 (1H, m), 6.11-6.22 (1H, m), 4.27-4.50 (4H, m); LCMS: 100%, MS (ESI); m/z 333.1[M+ H]+.
155		white solid; mp = 203.8-204.6°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.37-7.44 (1H, m), 7.19 (1H, d, *J* = 8.4 Hz), 6.90 -7.04 (4H, m), 6.88 (1H, d, *J* = 8.4 Hz), 6.53 (1H, t, *J* = 5.2 Hz), 6.30 (1H, d, *J* = 2.0 Hz), 6.26 (1H, dd, *J* = 8.0, 2.0 Hz), 5.10 (2H, s), 5.02 (1H, brs), 4.51 (2H, brs), 3.50-3.60 (2H, m), 3.34-3.38 (2H, m); LCMS: 100%, MS (ESI); m/z 409.0[M+H]+.
156		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.30 (1H, d, *J* = 8.8 Hz), 8.08 (1H, d, *J* = 2.0 Hz), 7.99 (1H, d, *J* = 9.2 Hz), 7.75 (1H, dd, *J* = 8.8, 2.4 Hz), 7.60 (1H, d, *J* = 8.4 Hz), 6.97 (1H, brs), 6.79 (1H, d, *J* = 8.0 Hz), 6.41 (1H, d, *J* = 2.0 Hz), 6.19 (1H, d, *J* = 6.4 Hz), 4.72 (2H, d, *J* = 5.6 Hz); LCMS: 93.1%, MS (ESI); m/z 323.9 [M+ H]+.
157		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.45 (2H, d, *J* = 8.4 Hz), 7.32 (2H, d, *J* = 8.0 Hz), 7.08 (1H, d, *J* = 8.4 Hz), 6.46 (1H, d, *J* = 2.0 Hz), 6.41 (1H, dd, *J* = 8.4, 2.0 Hz), 4.77 (2H, brs), 3.50-3.60 (2H, m), 3.48 (3H, s), 2.88-3.01 (2H, m), 2.73-2.85 (1H, m), 1.80-1.95 (4H, m); LCMS: 100 %, MS (ESI); m/z 390.9[M+ H]+.
158		off-white powder; mp = 101.8-104.0°C; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.49 (1H, brs), 8.56 (1H, d, *J* = 2.0 Hz), 7.87 (1H, dd, *J* = 8.4, 2.4 Hz), 7.40 (1H, d, *J* = 8.0 Hz), 6.85 (1H, brs), 6.79 (1H, d, *J* = 8.4 Hz), 6.41 (1H, d, *J* = 1.6 Hz), 6.19 (1H, d, *J* = 7.2 Hz), 4.54 (2H, d, *J* = 6.0 Hz), 4.42 (2H, brs); LCMS: 99.2%, MS (ESI); m/z 273.9[M+ H]+.
159		green solid; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.84-8.86 (1H, m), 8.33 (1H, d, *J* = 8.4 Hz), 7.91-8.00 (2H, m), 7.61-7.64 (1H, m), 7.49 (1H, dd, *J* = 8.0, 4.0 Hz), 7.13 (1H, brs), 6.81 (1H, d, *J* = 8.4 Hz), 6.43 (1H, d, *J* = 2.0 Hz), 6.21 (1H, dd, *J* = 8.0, 2.0 Hz), 4.68 (2H, d, *J* = 6.0 Hz); LCMS: 93.2 %, MS (ESI); m/z 290.3[M + H]+.
160		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.64-10.85 (1H, m), 8.25 (1H, d, *J* = 2.4 Hz), 7.81 (1H, dd, *J* = 8.8, 2.4 Hz), 6.88 (1H, d, *J* = 8.4 Hz), 6.76-6.86 (1H, m), 6.44 (1H, d, *J* = 1.6 Hz), 6.14-6.28 (1H, m), 5.50-5.56 (1H, m), 4.30-4.57 (2H, m), 3.70-3.81 (1H, m), 3.49-3.67 (3H, m), 2.26-2.37 (1H, m), 2.10-2.24 (1H, m); LCMS: 96.8%, MS (ESI); m/z 329.9[M+H]+.

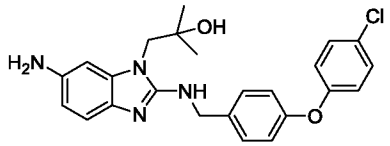
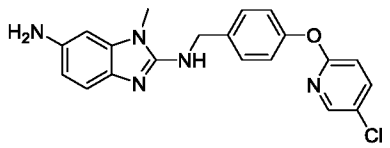
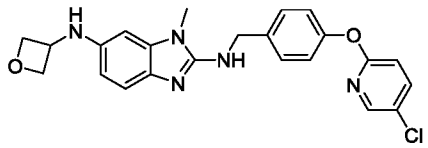
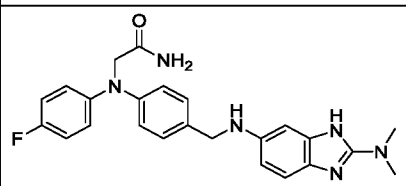
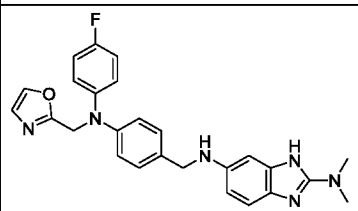
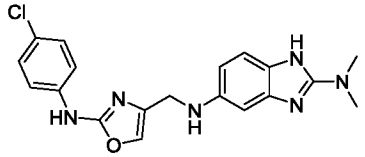
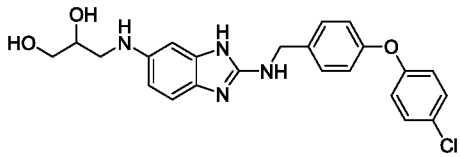
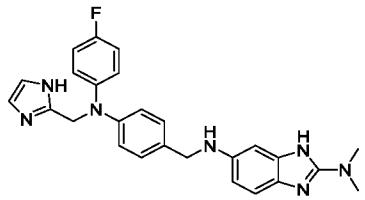
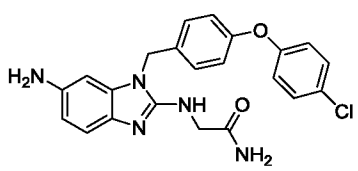
161		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.40 (2H, d, *J* = 8.8 Hz), 7.16 (2H, d, *J* = 8.8 Hz), 6.93-7.05 (4H, m), 6.89 (1H, d, *J* = 8.0 Hz), 6.22-6.30 (2H, m), 6.19 (1H, d, *J* = 6.8 Hz), 5.12 (2H, s), 4.47 (2H, brs), 4.06-4.19 (1H, m), 1.91-1.94 (2H, m), 1.48-1.56 (2H, m), 1.56-1.66 (4H, m); LCMS: 98.4%, MS (ESI); m/z 433.0[M+H]+.
162		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 6.71-6.81 (2H, m), 6.69 (1H, brs), 6.35-6.45 (3H, m), 6.20 (1H, d, *J* = 8.4 Hz), 5.58 (1H, brs), 4.25 (2H, d, *J* = 6.0 Hz), 3.09-3.18 (2H, m), 2.55-2.65 (2H, m), 1.65-1.80 (2H, m); LCMS: 96.9 %, MS (ESI); m/z 293.9[M + H]+.
163		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.32 (2H, d, *J* = 8.8 Hz), 7.01 (1H, d, *J* = 8.4 Hz), 7.00 (2H, d, *J* = 8.8 Hz), 6.50 (1H, s), 6.40 (1H, d, *J* = 8.4 Hz), 4.73 (2H, brs), 3.90 (2H, d, *J* = 6.0 Hz), 3.40-3.50 (5H, m), 2.80-2.87 (2H, m), 1.94-2.00 (1H, m), 1.80-1.88 (2H, m), 1.46-1.55 (2H, m); LCMS: 95%, MS (ESI); m/z 370.9[M+ H]+.
164		grey amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.30-10.40 (1H, m), 8.68 (1H, d, *J* = 1.2 Hz), 8.02 (2H, d, *J* = 8.4 Hz), 7.98 (2H, d, *J* = 1.6 Hz), 7.47 (2H, d, *J* = 8.0 Hz), 6.70-6.91 (2H, m), 6.41 (1H, d, *J* = 2.0 Hz), 6.10-6.22 (1H, m), 4.49 (2H, d, *J* = 6.0 Hz), 4.30-4.45 (2H, m); LCMS: 100%, MS (ESI); m/z 349.9 [M+ H]+.
165		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.37-7.45 (2H, m), 7.20 (2H, d, *J* = 8.4 Hz), 6.94-7.04 (4H, m), 6.87 (1H, d, *J* = 8.3 Hz), 6.51 (1H, brs), 6.33 (1H, d, *J* = 2.0 Hz), 6.28 (1H, dd, *J* = 8.0, 2.0 Hz), 5.15 (2H, s), 3.27-3.30 (2H, m), 1.08 (6H, s); LCMS: 97.8%, MS (ESI); m/z 437.0[M+H]+.
166		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.30-10.50 (1H, m), 8.16 (1H, d, *J* = 2.4 Hz), 7.92 (1H, dd, *J* = 8.8, 2.4 Hz), 7.38 (2H, d, *J* = 8.4 Hz), 7.01-7.09 (3H, m), 6.75-6.95 (2H, m), 6.24 (1H, d, *J* = 4.8 Hz), 6.08-6.20 (1H, m), 5.60-5.78 (1H, m), 4.81 (2H, t, *J* = 6.4 Hz), 4.35-4.50 (5H, m); LCMS: 98.13%, MS (ESI); m/z 422.0 [M+ H]+.
167		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.36-7.44 (4H, m), 6.93-7.05 (4H, m), 6.86 (2H, d, *J* = 8.4 Hz), 6.36 (1H, d, *J* = 1.6 Hz), 6.27 (1H, dd, *J* = 8.4, 2.0 Hz), 4.57 (2H, brs), 4.50 (2H, d, *J* = 6.0 Hz), 3.40 (3H, s); LCMS: 97.8%, MS (ESI); m/z 378.9[M+H]+.
168		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.93 (1H, d, *J* = 8.4 Hz), 7.48 (1H, d, *J* = 8.4 Hz), 7.14 (1H, brs), 6.81 (1H, d, *J* = 8.4 Hz), 6.43 (1H, d, *J* = 2.0 Hz), 6.22 (1H, dd, *J* = 8.0, 2.0 Hz), 4.53 (2H, s), 3.73-3.84 (1H, m), 1.79-1.93 (2H, m), 1.65-1.77 (2H, m), 1.59 (4H, m); LCMS: 94%, MS (ESI); m/z 335.1[M+ H]+.
169		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.44 (2H, d, *J* = 7.2 Hz), 7.38 (2H, t, *J* = 7.6 Hz), 7.25-7.34 (1H, m), 7.23 (2H, d, *J* = 8.8 Hz), 6.93 (2H, d, *J* = 8.8 Hz), 6.84 (1H, d, *J* = 8.0 Hz), 6.52 (1H, brs), 6.45 (1H, d, *J* = 2.0 Hz), 6.22 (1H, dd, *J* = 8.4, 2.0 Hz), 5.54 (1H, t, *J* = 6.0 Hz), 3.59-3.70 (2H, m); LCMS: 97.4%, MS (ESI); m/z 378.9[M+H]+.
170		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.38-7.45 (4H, m), 7.28 (1H, brs), 7.09 (1H, brs), 6.96-7.02 (4H, m), 6.88-6.96 (2H, m), 6.33 (1H, d, *J* = 2.0 Hz), 6.28 (1H, dd, *J* = 8.4, 2.0 Hz), 5.37 (1H, t, *J* = 6.0 Hz), 4.50 (2H, d, *J* = 5.6 Hz), 3.57 (2H, d, *J* = 5.6 Hz), 3.42 (3H, s); LCMS: 95.5%, MS (ESI); m/z 435.9[M+H]+.

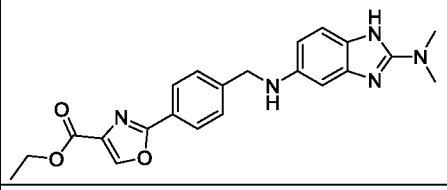
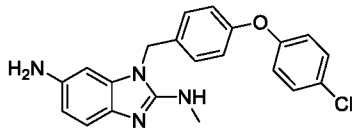
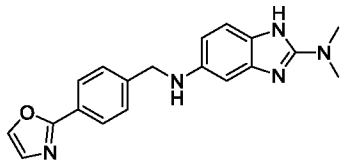
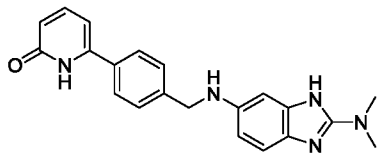
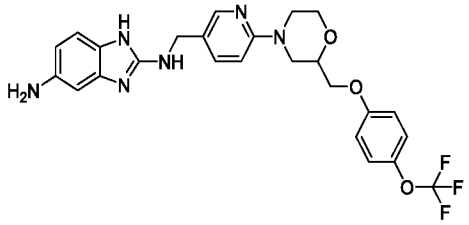
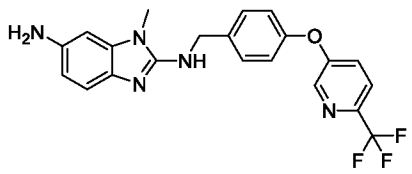
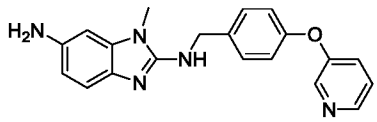
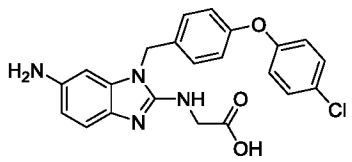
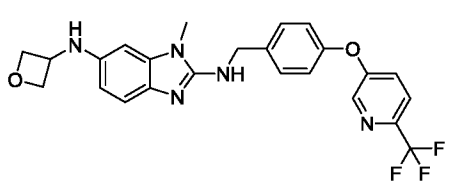
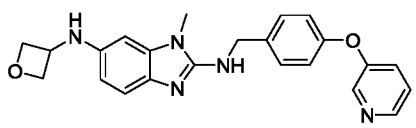
171		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.37-7.46 (4H, m), 6.95-7.04 (6H, m), 6.58 (1H, d, *J* = 2.0 Hz), 6.41 (1H, dd, *J* = 8.4, 2.1 Hz), 5.74 (1H, t, *J* = 7.2 Hz), 4.52 (2H, d, *J* = 6.0 Hz), 4.21 (2H, d, *J* = 7.2 Hz), 3.47 (3H, s); LCMS: 96.6%, MS (ESI); m/z 418.0[M+H]+.
172		grey powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 7.27 (2H, d, *J* = 8.4 Hz), 6.87 (2H, d, *J* = 8.4 Hz), 6.77 (1H, d, *J* = 8.4 Hz), 6.66 (1H, brs), 6.40 (1H, d, *J* = 1.6 Hz), 6.17 (1H, d, *J* = 8.4 Hz), 4.62-4.78 (1H, m), 4.34 (2H, d, *J* = 6.4 Hz), 2.56-2.74 (2H, m), 1.28 (3H, d, *J* = 6.0 Hz); LCMS: 99.4 %, MS (ESI); m/z 364.9[M+ H]+.
173		pale-yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.32-10.50 (1H, m), 8.16 (2H, d, *J* = 8.4 Hz), 7.56 (1H, s), 7.47 (2H, d, *J* = 8.0 Hz), 7.17 (1H, s), 6.88-6.98 (0.5H, m), 6.70-6.84 (1.5H, m), 6.40 (1H, s), 6.10-6.23 (1H, m), 4.25-4.60 (4H, m), 3.97 (3H, s); LCMS: 90%, MS (ESI); m/z 347.1[M+ H]+.
174		off-white powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 7.11-7.39 (6H, m), 6.93 (1H, d, *J* = 7.6 Hz), 6.42 (1H, d, *J* = 1.6 Hz), 6.34 (1H, d, *J* = 8.4 Hz), 4.66-4.83 (3H, m), 3.72 (1H, t, *J* = 8.8 Hz), 3.36-3.43 (4H, m), 2.91 (2H, d, *J* = 6.4 Hz); LCMS: 97.0%, MS (ESI); m/z 352.0[M+H]+.
175		off-white powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 8.03 (1H, s), 7.96 (2H, d, *J* = 8.4 Hz), 7.59 (2H, d, *J* = 8.4 Hz), 6.81 (1H, d, *J* = 8.0 Hz), 6.43 (1H, d, *J* = 1.6 Hz), 6.20 (1H, d, *J* = 7.6 Hz), 4.39 (2H, d, *J* = 5.6 Hz); LCMS: 100%, MS (ESI); m/z 340.1 [M+H]+.
176		grey powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 9.50-9.62 (1H, m), 7.34-7.42 (3H, m), 7.31 (1H, s), 7.07 (1H, d, *J* = 7.6 Hz), 6.97 (2H, d, *J* = 8.4 Hz), 4.56 (2H, d, *J* = 5.6 Hz), 4.18 (2H, t, *J* = 6.0 Hz), 2.67-2.85 (2H, m); LCMS: 100 %, MS (ESI); m/z 351.1[M+ H]+.
177		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.35-10.60 (1H, m), 8.16 (1H, d, *J* = 2.4 Hz), 7.92 (1H, dd, *J* = 8.8, 2.4 Hz), 7.39 (2H, d, *J* = 8.0 Hz), 7.14-7.25 (1H, m), 7.05-7.12 (3H, m), 6.77 -6.97 (3H, m), 6.38 (1H, s), 6.15-6.33 (1H, m), 4.90-5.10 (1H, m), 4.40-4.70 (2H, m), 1.31 (6H, s); LCMS: 96.3%, MS (ESI); m/z 451.0 [M+ H]+.
178		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (2H, d, *J* = 8.8 Hz), 7.54 (2H, d, *J* = 8.0 Hz), 6.83 (1H, d, *J* = 8.4 Hz), 6.44 (1H, d, *J* = 2.0 Hz), 6.22 (2H, dd, *J* = 8.0, 2.0 Hz), 4.28-4.35 (1H, m), 3.70-3.79 (1H, m), 3.57-3.68 (1H, m), 3.45-3.51 (2H, m), 2.25-2.35 (1H, m), 2.08-2.20 (1H, m); LCMS: 99.5 %, MS (ESI); m/z 390.9[M+ H]+.
179		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.60-10.89 (1H, m), 7.90 (2H, d, *J* = 8.0 Hz), 7.51 (2H, d, *J* = 8.0 Hz), 6.74-7.00 (1H, m), 6.14-6.45 (2H, m), 5.63-5.96 (1H, m), 4.31 (2H, d, *J* = 4.8 Hz), 3.83 (3H, s), 2.94 (3H, s), 2.93 (3H, s); LCMS: 99.3%, MS (ESI); m/z 324.9[M+ H]+.
180		off-white powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 10.29 (1H, brs), 7.42 (2H, d, *J* = 7.2 Hz), 7.36 (2H, t, *J* = 7.6 Hz), 7.28 (1H, t, *J* = 7.2 Hz), 7.18-7.24 (2H, m), 6.83-6.95 (3H, m), 6.58 (1H, brs), 6.27 (1H, d, *J* = 1.6 Hz), 6.13 (1H, d, *J* = 8.0 Hz), 5.71 (1H, brs), 5.52 (1H, t, *J* = 6.4 Hz), 4.81 (2H, t, *J* = 6.0 Hz), 4.31-4.49 (3H, m), 3.63 (2H, t, *J* = 6.0 Hz); LCMS: 99.1%, MS (ESI); m/z 435.0[M+H]+.

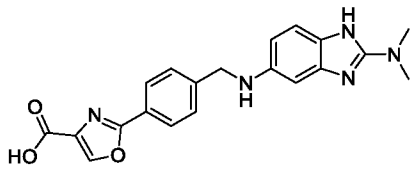
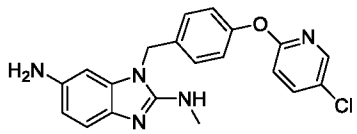
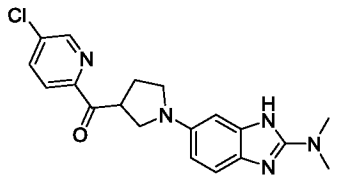
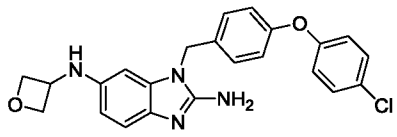
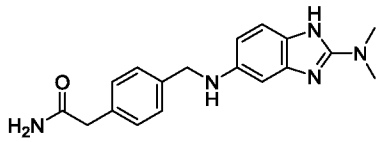
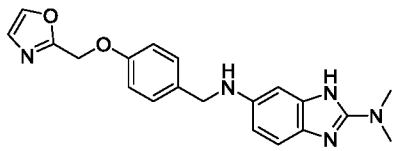
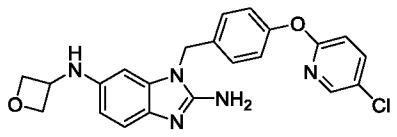
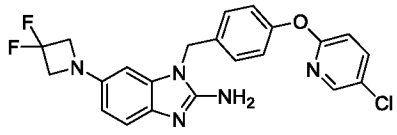
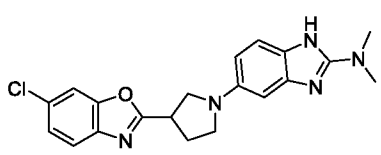
181		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.44 (1H, d, *J* = 4.0 Hz), 7.77 (1H, t, *J* = 7.2 Hz), 7.50 (1H, d, *J* = 8.0 Hz), 7.25-7.36 (4H, m), 7.16-7.25 (1H, m), 6.78 (1H, d, *J* = 8.4 Hz), 6.72 (1H, brs), 6.41 (1H, s), 6.19 (1H, d, *J* = 8.0 Hz), 5.32 (1H, s), 4.40 (2H, d, *J* = 4.4 Hz), 3.29 (3H, s); LCMS: 96.7%, MS (ESI); m/z 359.9[M+ H]+.
182		pale green powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 9.12 (1H, brs), 7.40-7.55 (4H, m), 7.15 (1H, d, *J* = 8.4 Hz), 7.07 (2H, d, *J* = 8.4 Hz), 6.99-7.02 (2H, m), 6.65 (1H, s), 6.59 (1H, d, *J* = 8.8 Hz), 4.62 (2H, d, *J* = 5.6 Hz), 3.72-3.80 (2H, m), 3.60 (3H, s), 3.14-3.23 (2H, m), 1.95-2.06 (2H, m); LCMS: 96.6 %, MS (ESI); m/z 419.0[M + H]+.
183		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.27 (2H, d, *J* = 8.8 Hz), 7.00-7.12 (3H, m), 6.79 (1H, s), 6.95 (1H, d, *J* = 8.4 Hz), 4.49-4.61 (1H, m), 3.48-3.55 (1H, m), 3.19-3.24 (1H, m), 3.05 (6H, s), 2.73-2.89 (2H, m), 1.98-2.10 (1H, m), 1.80-1.90 (1H, m), 1.62-1.76 (1H, m), 1.45-1.58 (1H, m); LCMS: 100%, MS (ESI); m/z 421.0[M+H]+.
184		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.37-7.44 (4H, m), 6.86-7.04 (6H, m), 6.17-6.28 (2H, m), 5.82 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.0 Hz), 4.46-4.56 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.43 (3H, s); LCMS: 98.4%, MS (ESI); m/z 434.9 [M+H]+.
185		pale yellow powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 10.65-10.86 (1H, m), 7.26 (2H, d, *J* = 8.0 Hz), 7.05-7.18 (2H, m), 6.95-7.04 (2H, m), 6.81-6.95 (3H, m), 6.20-6.45 (2H, m), 5.45-5.66 (1H, m), 4.49 (2H, s), 4.04-4.21 (4H, m), 2.97 (3H, s), 2.94 (3H, s), 1.17 (3H, t, *J* = 7.2 Hz); Based on H NMR, it is a mixture of tautomers; LCMS: 99.3 %, MS (ESI); m/z 462.1[M + H]+.
186		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.91 (1H, s), 7.38-7.40 (2H, m), 7.30-7.33 (2H, m), 6.89 (1H, d, *J* = 8.4 Hz), 6.48 (1H, d, *J* = 2.0 Hz), 6.30 (1H, dd, *J* = 8.4, 2.0 Hz), 4.34 (2H, s), 4.13 (2H, s); LCMS: 100%, MS (ESI); m/z 354.1 [M+H]+.
187		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.39-7.43 (2H, m), 7.21 (2H, d, *J* = 8.4 Hz), 6.96-7.03 (5H, m), 6.36-6.40 (3H, m), 5.26 (2H, s), 3.53 (2H, s), 1.32 (6H, s); LCMS: 100%, MS (ESI); m/z 437.0[M+H]+.
188		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.16-10.45 (1H, m), 8.44 (1H, d, *J* = 4.4 Hz), 7.77 (1H, t, *J* = 7.6 Hz), 7.51 (1H, d, *J* = 7.6 Hz), 7.26-7.35 (4H, m), 7.17-7.25 (1H, m), 6.55-6.88 (2H, m), 6.39 (1H, d, *J* = 1.6 Hz), 6.17 (1H, brs), 5.42 (1H, s), 4.20-4.63 (4H, m), 3.40-3.49 (2H, q, *J* = 6.8 Hz), 1.17 (3H, t, *J* = 7.0 Hz); LCMS: 95.4%, MS (ESI); m/z 373.8[M+ H]+.
189		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.29-10.48 (1H, m), 8.40-8.49 (1H, m), 7.72-7.82 (1H, m), 7.50 (1H, d, *J* = 7.6 Hz), 7.26-7.35 (4H, m), 7.19-7.26 (1H, m), 6.79-6.90 (2H, m), 6.24 (1H, d, *J* = 4.8 Hz), 6.06-6.17 (1H, m), 5.59-5.79 (1H, m), 5.32 (1H, s), 4.81 (2H, t, *J* = 6.0 Hz), 4.30-4.50 (5H, m), 3.29 (3H, s); LCMS: 95.7%, MS (ESI); m/z 416.0[M+ H]+.

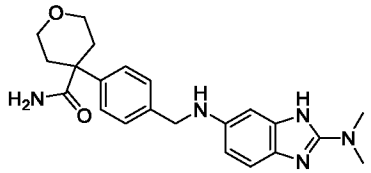
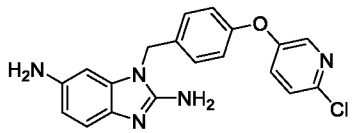
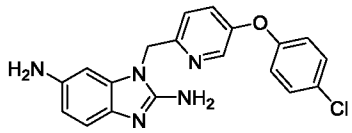
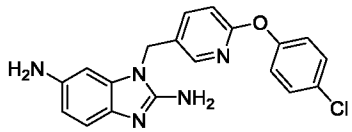
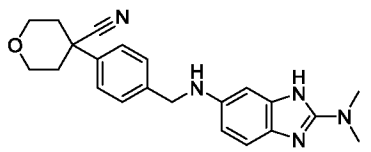
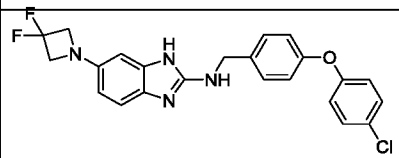
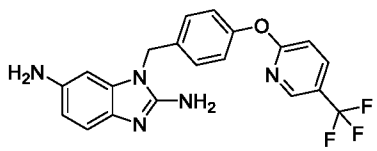
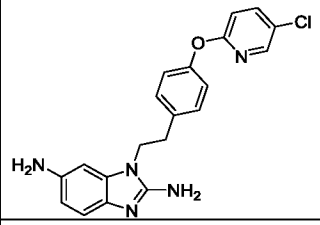
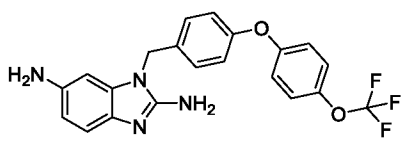
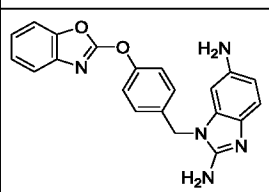
190		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.67-10.95 (1H, m), 8.18 (2H, d, *J* = 8.8 Hz), 7.53 (2H, d, *J* = 8.4 Hz), 6.88-7.07 (1H, m), 6.12-6.54 (2H, m), 4.23-4.40 (1H, m), 3.53 (1H, t, *J* = 8.8 Hz), 3.37-3.43 (1H, m, overlap with H2O signal), 3.20-3.30 (2H, m, overlap with H2O signal), 2.97 (6H, s), 2.25-2.34 (1H, m), 2.10-2.21 (1H, m); LCMS: 97.4%, MS (ESI, TOF); m/z 419.1985[M+H]+.
191		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.74-10.84 (1H, m), 7.32-7.42 (4H, m), 7.03 (2H, d, *J* = 9.2 Hz), 6.95 (2H, d, *J* = 8.4 Hz), 6.51-6.64 (1H, m), 6.05-6.18 (1H, m), 4.58-4.75 (1H, m), 4.43-4.50 (1H, m), 3.76-4.02 (1H, m), 2.96-2.98 (6H, m), 1.42-1.47 (3H, m); LCMS: 96.6%, MS (ESI); m/z 486.9 [M+ H]+.
192		pale brown powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.35-7.51 (4H, m), 6.91-7.06 (6H, m), 6.25 (1H, d, *J* = 2.0 Hz), 6.09 (1H, dd, *J* = 8.4, 2.0 Hz), 5.50 (1H, d, *J* = 6.8 Hz), 4.46-4.57 (3H, m), 3.90-4.05 (2H, m), 3.44 (3H, s), 3.30-3.45 (2H, m); LCMS: 96.0%, MS (ESI); m/z 435.0[M + H]+.
193		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.36-7.45 (4H, m), 7.01-7.09 (2H, m), 6.93-7.01 (4H, m), 6.43 (1H, d, *J* = 2.0 Hz), 6.21 (1H, dd, *J* = 8.4, 2.0 Hz), 4.51 (2H, d, *J* = 6.0 Hz), 4.17 (4H, t, *J* = 12.0 Hz), 3.46 (3H, s); LCMS: 100%, MS (ESI); m/z 455.0[M + H]+.
194		brown powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.92 (2H, d, *J* = 8.8 Hz), 7.08 (2H, d, *J* = 9.2 Hz), 6.95-7.05 (1H, m), 6.21-6.47 (2H, m), 5.20-5.30 (1H, m), 3.82 (3H, s), 3.60-3.70 (1H, m), 3.30-3.36 (3H, m), 2.97 (3H, s), 3.92 (3H, s), 2.37-2.40 (2H, m); LCMS: 95.3%, MS (ESI); m/z 380.8 [M+H]+.
195		off-white power; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.15 (1H, d, *J* = 2.8 Hz), 7.92 (1H, dd, *J* = 8.8, 2.8 Hz), 7.19 (2H, d, *J* = 8.4 Hz), 7.03-7.12 (3H, m), 6.82 (1H, d, *J* = 8.4 Hz), 6.32 (1H, d, *J* = 1.6 Hz), 6.25 (1H, dd, *J* = 8.0, 2.0 Hz), 6.14 (2H, brs), 5.11 (2H, s), 4.49 (2H, brs); LCMS: 97.1%, MS (ESI); m/z 365.9[M+H]+.
196		yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.40-7.60 (5H, m), 7.06 (1H, d, *J* = 8.4 Hz), 6.45-6.60 (2H, m), 6.32-6.37 (1H, m), 4.34 (2H, s), 3.83 (3H, s), 3.10 (6H, s); LCMS: 98.1%, MS (ESI); m/z 346.8[M+ H]+.
197		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.74 (1H, brs), 8.68 (1H, s), 7.90-8.05 (4H, m), 7.49 (2H, d, *J* = 8.0 Hz), 6.87 (1H, d, *J* = 6.8 Hz), 6.37 (1H, s), 6.15-6.45 (1H, m), 5.78 (1H, brs), 4.29 (2H, d, *J* = 5.6 Hz), 2.93 (6H, s); LCMS: 100%, MS (ESI); m/z 377.9[M+ H]+.
198		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.37 (1H, brs), 7.20-7.38 (4H, m), 6.52-6.95 (2H, m), 6.41 (1H, d, *J* = 2.0 Hz), 6.18 (1H, d, *J* = 6.4 Hz), 5.63 (1H, d, *J* = 4.0 Hz), 4.67 (1H, d, *J* = 4.0 Hz), 4.17-4.56 (4H, m), 1.06 (3H, s), 0.86 (3H, s); LCMS: 100%, MS (ESI); m/z 379.1[M+ H]+.
199		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.14 (1H, d, *J* = 2.4 Hz), 7.92 (1H, dd, *J* = 8.4, 2.4 Hz), 7.21 (2H, d, *J* = 8.4 Hz), 7.01-7.02 (3H, m), 6.74 (1H, d, *J* = 8.4 Hz), 6.41 (1H, d, *J* = 1.2 Hz), 6.29 (2H, brs), 6.14 (1H, dd, *J* = 8.4, 2.0 Hz), 5.11 (2H, s), 4.39 (2H, brs); LCMS: 92.3%, MS (ESI); m/z 365.8[M+H]+.

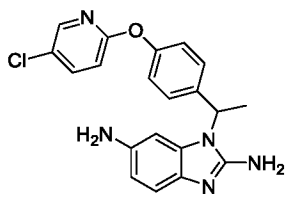
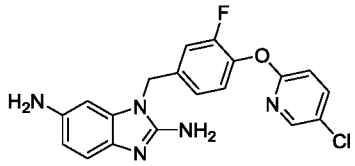
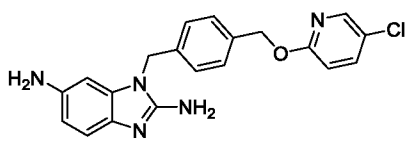
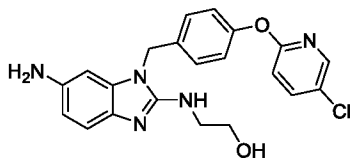
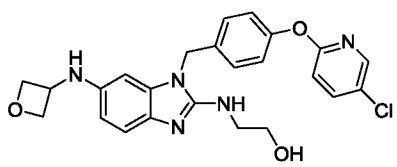
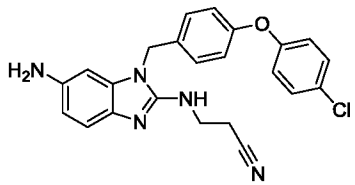
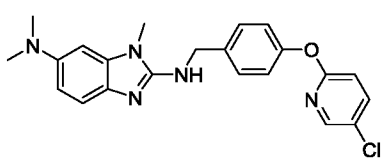
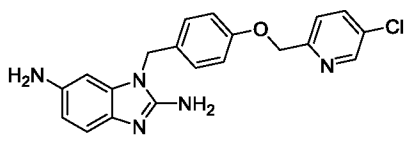
200		yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.25-10.60 (1H, m), 7.35-7.60 (5H, m), 6.65-7.00 (2H, m), 6.41 (1H, s), 6.35 (1H, d, *J* = 1.6 Hz), 6.10-6.25 (1H, m), 4.25-4.60 (4H, m), 3.82 (3H, s); LCMS: 100%, MS (ESI); m/z 318.9[M+ H]+.
201		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.40-10.60 (1H, m), 7.40-7.50 (5H, m), 6.80-7.10 (2H, m), 6.35 (1H, d, *J* = 2.0 Hz), 6.26 (1H, s), 6.10-6.20 (1H, m), 5.60-5.80 (1H, m), 4.81 (1H, t, *J* = 6.0 Hz), 4.30-4.60 (5H, m), 3.83 (3H, s); LCMS: 99.8%, MS (ESI); m/z 374.9[M+ H]+.
202		red amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.76-10.90 (1H, m), 8.38 (2H, d, *J* = 6.0 Hz), 6.90-7.03 (3H, m), 6.37-6.47 (1H, m), 6.17-6.30 (1H, m), 5.24-5.26 (1H, m), 3.64-3.71 (1H, m), 3.30-3.32 (3H, m), 2.99 (3H, s), 2.97 (3H, s), 2.37-2.45 (1H, m), 2.16-2.25 (1H, m); LCMS: 100%, MS (ESI); m/z 324.1[M+ H]+.
203		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.18 (1H, d, *J* = 2.4 Hz), 7.94 (1H, dd, *J* = 8.8, 2.4 Hz), 7.42 (2H, d, *J* = 8.4 Hz), 7.05-7.10 (3H, m), 6.88 (1H, d, *J* = 8.0 Hz), 6.60 (1H, t, *J* = 6.0 Hz), 6.46 (1H, d, *J* = 2.0 Hz), 6.28 (1H, dd, *J* = 8.0, 2.0 Hz), 5.26 (1H, s), 4.40-4.60 (4H, m), 3.75 (2H, s), 1.19 (6H, s); LCMS: 100%, MS (ESI); m/z 438.0[M+ H]+.
204		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.37-7.43 (2H, m), 7.24 (2H, d, *J* = 8.8 Hz), 6.92-7.03 (5H, m), 6.62 (1H, t, *J* = 5.2 Hz), 6.14-6.21 (2H, m), 5.82 (1H, d, *J* = 6.8 Hz), 5.14 (2H, s), 5.00 (1H, brs), 4.77 (2H, t, *J* = 6.4 Hz), 4.38-4.48 (1H, m), 4.29-4.37 (2H, m), 3.52-3.59 (2H, m), 3.30-3.45 (2H, m); LCMS: 99.4%, MS (ESI); m/z 465.0 [M+H]+.
205		off-white amorphous; 1H NMR (DMSO-*d*6, t = 80 °C, 400 MHz); δ 10.15 (1H, brs), 7.60-7.67 (2H, m), 7.46-7.52 (2H, m), 6.83 (1H, d, *J* = 8.4 Hz), 6.40-6.60 (2H, m), 6.24 (1H, d, *J* = 7.6 Hz), 4.56 (2H, s), 4.17 (2H, brs), 1.49-1.56 (6H, m); LCMS: 98.9%, MS (ESI); m/z 377.0[M+ H]+.
206		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.42 (2H, d, *J* = 8.8 Hz), 7.17 (2H, d, *J* = 8.4 Hz), 6.95-7.10 (5H, m), 6.38 (2H, d, *J* = 8.8 Hz), 6.32 (1H, s), 5.17-5.28 (2H, m), 4.99 (1H, brs), 4.25-4.35 (1H, m), 3.50-3.70 (2H, m), 3.10-3.22 (2H, m), 1.92-1.95 (1H, m), 1.70-1.80 (1H, m); LCMS: 97.8%, MS (ESI); m/z 434.9[M+H]+.
207		off-white powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 7.38-7.43 (2H, m), 7.25 (2H, d, *J* = 8.4 Hz), 7.05 (1H, t, *J* = 6.4 Hz), 6.96-7.02 (4H, m), 6.89 (1H, d, *J* = 8.4 Hz), 6.32 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.4, 2.0 Hz), 5.14 (2H, s), 4.54 (2H, brs), 4.10 (2H, q, *J* = 7.2 Hz), 4.05 (2H, d, *J* = 6.0 Hz), 1.19 (3H, t, *J* = 7.2 Hz); LCMS: 98.5%, MS (ESI); m/z 451.0[M+H]+.
208		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.18 (1H, d, *J* = 2.4 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.41 (2H, d, *J* = 8.4 Hz), 7.08 (3H, d, *J* = 8.8 Hz), 6.95 (1H, d, *J* = 8.4 Hz), 6.64 (1H, t, *J* = 6.0 Hz), 6.35 (1H, d, *J* = 1.6 Hz), 6.22 (1H, dd, *J* = 8.4, 2.0 Hz), 5.80 (1H, d, *J* = 7.6 Hz), 5.22 (1H, s), 4.83 (2H, t, *J* = 6.4 Hz), 4.47-4.59 (3H, m), 4.32-4.44 (2H, m), 3.80 (2H, s), 1.18 (6H, s); LCMS: 100%, MS (ESI); m/z 494.0[M+ H]+.

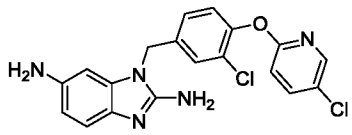
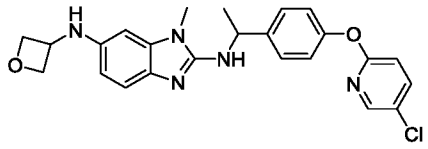
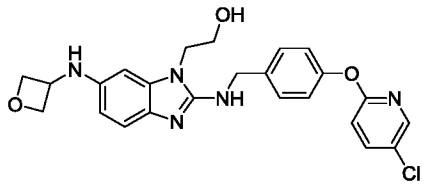
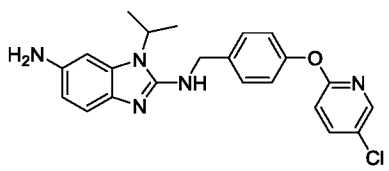
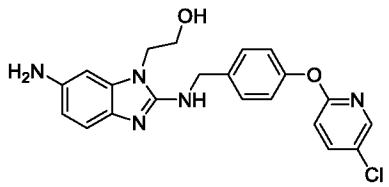
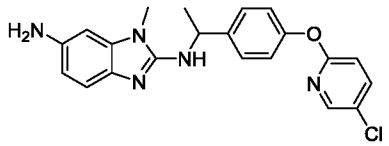
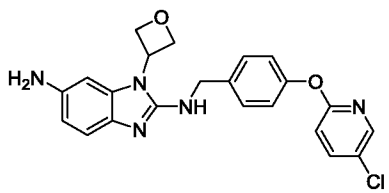
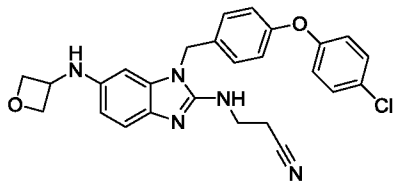
209		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.36-7.46 (4H, m), 6.95-7.04 (4H, m), 6.88 (1H, d, *J* = 8.4 Hz), 6.55 (1H, t, *J* = 6.0 Hz), 6.45 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.4, 2.0 Hz), 5.23 (1H, brs), 4.45-4.50 (4H, m), 3.74 (2H, s), 1.18 (6H, s); LCMS: 100%, MS (ESI); m/z 437.0[M+ H]+.
210		white power; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.18 (1H, d, *J* = 2.4 Hz), 7.94 (1H, dd, *J* = 8.8, 2.4 Hz), 7.44 (2H, d, *J* = 8.4 Hz), 7.04-7.13 (3H, m), 6.82-6.97 (2H, m), 6.37 (1H, d, *J* = 1.6 Hz), 6.28 (1H, dd, *J* = 8.0, 1.6 Hz), 4.42-4.65 (4H, m), 3.42 (3H, s); LCMS: 99.7%, MS (TOF, ESI); m/z 380.1267[M+H]+.
211		off-white power; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.4 Hz), 7.95 (1H, dd, *J* = 8.4, 2.4 Hz), 7.33-7.51 (3H, m), 7.05-7.18 (3H, m), 6.99 (1H, d, *J* = 8.8 Hz), 6.21-6.37 (2H, m), 5.99 (1H, d, *J* = 2.0 Hz), 4.86 (2H, t, *J* = 6.4 Hz), 4.48-4.61 (3H, m), 4.41 (2H, t, *J* = 6.0 Hz), 3.49 (3H, s); LCMS: 99.2%, MS (ESI); m/z 436.0[M+H]+.
212		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.54-10.91 (1H, m), 7.43 (1H, s), 7.23 (2H, d, *J* = 8.4 Hz), 6.95-7.19 (5H, m), 6.75-6.91 (3H, m), 6.37 (1H, s), 6.28 (1H, d, *J* = 7.6 Hz), 5.52 (1H, brs), 4.05-4.21 (4H, m), 2.93 (6H, s); LCMS: 99.0 %, MS (ESI); m/z 432.9[M + H]+.
213		pale-yellow powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 8.04 (1H, s), 7.25 (2H, d, *J* = 8.4 Hz), 7.06-7.18 (5H, m), 6.88-6.97 (3H, m), 6.42 (1H, d, *J* = 1.6 Hz), 6.38 (1H, d, *J* = 8.4 Hz), 5.78 (1H, brs), 5.01 (2H, s), 4.15 (2H, s), 3.01 (6H, s); LCMS: 97.6 %, MS (ESI); m/z 457.0[M+ H]+.
214		white powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 10.64-10.86 (1H, m), 10.19 (1H, brs), 7.63 (2H, d, *J* = 9.2 Hz), 7.41 (1H, d, *J* = 10.4 Hz), 7.33 (2H, d, *J* = 8.8 Hz), 6.80-6.96 (1H, m), 6.45-6.55 (1H, m), 6.24-6.40 (1H, m), 5.15-5.43 (1H, m), 4.02 (2H, t, *J* = 5.2 Hz), 2.96 (3H, s), 2.93 (3H, s); LCMS: 100%, MS (ESI); m/z 382.9[M+ H]+.
215		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.31-10.49 (1H, m), 7.29-7.46 (4H, m), 6.88-7.06 (4H, m), 6.65-6.88 (2H, m), 6.41 (1H, d, *J* = 6.4 Hz), 6.15-6.29 (1H, m), 4.50-4.81 (3H, m), 4.34-4.50 (2H, m), 3.55-3.71 (1H, m), 3.04-3.18 (1H, m), 2.70-2.91 (1H, m); LCMS: 100%, MS (ESI); m/z 439.0[M + H]+.
216		white powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 11.86 (1H, brs), 10.60-10.82 (1H, m), 7.19-7.25 (2H, m), 7.02-7.18 (4H, m), 6.74-7.00 (5H, m), 6.35-6.38 (1H, m), 6.18-6.31 (1H, m), 5.39-5.65 (1H, m), 4.80 (2H, s), 4.10 (2H, s), 2.94 (3H, s), 2.92 (3H, s); LCMS: 99.1 %, MS (ESI); m/z 456.0[M+ H]+.
217		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.41 (2H, d, *J* = 8.8 Hz), 7.33 (1H, brs), 7.25 (1H, d, *J* = 8.0 Hz), 6.94-7.06 (5H, m), 6.89 (1H, d, *J* = 8.0 Hz), 6.77 (1H, t, *J* = 6.0 Hz), 6.32 (1H, s), 6.27 (1H, d, *J* = 8.4 Hz), 5.13 (2H, s), 4.53 (2H, brs), 3.84 (2H, d, *J* = 5.6 Hz); LCMS: 99.4%, MS (ESI); m/z 422.0 [M+ H]+.

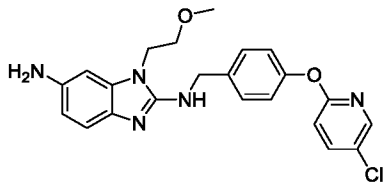
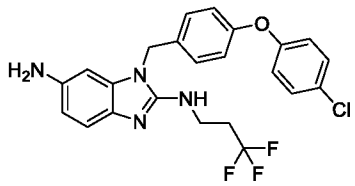
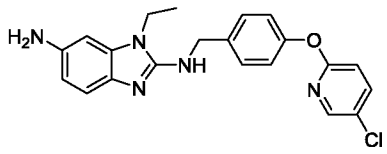
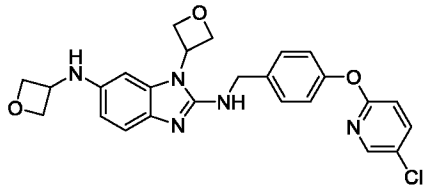
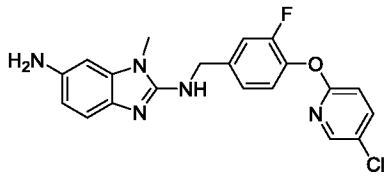
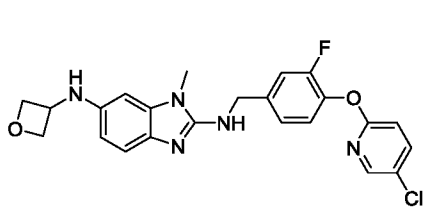
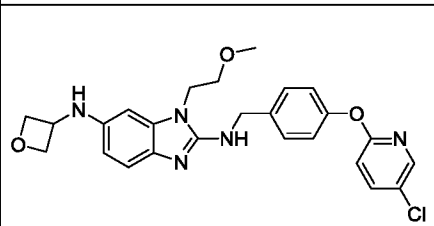
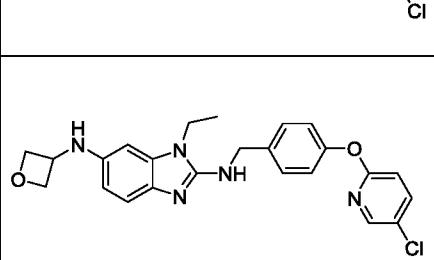
218		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.92 (1H, s), 7.98 (2H, d, *J* = 8.4 Hz), 7.55 (2H, d, *J* = 8.4 Hz), 7.09 (1H, d, *J* = 8.4 Hz), 6.49-6.59 (2H, m), 6.46 (1H, d, *J* = 2.0 Hz), 4.38 (2H, d, *J* = 5.2 Hz), 4.31 (2H, q, *J* = 7.2 Hz), 3.12 (6H, s), 1.30 (3H, t, *J* = 7.2 Hz); LCMS: 98.7%, MS (ESI); m/z 406.0[M+ H]+.
219		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.36-7.44 (1H, m), 7.17 (1H, d, *J* = 8.4 Hz), 6.95-7.03 (4H, m), 6.90 (1H, d, *J* = 8.4 Hz), 6.42 (1H, q, *J* = 4.4 Hz), 6.31 (1H, d, *J* = 2.0 Hz), 6.26 (1H, dd, *J* = 8.0, 2.0 Hz), 5.07 (2H, s), 4.50 (2H, brs), 2.85 (3H, d, *J* = 4.4 Hz); LCMS: 97.7%, MS (ESI); m/z 378.9 [M+ H]+.
220		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.18 (1H, s), 7.92 (2H, d, *J* = 8.4 Hz), 7.52 (2H, d, *J* = 8.4 Hz), 7.35 (1H, s), 6.91 (1H, d, *J* = 8.0 Hz), 6.37 (1H, *J* = 2.0 Hz), 6.34 (1H, *J* = 8.0, 2.0 Hz), 5.92 (1H, brs), 4.31 (2H, s), 2.97 (6H, s); LCMS: 100%, MS (ESI); m/z 333.9[M+ H]+.
221		yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 11.56 (1H, brs), 10.68-10.79 (1H, m), 7.70 (2H, d, *J* = 6.8 Hz), 7.45-7.53 (3H, m), 6.82-6.89 (1H, m), 6.50-6.60 (1H, m), 6.26-6.35 (3H, m), 5.71-5.83 (1H, m), 4.25-4.35 (2H, m), 2.94 (3H, s), 2.93 (3H, s); LCMS: 98.9%, MS (ESI); m/z 359.9[M+ H]+.
222		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.21 (1H, d, *J* = 2.4 Hz), 7.65 (1H, dd, *J* = 8.8, 2.4 Hz), 7.30 (2H, d, *J* = 8.4 Hz), 7.08 (2H, dd, *J* = 6.8, 2.4 Hz), 7.00 (1H, d, *J* = 8.4 Hz), 6.89 (1H, d, *J* = 8.8 Hz), 6.56 (1H, s), 6.43 (1H, d, *J* = 7.2 Hz), 4.42 (2H, d, *J* = 5.2 Hz), 4.20-4.30 (1H, m), 4.10-4.18 (2H, m), 3.95-4.05 (2H, m), 3.80-3.90 (1H, m), 3.55-3.65 (1H, m), 2.80-2.90 (1H, m), 2.65-2.75 (1H, m); LCMS: 98.1%, MS (ESI); m/z 515.0[M+ H]+.
223		pale-yellow amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.54 (1H, d, *J* = 2.8 Hz), 7.88 (1H, d, *J* = 8.8 Hz), 7.45-7.52 (3H, m), 7.17 (2H, d, *J* = 8.8 Hz), 6.84-6.93 (2H, m), 6.37 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.4, 2.0 Hz), 4.50-4.58 (4H, m); 3.41 (3H, s); LCMS: 100%, MS (ESI); m/z 414.0 [M+ H]+.
224		pale-yellow amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.32-8.37 (2H, m), 7.35-7.46 (4H, m), 7.03 (2H, *J* = 8.8 Hz), 6.83-6.88 (2H, m), 6.36 (1H, d, *J* = 2.8 Hz), 6.24-6.28 (1H, m), 4.53 (2H, brs), 4.50 (2H, d, *J* = 6.0 Hz), 3.40 (3H, s); LCMS: 100%, MS (ESI); m/z 345.9 [M+ H]+.
225		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 9.68 (1H, brs), 7.35-7.48 (5H, m), 6.96-7.17 (6H, m), 5.49 (2H, brs), 4.29 (2H, d, *J* = 6.4 Hz); LCMS: 100%, MS (ESI); m/z 423.0[M+H]+.
226		pale-yellow amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.53 (1H, d, *J* = 2.8 Hz), 7.87 (1H, d, *J* = 8.8 Hz), 7.45-7.54 (3H, m), 7.16 (2H, d, *J* = 8.8 Hz), 6.91-6.99 (2H, m), 6.25 (1H, d, *J* = 2.0 Hz), 6.21 (1H, dd, *J* = 8.4, 2.4 Hz), 5.84 (1H, d, *J* = 6.8 Hz), 4.80-4.88 (2H, m), 4.48-4.56 (3H, m), 4.39 (2H, t, *J* = 6.8 Hz), 3.44 (3H, s); LCMS: 100%, MS (ESI); m/z 469.9 [M+ H]+.
227		pale-yellow amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.32-8.36 (2H, m), 7.35-7.46 (4H, m), 7.03 (2H, d, *J* = 8.8 Hz), 6.89-6.96 (2H, m), 6.18-6.26 (2H, m), 5.83 (1H, d, *J* = 7.2 Hz), 4.84 (2H, d, *J* = 6.4 Hz), 4.48-4.55 (3H, m), 4.39 (2H, t, *J* = 5.6 Hz), 3.43 (3H, s); LCMS:

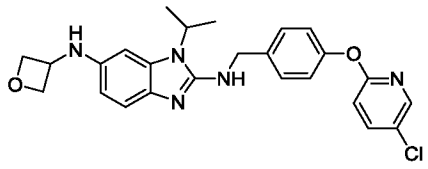
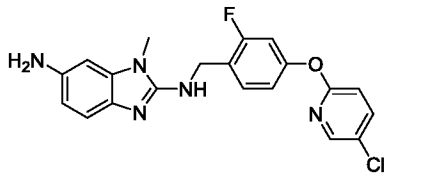
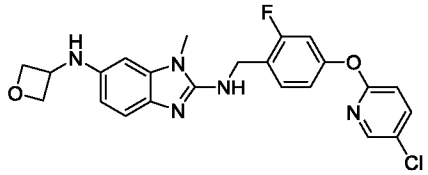
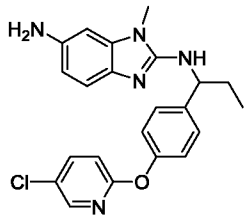
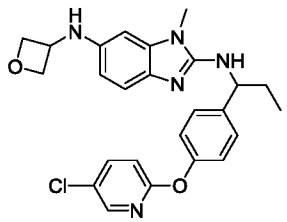
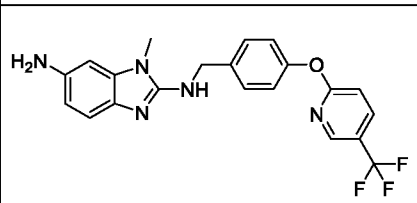
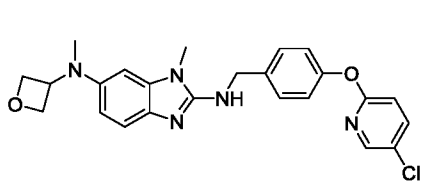
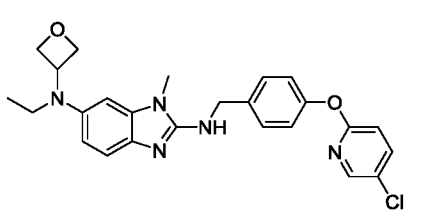
		100%, MS (ESI); m/z 402.2 [M+ H]+.
228		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.71 (1H, s), 7.94 (2H, d, *J* = 8.4 Hz), 7.54 (2H, d, *J* = 8.0 Hz), 6.91 (1H, d, *J* = 8.4 Hz), 6.27-6.43 (2H, m), 4.32 (2H, s), 2.97 (6H, s); LCMS: 97.9%, MS (ESI); m/z 377.9[M+ H]+.
229		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.16 (1H, d, *J* = 2.4 Hz), 7.94 (1H, dd, *J* = 8.8, 2.8 Hz), 7.17 (2H, d, *J* = 8.4 Hz), 7.04-7.12 (3H, m), 6.91 (1H, d, *J* = 8.4 Hz), 6.44 (1H, brs), 6.33 (1H, d, *J* = 2.0 Hz), 6.26 (1H, dd, *J* = 8.0, 1.6 Hz), 5.10 (2H, s), 4.51 (2H, brs), 2.86 (3H, d, *J* = 4.4 Hz); LCMS: 100.0%, MS (ESI); m/z 379.9[M+H]+.
230		pale yellow powder; 1H NMR (DMSO-*d*6+D2O, 400 MHz); δ 8.72 (1H, s), 7.94-8.11 (2H, m), 7.03 (1H, d, *J* = 8.0 Hz), 6.47 (1H, s), 6.32 (1H, d, *J* = 7.6 Hz), 4.40-4.54 (1H, m), 3.44-3.56 (1H, m), 3.29-3.40 (1H, m), 3.14-3.29 (2H, m), 2.97 (6H, s), 2.04-2.21 (1H, m), 2.22-2.35 (1H, m); LCMS: 100%, MS (ESI); m/z 369.9[M+ H]+.
231		white powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 7.36-7.43 (1H, m), 7.25 (1H, d, *J* = 8.8 Hz), 6.94-7.04 (2H, m), 6.89 (1H, d, *J* = 8.4 Hz), 6.14-6.23 (4H, m), 5.78 (1H, d, *J* = 6.8 Hz), 5.13 (2H, s), 4.78 (2H, t, *J* = 6.4 Hz), 4.38-4.80 (1H, m), 4.29-4.37 (2H, t, *J* = 6.0 Hz); LCMS: 98.8%, MS (ESI); m/z 421.0 [M+H]+.
232		white powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 10.60-10.80 (1H, m), 7.40-7.50 (1H, m), 7.27 (2H, d, *J* = 8.0 Hz), 7.17 (2H, d, *J* = 7.2 Hz), 6.80-6.95 (2H, m), 6.15-6.45 (2H, m), 5.45-5.75 (1H, m), 4.17 (2H, s), 3.30 (2H, s), 2.93 (3H, s), 2.91 (3H, s); LCMS: 95.2%, MS (ESI); m/z 324.0[M+ H]+.
233		pale-yellow powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 10.60-10.80 (1H, m), 8.14 (1H, s), 7.28 (2H, d, *J* = 8.4 Hz), 7.24 (1H, s), 6.95 (2H, d, *J* = 6.8 Hz), 6.77-6.91 (1H, m), 6.17-6.40 (2H, m), 5.44-5.65 (1H, m), 5.17 (2H, s), 4.13 (2H, s), 2.94 (3H, s), 2.91 (3H, s); LCMS: 98.8 %, MS (ESI); m/z 364.1[M+ H]+.
234		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.16 (1H, d, *J* = 2.4 Hz), 7.94 (1H, dd, *J* = 8.8, 2.8 Hz), 7.26 (2H, d, *J* = 8.8 Hz), 7.05-7.13 (3H, m), 6.91 (1H, d, *J* = 8.4 Hz), 6.13-6.25 (4H, m), 5.79 (1H, d, *J* = 7.2 Hz), 5.16 (2H, s), 4.79 (2H, t, *J* = 6.4 Hz), 4.40-4.50 (1H, m), 4.35 (2H, t, *J* = 6.0 Hz); LCMS: 97.8%, MS (ESI); m/z 421.9[M+H]+.
235		off-white powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 8.16 (1H, d, *J* = 2.4 Hz), 7.94 (1H, dd, *J* = 8.8, 2.8 Hz), 7.24 (2H, d, *J* = 8.4 Hz), 7.07-7.13 (3H, m), 7.03 (1H, d, *J* = 8.4 Hz), 6.45 (1H, d, *J* = 7.6 Hz), 6.33 (2H, brs), 6.23 (1H, dd, *J* = 8.4, 2.0 Hz), 5.22 (2H, s), 4.15 (4H, t, *J* = 12.0 Hz); LCMS: 100.0%, MS (ESI); m/z 442.1[M+H]+.
236		pale-yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.86 (1H, brs), 7.84 (1H, d, *J* = 2.0 Hz), 7.76 (1H, d, *J* = 8.8 Hz), 7.43 (1H, dd, *J* = 8.4, 2.0 Hz), 6.99 (1H, d, *J* = 8.4 Hz), 6.46 (1H, s), 6.27 (1H, d, *J* = 6.4 Hz), 3.85-4.00 (1H, m), 3.63-3.72 (2H, m), 3.35-3.43 (2H, m), 2.98 (3H, s), 2.33-2.45 (2H, m); LCMS: 99.0%, MS (ESI); m/z 382.0 [M+H]+.

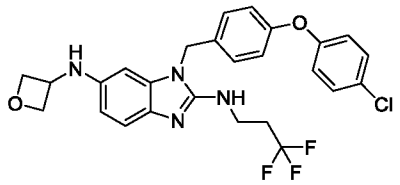
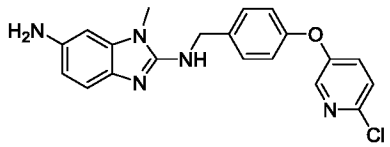
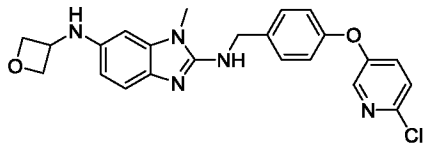
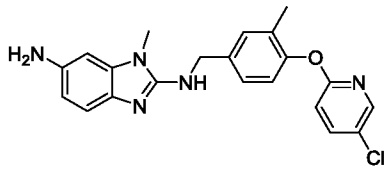
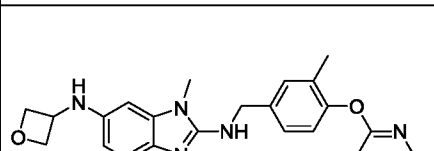
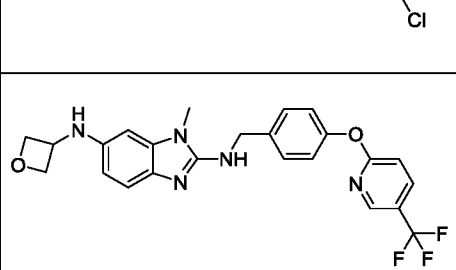
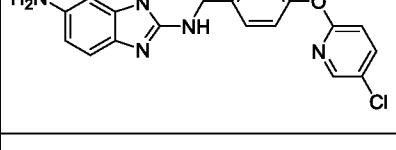
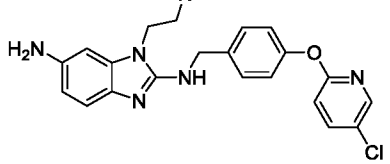
237		yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.72 (1H, brs), 7.25-7.40 (4H, m), 7.15 (1H, d, *J* = 6.8 Hz), 6.95 (1H, s), 6.87 (1H, d, *J* = 7.6 Hz), 6.37 (1H, s), 6.29 (1H, s), 5.63 (1H, brs), 4.19 (2H, d, *J* = 6.0 Hz), 3.68-3.79 (2H, m), 3.44-3.53 (2H, m), 2.94 (6H, s), 2.36-2.45 (2H, m), 1.71-1.83 (2H, m); LCMS: 97.1 %, MS (ESI); m/z 394.1[M+ H]+.
238		white powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 8.20 (1H, s), 7.45-7.54 (2H, m), 7.23 (2H, d, *J* = 8.4 Hz), 7.08 (2H, d, *J* = 8.8 Hz), 6.31 (1H, s), 6.26 (1H, dd, *J* = 2.0, 8.0 Hz), 6.10 (2H, s), 5.11 (2H, s), 4.48 (2H, s); LCMS: 99.8 %, MS (ESI); m/z 365.9[M+ H]+.
239		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.37 (1H, d, *J* = 2.8 Hz), δ 7.43-7.47 (3H, m), 7.00-7.07 (2H, m), 7.01 (1H, d, *J* = 8.8 Hz), 6.84 (1H, d, *J* = 8.0 Hz), 6.25-6.28 (2H, m), 6.09 (2H, brs), 5.18 (2H, s), 4.49 (2H, brs); LCMS: 100%, MS (ESI); m/z 366.0 [M+H]+.
240		grey powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.08 (1H, s), 7.64 (1H, d, *J* = 8.4 Hz), 7.44 (2H, d, *J* = 8.4 Hz), 7.14 (2H, d, *J* = 8.8 Hz), 7.04 (1H, d, *J* = 8.8 Hz), 6.82 (1H, d, *J* = 8.0 Hz), 6.37 (1H, s), 6.26 (1H, d, *J* = 8.4 Hz), 6.17 (2H, brs), 5.10 (2H, s), 4.49 (2H, brs); LCMS: 100%, MS (ESI); m/z 366.0 [M+H]+.
241		pale-yellow powder (amorphous) 1H NMR (DMSO-*d*6, 400 MHz); δ 7.41-7.52 (4H, m), 6.88 (2H, d, *J* = 8.4 Hz), 6.36 (1H, d, *J* = 1.6 Hz), 6.31 (1H, d, *J* = 8.4 Hz), 5.75 (1H, brs), 4.25 (2H, d, *J* = 4.4 Hz), 3.94-4.06 (2H, m), 3.60-3.71 (2H, m), 2.95 (6H, s), 1.96-2.13 (4H, m); LCMS: 97.5%, MS (ESI); m/z 376.1[M+ H]+.
242		pale white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.35-7.49 (4H, m), 7.13 (1H, d, *J* = 6.4 Hz), 6.95-7.09 (4H, m), 6.46 (1H, s), 6.32 (1H, d, *J* = 8.4 Hz), 4.53 (2H, d, *J* = 5.6 Hz), 4.22 (4H, t, *J* = 12.0 Hz); LCMS: 100%, MS (ESI); m/z 440.9[M + H]+.
243		white powder; 1H NMR (DMSO-*d*6); δ 8.54 (1H, s), 8.21 (1H, dd, *J* = 8.8, 2.0 Hz), 7.19-7.28 (3H, m), 7.15 (2H, d, *J* = 8.4 Hz), 6.84 (1H, d, *J* = 8.4 Hz), 6.34 (1H, d, *J* = 2.0 Hz), 6.26 (1H, dd, *J* = 8.4, 2.0 Hz), 6.15 (2H, brs), 5.14 (2H, s), 4.50 (2H, brs); LCMS: 97.7%, MS (ESI); m/z 400.0[M+ H]+.
244		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 9.10 (2H, brs), 8.19 (1H, d, *J* = 2.4 Hz), 7.95 (1H, dd, *J* = 8.4, 2.4 Hz), 7.65 (1H, s), 7.48 (1H, d, *J* = 8.4 Hz), 7.39 (2H, d, *J* = 8.4 Hz), 7.29 (1H, d, *J* = 8.0 Hz), 7.06 (2H, d, *J* = 8.4 Hz), 7.00 (1H, d, *J* = 8.8 Hz), 4.42 (2H, t, *J* = 7.4 Hz), 3.01 (2H, t, *J* = 7.4 Hz); LCMS: 100%, MS (ESI); m/z 379.9[M+ H]+.
245		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.36 (2H, d, *J* = 8.8 Hz), 7.23 (2H, d, *J* = 8.8 Hz), 6.98-7.11 (4H, m), 6.84 (1H, d, *J* = 8.0 Hz), 6.32 (1H, d, *J* = 2.0 Hz), 6.26 (1H, dd, *J* = 8.0, 2.0 Hz), 6.12 (2H, brs), 5.11 (2H, s), 4.49 (2H, brs); LCMS: 100 %, MS (ESI); m/z 415.0[M+ H]+
246		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.57-7.65 (1H, m), 7.42-7.54 (3H, m), 7.22-7.33 (4H, m), 6.86 (1H, d, *J* = 8.0 Hz), 6.33 (1H, d, *J* = 1.6 Hz), 6.28 (1H, dd, *J* = 8.0, 1.6 Hz), 6.18 (2H, brs), 5.18 (2H, s), 4.50 (2H, brs); LCMS: 99.7%, MS (ESI); m/z 372.0[M+ H]+.

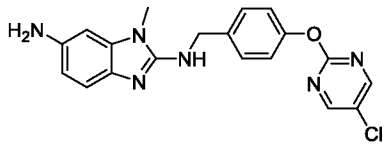
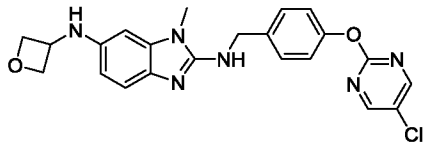
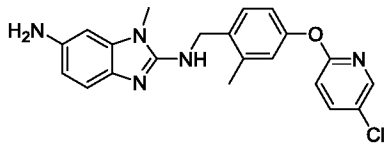
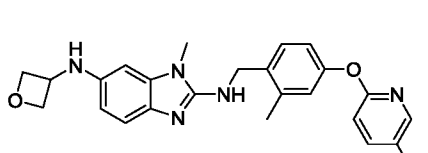
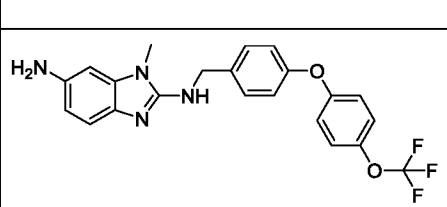
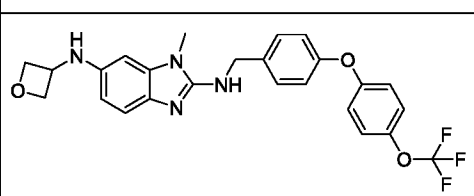
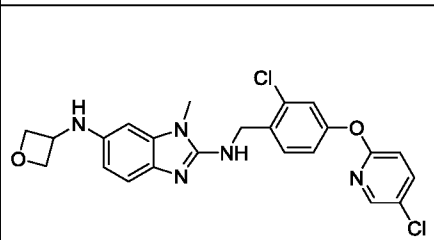
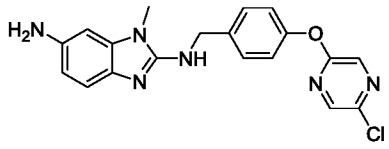
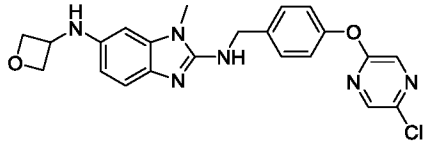
247		yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.18 (1H, d, *J* = 2.4 Hz), δ 7.95 (1H, dd, *J* = 8.8, 2.8 Hz), 7.27 (2H, d, *J* = 8.8 Hz), 7.08-7.14 (3H, m), 6.82 (1H, d, *J* = 8.0 Hz), 6.19-6.24 (2H, m), 6.02 (2H, brs), 5.64 (1H, q, *J* = 7.2 Hz), 4.39 (2H, brs), 1.83 (3H, d, *J* = 7.2 Hz); LCMS: 99.8%, MS (ESI); m/z 380.0 [M+H]+.
248		purple powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.15 (1H, d, *J* = 2.4 Hz), δ 7.97 (1H, dd, *J* = 8.8, 2.4 Hz), 7.31 (1H, t, *J* = 8.4 Hz), 7.20 (1H, d, *J* = 8.8 Hz), 7.14 (1H, d, *J* = 11.2 Hz), 7.01 (1H, d, *J* = 8.0 Hz), 6.87 (1H, d, *J* = 8.4 Hz), 6.43 (2H, brs), 6.38 (1H, s), 6.30 (1H, d, *J* = 7.2 Hz), 5.18 (2H, s); LCMS: 95.5%, MS (ESI); m/z 383.9 [M+H]+.
249		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.20 (1H, d, *J* = 2.4 Hz), 7.80 (1H, dd, *J* = 8.8, 2.8 Hz), 7.38 (2H, d, *J* = 8.0 Hz), 7.14 (2H, d, *J* = 8.0 Hz), 6.91 (1H, d, *J* = 8.8 Hz), 6.79-6.85 (1H, m), 6.24 (2H, dd, *J* = 4.4, 2.0 Hz), 6.08 (2H, brs), 5.27 (2H, s), 5.11 (2H, s), 4.45 (2H, brs); LCMS: 100%, MS (ESI); m/z 379.9 [M+H]+.
250		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.16 (1H, d, *J* = 2.4 Hz), 7.94 (1H, dd, *J* = 8.8, 2.4 Hz), 7.19 (2H, d, *J* = 8.8 Hz), 7.04-7.13 (3H, m), 6.89 (1H, d, *J* = 8.0 Hz), 6.58 (1H, t, *J* = 5.6 Hz), 6.32 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.0, 2.0 Hz), 5.13 (2H, s), 5.05 (1H, brs), 4.52 (2H, brs), 3.53-3.64 (2H, m), 3.36-3.43 (2H, m); LCMS: 100 %, MS (ESI); m/z 410.0[M+ H]+.
251		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.15 (1H, d, *J* = 2.4 Hz), 7.94 (1H, dd, *J* = 8.8, 2.8 Hz), 7.23 (2H, d, *J* = 8.4 Hz), 7.03-7.15 (3H, m), 6.96 (1H, d, *J* = 8.4 Hz), 6.64 (1H, t, *J* = 5.6 Hz), 6.21 (1H, s), 6.17 (1H, d, *J* = 8.4 Hz), 5.83 (1H, d, *J* = 6.8 Hz), 5.16 (2H, s), 4.99 (1H, t, *J* = 5.2 Hz), 4.78 (2H, t, *J* = 6.0 Hz), 4.38-4.50 (1H, m), 4.33 (2H, d, *J* = 6.0 Hz), 3.54-3.63 (2H, m), 3.36-3.44 (2H, m); LCMS: 99.4 %, MS (ESI); m/z 466.0[M+ H]+.
252		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.36-7.43 (2H, m), 7.22 (1H, d, *J* = 8.8 Hz), 6.95-7.02 (5H, m), 6.93 (1H, d, *J* = 8.4 Hz), 6.33 (1H, d, *J* = 2.0 Hz), 6.28 (1H, dd, *J* = 8.0, 2.0 Hz), 5.11 (2H, s), 4.55 (2H, brs), 3.54 (2H, q, *J* = 6.0 Hz), 2.88 (2H, t, *J* = 6.8 Hz); LCMS: 100%, MS (ESI); m/z 418.0[M+H]+.
253		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.4 Hz), 7.93 (1H, dd, *J* = 8.4, 2.4 Hz), 7.44 (2H, d, *J* = 8.4 Hz), 6.93-7.16 (5H, m), 6.60 (1H, d, *J* = 1.6 Hz), 6.46-6.49 (1H, m), 4.54 (2H, d, *J* = 5.6 Hz), 3.49 (3H, s), 2.83 (6H, s); LCMS: 99.9%, MS (ESI); m/z 407.9 [M+H]+.
254		white amorphous; 1H NMR (DMSO-*d*6); δ 8.61 (1H, d, *J* = 2.4 Hz), 7.95 (1H, dd, *J* = 8.4, 2.4 Hz), 7.52 (1H, d, *J* = 8.4 Hz), 7.12 (2H, d, *J* = 8.4 Hz), 6.97 (2H, d, *J* = 8.4 Hz), 6.82 (1H, d, *J* = 8.0 Hz), 6.29 (1H, d, *J* = 1.6 Hz), 6.24 (1H, dd, *J* = 8.0, 2.0 Hz), 6.08 (2H, brs), 5.14 (2H, s), 5.03 (2H, s), 4.45 (2H, s); LCMS: 100%, MS (ESI); m/z 379.9[M+ H]+.

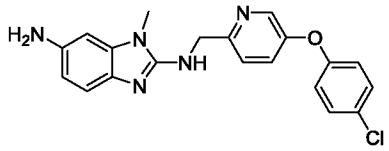
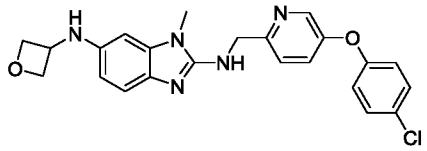
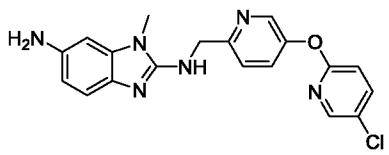
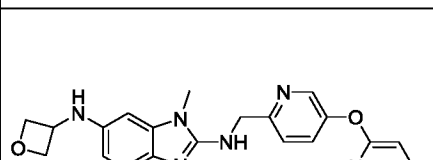
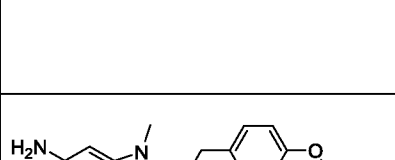
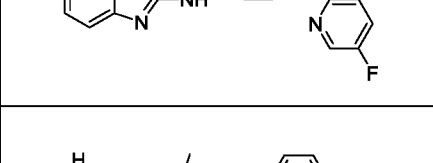
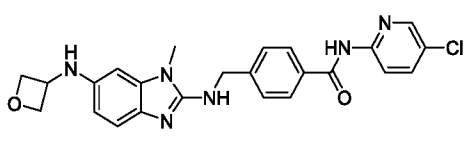
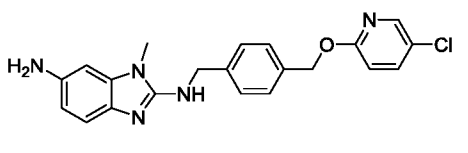
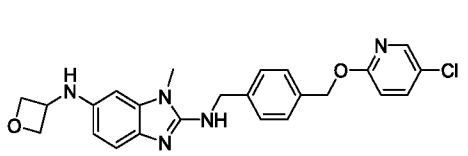
255		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.14 (1H, d, *J* = 2.4 Hz), 7.97 (1H, dd, *J* = 8.4, 2.4 Hz), 7.26-7.37 (2H, m), 7.10-7.22 (2H, m), 6.85 (1H, d, *J* = 8.4 Hz), 6.35 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.0, 1.6 Hz), 6.18 (2H, brs), 5.15 (2H, s), 4.53 (2H, brs); LCMS: 100%, MS (ESI); m/z 399.9[M+ H]+.
256		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.0 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.46 (2H, d, *J* = 8.8 Hz), 7.02-7.10 (3H, m), 6.90 (1H, d, *J* = 8.4 Hz), 6.70 (1H, d, *J* = 8.0 Hz), 6.23 (1H, d, *J* = 2.0 Hz), 6.19 (1H, dd, *J* = 8.4, 2.0 Hz), 5.83 (1H, d, *J* = 7.2 Hz), 5.00-5.12 (1H, m), 4.83 (2H, t, *J* = 6.4 Hz), 4.45-4.55 (1H, m), 4.35-4.40 (2H, m), 3.46 (3H, s), 1.50 (3H, d, *J* = 6.8 Hz); LCMS: 99.6 %, MS (ESI); m/z 450.1 [M+H]+.
257		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.8 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.41 (2H, d, *J* = 8.4 Hz), 6.90-7.00 (3H, m), 6.93 (1H, d, *J* = 8.4 Hz), 6.79 (1H, t, *J* = 6.0 Hz), 6.31 (1H, d, *J* = 1.6 Hz), 6.20 (1H, dd, *J* = 8.4, 2.0 Hz), 5.82 (1H, d, *J* = 7.2 Hz), 5.03 (1H, brs), 4.83 (2H, t, *J* = 6.4 Hz), 4.45-4.56 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.98 (2H, t, *J* = 5.2 Hz), 3.59-3.70 (2H, m); LCMS: 100%, MS (ESI); m/z 466.1[M+ H]+.
258		off-white solid; 1H NMR (CDCl3, 400 MHz); δ 8.11 (1H, d, *J* = 2.4 Hz), 7.66 (1H, dd, *J* = 8.8, *J* = 2.8 Hz), 7.46 (2H, d, *J* = 8.8 Hz), 7.31 (1H, d, *J* = 8.4 Hz), 7.11 (2H, d, *J* = 8.4 Hz), 6.91 (1H, d, *J* = 8.8 Hz), 6.66 (1H, d, *J* = 2.0 Hz), 6.54 (1H, dd, *J* = 8.4 Hz, *J* = 2.0 Hz), 4.67 (2H, d, *J* = 4.8 Hz), 4.29-4.38 (1H, m), 4.24 (1H, brs), 3.55 (2H, brs), 1.56 (6H, d, *J* = 6.8 Hz); LCMS: 99.6 %, MS (ESI); m/z 408.1 [M+H]+.
259		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.18 (1H, d, *J* = 2.8 Hz), 7.94 (1H, dd, *J* = 8.8, 2.8 Hz), 7.42 (2H, d, *J* = 8.4 Hz), 7.05-7.10 (3H, m), 6.87 (1H, d, *J* = 8.0 Hz), 6.75 (1H, t, *J* = 5.2 Hz), 6.41 (1H, d, *J* = 1.6 Hz), 6.27 (1H, dd, *J* = 8.0, 1.6 Hz), 5.06 (1H, t, *J* = 4.8 Hz), 4.57 (2H, brs), 4.50 (2H, d, *J* = 6.0 Hz), 3.95 (2H, t, *J* = 5.2 Hz), 3.64 (2H, q, *J* = 5.2 Hz); LCMS: 99.3%, MS (ESI); m/z 410.0[M+ H]+.
260		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.19 (1H, d, *J* = 2.8 Hz), 7.94 (1H, dd, *J* = 8.8, 2.8 Hz), 7.47 (2H, d, *J* = 8.4 Hz), 7.05-7.10 (3H, m), 6.83 (1H, d, *J* = 8.4 Hz), 6.65 (1H, d, *J* = 8.0 Hz), 6.35 (1H, d, *J* = 1.6 Hz), 6.25 (1H, dd, *J* = 8.4, 2.0 Hz), 5.00-5.09 (1H, m), 4.55 (2H, brs), 3.44 (3H, s), 1.51 (3H, d, *J* = 7.2 Hz); LCMS: 98.2%, MS (ESI); m/z 394.0 [M+H]+.
261		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.8 Hz), 7.94 (1H, dd, *J* = 8.8, 2.4 Hz), 7.42 (2H, d, *J* = 8.4 Hz), 7.04-7.14 (3H, m), 7.01 (1H, d, *J* = 1.2 Hz), 6.95 (1H, d, *J* = 8.4 Hz), 6.76 (1H, t, *J* = 5.6 Hz), 6.35 (1H, dd, *J* = 8.8, 2.4 Hz), 5.53-5.65 (1H, m), 5.04-5.17 (2H, m), 4.90-5.03 (2H, m), 4.71 (2H, brs), 4.45 (2H, d, *J* = 5.6 Hz); LCMS: 98.3%, MS (ESI); m/z 422.1[M+ H]+.
262		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.39 (2H, d, *J* = 8.8 Hz), 7.27 (2H, d, *J* = 8.8 Hz), 7.07 (1H, t, *J* = 5.6 Hz), 6.94-7.02 (5H, m), 6.17-6.24 (2H, m), 5.87 (1H, d, *J* = 6.8 Hz), 5.14 (2H, s), 4.78 (2H, t, *J* = 6.4 Hz), 4.39-4.48 (1H, m), 4.34 (2H, t, *J* = 6.0 Hz), 3.55 (2H, q, *J* = 6.0 Hz), 2.88 (2H, t, *J* = 6.4 Hz); LCMS: 98.6%, MS (ESI); m/z 474.2 [M+H]+.

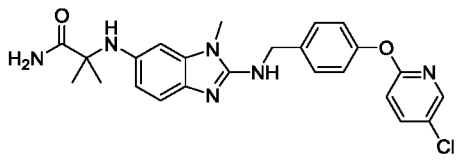
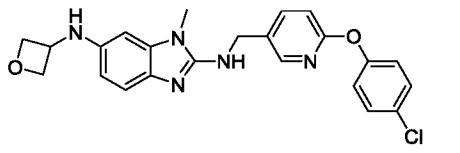
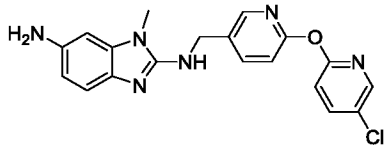
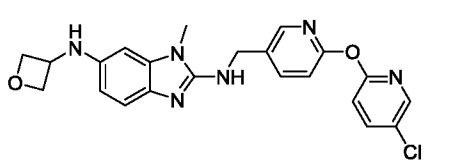
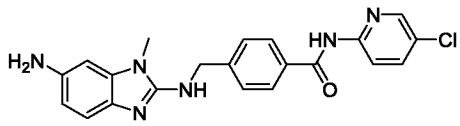
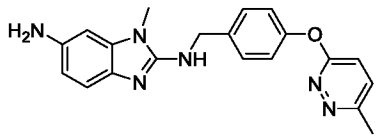
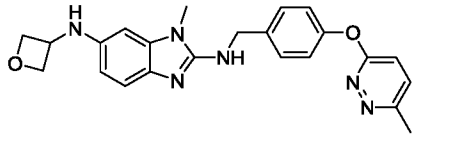
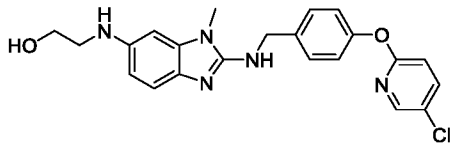
263		yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.18 (1H, d, *J* = 2.8 Hz), 7.94 (1H, dd, *J* = 8.8, 2.8 Hz), 7.42 (2H, d, *J* = 8.8 Hz), 7.05-7.11 (3H, m), 6.86 (1H, d, *J* = 8.0 Hz), 6.78 (1H, t, *J* = 5.6 Hz), 6.41 (1H, d, *J* = 1.6 Hz), 6.26 (1H, dd, *J* = 8.0, 2.0 Hz), 4.49-4.51 (4H, m), 4.06 (2H, t, *J* = 5.6 Hz), 3.57 (2H, t, *J* = 4.8 Hz), 3.24 (3H, s); LCMS: 98.5%, MS (ESI); m/z 424.1 [M+ H]+.
264		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.37-7.44 (2H, m), 7.18 (2H, d, *J* = 8.8 Hz), 6.95-7.03 (4H, m), 6.93 (1H, d, *J* = 8.4 Hz), 6.75 (1H, t, *J* = 5.6 Hz), 6.31 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.4, 2.0 Hz), 5.08 (2H, s), 4.5 (2H, brs), 3.53 (2H, q, *J* = 6.4 Hz), 2.59-2.70 (2H, m); LCMS: 100%, MS (ESI); m/z 461.0[M+H] +.
265		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.4 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.41 (2H, d, *J* = 8.8 Hz), 7.05-7.10 (3H, m), 6.92 (1H, t, *J* = 6.0 Hz), 6.85 (1H, d, *J* = 8.4 Hz), 6.39 (1H, d, *J* = 1.6 Hz), 6.26 (1H, dd, *J* =8.0, 2.0 Hz), 4.43-4.60 (4H, m), 3.93 (2H, q, *J* = 7.2 Hz), 1.20 (3H, t, *J* = 7.2 Hz); LCMS: 99.2 %, MS (ESI); m/z 394.1 [M+H]+.
266		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.16 (1H, d, *J* = 2.4 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.42 (2H, d, *J* = 8.4 Hz), 7.01-7.16 (4H, m), 6.84-6.97 (2H, m), 6.26 (1H, dd, *J* = 8.4, 2.0 Hz), 6.05 (1H, d, *J* = 6.0 Hz), 5.51-5.68 (1H, m), 5.04-5.12 (2H, m), 4.96-5.04 (2H, m), 4.82 (2H, t, *J* = 6.0 Hz), 4.39-4.54 (5H, m); LCMS: 98.8%, MS (ESI); m/z 478.1[M+ H]+.
267		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.16 (1H, d, *J* = 2.4 Hz), 7.97 (1H, dd, *J* = 8.8, 2.4 Hz), 7.36 (1H, d, *J* = 11.2 Hz), 7.24-7.30 (2H, m), 7.20 (1H, d, *J* = 8.8 Hz), 6.97 (1H, t, *J* = 6.0 Hz), 6.87 (1H, d, *J* = 8.4 Hz), 6.37 (1H, d, *J* = 1.6 Hz), 6.27 (1H, dd, *J* = 8.4, 2.0 Hz), 4.56 (2H, brs), 4.52 (2H, d, *J* = 5.6 Hz), 3.42 (3H, s); LCMS: 100%, MS (ESI); m/z 398.0[M+ H]+.
268		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.16 (1H, d, *J* = 2.4 Hz), 7.98 (1H, dd, *J* = 8.8, 2.8 Hz), 7.36 (1H, d, *J* = 11.2 Hz), 7.23-7.31 (2H, m), 7.20 (1H, d, *J* = 8.8 Hz), 7.04 (1H, t, *J* = 6.0 Hz), 6.95 (1H, d, *J* = 8.0 Hz), 6.27 (1H, d, *J* = 2.0 Hz), 6.23 (1H, dd, *J* = 8.0, 2.0 Hz), 5.87 (1H, d, *J* = 7.2 Hz), 4.85 (2H, t, *J* = 6.4 Hz), 4.46-4.60 (3H, m), 4.40 (2H, t, *J* = 6.0 Hz), 3.46 (3H, s); LCMS: 100%, MS (ESI); m/z 454.1[M+ H]+.
269		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.4 Hz), 7.94 (1H, dd, *J* = 8.8, 2.8 Hz), 7.41 (2H, d, *J* = 8.0 Hz), 7.05-7.10 (3H, m), 6.93 (1H, d, *J* = 8.4 Hz), 6.84 (1H, t, *J* = 5.6 Hz), 6.31 (1H, s), 6.20 (1H, dd, *J* = 8.4, 2.0 Hz), 5.84 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.45-4.56 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 4.10 (2H, t, *J* = 5.2 Hz), 3.58 (2H, t, *J* = 5.2 Hz), 3.25 (3H, s); LCMS: 100%, MS (ESI); m/z 480.2[M+ H]+.
270		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.8 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.40 (2H, d, *J* = 8.8 Hz), 7.05-7.10 (3H, m), 6.99 (1H, t, *J* = 6.0 Hz), 6.93 (1H, d, *J* = 8.4 Hz), 6.28 (1H, d, *J* = 2.0 Hz), 6.19 (1H, dd, *J* =8.4, 2.0 Hz), 5.83 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.47-4.56 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.97 (2H, q, *J* = 6.8 Hz), 1.20 (2H, d, *J* = 7.2 Hz); LCMS: 100 %, MS (ESI); m/z 450.0 [M+H]+.

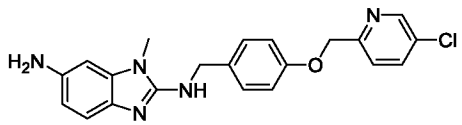
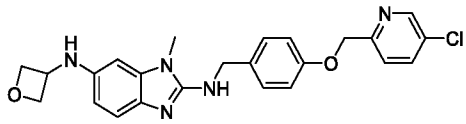
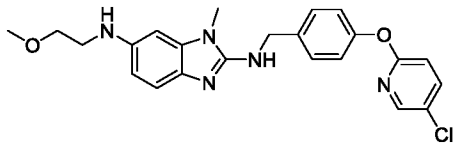
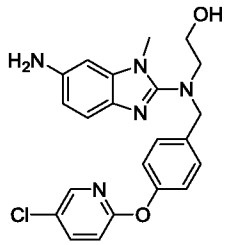
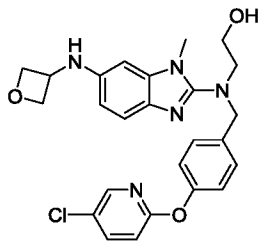
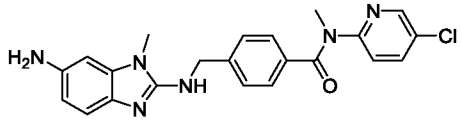
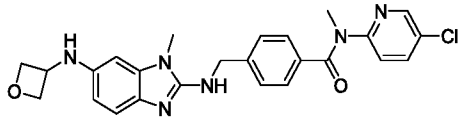
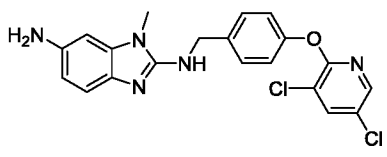
271		brown powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.16 (1H, d, *J* = 2.8 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.40 (2H, d, *J* = 8.4 Hz), 7.05-7.10 (3H, m), 6.94 (1H, d, *J* = 8.4 Hz), 6.84 (1H, t, *J* = 5.6 Hz), 6.47 (1H, d, *J* = 1.6 Hz), 6.16 (1H, dd, *J* = 8.4, 2.0 Hz), 5.80 (1H, d, *J* = 7.2 Hz), 4.83 (2H, t, *J* = 6.8 Hz), 4.56-4.65 (1H, m), 4.45-4.55 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 1.47 (2H, d, *J* = 6.8 Hz); LCMS: 98.8 %, MS (ESI); m/z 464.1 [M+H]+.
272		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.20 (1H, d, *J* = 2.4 Hz), 7.97 (1H, dd, *J* = 8.8, 2.8 Hz), 7.48 (1H, t, *J* = 8.8 Hz), 7.13 (1H, d, *J* = 9.2 Hz), 7.10 (1H, dd, *J* = 11.2, 2.4 Hz), 6.95 (1H, dd, *J* = 8.4, 2.4 Hz), 6.83-6.92 (2H, m), 6.37 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.4, 2.4 Hz), 4.56 (2H, brs), 4.53 (2H, d, *J* = 6.0 Hz), 3.42 (3H, s); LCMS: 99.6%, MS (ESI); m/z 398.0[M+ H]+.
273		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.20 (1H, d, *J* = 2.4 Hz), 7.96 (1H, dd, *J* = 8.8, 2.4 Hz), 7.48 (1H, t, *J* = 8.4 Hz), 7.05-7.18 (2H, m), 6.89-7.02 (3H, m), 6.16-6.33 (2H, m), 5.87 (1H, d, *J* = 7.2 Hz), 4.85 (2H, t, *J* = 6.4 Hz), 4.46-4.62 (3H, m), 4.34-4.45 (2H, m), 3.46 (3H, s); LCMS: 98.6%, MS (ESI); m/z 454.1[M+ H]+.
274		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.18 (1H, d, *J* = 2.8 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.46 (2H, d, *J* = 8.4 Hz), 7.01-7.12 (3H, m), 6.81 (1H, d, *J* = 8.4 Hz), 6.61 (1H, d, *J* = 2.4 Hz), 6.33 (1H, d, *J* = 1.6 Hz), 6.23 (1H, dd, *J* = 8.0, 2.0 Hz), 4.75-4.86 (1H, m), 4.52 (1H, brs), 3.44 (3H, s), 1.84-1.95 (1H, m), 1.70-1.83 (1H, m), 0.93 (3H, t, *J* = 7.2 Hz); LCMS: 97.2 %, MS (ESI); m/z 408.0[M+ H]+.
275		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.18 (1H, d, *J* = 2.4 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.46 (2H, d, *J* = 8.4 Hz), 7.02-7.12 (3H, m), 7.07 (1H, d, *J* = 8.4 Hz), 6.89 (1H, t, *J* = 8.4 Hz), 6.22 (1H, d, *J* = 2.0 Hz), 6.18 (1H, dd, *J* = 8.4, 2.0 Hz), 5.82 (1H, d, *J* = 7.2 Hz), 4.76-4.88 (3H, m), 4.45-4.51 (1H, m), 4.35-4.44 (2H, m), 3.48 (3H, s), 1.85-1.96 (1H, m), 1.73-1.84 (1H, m), 0.94 (3H, t, *J* = 7.2 Hz); LCMS: 95.9 %, MS (ESI); m/z 464.2[M+ H]+.
276		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.55 (1H, s), 8.22 (1H, dd, *J* = 8.8, 2.4 Hz), 7.46 (2H, d, *J* = 8.8 Hz), 7.23 (1H, d, *J* = 8.8 Hz), 7.14 (2H, d, *J* = 8.4 Hz), 6.93 (1H, t, *J* = 6.0 Hz), 6.86 (1H, d, *J* = 8.0 Hz), 6.34 (1H, d, *J* = 1.6 Hz), 6.27 (1H, dd, *J* = 8.4, 2.0 Hz), 4.55 (2H, brs), 4.52 (2H, d, *J* = 6.0 Hz), 3.42 (3H, s); LCMS: 100%, MS (ESI); m/z 414.1[M+ H]+.
277		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.16 (1H, d, *J* = 2.4 Hz), 7.94 (1H, dd, *J* = 8.8, 2.8 Hz), 7.42 (2H, d, *J* = 8.8 Hz), 7.05-7.13 (4H, m), 7.02 (1H, d, *J* = 8.4 Hz), 6.59 (1H, d, *J* = 2.0 Hz), 6.40 (1H, dd, *J* = 8.4, 2.0 Hz), 4.69-4.75 (2H, m), 4.54 (2H, d, *J* = 6.0 Hz), 4.43-4.49 (2H, m), 4.34-4.41 (1H, m), 3.49 (3H, s), 2.70 (3H, s); LCMS: 98.7%, MS (ESI); m/z 450.0 [M+H]+.
278		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.16 (1H, d, *J* = 2.0 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.43 (2H, d, *J* = 8.8 Hz), 7.13 (1H, t, *J* = 6.0 Hz), 7.05-7.10 (3H, m), 7.03 (1H, d, *J* = 8.4 Hz), 6.61 (1H, d, *J* = 2.0 Hz), 6.44 (1H, dd, *J* = 8.0, 2.0 Hz), 4.68 (2H, t, *J* = 6.4 Hz), 4.55 (2H, d, *J* = 6.0 Hz), 4.44-4.52 (1H, m), 4.36 (2H, t, *J* = 6.4 Hz), 3.49 (3H, s), 3.12 (2H, q, *J* = 6.8 Hz) 0.83 (3H, t, *J* = 7.2 Hz); LCMS: 99.8%, MS (ESI); m/z 464.1 [M+H]+.

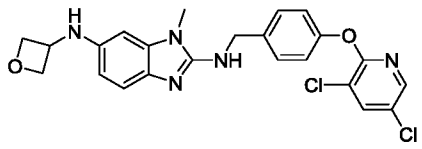
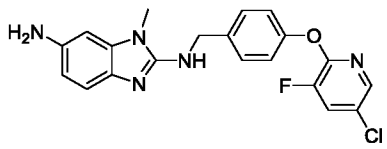
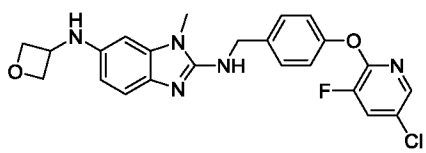
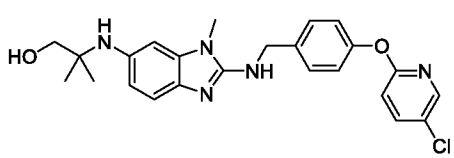
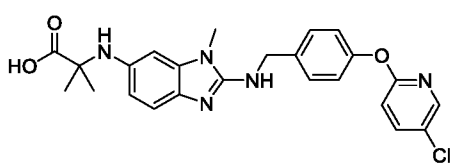
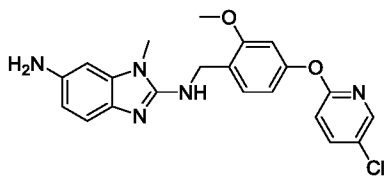
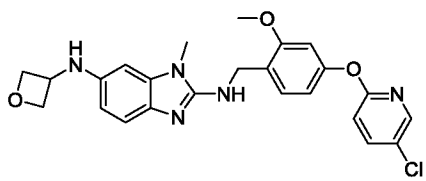
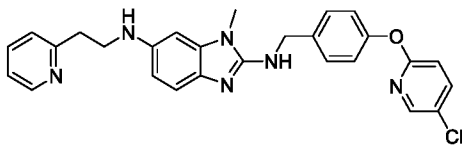
279		white powder; mp = 155.5-159.8oC; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.37-7.43 (2H, m), 7.23 (2H, d, *J* = 8.4 Hz), 6.95-7.03 (5H, m), 6.80-6.84 (1H, m), 6.16-6.23 (2H, m), 5.86 (1H, d, *J* = 6.8 Hz), 5.11 (2H, s), 4.78 (2H, t, *J* = 6.4 Hz), 4.41-4.48 (1H, m), 4.33 (2H, d, *J* = 6.0 Hz), 3.54 (2H, q, *J* = 6.8 Hz), 2.60-2.71 (2H, m); LCMS: 98.9%, MS (ESI); m/z 417.0 [M+H]+.
280		yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.19 (1H, d, *J* = 2.8 Hz), 7.41-7.52 (4H, m), 7.07 (2H, d, *J* = 8.8 Hz), 6.75-6.85 (2H, m), 6.37 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.4, 2.0 Hz), 4.55 (2H, brs), 4.51 (1H, d, *J* = 5.6 Hz), 3.41 (3H, s); LCMS: 98.7 %, MS (ESI); m/z 380.0[M + H]+.
281		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.19 (1H, d, *J* = 2.4 Hz), 7.41-7.56 (4H, m), 7.07 (2H, d, *J* = 8.4 Hz), 6.90-6.95 (2H, m), 6.25 (1H, s), 6.21 (1H, dd, *J* = 8.4, 2.0 Hz), 5.85 (1H, d, *J* = 6.8 Hz), 4.85 (2H, t, *J* = 6.4 Hz), 4.46-4.57 (3H, m), 4.40 (2H, t, *J* = 6.0 Hz), 3.44 (3H, s); LCMS: 98.1%, MS (ESI); m/z 436.1[M+ H]+.
282		brown powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.14 (1H, d, *J* = 2.4 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.31 (1H, s), 7.25 (1H, d, *J* = 8.4 Hz), 7.07 (1H, d, *J* = 8.8 Hz), 7.00 (1H, d, *J* = 8.0 Hz), 6.83-6.90 (2H, m), 6.36 (1H, d, *J* = 1.6 Hz), 6.26 (1H, dd, *J* = 8.0, 2.0 Hz), 4.54 (2H, brs), 4.48 (2H, d, *J* = 5.6 Hz), 3.41 (3H, s), 2.04 (3H, s); LCMS: 100 %, MS (ESI); m/z 394.0 [M+H]+.
283		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.14 (1H, d, *J* = 2.8 Hz), 7.92 (1H, dd, *J* = 8.8, 2.8 Hz), 7.30 (1H, s), 7.25 (1H, d, *J* = 8.0 Hz), 7.07 (1H, d, *J* = 8.8 Hz), 7.00 (1H, d, *J* = 8.0 Hz), 6.89-6.96 (2H, m), 6.25 (1H, d, *J* = 1.6 Hz), 6.21 (1H, dd, *J* = 8.4, 2.0 Hz), 5.85 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.0 Hz), 4.46-4.56 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.45 (3H, s), 2.03 (3H, s); LCMS: 99.8 %, MS (ESI); m/z 450.1 [M+H]+.
284		grey powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.54 (1H, s), 8.21 (1H, dd, *J* = 8.8, 2.4 Hz), 7.45 (2H, d, *J* = 8.0 Hz), 7.22 (1H, d, *J* = 8.4 Hz), 7.13 (2H, d, *J* = 8.4 Hz), 6.98 (1H, t, *J* = 5.6 Hz), 6.93 (1H, d, *J* = 8.4 Hz), 6.25 (1H, s), 6.21 (1H, dd, *J* = 8.0, 2.0 Hz), 5.84 (1H, d, *J* = 6.8 Hz), 4.79-4.88 (2H, m), 4.45-4.57 (3H, m), 4.35-4.44 (2H, m), 3.45 (3H, s); LCMS: 99.6%, MS (ESI); m/z 470.0[M+ H]+.
285		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.20 (1H, d, *J* = 2.4 Hz), 7.97 (1H, dd, *J* = 8.8, 2.8 Hz), 7.46 (1H, d, *J* = 8.8 Hz), 7.33 (1H, d, *J* = 2.4 Hz), 7.14 (1H, d, *J* = 8.8 Hz), 7.10 (1H, dd, *J* = 8.8, 2.4 Hz), 6.97 (1H, t, *J* = 6.0 Hz), 6.85 (1H, d, *J* = 8.4 Hz), 6.38 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.0, 2.0 Hz), 4.51-4.61 (4H, m), 3.45 (3H, s); LCMS: 100%, MS (ESI); m/z 414.0[M+ H]+.
286		off-white powder; 1H NMR (DMSO–*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.8 Hz), 7.94 (1H, dd, *J* = 8.8, 2.8 Hz), 7.42 (2H, d, *J* = 8.0 Hz), 7.13 (1H, t, *J* = 5.6 Hz), 7.06-7.10 (3H, m), 6.86 (1H, d, *J* = 8.4 Hz), 6.39 (1H, d, *J* = 1.6 Hz), 6.26 (1H, dd, *J* = 8.4, 2.0 Hz), 4.55 (2H, brs), 4.50 (2H, d, *J* = 5.6 Hz), 3.95 (2H, t, *J* = 6.8 Hz), 2.47-2.49 (2H, m), 2.20 (6H, s); LCMS: 100%, MS (ESI); m/z 437.0 [M+H]+.
287		white amorphous; 1H NMR (CDCl3, 400 MHz); δ 8.20 (1H, s) 7.83 (1H, dd, *J* = 8.4, 2.0 Hz), 7.35 (2H, d, *J* = 8.8 Hz), 7.26-7.29 (1H, m), 7.07 (2H, d, *J* = 8.4 Hz), 6.91 (1H, d, *J* = 8.4 Hz), 6.54 (1H, dd, *J* = 8.0, 2.0 Hz), 6.45 (1H, d, *J* = 1.6 Hz), 4.65 (2H, d, *J* = 5.6 Hz), 4.21 (1H, t, *J* = 5.2 Hz), 3.58 (2H, brs), 3.41 (3H, s); LCMS: 100%, MS (ESI); m/z 380.0[M+H] +.

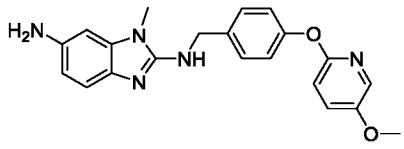
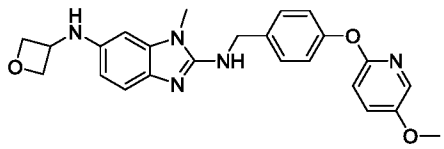
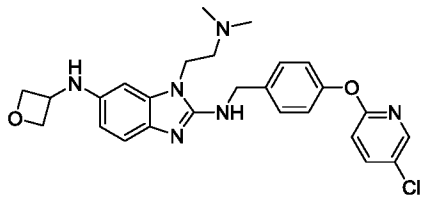
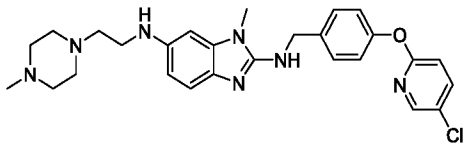
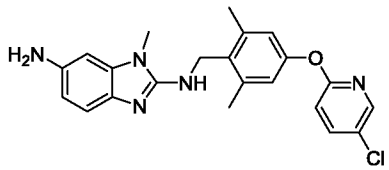
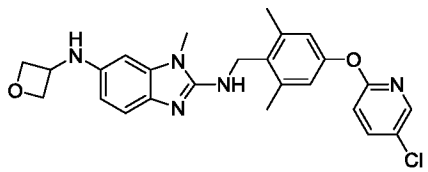
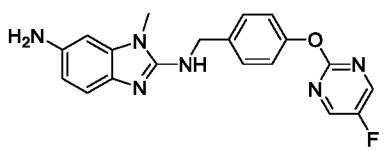
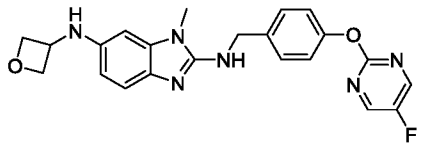
288		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.73 (2H, s), 7.44 (2H, d, *J* = 8.4 Hz), 7.15 (2H, d, *J* = 8.4 Hz), 6.92 (1H, t, *J* = 6.0 Hz), 6.86 (1H, d, *J* = 8.0 Hz), 6.36 (1H, d, *J* = 2.0 Hz), 6.26 (1H, dd, *J* = 8.4, 2.0 Hz), 4.58 (2H, brs), 4.51 (2H, d, *J* = 5.6 Hz), 3.41 (3H, s); LCMS: 99.7 %, MS (ESI); m/z 381.0[M+ H]+.
289		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.73 (2H, s), 8.32 (1H, s), 7.44 (2H, d, *J* = 8.4 Hz), 7.15 (2H, d, *J* = 8.4 Hz), 6.89-7.01 (2H, m), 6.25 (1H, s), 6.21 (1H, dd, *J* = 2.4, 8.4 Hz), 5.84 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.45-4.57 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.45 (3H, s); LCMS: 100 %, MS (ESI); m/z 437.1[M + H]+.
290		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.18 (1H, d, *J* = 2.4 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.35 (1H, d, *J* = 8.4 Hz), 7.06 (1H, d, *J* = 8.8 Hz), 6.96 (1H, s), 6.91 (1H, d, *J* = 8.0 Hz), 6.86 (1H, d, *J* = 8.4 Hz), 6.73 (1H, t, *J* = 5.6 Hz), 6.37 (1H, s), 6.26 (1H, dd, *J* = 8.0, 1.2 Hz), 4.64 (2H, brs), 4.46 (2H, d, *J* = 5.2 Hz), 3.42 (3H, s), 2.34 (3H, s); LCMS: 98.8%, MS (ESI); m/z 394.1[M+ H]+.
291		off-white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.8 Hz), 7.92 (1H, dd, *J* = 8.8, 2.4 Hz), 7.34 (1H, d, *J* = 8.4 Hz), 7.05 (1H, d, *J* = 8.8 Hz), 6.85-7.00 (3H, m), 6.81 (1H, t, *J* = 5.6 Hz), 6.26 (1H, d, *J* = 1.2 Hz), 6.22 (1H, d, *J* = 8.4 Hz), 5.84 (1H, d, *J* = 7.2 Hz), 4.85 (2H, t, *J* = 6.0 Hz), 4.44-4.56 (3H, m), 4.40 (2H, t, *J* = 6.0 Hz), 3.46 (3H, s), 2.34 (3H, s); LCMS: 99.6%, MS (ESI); m/z 450.0[M+ H]+.
292		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.44 (2H, d, *J* = 8.4 Hz), 7.37 (2H, d, *J* = 8.4 Hz), 7.01-7.12 (4H, m), 6.82-6.93 (2H, m), 6.37 (1H, d, *J* = 1.6 Hz), 6.27 (1H, dd, *J* = 8.4, 2.0 Hz), 4.55 (2H, s), 4.50 (2H, d, *J* = 6.0 Hz), 3.41 (3H, s); LCMS: 98.5 %, MS (ESI); m/z 429.1[M+ H]+.
293		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.44 (2H, d, *J* = 8.4 Hz), 7.37 (2H, d, *J* = 8.4 Hz), 6.98-7.10 (4H, m), 6.89-6.98 (2H, m), 6.26 (1H, d, *J* = 2.0 Hz), 6.22 (1H, dd, *J* = 8.4, 2.0 Hz), 5.85 (1H, d, *J* = 7.2 Hz), 4.85 (2H, t, *J* = 6.4 Hz), 4.45-4.57 (3H, m), 4.40 (2H, t, *J* = 6.0 Hz), 3.44 (3H, s); LCMS: 97.4%, MS (ESI); m/z 485.2[M+ H]+.
294		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.19 (1H, d, *J* = 2.8 Hz), 7.96 (1H, dd, *J* = 8.8, 2.8 Hz), 7.45 (1H, d, *J* = 8.4 Hz), 7.32 (1H, d, *J* = 2.4 Hz), 7.13 (1H, d, *J* = 8.8 Hz), 7.09 (1H, dd, *J* = 8.4, 2.4 Hz), 7.01 (1H, t, *J* = 5.6 Hz), 6.93 (1H, d, *J* = 8.4 Hz), 6.27 (1H, d, *J* = 1.6 Hz), 6.22 (1H, dd, *J* = 8.4, 2.0 Hz), 5.86 (1H, d, *J* = 6.8 Hz), 4.85 (2H, t, *J* = 6.4 Hz), 4.57 (2H, d, *J* = 5.6 Hz), 4.45-4.55 (1H, m), 4.40 (2H, t, *J* = 6.0 Hz), 3.49 (3H, s); LCMS: 99.4%, MS (ESI); m/z 470.1[M+ H]+.
295		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.41 (1H, d, *J* = 1.2 Hz), 8.32 (1H, s), 7.45 (2H, d, *J* = 8.4 Hz), 7.16 (2H, d, *J* = 8.4 Hz), 6.90 (1H, t, *J* = 6.0 Hz), 6.86 (1H, d, *J* = 8.0 Hz), 6.36 (1H, d, *J* = 1.6 Hz), 6.26 (1H, dd, *J* = 8.0, 2.0 Hz), 4.54 (2H, brs), 4.51 (2H, d, *J* = 6.0 Hz), 3.41 (3H, s); LCMS: 98.7 %, MS (ESI); m/z 381.0[M+ H]+.
296		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.41 (1H, s), 8.32 (1H, s), 7.44 (2H, d, *J* = 8.4 Hz), 7.16 (2H, d, *J* = 8.4 Hz), 6.89-7.02 (2H, m), 6.24 (1H, s), 6.21 (1H, d, *J* = 8.0 Hz), 5.85 (1H, d, *J* = 6.8 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.46-4.58 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.44 (3H, s); LCMS: 97.5 %, MS (ESI); m/z 437.0[M+ H]+.

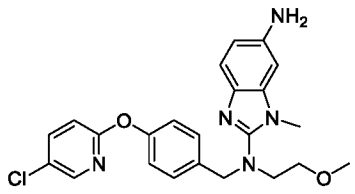
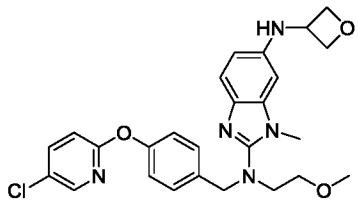
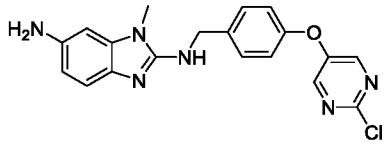
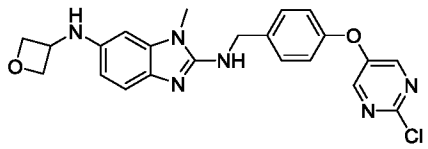
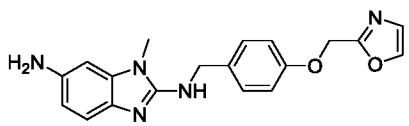
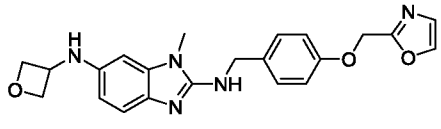
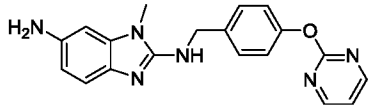
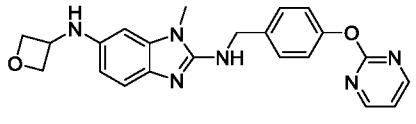
297		white power; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.35 (1H, s), 7.43-7.46 (4H, m), 7.01-7.07 (3H, m), 6.84 (1H, d, *J* = 8.0 Hz), 6.37 (1H, s), 6.26 (1H, dd, *J* = 8.0, 2.0 Hz), 4.59 (2H, d, *J* = 6.0 Hz), 4.56 (2H, brs), 3.44 (3H, s); LCMS: 99.5%, MS (ESI); m/z 380.0 [M+H]+.
298		white power; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.34 (1H, s), 7.41-7.45 (4H, m), 7.03-7.07 (3H, m), 6.92 (1H, d, *J* = 8.8 Hz), 6.25 (1H, s), 6.21 (1H, d, *J* = 8.4 Hz), 5.84 (1H, d, *J* = 6.8 Hz), 4.84 (2H, t, *J* = 6.0 Hz), 4.59 (2H, d, *J* = 5.6 Hz), 4.48-4.51 (1H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.46 (3H, s); LCMS: 100%, MS (ESI); m/z 436.0[M+H] +.
299		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.39 (1H, d, *J* = 2.4 Hz), 8.18 (1H, d, *J* = 2.8 Hz), 7.98 (1H, dd, *J* = 8.8, 2.8 Hz), 7.58 (1H, dd, *J* = 8.8, 2.8 Hz), 7.46 (1H, d, *J* = 8.8 Hz), 7.20 (1H, d, *J* = 8.8 Hz), 7.04 (1H, t, *J* = 6.0 Hz), 6.85 (1H, d, *J* = 8.0 Hz), 6.38 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.0, 2.0 Hz), 4.60 (2H, d, *J* = 6.0 Hz), 4.55 (2H, brs), 3.45 (3H, s); LCMS: 99.3 %, MS (ESI); m/z 381.0 [M+H]+.
300		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.39 (1H, d, *J* = 2.4 Hz), 8.17 (1H, d, *J* = 2.4 Hz), 7.98 (1H, dd, *J* = 8.8, 2.8 Hz), 7.58 (1H, dd, *J* = 8.4, 2.8 Hz), 7.45 (1H, d, *J* = 8.4 Hz), 7.19 (1H, d, *J* = 8.8 Hz), 7.09 (1H, t, *J* = 5.6 Hz), 6.92 (1H, d, *J* = 8.0 Hz), 6.26 (1H, d, *J* = 2.0 Hz), 6.21 (1H, dd, *J* = 8.4, 2.0 Hz), 5.85 (1H, d, *J* = 7.2 Hz), 4.84 (1H, t, *J* = 6.0 Hz), 4.61 (1H, d, *J* = 6.0 Hz), 4.45-4.57 (1H, m), 4.39 (1H, t, *J* = 6.0 Hz), 3.48 (3H, s); LCMS: 99.0 %, MS (ESI); m/z 437.0 [M + H]+.
301		pale yellow solid; mp = 121.4-124.6 oC; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.12 (1H, d, *J* = 3.2 Hz), 7.74-7.85 (1H, m), 7.42 (2H, d, *J* = 8.4 Hz), 7.02-7.12 (3H, m), 6.82-6.92 (2H, m), 6.36 (1H, d, *J* = 2.0 Hz), 6.26 (1H, dd, *J* = 8.4, 2.0 Hz), 4.54 (2H, brs), 4.50 (2H, d, *J* = 5.6 Hz), 3.41 (3H, s); LCMS: 98.8 %, MS (ESI); m/z 364.0[M+ H]+.
302		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.11 (1H, d, *J* = 3.2 Hz), 7.76-7.85 (1H, m), 7.41 (2H, d, *J* = 8.4 Hz), 7.01-7.12 (3H, m), 6.90-6.97 (2H, m), 6.24 (1H, s), 6.21 (1H, dd, *J* = 8.4, 2.0 Hz), 5.84 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.0 Hz), 4.45-4.57 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.44 (3H, s); LCMS: 98.4 %, MS (ESI); m/z 420.1[M+ H]+.
303		white power; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.92 (1H, brs), 8.42 (1H, d, *J* = 2.4 Hz), 8.22 (1H, d, *J* = 8.8 Hz), 7.92-7.98 (3H, m), 7.48 (2H, d, *J* = 8.4 Hz), 7.04 (1H, t, *J* = 6.0 Hz), 6.91(1H, d, *J* = 8.0 Hz), 6.25 (1H, s), 6.20 (1H, d, *J* = 8.4 Hz), 5.83 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.0 Hz), 4.58 (2H, d, *J* = 6.0 Hz), 4.45-4.55 (1H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.46 (3H, s); LCMS: 100%, MS (ESI); m/z 463.2[M+H] +.
304		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.21 (1H, d, *J* = 2.4 Hz), 7.80 (1H, dd, *J* = 8.8, 2.4 Hz), 7.33-7.42 (4H, m), 6.91 (1H, d, *J* = 8.4 Hz), 6.81-6.89 (2H, m), 6.36 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.4, 2.0 Hz), 5.29 (2H, s), 4.54 (2H, brs), 4.50 (2H, d, *J* = 6.0 Hz), 3.40 (3H, s); LCMS: 98.1%, MS (ESI); m/z 394.1[M+ H]+.
305		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.21 (1H, d, *J* = 2.4 Hz), 7.80 (1H, dd, *J* = 8.8, 2.8 Hz), 7.31-7.42 (4H, m), 6.97-6.85 (3H, m), 6.24 (1H, d, *J* = 2.0 Hz), 6.20 (1H, dd, *J* = 8.0, 2.0 Hz), 5.83 (1H, d, *J* = 6.8 Hz), 5.29 (2H, s), 4.84 (2H, t, *J* = 6.4 Hz), 4.44-4.58 (3H, m), 4.33-4.43 (2H, m), 3.43 (3H, s); LCMS: 99.1%, MS (ESI); m/z 450.0[M+ H]+.

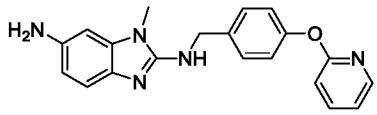
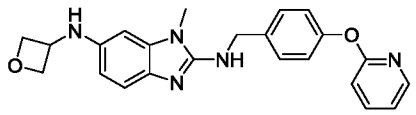
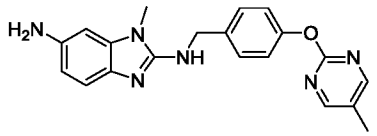
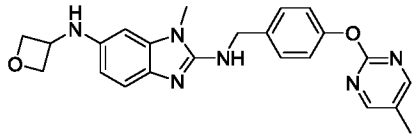
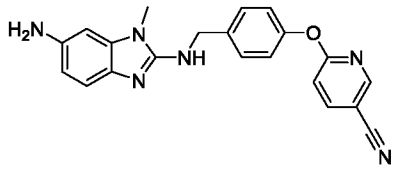
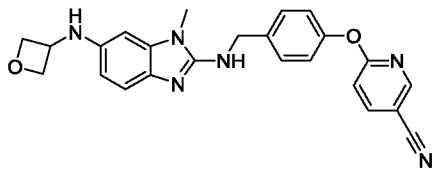
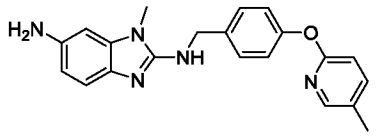
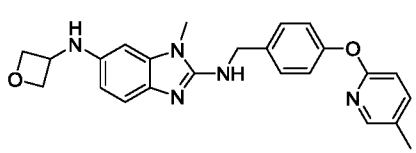
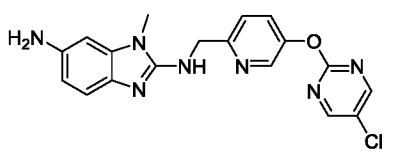
306		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.8 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.42 (2H, d, *J* = 8.4 Hz), 7.21-7.23 (1H, m), 7.05-7.09 (3H, m), 6.96-7.02 (2H, m), 6.93 (1H, d, *J* = 8.4 Hz), 6.33 (1H, d, *J* = 1.6 Hz), 6.29 (1H, dd, *J* = 8.4, 2.0 Hz), 5.14 (1H, brs), 4.52 (2H, d, *J* = 6.0 Hz), 3.40 (3H, s) 1.33 (6H, s); LCMS: 99.1%, MS (ESI); m/z 465.1 [M+H]+.
307		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.16 (1H, d, *J* = 2.4 Hz), 7.90 (1H, dd, *J* = 8.0, 2.4 Hz), 7.40-7.46 (2H, m), 7.09-7.16 (2H, m), 7.02 (1H, d, *J* = 8.0 Hz), 6.89-6.96 (2H, m), 6.24 (1H, d, *J* = 2.4 Hz), 6.21 (1H, dd, *J* = 8.4, 2.4 Hz), 5.85 (1H, d, *J* = 6.8 Hz), 4.82-4.86 (2H, m), 4.43-4.55 (3H, m), 4.38 (2H, t, *J* = 6.0 Hz), 3.41 (3H, s); LCMS: 99.0%, MS (ESI); m/z 436.1 [M+H]+.
308		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.25-8.30 (2H, m), 7.99 (1H, dd, *J* = 8.4, 2.8 Hz), 7.94 (1H, dd, *J* = 8.0, 2.4 Hz), 7.18 (1H, d, *J* = 8.8 Hz), 7.11 (1H, d, *J* = 8.0 Hz), 6.92 (1H, t, *J* = 6.0 Hz), 6.87 (1H, d, *J* = 8.0 Hz), 6.36 (1H, d, *J* = 1.6 Hz), 6.27 (1H, dd, *J* = 8.0, 2.0 Hz), 4.55 (2H, brs), 4.50 (2H, t, *J* = 5.6 Hz), 3.39 (3H, s); LCMS: 99.0%, MS (ESI); m/z 381.0[M+ H]+.
309		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.25-8.35 (2H, m), 7.99 (1H, dd, *J* = 8.8, 2.8 Hz), 7.93 (1H, dd, *J* = 8.4, 2.4 Hz), 7.18 (1H, d, *J* = 8.8 Hz), 7.12 (1H, d, *J* = 8.4 Hz), 6.98 (1H, t, *J* = 5.6 Hz), 6.95 (1H, d, *J* = 8.0 Hz), 6.25 (1H, d, *J* = 1.6 Hz), 6.22 (1H, dd, *J* = 8.4, 2.4 Hz), 5.86 (1H, d, *J* = 6.8 Hz), 4.85 (2H, t, *J* = 6.4 Hz), 4.45-4.60 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.39 (3H, s); LCMS: 98.4%, MS (ESI); m/z 437.0[M+ H]+.
310		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 10.94 (1H, brs), 8.43 (1H, d, *J* = 2.4 Hz), 8.23 (1H, d, *J* = 8.8 Hz), 7.94-7.98 (3H, m), 7.49 (2H, d, *J* = 8.4 Hz), 6.99 (1H, t, *J* = 6.0 Hz), 6.84 (1H, d, *J* = 8.0 Hz), 6.36 (1H, d, *J* = 1.6 Hz), 6.25 (1H, dd, *J* = 8.0, 2.0 Hz), 4.58 (2H, d, *J* = 6.0 Hz), 4.55 (2H, brs), 3.43 (3H, s); LCMS: 98.6%, MS (ESI); m/z 407.0 [M+H]+.
311		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.62 (1H, d, *J* = 8.8 Hz), 7.45 (2H, d, *J* = 8.4 Hz), 7.32 (1H, d, *J* = 8.8 Hz), 7.12 (2H, d, *J* = 8.4 Hz), 6.82-6.92 (2H, m), 6.36 (1H, d, *J* = 1.6 Hz), 6.26 (1H, dd, *J* = 8.0, 2.0 Hz), 4.46-4.55 (4H, m), 3.41 (3H, s), 2.54 (3H, s); LCMS: 97.7 %, MS (ESI); m/z 361.1[M+ H]+.
312		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.61 (1H, d, *J* = 9.2 Hz), 7.44 (2H, d, *J* = 8.4 Hz), 7.32 (1H, d, *J* = 8.8 Hz), 7.12 (2H, d, *J* = 8.8 Hz), 6.94 (2H, d, *J* = 8.0 Hz), 6.25 (1H, d, *J* = 2.0 Hz), 6.21 (1H, dd, *J* = 8.4, 2.4 Hz), 5.84 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.45-4.57 (3H, m), 4.39 (2H, t, *J* = 5.6 Hz), 3.44 (3H, s), 2.53 (3H, s); LCMS: 96.4 %, MS (ESI); m/z 417.1[M+ H]+.
313		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.0 Hz), 7.94 (1H, dd, *J* = 8.4, 2.4 Hz), 7.43 (2H, d, *J* = 8.8 Hz), 7.06-7.10 (3H, m), 6.88-6.73 (2H, m), 6.39 (1H, d, *J* = 2.0 Hz), 6.31 (1H, dd, *J* = 8.0, 2.0 Hz), 4.90 (1H, brs), 4.66 (1H, t, *J* = 5.6 Hz), 4.51 (2H, d, *J* = 5.6 Hz), 3.57 (2H, q, *J* = 6.0 Hz), 3.45 (3H, s), 3.00-3.10 (2H, m); LCMS: 99.0%, MS (ESI); m/z 424.0 [M+H]+.

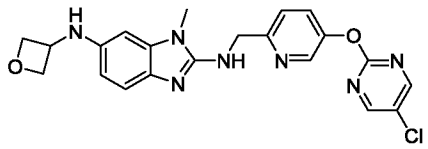
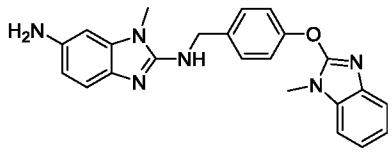
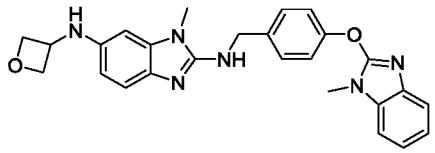
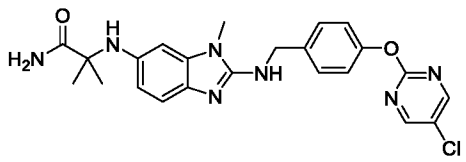
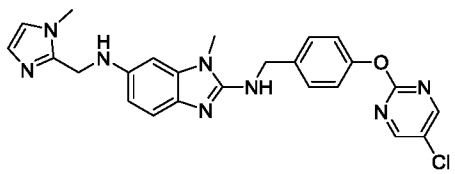
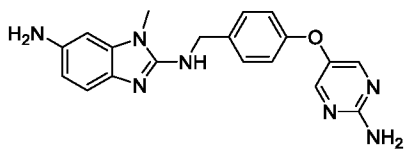
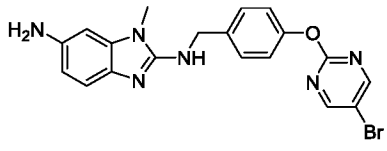
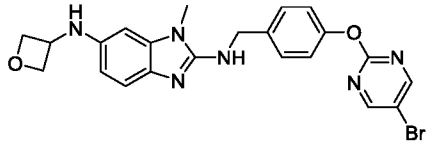
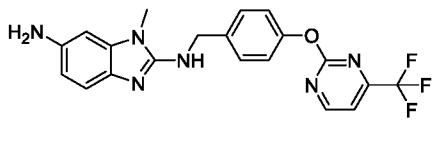
314		white solid; m.p = 96.6-100.9 °C; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.62 (1H, d, *J* = 2.4 Hz), 7.95 (1H, dd, *J* = 8.4, 2.4 Hz), 7.53 (1H, d, *J* = 8.4 Hz), 7.31 (2H, d, *J* = 8.8 Hz), 6.96 (2H, d, *J* = 8.4 Hz), 6.85 (1H, d, *J* = 8.0 Hz), 6.75 (1H, t, *J* = 6.0 Hz), 6.35 (1H, d, *J* = 1.6 Hz), 6.26 (1H, dd, *J* = 8.0, 2.0 Hz), 5.16 (2H, s), 4.55 (2H, brs), 4.42 (2H, d, *J* = 5.6 Hz), 3.38 (3H, s); LCMS: 97.0%, MS (ESI); m/z 394.1[M+ H]+.
315		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.62 (1H, d, *J* = 2.4 Hz), 7.95 (1H, dd, *J* = 8.8, 2.8 Hz), 7.53 (1H, d, *J* = 8.4 Hz), 7.31 (2H, d, *J* = 8.8 Hz), 6.88-7.01 (3H, m), 6.81 (1H, t, *J* = 6.0 Hz), 6.23 (1H, d, *J* = 2.0 Hz), 6.20 (1H, dd, *J* = 8.4, 2.0 Hz), 5.83 (1H, d, *J* = 6.8 Hz), 5.15 (2H, s), 4.84 (2H, t, *J* = 6.4 Hz), 4.46-4.56 (1H, m), 4.34-4.45 (4H, m), 3.41 (3H, s); LCMS: 100%, MS (ESI); m/z 450.1[M+ H]+.
316		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.8 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.43 (2H, d, *J* = 8.4 Hz), 7.00-7.13 (3H, m), 6.83-6.98 (2H, m), 6.42 (1H, d, *J* = 2.0 Hz), 6.32 (1H, dd, *J* = 8.0, 2.0 Hz), 4.94 (1H, t, *J* = 6.0 Hz), 4.52 (2H, d, *J* = 6.0 Hz), 3.50 (2H, t, *J* = 5.6 Hz), 3.45 (3H, s), 3.28 (3H, s), 3.18 (2H, q, *J* = 5.8 Hz); LCMS: 98.0%, MS (ESI); m/z 438.1[M+ H]+.
317		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.19 (1H, d, *J* = 2.8 Hz), 7.94 (1H, dd, *J* = 8.8, 2.8 Hz), 7.40 (2H, d, *J* = 8.8 Hz), 6.99-7.15 (4H, m), 6.45 (1H, d, *J* = 1.6 Hz), 6.40 (1H, dd, *J* = 8.4, 2.4 Hz), 4.90 (1H, t, *J* = 5.6 Hz), 4.77 (2H, brs), 4.44 (2H, s), 3.59 (2H, q, *J* = 5.6 Hz), 3.52 (3H, s), 3.24 (1H, t, *J* = 6.0 Hz); LCMS: 100 %, MS (ESI); m/z 424.0 [M+H]+.
318		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.19 (1H, d, *J* = 2.8 Hz), 7.94 (1H, dd, *J* = 8.8, 2.4 Hz), 7.40 (2H, d, *J* = 8.8 Hz), 7.12 (1H, d, *J* = 8.4 Hz), 7.04-7.10 (3H, m), 6.38 (1H, dd, *J* = 8.4, 2.0 Hz), 6.30 (1H, d, *J* = 2.0 Hz), 6.08 (1H, d, *J* = 6.8 Hz), 4.87 (1H, t, *J* = 6.4 Hz), 4.50-4.62 (1H, m), 4.45 (2H, brs), 4.40 (1H, t, *J* = 6.0 Hz), 3.53-3.62 (5H, m), 3.24 (2H, t, *J* = 6.0 Hz); LCMS: 100 %, MS (ESI); m/z 480.1 [M+H]+.
319		white power; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.41 (1H, d, *J* = 2.4 Hz), 7.80 (1H, dd, *J* = 8.8, 2.8 Hz), 7.19-7.33 (5H, m), 6.89 (1H, d, *J* = 8.4 Hz), 6.43 (1H, s), 6.33 (1H, d, *J* = 7.6 Hz), 4.53 (2H, d, *J* = 5.2 Hz), 3.44 (6H, s); LCMS: 100%, MS (ESI); m/z 421.1 [M+H]+.
320		white power; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.41 (1H, d, *J* = 2.4 Hz), 7.99 (1H, dd, *J* = 8.8, 2.4 Hz), 7.18-7.30 (5H, m), 6.89-6.94 (2H, m), 6.24 (1H, s), 6.20 (1H, d, *J* = 8.4 Hz), 5.83 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.48-4.53 (3H, m), 4.38 (2H, t, *J* = 6.4 Hz), 3.42 (6H, s); LCMS: 100%, MS (ESI); m/z 477.1[M+H] +.
321		white power; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.33 (1H, d, *J* = 2.0 Hz), 8.13 (1H, d, *J* = 2.4 Hz), 7.44 (2H, d, *J* = 8.4 Hz), 7.11 (2H, d, *J* = 8.8 Hz), 6.91 (1H, t, *J* = 6.0 Hz), 6.85 (1H, d, *J* = 8.0 Hz), 6.36 (1H, d, *J* = 2.0 Hz), 6.26 (1H, dd, *J* = 8.0, 2.0 Hz); LCMS: 100 %, MS (ESI); m/z 414.0[M+ H]+.

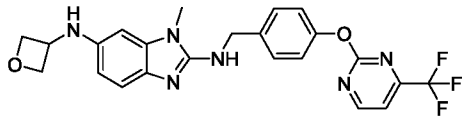
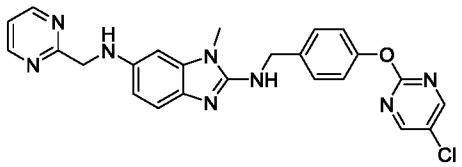
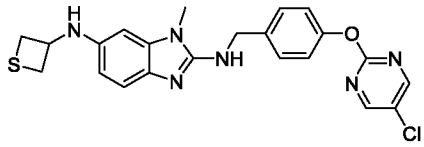
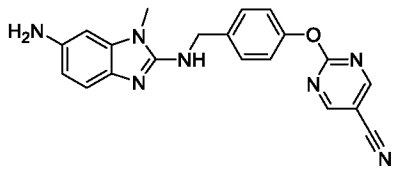
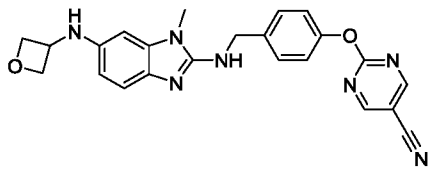
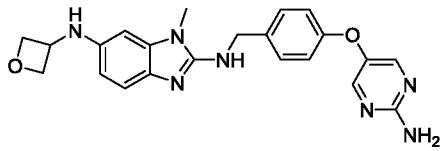
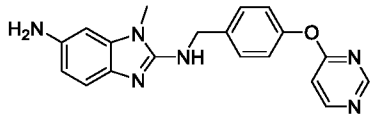
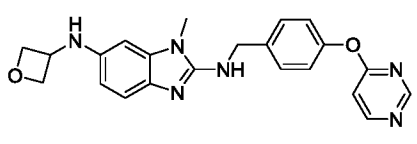
322		white power; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.32 (1H, d, *J* = 2.0 Hz), 8.12 (1H, d, *J* = 2.4 Hz), 7.43 (2H, d, *J* = 8.8 Hz), 7.11 (2H, d, *J* = 8.4 Hz), 6.89-7.00 (2H, m), 6.25 (1H, d, *J* = 2.0 Hz), 6.21 (1H, dd, *J* = 8.4, 2.0 Hz), 5.84 (1H, d, *J* = 6.8 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.45-4.57 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.44 (3H, s); LCMS: 99.7%, MS (ESI); m/z 470.0[M+ H]+.
323		white power; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.20 (1H, dd, *J* = 10.0, 2.4 Hz), 8.02 (1H, d, *J* = 2.0 Hz), 7.44 (2H, d, *J* = 8.4 Hz), 7.14 (2H, d, *J* = 8.8 Hz), 6.93 (1H, t, *J* = 6.0 Hz), 6.86 (1H, d, *J* = 8.0 Hz), 6.37 (1H, d, *J* = 1.6 Hz), 6.27 (1H, dd, *J* = 8.0, 2.0 Hz), 4.57 (2H, brs), 4.51 (2H, d, *J* = 6.0 Hz), 3.41 (3H, s); LCMS: 100 %, MS (ESI); m/z 398.0[M+ H]+.
324		white power; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.20 (1H, dd, *J* = 10.0, 2.0 Hz), 8.01 (1H, d, *J* = 2.0 Hz), 7.43 (2H, d, *J* = 8.4 Hz), 7.13 (2H, d, *J* = 8.8 Hz), 6.89-7.00 (2H, m), 6.25 (1H, d, *J* = 2.0 Hz), 6.21 (1H, dd, *J* = 8.4, 2.4 Hz), 5.84 (1H, d, *J* = 6.8 Hz), 4.84 (2H, t, *J* = 6.8 Hz), 4.45-4.57 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.44 (3H, s); LCMS: 98.6%, MS (ESI); m/z 454.1[M+ H]+.
325		off-white powder; 1H NMR (DMSO-d6, 400 MHz); δ 8.17 (1H, d, *J* = 2.8 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.43 (2H, d, *J* = 8.4 Hz), 7.02-7.11 (4H, m), 6.94 (1H, d, *J* = 8.4 Hz), 6.62 (1H, d, *J* = 2.0 Hz), 6.49 (1H, dd, *J* = 8.4, 2.0 Hz), 4.75 (1H, t, *J* = 5.2 Hz), 4.54 (2H, d, *J* = 5.6 Hz), 3.46 (3H, s), 3.27 (2H, d, *J* = 5.6 Hz), 1.10 (6H, s); LCMS: 98.9%, MS (ESI); m/z 452.0 [M+H]+.
326		off-white solid; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.4 Hz), 7.94 (1H, dd, *J* = 8.8, 2.8 Hz), 7.42 (2H, d, *J* = 8.4 Hz), 7.05-7.10 (3H, m), 7.02 (1H, t, *J* = 4.8 Hz), 6.92 (1H, d, *J* = 8.4 Hz), 6.36 (1H, d, *J* = 2.0 Hz), 6.31 (1H, dd, *J* = 8.4, 2.0 Hz), 4.52 (2H, d, *J* = 5.2 Hz), 3.41 (3H, s), 1.40 (6H, s); LCMS: 93.1 %, MS (ESI); m/z 466.1 [M+H]+.
327		yellow powder; 1H NMR (Methanol-*d*4, 400 MHz); δ 8.16 (1H, d, *J* = 2.8 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.55-7.62 (2H, m), 7.45 (1H, d, *J* = 8.4 Hz), 7.39 (1H, dd, *J* = 8.4, 2.0 Hz), 7.04 (1H, d, *J* = 8.8 Hz), 6.90 (1H, d, *J* = 2.0 Hz), 6.75 (1H, dd, *J* = 8.4, 2.4 Hz), 4.73 (2H, s), 3.84 (3H, s), 3.76 (3H, s); LCMS: 100%, MS (ESI); m/z 410.0 [M+H]+.
328		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.19 (1H, d, *J* = 2.4 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.27 (1H, d, *J* = 8.4 Hz), 7.06 (1H, d, *J* = 8.4 Hz), 6.91 (1H, d, *J* = 8.0 Hz), 6.81 (1H, d, *J* = 2.0 Hz), 6.76 (1H, t, *J* = 6.0 Hz), 6.64 (1H, dd, *J* = 8.4, 2.4 Hz), 6.25 (1H, d, *J* = 1.6 Hz), 6.20 (1H, dd, *J* = 8.4, 2.0 Hz), 5.84 (1H, d, *J* = 6.8 Hz), 4.84 (1H, t, *J* = 6.4 Hz), 4.49-4.57(1H, m), 4.47 (2H, d, *J* = 6.0 Hz), 4.39 (1H, t, *J* = 6.0 Hz), 3.80 (3H, s), 3.47 (3H, s); LCMS: 98.9 %, MS (ESI); m/z 466.0 [M+H]+.
329		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.51 (1H, dd, *J* = 4.8, 0.8 Hz), 8.17 (1H, d, *J* = 2.4 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.70 (1H, dt, *J* = 8.0, 2.0 Hz), 7.43 (2H, d, *J* = 8.8 Hz), 7.32 (1H, d, *J* = 7.6 Hz), 7.18-7.25 (1H, m), 7.03-7.14 (3H, m), 6.87-6.97 (2H, m), 6.40 (1H, d, *J* = 2.0 Hz), 6.32 (1H, dd, *J* = 8.4, 2.4 Hz), 5.15 (1H, t, *J* = 6.0 Hz), 4.51 (2H, d, *J* = 6.0 Hz), 3.45 (3H, s), 3.35-3.40 (2H, m), 3.00 (2H, t, *J* = 7.2 Hz); LCMS: 96.1%, MS (ESI); m/z 485.1[M+ H]+.

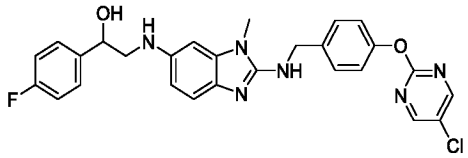
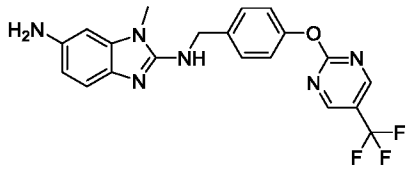
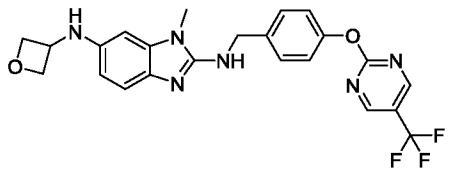
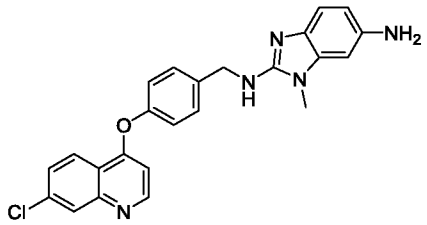
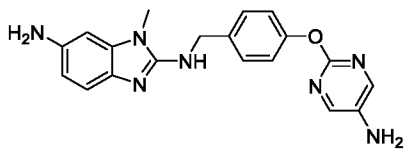
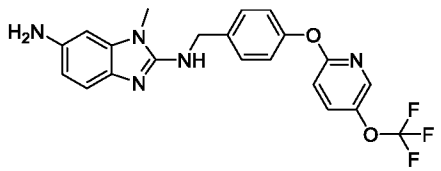
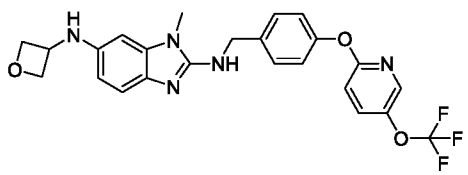
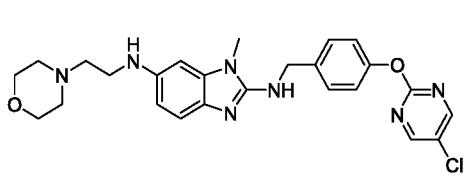
330		white powder (amorphous); (note: HNMR showed 10% of methyl isomer); 1H NMR (DMSO-*d*6, 400 MHz); δ 7.84 (1H, d, *J* = 3.2 Hz), 7.48 (1H, dd, *J* = 8.8, 3.2 Hz), 7.39 (2H, d, *J* = 8.8 Hz), 6.93-7.05 (3H, m), 6.80-6.90 (2H, m), 6.36 (1H, d, *J* = 1.6 Hz), 6.26 (1H, dd, *J* = 8.0, 2.0 Hz), 4.54 (2H, brs), 4.48 (2H, d, *J* = 6.0 Hz), 3.78 (3H, s), 3.40 (3H, s); LCMS: 98.8 %, MS (ESI); m/z 376.1[M+ H]+.
331		white powder (amorphous); (Note: HNMR showed 10% of methyl isomer); 1H NMR (DMSO-*d*6, 400 MHz); δ 7.84 (1H, d, *J* = 2.8 Hz), 7.48 (1H, dd, *J* = 8.8, 3.2 Hz), 7.38 (2H, d, *J* = 8.8 Hz), 6.89-7.02 (5H, m), 6.24 (1H, d, *J* = 2.0 Hz), 6.20 (1H, dd, *J* = 8.4, 2.0 Hz), 5.84 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.45-4.57 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.78 (3H, s), 3.44 (3H, s); LCMS: 100 %, MS (ESI); m/z 432.1[M+ H]+.
332		white powder (amorphous); 1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.4 Hz), 7.94 (1H, dd, *J* = 8.8, 2.8 Hz), 7.40 (2H, d, *J* = 8.4 Hz), 7.21 (1H, t, *J* = 6.0 Hz), 7.06-7.10 (3H, m), 6.93 (1H, d, *J* = 8.4 Hz), 6.27 (1H, d, *J* = 1.6 Hz), 6.19 (1H, dd, *J* = 8.4, 2.0 Hz), 5.85 (1H, d, *J* = 6.8 Hz), 4.80-4.86 (2H, m), 4.47-4.55 (3H, m), 4.36-4.42 (2H, m), 3.99 (2H, t, *J* = 6.8 Hz), 2.51-2.54 (2H, m, overlapped with DMSO peak), 2.20 (6H, s); LCMS: 96.1%, MS (ESI); m/z 493.1 [M+H]+.
333		white powder (amorphous); 1H NMR (CDCl3, 400 MHz); δ 8.12 (1H, d, *J* = 2.8 Hz), 7.66 (1H, dd, *J* = 8.8, 2.4 Hz), 7.48 (2H, d, *J* = 8.4 Hz), 7.34 (1H, d, *J* = 8.4 Hz), 7.12 (2H, d, *J* = 8.4 Hz), 6.92 (1H, d, *J* = 8.8 Hz), 6.53 (1H, dd, *J* = 8.4, 2.0 Hz), 6.40 (1H, d, *J* = 1.6 Hz), 4.70 (2H, d, *J* = 5.6 Hz), 4.14 (1H, t, *J* = 5.4 Hz), 3.45 (3H, s), 3.21 (2H, t, *J* = 5.6 Hz), 2.68 (2H, t, *J* = 5.8 Hz), 2.30-2.65 (8H, m), 2.31 (3H, s); LCMS: 100%, MS (ESI); m/z 506.2[M+ H]+.
334		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.20 (1H, d, *J* = 2.0 Hz), 7.94 (1H, dd, *J* = 8.8, 2.4 Hz), 7.07 (1H, d, *J* = 8.8 Hz), 6.93 (1H, d, *J* = 8.4 Hz), 6.84 (2H, s), 6.36 (1H, s), 6.29 (1H, d, *J* = 8.0 Hz), 6.22 (1H, brs), 4.59 (2H, brs), 4.43 (2H, d, *J* = 4.0 Hz), 3.36 (3H, s), 2.38 (6H, s); LCMS: 100%, MS (ESI); m/z 408.1[M+ H]+.
335		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.20 (1H, d, *J* = 2.8 Hz), 7.94 (1H, dd, *J* = 8.8, 2.8 Hz), 7.07 (1H, d, *J* = 8.8 Hz), 7.01 (1H, d, *J* = 9.2 Hz), 6.84 (2H, s), 6.18-6.32 (3H, m), 5.86 (1H, d, *J* = 6.8 Hz), 4.85 (2H, t, *J* = 6.4 Hz), 4.48-4.58 (1H, m), 4.45 (2H, d, *J* = 4.4 Hz), 4.40 (2H, t, *J* = 6.0 Hz), 3.39 (3H, s), 2.37 (6H, s); LCMS: 99.4%, MS (ESI); m/z 464.1[M+ H]+.
336		pale yellow powder (amorphous); 1H NMR (DMSO-*d*6, 400 MHz); δ 8.71 (2H, s), 7.44 (2H, d, *J* = 8.4 Hz), 7.13 (2H, d, *J* = 8.8 Hz), 6.91 (1H, t, *J* = 6.0 Hz), 6.86 (1H, d, *J* = 8.4 Hz), 6.36 (1H, d, *J* = 1.2 Hz), 6.26 (1H, dd, *J* = 8.0, 1.6 Hz), 4.55 (2H, brs), 4.51 (2H, d, *J* = 6.0 Hz), 3.41 (3H, s); LCMS: 100%, MS (ESI); m/z 365.0[M+H]+.
337		pale yellow amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.71 (2H, s), 7.43 (2H, d, *J* = 8.0 Hz), 7.13 (2H, d, *J* = 8.4 Hz), 6.97 (1H, brs), 6.93 (1H, d, *J* = 8.0 Hz), 6.25 (1H, d, *J* = 1.6 Hz), 6.21 (1H, dd, *J* = 8.4, 2.0 Hz), 5.85 (1H, d, *J* = 7.2 Hz), 4.82-4.86 (2H, m), 4.47-4.55 (3H, m), 4.36-4.42 (2H, m), 3.45 (3H, s); LCMS: 99.5%, MS (ESI); m/z 421.1[M+H]+.

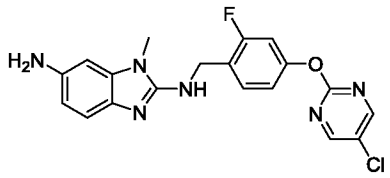
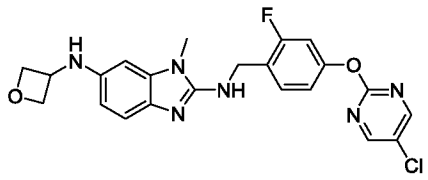
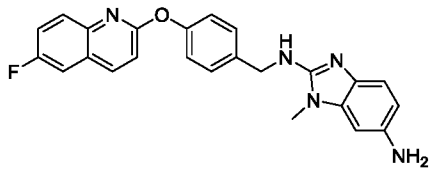
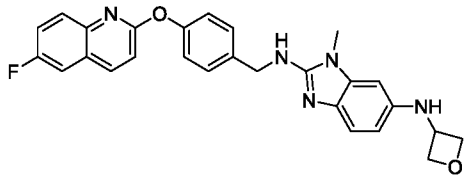
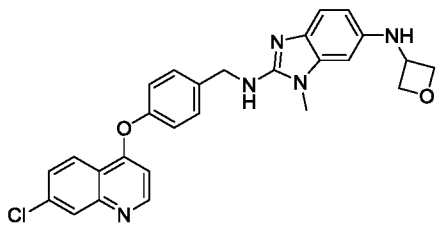
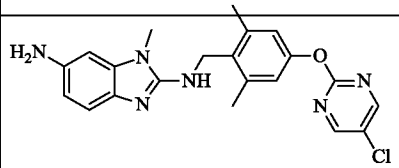
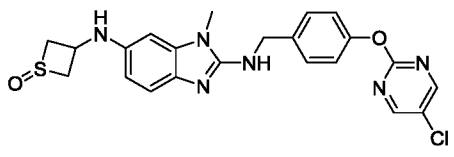
338		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.18 (1H, d, *J* = 2.8 Hz), 7.94 (1H, dd, *J* = 8.8, 2.8 Hz), 7.38 (1H, d, *J* = 8.8 Hz), 7.01-7.12 (4H, m), 6.45 (1H, d, *J* = 1.6 Hz), 6.40 (1H, dd, *J* = 8.8, 2.0 Hz), 4.78 (2H, brs), 4.43 (2H, s), 3.53-3.47 (5H, m), 3.29-3.34 (2H, m), 3.21 (3H, s); LCMS: 99.6 %, MS (ESI); m/z 438.1 [M+H]+.
339		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.18 (1H, d, *J* = 2.4 Hz), 7.94 (1H, dd, *J* = 8.4, 2.4 Hz), 7.37 (2H, d, *J* = 8.8 Hz), 7.13 (1H, d, *J* = 8.4 Hz), 7.00-7.10 (3H, m), 6.38 (1H, dd, *J* = 8.8, 2.4 Hz), 6.30 (1H, d, *J* = 2.0 Hz), 6.09 (1H, d, *J* = 6.4 Hz), 4.86 (2H, t, *J* = 6.4 Hz), 4.51-4.58 (1H, m), 4.44 (2H, s), 4.40 (2H, t, *J* = 6.0 Hz), 3.55 (3H, s), 3.49 (2H, t, *J* = 5.6 Hz), 3.28-3.33 (2H, m), 3.21 (3H, s); LCMS: 99.6 %, MS (ESI); m/z 494.1 [M+H]+.
340		pale yellow powder (amorphous); 1H NMR (DMSO-*d*6, 400 MHz); δ 8.58 (2H, s), 7.46 (2H, d, *J* = 8.8 Hz), 7.15 (2H, d, *J* = 8.4 Hz), 6.81-6.92 (2H, m), 6.36 (1H, d, *J* = 2.0 Hz), 6.26 (1H, dd, *J* = 8.4, 2.0 Hz), 4.55 (2H, brs), 4.51 (2H, d, *J* = 5.6 Hz), 3.40 (3H, s); LCMS: 100%, MS (ESI); m/z 381.0[M+H]+.
341		pale yellow amorphous;1H NMR (DMSO-*d*6, 400 MHz); δ 8.57 (2H, s), 7.45 (2H, d, *J* = 8.4 Hz), 7.15 (2H, d, *J* = 8.4 Hz), 6.92-6.95 (2H, m), 6.14-6.28 (2H, m), 5.85 (1H, d, *J* = 6.4 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.35-4.45 (3H, m), 4.39 (2H, t, *J* = 5.6 Hz), 3.44 (3H, s); LCMS: 100%, MS (ESI); m/z 436.9[M+H]+.
342		grey powder (amorphous); 1H NMR (DMSO-*d*6, 400 MHz); δ 8.15 (1H, s), 7.32 (2H, d, *J* = 8.4 Hz), 7.26 (1H, s), 6.97 (2H, d, *J* = 8.4 Hz), 6.85 (1H, d, *J* = 8.4 Hz), 6.77 (1H, brs), 6.35 (1H, s), 6.26 (1H, dd, *J* = 8.0, 2.4 Hz), 5.19 (2H, s), 4.55 (2H, brs), 4.42 (2H, d, *J* = 6.0 Hz), 3.38 (3H, s); LCMS: 100 %, MS (ESI); m/z 350.2[M+ H]+.
343		white powder (amorphous); 1H NMR (DMSO-*d*6, 400 MHz); δ 8.15 (1H, s), 7.31 (2H, d, *J* = 8.4 Hz), 7.25 (1H, s), 6.90-7.02 (3H, m), 6.82 (1H, t, *J* = 6.0 Hz), 6.15-6.25 (2H, m), 5.83 (1H, d, *J* = 6.8 Hz), 5.19 (2H, s), 4.77-4.89 (2H, m), 4.34-4.55 (5H, m), 3.41 (3H, s); LCMS: 100 %, MS (ESI); m/z 406.0[M+ H]+.
344		pale-yellow power; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.61 (2H, d, *J* = 4.8 Hz), 7.45 (2H, d, *J* = 8.4 Hz), 7.25 (1H, t, *J* = 4.8 Hz), 7.14 (2H, d, *J* = 8.4 Hz), 6.92 (1H, d, *J* = 8.4 Hz), 6.43 (1H, s), 6.33 (1H, d, *J* = 8.0 Hz), 4.54 (2H, d, *J* = 5.6 Hz), 3.46 (3H, s); LCMS: 98.4%, MS (ESI); m/z 347.0 [M+H]+.
345		pale-yellow power; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.61 (2H, d, *J* = 4.4 Hz), 7.43 (2H, d, *J* = 8.4 Hz), 7.24 (2H, t, *J* = 4.8 Hz), 7.11 (2H, d, *J* = 8.4 Hz), 6.93-6.98 (2H, m), 6.25 (1H, s), 6.21 (1H, d, *J* = 8.4 Hz), 5.83 (1H, d, *J* = 6.8 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.49-4.53 (3H, m), 4.39 (2H, t, *J* = 5.6 Hz), 3.45 (3H, s); LCMS: 99.5%, MS (ESI); m/z 403.0[M+H]+.

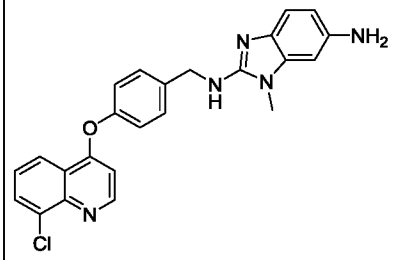
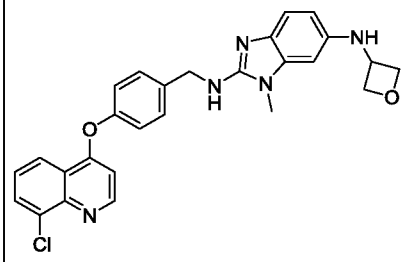
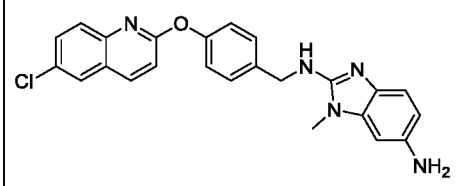
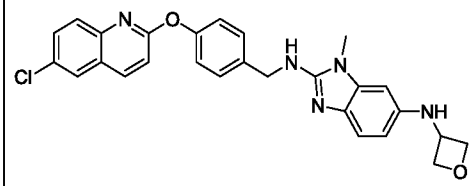
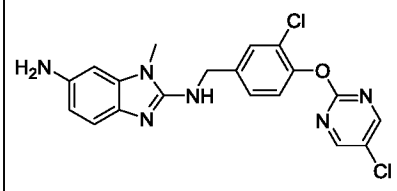
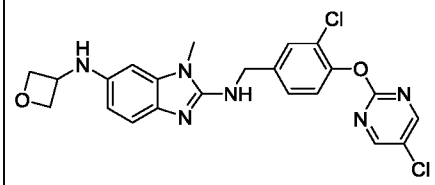
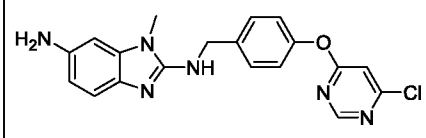
346		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.12 (1H, dd, *J* = 4.8, 1.2 Hz), 7.77-7.89 (1H, m), 7.43 (2H, d, *J* = 8.0 Hz), 7.04-7.12 (3H, m), 7.00 (1H, d, *J* = 8.4 Hz), 6.92 (1H, t, *J* = 5.2 Hz), 6.88 (1H, d, *J* = 8.0 Hz), 6.37 (1H, d, *J* = 1.6 Hz), 6.28 (1H, dd, *J* = 8.0, 1.6 Hz), 4.36-4.83 (4H, m), 3.42 (3H, s); LCMS: 100 %, MS (ESI); m/z 346.0 [M+H]+.
347		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.11 (1H, dd, *J* = 4.8, 1.6 Hz), 7.78-7.88 (1H, m), 7.41 (2H, d, *J* = 8.4 Hz), 7.03-7.13 (3H, m), 7.00 (1H, d, *J* = 8.8 Hz), 6.90-7.02 (2H, m), 6.25 (1H, d, *J* = 2.0 Hz), 6.21(1H, dd, *J* = 8.0, 2.0 Hz), 5.84 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.45-4.62 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.44 (3H, s); LCMS: 100 %, MS (ESI); m/z 402.0 [M+H]+.
348		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.45 (2H, s), 7.45 (2H, d, *J* = 8.4 Hz), 7.13 (2H, d, *J* = 8.4 Hz), 6.96 (1H, d, *J* = 8.4 Hz), 6.47 (1H, s), 6.38 (1H, d, *J* = 8.4 Hz), 4.56 (2H, d, *J* = 5.2 Hz), 3.48 (3H, s), 2.20 (3H, s); LCMS: 97.8%, MS (ESI); m/z 361.0 [M+H]+.
349		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.44 (2H, s), 7.41 (2H, d, *J* = 8.0 Hz), 7.08 (2H, d, *J* = 8.4 Hz), 6.92-6.96 (2H, m), 6.25 (1H, s), 6.21 (1H, d, *J* = 8.4 Hz), 5.83 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.47-4.52 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.44 (3H, s), 2.19 (3H, s); LCMS: 98.5%, MS (ESI); m/z 417.1[M+H]+.
350		off white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.62 (1H, d, *J* = 2.0 Hz), 8.30 (1H, dd, *J* = 8.8, 2.4 Hz), 7.47 (2H, d, *J* = 8.0 Hz), 7.23 (1H, d, *J* = 8.8 Hz), 7.14 (2H, d, *J* = 8.4 Hz), 6.85-6.94 (2H, m), 6.37 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.0, 2.0 Hz), 4.45-4.61 (4H, m), 3.42 (3H, s); LCMS: 99.8 %, MS (ESI); m/z 371.1[M+ H]+.
351		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.62 (1H, d, *J* = 2.0 Hz), 8.30 (1H, dd, *J* = 8.8, 2.4 Hz), 7.46 (2H, d, *J* = 8.8 Hz), 7.23 (1H, d, *J* = 8.8 Hz), 7.14 (2H, d, *J* = 8.4 Hz), 6.90-7.01 (2H, m), 6.26 (1H, s), 6.22 (1H, dd, *J* = 8.4, 2.0 Hz), 5.85 (1H, d, *J* = 7.2 Hz), 4.85 (2H, t, *J* = 6.4 Hz), 4.48-4.59 (3H, m), 4.40 (2H, t, *J* = 6.0 Hz), 3.45 (3H, s); LCMS: 98.3%, MS (ESI); m/z 427.1[M+ H]+.
352		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.95 (1H, d, *J* = 2.4 Hz), 7.65 (1H, dd, *J* = 8.4, 2.4 Hz), 7.41 (2H, d, *J* = 8.4 Hz), 7.03 (2H, d, *J* = 8.4 Hz), 6.95-6.83 (3H, m), 6.37 (1H, d, *J* = 1.6 Hz), 6.27 (1H, dd, *J* = 8.0, 2.0 Hz), 4.54 (2H, s), 4.50 (2H, d, *J* = 6.0 Hz), 3.41 (3H, s), 2.23 (3H, s); LCMS: 98.3 %, MS (ESI); m/z 360.0[M+ H]+.
353		a white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.95 (1H, s), 7.65 (1H, dd, *J* = 8.4, 2.4 Hz), 7.40 (2H, d, *J* = 8.4 Hz), 7.02 (2H, d, *J* = 8.4 Hz), 6.86-6.98 (3H, m), 6.16-6.31 (2H, m), 5.84 (1H, d, *J* = 7.2 Hz), 4.85 (2H, t, *J* = 6.4 Hz), 4.46-4.57 (3H, m), 4.40 (2H, t, *J* = 6.0 Hz), 3.44 (3H, s), 2.23 (3H, s); LCMS: 98.0%, MS (ESI); m/z 416.2[M+ H]+.
354		pale yellow powder (amorphous); 1H NMR (DMSO-*d*6, 400 MHz); δ 8.77 (2H, s), 8.46 (1H, d, *J* = 2.8 Hz), 7.66 (1H, dd, *J* = 8.4, 2.8 Hz), 7.48 (1H, d, *J* = 8.8 Hz), 7.05 (1H, t, *J* = 6.0 Hz), 6.84 (1H, d, *J* = 8.0 Hz), 6.38 (1H, d, *J* = 1.6 Hz), 6.26 (1H, dd, *J* = 8.4, 2.0 Hz), 4.61 (2H, d, *J* = 6.0 Hz), 4.55 (2H, s), 3.45 (3H, s); LCMS: 99.5%, MS (ESI); m/z 382.0[M+H]+.

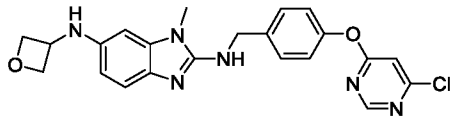
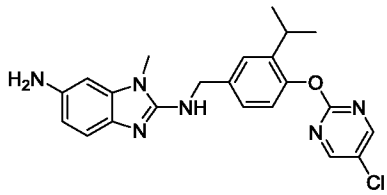
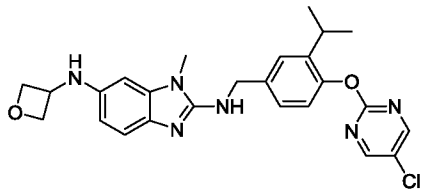
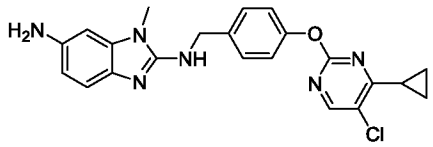
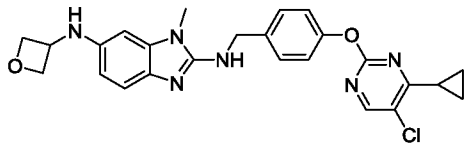
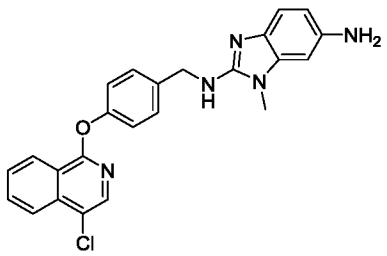
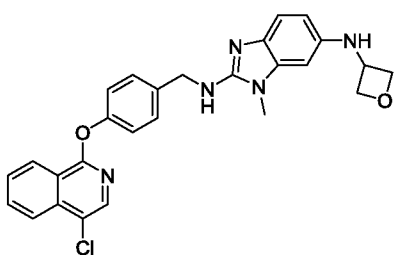
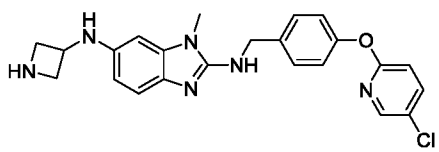
355		pale yellow amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.76 (2H, s), 8.46 (1H, d, *J* = 2.4 Hz), 7.66 (1H, dd, *J* = 8.4, 2.8 Hz), 7.47 (1H, d, *J* = 8.8 Hz), 7.10 (1H, t, *J* = 6.0 Hz), 6.92 (1H, d, *J* = 8.0 Hz), 6.26 (1H, d, *J* = 1.6 Hz), 6.21 (1H, dd, *J* = 8.4, 2.0 Hz), 5.85 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.0 Hz), 4.62 (2H, d, *J* = 6.0 Hz), 4.547-4.55 (1H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.48 (3H, s); LCMS: 100%, MS (ESI); m/z 438.1[M+H]+.
356		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.40-7.53 (3H, m), 7.25-7.40 (3H, m), 7.05-7.20 (2H, m), 6.82-6.96 (2H, m), 6.37 (1H, d, *J* = 1.2 Hz), 6.27 (1H, dd, *J* = 8.0, 2.0 Hz), 4.40-4.65 (4H, m), 3.71 (3H, s), 3.42 (3H, s); LCMS: 100%, MS (ESI); m/z 399.1[M+H]+.
357		white amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.40-7.52 (3H, m), 7.27-7.39 (3H, m), 7.06-7.19 (2H, m), 6.91-7.02 (2H, m), 6.26 (1H, d, *J* = 2.0 Hz), 6.22 (1H, dd, *J* = 8.0, 2.0 Hz), 5.83 (1H, d, *J* = 7.6 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.45-4.62 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.70 (3H, s), 3.45 (3H, s); LCMS: 100%, MS (ESI); m/z 455.2[M+H]+.
358		pale-yellow powder (amorphous); 1H NMR (DMSO-*d*6, 400 MHz); δ 8.73 (2H, s), 7.44 (2H, d, *J* = 8.4 Hz), 7.22 (1H, brs), 7.14 (2H, d, *J* = 8.4 Hz), 6.96-7.05 (2H, m), 6.92 (1H, d, *J* = 8.4 Hz), 6.33 (1H, d, *J* = 1.6 Hz), 6.30 (1H, dd, *J* = 8.4, 2.0 Hz), 5.15 (1H, brs), 4.52 (2H, d, *J* = 6.4 Hz), 3.40 (3H, s), 1.32 (6H, s); LCMS: 99.1 %, MS (ESI); m/z 466.1[M + H]+.
359		yellow powder (amorphous); 1H NMR (DMSO-*d*6, 400 MHz); δ 8.73 (2H, s), 7.44 (2H, d, *J* = 8.8 Hz), 7.14 (2H, d, *J* = 8.0 Hz), 7.05 (1H, s), 6.87-7.00 (2H, m), 6.79 (1H, s), 6.57 (1H, s), 6.42 (1H, d, *J* = 8.4 Hz), 5.46 (1H, brs), 4.51 (2H, d, *J* = 5.6 Hz), 4.24 (2H, d, *J* = 4.8 Hz), 3.64 (3H, s), 3.44 (3H, s); LCMS: 99.53%, MS (ESI); m/z 475.1[M+H]+.
360		white powder (amorphous); 1H NMR (DMSO-*d*6, 400 MHz); δ 8.11 (2H, s), 7.35 (1H, d, *J* = 8.4 Hz), 6.89 (2H, d, *J* = 8.8 Hz), 6.75-6.88 (2H, m), 6.62 (2H, brs), 6.35 (1H, d, *J* = 1.2 Hz), 6.25 (1H, dd, *J* = 8.0, 1.6 Hz), 4.53 (2H, brs), 4.44 (2H, d, *J* = 5.6 Hz), 3.38 (3H, s); LCMS: 97.1%, MS (ESI); m/z 362.1[M+ H]+.
361		pale-yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.78 (2H, s), 7.44 (2H, d, *J* = 8.4 Hz), 7.16 (2H, d, *J* = 8.4 Hz), 7.02 (1H, brs), 6.86 (1H, d, *J* = 8.0 Hz), 6.37 (1H, s), 6.27 (1H, dd, *J* = 8.4, 1.6 Hz), 4.77 (2H, brs), 4.51 (2H, d, *J* = 5.6 Hz), 3.42 (3H, s); LCMS: 98.8%, MS (ESI); m/z 425.0 [M+H]+.
362		pale-yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.77 (2H, s), 7.43 (2H, d, *J* = 8.0 Hz), 7.14 (2H, t, *J* = 8.4 Hz), 6.90-6.98 (2H, m), 6.25 (1H, s), 6.21 (1H, d, *J* = 8.4 Hz), 5.83 (1H, d, *J* = 6.8 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.47-4.52 (3H, m), 4.39 (2H, t, *J* = 5.6 Hz), 3.45 (3H, s); LCMS: 100%, MS (ESI); m/z 482.9[M+3]+.
363		pale-yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.95 (1H, d, *J* = 4.8 Hz), 7.76 (1H, d, *J* = 5.2 Hz), 7.47 (2H, d, *J* = 8.4 Hz), 7.22 (2H, d, *J* = 8.8 Hz), 6.90 (1H, d, *J* = 8.0 Hz), 6.41 (1H, s), 6.31 (1H, d, *J* = 8.4 Hz), 4.55 (2H, d, *J* = 5.6 Hz), 3.45 (3H, s); LCMS: 97.7%, MS (ESI); m/z 415.1 [M+H]+.

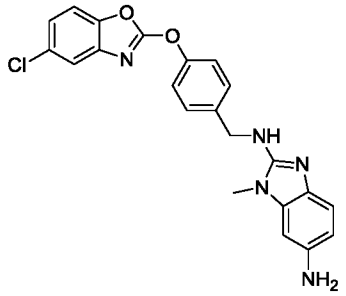
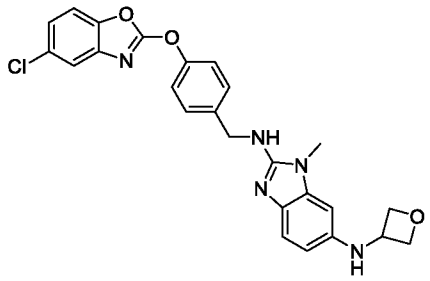
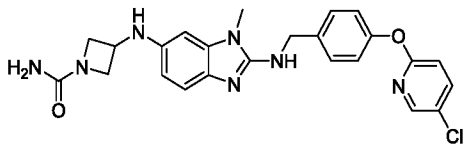
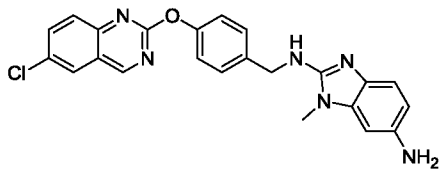
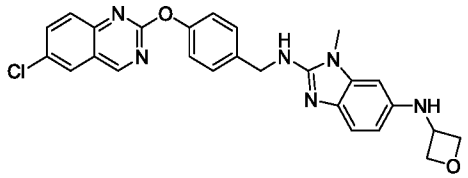
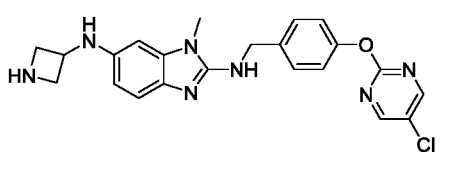
364		pale-yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.96 (1H, d, *J* = 4.4 Hz), 7.75 (1H, d, *J* = 4.8 Hz), 7.46 (2H, d, *J* = 8.4 Hz), 7.20 (2H, d, *J* = 8.4 Hz), 6.93-6.99 (2H, m), 6.25 (1H, s), 6.21 (1H, d, *J* = 8.8 Hz), 5.83 (1H, d, *J* = 6.8 Hz), 4.84 (2H, t, *J* = 6.0 Hz), 4.47-4.55 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.45 (3H, s); LCMS: 100%, MS (ESI); m/z 471.1[M+H]+.
365		yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.79 (2H, d, *J* = 5.2 Hz), 8.72 (2H, s), 7.44 (2H, d, *J* = 8.4 Hz), 7.39 (1H, t, *J* = 4.8 Hz), 7.12-7.17 (2H, m), 6.95 (1H, t, *J* = 6.0 Hz), 6.91 (1H, d, *J* = 8.4 Hz), 6.50 (1H, d, *J* = 2.0 Hz), 6.39 (1H, dd, *J* = 8.4, 2.0 Hz), 5.63 (1H, t, *J* = 6.0 Hz), 4.52 (2H, d, *J* = 5.6 Hz), 4.45 (2H, d, *J* = 5.6 Hz), 3.43 (3H, s); LCMS: 96.7%, MS (ESI); m/z 473.1[M+H]+.
366		pale-yellow power; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.72 (2H, s), 7.43 (2H, d, *J* = 8.8 Hz), 7.14 (2H, d, *J* = 8.4 Hz), 6.96 (1H, t, *J* = 6.0 Hz), 6.91 (1H, d, *J* = 8.4 Hz), 6.42 (1H, s), 6.27 (1H, dd, *J* = 8.8, 1.6 Hz), 5.76 (1H, d, *J* = 9.6 Hz), 4.70-4.78 (1H, m), 4.51 (2H, t, *J* = 6.0 Hz), 3.46 (3H, s), 3.30-3.35 (2H, m, after exchage with D2O), 3.25 (2H, t, *J* = 8.4 Hz); LCMS: 98.5%, MS (ESI); m/z 453.0 [M+H]+.
367		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 9.12 (2H, s), 7.47 (2H, d, *J* = 8.0 Hz), 7.19 (2H, d, *J* = 8.0 Hz), 6.93 (1H, t, *J* = 6.0 Hz), 6.86 (1H, d, *J* = 8.4 Hz), 6.37 (1H, d, *J* = 1.6 Hz), 6.27 (1H, dd, *J* = 8.0, 2.0 Hz), 4.52 (2H, d, *J* = 6.0 Hz), 3.41 (3H, s); LCMS: 99.3%, MS (ESI); m/z 372.1 [M+H]+.
368		pale yellow amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 9.12 (2H, s), 7.46 (2H, d, *J* = 8.4 Hz), 7.19 (2H, d, *J* = 8.4 Hz), 6.98 (1H, t, *J* = 6.0 Hz), 6.93 (1H, d, *J* = 8.4 Hz), 6.25 (1H, d, *J* = 2.0 Hz), 6.21 (1H, dd, *J* = 8.0, 2.0 Hz), 5.84 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.0 Hz), 4.47-4.56 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), (2H, m) 3.45 (3H, s); LCMS: 100%, MS (ESI); m/z 428.0[M+H] +.
369		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.12 (2H, s), 7.35 (1H, d, *J* = 8.4 Hz), 6.80-7.00 (4H, m), 6.63 (1H, s), 6.75-6.88 (2H, m), 6.63 (2H, s), 6.24 (1H, d, *J* = 1.6 Hz), 6.21 (1H, dd, *J* = 8.8, 2.0 Hz), 5.83 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.8 Hz), 4.50-4.60 (1H, m), 4.46 (2H, d, *J* = 6.0 Hz), 4.39 (2H, t, *J* = 6.0 Hz), 3.46 (3H, s); LCMS: 100%, MS (ESI); m/z 418.1[M+ H]+.
370		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.74 (1H, s), 8.67 (1H, d, *J* = 5.6 Hz), 7.48 (2H, d, *J* = 8.8 Hz), 7.09-7.21 (3H, m), 6.92 (1H, t, *J* = 6.0 Hz), 6.87 (1H, d, *J* = 8.4 Hz), 6.37 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.0, 2.0 Hz), 4.49-4.61 (4H, m), 3.43 (3H, s); LCMS: 99.0 %, MS (ESI); m/z 347.1[M+ H]+.
371		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.74 (1H, s), 8.67 (1H, d, *J* = 2.0 Hz), 7.47 (2H, d, *J* = 8.8 Hz), 7.09-7.26 (3H, m), 6.98 (1H, t, *J* = 5.6 Hz), 6.95 (1H, d, *J* = 8.0 Hz), 6.26 (1H, d, *J* = 1.6 Hz), 6.22 (1H, dd, *J* = 8.0, 1.6 Hz), 5.85 (1H, d, *J* = 6.8 Hz), 4.85 (2H, t, *J* = 6.4 Hz), 4.44-4.69 (3H, m), 4.40 (2H, t, *J* = 6.0 Hz), 3.46 (3H, s); LCMS: 100%, MS (ESI); m/z 403.2[M+ H]+.

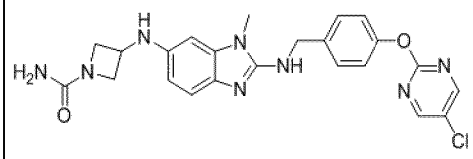
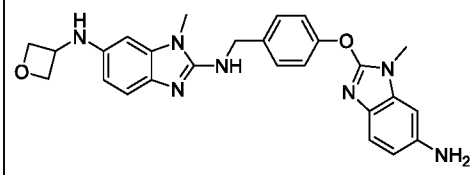
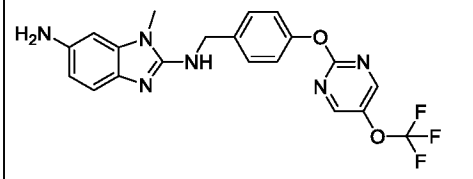
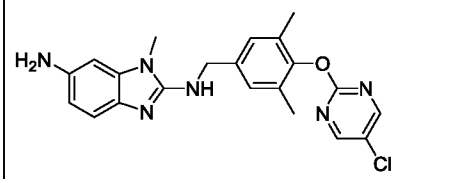
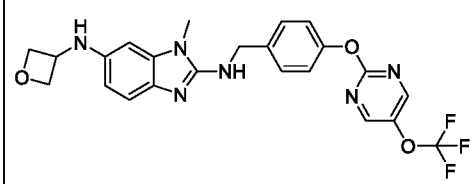
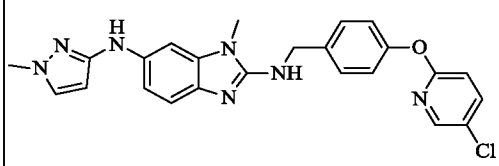
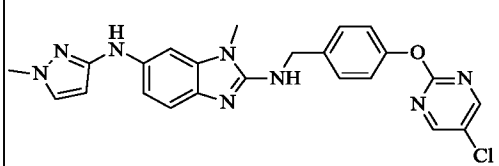
372		yellow amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.73 (2H, s), 7.40-7.48 (4H, m), 7.10-7.20 (4H, m), 6.87-6.95 (2H, m), 6.41 (1H, s), 6.34 (1H, d, *J* = 8.4 Hz), 5.51 (1H, brs), 4.92-4.97 (1H, m), 4.74-4.80 (1H, m), 4.51 (2H, d, *J* = 6.0 Hz), 3.44 (3H, s), 3.17-3.25 (1H, m), 3.02-3.17 (1H,m); LCMS: 99.77%, MS (ESI); m/z 519.1[M+H] +.
373		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 9.09 (2H, s), 7.47 (2H, d, *J* = 7.6 Hz), 7.20 (2H, d, *J* = 7.6 Hz), 6.90-6.99 (1H, m), 6.86 (1H, d, *J* = 8.0 Hz), 6.37 (1H, s), 6.26 (1H, d, *J* = 8.4 Hz), 4.45-4.65 (4H, m), 3.41 (3H, s); LCMS: 99.7 %, MS (ESI); m/z 415.1[M+ H]+.
374		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 9.09 (2H, s), 7.46 (2H, d, *J* = 8.4 Hz), 7.20 (2H, d, *J* = 8.4 Hz), 6.99 (1H, t, *J* = 6.0 Hz), 6.93 (1H, d, *J* = 8.4 Hz), 6.17-6.28 (2H, m), 5.85 (1H, d, *J* = 6.8 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.46-4.60 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.45 (3H, s); LCMS: 98.2 %, MS (ESI); m/z 471.1[M + H]+.
375		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.71(1H, d, *J* = 5.6 Hz), 8.33 (1H, d, *J* = 8.8 Hz), 8.09 (1H, d, *J* = 2.0 Hz), 7.68 (1H, dd, *J* = 9.2, 2.4 Hz), 7.55 (2H, d, *J* = 8.4 Hz), 7.26 (2H, d, *J* = 8.4 Hz), 6.95 (1H, t, *J* = 6.0 Hz), 6.88 (1H, d, *J* = 8.4 Hz), 6.60 (1H, d, *J* = 5.6 Hz), 6.37 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.0, 2.0 Hz), 4.45-4.69 (4H, m), 3.43 (3H, s); LCMS: 99.3%, MS (ESI); m/z 430.0[M+H] +.
376		grey powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.95 (2H, s), 7.38 (2H, d, *J* = 8.0 Hz), 7.00 (2H, d, *J* = 8.4 Hz), 6.82-6.90 (2H, m), 6.36 (1H, d, *J* = 1.6 Hz), 6.26 (1H, dd, *J* = 8.4, 2.0 Hz), 5.21 (2H, s), 4.55 (2H, brs), 4.48 (2H, d, *J* = 5.6 Hz), 3.40 (3H, s); LCMS: 94.7%, MS (ESI); m/z 362.0[M+H] +.
377		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.24 (1H, d, *J* = 2.8 Hz), 7.95 (1H, dd, *J* = 8.8, 2.0 Hz), 7.45 (2H, d, *J* = 8.4 Hz), 7.16 (1H, d, *J* = 9.2 Hz), 7.12 (2H, d, *J* = 8.4 Hz), 6.83-6.95 (2H, m), 6.37 (1H, d, *J* = 1.6 Hz), 6.27 (1H, dd, *J* = 8.0, 2.0 Hz), 4.56 (2H, brs), 4.52 (2H, d, *J* = 6.0 Hz), 3.42 (3H, s); LCMS: 99.9%, MS (ESI); m/z 430.1[M+H] +.
378		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.23 (1H, d, *J* = 2.8 Hz), 7.95 (1H, dd, *J* = 8.8, 2.4 Hz), 7.44 (2H, d, *J* = 8.4 Hz), 7.16 (1H, d, *J* = 8.8 Hz), 7.12 (2H, d, *J* = 8.4 Hz), 6.90-7.01 (2H, m), 6.26 (1H, d, *J* = 1.6 Hz), 6.22 (2H, dd, *J* = 8.4, 2.0 Hz), 5.85 (1H, d, *J* = 6.8 Hz), 4.85 (2H, t, *J* = 6.0 Hz), 4.46-4.58 (3H, m), 4.40 (2H, t, *J* = 6.0 Hz), 3.45 (3H, s); LCMS: 97.9%, MS (ESI); m/z 486.1[M+H] +.
379		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.73 (2H, s), 7.45 (2H, d, *J* = 8.4 Hz), 7.15 (2H, d, *J* = 8.4 Hz), 6.85-6.98 (2H, m), 6.42 (1H, d, *J* = 2.0 Hz), 6.31 (1H, dd, *J* = 8.4, 2.0 Hz), 4.82 (1H, t, *J* = 5.6 Hz), 4.52 (2H, d, *J* = 5.6 Hz), 3.59 (4H, t, *J* = 4.6 Hz), 3.45 (3H, s), 3.12 (2H, q, *J* = 6.0 Hz), 2.51-2.54 (2H, m), 2.35-2.46 (4H, m); LCMS: 99.5%, MS (ESI); m/z 494.1[M+H] +.

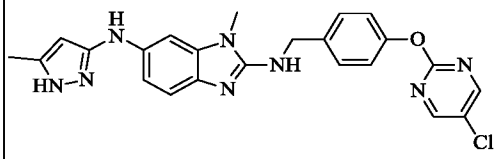
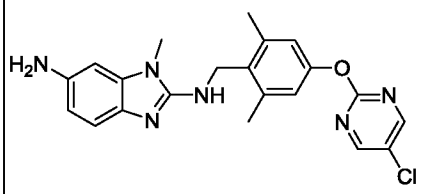
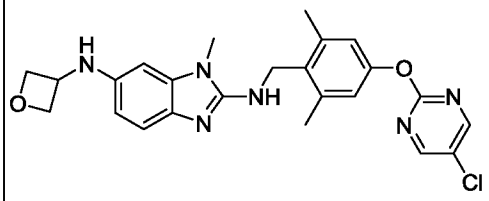
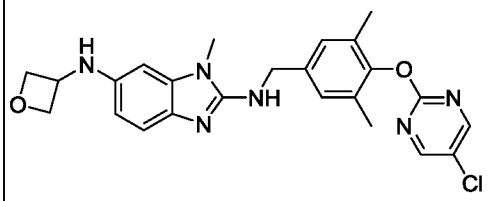
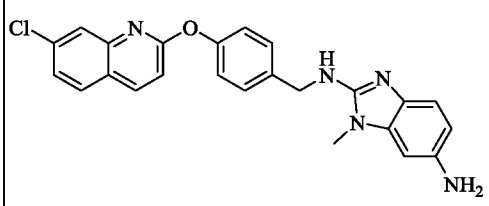
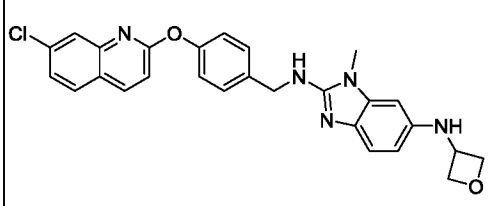
380		grey powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.76 (2H, s), 7.50 (1H, t, *J* = 8.8 Hz), 7.21 (1H, dd, *J* = 10.8, 2.0 Hz), 7.03 (1H, dd, *J* = 8.4, 2.0 Hz), 6.84-6.93 (2H, m), 6.37 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.0, 2.0 Hz), 4.48-4.62 (4H, m), 3.42 (3H, s); LCMS: 100%, MS (ESI); m/z 399.0[M+ H]+.
381		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.76 (2H, s), 7.50 (1H, t, *J* = 8.8 Hz), 7.21 (1H, dd, *J* = 11.2, 2.4 Hz), 7.03 (1H, dd, *J* = 8.4, 2.0 Hz), 6.92-7.00 (2H, m), 6.18-6.31 (2H, m), 5.86 (1H, d, *J* = 7.2 Hz), 4.85 (2H, t, *J* = 6.4 Hz), 4.46-4.61 (3H, m), 4.40 (2H, t, *J* = 6.0 Hz), 3.46 (3H, s); LCMS: 100 %, MS (ESI); m/z 455.1[M + H]+.
382		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.38 (1H, d, *J* = 8.8 Hz), 7.76 (1H, dd, *J* = 9.2, 2.8 Hz), 7.68 (1H, dd, *J* = 9.2, 5.2 Hz), 7.53 (1H, td, *J* = 8.8, 3.2 Hz), 7.43-7.48 (2H, m), 7.31 (1H, d, *J* = 9.2 Hz), 7.15-7.21 (2H, m), 6.94 (1H, t, *J* = 5.8 Hz), 6.88 (1H, d, *J* = 8.0 Hz), 6.37 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.4, 2.0 Hz), 4.46-4.65 (4H, m), 3.43 (3H, s); LCMS: 100%, MS (ESI); m/z 414.1[M+H] +.
383		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.38 (1H, d, *J* = 8.8 Hz), 7.76 (1H, dd, *J* = 9.2, 2.8 Hz), 7.68 (1H, dd, *J* = 8.8, 5.2 Hz), 7.52 (1H, td, *J* = 8.8, 2.8 Hz), 7.46 (2H, d, *J* = 8.4 Hz), 7.30 (1H, d, *J* = 8.8 Hz), 7.18 (2H, d, *J* = 8.4 Hz), 6.92-7.02 (2H, m), 6.26 (1H, d, *J* = 2.0 Hz), 6.22 (1H, dd, *J* = 8.0, 2.0 Hz), 5.84 (1H, d, *J* = 7.2 Hz), 4.85 (2H, t, *J* = 6.0 Hz), 4.56 (2H, d, *J* = 5.6 Hz), 4.47-4.55 (1H, m), 4.40 (2H, t, *J* = 6.0 Hz), 3.46 (3H, s); LCMS: 100%, MS (ESI); m/z 470.1[M+H] +.
384		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.70 (1H, d, *J* = 5.2 Hz), 8.32 (1H, d, *J* = 8.8 Hz), 8.08 (1H, d, *J* = 2.0 Hz), 7.68 (1H, dd, *J* = 9.2, 2.4 Hz), 7.54 (2H, d, *J* = 8.0 Hz), 7.26 (2H, d, *J* = 8.4 Hz), 7.02 (1H, t, *J* = 6.0 Hz), 6.95 (1H, d, *J* = 8.4 Hz), 6.59 (1H, d, *J* = 5.2 Hz), 6.26 (1H, d, *J* = 1.6 Hz), 6.22 (1H, dd, *J* = 8.0, 2.0 Hz), 5.85 (1H, d, *J* = 6.8 Hz), 4.85 (2H, t, *J* = 6.4 Hz), 4.58 (2H, d, *J* = 6.0 Hz), 4.45-4.55 (1H, m), 4.40 (2H, d, *J* = 6.0 Hz), 3.46 (3H, s); LCMS: 97.1%, MS (ESI); m/z 481.2[M+H] +.
385		pale yellow powder; 1H-NMR (DMSO-*d*6, 400 MHz): δ 8.75 (2H, s), 6.86-6.97 (3H, m), 6.36 (1H, s), 6.29 (1H, d, *J* = 8.0 Hz), 6.22 (1H, t, *J* = 4.8 Hz), 4.56 (2H, brs), 4.44 (2H, d, *J* = 4.8 Hz), 3.36 (3H, s), 2.39 (6H, s); LCMS: 100%, MS (ESI); m/z 409.2[M+ H]+.
386		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.73 (2H, s), 7.44 (2H, d, *J* = 8.4 Hz), 7.15 (2H, t, *J* = 8.4 Hz), 7.01 (1H, brs), 6.96 (1H, d, *J* = 8.4 Hz), 6.30 (1H, s), 6.23 (1H, d, *J* = 8.4 Hz), 5.73 (1H, d, *J* = 4.8 Hz), 4.61-4.63 (1H, m), 4.53 (2H, d, *J* = 5.6 Hz), 3.44-3.52 (7H, m); LCMS: 98.9%, MS (ESI); m/z 469.2[M+H] +.

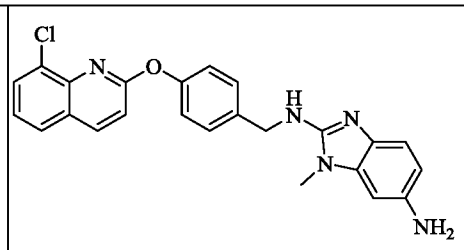
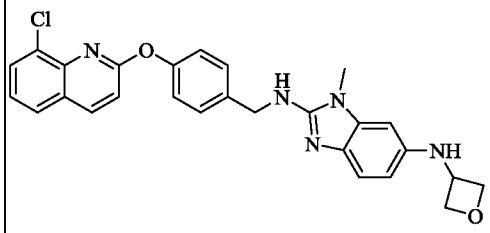
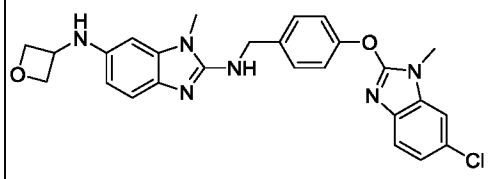
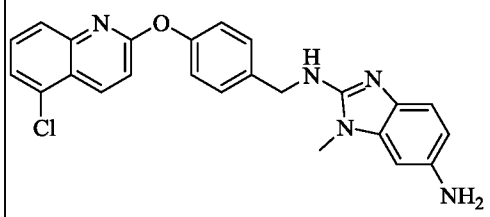
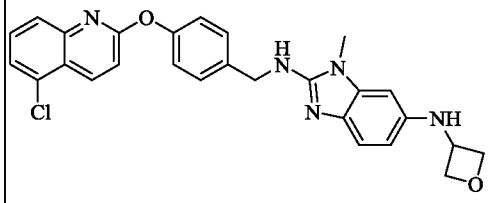
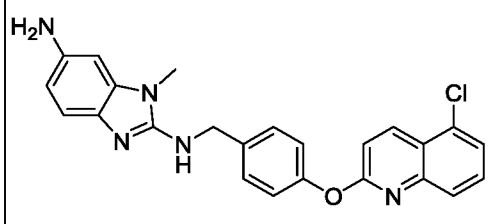
387		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.78 (1H, d, *J* = 5.2 Hz), 8.30 (1H, d, *J* = 8.4 Hz), 8.02 (1H, d, *J* = 6.4 Hz), 7.63 (1H, t, *J* = 8.0 Hz), 7.55 (2H, d, *J* = 8.8 Hz), 7.27 (2H, d, *J* = 8.0 Hz), 6.94 (1H, t, *J* = 6.0 Hz), 6.87 (1H, d, *J* = 8.0 Hz), 6.69 (1H, d, *J* = 4.8 Hz), 6.37 (1H, s), 6.27 (1H, dd, *J* = 8.0, 2.0 Hz), 4.48-4.65 (4H, m), 3.43 (3H, s); LCMS: 98.7 %, MS (ESI); m/z 430.1[M+ H]+.
388		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.78 (1H, d, *J* = 5.2 Hz), 8.30-8.35 (1H, m), 8.02 (1H, dd, *J* = 7.6, 1.6 Hz), 7.62 (1H, t, *J* = 8.4 Hz), 7.55 (2H, d, *J* = 8.4 Hz), 7.26 (2H, d, *J* = 8.4 Hz), 7.01 (1H, t, *J* = 6.0 Hz), 6.95 (1H, d, *J* = 8.4 Hz), 6.68 (1H, d, *J* = 5.2 Hz), 6.26 (1H, d, *J* = 2.0 Hz), 6.22 (1H, dd, *J* = 8.4, 2.0 Hz), 5.85 (1H, d, *J* = 6.8 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.58 (2H, d, *J* = 6.0 Hz), 4.45-4.56 (1H, m), 4.40 (2H, t, *J* = 6.0 Hz), 3.46 (3H, s); LCMS: 97.1%, MS (ESI); m/z 486.1[M + H]+.
389		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.38 (1H, d, *J* = 9.2 Hz), 8.07 (1H, d, *J* = 1.6 Hz), 7.60-7.67 (2H, m), 7.47 (2H, d, *J* = 8.4 Hz), 7.32 (1H, d, *J* = 8.8 Hz), 7.19 (2H, d, *J* = 8.4 Hz), 6.92 (1H, t, *J* = 6.0 Hz), 6.88 (1H, d, *J* = 8.4 Hz), 6.37 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.4, 2.0 Hz), 4.50-4.60 (4H, m), 3.43 (3H, s); LCMS: 99.4%, MS (ESI); m/z 430.1[M+H] +.
390		pale yellow amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.38 (1H, d, *J* = 9.2 Hz), 8.07 (1H, s), 7.60-7.66 (2H, m), 7.46 (2H, d, *J* = 8.4 Hz), 7.31 (1H, d, *J* = 9.2 Hz), 7.19 (2H, d, *J* = 8.4 Hz), 6.93-7.00 (2H, m), 6.26 (1H, d, *J* = 2.0 Hz), 6.22 (1H, dd, *J* = 8.4, 2.0 Hz), 5.83 (1H, d, *J* = 7.2 Hz), 4.85 (2H, t, *J* = 6.4 Hz), 4.47-4.60 (3H, m), 4.40 (2H, t, *J* = 6.0 Hz), 3.46 (3H, s); LCMS: 100%, MS (ESI); m/z 486.1[M+H] +.
391		pale yellow amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.77 (2H, s), 7.59 (1H, d, *J* = 1.6 Hz), 7.43 (1H, dd, *J* = 8.4, 2.0 Hz), 7.35 (1H, d, *J* = 8.4 Hz), 6.99 (1H, t, *J* = 6.0 Hz), 6.86 (1H, d, *J* = 8.4 Hz), 6.37 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.4, 2.0 Hz), 4.56 (2H, brs), 4.52 (2H, d, *J* = 6.0 Hz), 3.42 (3H, s); LCMS: 100%, MS (ESI); m/z 415.0 [M+H]+.
392		pale yellow amorphous; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.77 (2H, s), 7.58 (1H, d, *J* = 2.0 Hz), 7.43 (1H, dd, *J* = 8.4, 2.0 Hz), 7.35 (1H, d, *J* = 2.4 Hz), 7.05 (1H, t, *J* = 6.0 Hz), 6.94 (1H, d, *J* = 8.4 Hz), 6.26 (1H, d, *J* = 1.6 Hz), 6.22 (1H, dd, *J* = 8.4, 2.0 Hz), 5.86 (1H, d, *J* = 6.8 Hz), 4.84 (2H, t, *J* = 6.4 Hz) 4.47-4.56 (3H, m) 4.39 (2H, t, *J* = 6.0 Hz) 3.46 (3H, s); LCMS: 100%, MS (ESI); m/z 471.0[M+H] +.
393		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.61 (1H, s), 7.46 (2H, d, *J* = 8.4 Hz), 7.37 (1H, s), 7.16 (2H, d, *J* = 8.8 Hz), 6.91 (1H, t, *J* = 5.6 Hz), 6.85 (1H, d, *J* = 8.0 Hz), 6.35 (1H, d, *J* = 2.0 Hz), 6.25 (1H, dd, *J* = 8.0, 2.0 Hz), 4.46-4.57 (4H, m), 3.40 (3H, s); LCMS: 100 %, MS (ESI); m/z 381.0[M+ H]+.

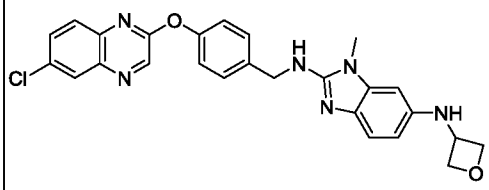
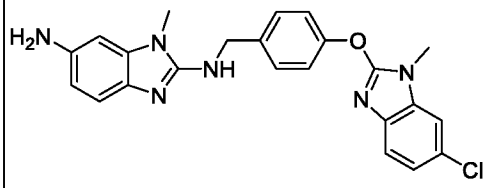
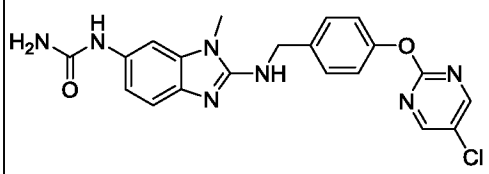
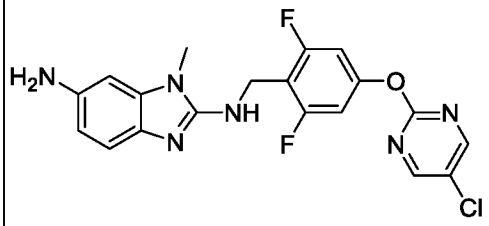
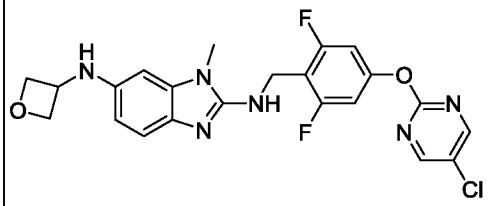
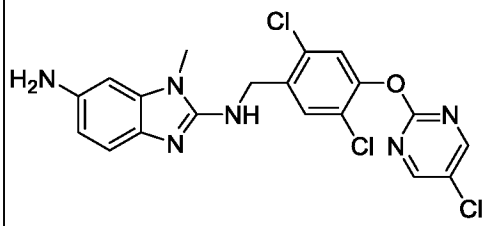
394		yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.63 (1H, s), 7.47 (2H, d, *J* = 8.8 Hz), 7.38 (1H, s), 7.18 (2H, d, *J* = 8.4 Hz), 6.98 (1H, t, *J* = 6.0 Hz), 6.94 (1H, d, *J* = 8.0 Hz), 6.26 (1H, d, *J* = 1.6 Hz), 6.22 (1H, dd, *J* = 8.0, 2.0 Hz), 5.85 (1H, d, *J* = 7.2 Hz), 4.85 (2H, t, *J* = 6.4 Hz), 4.45-4.61 (3H, m), 4.40 (2H, t, *J* = 5.6 Hz), 3.45 (3H, s); LCMS: 99.3%, MS (ESI); m/z 437.0[M+ H]+.
395		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.73 (2H, s), 7.44 (1H, d, *J* = 1.6 Hz), 7.26 (1H, dd, *J* = 8.4, 1.6 Hz), 7.02-7.05 (2H, m), 6.87 (1H, d, *J* = 8.0 Hz), 6.38 (1H, d, *J* = 1.6 Hz), 6.28 (1H, dd, *J* = 8.4, 1.6 Hz), 4.51 (2H, d, *J* = 6.0 Hz), 3.43 (3H, s), 2.89-2.97 (1H, m), 1.11 (6H, d, *J* = 6.8 Hz); LCMS: 99.2%, MS (ESI); m/z 423.1 [M+H]+.
396		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.72 (2H, s), 7.43 (1H, d, *J* = 1.6 Hz), 7.25 (1H, dd, *J* = 8.0, 1.6 Hz), 7.02 (1H, d, *J* = 8.4 Hz), 6.92-6.95 (2H, m), 6.25 (1H, d, *J* = 1.6 Hz), 6.21 (1H, dd, *J* = 8.4, 2.0 Hz), 5.84 (2H, d, *J* = 6.8 Hz), 4.84 (2H, t, *J* = 6.0 Hz), 4.49-4.54 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.45 (3H, s), 2.89-2.96 (1H, m), 1.10 (6H, d, *J* = 6.8 Hz); LCMS: 99.3%, MS (ESI); m/z 479.2[M+H] +.
397		white powder; 1H NMR (CDCl3, 400 MHz); δ 8.28 (1H, s), 7.48 (2H, d, *J* = 8.4 Hz), 7.32 (2H, d, *J* = 8.4 Hz), 7.15 (1H, d, *J* = 8.4 Hz), 6.56 (1H, d, *J* = 8.0 Hz), 6.48 (1H, s), 4.71 (2H, d, *J* = 3.6 Hz), 4.24 (1H, brs), 3.45 (3H, s), 2.41-2.52 (1H, m), 1.12-1.30 (4H, m); LCMS: 99.8%, MS (ESI); m/z 421.1[M+H] +.
398		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.51 (1H, s), 7.42 (2H, d, *J* = 8.4 Hz), 7.12 (2H, d, *J* = 8.4 Hz), 6.91-7.00 (2H, m), 6.25 (1H, d, *J* = 1.6 Hz), 6.22 (1H, dd, *J* = 8.4, 1.6 Hz), 5.85 (1H, d, *J* = 7.2 Hz), 4.85 (2H, t, *J* = 6.4 Hz), 4.47-4.59 (3H, m), 4.40 (2H, t, *J* = 6.0 Hz), 3.45 (3H, s), 2.38-2.46 (1H, m), 1.01-2.01 (2H, m), 0.80-1.05 (2H, m); LCMS: 99.7%, MS (ESI); m/z 477.1[M+H] +.
399		off-white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.45 (1H, d, *J* = 8.0 Hz), 8.14 (1H, d, *J* = 8.4 Hz), 8.07 (1H, s), 8.03 (1H, t, *J* = 7.6 Hz), 7.86 (1H, t, *J* = 7.8 Hz), 7.48 (2H, d, *J* = 8.0 Hz), 7.22 (2H, d, *J* = 8.4 Hz), 7.01 (1H, brs), 6.88 (1H, d, *J* = 8.4 Hz), 6.38 (1H, d, *J* = 1.2 Hz), 6.28 (1H, dd, *J* = 8.0, 2.0 Hz), 4.55 (2H, d, *J* = 5.6 Hz), 3.43 (3H, s); LCMS: 99.8%, MS (ESI); m/z 430.1[M+H] +.
400		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.45 (1H, d, *J* = 8.4 Hz), 8.14 (1H, d, *J* = 8.4 Hz), 8.07 (1H, s), 7.99-8.06 (1H, m), 7.86 (1H, t, *J* = 7.4 Hz), 7.47 (2H, d, *J* = 8.4 Hz), 7.21 (2H, d, *J* = 8.4 Hz), 6.99 (1H, t, *J* = 6.2 Hz), 6.95 (1H, d, *J* = 8.4 Hz), 6.26 (1H, d, *J* = 2.0 Hz), 6.22 (1H, dd, *J* = 8.0, 2.0 Hz), 5.84 (1H, d, *J* = 6.8 Hz), 4.85 (2H, t, *J* = 6.4 Hz), 4.47-4.60 (3H, m), 4.40 (2H, t, *J* = 6.0 Hz), 3.46 (3H, s); LCMS: 100%, MS (ESI); m/z 486.1[M+H] +.
401		white powder; 1H NMR (CDCl3, 400 MHz); δ 8.11 (1H, d, *J* = 2.4 Hz), 7.65 (1H, dd, *J* = 8.8, 2.8 Hz), 7.46 (2H, d, *J* = 8.4 Hz), 7.32 (1H, d, *J* = 8.4 Hz), 7.11 (2H, d, *J* = 8.4 Hz), 6.91 (1H, d, *J* = 8.4 Hz), 6.42 (1H, dd, *J* = 8.4, 1.6 Hz), 6.28 (1H, d, *J* = 2.0 Hz), 4.67 (2H, d, *J* = 4.0 Hz), 4.35-4.47 (1H, m), 4.25 (1H, brs), 3.97 (2H, t, *J* = 7.2 Hz), 3.54 (2H, t, *J* = 7.0 Hz), 3.43 (3H, s); LCMS: 98.6%, MS (ESI); m/z

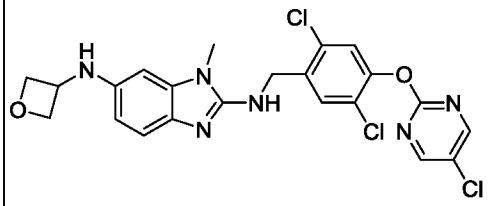
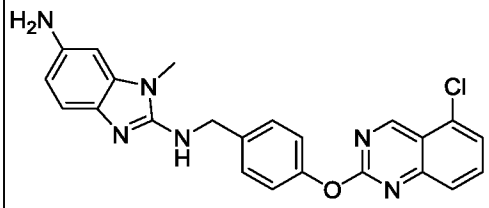
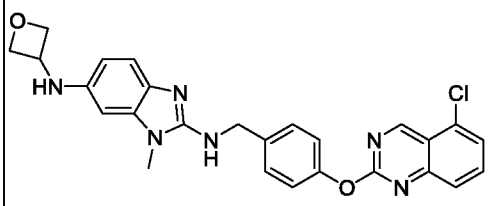
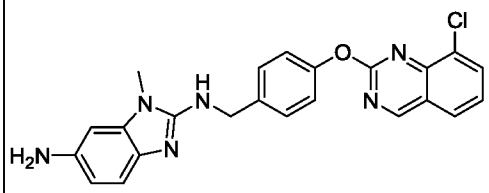
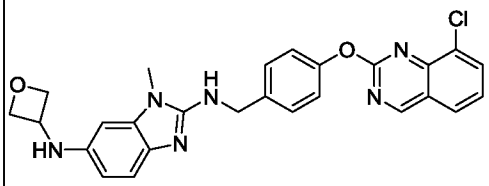
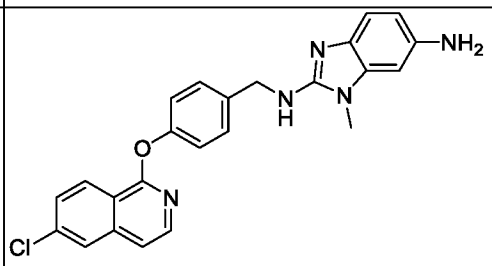
		435.1[M+H] +.
402		white powder; 1H NMR (CDCl3, 400 MHz); δ 7.52 (2H, d, *J* = 8.4 Hz), 7.45 (1H, d, *J* = 2.0 Hz), 7.33-7.40 (3H, m), 7.29 (1H, s), 7.22 (1H, dd, *J* = 8.4, 2.0 Hz), 6.55 (1H, dd, *J* = 8.4, 2.0 Hz), 6.47 (1H, d, *J* = 2.0 Hz), 4.61-4.82 (3H, m), 3.46 (3H, s); LCMS: 98.4%, MS (ESI); m/z 420.1[M+H] +.
403		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.66 (1H, d, *J* = 8.4 Hz), 7.62 (1H, d, *J* = 2.0 Hz), 7.51 (2H, d, *J* = 8.8 Hz), 7.44 (2H, d, *J* = 8.4 Hz), 7.32 (1H, dd, *J* = 8.8, 2.4 Hz), 7.00 (1H, t, *J* = 6.0 Hz), 6.94 (1H, d, *J* = 8.4 Hz), 6.26 (1H, d, *J* = 2.0 Hz), 6.22 (1H, dd, *J* = 8.4, 2.0 Hz), 5.84 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.47-4.60 (3H, m), 4.40 (2H, t, *J* = 6.0 Hz), 3.46 (3H, s); LCMS: 99.2%, MS (ESI); m/z 476.2[M+H] +.
404		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.4 Hz), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.43 (2H, d, *J* = 8.8 Hz), 7.03-7.11 (3H, m), 6.91-7.00 (2H, m), 6.29 (1H, d, *J* = 2.0 Hz), 6.24 (1H, dd, *J* = 8.4, 2.0 Hz), 5.75-5.84 (2H, m), 5.73 (1H, d, *J* = 4.8 Hz), 4.52 (2H, d, *J* = 5.6 Hz), 4.10-4.30 (3H, m), 3.56 (2H, d, *J* = 4.0 Hz), 3.45 (3H, s); LCMS: 99.7%, MS (ESI); m/z 478.2[M+H] +.
405		yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 9.52 (1H, s), 8.26 (1H, d, *J* = 2.4 Hz), 7.91 (1H, dd, *J* = 9.2, 2.4 Hz), 7.75 (1H, d, *J* = 9.2 Hz), 7.47 (2H, d, *J* = 8.4 Hz), 7.22 (2H, d, *J* = 8.4 Hz), 6.92 (1H, t, *J* = 6.0 Hz), 6.88 (1H, d, *J* = 8.0 Hz), 6.37 (1H, d, *J* = 2.0 Hz), 6.27 (1H, dd, *J* = 8.4, 2.0 Hz), 4.48-4.64 (4H, m), 3.43 (3H, s); LCMS: 99.4%, MS (ESI); m/z 431.1[M+ H]+.
406		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 9.51 (1H, s), 8.26 (1H, d, *J* = 2.4 Hz), 7.91 (1H, dd, *J* = 9.2, 2.4 Hz), 7.74 (1H, d, *J* = 9.2 Hz), 7.46 (2H, d, *J* = 8.4 Hz), 7.21 (2H, d, *J* = 8.4 Hz), 6.93-7.04 (2H, m), 6.26 (1H, s), 6.22 (1H, dd, *J* = 8.0, 2.0 Hz), 5.83 (1H, d, *J* = 7.2 Hz), 4.84 (2H, t, *J* = 6.4 Hz), 4.46-4.60 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.46 (3H, s); LCMS: 97.3%, MS (ESI); m/z 487.2[M + H]+.
407		off-white powder; 1H NMR (CDCl3, 400 MHz); δ 8.50 (2H, s), 7.51 (2H, d, *J* = 8.4 Hz), 7.32 (1H, d, *J* = 8.4 Hz), 7.18 (2H, d, *J* = 8.4 Hz), 6.43(1H, dd, *J* = 8.4, 1.6 Hz), 6.28 (1H, s), 4.71 (2H, d, *J* = 3.2 Hz), 4.34-4.46 (1H, m), 4.21 (1H, brs), 3.97 (2H, t, *J* = 7.2 Hz), 3.54 (2H, t, *J* = 7.2 Hz), 3.44 (3H, s); LCMS: 98.5%, MS (ESI); m/z 436.1[M+H] +.

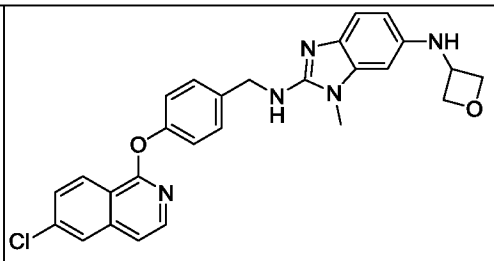
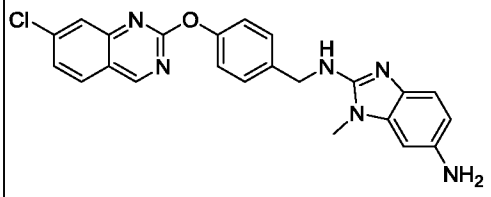
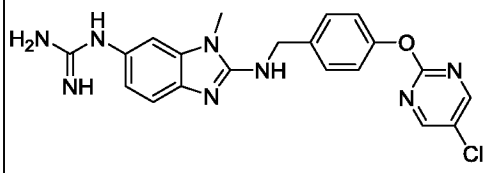
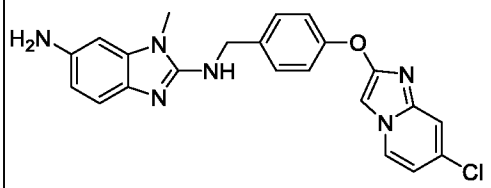
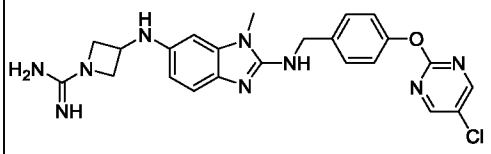
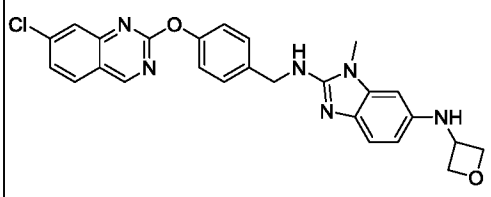
408		white powder; 1H NMR (CDCl3, 400 MHz); δ 8.50 (2H, s), 7.51 (1H, d, *J* = 8.4 Hz), 7.35 (1H, d, *J* = 8.4 Hz), 7.18 (2H, d, *J* = 8.8 Hz), 6.41 (1H, dd, *J* = 8.4, 2.0 Hz), 6.28 (1H, d, *J* = 2.0 Hz), 4.72 (2H, d, *J* = 5.6 Hz), 4.29-4.43 (5H, m), 4.26 (1H, t, *J* = 5.0 Hz), 3.93 (1H, brs), 3.76-3.86 (2H, m), 3.45 (3H, s); LCMS: 97.7%, MS (ESI); m/z 479.2[M+H] +.
409		white powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 7.43 (2H, d, *J* = 8.4 Hz), 7.27 (2H, d, *J* = 8.8 Hz), 7.03 (1H, d, *J* = 8.4 Hz), 6.90-6.98 (2H, m), 6.52 (1H, s), 6.42 (1H, d, *J* = 8.4 Hz), 6.25 (1H, s), 6.21 (1H, d, *J* = 8.4 Hz), 5.82 (1H, d, *J* = 6.8 Hz), 4.77-4.91 (4H, m), 4.47-4.57 (3H, m), 4.39 (2H, t, *J* = 6.0 Hz), 3.54 (3H, s), 3.44 (3H, s); LCMS: 98.5%, MS (ESI); m/z 470.3[M+H] +.
410		yellow powder; 1H NMR (CDCl3, 400 MHz); δ 8.50 (2H, s), 7.53 (2H, d, *J* = 8.4 Hz), 7.31 (1H, d, *J* = 8.4 Hz), 7.20 (2H, d, *J* = 8.4 Hz), 6.55 (1H, dd, *J* = 8.0, 2.0 Hz), 6.47 (1H, d, *J* = 1.6 Hz), 4.72 (2H, d, *J* = 4.8 Hz), 4.18 (1H, brs), 3.43 (3H, s); LCMS: 96.9%, MS (ESI); m/z 431.1[M+H] +.
411		pale yellow powder; 1H NMR (DMSO-*d*6, 400 MHz); δ 8.73 (2H, s), 7.15 (2H, s), 6.81-6.90 (2H, m), 6.37 (1H, d, *J* = 1.6 Hz), 6.27 (1H, dd, *J* = 8.0, 2.0 Hz), 4.55 (2H, brs), 4.45 (2H, d, *J* = 6.0 Hz), 3.42 (3H, s), 2.02 (6H, s); LCMS: 100%, MS (ESI); m/z 409.1[M+ H]+.
412		yellow powder; 1H NMR (CDCl3, 400 MHz); δ 8.50 (2H, s), 7.52 (2H, d, *J* = 8.8 Hz), 7.34 (1H, d, *J* = 8.4 Hz), 7.19 (2H, d, *J* = 8.4 Hz), 6.40 (1H, dd, *J* = 8.4, 2.0 Hz), 6.24 (1H, d, *J* = 2.0 Hz), 5.03 (2H, t, *J* = 6.4 Hz), 4.73 (2H, d, *J* = 4.4 Hz), 4.63-4.70 (1H, m), 4.56 (2H, t, *J* = 6.0 Hz), 4.36 (1H, brs), 3.46 (3H, s); LCMS: 100%, MS (ESI); m/z 487.3[M+H] +.
413		1H NMR (DMSO-*d*6, 400 MHz); δ 8.17 (1H, d, *J* = 2.8 Hz), 8.02 (1H, s), 7.93 (1H, dd, *J* = 8.8, 2.8 Hz), 7.45-7.42 (3H, m), 7.23 (1H, d, *J* = 2.4 Hz), 7.09-7.06 (3H, m), 7.05-6.98 (m, 2H) 6.85 (1H, dd, *J* = 8.8, 2.8 Hz), 5.73 (1H, d, *J* = 2.4 Hz), 4.53 (2H, d, *J* = 6.0 Hz) 3.71 (3H, s), 3.46 (3H, s); LCMS: 100%, MS (ESI); m/z 460.3[M+H]+.
414		pale yellow solid; 1H NMR (DMSO-d6, 400 MHz); δ 8.74 (2H, s), 8.03 (1H, s) 7.48-7.45 (m, 3H), 7.23 (1H, d, J = 1.6 Hz), 7.17 (2H, d, J = 8.4 Hz), 7.04-6.99 (2H, m), 6.86 (1H, dd, J = 8.8, 2.8 Hz), 5.74 (1H, d, J = 1.6 Hz), 4.56 (2H, d, J = 5.6 Hz) 3.73 (3H, s), 3.48 (3H, s); LCMS: 99.4%, MS (ESI); m/z 461.2[M+H]+.

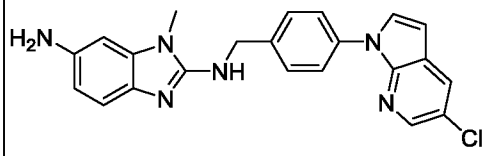
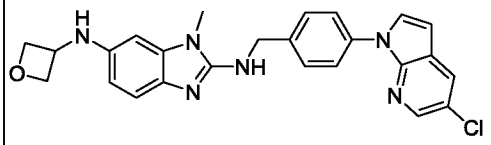
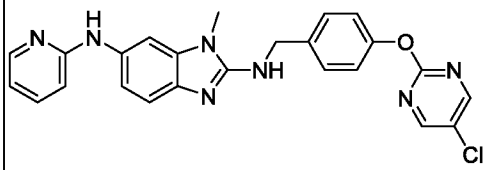
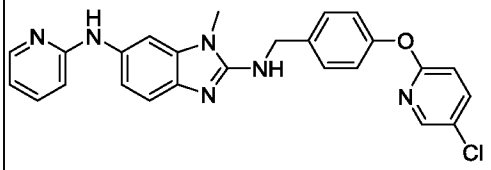
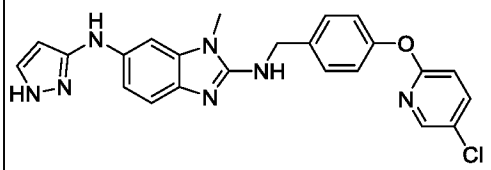
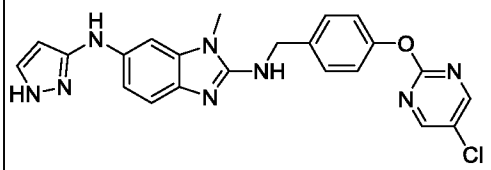
415		yellow powder; 1H NMR (DMSO-d6, 400 MHz); δ 11.48 (1H, s), 8.73 (2H, s), 7.92-7.91 (1H, m), 7.46 (2H, d, J = 8.4 Hz), 7.33 (1H, s), 7.16 (2H, d, J = 8.4 Hz), 7.02-6.07 (2H, m), 6.78-6.75 (1H, m), 5.55 (1H, s), 4.54 (2H, d, J = 5.2 Hz), 3.46 (s, 3H), 2.16 (s, 3H); LCMS: 95.5%, MS (ESI); m/z 461.2[M+H]+.
416		pale yellow powder (amorphous); 1H-NMR (DMSO-d6, 400 MHz): δ 8.75 (2H, s), 6.86-6.97 (3H, m), 6.36 (1H, s), 6.29 (1H, d, J = 8.0 Hz), 6.22 (1H, t, J = 4.8 Hz), 4.56 (2H, brs), 4.44 (2H, d, J = 4.8 Hz), 3.36 (3H, s), 2.39 (6H, s); LCMS: 100%, MS (ESI): m/z 409.2[M+ H]+.
417		off-white powder (amorphous); 1H-NMR (DMSO-d6, 400 MHz): δ 8.74 (2H, s), 7.00 (1H, d, J = 8.8 Hz), 6.90 (2H, s), 6.29 (1H, t, J = 4.8 Hz), 6.19-6.25 (2H, m), 5.85 (1H, d, J = 7.2 Hz), 4.84 (2H, t, J = 6.4 Hz), 4.47-4.56 (1H, m), 4.44 (1H, d, J = 4.8 Hz), 4.39 (1H, t, J = 6.0 Hz), 3.37 (3H, s, D2O added), 2.38 (6H, s); LCMS: 100%, MS (ESI): m/z 465.2[M + H]+.
418		a white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.73 (2H, s), 8.14 (2H, s), 6.94 (1H, d, J = 8.4 Hz), 6.90 (1H, t, J = 5.6 Hz), 6.25 (1H, d, J = 2.0 Hz), 6.22 (1H, dd, J = 8.4, 2.0 Hz), 5.84 (1H, d, J = 7.2 Hz), 4.85 (2H, t, J = 6.0 Hz), 4.49-4.54 (1H, m), 4.46 (1H, d, J = 6.0 Hz), 4.40 (2H, t, J = 6.0 Hz), 3.45 (3H, s), 2.01 (6H, s); LCMS: 96.9%, MS (ESI): m/z 465.2[M+H] +.
419		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.43 (1H, d, J = 9.2 Hz), 7.98 (1H, d, J = 8.4 Hz), 7.68 (1H, d, J = 2.4 Hz), 7.51 (1H, dd, J = 8.4, 2.0 Hz), 7.47 (2H, d, J = 8.4 Hz), 7.28 (1H, d, J = 8.8 Hz), 7.20 (2H, d, J = 8.8 Hz), 6.93 (1H, t, J = 6.0 Hz), 6.88 (1H, d, J = 8.0 Hz), 6.38 (1H, d, J = 2.0 Hz), 6.27 (1H, dd, J = 8.4, 2.0 Hz), 4.50-4.55 (4H, m), 3.43 (3H, s); LCMS: 100%, MS (ESI): m/z 430.1[M+H] +.
420		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.43 (1H, d, J = 8.8 Hz), 7.98 (1H, d, J = 8.4 Hz), 7.67 (1H, d, J = 2.0 Hz), 7.51 (1H, dd, J = 8.4, 2.0 Hz), 7.46 (2H, d, J = 8.8 Hz), 7.28 (1H, d, J = 8.8 Hz), 7.19 (2H, d, J = 8.4 Hz), 6.93-7.02 (2H, m), 6.26 (1H, d, J = 2.0 Hz), 6.22 (1H, dd, J = 8.4, 2.0 Hz), 5.84 (1H, d, J = 7.2 Hz), 4.85 (2H, t, J = 6.4 Hz), 4.56 (2H, d, J = 6.0 Hz), 4.46-4.54 (1H, m), 4.40 (2H, t, J = 5.8 Hz), 3.46 (3H, s); LCMS: 99.8%, MS (ESI): m/z 486.2[M+H] +.

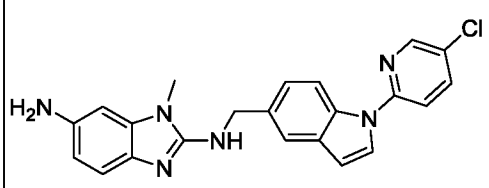
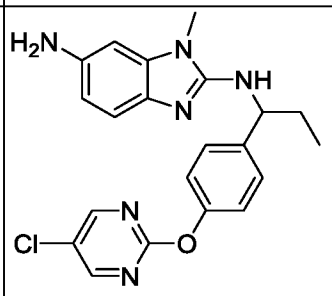
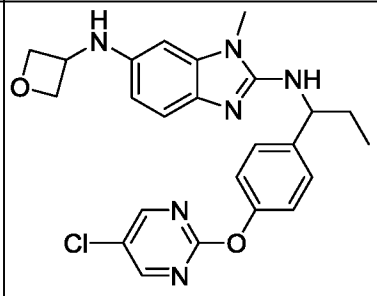
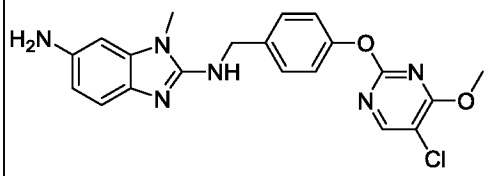
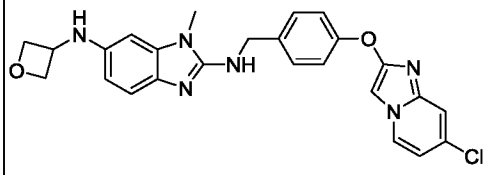
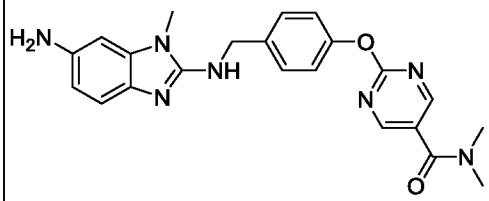
421		white amorphous; 1H-NMR (DMSO-d6, 400 MHz): δ 8.47 (1H, d, J = 9.2 Hz), 7.94 (1H, dd, J = 8.0, 1.2 Hz), 7.85 (1H, dd, J = 8.0, 1.2 Hz), 7.43-7.50 (3H, m), 7.29-7.33 (3H, m), 6.93 (1H, brs), 6.88 (1H, d, J = 8.0 Hz), 6.37 (1H, d, J = 2.0 Hz), 6.27 (1H, dd, J = 8.0, 2.0 Hz), 4.50-4.65 (4H, m), 3.43 (3H, s); LCMS: 100%, MS (ESI): m/z 430.1[M+H] +.
422		white amorphous; 1H-NMR (DMSO-d6, 400 MHz): δ 8.47 (1H, d, J = 9.2 Hz), 7.94 (1H, dd, J = 8.0, 1.2 Hz), 7.85 (1H, dd, J = 7.6, 1.2 Hz), 7.42-7.51 (3H, m), 7.27-7.34 (3H, m), 6.91-7.00 (2H, m), 6.26 (1H, d, J = 2.0 Hz), 6.22 (1H, dd, J = 8.0, 2.0 Hz), 5.83 (1H, d, J = 7.6 Hz), 4.84 (2H, t, J = 6.0 Hz), 4.57 (2H, d, J = 5.6 Hz), 4.47-4.55 (1H, m), 4.40 (2H, t, J = 6.0 Hz), 3.46 (3H, s); LCMS: 100%, MS (ESI): m/z 486.2[M+H] +.
423		white solid; mp 138.9-140.8 °C; 1H-NMR (DMSO-d6, 400 MHz): δ 7.61 (1H, d, J = 2.0 Hz), 7.47 (2H, d, J = 8.8 Hz), 7.29-7.40 (3H, m), 7.12 (1H, dd, J = 8.8, 2.0 Hz), 6.90-7.02 (2H, m), 6.25 (1H, d, J = 2.0 Hz), 6.21 (1H, dd, J = 8.4, 2.4 Hz), 5.84 (1H, d, J = 7.2 Hz), 4.84 (2H, t, J = 6.4 Hz), 4.46-4.59 (3H, m), 4.40 (2H, t, J = 6.0 Hz), 3.71 (3H, s), 3.45 (3H, s); LCMS: 98.5%, MS (ESI): m/z 489.2[M+H] +.
424		off-white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.58 (1H, d, J = 8.8 Hz), 7.58-7.67 (3H, m), 7.48 (2H, d, J = 8.4 Hz), 7.40 (1H, d, J = 8.8 Hz), 7.21 (2H, d, J = 8.4 Hz), 6.93 (1H, t, J = 6.0 Hz), 6.88 (1H, d, J = 8.0 Hz), 6.38 (1H, d, J = 1.6 Hz), 6.28 (1H, dd, J = 8.0, 2.0 Hz), 4.49-4.60 (4H, m), 3.43 (3H, s); LCMS: 95.9%, MS (ESI): m/z 430.1[M+H] +.
425		white solid; mp: 102.3-107.3 oC; 1H-NMR (DMSO-d6, 400 MHz): δ 8.43 (1H, d, J = 8.8 Hz), 7.98 (1H, d, J = 8.4 Hz), 7.67 (1H, d, J = 2.0 Hz), 7.51 (1H, dd, J = 8.4, 2.0 Hz), 7.46 (2H, d, J = 8.8 Hz), 7.28 (1H, d, J = 8.8 Hz), 7.19 (2H, d, J = 8.4 Hz), 6.93-7.02 (2H, m), 6.26 (1H, d, J = 2.0 Hz), 6.22 (1H, dd, J = 8.4, 2.0 Hz), 5.84 (1H, d, J = 7.2 Hz), 4.85 (2H, t, J = 6.4 Hz), 4.56 (2H, d, J = 6.0 Hz), 4.46-4.54 (1H, m), 4.40 (2H, t, J = 6.0 Hz), 3.46 (3H, s); LCMS: 99.8%, MS (ESI): m/z 486.2[M+H] +.
426		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.90 (1H, s), 8.15 (1H, s), 7.74-7.77 (2H, m), 7.49 (2H, d, J = 8.8 Hz), 7.27 (2H, dd, J = 6.8, 2.0 Hz), 6.95 (3H, t, J = 5.6 Hz), 6.87 (1H, d, J = 8.0 Hz), 6.37 (1H, d, J = 1.6 Hz), 6.27 (1H, dd, J = 8.4, 2.0 Hz), 4.45-4.70 (4H, m), 3.43 (3H, s); LCMS: 100%, MS (ESI): m/z 431.1[M+ H]+.

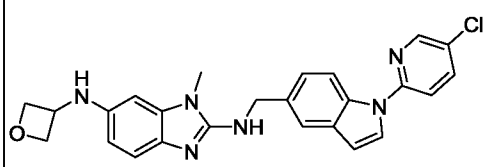
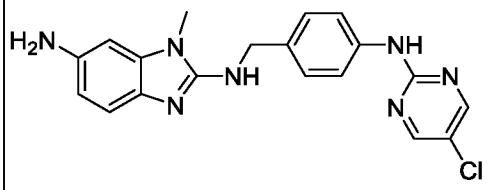
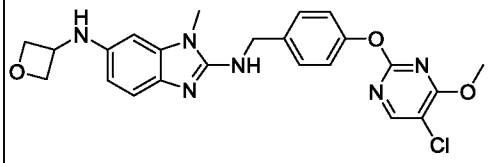
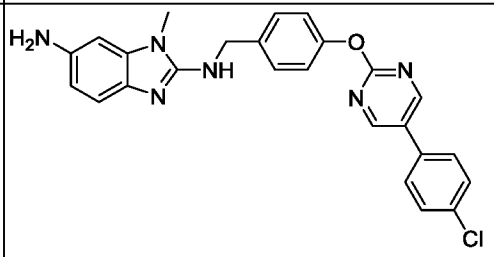
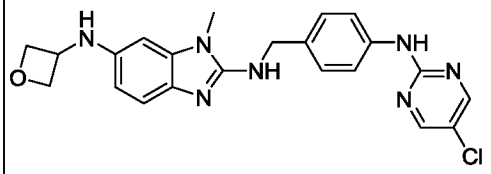
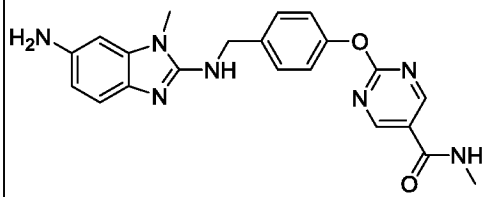
427		pale yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.90 (1H, s), 8.15 (1H, s), 7.74 (2H, s), 7.49 (2H, d, J = 8.4 Hz), 7.27 (2H, dd, J = 8.8 Hz), 6.99 (1H, t, J = 6.4 Hz), 6.95 (1H, d, J = 8.4 Hz), 6.26 (1H, d, J = 2.0 Hz), 6.22 (1H, dd, J = 8.4, 2.0 Hz), 5.83 (1H, d, J = 7.2 Hz), 4.84 (2H, t, J = 6.4 Hz), 4.45-4.70 (3H, m), 4.40 (2H, t, J = 6.0 Hz), 3.46 (3H, s); LCMS: 100%, MS (ESI): m/z 487.2[M+ H]+.
428		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 7.61 (1H, d, J = 2.0 Hz), 7.48 (2H, d, J = 8.4 Hz), 7.30-7.40 (3H, m), 7.12 (1H, dd, J = 8.0, 2.0 Hz), 6.93 (1H, t, J = 6.0 Hz), 6.88 (1H, d, J = 8.0 Hz), 6.37 (1H, d, J = 1.6 Hz), 6.27 (1H, dd, J = 8.4, 2.4 Hz), 4.56 (1H, brs), 4.53 (2H, d, J = 5.6 Hz), 3.71 (3H, s), 3.42 (3H, s); LCMS: 100%, MS (ESI): m/z 433.2[M+H] +.
429		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 13.10 (1H, brs), 9.39 (1H, t, J = 5.2 Hz), 8.88 (1H, s), 8.74 (2H, s), 7.78 (1H, d, J = 2.0 Hz), 7.53 (2H, d, J = 8.4 Hz), 7.21-7.31 (3H, m), 7.08 (1H, d, J = 8.4 Hz), 5.94 (2H, brs), 4.70 (2H, d, J = 6.0 Hz), 3.63 (3H, s); LCMS: 100%, MS (ESI): m/z 424.2[M + H]+.
430		pale yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.80 (2H, s), 7.12-7.21 (2H, m), 6.91 (1H, d, J = 8.0 Hz), 6.64 (1H, t, J = 5.2 Hz), 6.36 (1H, d, J = 2.0 Hz), 6.29 (1H, dd, J = 8.4, 2.0 Hz), 4.57 (2H, brs), 4.51 (2H, d, J = 4.8 Hz); LCMS: 97.4%, MS (ESI): m/z 417.1 [M+H]+.
431		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.80 (2H, s), 7.17 (2H, d, J = 8.4 Hz), 6.99 (1H, d, J = 8.8 Hz), 6.70 (1H, t, J = 5.6 Hz), 6.20-6.25 (2H, m), 5.86 (1H, d, J = 7.2 Hz), 4.84 (2H, t, J = 6.4 Hz), 4.48-4.55 (3H, m), 4.40 (2H, t, J = 6.0 Hz), 3.39 (3H, s); LCMS: 100%, MS (ESI): m/z 473.1[M+H] +.
432		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.80 (2H, s), 7.70 (1H, s), 7.59 (1H, s), 7.02 (1H, t, J = 6.0 Hz), 6.86 (1H, d, J = 8.0 Hz), 6.39 (1H, d, J = 2.0 Hz), 6.28 (1H, dd, J = 8.0, 2.0 Hz), 4.50-4.66 (4H, m), 3.46 (3H, s); LCMS: 97.1%, MS (ESI): m/z 449.0[M+ H]+.

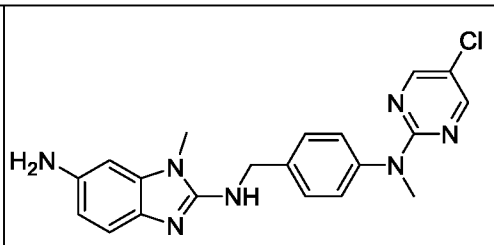
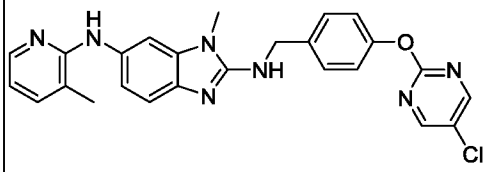
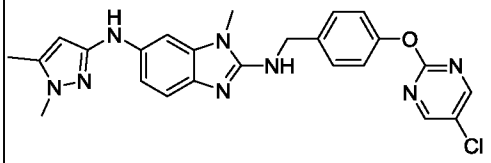
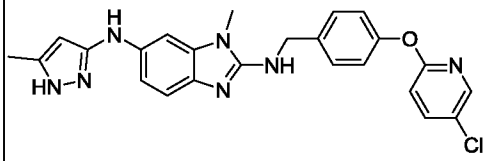
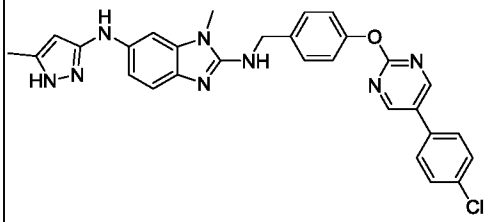
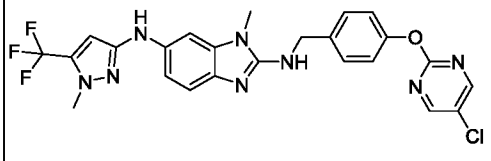
433		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.80 (2H, s), 7.70 (1H, s), 7.58 (1H, s), 7.08 (1H, t, J = 6.0 Hz), 6.94 (1H, d, J = 8.4 Hz), 6.28 (1H, d, J = 2.0 Hz), 6.23 (1H, dd, J = 8.0, 2.0 Hz), 5.88 (1H, d, J = 6.8 Hz), 4.85 (2H, t, J = 6.4 Hz), 4.57 (2H, d, J = 6.0 Hz), 4.46-4.54 (1H, m), 4.40 (2H, t, J = 6.0 Hz), 3.50 (3H, s); LCMS: 100%, MS (ESI): m/z 507.0[M + H]+.
434		off-white powder; 1H-NMR (CDCl3, 400 MHz): δ 9.67 (1H, s), 7.71-7.80 (2H, m), 7.49-7.58 (3H, m), 7.29-7.33 (2H, m), 6.57 (1H, dd, J = 8.4, 2.0 Hz), 6.49 (1H, d, J = 2.0 Hz), 4.76 (2H, s), 4.63 (1H, brs), 3.48 (3H, s); LCMS: 97.5%, MS (ESI): m/z 431.2[M+H]
435		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 9.68 (1H, s), 7.88 (1H, t, J = 8.0 Hz), 7.65-7.72 (2H, m), 7.47 (2H, d, J = 8.4 Hz), 7.22 (2H, d, J = 8.4 Hz), 6.98 (1H, brs), 6.95 (1H, d, J = 8.4 Hz), 6.25 (1H, s), 6.20 (1H, dd, J = 8.4, 2.0 Hz), 5.84 (1H, d, J = 6.8 Hz), 4.84 (2H, t, J = 6.4 Hz), 4.46-4.58 (3H, m), 4.39 (2H, t, J = 6.0 Hz), 3.44 (3H, s); LCMS: 99.1%, MS (ESI): m/z 487.2[M+H] +.
436		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 9.58 (1H, s), 8.08-8.17 (2H, m), 7.59 (1H, t, J = 8.0 Hz), 7.47 (2H, d, J = 8.4 Hz), 7.27 (2H, d, J = 8.8 Hz), 6.90 (1H, t, J = 6.0 Hz), 6.88 (1H, d, J = 8.0 Hz), 6.37 (1H, d, J = 1.6 Hz), 6.26 (1H, dd, J =8.0, 2.0 Hz), 4.47-4.61 (4H, m), 3.43 (3H, s); LCMS: 99.1%, MS (ESI): m/z 431.1[M+ H]+.
437		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 9.57 (1H, s), 8.06-8.19 (2H, m), 7.59 (1H, t, J = 8.0 Hz), 7.47 (2H, d, J = 8.4 Hz), 7.27 (2H, d, J = 8.4 Hz), 7.02-7.23 (1H, brs), 6.97 (1H, d, J = 8.0 Hz), 6.28 (1H, s), 6.24 (1H, d, J = 8.4 Hz), 5.89 (1H, d, J = 6.8 Hz), 4.85 (2H, t, J = 6.4 Hz), 4.46-4.62 (3H, m), 4.40 (2H, t, J = 6.0 Hz), 3.47 (3H, s); LCMS: 97.8%, MS (ESI): m/z 487.2[M + H]+.
438		pale green powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.38 (1H, d, J = 8.8 Hz), 8.14 (1H, d, J = 2.0 Hz), 7.96 (1H, d, J = 6.0 Hz), 7.74 (1H, d, J = 9.2, 2.0 Hz), 7.40-7.55 (3H, m), 7.21 (2H, d, J = 8.4 Hz), 6.94 (1H, brs), 6.89 (1H, d, J = 8.0 Hz), 6.38 (1H, d, J = 2.0 Hz), 6.28 (1H, d, J = 8.4, 2.0 Hz), 4.42-4.69 (4H, m), 3.45 (3H, s); LCMS: 100%, MS (ESI): m/z 430.1[M+ H]+.

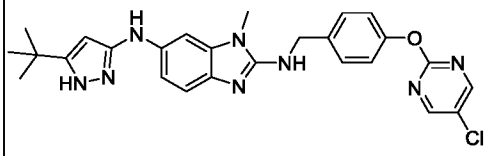
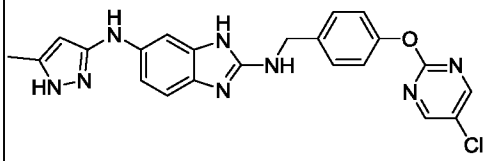
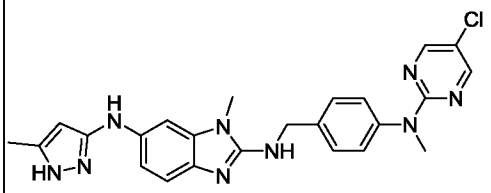
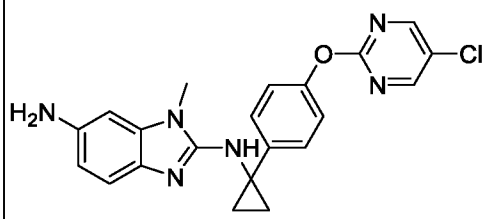
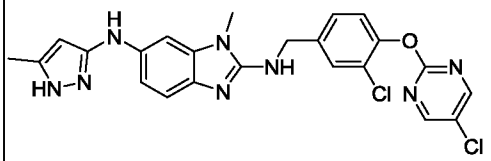
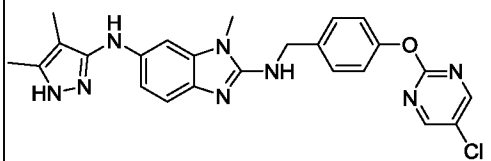
439		off-white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.36 (1H, d, J = 8.8 Hz), 8.12 (1H, d, J = 2.0 Hz), 7.93 (1H, d, J = 5.6 Hz), 7.71 (1H, dd, J = 8.8, 2.0 Hz), 7.47 (1H, d, J = 6.0 Hz), 7.45 (2H, d, J = 8.4 Hz), 7.18 (2H, d, J = 8.4 Hz), 6.96 (1H, brs), 6.94 (1H, d, J = 8.0 Hz), 6.24 (1H, d, J = 1.6 Hz), 6.20 (1H, dd, J = 8.0, 2.0 Hz), 5.82 (1H, d, J = 7.6 Hz), 4.83 (2H, t, J = 6.4 Hz), 4.43-4.56 (3H, m), 4.38 (2H, t, J = 6.0 Hz), 3.44 (3H, s); LCMS: 99.1%, MS (ESI): m/z 486.2[M+H] +.
440		off-white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 9.55 (1H, s), 8.16 (1H, d, J = 8.4 Hz), 7.83 (1H, s), 7.63 (1H, dd, J = 8.8, 2.0 Hz), 7.47 (2H, d, J = 8.0 Hz), 7.22 (2H, d, J = 8.4 Hz), 6.98 (1H, brs), 6.89 (1H, d, J = 8.0 Hz), 6.38 (1H, d, J = 1.6 Hz), 6.28 (1H, dd, J = 8.0, 1.6 Hz), 4.67 (2H, brs), 4.55 (2H, d, J = 5.6 Hz), 3.43 (3H, s); LCMS: 98.1%, MS (ESI): m/z 431.2[M+H] +.
441		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 13.90 (1H, brs), 10.08 (1H, s), 9.80 (1H, brs), 8.74 (2H, s), 7.40-7.65 (8H, m), 7.24 (2H, d, J = 8.8 Hz), 7.09-7.18 (1H, m), 4.79 (2H, d, J = 6.0 Hz), 3.73 (3H, s); LCMS: 100%, MS (ESI): m/z 423.2[M+ H]+.
442		off-white powder; 1H-NMR (CDCl3, 400 MHz): δ 8.48 (1H, d, J = 7.6 Hz), 7.95 (1H, s), 7.49 (2H, d, J = 8.8 Hz), 7.14 (2H, d, J = 8.8 Hz), 7.02 (1H, brs), 6.89 (1H, d, J = 8.0 Hz), 6.84 (1H, dd, J = 7.6, 2.4 Hz), 6.74 (1H, d, J = 2.0 Hz), 6.39 (1H, d, J = 1.6 Hz), 6.29 (1H, dd, J = 8.0, 1.6 Hz), 4.54 (2H, d, J = 5.6 Hz), 3.43 (3H, s); LCMS: 98.7%, MS (ESI): m/z 419.1[M+H] +.
443		white powder (hydroscopic); 1H-NMR (DMSO-d6, 400 MHz): δ 13.11 (1H, s), 9.40 (1H, t, J = 6.0 Hz), 8.74 (2H, s), 7.54 (2H, d, J = 8.4 Hz), 7.33-7.48 (4H, m), 7.12-7.28 (4H, m), 6.61 (1H, s), 6.54 (1H, d, J = 8.4 Hz), 4.70 (2H, d, J = 6.0 Hz), 4.40-4.50 (2H, m), 4.28-4.39 (1H, m), 3.77-3.86 (2H, m), 3.63 (3H, s); LCMS: 99.4%, MS (ESI): m/z 478.3[M+ H]+.
444		yellow powder; 1H NMR (DMSO-d6, 400 MHz): δ 9.55 (1H, s), 8.16 (1H, d, J = 8.8 Hz), 7.82 (1H, d, J = 1.6 Hz), 7.63 (1H, dd, J = 8.4, 2.0 Hz), 7.46 (2H, d, J = 8.4 Hz), 7.21 (2H, d, J = 8.4 Hz), 7.04 (1H, brs), 6.96 (1H, d, J = 8.0 Hz), 6.26 (1H, d, J = 1.6 Hz), 6.20-6.25 (1H, dd, J = 8.0, 2.0 Hz), 5.86 (1H, d, J = 6.8 Hz), 4.85 (2H, t, J = 6.0 Hz), 4.56 (2H, d, J = 6.0 Hz), 4.47-4.54 (1H, m), 4.40 (2H, d, J = 6.0 Hz), 3.46 (3H, s); LCMS: 96.9%, MS (ESI): m/z 487.2[M+H] +.

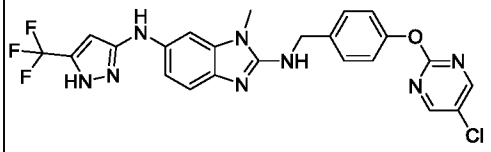
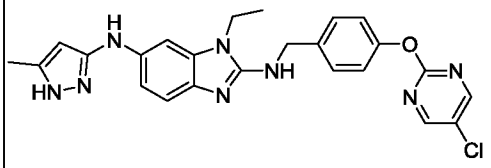
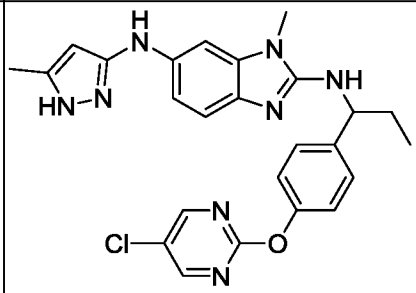
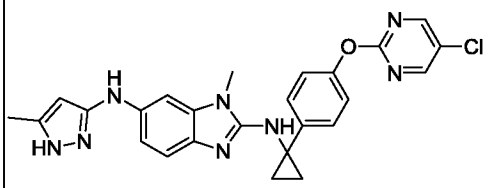
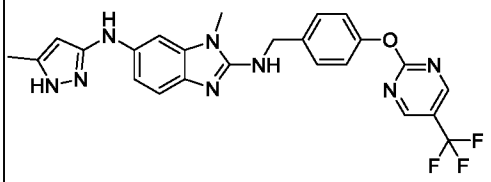
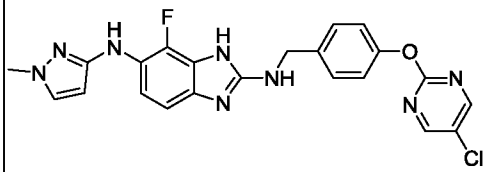
445		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.29 (1H, d, J = 2.4 Hz), 8.21 (1H, d, J = 2.4 Hz), 7.99 (1H, d, J = 3.6 Hz), 7.76 (2H, d, J = 8.4 Hz), 7.55 (2H, d, J = 8.8 Hz), 6.94 (1H, t, J = 6.0 Hz), 6.86 (1H, d, J = 8.0 Hz), 6.71 (1H, d, J = 8.0 Hz), 6.37 (1H, d, J = 1.6 Hz), 6.26 (1H, d, J = 8.4, 2.0 Hz), 4.40-4.60 (4H, m), 3.43 (3H, s); LCMS: 99.3%, MS (ESI): m/z 403.1[M+ H]+.
446		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.28 (1H, d, J = 2.4 Hz), 8.21 (1H, d, J = 2.4 Hz), 7.99 (1H, d, J = 4.0 Hz), 7.76 (2H, d, J = 8.4 Hz), 7.55 (2H, d, J = 8.4 Hz), 7.00 (1H, t, J = 6.0 Hz), 6.94 (1H, d, J = 8.4 Hz), 6.70 (1H, d, J = 3.6 Hz), 6.26 (1H, d, J = 2.0 Hz), 6.21 (1H, dd, J = 8.4, 2.0 Hz), 5.84 (1H, d, J = 7.2 Hz), 4.84 (2H, t, J = 6.8 Hz), 4.57 (2H, d, J = 6.0 Hz), 4.55-4.60 (1H, m), 4.39 (2H, d, J = 6.0 Hz), 3.46 (3H, s); LCMS: 98.3%, MS (ESI): m/z 459.3[M+ H]+.
447		pale yellow solid; 1H-NMR (DMSO-d6, 400 MHz): δ 8.72 (2H, s), 8.68 (1H, brs), 8.07 (1H, dd, J = 4.8, 1.2 Hz), 7.54 (1H, d, J = 2.0 Hz), 7.40-7.49 (3H, m), 7.11-7.20 (3H, m), 7.07 (1H, d, J = 8.0 Hz), 7.00 (1H, dd, J = 8.4, 2.0 Hz), 6.72 (1H, d, J = 8.4 Hz), 6.61 (1H, dd, J = 6.8, 6.0 Hz), 4.56 (2H, d, J = 6.0 Hz), 3.50 (3H, s); LCMS: 100 %, MS (ESI): m/z 458.2[M+ H]+.
448		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.69 (1H, s), 8.17 (1H, d, J = 2.8 Hz), 8.08 (1H, dd, J = 4.8, 2.0 Hz), 7.94 (1H, dd, J = 8.8, 2.8 Hz), 7.55 (1H, d, J = 2.0 Hz), 7.42-7.49 (3H, m), 7.15 (1H, t, J = 6.0 Hz), 7.06-7.11 (4H, m), 7.01 (1H, dd, J = 8.1, 2.0 Hz), 6.73 (1H, d, J = 8.4 Hz), 6.62 (1H, dd, J = 6.4, 5.2 Hz), 4.57 (2H, d, J = 6.0 Hz), 3.51 (3H, s); LCMS: 99.3%, MS (ESI): m/z 457.2[M+H] +.
449		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.80 (1H, brs), 8.17 (1H, d, J = 2.8 Hz), 8.02 (1H, brs), 7.93 (1H, dd, J = 8.8, 2.8 Hz), 7.50 (1H, d, J = 2.4 Hz), 7.44 (2H, d, J = 8.4 Hz), 7.33 (1H, s), 7.06-7.10 (3H, m), 6.97-7.03 (2H, m), 6.78 (1H, dd, J = 8.4, 2.0 Hz), 5.78 (1H, d, J = 2.4 Hz), 4.54 (2H, d, J = 5.6 Hz), 3.46 (3H, s); LCMS: 97.2%, MS (ESI): m/z 446.1[M + H] +.
450		pale yellow solid; 1H-NMR (DMSO-d6, 400 MHz): δ 11.81 (1H, brs), 8.72 (2H, s), 8.02 (1H, s), 7.48 (1H, s), 7.45 (2H, d, J = 8.4 Hz), 7.33 (1H, s), 7.14 (2H, d, J = 8.4 Hz), 7.01 (1H, t, J = 6.0 Hz), 6.98 (1H, d, J = 8.4 Hz), 6.77 (1H, d, J = 8.8 Hz), 5.77 (1H, d, J = 2.0 Hz), 4.53 (2H, d, J = 6.0 Hz), 3.45 (3H, s); LCMS: 100%, MS (ESI): m/z 447.2[M + H]+.

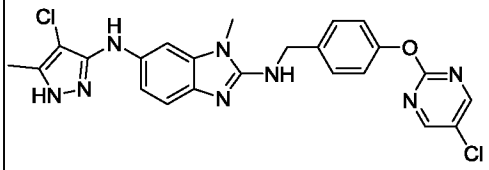
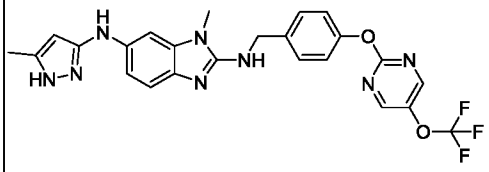
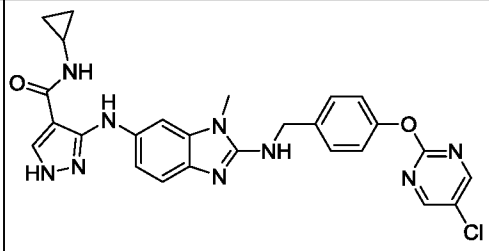
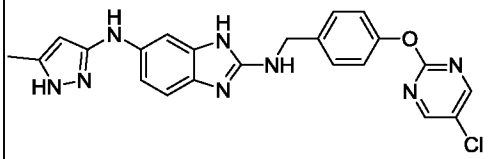
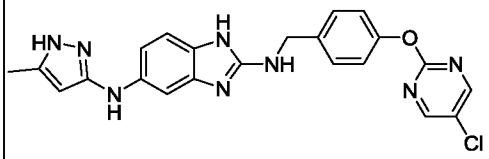
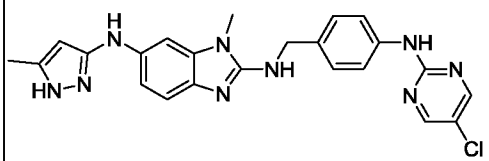
451		off-white solid; 1H-NMR (CDCl3, 400 MHz): δ 8.61 (1H, d, J = 2.8 Hz), 8.34 (1H, d, J = 8.8 Hz), 8.09 (1H, dd, J = 8.8, 2.4 Hz), 8.02 (1H, d, J = 3.2 Hz), 7.83 (1H, d, J = 8.8 Hz), 7.34 (1H, d, J = 8.4 Hz), 6.85-6.95 (2H, m), 6.76 (1H, d, J = 3.6 Hz), 6.38 (1H, d, J = 1.6 Hz), 6.28 (1H, dd, J = 8.4, 2.0 Hz), 4.41-4.72 (4H, m), 3.43 (3H, s); LCMS: 99.6%, MS (ESI): m/z 403.2[M + H] +.
452		pale yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.71 (2H, s), 7.46 (2H, d, J = 8.4 Hz), 7.12 (2H, d, J = 8.4 Hz), 6.80 (1H, d, J = 8.0 Hz), 6.60 (1H, d, J = 8.4 Hz), 6.32 (1H, d, J = 1.6 Hz), 6.22 (1H, dd, J = 8.4, 2.0 Hz), 4.79 (1H, q, J = 8.0 Hz), 4.50 (2H, brs), 3.43 (3H, s), 1.65-1.96 (2H, m), 0.93 (3H, t, J = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 409.2[M + H]+.
453		pale yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.73 (2H, s), 7.49 (2H, d, J = 8.8 Hz), 7.15 (2H, d, J = 8.4 Hz), 6.91 (1H, d, J = 8.4 Hz), 6.74 (1H, brs), 6.24 (1H, d, J = 1.6 Hz), 6.20 (1H, dd, J = 8.4, 2.0 Hz), 5.85 (1H, d, J = 6.8 Hz), 4.75-4.91 (3H, m), 4.45-4.61 (1H, m), 4.39 (2H, td, J = 6.0, 2.4 Hz), 3.49 (3H, s), 1.69-2.01 (2H, m), 0.95 (3H, t, J = 7.2 Hz); LCMS: 98.7%, MS (ESI): m/z 465.3[M + H] +.
454		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.39 (1H, s), 7.44 (2H, d, J = 8.4 Hz), 7.16 (2H, d, J = 8.8 Hz), 6.87-6.94 (1H, m), 6.85 (1H, d, J = 8.0 Hz), 6.36 (1H, d, J = 2.0 Hz), 6.26 (1H, dd, J = 8.4, 2.0 Hz), 4.55 (2H, brs), 4.51 (2H, d, J = 5.6 Hz), 3.97 (3H, s), 3.41 (3H, s); LCMS: 100%, MS (ESI): m/z 411.1[M + H]+.
455		off-white power; 1H-NMR (DMSO-d6, 400 MHz): δ 8.48 (1H, d, J = 7.6 Hz), 7.95 (1H, s), 7.48 (2H, d, J = 8.4 Hz), 7.12 (2H, d, J = 8.4 Hz), 6.91-6.98 (2H, m), 6.83 (1H, dd, J = 7.6, 2.4 Hz), 6.73 (1H, d, J = 2.4 Hz), 6.20-6.30 (2H, m), 5.83 (1H, d, J = 6.8 Hz), 4.85 (2H, t, J = 6.4 Hz), 4.40 (2H, t, J = 6.0 Hz), 4.49-4.60 (3H, m), 3.45 (3H, s); LCMS: 97.2%, MS (ESI): m/z 475.0[M+H] +.
456		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.72 (2H, s), 7.45 (2H, d, J = 8.8 Hz), 7.17 (2H, d, J = 8.8 Hz), 6.90 (1H, t, J = 6.0 Hz), 6.86 (1H, d, J = 8.0 Hz), 6.36 (1 H, d, J = 2.0 Hz), 6.26 (1 H, dd, J = 8.4, 2.0 Hz), 4.50-4.53 (4H, m), 3.41 (3H, s), 2.98 (6H, s); LCMS: 100%, MS (ESI): m/z 418.3[M + H] +.

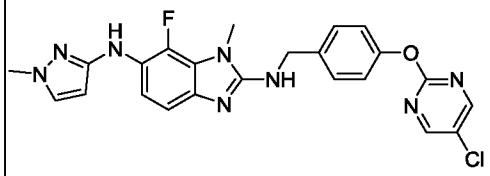
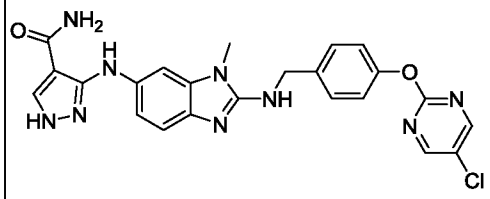
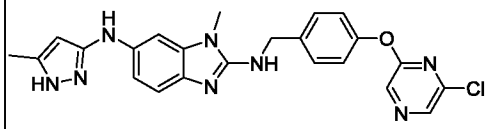
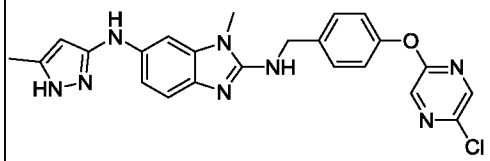
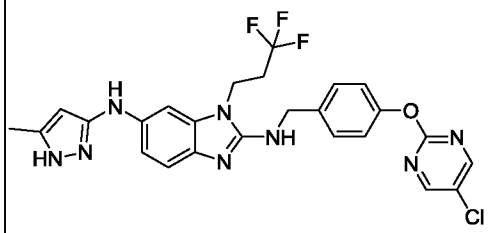
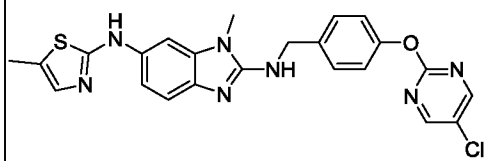
457		off-white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.61 (1H, d, J = 2.4 Hz), 8.33 (1H, dd, J = 8.8 Hz), 8.08 (1H, dd, J = 8.8, 2.4 Hz), 8.01 (1H, d, J = 3.2 Hz), 7.82 (1H, d, J = 8.8 Hz), 7.64 (1H, s), 7.33 (1H, d, J = 8.4 Hz), 6.83-6.97 (2H, m), 6.75 (1H, d, J = 3.2 Hz), 6.25 (1H, s), 6.21 (1H, d, J = 8.4 Hz), 5.82 (1H, d, J = 7.6 Hz), 4.85 (2H, t, J = 6.4 Hz), 4.62 (2H, d, J = 6.0 Hz), 4.46-4.57 (1H, m), 4.40 (2H, t, J = 6.0 Hz), 3.45 (3H, s); LCMS: 97.8%, MS (ESI): m/z 459.1[M+H] +.
458		off-white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 9.80 (1H, s), 8.51 (2H, s), 7.61 (2H, d, J = 8.4 Hz), 7.31 (2H, d, J = 8.4 Hz), 6.86 (1H, d, J = 8.0 Hz), 6.77 (1H, t, J = 5.8 Hz), 6.36 (1H, d, J = 1.6 Hz), 6.26 (1H, dd, J = 8.4, 2.0 Hz), 4.56 (2H, brs), 4.44 (2H, d, J = 6.0 Hz), 3.40 (3H, s); LCMS: 98.5%, MS (ESI): m/z 380.1[M + H] +.
459		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.39 (1H, s), 7.43 (2H, d, J = 8.4 Hz), 7.15 (2H, d, J = 8.4 Hz), 6.90-6.97 (2H, m), 6.25 (1H, d, J = 2.0 Hz), 6.21 (1H, dd, J = 8.4, 2.0 Hz), 5.82 (1H, d, J = 7.2 Hz), 4.84 (2H, t, J = 6.4 Hz), 4.45-4.56 (3H, m), 4.39 (2H, t, J = 6.0 Hz), 3.97 (3H, s), 3.44 (3H, s); LCMS: 99.5%, MS (ESI): m/z 467.1[M + H]+.
460		off-white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.95 (2H, s), 7.74-7.77 (2H, m), 7.54-7.59 (2H, m), 7.46 (2H, d, J = 8.8 Hz), 7.17 (2H, d, J = 8.8 Hz), 6.90 (1H, t, J = 5.8 Hz), 6.87 (1H, d, J = 8.0 Hz), 6.37 (1H, d, J = 2.0 Hz), 6.27 (1H, dd, J = 8.4, 2.0 Hz), 4.47-4.58 (4H, m), 3.42 (3H, s); LCMS: 100%, MS (ESI): m/z 457.1[M+H]+.
461		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 9.80 (1H, brs), 8.51 (2H, s), 7.61 (2H, d, J = 8.8 Hz), 7.30 (2H, d, J = 8.8 Hz), 6.93 (1H, d, J = 8.4 Hz), 6.81 (1H, t, J = 5.8 Hz), 6.24 (1H, d, J = 1.6 Hz), 6.20 (1H, dd, J = 8.4, 1.6 Hz), 5.82 (1H, d, J = 7.2 Hz), 4.84 (2H, t, J = 6.4 Hz), 4.48-4.56 (1H, m), 4.45 (2H, d, J = 6.0 Hz), 4.36-4.42 (2H, t, J = 5.8 Hz), 3.43 (3H, s); LCMS: 99.7%, MS (ESI): m/z 436.1[M + H] +.
462		pale yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.96 (1H, s), 8.65 (1H, brs), 7.47 (2H, d, J = 8.4 Hz), 7.18 (2H, d, J = 8.8 Hz), 6.92 (1H, brs), 6.88 (1H, d, J = 8.4 Hz), 6.37 (1H, d, J = 2.0 Hz), 6.27 (1H, dd, J = 8.0, 2.0 Hz), 4.50-4.70 (4H, m), 3.43 (3H, s), 2.80(3H, d, J = 4.8 Hz); LCMS: 99.3%, MS (ESI): m/z 404.2 [M + H] +.

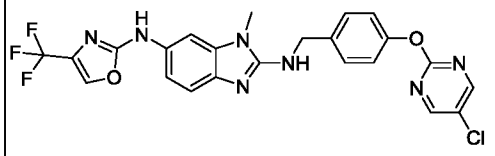
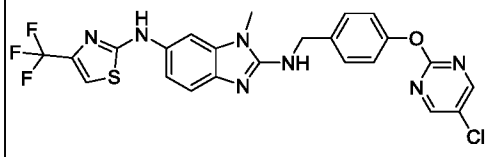
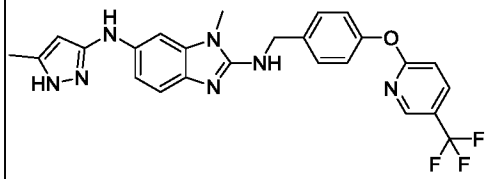
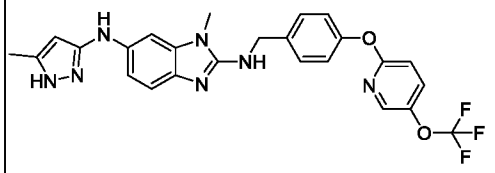
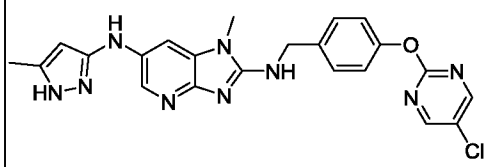
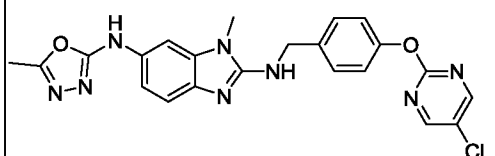
463		brown powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.40 (2H, s), 7.40 (2H, d, J = 8.4 Hz), 7.26 (2H, d, J = 8.4 Hz), 6.90 (1H, t, J = 5.8 Hz), 6.86 (1H, d, J = 8.4 Hz), 6.36 (1H, d, J = 1.6 Hz), 6.26 (1H, dd, J = 8.4, 1.6 Hz), 4.59 (2H, brs), 4.50 (2H, d, J = 5.6 Hz), 3.41 (6H, s); LCMS: 100%, MS (ESI): m/z 394.2[M+H] +.
464		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.72 (2H, s), 7.90 (1H, d, J = 3.6 Hz), 7.59 (1H, s), 7.49 (1H, d, J = 1.6 Hz), 7.46 (2H, d, J = 8.8 Hz), 7.34 (1H, d, J = 6.8 Hz), 7.10-7.19 (4H, m), 7.05 (1H, d, J = 8.8 Hz), 6.57-6.62 (1H, m), 4.57 (2H, d, J = 5.6 Hz), 3.49 (3H, s), 2.22 (3H, s); LCMS: 96.4 %, MS (ESI): m/z 472.2[M+ H]+.
465		pale yellow solid; 1H-NMR (DMSO-d6, 400 MHz): δ 8.74 (2H, s), 7.91 (1H, brs), 7.47 (2H, d, J = 8.4 Hz), 7.22 (1H, d, J = 2.0 Hz), 7.16 (2H, d, J = 8.8 Hz), 7.04 (1H, t, J = 6.0 Hz), 6.99 (1H, d, J = 8.4 Hz), 6.84 (1H, dd, J = 8.4, 2.0 Hz), 5.58 (1H, s), 4.55 (2H, d, J = 5.6 Hz), 3.60 (3H, s), 3.48 (3H, s), 2.19 (3H, s); LCMS: 98.3 %, MS (ESI): m/z 475.3[M+ H]+.
466		off-white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.48 (1H, brs), 8.17 (1H, d, J = 2.0 Hz), 7.90-7.95 (2H, m), 7.44 (2H, d, J = 8.8 Hz), 7.32-7.35 (1H, m), 7.04-7.15 (3H, m), 6.92-7.04 (2H, m), 6.77 (1H, d, J = 8.0 Hz), 5.55 (1H, s), 4.54 (2H, d, J = 6.0 Hz), 3.46 (3H, s), 2.16 (3H, s); LCMS: 100%, MS (ESI): m/z 460.3[M + H] +.
467		off-white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.48 (1H, s), 8.95 (2H, s), 7.92 (1H, s), 7.75 (2H, d, J = 8.4 Hz), 7.56 (2H, d, J = 8.4 Hz), 7.47 (2H, d, J = 8.4 Hz), 7.34 (1H, s), 7.17 (2H, d, J = 8.0 Hz), 7.01 (1H, t, J = 5.6 Hz), 6.98 (1H, d, J = 8.4 Hz), 6.77 (1H, d, J = 7.2 Hz), 5.55 (1H, s), 4.55 (2H, d, J = 5.6 Hz), 3.47 (3H, s), 2.16 (3H, s); LCMS: 100%, MS (ESI): m/z 537.1[M+H]+.
468		pale yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.74 (2H, s), 8.38 (1H, brs), 7.47 (2H, d, J = 8.8 Hz), 7.24 (1H, d, J = 2.0 Hz), 7.17 (2H, d, J = 8.4 Hz), 7.12 (1H, brs), 7.05 (2H, d, J = 8.4 Hz), 6.89 (1H, dd, J = 8.4, 2.0 Hz), 6.27 (1H, s), 4.57 (2H, d, J = 5.6 Hz), 3.85 (3H, s), 3.51 (3H, s); LCMS: 100%, MS (ESI): m/z 529.4[M + H]+.

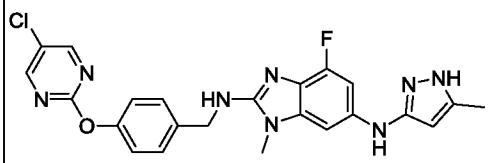
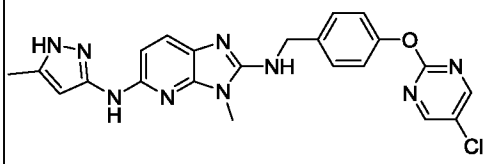
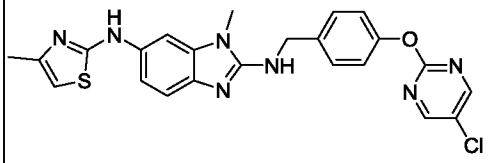
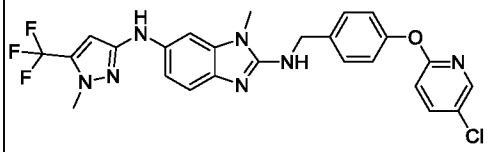
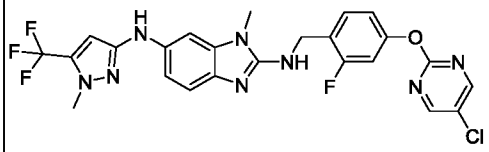
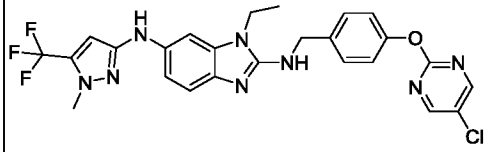
469		off-white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.57 (1H, brs), 8.74 (2H, s), 7.94 (1H, brs), 7.35-7.51 (3H, m), 7.17 (2H, d, J = 8.4 Hz), 7.01 (1H, brs), 6.99 (1H, d, J = 8.4 Hz), 6.77 (1H, d, J = 8.8 Hz), 5.53 (1H, s), 4.56 (2H, d, J = 5.6 Hz), 3.46 (3H, s), 1.26 (9H, s); LCMS: 97.9 %, MS (ESI): m/z 503.2[M + H]+.
470		yellow solid; 1H-NMR (DMSO-d6, 400 MHz): δ 11.52 (1H, brs), 8.72 (2H, s), 8.06 (1H, brs), 7.93 (1H, brs), 7.40-7.53 (3H, m), 7.18 (2H, d, J = 8.4 Hz), 7.01 (1H, d, J = 8.4 Hz), 6.84 (1H, d, J = 8.0), 5.53 (1H, s), 4.51 (2H, d, J = 3.6 Hz), 2.15 (3H, s); LCMS: 95.9%, MS (ESI): m/z 447.2[M + H] +.
471		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.48 (1H, brs), 8.40 (2H, s), 7.91 (1H, brs), 7.41 (2H, d, J = 8.4 Hz), 7.33 (1H, s), 7.26 (2H, d, J = 8.0 Hz), 6.93-7.05 (2H, m), 6.77 (1H, d, J = 7.2 Hz), 5.55 (1H, s), 4.53 (2H, d, J = 5.2 Hz), 3.46 (3H, s), 3.42 (3H, s), 2.16 (3H, s); LCMS: 97.7%, MS (ESI): m/z 474.2[M + H] +.
472		off-white solid; 1H-NMR (DMSO-d6, 400 MHz): δ 8.72 (2H, s), 7.21-7.39 (3H, m), 7.08 (2H, d, J = 8.4 Hz), 6.84 (1H, d, J = 8.0 Hz), 6.37 (1H, brs), 6.26 (1H, d, J = 7.6 Hz), 4.55 (2H, brs), 3.43 (3H, s), 1.20-1.38 (4H, m); LCMS: 99.8%, MS (ESI): m/z 407.1[M + H] +.
473		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.49 (1H, brs), 8.77 (2H, s), 7.95 (1H, brs), 7.60 (1H, d, J = 1.6 Hz), 7.46 (1H, dd, J = 8.4, 2.0 Hz), 7.32-7.42 (2H, m), 7.10 (1H, brs), 6.99 (1H, d, J = 8.4 Hz), 6.75-6.80 (1H, m), 5.55(1H, s), 4.55 (2H, d, J = 4.8 Hz), 3.47 (3H, s), 2.16 (3H, s); LCMS: 100%, MS (ESI): m/z 495.2 [M + H]+.
474		off-white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.42 (1H, brs), 8.72 (2H, s), 7.44 (2H, d, J = 8.8 Hz), 7.21-7.34 (2H, m), 7.14 (2H, d, J = 8.8 Hz), 7.02 (1H, brs), 6.95 (1H, d, J = 8.4 Hz), 6.76-6.88 (1H, m), 4.53 (2H, d, J = 5.6 Hz), 3.43 (3H, s), 2.08 (3H, s), 1.82 (3H, s); LCMS: 100 %, MS (ESI): m/z 475.2[M+ H]+.

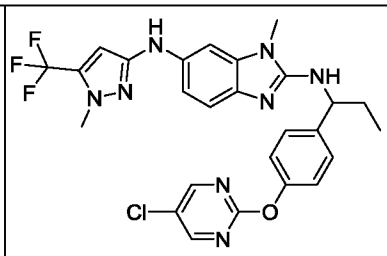
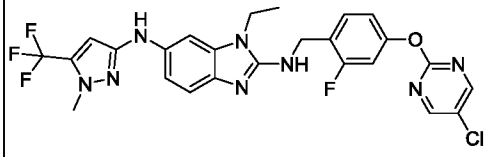
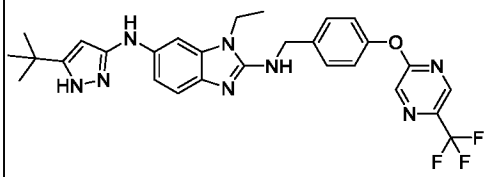
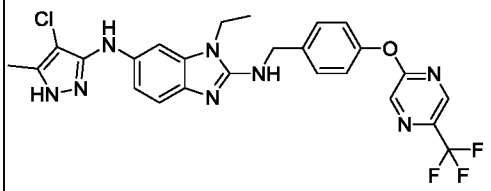
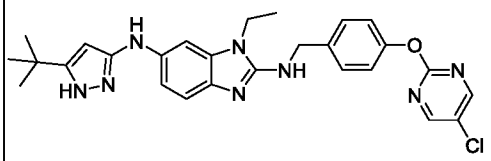
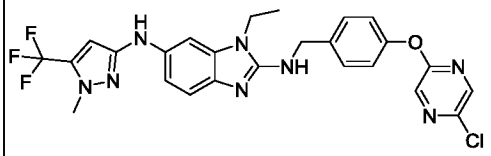
475		brown powder; 1H NMR (DMSO-d6): δ 12.78 (1H, brs), 8.73 (2H, s), 8.27 (1H, brs), 7.45 (2H, d, J = 8.4 Hz), 7.11-7.23 (3H, m), 7.07 (1H, d, J = 8.0 Hz), 6.85 (1H, brs), 6.66 (1H, d, J = 8.0 Hz), 6.08 (1H, s), 4.56 (2H, d, J = 6.0 Hz), 3.50 (3H, s); LCMS: 100%, MS (ESI): m/z 515.1[M+H] +.
476		pale yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.49 (1H, brs), 8.72 (2H, s), 7.91 (1H, brs), 7.43 (2H, d, J = 8.8 Hz), 7.37 (1H, s), 7.14 (2H, d, J = 8.4 Hz), 7.04 (1H, brs), 6.96 (1H, d, J = 8.4 Hz), 6.75 (1H, d, J = 8.0 Hz), 5.53 (1H, s), 4.54 (2H, d, J = 6.0 Hz), 3.96 (2H, q, J = 7.2 Hz), 2.14 (3H, s), 1.22 (3H, t, J = 6.8 Hz); LCMS: 100 %, MS (ESI): m/z 475.2[M + H]+.
477		off-white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.46 (1H, brs), 8.72 (2H, s), 7.89 (1H, s), 7.48 (2H, d, J = 8.4 Hz), 7.29 (1H, s), 7.13 (2H, d, J = 8.4 Hz), 6.92 (1H, d, J = 8.4 Hz), 6.70-6.74 (2H, m), 5.54 (1H, s), 4.80-4.87 (1H, m), 3.48 (3H, s), 2.15 (3H, s), 1.76-1.94 (2H, m), 0.94 (3H, t, J = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 489.2[M + H]+.
478		red powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.49 (1H, brs), 8.72 (2H, s), 7.91 (1H, brs), 7.40 (1H, brs), 7.21-7.38 (3H, m), 7.08 (2H, d, J = 8.8 Hz), 6.95 (1H, d, J = 8.4 Hz), 6.75 (1H, d, J = 8.0 Hz), 5.55 (1H, s), 3.48 (3H, s), 2.16 (3H, s), 1.20-1.39 (4H, m); LCMS: 89.0%, MS (ESI): m/z 487.2[M + H] +.
479		off-white powder; 1H NMR (DMSO-d6): δ 11.48 (1H, brs), 9.09 (2H, s), 7.91 (1H, brs), 7.48 (2H, d, J = 8.8 Hz), 7.34 (1H, s), 7.21 (2H, d, J = 8.4 Hz), 7.03 (1H, t, J = 6.0 Hz), 6.97 (1H, d, J = 8.0 Hz), 6.77 (1H, d, J = 8.0 Hz), 5.55 (1H, s), 4.56 (2H, d, J = 6.0 Hz), 3.46 (3H, s), 2.16 (3H, s); LCMS: 100%, MS (ESI): m/z 495.2[M + H] +.
480		off-white powder; 1H NMR (DMSO-d6): δ 8.74 (2H, s), 7.79 (1H, brs), 7.59 (1H, brs), 7.42-7.50 (3H, m), 7.21 (3H, d, J = 8.4 Hz), 6.94 (1H, d, J = 9.2 Hz), 5.76 (1H, d, J = 2.0 Hz), 4.59 (2H, d, J = 6.0 Hz), 3.70 (3H, s); LCMS: 99.0%, MS (ESI): m/z 465.1[M + H] +.

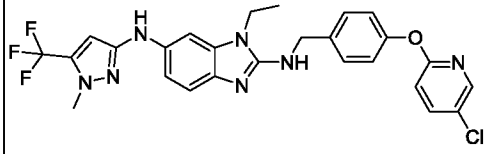
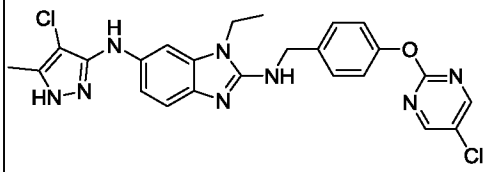
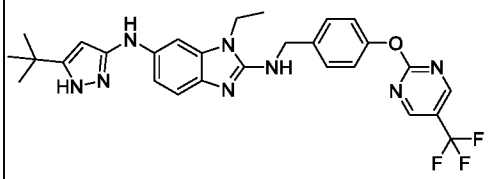
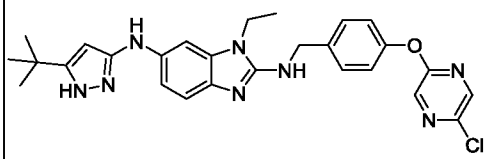
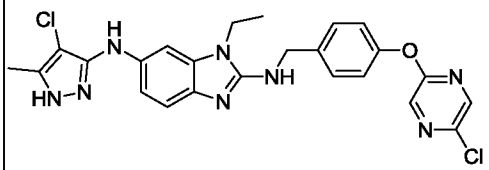
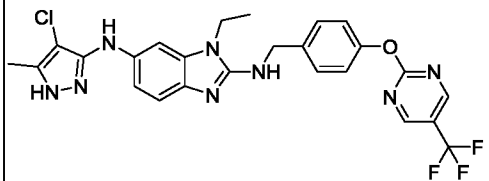
481		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 12.02 (1H, brs), 8.76 (2H, s), 7.52 (1H, brs), 7.47 (2H, d, J = 8.8 Hz), 7.30 (1H, s), 7.17 (2H, d, J = 8.0 Hz), 7.07 (1H, brs), 7.00 (1H, d, J = 8.8 Hz), 6.94 (1H, d, J = 8.0 Hz), 4.56 (2H, d, J = 6.0 Hz), 3.46 (3H, s), 2.18 (3H, s); LCMS: 95.4%, MS (ESI): m/z 475.2[M + H]+. From LCMS, the product contains 4.6% impurity of de-Cl of compound 1.
482		off-white powder; 1H-NMR (CDCl3, 400 MHz): δ 8.50 (2H, s), 7.52 (2H, d, J = 8.4 Hz), 7.37 (1H, d, J = 8.4 Hz), 7.20 (2H, d, J = 8.4 Hz), 7.07 (1H, s), 6.83 (1H, dd, J = 8.4, 1.6 Hz), 6.05 (1H, brs), 5.75 (1H, s), 4.73 (2H, s), 4.33 (1H, brs), 3.41 (3H, s), 2.28 (3H, s); LCMS: 98.0%, MS (ESI): m/z 511.1[M+H]+.
483		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 12.25 (1H, brs), 8.95 (1H, s), 8.72 (2H, s), 8.11 (1H, s), 8.02 (1H, s), 7.55 (1H, s), 7.45 (2H, d, J = 8.4 Hz), 7.15 (2H, d, J = 8.8 Hz), 7.10 (1H, brs), 7.04 (1H, d, J = 8.8 Hz), 6.94 (1H, d, J = 8.4 Hz), 4.55 (2H, d, J = 5.6 Hz), 3.49 (3H, s), 2.64-2.81 (1H, m), 0.60-0.76 (2H, m), 0.41-0.53 (2H, m); LCMS: 100%, MS (ESI): m/z 530.4[M+ H]+.
484		off-white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.43 (1H, brs), 10.60 (0.6H, brs), 10.48 (0.4H, brs), 8.74 (2H, s), 7.83 (0.6H, brs), 7.70 (0.4H, brs), 7.31-7.48 (2.6H, m), 7.10-7.26 (2.4H, m), 6.83-7.01 (2H, m), 6.62-6.80 (1H, m), 5.53 (1H, s), 4.41-4.55 (2H, m), 2.16 (3H, s); LCMS: 99.6%, MS (ESI): m/z 447.1[M + H] +.
485		off-white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.44 (1H, brs), 10.33-10.78 (1H, m), 8.74 (2H, s), 7.65-7.90 (1H, m), 7.44 (2H, d, J = 8.4 Hz), 7.21-7.40 (1H, m), 7.16 (2H, d, J = 8.8 Hz), 6.81-7.00 (2H, m), 6.73 (1H, d, J = 7.2 Hz), 5.53 (1H, s), 4.48 (2H, d, J = 5.6 Hz), 2.16 (3H, s); LCMS: 99.3%, MS (ESI): m/z 447.2[M + H] +.
486		off-white powder; 1H NMR (DMSO-d6): δ 11.48 (1H, brs), 9.80 (1H, brs), 8.51 (2H, s), 7.91 (1H, brs), 7.62 (2H, d, J = 8.8 Hz), 7.25-7.39 (3H, m), 6.98 (1H, d, J = 8.4 Hz), 6.90 (1H, brs), 6.76 (1H, d, J = 7.2 Hz), 5.55 (1H, s), 4.47 (2H, d, J = 5.6 Hz), 3.44 (3H, s), 2.16 (3H, s); LCMS: 95.9%, MS (ESI): m/z 460.2[M + H] +.

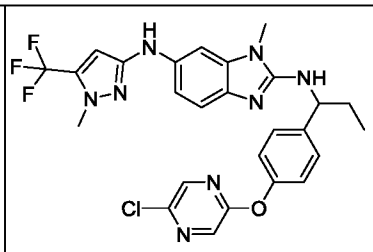
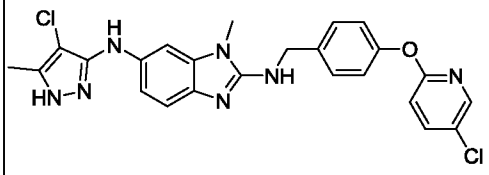
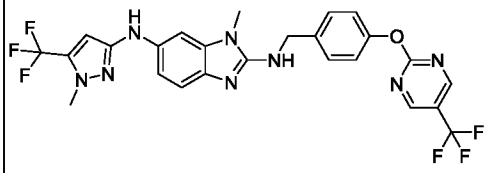
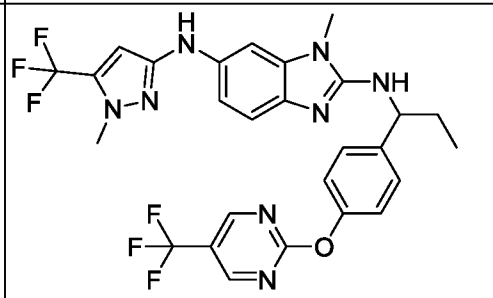
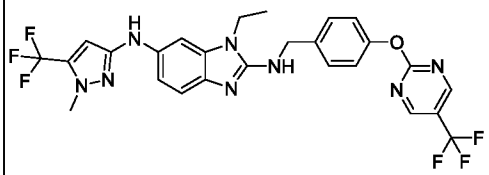
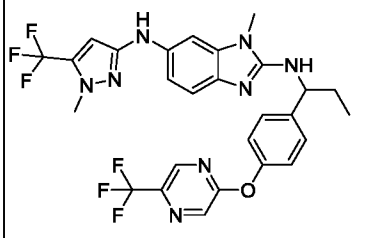
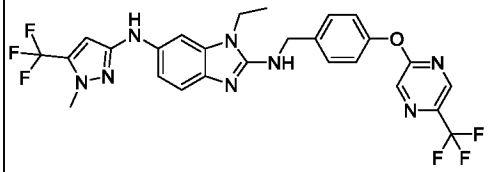
487		off-white powder; 1H NMR (DMSO-d6): δ 8.73 (2H, s), 7.56 (1H, brs), 7.46 (2H, d, J = 8.4 Hz), 7.37-7.43 (2H, m), 7.23 (1H, t, J = 6.0 Hz), 7.17 (2H, d, J = 8.4 Hz), 6.86 (1H, d, J = 8.8 Hz), 5.71 (1H, d, J = 2.4 Hz), 4.55 (2H, d, J = 6.0 Hz), 3.69 (3H, s), 3.68 (3H, s); LCMS: 98.6%, MS (ESI): m/z 479.2[M + H] +.
488		pale yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 12.27 (1H, brs), 8.91 (1H, s), 8.72 (2H, s), 8.14 (1H, brs), 7.53 (2H, brs), 7.45 (2H, d, J = 8.8 Hz), 7.10-7.21 (3H, m), 6.82-7.09 (3H, m), 4.55 (2H, d, J = 5.6 Hz), 3.49 (3H, s); LCMS: 100%, MS (ESI): m/z 489.9[M + H]+.
489		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.49 (1H, brs), 8.54 (1H, s), 8.49 (1H, s), 7.95 (1H, brs), 7.47 (2H, d, J = 8.4 Hz), 7.35 (1H, s), 7.20 (2H, d, J = 8.4 Hz), 6.99 (1H, d, J = 8.8 Hz), 6.70-6.80 (1H, m), 5.56 (1H, s), 4.56 (2H, d, J = 6.0 Hz), 3.47 (3H, s), 2.16 (3H, s); LCMS: 99%, MS (ESI): m/z 461.2[M + H]+.
490		light yellow powder; 1H NMR (DMSO-d6): δ 11.48 (1H, brs), 8.41 (1H, s), 8.32 (1H, s), 7.92 (1H, brs), 7.46 (2H, d, J = 8.4 Hz), 7.34 (1H, s), 7.17 (2H, d, J = 8.4 Hz), 7.03 (1H, brs), 6.98 (1H, d, J = 8.4 Hz), 6.77 (1H, d, J = 7.6 Hz), 5.55 (1H, s), 4.54 (2H, d, J = 5.6 Hz), 3.46 (3H, s), 2.16 (3H, s); LCMS: 100%, MS (ESI): m/z 461.2[M + H] +.
491		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.51 (1H, brs), 8.74 (2H, s), 7.97 (1H, brs), 7.47 (2H, d, J = 8.4 Hz), 7.31 (1H, s), 7.09-7.22 (3H, m), 7.01 (1H, d, J = 8.4 Hz), 6.86 (1H, d, J = 7.6 Hz), 5.57 (1H, s), 4.56 (2H, d, J = 5.2 Hz), 4.24 (2H, t, J = 7.2 Hz), 2.61-2.80 (2H, m), 2.17 (3H, s); LCMS: 98.6%, MS (ESI): m/z 543.3[M + H] +.
492		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 9.75 (1H, brs), 8.73 (2H, s), 7.62 (1H, s), 7.47 (1H, d, J = 8.8 Hz), 7.17 (1H, d, J = 8.8 Hz), 7.11 (1H, d, J = 8.0 Hz), 6.99 (1H, d, J = 8.0 Hz), 6.86 (1H, s), 4.58 (1H, d, J = 5.6 Hz), 3.52 (3H, s), 2.27 (3H, s). LCMS: 96.4%, MS (ESI): m/z 478.0[M + H]+.

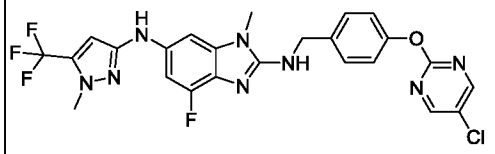
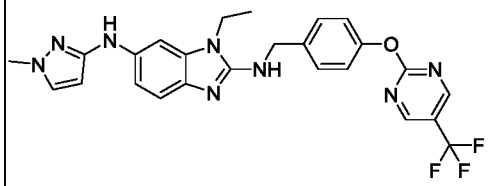
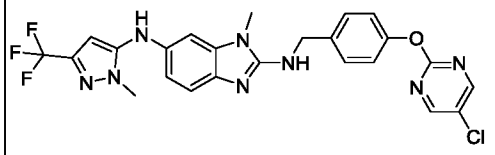
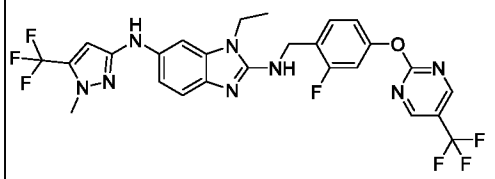
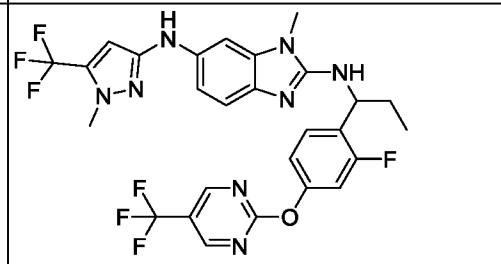
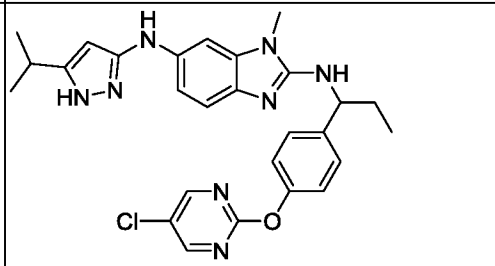
493		off-white powder; 1H NMR (DMSO-d6, 400 MHz): δ 10.24 (1H, brs), 8.73 (2H, s), 8.28-8.35 (1H, m), 7.46 (2H, d, J = 8.8 Hz), 7.38 (1H, d, J = 1.6 Hz), 7.27 (1H, t, J = 6.0 Hz), 7.16 (2H, d, J = 8.8 Hz), 7.13 (1H, s), 7.08-7.12 (1H, dd, J = 8.4, 2.0 Hz), 4.57 (2H, d, J = 6.0 Hz), 3.51 (3H, s); LCMS: 100%, MS (ESI): m/z 516.1[M + H] +.
494		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 10.29 (1H, brs), 8.73 (2H, s), 7.45-7.60 (3H, m), 7.30-7.45 (2H, m), 7.10-7.25 (3H, m), 7.04 (1H, d, J = 8.8 Hz), 4.58 (1H, d, J = 6.0 Hz), 3.52 (3H, s); LCMS: 100%, MS (ESI): m/z 532.0[M + H]+.
495		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.49 (1H, brs), 8.55 (1H, s), 8.20 (1H, dd, J = 8.8, 2.4 Hz), 7.93 (1H, brs), 7.47 (2H, d, J = 8.0 Hz), 7.33 (1H, s), 7.23 (1H, d, J = 8.4 Hz), 7.15 (2H, d, J = 8.4 Hz), 7.05 (1H, t, J = 5.6 Hz), 6.98 (1H, d, J = 8.4 Hz), 6.77 (1H, d, J = 8.0 Hz), 5.56 (1H, s), 4.50 (2H, d, J = 6.0 Hz), 3.47 (3H, s), 2.16 (3H, s); LCMS: 100%, MS (ESI): m/z 494.2 [M + H]+.
496		off-white powder; 1H NMR (DMSO-d6, 400 MHz): δ 11.48 (1H, brs), 8.23 (1H, d, J = 2.4 Hz), 7.86-8.01 (2H, m), 7.45 (2H, d, J = 8.4 Hz), 7.34 (1H, s), 7.16 (1H, d, J = 9.2 Hz), 7.11 (2H, d, J = 8.8 Hz), 7.01 (1H, t, J = 5.6 Hz), 6.98 (1H, d, J = 8.4 Hz), 6.77 (1H, d, J = 7.2 Hz), 5.55 (1H, s), 4.54 (2H, d, J = 5.6 Hz), 3.46 (3H, s), 2.16 (3H, s); LCMS: 100%, MS (ESI): m/z 510.1[M + H] +.
497		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.60 (1H, brs), 8.75 (2H, s), 8.22 (1H, brs), 7.95 (1H, s), 7.75 (1H, s), 7.61 (1H brs), 7.48 (2H, d, J = 8.4 Hz), 7.19 (2H, d, J = 8.0 Hz), 5.57 (1H, s), 4.61 (2H, d, J = 4.4 Hz), 3.52 (3H, s), 2.19 (3H, s); LCMS: 96.4%, MS (ESI): m/z 462.0[M + H] +.
498		off-white powder; 1H NMR (DMSO-d6, 400 MHz): δ 10.04 (1H, s), 8.73 (2H, s), 7.50 (1H, d, J = 2.0 Hz), 7.46 (2H, d, J = 8.8 Hz), 7.25 (1H, t, J = 6.0 Hz), 7.17 (2H, d, J = 8.4 Hz), 7.11 (1H, d, J = 8.4 Hz), 6.99 (1H, dd, J = 8.4, 2.0 Hz), 4.57 (2H, d, J = 6.0 Hz), 3.52 (3H, s), 2.38 (3H, s); LCMS: 99.2%, MS (ESI): m/z 463.0[M + H] +.

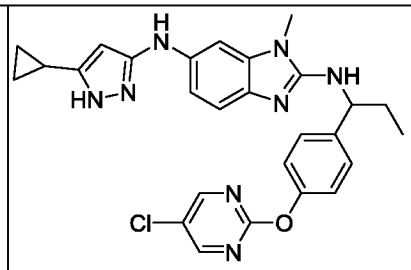
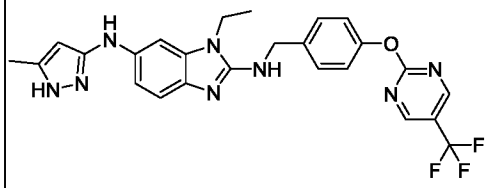
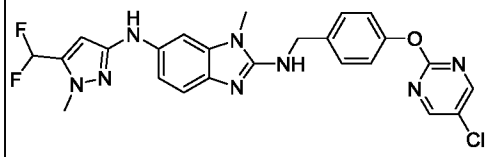
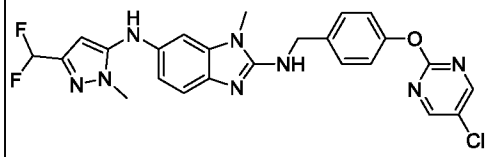
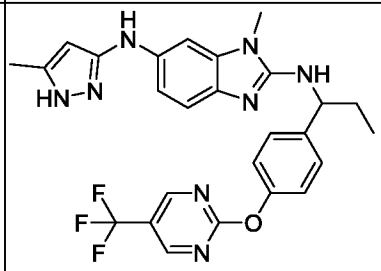
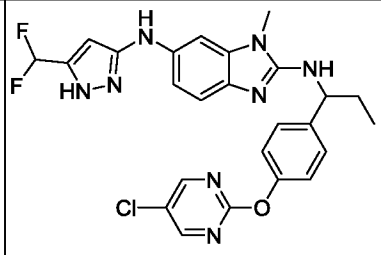
499		off-white powder; 1H NMR (DMSO-d6, 400 MHz): δ 11.56 (1H, brs), 8.73 (2H, s), 8.15 (1H, brs), 7.46 (2H, d, J = 8.4 Hz), 7.10-7.20 (3H, m), 7.05 (1H, s), 6.79 (1H, d, J = 13.6 Hz), 5.56 (1H, s), 4.56 (2H, d, J = 5.6 Hz), 3.46 (3H, s), 2.17 (3H, s); LCMS: 99.0%, MS (ESI): m/z 479.0[M + H] +.
500		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.75 (1H, s), 8.68 (2H, s), 8.63 (1H, s), 7.81 (1H, t, J = 6.0 Hz), 7.50 (1H, d, J = 8.0 Hz), 7.41 (2H, d, J = 8.8 Hz), 7.07 (2H, d, J = 8.8 Hz), 7.01 (1H, d, J = 8.0 Hz), 5.57 (1H, s), 4.61 (2H, d, J = 6.0 Hz), 3.54 (3H, s), 2.17 (3H, s); LCMS: 93.0%, MS (ESI): m/z 462.1[M + H]+.
501		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 9.83 (1H, brs), 8.73 (2H, s), 7.35-7.70 (4H, m), 7.00-7.25 (5H, m), 6.32 (1H, s), 4.58 (2H, d, J = 6.0 Hz), 3.52 (3H, s), 2.20 (3H, s); LCMS: 98.7%, MS (ESI): m/z 478.1[M + H]+.
502		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.37 (1H, s), 8.18 (1H, d, J = 2.4 Hz), 7.94 (1H, dd, J = 8.8, 2.8 Hz), 7.45 (2H, d, J = 8.4 Hz), 7.23 (1H, d, J = 2.0 Hz), 7.01-7.16 (5H, m), 6.88 (1H, dd, J = 8.0, 2.0 Hz), 6.26 (1H, s), 4.55 (2H, d, J = 6.0 Hz), 3.84 (3H, s), 3.50 (3H, s); LCMS: 100%, MS (ESI): m/z 528.2[M + H] +.
503		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.76 (2H, s), 8.39 (1H, brs), 7.52 (1H, t, J = 8.4 Hz), 7.20-7.25 (2H, m), 7.11 (1H, brs), 7.05 (2H, d, J = 8.0 Hz), 6.88 (1H, dd, J = 8.4, 2.0 Hz), 6.26 (1H, s), 4.58 (2H, d, J = 5.6 Hz), 3.83 (3H, s), 3.51 (3H, s); LCMS: 97.3%, MS (ESI): m/z 547.1[M + H]+.
504		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.74 (2H, s), 8.38 (1H, brs), 7.46 (2H, d, J = 8.4 Hz), 7.24-7.35 (2H, m), 7.18 (2H, d, J = 8.4 Hz), 7.06 (1H, d, J = 8.0 Hz), 6.92 (1H, d, J = 8.4 Hz), 6.26 (1H, s), 4.58 (2H, d, J = 5.6 Hz), 4.03 (2H, q, J = 6.8 Hz), 3.84 (3H, s), 1.26 (3H, t, J = 6.8 Hz); LCMS: 98.4 %, MS (ESI): m/z 543.0[M + H]+.

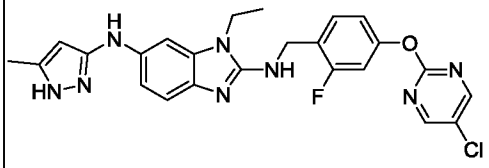
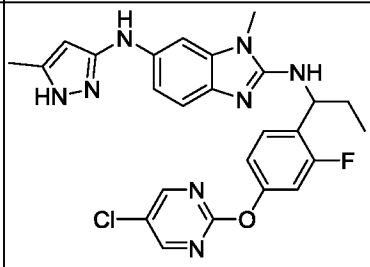
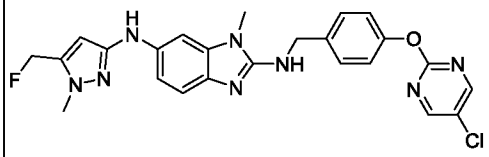
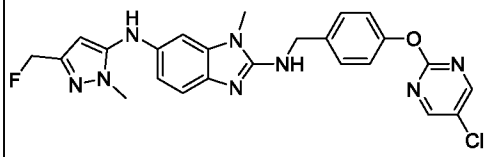
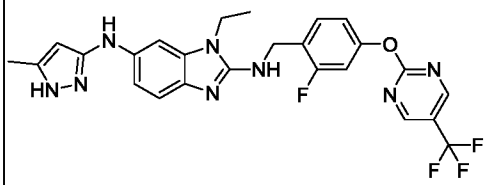
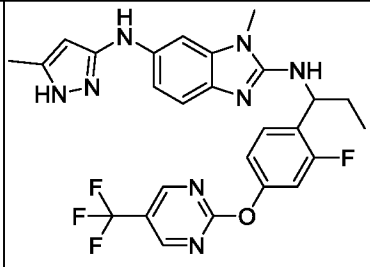
505		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.72 (2H, s), 8.34 (1H, brs), 7.50 (2H, d, J = 8.4 Hz), 7.20 (1H, d, J = 1.6 Hz), 7.15 (2H, d, J = 8.8 Hz), 7.00 (1H, d, J = 8.4 Hz), 6.86 (1H, dd, J = 2.4, 0.4 Hz), 6.81 (1H, d, J = 8.4 Hz), 6.24 (1H, s), 4.82-4.88 (1H, m), 3.83 (3H, s), 3.52 (3H, s), 1.76-1.94 (2H, m), 0.95 (3H, t, J = 7.2 Hz); LCMS: 99.8%, MS (ESI): m/z 557.1[M + H]+.
506		off-white solid; 1H-NMR (DMSO-d6, 400 MHz): δ 8.78 (2H, s), 8.56 (1H, brs), 7.51 (1H, t, J = 8.4 Hz), 7.35 (1H ,brs), 7.27 (1H, d, J = 9.2 Hz), 7.09-7.20 (2H, m), 6.95-7.06 (1H, m), 6.28 (1H, s), 4.63 (2H, d, J = 5.2 Hz), 4.00-4.10 (2H, m), 3.85 (3H, s), 1.28 (3H, t, J = 6.8 Hz); LCMS: 99.8%, MS (ESI): m/z 561.0[M + H] +.
507		off-white powder; 1H NMR (DMSO-d6, 400 MHz): δ 11.59 (1H, brs), 8.73 (1H, s), 8.70 (1H, s), 7.95 (1H, brs), 7.40-7.57 (3H, m), 7.22 (2H, d, J = 8.4 Hz), 7.07 (1H, t, J = 6.0 Hz), 6.98 (1H, d, J = 8.4 Hz), 6.74 (1H, d, J = 8.4 Hz), 5.51 (1H, s), 4.57 (2H, d, J = 6.0 Hz), 3.97 (2H, q, J = 6.8 Hz), 1.21-1.28 (12H, m); LCMS: 98.9%, MS (ESI): m/z 551.0[M + H] +.
508		off-white solid; 1H-NMR (DMSO-d6, 400 MHz): δ 12.09 (1H, brs), 8.74 (1H, s), 8.70 (1H, s), 7.60 (1H, brs), 7.49 (2H, d, J = 8.4 Hz), 7.43 (1H, s), 7.24 (2H, d, J = 8.4 Hz), 6.91-7.10 (2H, m), 4.59 (2H, d, J = 6.0 Hz), 4.00 (2H, q, J = 6.8 Hz), 2.18 (3H, s), 1.25 (3H, t, J = 6.8 Hz); LCMS: 100%, MS (ESI): m/z 543.0[M + H] +.
509		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.59 (1H, brs), 8.72 (2H, s), 7.94 (1H, brs), 7.50 (1H, s), 7.43 (2H, d, J = 8.8 Hz), 7.14 (2H, d, J = 8.4 Hz), 7.04 (1H, brs), 6.96 (1H, d, J = 8.0 Hz), 6.72 (1H, d, J = 8.4 Hz), 5.49 (1H, s), 4.54 (2H, d, J = 5.6 Hz), 3.95-4.00 (2H, m), 1.20-1.25 (12H, m); LCMS: 98.7 %, MS (ESI): m/z 517.1[M+ H]+.
510		off-white powder; 1H NMR (DMSO-d6): δ 8.41 (1H, d, J = 1.2 Hz), 8.35 (1H, s), 8.32 (1H, d, J = 1.6 Hz), 7.45 (2H, d, J = 8.8 Hz), 7.22 (1H, d, J = 1.6 Hz), 7.17 (2H, d, J = 8.4 Hz), 7.13 (1H, t, J = 5.6 Hz), 7.03 (1H, d, J = 8.4 Hz), 6.90 (1H, dd, J = 8.4, 2.0 Hz), 6.24 (1H, s), 4.56 (2H, d, J = 5.6 Hz), 4.01 (2H, q, J = 6.8 Hz), 3.82 (3H, s), 1.24 (3H, t, J = 6.8 Hz); LCMS: 100%, MS (ESI): m/z 543.1[M + H] +.

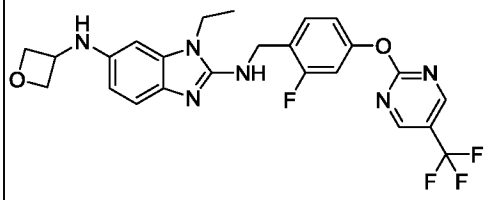
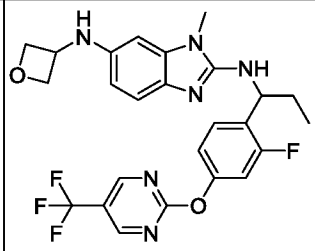
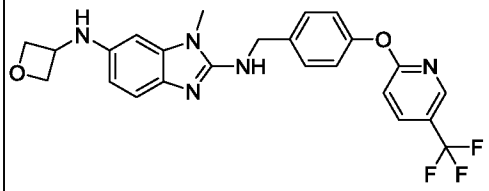
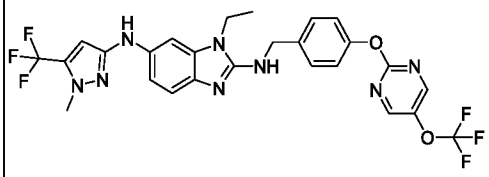
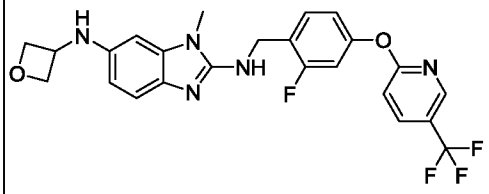
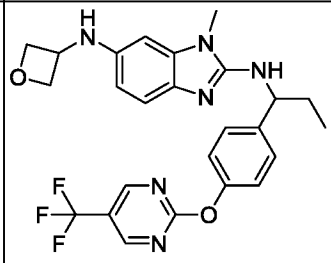
511		white powder; 1H-NMR (CDCl3, 400 MHz): δ 8.35 (1H, s), 8.17 (1H, d, J = 2.8 Hz), 7.94 (1H, dd, J = 8.8, 2.8 Hz), 7.42 (2H, d, J = 8.4 Hz), 7.22 (1H, d, J = 1.6 Hz), 7.06-7.16 (4H, m), 7.04 (1H, d, J = 8.8 Hz), 6.90 (1H, dd, J = 8.0, 2.0 Hz), 6.24 (1H, s), 4.55 (2H, d, J = 6.0 Hz), 4.01 (2H, q, J = 6.8 Hz), 3.83 (3H, s), 1.24 (3H, t, J = 7.2 Hz); LCMS: 99.0%, MS (ESI): m/z 542.0[M + H]+.
512		off-white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 12.05 (1H, brs), 8.74 (2H, s), 7.51 (1H, brs), 7.44 (2H, d, J = 8.4 Hz), 7.39 (1H, s), 7.16 (2H, d, J = 8.4 Hz), 7.10 (1H, s), 6.93-7.05 (2H, m), 4.60 (2H, d, J = 6.4 Hz), 3.97 (2H, q, J = 6.8 Hz), 2.17 (3H, s), 1.24 (3H, t, J = 7.2 Hz); LCMS: 97.6 %, MS (ESI): m/z 508.9[M + H]+.
513		off-white powder; 1H NMR (DMSO-d6, 400 MHz): δ 11.60 (1H, brs), 9.09 (2H, s), 7.96 (1H, brs), 7.51 (1H, s), 7.47 (2H, d, J = 8.0 Hz), 7.21 (2H, d, J = 8.4 Hz), 7.08 (1H, t, J = 6.0 Hz), 6.98 (1H, d, J = 8.4 Hz), 6.74 (1H, d, J = 8.4 Hz), 5.51 (1H, s), 4.57 (2H, d, J = 6.0 Hz), 3.98 (2H, q, J = 6.8 Hz), 1.20-1.28 (12H, m); LCMS: 94.2%, MS (ESI): m/z 551.1[M + H] +.
514		white powder; 1H NMR (DMSO-d6, 400MHz): δ 11.59 (1H, brs), 8.41 (1H, s), 8.32 (1H, s), 7.95 (1H, brs), 7.50 (1H, s), 7.45 (2H, d, J = 8.4 Hz), 7.17 (2H, d, J = 8.8 Hz), 7.06 (1H, brs), 6.98 (1H, d, J = 8.0 Hz), 6.74 (1H, d, J = 8.4 Hz), 5.51 (1H, s), 4.55 (2H, d, J = 5.6 Hz), 3.97 (2H, q, J = 6.8 Hz), 1.21-1.26 (12H, m); LCMS: 99.4%, MS (ESI): m/z 517.0[M + H] +.
515		off-white solid; 1H-NMR (DMSO-d6, 400 MHz): δ 12.07 (1H, brs), 8.43 (1H, s), 8.34 (1H, s), 7.55 (1H, brs), 7.46 (2H, d, J = 8.4 Hz), 7.40 (1H, s), 7.11-7.27 (3H, m), 6.95-7.04 (2H, m), 4.57 (2H, d, J = 5.6 Hz), 3.90-4.00 (2H, m), 2.18 (3H, s), 1.25 (3H, t, J = 6.8 Hz); LCMS: 100%, MS (ESI): m/z 508.9[M + H] +.
516		yellow solid; 1H-NMR (DMSO-d6, 400 MHz): δ 12.06 (1H, brs), 9.10 (2H, s), 7.44-7.59 (3H, m), 7.39 (1H, s), 7.22 (2H, d, J = 8.4 Hz), 7.12 (1H ,brs), 6.97-7.06 (2H, m), 4.58 (2H, d, J = 6.0 Hz), 3.98 (2H, q, J = 6.8 Hz), 2.18 (3H, s), 1.25 (3H, t, J = 6.8 Hz); LCMS: 100%, MS (ESI): m/z 543.0[M + H] +.

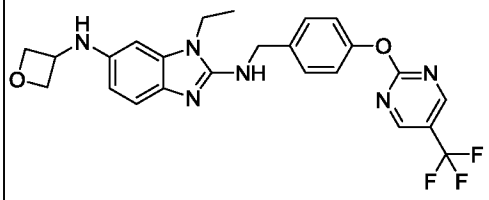
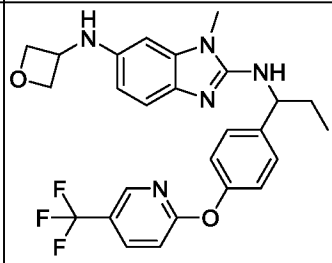
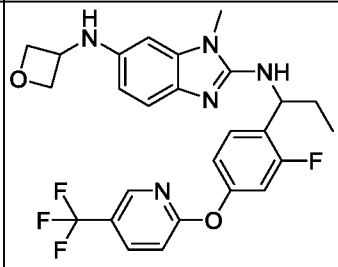
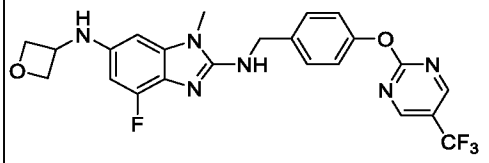
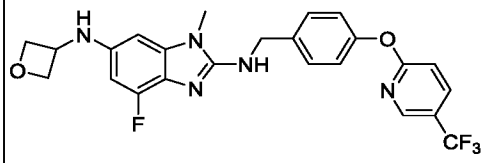
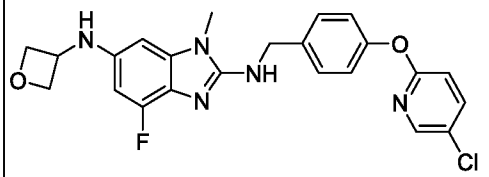
517		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.41 (1H, d, J = 1.2 Hz), 8.36 (1H, brs), 8.32 (1H, d, J = 1.2 Hz), 7.50 (2H, d, J = 8.4 Hz), 7.20 (1H, s), 7.15 (2H, d, J = 8.8 Hz), 6.99 (1H, d, J = 8.4 Hz), 6.80-6.85 (2H, m), 6.24 (1H, s), 4.80-4.90 (1H, m), 3.83 (3H, s), 3.52 (3H, s), 1.74-1.97 (2H, m), 0.94 (3H, t, J = 8.8 Hz); LCMS: 100%, MS (ESI): m/z 557.0[M + H]+.
518		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 12.02 (1H, brs), 8.17 (1H, d, J = 2.4 Hz), 7.94 (1H, dd, J = 8.8, 2.8 Hz), 7.49 (1H, s), 7.44 (2H, d, J = 8.8 Hz), 7.35 (1H, s), 7.01-7.11 (4H, m), 6.94-7.01 (2H, m), 4.54 (2H, d, J = 6.0 Hz), 3.45 (3H, s), 2.17 (3H, s); LCMS: 99.1%, MS (ESI): m/z 493.9[M + H]+.
519		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 9.10 (2H, s), 8.39 (1H, brs), 7.50 (2H, d, J = 8.4 Hz), 7.25 (1H, d, J = 2.0 Hz), 7.22 (2H, d, J = 8.8 Hz), 7.14 (1H, brs), 7.05 (1H, d, J = 8.0 Hz), 6.89 (1H, dd, J = 8.4, 2.0 Hz), 6.27 (1H, s), 4.58 (2H, d, J = 6.0 Hz), 3.84 (3H, s), 3.51 (3H, s); LCMS: 100 %, MS (ESI): m/z 563.0[M + H]+.
520		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 9.09 (2H, s), 8.35 (1H, brs), 7.52 (2H, d, J = 8.4 Hz), 7.15-7.24 (3H, m), 6.99 (1H, d, J = 8.8 Hz), 6.78-6.89 (2H, m), 6.24 (1H, s), 4.79-4.95 (1H, m), 3.83 (3H, s), 3.53 (3H, s), 1.72-2.00 (2H, m), 0.96 (3H, t, J = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 591.0[M + H]+.
521		pale yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 9.10 (2H, s), 8.36 (1H, brs), 7.48 (2H, d, J = 8.8 Hz), 7.21-7.27 (3H, m), 7.17 (1H, brs), 7.05 (1H, d, J = 8.4 Hz), 6.91 (1H, dd, J = 8.4, 2.0 Hz), 6.25 (1H, s), 4.59 (2H, d, J = 5.6 Hz), 4.03 (2H, q, J = 7.2 Hz), 3.84 (3H, s), 1.26 (3H, t, J = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 577.0[M + H]+.
522		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.72 (1H, s), 8.69 (1H, s), 8.36 (1H, brs), 7.53 (2H, d, J = 8.4 Hz), 7.19-7.24 (3H, m), 7.00 (1H, d, J = 8.0 Hz), 6.77-6.90 (2H, m), 6.24 (1H, s), 4.82-4.91 (1H, m), 3.83 (3H, s), 3.53 (3H, s), 1.73-1.99 (2H, m), 0.95 (3H, t, J = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 590.9[M + H]+.
523		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.73 (1H, s), 8.70 (1H, s), 8.35 (1H, brs), 7.48 (2H, d, J = 8.4 Hz), 7.20-7.30 (3H, m), 7.15 (1H, t, J = 6.0 Hz), 7.03 (1H, d, J = 8.4 Hz), 6.89 (1H, dd, J = 8.4, 2.4 Hz), 6.24 (1H, s), 4.57 (1H, d, J = 6.0 Hz), 4.02 (2H, q, J = 6.8 Hz), 3.83 (3H, s), 1.24 (3H, t, J = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 577.1[M + H]+.

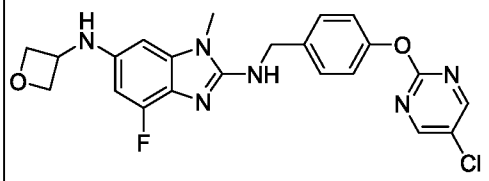
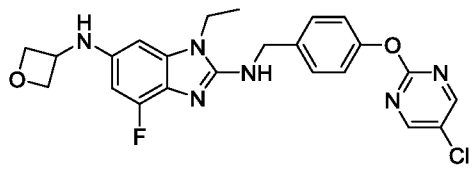
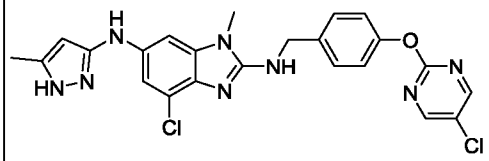
524		a white powder; 1H NMR (DMSO-d6, 400 MHz): δ 8.73 (2H, s), 8.60 (1H, brs), 7.46 (2H, d, J = 8.4 Hz), 7.25 (1H, t, J = 6.0 Hz), 7.17 (2H, d, J = 8.4 Hz), 6.99 (1H, s), 6.87 (1H, d, J = 13.2 Hz), 6.29 (1H, s), 4.57 (2H, d, J = 6.0 Hz), 3.85 (3H, s), 3.50 (3H, s); LCMS: 100%, MS (ESI): m/z 546.9[M + H] +.
525		off-white solid; 1H-NMR (DMSO-d6, 400 MHz): δ 9.10 (2H, s), 8.01 (1H, brs), 7.42-7.51 (3H, m), 7.20-7.31 (3H, m), 7.11 (1H, brs), 7.00 (1H, d, J = 8.4 Hz), 6.88 (1H, d, J = 8.4 Hz), 5.73 (1H, d, J = 2.0 Hz), 4.57 (2H, d, J = 5.6 Hz), 4.00 (2H, q, J = 6.8 Hz), 3.72 (3H, s), 1.25 (3H, t, J = 7.2 Hz); LCMS: 99.2%, MS (ESI): m/z 509.0[M + H] +.
526		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.74 (2H, s), 8.02 (1H, brs), 7.46 (2H, d, J = 8.4 Hz), 7.23 (1H, brs), 7.17 (2H, d, J = 8.4 Hz), 7.10 (1H, d, J = 8.0 Hz), 6.83 (1H, d, J = 1.6 Hz), 6.69 (1H, dd, J = 8.4, 2.0 Hz), 6.14 (1H, s), 4.57 (2H, d, J = 6.0 Hz), 3.74 (3H, s), 3.50 (3H, s); LCMS: 98.4%, MS (ESI): m/z 529.1[M + H]+.
527		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 9.13 (2H, s), 8.38 (1H, brs), 7.52 (1H, t, J = 8.8 Hz), 7.29 (1H, dd, J = 10.8, 2.4 Hz), 7.25 (1H, d, J = 2.0 Hz), 7.16 (1H, brs), 7.11 (1H, dd, J = 8.4, 1.6 Hz), 7.06 (1H, d, J = 8.4 Hz), 6.91 (1H, dd, J = 8.0, 2.0 Hz), 6.26 (1H, s), 4.61 (2H, d, J = 6.0 Hz), 4.04 (2H, q, J = 2.8 Hz), 3.84 (3H, s), 1.26 (3H, t, J = 6.8 Hz); LCMS: 100 %, MS (ESI): m/z 595.1[M + H]+.
528		white solid; 1H NMR (DMSO-d6, 400 MHz): δ 9.12 (2H, s), 8.38 (1H, brs), 7.60 (1H, t, J = 8.8 Hz), 7.19-7.28 (2H, m), 7.06-7.13 (1H, m), 7.01 (1H, d, J = 8.4 Hz), 6.80-6.94 (2H, m), 6.25 (1H, s) 5.10-5.20 (1H, m), 3.83 (3H, s) 3.55 (3H, s), 1.74-1.98 (2H, m), 0.99 (3H, t, J = 7.2 Hz); LCMS: 99.2%, MS (ESI): m/z 609.0[M + H] +.
529		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.53 (1H, brs), 8.71 (2H, s), 7.90 (1H, brs), 7.48 (2H, d, J = 8.4 Hz), 7.31 (1H, s), 7.13 (2H, d, J = 8.4 Hz), 6.92 (1H, d, J = 8.4 Hz), 6.60-6.81 (2H, m), 5.51 (1H, s), 4.83 (1H, q, J = 8.0 Hz), 3.47 (3H, s), 2.75-2.91 (1H, m), 1.70-2.01 (2H, m), 1.18 (6H, d, J = 7.2 Hz), 0.94 (3H, t, J = 7.2 Hz); LCMS: 98.0%, MS (ESI): m/z 517.1[M + H]+.

530		pale yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.51 (1H, brs), 8.69 (2H, s), 7.85 (1H, brs), 7.45 (2H, d, J = 8.8 Hz), 7.23 (1H, s), 7.11 (2H, d, J = 8.4 Hz), 6.89 (1H, d, J = 8.4 Hz), 6.61-6.82 (2H, m), 5.41 (1H, s), 4.70-4.85 (1H, m), 3.66 (3H, s), 1.65-1.96 (3H, m), 0.76-0.99 (5H, m), 0.55-0.64 (2H, m); LCMS: 96.3%, MS (ESI): m/z 537.0[M + Na]+.
531		white powder; 1H NMR (DMSO-d6, 400 MHz): δ 11.50 (1H, brs), 9.09 (2H, s), 7.95 (1H, brs), 7.47 (2H, d, J = 8.4 Hz), 7.38 (1H, s), 7.21 (2H, d, J = 8.4 Hz), 7.14 (1H, brs), 6.98 (1H, d, J = 8.4 Hz), 6.77 (1H, d, J = 8.0 Hz), 5.54 (1H, s), 4.57 (2H, d, J = 5.6 Hz), 3.95-4.00 (2H, m), 2.16 (3H, s), 1.24 (3H, t, J = 6.8 Hz); LCMS: 100%, MS (ESI): m/z 509.0[M + H] +.
532		light-yellow powder; 1H NMR (DMSO-d6, 400 MHz): δ 8.73 (2H, s), 8.23 (1H, brs), 7.46 (2H, d, J = 8.0 Hz), 7.07- 7.35 (1H, m), 7.22 (1H, s), 7.16 (2H, d, J = 8.4 Hz), 7.08 (1H, brs), 7.02 (1H, d, J = 8.4 Hz), 6.84-6.89 (1H, m), 6.06 (1H, s), 4.54 (2H, d, J = 5.6 Hz), 3.78 (3H, s), 3.48 (3H, s); LCMS: 99.3%, MS (ESI): m/z 510.9[M + H] +.
533		light-yellow powder; 1H NMR (DMSO-d6, 400 MHz): δ 8.73 (2H, s), 7.88 (1H, s), 7.45 (2H, d, J = 8.4 Hz), 7.12- 7.40 (3H, m), 7.07 (1H, d, J = 8.0 Hz), 6.80 (1H, t, J = 55.2 Hz), 6.78 (1H, s), 6.62-6.68 (1H, m), 5.98 (1H, s), 4.56 (1H, d, J = 5.6 Hz), 3.69 (3H, s), 3.49 (3H, s); LCMS: 97.7%, MS (ESI): m/z 511.0[M + H] +.
534		pale yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.45 (1H, brs), 9.07 (2H, s), 7.89 (1H, brs), 7.50 (2H, d, J = 8.4 Hz), 7.29 (1H, s), 7.18 (2H, d, J = 8.4 Hz), 6.91 (1H, d, J = 8.4 Hz), 6.60-6.81 (2H, m), 5.53 (1H, s), 4.80-4.90 (1H, m), 3.48 (3H, s), 2.14 (3H, s), 1.65-1.96 (2H, m), 0.94 (3H, t, J = 6.8 Hz); LCMS: 96.7%, MS (ESI): 523.0 m/z [M + H]+.
535		pale yellow powder; 1H-NMR (CDCl3, 400 MHz): δ 8.43 (2H, s), 7.41 (2H, d, J = 8.4 Hz), 7.01-7.20 (3H, m), 6.41-6.85 (3H, m), 6.16 (1H, brs), 6.01(1H, s), 4.90-5.06 (1H, m), 4.44 (1H, brs), 3.30 (3H, s), 1.76-2.11 (2H, m), 0.93 (3H, t, J = 7.2 Hz); LCMS: 96.1%, MS (ESI): 525.0 m/z [M + H]+.

536		pale yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.51 (1H, brs), 8.76 (2H, s), 7.94 (1H, brs), 7.45-7.55 (1H, m), 7.40 (1H, s), 7.21 (1H, d, J = 10.8 Hz), 6.90-7.12 (3H, m), 6.71-6.82 (1H, m), 5.54 (1H, s), 4.58 (2H, d, J = 5.2 Hz), 3.95-4.00 (2H, m), 2.16 (3H, s), 1.24 (3H, t, J = 6.8 Hz); LCMS: 100%, MS (ESI): 492.9 m/z [M+ H]+.
537		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 11.48 (1H, brs), 8.76 (2H, s), 7.93 (1H, brs), 7.57 (1H, t, J = 8.8 Hz), 7.32 (1H, s), 7.17 (1H, d, J = 10.8 Hz), 7.05 (1H, d, J = 8.4 Hz), 6.94 (1H, d, J = 8.4 Hz), 6.50-6.85 (2H, m), 5.55 (1H, s), 5.08-5.20 (1H, m), 3.51 (3H, s), 2.16 (3H, s), 1.60-1.95 (2H, m), 0.98 (3H, t, J = 7.2 Hz); LCMS: 98.6%, MS (ESI): m/z 507.0 [M+H]+.
538		white powder; 1H NMR (DMSO-d6, 400 MHz): δ 8.73 (2H, s), 8.11 (1H, brs), 7.46 (2H, d, J = 8.0 Hz), 7.21 (1H, s), 7.16 (2H, d, J = 8.4 Hz), 7.07 (1H, brs), 7.02 (1H, d, J = 8.4 Hz), 6.85 (1H, d, J = 7.2 Hz), 5.96 (1H, d, J = 2.8 Hz), 5.43 (2H, d, J = 48.4 Hz), 4.55 (2H, d, J = 5.2 Hz), 3.73 (3H, s), 3.48 (3H, s); LCMS: 89.5%, MS (ESI): m/z 493.1[M + H] +.
539		white powder ; 1H NMR (DMSO-d6, 400 MHz): δ 8.73 (2H, s), 7.76 (1H, brs), 7.46 (2H, d, J = 8.4 Hz), 7.15-7.17 (3H, m), 7.05 (1H, d, J = 8.0 Hz), 6.74 (1H, s), 6.62 (1H, dd, J = 8.4, 1.6 Hz), 5.96 (1H, s), 5.19 (2H, d, J = 48.8 Hz), 4.56 (2H, d, J = 6.0 Hz), 3.65 (3H, s), 3.48 (3H, s); LCMS: 95.3%, MS (ESI): m/z 493.1[M + H] +.
540		white powder; 1H NMR (DMSO-d6, 400 MHz): δ 9.12 (2H, s), 7.95 (1H, brs), 7.51 (1H, t, J =8.4 Hz), 7.37 (1H, s), 7.28 (1H, dd, J =10.8, 2.0 Hz), 7.03-7.14 (2H, m), 6.98 (1H, d, J = 8.4 Hz), 6.77 (1H, dd, J = 8.4, 1.6 Hz), 5.54 (1H, s), 4.59 (2H, d, J = 5.2 Hz), 3.94-4.03 (2H, m), 2.16 (3H, q, 6.8 Hz), 1.24 (3H, t, J =6.8 Hz); LCMS: 100%, MS (ESI): m/z 527.0[M+H] +.
541		white powder; 1H NMR (DMSO-d6, 400 MHz): δ 11.48 (1 H, brs), 9.12 (2 H, s), 7.95 (1 H, brs), 7.58 - 7.62 (1 H, m), 7.32 (1 H, s), 7.24 (1 H, d, J=10.8 Hz), 7.10 (1 H, d, J=8.0 Hz), 6.95 (1 H, d, J=8.0 Hz), 6.80 - 6.90 (1 H, brs), 6.76 (1 H, d, J=7.6 Hz), 5.55 (1 H, s), 5.12 - 5.13 (1 H, m), 3.52 (3 H, s), 2.33 (3 H, s), 1.80 - 1.92 (2 H, m), 0.97 (3 H, t, J=7.2 Hz); LCMS: 95.9%, MS (ESI): m/z 541.0[M + H] +.

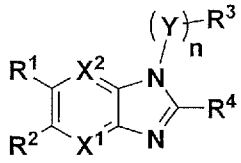
542		white solid; 1H-NMR (DMSO-d6, 400 MHz): δ 9.11 (2H, s), 7.47 (1H, t, J = 8.4 Hz), 7.26 (1H, d, J = 10.8 Hz), 7.07 (1H, d, J = 8.4 Hz), 6.95-7.05 (1H, m), 6.93 (1H, d, J = 8.4 Hz), 6.28 (1H, s), 6.19 (1H, d, J = 8.4 Hz), 5.84 (1H, d, J = 7.2 Hz), 4.83 (2H, t, J = 6.4 Hz), 4.45-4.65 (3H, m), 4.38 (2H, t, J = 6.0 Hz), 3.90-4.10 (2H, m), 1.20 (3H, t, J = 6.8 Hz); LCMS: 100%, MS (ESI): m/z 503.0[M + H]+
543		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 9.12 (2H, s), 7.58 (1H, t, J = 8.4 Hz), 7.23 (1H, d, J = 11.2 Hz), 7.09 (1H, d, J = 6.8 Hz), 6.90 (1H, d, J = 8.0 Hz), 6.76 (1H, brs), 6.15-6.25 (2H, m), 5.85 (1H, d, J = 5.2 Hz), 5.05-5.15 (1H, m), 4.70-4.90 (2H, m), 4.45-4.55 (1H, m), 4.30-4.40 (2H, m), 3.50 (3H, s), 1.60-2.00 (2H, m), 0.97 (3H, t, J = 7.2 Hz); LCMS: 98.15%, MS (ESI): m/z 517.0 [M+H]+.
544		white powder; 1H NMR (DMSO-d6, 400 MHz): δ 8.54 (1H, s), 8.21 (1H, dd, J = 8.8, 2.0 Hz), 7.45 (2H, d, J = 8.4 Hz), 7.22 (1H, d, J = 8.8 Hz), 7.14 (2H, d, J = 8.4 Hz), 6.95-7.00 (1H, m), 6.94 (1H, d, J = 8.0 Hz), 6.25 (1H, s), 6.22 (1H, d, J = 8.4 Hz), 5.85 (1H, d, J = 6.8 Hz), 4.84 (2H, t, J = 6.4 Hz), 4.45-4.58 (3H, m), 4.39 (2H, t, J = 6.0 Hz), 3.45 (3H, s); LCMS: 100%, MS (ESI): m/z 470.0[M + H] +.
545		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.83 (2H, s), 8.37 (1H, brs), 7.45 (2H, d, J = 8.4 Hz), 7.16-7.26 (3H, m), 7.05 (1H, d, J = 8.4 Hz), 6.91 (1H, d, J = 8.4 Hz), 6.25 (1H, s), 4.57 (2H, d, J = 4.8 Hz), 4.02-1-4.04 (2H, m), 3.83 (3H, s), 1.25 (3H, t, J = 6.8 Hz); LCMS: 100%, MS (ESI): m/z 593.0[M + H]+.
546		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.57 (1H, s), 8.24 (1H, dd, J = 8.8, 2.4 Hz), 7.50 (1H, t, J = 8.4 Hz), 7.28 (1H, d, J = 8.4 Hz), 7.18 (1H, dd, J = 10.8, 2.4 Hz), 7.01 (2H, dd, J = 8.4, 2.0 Hz), 6.95 (1H, d, J = 8.4 Hz), 6.26 (1H, d, J = 1.2 Hz), 6.23 (1H, d, J = 8.0, 1.2 Hz), 5.87 (1H, d, J = 6.8 Hz), 4.84 (2H, t, J = 6.4 Hz), 4.46-4.61 (3H, m), 4.34-4.44 (2H, m), 3.46 (3H, s); LCMS: 100%, MS (ESI): m/z 487.9[M + H]+.
547		pale yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 9.05 (2H, s), 7.47 (2H, d, J = 8.4 Hz), 7.15 (2H, d, J = 8.8 Hz), 6.86 (1H, d, J = 8.0 Hz), 6.65 (1H, d, J = 8.4 Hz), 6.19 (1H, d, J = 1.6 Hz), 6.15 (1H, dd, J = 8.4, 2.0 Hz), 5.78 (1H, d, J = 7.2 Hz), 4.74-4.88 (3H, m), 4.35-4.50 (1H, m), 4.29-4.38 (2H, m), 3.44 (3H, s), 1.71-1.95 (2H, m), 0.91 (3H, t, J = 7.2 Hz); LCMS: 100%, MS (ESI): m/z 499.0[M + H]+.

548		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 9.09 (2H, s), 7.45 (2H, d, J = 8.4 Hz), 7.20 (2H, d, J = 8.4 Hz), 7.04 (1H, brs), 6.93 (1H, d, J = 8.4 Hz), 6.29 (1H, d, J = 1.6 Hz), 6.19 (1H, dd, J = 8.0, 1.6 Hz), 5.84 (1H, d, J = 7.2 Hz), 4.84 (2H, t, J = 6.0 Hz), 4.47-4.57 (3H, m), 4.36-4.42 (2H, m), 3.98 (2H, q , J = 6.8 Hz), 1.20 (3H, t, J = 7.2 Hz); LCMS: 99.5%, MS (ESI): m/z 485.0[M + H]+.
549		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.53 (1H, s), 8.18 (1H, dd, J = 8.8, 2.4 Hz), 7.46 (2H, d, J = 8.8 Hz), 7.19 (1H, d, J = 8.8 Hz), 7.10 (2H, d, J = 8.8 Hz), 6.87 (1H, d, J = 8.0 Hz), 6.66 (1H, d, J = 8.4 Hz), 6.20 (1H, s), 6.16 (1H, dd, J = 8.4, 2.0 Hz), 5.80 (1H, d, J = 6.8 Hz), 4.72-4.85 (3H, m), 4.40-4.50 (1H, m), 4.33-4.41 (2H, m), 3.45 (3H, s), 1.69-1.96 (2H, m), 0.92 (3H, t, J = 7.6 Hz); LCMS: 100%, MS (ESI): m/z 498.1[M + H]+.
550		white powder; 1H NMR (DMSO-d6, 400 MHz): δ 8.58 (1H, s.), 8.23 (1H, d, J = 8.8 Hz), 7.56 (1H, t, J = 8.4 Hz), 7.26 (1H, d, J = 8.8 Hz), 7.13 (1H, d, J = 10.8 Hz), 7.01 (1H, d, J = 8.0 Hz), 6.90 (1H, d, J = 8.0 Hz), 6.73 (1H, d, J = 8.0 Hz), 6.13-6.25 (2H, m), 5.83 (1H, d, J = 6.8 Hz), 5.06-5.15 (1H, m), 4.83 (2H, t, J = 6.4 Hz), 4.44-4.55 (1H, m), 4.33-4.41 (2H, m), 3.50 (3H, s), 1.68- 1.96 (2H, m), 0.97 (3H, t, J = 7.2 Hz); LCMS: 99.3%, MS (ESI): m/z 516.0 [M + H]+.
551		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 9.08 (2H, s), 7.45 (2H, d, J = 8.4 Hz), 7.19 (2H, d, J = 8.4 Hz), 7.11 (1H, t, J = 6.0 Hz), 6.00-6.15 (3H, m), 4.83 (2H, t, J = 6.4 Hz), 4.46-4.57 (3H, m), 4.36 (2H, t, J = 6.0 Hz), 3.44 (3H, s); LCMS: 100%, MS (ESI): m/z 489.0[M + H]+.
552		white powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.51 (1H, s), 8.18 (1H, dd, J = 8.4, 2.0 Hz), 7.42 (2H, d, J = 8.8 Hz), 7.19 (1H, d, J = 8.8 Hz), 7.02-7.16 (3H, m), 5.95-6.12 (3H, m), 4.81 (2H, t, J = 6.4 Hz), 4.42-4.56 (3H, m), 4.34 (2H, t, J = 6.4 Hz), 3.42 (3H, s); LCMS: 100.0%, MS (ESI): m/z 488.0[M + H]+.
553		yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.14 (1H, d, J = 2.4 Hz), 7.91 (1H, dd, J = 8.4, 2.4 Hz), 7.40 (2H, d, J = 8.0 Hz), 6.97-7.12 (3H, m), 5.95-6.27 (3H, m), 4.82 (2H, t, J = 6.4 Hz), 4.41-4.60 (3H, m), 4.35 (2H, t, J = 5.6 Hz), 3.44 (3H, s); LCMS: 86.5%, MS (ESI): m/z 476.0[M + Na]+.

554		pale yellow powder; 1H-NMR (DMSO-d6, 400 MHz): δ 8.70 (2H, s), 7.41 (2H, d, J = 8.0 Hz), 7.12 (2H, d, J = 8.0 Hz), 7.07 (1H, t, J = 6.0 Hz), 5.95-6.10 (3H, m), 4.81 (2H, t, J = 6.0 Hz), 4.45-4.55 (3H, m), 4.34 (2H, t, J = 6.0 Hz), 3.42 (3H, s); LCMS: 99.3%, MS (ESI): m/z 455.0[M + H]+.
555		white powder; ^{1}H-NMR (DMSO-d6, 400 MHz): δ 8.73 (2H, s), 7.42 (2H, d, J = 8.0 Hz), 7.16 (3H, d, J = 8.0 Hz), 5.98-6.17 (3H, m), 4.84 (2H, t, J = 6.4 Hz), 4.47-4.60 (3H, m), 4.34-4.42 (2H, m), 3.98 (2H, q, J = 6.8 Hz), 1.19 (3H, t, J = 6.8 Hz); LCMS: 100%, MS (ESI): m/z 469.0[M + H]+.
556		pink powder; ^{1}H NMR (DMSO-d6, 400 MHz): δ 11.57 (1H, brs), 8.74 (2H, s), 8.14 (1H, s), 7.47 (2H, d, J = 8.0 Hz), 7.15-7.25 (4H, m), 7.03 (1H, s), 5.55 (1H, s), 4.59 (2H, d, J = 5.6 Hz), 3.47 (3H, s), 2.17 (3H, s); LCMS: 100%, MS (ESI): m/z = 517.0 [M + Na] +.

Claims

1. A compound having the general formula I:



Formula I

wherein

n is 0 or 1;

X^1 and X^2 are independently, at each occurrence, CR^5 or N;

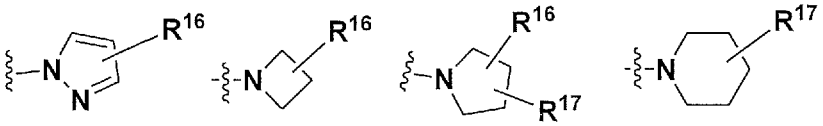
Y is C_1-C_6 alkylene, wherein alkylene is optionally substituted with one to two C_1-C_3 alkyl groups;

R^1 is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkoxy, $-NH_2$, $-NHR^6$, $-NR^7R^8$ and $-NH-(R^9)_n-R^{10}$, n being 0 or 1;

R^2 is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl,$-NH_2$, $-NHR^6$, $-NR^7R^8$ and $-NH-(R^9)_n-R^{10}$ group, n being 0 or 1;

R^3 is selected from the group consisting of hydrogen, hydroxyl, OR^{11}, $-NR^7R^8$, C_1-C_6 alkoxy, C_1-C_6 alkyl, C_3-C_{10}cycloalkyl, C_1-C_3 haloalkyl,$-C(O)NHR^{11}$, aryl, heteroaryl and heterocyclyl group, wherein each of said cycloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^4 is selected from the group consisting of $-NH_2$, $-N(R^{12})(V)_pR^{13}$, $-NH(V)_p-OR^{14}$, $-NHC(O)R^{15}$, and groups of formula Ia shown below,



Formula Ia

wherein,

p is 0 or 1,

V is C_1-C_6 alkylene, wherein alkylene is optionally substituted with one to three C_1-C_3 alkyl, C_3-C_6 cycloalkyl or phenyl groups, or wherein a carbon atom of said alkylene forms part of a C_3-C_6 cycloalkyl group;

R^5 is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl and C_1-C_6 alkoxy group;

R^6 is selected from the group consisting of C_1-C_6 alkyl, C_3-C_{10}cycloalkyl, C_1-C_6 haloalkyl, aryl, heteroaryl and heterocyclyl group, wherein each of said alkyl, cycloalkyl, haloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

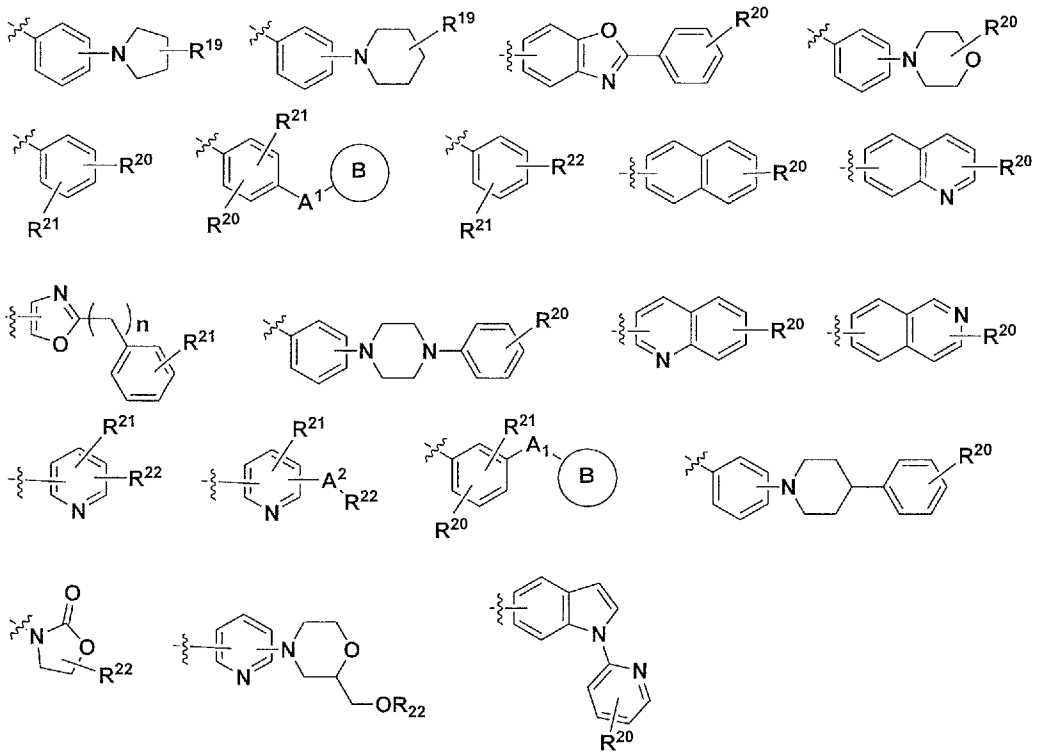
R^7 and R^8 are independently, at each occurrence, C_1-C_6 alkyl or heterocyclyl; or
R^7 and R^8 are connected to each other to make a four, five or six membered heterocyclyl or heteroaryl group, wherein each of said heterocyclyl and heteroaryl is optionally and independently substituted with one to four R^a groups;

R^9 is C_1-C_4 alkylene, wherein said alkylene is optionally substituted with one to three C_1-C_3 alkyl groups;
R^{10} is selected from the group consisting of hydroxyl, -OR^{11}, -CN, -C(O)OR^{18}, -C(O)NH_2, -C(NH)NH_2, aryl, heteroaryl and heterocyclyl group wherein each of said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{11} is independently, at each occurrence, selected from the group consisting of aryl, e.g. phenyl or benzyl, heteroaryl and heterocyclyl group wherein each of said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{12} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_4 alkyl-hydroxyl and C_1-C_4 alkyl-alkoxy;

R^{13} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_3-C_{10} cycloalkyl, C_1-C_4 alkyl-hydroxyl, -OH, -$C(O)NH_2$, -$C(O)OR^{18}$, -CN, C_1-C_3 haloalkyl and heterocyclyl, and groups of formula Ib shown below,



Formula Ib

wherein,

n is 0 or 1;

A^1 is -O-, -CH_2O-, -OCH_2-, -S-, -SO_2-, -SO_2NH-, -C(O)-, -C(O)NH-, -$C(O)N(R^7)$-, -CH(OH)-, -$CH(OR^7)$-, -NH-, -$N(CH_3)$- or -$N(CH_2COOR^7)$-;

A^2 is –O- or NH-;

B is selected from the group consisting of aryl, e.g. phenyl or benzyl, heteroaryl and heterocyclyl group wherein each of said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{14} is selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl, wherein each of said alkyl and aryl is optionally and independently substituted with one to four halogen or C_1-C_3 haloalkoxy groups;

R^{15} is aryl, wherein aryl is optionally substituted with one to four halogen groups;

R^{16} is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl and hydroxyl ;

R^{17} is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, -$C(O)R^{11}$, -$C(O)NHR^{11}$, -OR^{11} and aryl , wherein each of said alkyl and aryl is optionally and independently substituted with one to four R^a groups;

R^{18} is hydrogen or C_1-C_6 alkyl;

R^{19} is selected from the group consisting of hydrogen, -OR^{22} and -CH_2OR^{22};

R^{20} is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, –$C(O)R^a$ and C_1-C_6 haloalkoxy;

R^{21} is selected from the group consisting of hydrogen, halogen and C_1-C_6 alkyl group;

R^{22} is selected from the group consisting of C_1-C_6 haloalkyl, aryl, e.g. phenyl or benzyl, and heteroaryl, wherein each of said haloalkyl, aryl and heteroaryl is optionally and independently substituted with one to four R^a groups;

R^a is independently, at each occurrence, selected from the group consisting of hydrogen, halogen, C_1-C_3 alkyl, C_3-C_{10} cycloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_6 haloalkoxy, hydroxyl, C_1-C_3 alkylhydroxyl, –CH_2OR^c, –OCH_2R^c, -OR^c, -CN, NO_2, -NR^bR^c, -$C(O)NR^bR^c$, -$C(NH)NH_2$, -$C(O)R^c$, -$C(O)OR^c$, sulfonyl, sulfoxide, heterocyclyl, heteroaryl and aryl, e.g. phenyl, benzyl, wherein each of said alkyl, haloalkyl, haloalkoxy, alkoxy, cycloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four C_1-C_3 alkyl, C_1-C_4 alkoxy, halogen, C_1-C_3 haloalkyl, -CN, -$C(O)NH_2$, -COOH, -CO_2Et and heteroaryl;

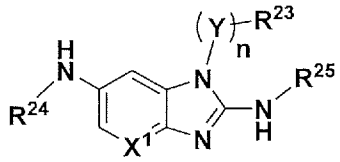
R^b and R^c are independently, at each occurrence, selected from the group consisting of hydrogen, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_1-C_6 alkyl-O-alkyl, C_2-C_{10} alkenyl, C_1-C_4 alkoxy, C_1-C_3 alkylhydroxyl, C_3-C_{10} cycloalkenyl, C_2-C_{10} alkynyl, C_1-C_6 haloalkyl, aryl, e.g. phenyl

or benzyl, heteroaryl, and heterocyclyl wherein each of said alkyl, cycloalkyl, alkyl-O-alkyl, alkenyl, alkoxy, cycloalkenyl, alkynyl, haloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four C_1-C_3 alkyl, C_1-C_4 alkoxy, halogen, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, hydroxyl, -C(O)NH_2, -COOH, -COOMe, -COOEt, -CN, -NO_2, -NH_2; or

R^b and R^c are connected to each other to make a four, five or six membered saturated or unsaturated cyclic or heterocyclic ring;

and pharmaceutically acceptable salts thereof.

2. The compound according to claim 1 having the general formula II:



Formula II

wherein

n is 0 or 1;

X^1 is CR^5 or N;

Y is C_1-C_6 alkylene, wherein alkylene is optionally substituted with one to two C_1-C_3 alkyl groups;

R^5 is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl and C_1-C_6 alkoxy group;

R^{23} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_3 haloalkyl, aryl, heteroaryl and heterocyclyl group, wherein each of said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{24} is selected from the group consisting of hydrogen, C_3-C_{10}cycloalkyl, aryl, heteroaryl and heterocyclyl group, wherein each of said cycloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{25} is selected from the group consisting of hydrogen, $-(V)_pR^{26}$ and $-(V)_p-OR^{14}$;

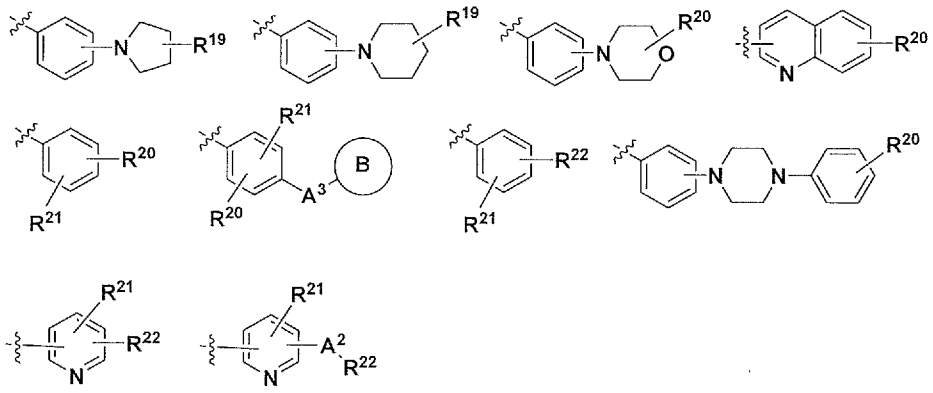
wherein,

p is 0 or 1,

V is C_1-C_6 alkylene, wherein alkylene is optionally substituted with one to three C_1-C_3 alkyl or phenyl groups, or wherein a carbon atom of said alkylene forms part of a C_3-C_6 cycloalkyl group;

R^{14} is selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl, wherein each of said alkyl and aryl is optionally and independently substituted with one to four halogen or C_1-C_3 haloalkoxy groups;

R^{26} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, -CN and C_1-C_3 haloalkyl, and groups of formula IIa shown below,



Formula IIa

wherein,

A^2 is -O- or NH-;

A^3 is -O-, $-CH_2O-$, $-OCH_2-$, or –NH-;

B is selected from the group consisting of aryl, e.g. phenyl or benzyl, heteroaryl and heterocyclyl group wherein each of said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{19} is selected from the group consisting of hydrogen, $-OR^{22}$ and $-CH_2OR^{22}$;

R^{20} is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy and C_1-C_6 haloalkoxy;

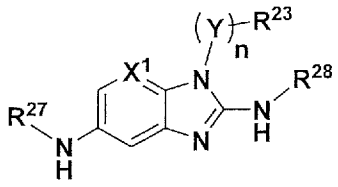
R^{21} is selected from the group consisting of hydrogen, halogen and C_1-C_6 alkyl;

R^{22} is selected from the group consisting of aryl, e.g. phenyl or benzyl, and heteroaryl, wherein each of said aryl and heteroaryl is optionally and independently substituted with one to four R^a groups;

R^a is independently, at each occurrence, selected from the group consisting of hydrogen, halogen, C_1-C_3 alkyl, C_3-C_{10} cycloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_6 haloalkoxy, hydroxyl, C_1-C_3 alkylhydroxyl, $–CH_2OR^c$, $–OCH_2R^c$, $-OR^c$, -CN, NO_2, $-NR^bR^c$, $-C(O)NR^bR^c$, $-C(NH)NH_2$, $-C(O)R^c$, $-C(O)OR^c$, sulfonyl, sulfoxide, heterocyclyl, heteroaryl and aryl, e.g. phenyl, benzyl, wherein each of said alkyl, haloalkyl, haloalkoxy, alkoxy, cycloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four C_1-C_3 alkyl, C_1-C_4 alkoxy, halogen, C_1-C_3 haloalkyl, -CN, $-C(O)NH_2$, -COOH, $-CO_2Et$ and heteroaryl;

R^b and R^c are independently, at each occurence, selected from the group consisting of hydrogen, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_1-C_6 alkyl-O-alkyl, C_2-C_{10} alkenyl, C_1-C_4 alkoxy, C_1-C_3 alkylhydroxyl, C_3-C_{10} cycloalkenyl, C_2-C_{10} alkynyl, C_1-C_6 haloalkyl, aryl, e.g. phenyl or benzyl, heteroaryl, and heterocyclyl wherein each of said alkyl, alkyl-O-alkyl, alkenyl, alkoxy, cycloalkenyl, alkynyl, haloalkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four C_1-C_3 alkyl, C_1-C_4 alkoxy, halogen, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, hydroxyl, $-C(O)NH_2$, -COOH, -COOMe, -COOEt, -CN, $-NO_2$, $-NH_2$; or
R^b and R^c are connected to each other to make a four, five or six membered saturated or unsaturated cyclic or heterocyclic ring;
and pharmaceutically acceptable salts thereof.

3. The compound according to claim 1 having the general formula III:



Formula III

wherein

n is 0 or 1;

X^1 is CR^5 or N;

Y is C_1-C_6 alkylene, wherein alkylene is optionally substituted with one to two C_1-C_3 alkyl groups;

R^5 is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl and C_1-C_6 alkoxy group;

R^{23} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, aryl, heteroaryl and heterocyclyl group, wherein each of said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{27} is selected from the group consisting of hydrogen, -R^6, and -R^9-R^{10} ;

wherein,

R^6 is selected from the group consisting of C_1-C_6 alkyl, C_3-C_{10}cycloalkyl, C_1-C_6 haloalkyl, aryl, heteroaryl and heterocyclyl group, wherein said alkyl, cycloalkyl, haloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^9 is C_1-C_4 alkylene, wherein said alkylene is optionally substituted with one to three C_1-C_3 alkyl groups;

R^{10} is selected from the group consisting of hydroxyl, $-OR^{11}$, $-C(O)OR^{18}$, $-C(O)NH_2$, aryl, heteroaryl and heterocyclyl group wherein each of said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{11} is independently, at each occurrence selected from the group consisting of aryl, e.g. phenyl or benzyl, heteroaryl and heterocyclyl group wherein said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{18} is hydrogen or C_1-C_6 alkyl;

R^{28} is selected from the group consisting of hydrogen, $-(V)_pR^{29}$ and $-(V)_p$-OR^{14} group;

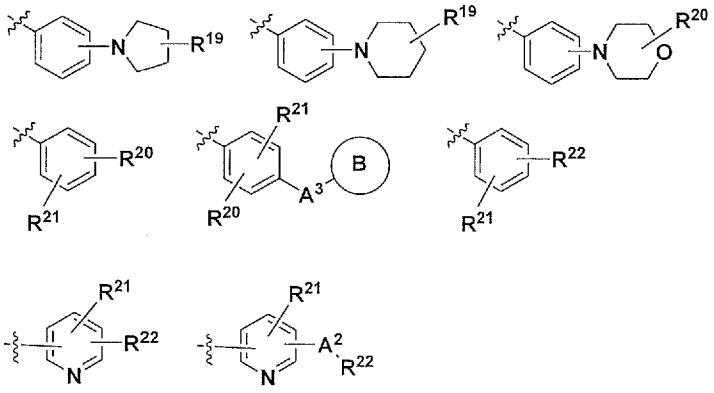
wherein,

p is 0 or 1,

V is C_1-C_6 alkylene, wherein alkylene is optionally substituted with one to three C_1-C_6 alkyl or phenyl groups;

R^{14} is selected from the group consisting of hydrogen, C_1-C_6 alkyl and aryl, wherein each of said alkyl and aryl is optionally and independently substituted with one to four halogen or C_1-C_3 haloalkoxy groups;

R^{29} is selected from the group consisting of hydrogen, C_1-C_6 alkyl and C_1-C_3 haloalkyl, and groups of formula IIIa shown below,



Formula IIIa

wherein,

A^2 is -O- or NH-;

A^3 is -O-, -CH_2O-, -OCH_2-, or –NH-;

B is selected from the group consisting of aryl, e.g. phenyl or benzyl, heteroaryl and heterocyclyl group wherein each of said aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups;

R^{19} is selected from the group consisting of hydrogen, -OR^{22} and -CH_2OR^{22} ;

R^{20} is selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy and C_1-C_6 haloalkoxy;

R^{21} is selected from the group consisting of hydrogen, halogen and C_1-C_6 alkyl;

R^{22} is selected from the group consisting of aryl, e.g. phenyl or benzyl, and heteroaryl, wherein said aryl and heteroaryl is optionally and independently substituted with one to four R^a groups;

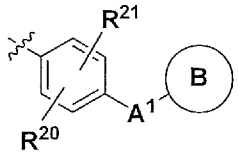
R^a is independently, at each occurrence, selected from the group consisting of hydrogen, halogen, C_1-C_3 alkyl, C_3-C_{10} cycloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, C_1-C_6 haloalkoxy, hydroxyl, C_1-C_3 alkylhydroxyl, –CH_2OR^c, –OCH_2R^c, -OR^c, -CN, NO_2, -NR^bR^c, -$C(O)NR^bR^c$, -$C(NH)NH_2$, -$C(O)R^c$, -$C(O)OR^c$, sulfonyl, sulfoxide, heterocyclyl, heteroaryl and aryl, e.g. phenyl, benzyl, wherein each of said alkyl, haloalkyl, haloalkoxy, alkoxy, cycloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four C_1-C_3 alkyl, C_1-C_4 alkoxy, halogen, C_1-C_3 haloalkyl, -CN, -$C(O)NH_2$, -COOH, -CO_2Et and heteroaryl;

R^b and R^c are independently, at each occurrence, selected from the group consisting of hydrogen, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_1-C_6 alkyl-O-alkyl, C_2-C_{10} alkenyl, C_1-C_4 alkoxy, C_1-C_3 alkylhydroxyl, C_3-C_{10} cycloalkenyl, C_2-C_{10} alkynyl, C_1-C_6 haloalkyl, alkyl-O-alkyl, alkenyl, alkoxy, cycloalkenyl, alkynyl, haloalkyl, aryl, e.g. phenyl or benzyl, heteroaryl, and heterocyclyl wherein each of said alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl is optionally and independently substituted with one to four C_1-C_3 alkyl, C_1-C_4 alkoxy, halogen,

C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, hydroxyl, -C(O)NH_2,
-COOH, -COOMe , -COOEt, -CN, -NO_2, -NH_2; or
R^b and R^c are connected to each other to make a four, five or six membered saturated or unsaturated cyclic or heterocyclic ring;
and pharmaceutically acceptable salts thereof.

4. The compound according to any of claims 1-3, having one of the formulae 1- 556, as shown in tables 1-6 and/or example 7 and/or table 7, or a pharmaceutically acceptable salt thereof, preferably having one of the formulae 1-12, 14-16, 19-21, 24, 28-34, 36-40, 44, 48, 51-54, 56-68, 70, 71, 73-77, 79-81, 84, 86-173, 175-192, 194-234, 236-241, 243, 244, 246-261, 263-278, 280-321, 323-354, 356-385, 387- 428, 430-440, 442-446, 449-463, 465-471, 473-487, 489-492, 495-496, 499, 501, 503, 505, 507, 509, 512-514, 525, 529-544, 546-556 as indicated in Tables 1 and 7, or formula 14 as indicated in Tables 2 and 7, or one of the formulae 53, 54, 86, 90, 91, 95, 99, 103, 226 as indicated in Tables 5 - 7; or one of the formulae 14, 17, 24, 29, 30, 32, 33, 38, 43-46, 48, 49, 51-60, 62, 65-70, 73, 74, 79-81, 84, 86-88, 90-107, 109-113, 116, 118-132, 134-138, 140, 145, 147-150, 152, 153, 155, 160-162, 164-166, 168, 169, 172, 175-177, 179, 180, 184-187, 190-197, 199, 200, 202-220, 223, 224, 226, 227, 229-231, 233-236, 238-255, 257-262, 264, 265, 267-302, 304-306, 313, 316, 322-333, 335, 340, 342, 346, 347, 349, 350, 352, 353, 357-359, 361, 365-369, 372-375, 377-380, 382-384, 387, 389-393, 395-403, 405-407, 410, 412-415, 419-428, 430-432, 434-437, 440, 442, 445-453, 455, 457-458, 460-461, 463-482, 486-487, 489-496, 499, 501-553, 556 as indicated in Tables 3 and 7, or one of the formulae, 11, 12, 14, 24, 30, 32, 48, 52-54, 62, 65, 77, 79-81, 86-88, 92, 94, 97, 98, 101-103, 106, 109-111, 113, 119, 120, 122, 123, 125, 130, 136-138, 145, 147, 149, 155, 165, 166, 176, 177, 184, 193, 195, 199, 204, 211, 226, 227, 229, 231, 233, 234, 238, 239, 243, 249, 251, 253, 256, 268-271, 275, 277, 279, 281, 284, 288, 289, 296, 306, 311, 324, 328, 336, 341, 345, 350, 351, 358, 360, 362, 367-369, 373, 374, 378, 381, 392, 412-415, 430, 431, 433, 447-450, 461, 464-466, 468-471, 473-477, 479, 481, 482, 486, 487, 489-496, 498, 499, 501-506, 508, 509, 512-514, 516-519, 525-538, 540-547, 550, 553-554 as indicated in Tables 4 and 7; or having the formula 211 as indicated in Figure 1 and Table 7; or a pharmaceutically acceptable salt thereof.

5. The compound according to claim 1, wherein R^4 is –$N(R^{12})(V)_pR^{13}$, R^{12} is H, V is C_1-alkylene, p is 1, R^{13} is



and B is heteroaryl which is optionally substituted with one to four R^a groups.

6. The compound according to any of claims 1 or 5 wherein R^1 is $-NH_2$ or $-NHR^6$, R^6 is heteroaryl or heterocyclyl wherein each of said heteroaryl and heterocyclyl is optionally and independently substituted with one to four R^a groups.

7. The compound according to any of claims 1- 6 or a pharmaceutically acceptable salt thereof, for use in the treatment of a disease associated with the 5LOX-pathway and/or the prostaglandin E synthase (PGES) pathway, said disease being selected from inflammatory diseases, e.g. asthma, atherosclerosis, pain, or COPD, cancer, stroke and Alzheimer's disease.

8. The compound according to any of claims 1- 7, wherein said compound has an inhibitory activity on an enzyme involved in an inflammatory pathway or several inflammatory pathways, e.g. the arachidonate 5-lipoxygenese pathway and/or the prostaglandin E synthase pathway, preferably on arachidonate 5-lipoxygenase (5-lipoxygenase, 5-LO, 5-LOX, Alox5), at a concentration of said compound between 0.001-50μM, particularly preferably having an IC_{50} on arachidonate 5-lipoxygenase of less than 1μM and/or having an EC_{50} of less than 10μM on the production of leukotriene B4 (LTB4) in rat basophilic leucocyte cells (RBL) and/or rat whole blood (RWB), and/or having a 40-70 % inhibitory activity, preferably a>70 % inhibitory activity on the production of prostaglandin E2 in HeLaS3 cells, stimulated with TNF-α, at a concentration of 10μM of said compound.

9. A composition comprising a compound or a pharmaceutically acceptable salt thereof, as defined in any of claims 1- 6, and a pharmaceutically acceptable carrier.

10. The composition according to claim 9, for use in the treatment of a disease associated with the 5LOX-pathway and/or the prostaglandin E synthase (PGES) pathway, said disease

being selected from inflammatory diseases, e.g. asthma, atherosclerosis, pain, or COPD, cancer, stroke and Alzheimer's disease.

11. The compound or composition for use according to any of claims 7-8, 10 wherein said inflammatory disease is one or several of asthma, allergic rhinitis, dermatitis, chronic obstructive pulmonary disease (COPD), inflammation post infection, arthritis, atherosclerosis, allergies, such as hay fever, autoimmune diseases, such as lupus erythematosus, inflammatory bowel diseases, such as Crohn's disease, celiac disease, acne, or pain, e.g. inflammatory and/or neuropathic pain.

12. The compound or composition for use according to any of claims 7-8, 10-11 wherein said treatment comprises administering a suitable amount of a compound as defined in any of claims 1-6 , or of a composition as defined in claim 9 , to a patient in need thereof, suffering from an inflammatory disease, and/or of cancer, and/or of stroke, and/or of Alzheimer's disease.

13. A method of treatment of a disease associated with the 5-LOX-pathway and/or the prostaglandin E synthase (PGES) pathway, said disease being selected from inflammatory diseases, cancer and Alzheimer's disease, said method comprising the application of a suitable amount of a compound as defined in any of claims 1-6 or of a composition as defined in claim 9 , to a patient in need thereof, suffering from a disease associated with the 5-LOX-pathway and/or the prostaglandin E synthase (PGES) pathway.

14. The method of treatment according to claim 13 , wherein said inflammatory disease is selected from asthma, allergic rhinitis, dermatitis, chronic obstructive pulmonary disease (COPD), inflammation post infection, arthritis, atherosclerosis, allergies, such as hay fever, autoimmune diseases, such as lupus erythematosus, inflammatory bowel diseases, such as Crohn's disease, celiac disease, acne, and pain, e.g. inflammatory and/or neuropathic pain.

15. The compound or composition for use according to claim 12 or the method of treatment according to any of claims 13-14, wherein said suitable amount is an amount in the range of 0.01mg/kg body weight to 1g/kg body weight of said patient.

16. A compound that competitively inhibits the specific binding of a compound as defined in any of claims 1-6 to arachidonate 5-lipoxygenase (5-lipoxygenase, 5-LO, 5-LOX, Alox5) or to prostaglandin E synthase (PGES).

17. A method of treatment of an inflammatory disease, in particular asthma, atherosclerosis, pain, chronic obstructive pulmonary disease (COPD), inflammation post infection, allergic rhinitis, arthritis, pain, e.g. inflammatory or neuropathic pain, allergies, such as hay fever, autoimmune diseases, such as lupus erythematosus, inflammatory bowel diseases, such as Crohn's disease, celiac disease, acne, and/or dermatitis, or a method of treatment of cancer/and or of Alzheimer's disease, said method comprising the application of a suitable amount of a compound according to claim 16, to a patient in need thereof.

18. The method of treatment according to claim 17 wherein said patient is a patient suffering from an inflammatory disease and/or from cancer and/or from stroke and/or from Alzheimer's disease.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2015/067644

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D235/20 C07D401/04 C07D401/06 C07D401/12 C07D401/14
C07D403/04 C07D403/12 C07D403/14 C07D405/12 C07D405/14
C07D409/14 C07D413/12 C07D413/14 C07D417/14 C07D471/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, CHEM ABS Data, WPI Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 419 210 A1 (PFIZER [US]) 27 March 1991 (1991-03-27) the whole document	1,3,7-15
X	WO 2012/076672 A1 (BOEHRINGER INGELHEIM INT [DE]; PRIEPKE HENNING [DE]; KUELZER RAIMUND [) 14 June 2012 (2012-06-14) the whole document	1,2,6-15

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 September 2015	06/11/2015

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Fink, Dieter

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Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LEE JIN HA ET AL: "A facile synthesis of 2-acyl- and 2-alkylaminobenzimidazoles for 5- lipoxygenase inhibitors", HETEROCYCLES : AN INTERNATIONAL JOURNAL FOR REVIEWS AND COMMUNICATIONS IN HETEROCYCLIC CHEMISTRY, JAPAN INSTITUTE OF HETEROCYCLIC CHEMISTRY, JP, vol. 70, 1 January 2006 (2006-01-01), pages 571-580, XP009186220, ISSN: 0385-5414 the whole document; in particular, page 575, table 2	1,7-15
X	WO 2005/042520 A1 (MERCK PATENT GMBH [DE]; STAEHLE WOLFGANG [DE]; BUCHSTALLER HANS-PETER) 12 May 2005 (2005-05-12) the whole document; in particular, page 48, compound (41)	1,2,6-15
X	WO 2004/085425 A1 (AMGEN INC [US]) 7 October 2004 (2004-10-07) the whole document; in particular, claim 1, pages 177-178, the compounds 60, 65, and 68 of table 5, and page 41, line 30 - page 46, line 18	1-3,5-15
X	WO 03/030902 A1 (TULARIK INC [US]; FRENKEL ALEXANDER DAVID [GB]; LIVELY SARAH ELIZABETH) 17 April 2003 (2003-04-17) the whole document; in particular, claims 1, 18, 40, and 42, the compounds 9 and 10 of figure 1a, the compound 63 of figure 3a, and page 32, line 13 - page 33, line 2	1-3,5-15
X	WO 2005/070920 A1 (SQUIBB BRISTOL MYERS CO [US]; HERPIN TIMOTHY F [US]; MORTON GEORGE C [) 4 August 2005 (2005-08-04) the whole document; in particular, claim 1, pages 75-76, the compounds 63, 67, 68, 72, 75, 76, 79, and 82 of table 1, and page 157, line 22 - page 159, line 20	1-3,6,7, 9-12,15
X	WO 00/31067 A1 (CELLTECH THERAPEUTICS LTD [GB]; ALEXANDER RIKKI PETER [GB]; LANGHAM BA) 2 June 2000 (2000-06-02) the whole document; in particular, claim 1, the intermediate 101 on page 66, the compound of the example 41 on page 92, and page 24, line 22 - page 25, line 6	1,5,7-15

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 9 July 2015 (2015-07-09), file chemcats - Chemical library; supplier: aurora fine chemicals: XP002745110, Database accession no. 1797682-22-4 the whole document -----	1,5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2015/067644

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 16-18
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

Continuation of Box II.2

Claims Nos.: 16-18

Present independent claim 16 relates to compounds defined only by their desired function (..."a compound that competitively inhibits the specific binding of a compound as defined in any of claims 1-6 to arachidonate 5-lipoxygenase.....or to prostaglandin E synthase...") rather than their structural features. This is contrary to the requirements of clarity (Article 6 PCT), because the result-to-be-achieved type of definition does not allow the scope of this compound claim to be ascertained. Furthermore, the description does not provide any support and/or disclosure in the sense of Article 6 and 5 PCT for such compounds. The fact that any compound could be screened does not overcome this objection, as the skilled person would not have knowledge beforehand as to whether it would fall within the scope claimed. Undue experimentation would be required to screen compounds randomly. The non-compliance with the substantive provisions is to such an extent, that no search has been carried out on claim 16.

Consequently, the present method claims 17 and 18, the definition of which depends essentially only on the compounds of claim 16, have not been searched either.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2015/067644

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0419210 A1	27-03-1991	AT 113586 T	15-11-1994
		CA 2025849 A1	23-03-1991
		DE 69013836 D1	08-12-1994
		DE 69013836 T2	23-03-1995
		DK 0419210 T3	09-01-1995
		EP 0419210 A1	27-03-1991
		ES 2062395 T3	16-12-1994
		IE 903408 A1	10-04-1991
		JP H06759 B2	05-01-1994
		JP H03109378 A	09-05-1991
		PT 95371 A	22-05-1991
		US 5141950 A	25-08-1992
WO 2012076672 A1	14-06-2012	EP 2649052 A1	16-10-2013
		JP 2013544867 A	19-12-2013
		US 2012309738 A1	06-12-2012
		WO 2012076672 A1	14-06-2012
WO 2005042520 A1	12-05-2005	AR 046140 A1	23-11-2005
		AU 2004285643 A1	12-05-2005
		BR PI0415760 A	19-12-2006
		CA 2543346 A1	12-05-2005
		CN 1871232 A	29-11-2006
		DE 10349587 A1	25-05-2005
		EP 1675849 A1	05-07-2006
		JP 4856546 B2	18-01-2012
		JP 2007509096 A	12-04-2007
		KR 20060123124 A	01-12-2006
		MX PA06004405 A	14-06-2006
		US 2007066660 A1	22-03-2007
		US 2009082404 A1	26-03-2009
		WO 2005042520 A1	12-05-2005
		ZA 200604148 A	26-09-2007
WO 2004085425 A1	07-10-2004	AU 2004223827 A1	07-10-2004
		CA 2518909 A1	07-10-2004
		EP 1638954 A1	29-03-2006
		JP 2006520805 A	14-09-2006
		MX PA05010086 A	10-02-2006
		US 2004209892 A1	21-10-2004
		WO 2004085425 A1	07-10-2004
WO 03030902 A1	17-04-2003	AT 511840 T	15-06-2011
		CA 2458533 A1	17-04-2003
		EP 1434579 A1	07-07-2004
		ES 2367422 T3	03-11-2011
		JP 4445262 B2	07-04-2010
		JP 2005532251 A	27-10-2005
		US 2003144286 A1	31-07-2003
		US 2007037803 A1	15-02-2007
		US 2010048565 A1	25-02-2010
		WO 03030902 A1	17-04-2003
WO 2005070920 A1	04-08-2005	AR 047449 A1	18-01-2006
		EP 1706398 A1	04-10-2006
		JP 2007518809 A	12-07-2007
		PE 07672005 A1	06-10-2005
		TW 200530217 A	16-09-2005

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2015/067644

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		US 2005203146 A1	15-09-2005
		US 2008275090 A1	06-11-2008
		WO 2005070920 A1	04-08-2005
WO 0031067 A1	02-06-2000	AU 1283200 A	13-06-2000
		EP 1133488 A1	19-09-2001
		JP 2002530400 A	17-09-2002
		US 6319922 B1	20-11-2001
		US 2002035092 A1	21-03-2002
		WO 0031067 A1	02-06-2000