

anonychia [*Nat. Genet.* (2006), 38(11), 1245-7], neural tube defects [*N. Engl. J. Med.* (2007), 356(14), 1432-7], alpha-thalassemia (ATRX) syndrome [*The Journal of Neuroscience* (2008), 28(47), 12570 –12580], fragile X syndrome [*PLoS Genetics* (2010), 6(4), e1000898], ICF syndrome, Angelman syndrome [*Brain Research Bulletin* (2002), 57(1), 109-119], Prader-Willi syndrome [*Journal of Neuroscience* (2006), 26(20), 5383-5392], Beckwith-Wiedemann Syndrome [*Pediatric and Developmental Pathology* (2003), 6(4), 299-306] and Rett syndrome.

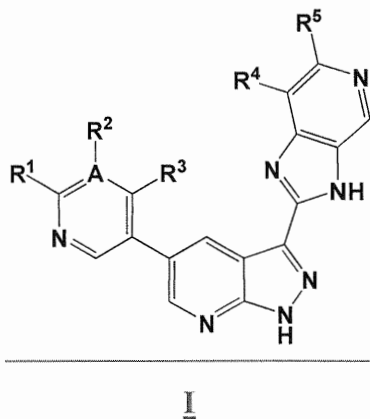
[0009] Regulation of cell signaling by the Wnt signaling pathway is critical for the formation of neuronal circuits. Wnt pathway modulates in neural tissue, among other things, axon pathfinding, dendritic development, and synaptic assembly. Through different receptors, Wnt pathway activates and/or regulates diverse signaling pathways and other processes that lead to local changes on the cytoskeleton or global cellular changes involving nuclear function. Recently, a link between neuronal activity, essential for the formation and refinement of neuronal connections, and Wnt signaling has been uncovered. Indeed, neuronal activity regulates the release of various Wnt proteins and the localization of their receptors. Wnt pathway mediates synaptic structural changes induced by neuronal activity or experience. Evidence suggests that dysfunction in Wnt signaling contributes to neurological disorders [*Brain Research Reviews* (2000), 33(1), 1–12; *Oncogene* (2006) 25(57), 7545-7553; *Molecular Neurodegeneration* (2008), 3, 9; *Neurobiology of Disease* (2010), 38(2), 148–153; *Journal of Neurodevelopmental Disorders* (2011), 3(2), 162–174 and *Cold Spring Harbor Perspectives in Biology* February (2012), 4(2)].

SUMMARY OF THE INVENTION

[0010] The present ~~invention~~-disclosure makes available methods and reagents, involving contacting a cell with an agent, such as a 1H-pyrazolo[3,4-*b*]pyridine compound, in a sufficient amount to antagonize Wnt activity, e. g., to reverse or control an aberrant growth state or correct a genetic disorder due to mutations in Wnt signaling components.

[0011] Some embodiments disclosed herein include Wnt inhibitors containing a 1H-pyrazolo[3,4-*b*]pyridine core. Other embodiments disclosed herein include pharmaceutical compositions and methods of treatment using these compounds.

[0011a] In one aspect, there is provided a compound or pharmaceutically acceptable salt or prodrug thereof having the structure of Formula I:



wherein:

R^1 and R^2 are independently selected from the group consisting of H, lower alkyl, halide, $-(C_{1-9} \text{ alkyl})_n\text{aryl}(R^6)_q$, $-(C_{1-9} \text{ alkyl})_n\text{heteroaryl}(R^7)_q$, $-(C_{1-9} \text{ alkyl})_n\text{heterocyclyl}(R^8)_q$, $-(C_{1-9} \text{ alkyl})_nN(R^9)_2$, $-OR^{10}$ and $-NHC(=O)R^{11}$;

R^3 is selected from the group consisting of H, halide and lower alkyl;

with the proviso that at least two of R^1 , R^2 and R^3 are H;

R^4 and R^5 are independently selected from the group consisting of H, $-C(=O)N(R^{12})_2$, $-\text{aryl}(R^{13})_q$, $-\text{heterocyclyl}(R^{14})_q$, and $-\text{heteroaryl}(R^{15})_q$;

with the proviso that at least one of R^4 and R^5 is H;

each R^6 is a substituent attached to the aryl ring and independently selected from the group consisting of H, $-C_{1-9} \text{ alkyl}$, halide, CF_3 and CN;

each R^7 is a substituent attached to the heteroaryl ring and independently selected from the group consisting of H, $-C_{1-9} \text{ alkyl}$, halide, CF_3 and CN;

each R^8 is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, halide, $-(C_{1-3} \text{ alkyl})_n\text{aryl}(R^6)_q$, and $-C_{1-4} \text{ alkyl}$;

each R^9 is independently selected from the group consisting of H, $-C_{1-9} \text{ alkyl}$, $-(C_{1-3} \text{ alkyl})_n\text{aryl}(R^6)_q$, $-(C_{1-3} \text{ alkyl})_n\text{carbocyclyl}$ and $-(C_{1-9} \text{ alkyl})N(R^{16})_2$;

alternatively, two adjacent R^9 or two adjacent R^{12} , may be taken together with the atoms to which they are attached to form a $\text{heterocyclyl}(R^{17})_q$;

R^{10} is selected from the group consisting of H, $-CF_3$, $-(C_{1-3} \text{ alkyl})_n\text{aryl}(R^6)_q$, and $-C_{1-9} \text{ alkyl}$;

R^{11} is selected from the group consisting of $-(C_{1-3} \text{ alkyl})_n \text{ aryl}(R^6)_q$, $-(C_{1-3} \text{ alkyl})_n \text{ carbocyclyl}$, $-C_{1-9} \text{ alkyl}$ and $-\text{CF}_3$;

each R^{12} is independently selected from the group consisting of H, $-(C_{1-9} \text{ alkyl})_n \text{ aryl}(R^6)_q$ and $-C_{1-9} \text{ alkyl}$;

each R^{13} is a substituent attached to the aryl ring and independently selected from the group consisting of H, halide, $-\text{CF}_3$, CN, $-(C_{1-3} \text{ alkyl})_n \text{ heterocyclyl}(R^8)_q$, $-(C_{1-9} \text{ alkyl})_n \text{N}(R^9)_2$ and $-(C_{1-9} \text{ alkyl})_n \text{NHSO}_2 R^{18}$;

each R^{14} is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, lower alkyl, halide, $-\text{CF}_3$ and CN;

each R^{15} is a substituent attached to the heteroaryl ring and independently selected from the group consisting of H, lower alkyl, halide, $-\text{CF}_3$, CN, $-\text{C}(=\text{O})(C_{1-3} \text{ alkyl})$, $-(C_{1-9} \text{ alkyl})_n \text{N}(R^9)_2$ and $-(C_{1-9} \text{ alkyl})_n \text{NHSO}_2 R^{18}$;

each R^{16} is independently selected from the group consisting of H and lower alkyl;

each R^{17} is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, $-(C_{1-9} \text{ alkyl})_n \text{ aryl}(R^6)_q$, and $-C_{1-9} \text{ alkyl}$;

each R^{18} is a lower alkyl;

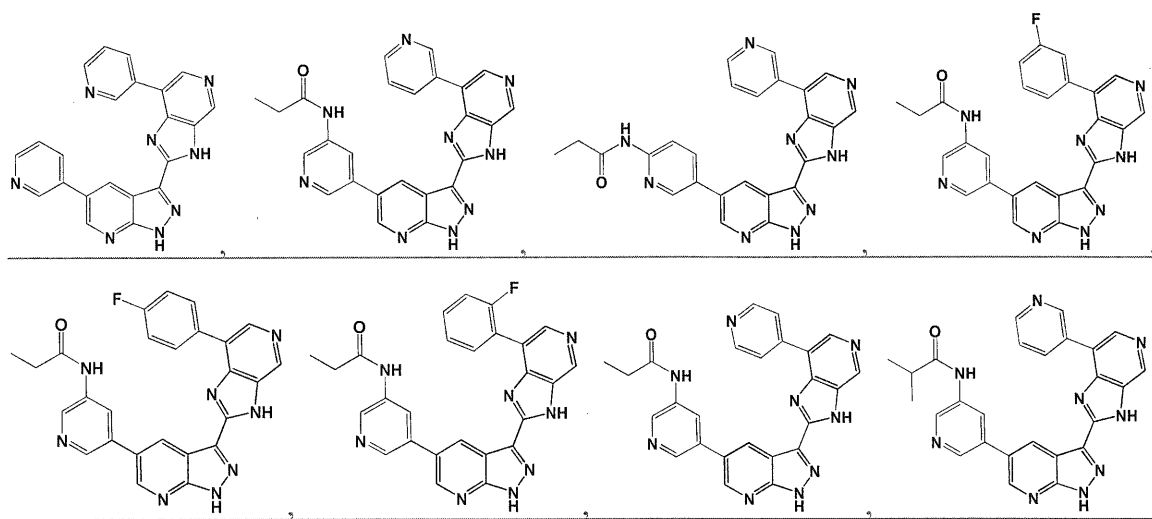
A is N or C;

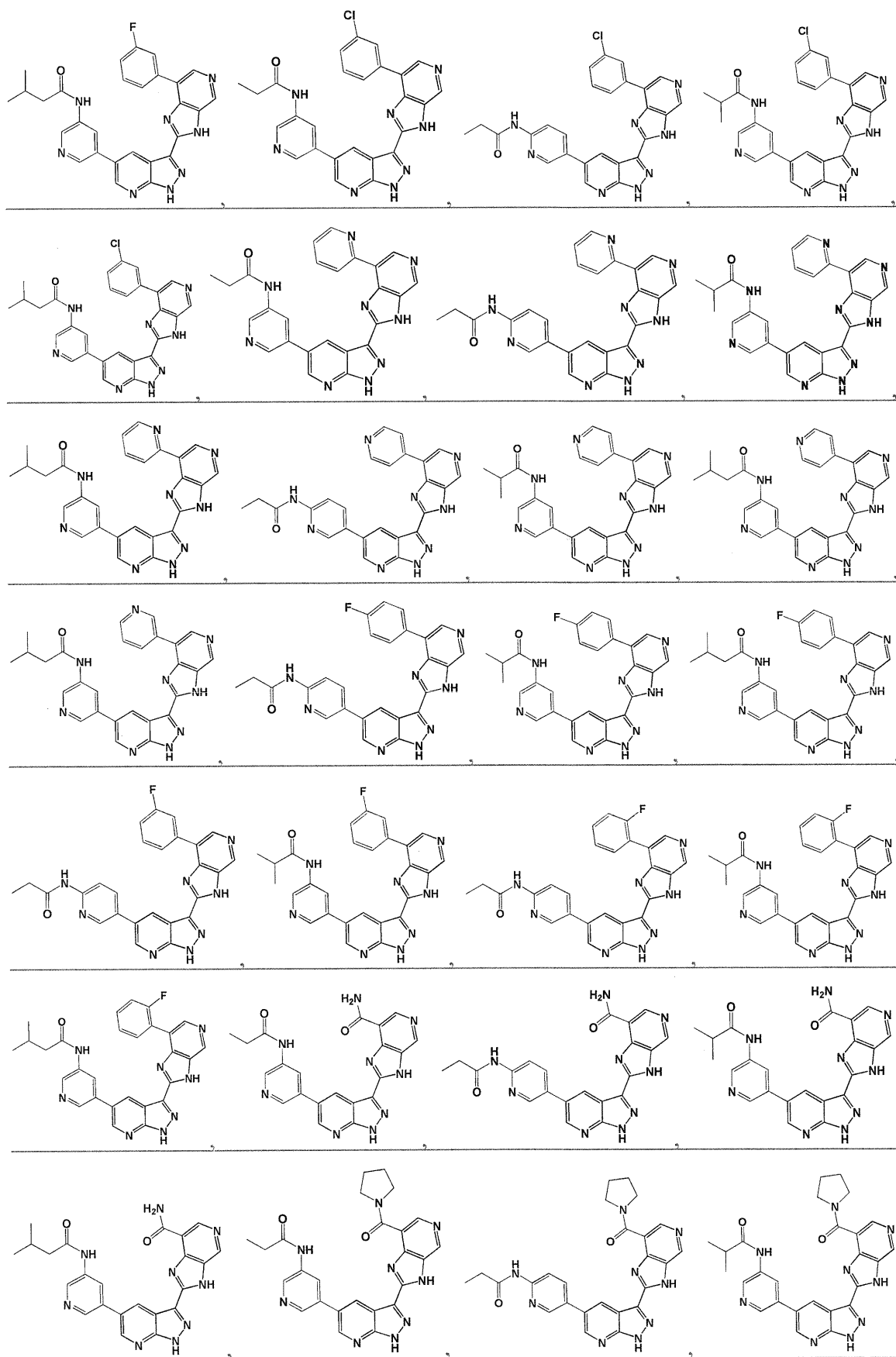
with the proviso that if A is N then R^2 is nil;

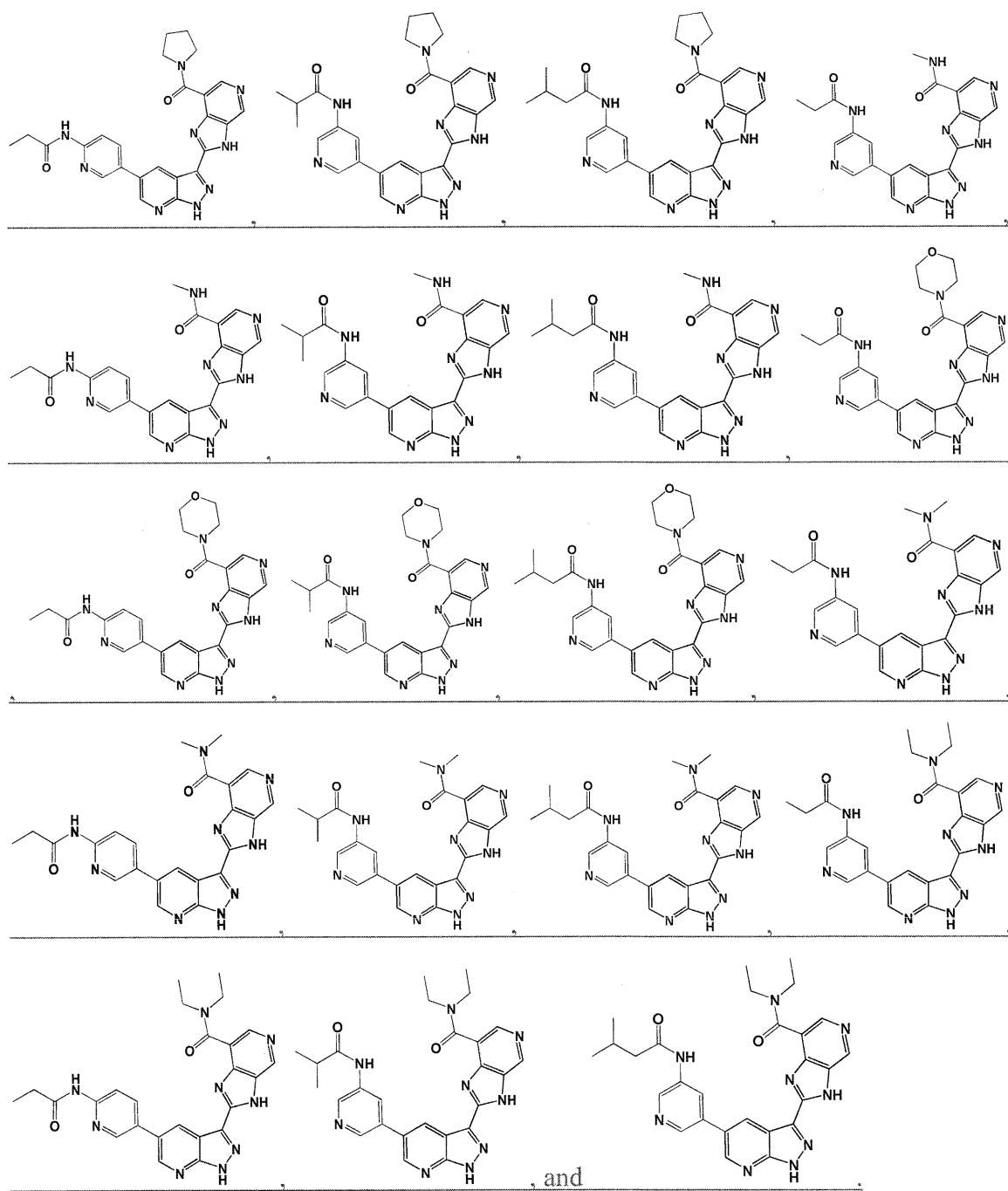
each q is an integer of 1 to 5;

each n is an integer of 0 or 1; and

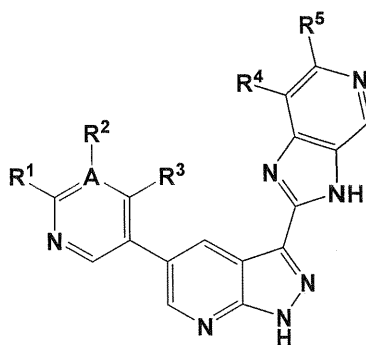
with the proviso that Formula I is not a structure selected from the group consisting of:







[0012] One embodiment disclosed herein includes a compound having the structure of Formula I or a pharmaceutically acceptable salt thereof:



I

[0013] In some embodiments of Formula (I):

R^1 and R^2 are independently selected from the group consisting of H, lower alkyl, halide, $-(C_{1-9} \text{ alkyl})_n\text{aryl}(R^6)_q$, $-(C_{1-9} \text{ alkyl})_n\text{heteroaryl}(R^7)_q$, $-(C_{1-9} \text{ alkyl})_n\text{heterocyclyl}(R^8)_q$, $-(C_{1-9} \text{ alkyl})_nN(R^9)_2$, $-OR^{10}$ and $-NHC(=O)R^{11}$;

R^3 is selected from the group consisting of H, halide and lower alkyl;

with the proviso that at least two of R^1 , R^2 and R^3 are H;

R^4 and R^5 are independently selected from the group consisting of H, $-C(=O)N(R^{12})_2$, $-\text{aryl}(R^{13})_q$, $-\text{heterocyclyl}(R^{14})_q$, and $-\text{heteroaryl}(R^{15})_q$;

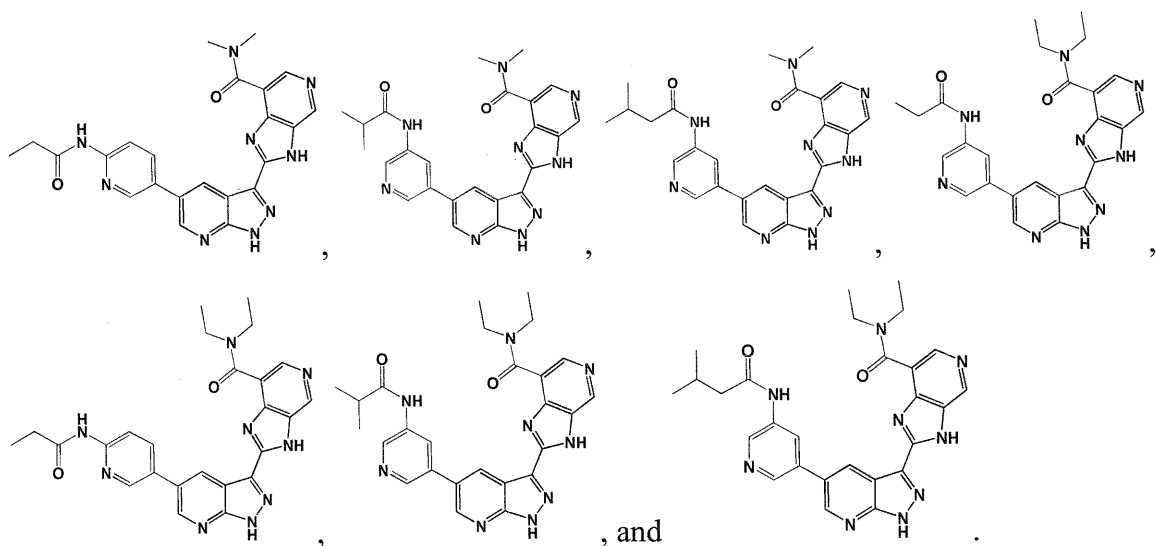
with the proviso that at least one of R^4 and R^5 is H;

each R^6 is a substituent attached to the aryl ring and independently selected from the group consisting of H, $-C_{1-9} \text{ alkyl}$, halide, CF_3 and CN;

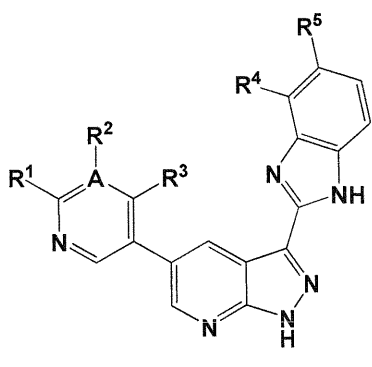
each R^7 is a substituent attached to the heteroaryl ring and independently selected from the group consisting of H, $-C_{1-9} \text{ alkyl}$, halide, CF_3 and CN;

each R^8 is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, halide, $-(C_{1-3} \text{ alkyl})_n\text{aryl}(R^6)_q$, and $-C_{1-4} \text{ alkyl}$;

each R^9 is independently selected from the group consisting of H, $-C_{1-9} \text{ alkyl}$, $-(C_{1-3} \text{ alkyl})_n\text{aryl}(R^6)_q$, $-(C_{1-3} \text{ alkyl})_n\text{carbocyclyl}$ and $-(C_{1-9} \text{ alkyl})N(R^{16})_2$;



[0013a] In one aspect, there is provided a compound or pharmaceutically acceptable salt or prodrug thereof having the structure of Formula II:



II

wherein:

R^1 and R^2 are independently selected from the group consisting of H, lower alkyl, halide, $-(C_{1-9} \text{ alkyl})_n \text{ aryl}(R^6)_q$, $-(C_{1-9} \text{ alkyl})_n \text{ heteroaryl}(R^7)_q$, $-(C_{1-9} \text{ alkyl})_n \text{ heterocyclyl}(R^8)_q$, $-(C_{1-9} \text{ alkyl})_n N(R^9)_2$, $-OR^{10}$ and $-NHC(=O)R^{11}$;

R^3 is selected from the group consisting of H, halide and lower alkyl;

with the proviso that at least two of R^1 , R^2 and R^3 are H;

R^4 and R^5 are independently selected from the group consisting of H, $-C(=O)N(R^{12})_2$, $-\text{aryl}(R^{13})_q$, $-\text{heterocyclyl}(R^{14})_q$, and $-\text{heteroaryl}(R^{15})_q$;

with the proviso that at least one of R^4 and R^5 is H;

each R^6 is a substituent attached to the aryl ring and independently selected from the group consisting of H, $-C_{1-9} \text{ alkyl}$, halide, CF_3 and CN;

each R^7 is a substituent attached to the heteroaryl ring and independently selected from the group consisting of H, $-C_{1-9}$ alkyl, halide, CF_3 and CN;

each R^8 is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, halide, $-(C_{1-3} \text{ alkyl})_n \text{ aryl}(R^6)_q$, and $-C_{1-4}$ alkyl;

each R^9 is independently selected from the group consisting of H, $-C_{1-9}$ alkyl, $-(C_{1-3} \text{ alkyl})_n \text{ aryl}(R^6)_q$, $-(C_{1-3} \text{ alkyl})_n \text{ carbocyclyl}$ and $-(C_{1-9} \text{ alkyl})N(R^{16})_2$;

alternatively, two adjacent R^9 or two adjacent R^{12} , may be taken together with the atoms to which they are attached to form a heterocyclyl(R^{17})_q;

R^{10} is selected from the group consisting of H, $-CF_3$, $-(C_{1-3} \text{ alkyl})_n \text{ aryl}(R^6)_q$, and $-C_{1-9}$ alkyl;

R^{11} is selected from the group consisting of $-(C_{1-3} \text{ alkyl})_n \text{ aryl}(R^6)_q$, $-(C_{1-3} \text{ alkyl})_n \text{ carbocyclyl}$, $-C_{1-9}$ alkyl and $-CF_3$;

each R^{12} is independently selected from the group consisting of H, $-(C_{1-9} \text{ alkyl})_n \text{ aryl}(R^6)_q$ and $-C_{1-9}$ alkyl;

each R^{13} is a substituent attached to the aryl ring and independently selected from the group consisting of H, halide, $-CF_3$, CN, $-(C_{1-3} \text{ alkyl})_n \text{ heterocyclyl}(R^8)_q$, $-(C_{1-9} \text{ alkyl})_n N(R^9)_2$ and $-(C_{1-9} \text{ alkyl})_n NHSO_2 R^{18}$;

each R^{14} is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, lower alkyl, halide, $-CF_3$ and CN;

each R^{15} is a substituent attached to the heteroaryl ring and independently selected from the group consisting of H, lower alkyl, halide, $-CF_3$, CN, $-C(=O)(C_{1-3} \text{ alkyl})$, $-(C_{1-9} \text{ alkyl})_n N(R^9)_2$ and $-(C_{1-9} \text{ alkyl})_n NHSO_2 R^{18}$;

each R^{16} is independently selected from the group consisting of H and lower alkyl;

each R^{17} is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, $-(C_{1-9} \text{ alkyl})_n \text{ aryl}(R^6)_q$, and $-C_{1-9}$ alkyl;

each R^{18} is a lower alkyl;

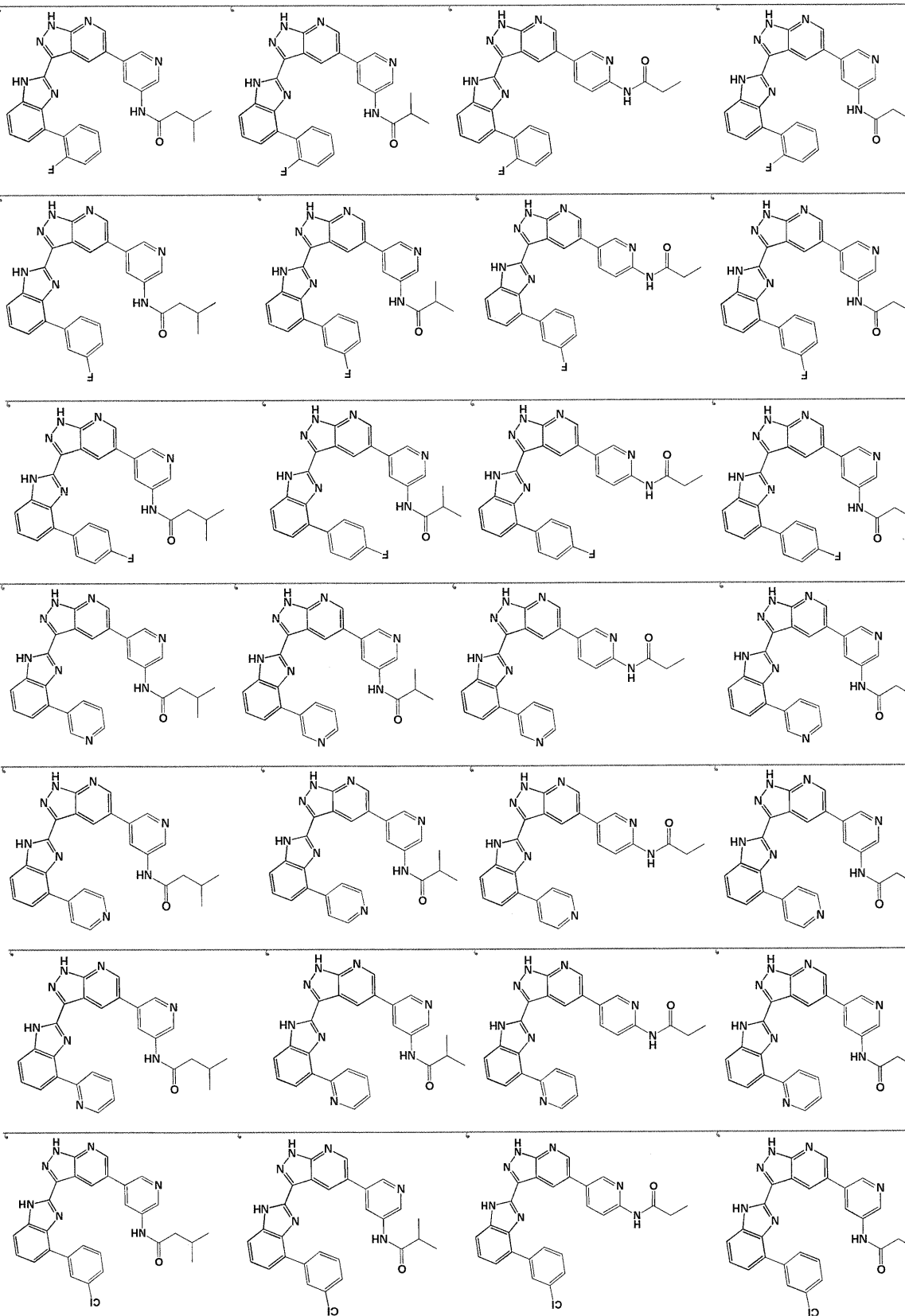
A is N or C;

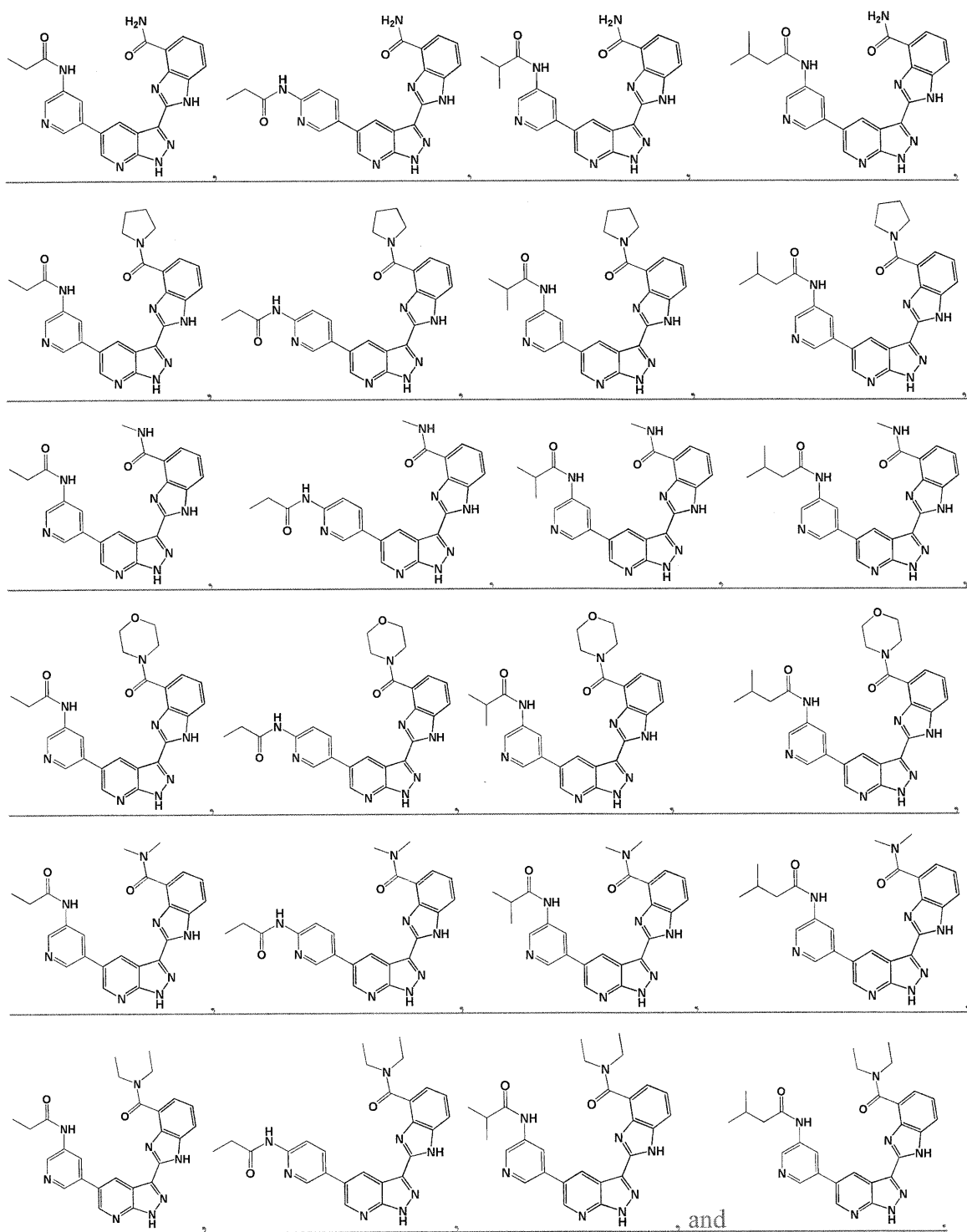
with the proviso that if A is N then R^2 is nil;

each q is an integer of 1 to 5;

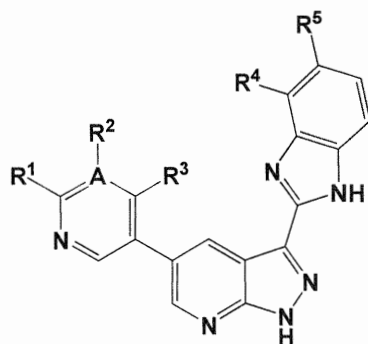
each n is an integer of 0 or 1; and

with the proviso that Formula II is not a structure selected from the group consisting of:





[0014] Another embodiment disclosed herein includes a compound having the structure of Formula II or a pharmaceutically acceptable salt thereof:



II

[0015] In some embodiments of Formula (II):

R^1 and R^2 are independently selected from the group consisting of H, lower alkyl, halide, $-(C_{1-9} \text{ alkyl})_n\text{aryl}(R^6)_q$, $-(C_{1-9} \text{ alkyl})_n\text{heteroaryl}(R^7)_q$, $-(C_{1-9} \text{ alkyl})_n\text{heterocyclyl}(R^8)_q$, $-(C_{1-9} \text{ alkyl})_nN(R^9)_2$, $-OR^{10}$ and $-NHC(=O)R^{11}$;

R^3 is selected from the group consisting of H, halide and lower alkyl;

with the proviso that at least two of R^1 , R^2 and R^3 are H;

R^4 and R^5 are independently selected from the group consisting of H, $-C(=O)N(R^{12})_2$, $-\text{aryl}(R^{13})_q$, $-\text{heterocyclyl}(R^{14})_q$, and $-\text{heteroaryl}(R^{15})_q$;

with the proviso that at least one of R^4 and R^5 is H;

each R^6 is a substituent attached to the aryl ring and independently selected from the group consisting of H, $-C_{1-9} \text{ alkyl}$, halide, CF_3 and CN;

[0016] Some embodiments include stereoisomers and pharmaceutically acceptable salts of a compound of general Formulas (I) or (II).

[0017] Some embodiments include pro-drugs of a compound of general Formulas (I) or (II).

[0017a] In one aspect, there is provided a pharmaceutical composition comprising a compound as described herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

[0018] Some embodiments of the present ~~disclosure~~invention include pharmaceutical compositions comprising a compound of general Formulas (I) or (II) and a pharmaceutically acceptable carrier, diluent, or excipient.

[0018a] In one aspect, there is provided a compound as described herein, or a pharmaceutically acceptable salt thereof, for use in treating a disorder or disease in a patient, wherein the disorder or disease is selected from the group consisting of: diabetic retinopathy, pulmonary fibrosis, idiopathic pulmonary fibrosis (IPF), rheumatoid arthritis, scleroderma, a mycotic or viral infection, a bone or cartilage disease, Alzheimer's disease, dementia, Parkinson's disease, lung disease, and cancer.

[0018b] In one aspect, there is provided a compound as described herein, or a pharmaceutically acceptable salt thereof, for use in treating a disorder or disease in a patient, wherein the disorder or disease is selected from the group consisting of: polyposis coli, osteoporosis-pseudoglioma syndrome, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia syndrome, Müllerian-duct regression and virilization, SERKAL syndrome, diabetes mellitus type 2, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzal phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication syndrome, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease, and Rett syndrome.

[0019] Other embodiments disclosed herein include methods of inhibiting one or more members of the Wnt pathway, including one or more Wnt proteins by administering to a subject affected by a disorder or disease in which aberrant Wnt signaling is implicated, such as cancer and other diseases associated with abnormal angiogenesis, cellular proliferation, cell cycling and mutations in Wnt signaling components, a compound according to Formulas (I) or (II). Accordingly, the compounds

and compositions provided herein can be used to treat cancer, to reduce or inhibit angiogenesis, to reduce or inhibit cellular proliferation and correct a genetic disorder due to mutations in Wnt signaling components. Non-limiting examples of diseases which can be treated with the compounds and compositions provided herein include a variety of cancers, diabetic retinopathy, pulmonary fibrosis, idiopathic pulmonary fibrosis, rheumatoid arthritis, scleroderma, mycotic and viral infections, osteochondrodysplasia, Alzheimer's disease, lung disease, osteoarthritis, polyposis coli, osteoporosis-pseudoglioma syndrome, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-ameliasyndrome, Müllerian-duct regression and virilization, SERKAL syndrome, diabetes mellitus type 2, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzal phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication syndrome, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease and Rett syndrome.

[0020] Another embodiment disclosed herein includes a pharmaceutical composition that has a compound according to any of the above formulas and a pharmaceutically acceptable carrier, diluent, or excipient.

[0021] Some embodiments of the present ~~invention~~-disclosure include methods to prepare a compound of general Formulas (I) or (II).

[0022] It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the ~~disclosure~~invention, as claimed.

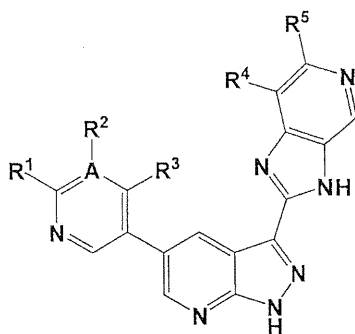
DETAILED DESCRIPTION OF THE INVENTION

[0023] Compositions and methods for inhibiting one or more members of the Wnt pathway, including one or more Wnt proteins would be of tremendous benefit. Certain embodiments provide such compositions and methods. Certain related compounds and methods are disclosed in U.S. Application Ser. No. 12/968,505, filed December 15, 2010, which claims priority to U.S. Provisional Application Ser. No. 61/288,544, all of which are incorporated by reference in their entirety herein.

[0024] Some embodiments relate to a method for treating a disease including, but not limited to, cancers, diabetic retinopathy, idiopathic pulmonary fibrosis, pulmonary fibrosis, rheumatoid arthritis, scleroderma, mycotic and viral infections, bone and cartilage diseases, Alzheimer's disease, lung disease, osteoarthritis, polyposis coli, bone density and vascular defects in the eye (Osteoporosis-pseudoglioma Syndrome, OPPG), familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia, Müllerian-duct regression and virilization, SERKAL syndrome, type II diabetes, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman's syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease and Rett syndrome.

WHAT IS CLAIMED IS:

1. A compound or pharmaceutically acceptable salt or prodrug thereof having the structure of Formula I:



I

wherein:

R^1 and R^2 are independently selected from the group consisting of H, lower alkyl, halide, $-(C_{1-9} \text{ alkyl})_n \text{ aryl}(R^6)_q$, $-(C_{1-9} \text{ alkyl})_n \text{ heteroaryl}(R^7)_q$, $-(C_{1-9} \text{ alkyl})_n \text{ heterocyclyl}(R^8)_q$, $-(C_{1-9} \text{ alkyl})_n \text{ N}(R^9)_2$, $-OR^{10}$ and $-NHC(=O)R^{11}$;

R^3 is selected from the group consisting of H, halide and lower alkyl;

with the proviso that at least two of R^1 , R^2 and R^3 are H;

R^4 and R^5 are independently selected from the group consisting of H, $-C(=O)N(R^{12})_2$, $-\text{aryl}(R^{13})_q$, $-\text{heterocyclyl}(R^{14})_q$, and $-\text{heteroaryl}(R^{15})_q$;

with the proviso that at least one of R^4 and R^5 is H;

each R^6 is a substituent attached to the aryl ring and independently selected from the group consisting of H, $-C_{1-9} \text{ alkyl}$, halide, CF_3 and CN;

each R^7 is a substituent attached to the heteroaryl ring and independently selected from the group consisting of H, $-C_{1-9} \text{ alkyl}$, halide, CF_3 and CN;

each R^8 is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, halide, $-(C_{1-3} \text{ alkyl})_n \text{ aryl}(R^6)_q$, and $-C_{1-4} \text{ alkyl}$;

each R^9 is independently selected from the group consisting of H, $-C_{1-9} \text{ alkyl}$, $-(C_{1-3} \text{ alkyl})_n \text{ aryl}(R^6)_q$, $-(C_{1-3} \text{ alkyl})_n \text{ carbocyclyl}$ and $-(C_{1-9} \text{ alkyl})N(R^{16})_2$;

alternatively, two adjacent R^9 or two adjacent R^{12} , may be taken together with the atoms to which they are attached to form a heterocyclyl(R^{17})_q;

R^{10} is selected from the group consisting of H, $-CF_3$, $-(C_{1-3} \text{ alkyl})_n \text{aryl}(R^6)_q$, and $-C_{1-9} \text{ alkyl}$;

R^{11} is selected from the group consisting of $-(C_{1-3} \text{ alkyl})_n \text{aryl}(R^6)_q$, $-(C_{1-3} \text{ alkyl})_n \text{carbocyclyl}$, $-C_{1-9} \text{ alkyl}$ and $-CF_3$;

each R^{12} is independently selected from the group consisting of H, $-(C_{1-9} \text{ alkyl})_n \text{aryl}(R^6)_q$ and $-C_{1-9} \text{ alkyl}$;

each R^{13} is a substituent attached to the aryl ring and independently selected from the group consisting of H, halide, $-CF_3$, CN, $-(C_{1-3} \text{ alkyl})_n \text{heterocyclyl}(R^8)_q$, $-(C_{1-9} \text{ alkyl})_n N(R^9)_2$ and $-(C_{1-9} \text{ alkyl})_n NHSO_2 R^{18}$;

each R^{14} is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, lower alkyl, halide, $-CF_3$ and CN;

each R^{15} is a substituent attached to the heteroaryl ring and independently selected from the group consisting of H, lower alkyl, halide, $-CF_3$, CN, $-C(=O)(C_{1-3} \text{ alkyl})$, $-(C_{1-9} \text{ alkyl})_n N(R^9)_2$ and $-(C_{1-9} \text{ alkyl})_n NHSO_2 R^{18}$;

each R^{16} is independently selected from the group consisting of H and lower alkyl;

each R^{17} is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, $-(C_{1-9} \text{ alkyl})_n \text{aryl}(R^6)_q$, and $-C_{1-9} \text{ alkyl}$;

each R^{18} is a lower alkyl;

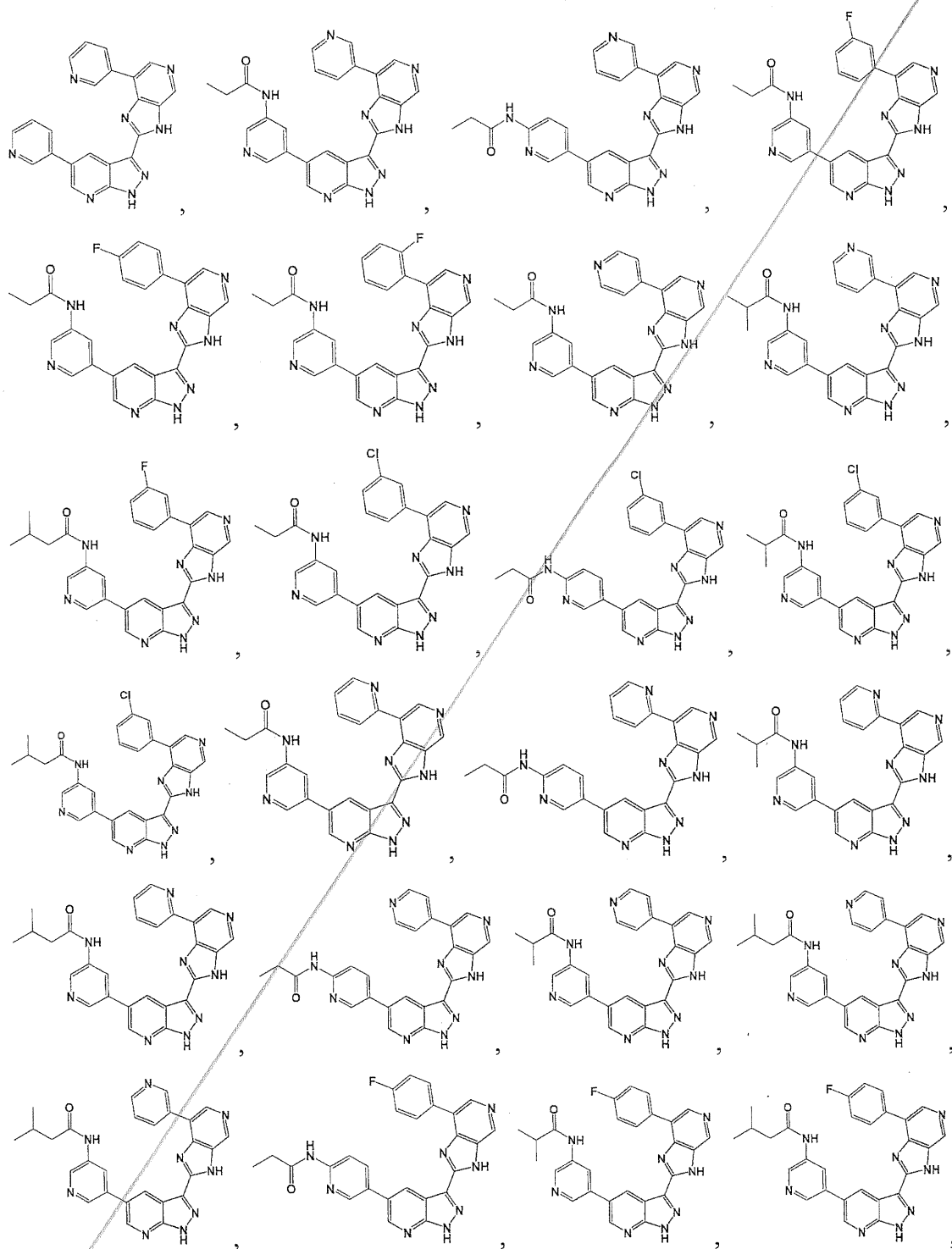
A is N or C;

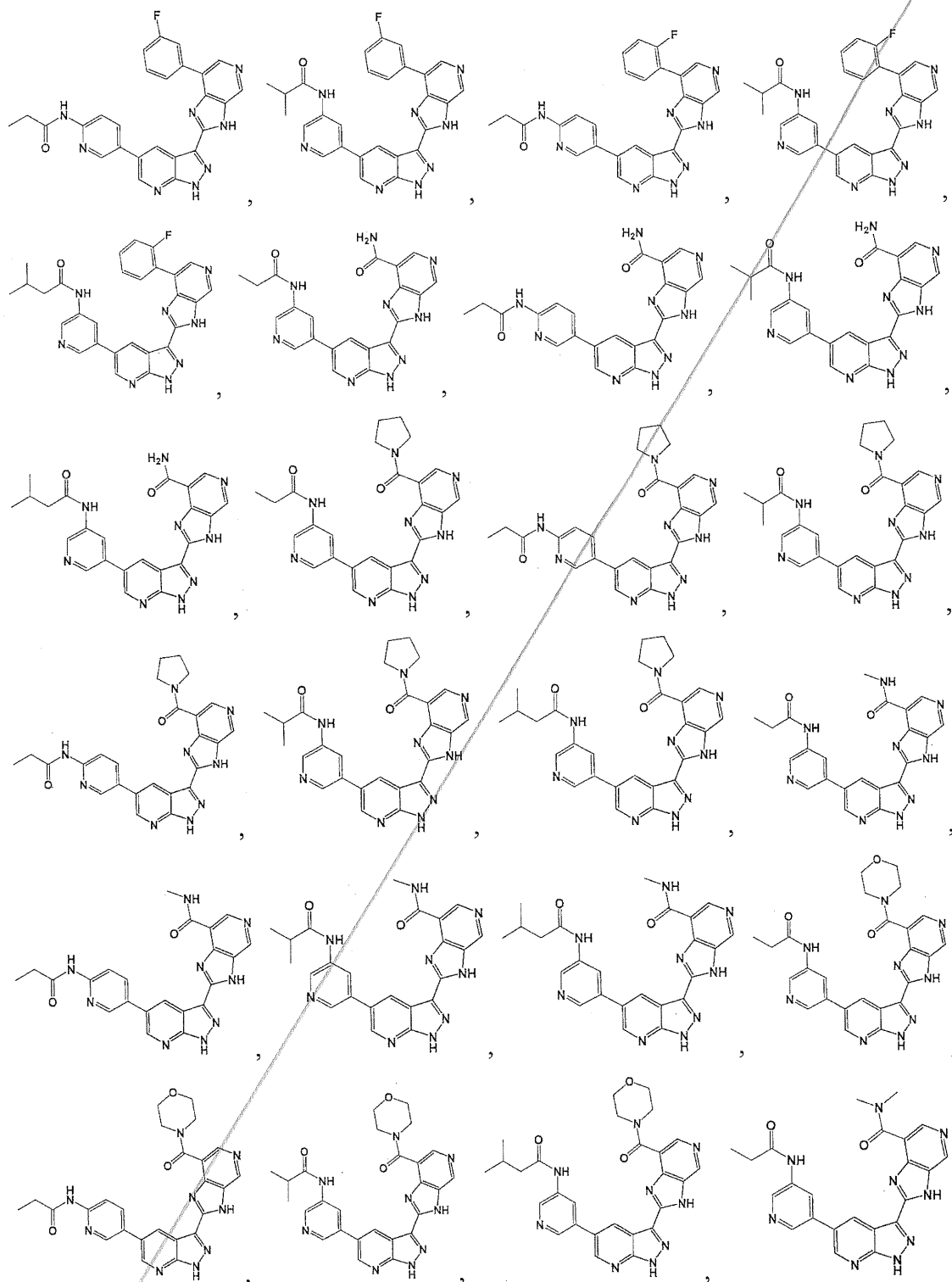
with the proviso that if A is N then R^2 is nil;

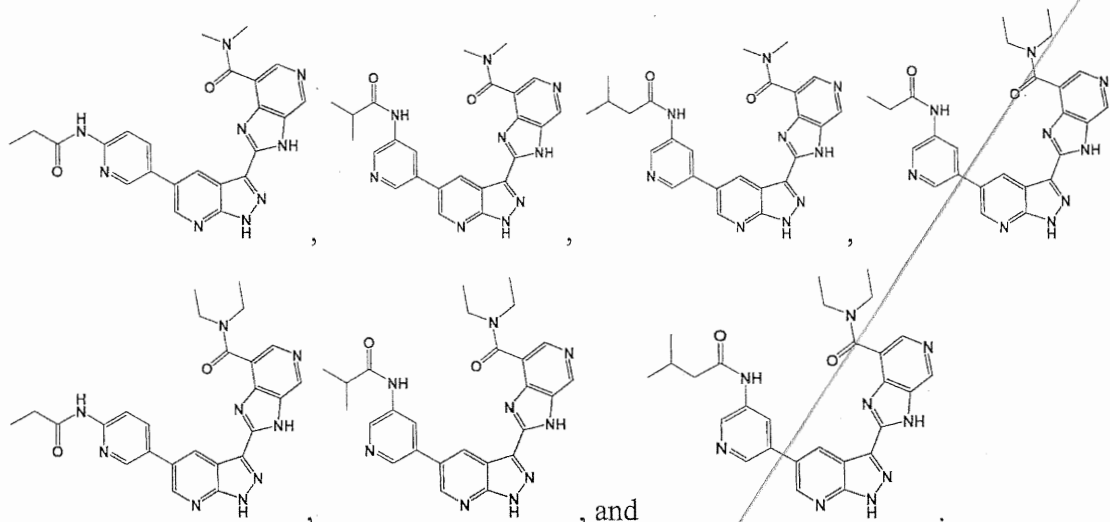
each q is an integer of 1 to 5;

each n is an integer of 0 or 1; and

with the proviso that Formula I is not a structure selected from the group consisting of:





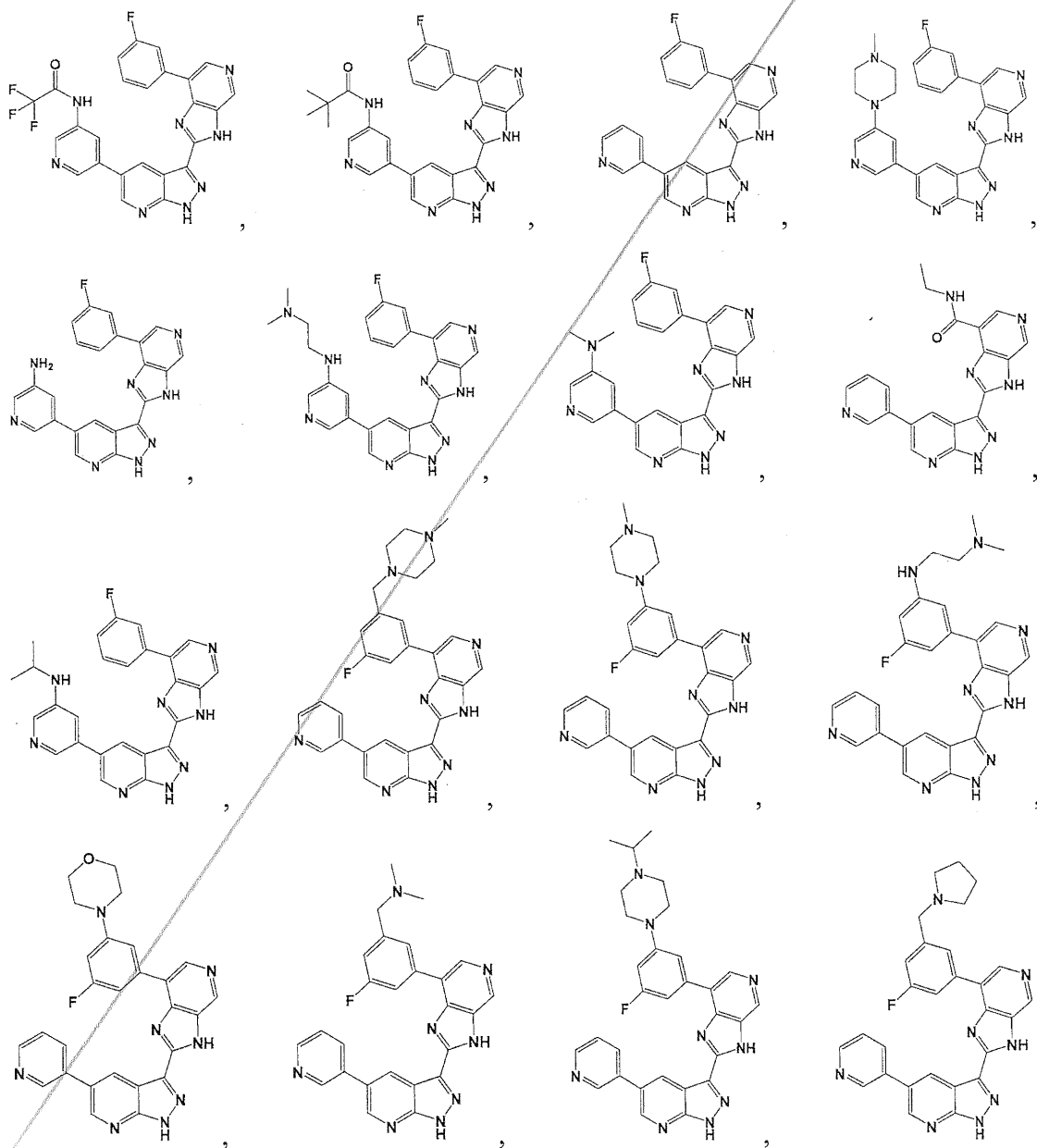


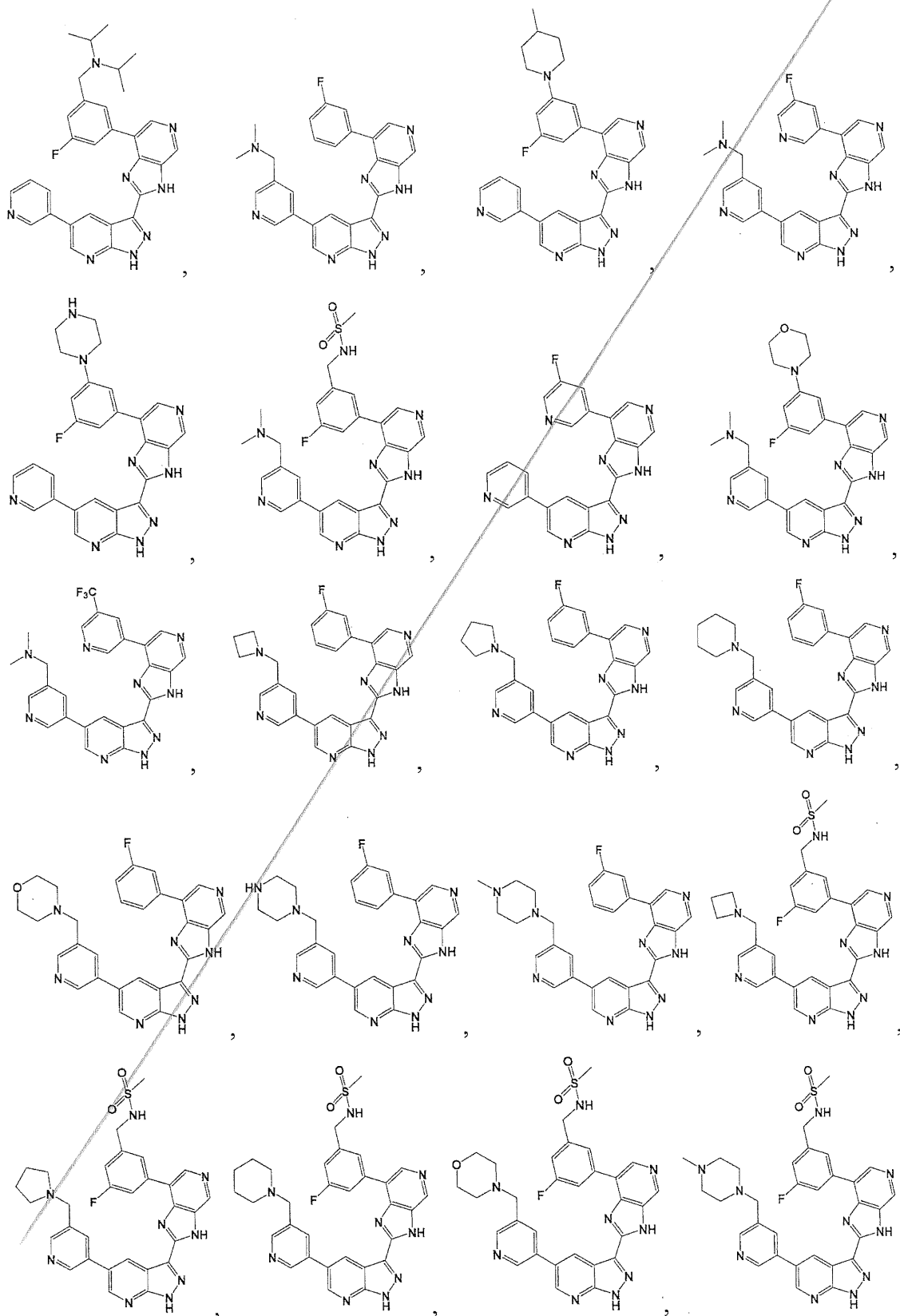
2. The compound of claim 1 wherein aryl is phenyl.
3. The compound of claim 1 wherein heteroaryl is pyridinyl.
4. The compound of claim 1 wherein heterocyclyl is selected from the group consisting of azetidiny, pyrrolidinyl, morpholinyl, piperazinyl and piperidinyl.
5. The compound of claim 1 wherein R² is selected from the group consisting of H, -(C₁₋₉ alkyl)_nheterocyclyl(R⁸)_q, -NHC(=O)R¹¹ and -(C₁₋₉ alkyl)_nN(R⁹)₂ and R¹ and R³ are both H.
6. The compound of claim 5 wherein R² is -CH₂N(R⁹)₂ or -N(R⁹)₂.
7. The compound of claim 6 wherein R⁹ is independently selected from the group consisting of H, Me, Et, -CH₂phenyl and -CH₂carbocyclyl.
8. The compound of claim 5 wherein R² is -NHC(=O)R¹¹.
9. The compound of claim 8 wherein R¹¹ is selected from the group consisting of -C₁₋₅ alkyl, carbocyclyl, phenyl(R⁶)_q, and -CH₂phenyl(R⁶)_q.
10. The compound as in any of claims 6-9, in which R⁴ is phenyl(R¹³)_q.
11. The compound as in any of claims 6-9, in which R⁴ is -heterocyclyl(R¹⁴)_q.
12. The compound as in any of claims 6-9, in which R⁴ is -heteroaryl(R¹⁵)_q.
13. The compound of claim 10 wherein R¹³ is one substituent attached to the phenyl comprising a fluorine atom.
14. The compound of claim 10 wherein R¹³ is two substituents each attached to the phenyl comprising a fluorine atom and either a -(CH₂)_nN(R⁵)₂ or a -(CH₂)_nNHSO₂R¹⁸.

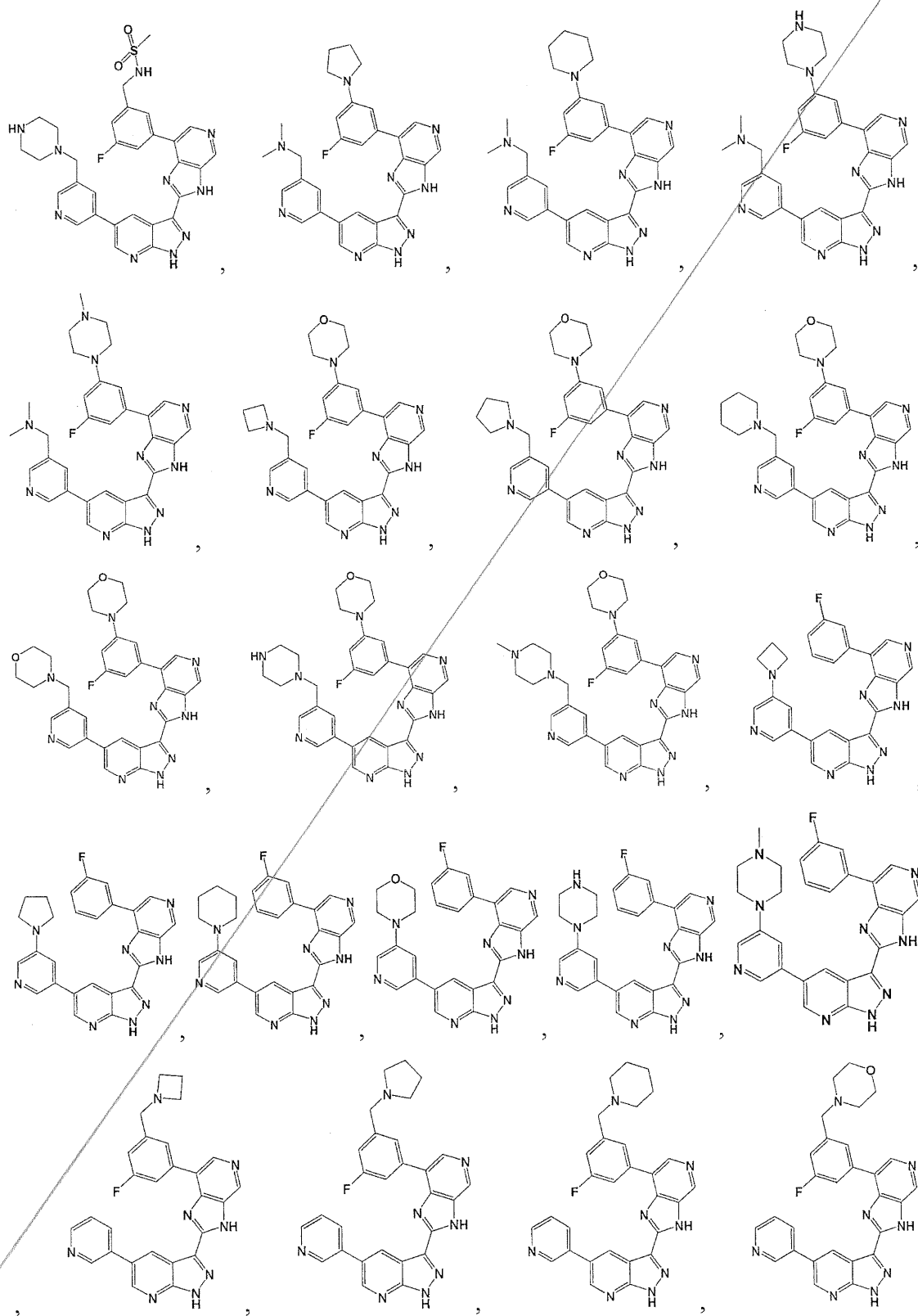
15. The compound of claim 11 wherein the heterocyclyl is selected from the group consisting of piperazinyl and piperidinyl; and the R¹⁴ is H or Me.

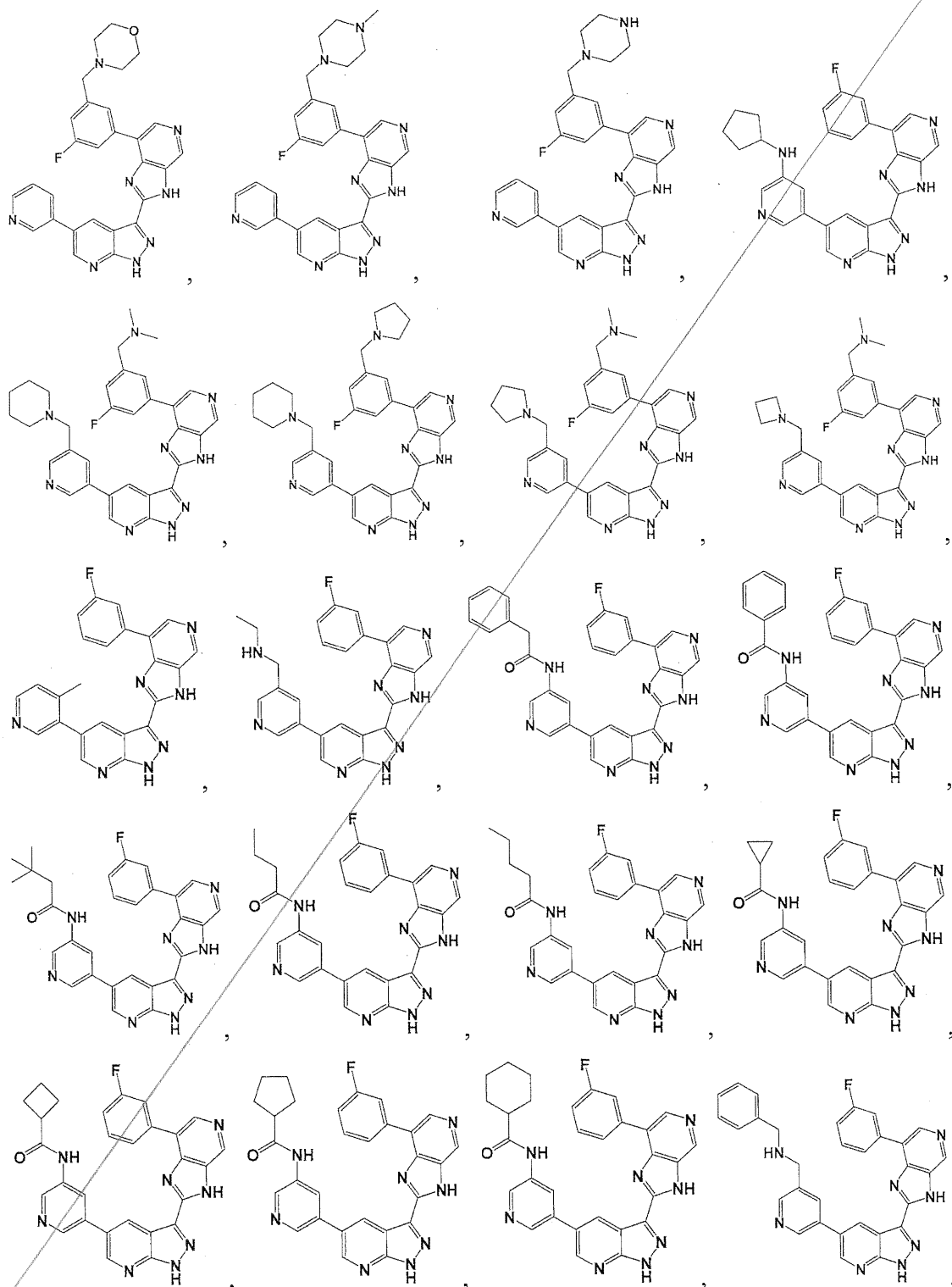
16. The compound of claim 12 wherein the heteroaryl is selected from the group consisting of pyridinyl, furyl, thiophenyl and imidazolyl; and R¹⁵ is lower alkyl or halide.

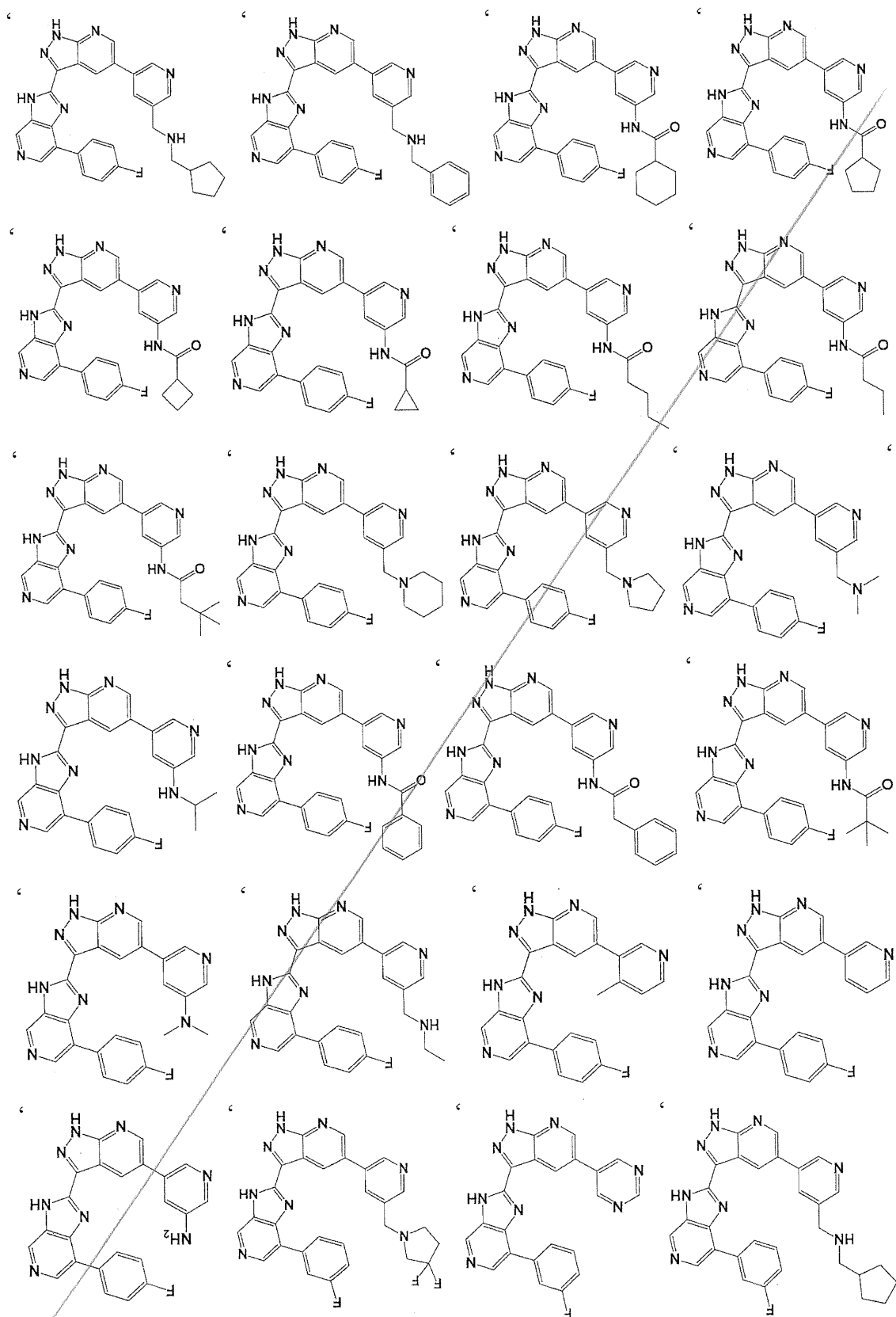
17. The compound of claim 1 having a structure selected from the group consisting of:

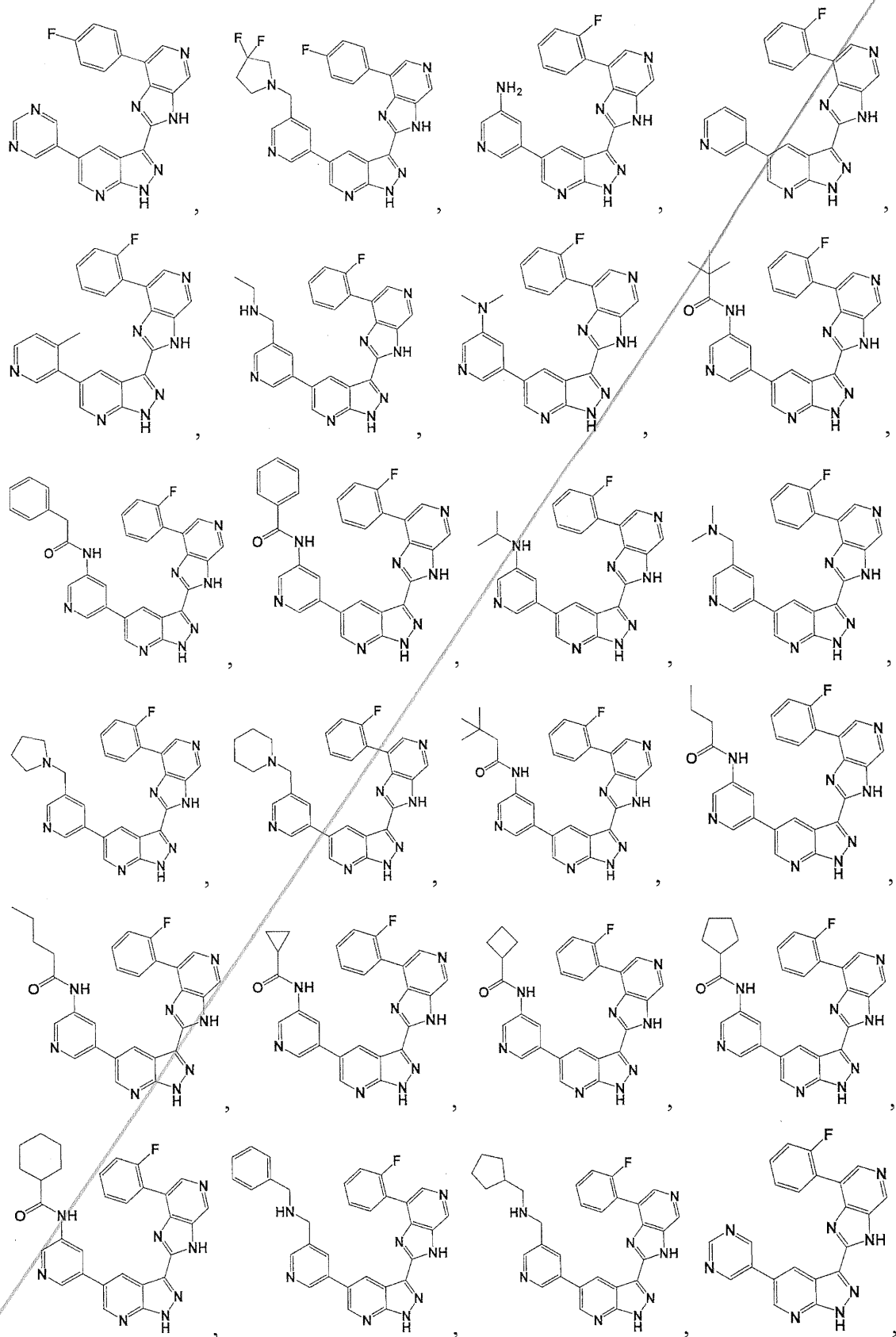


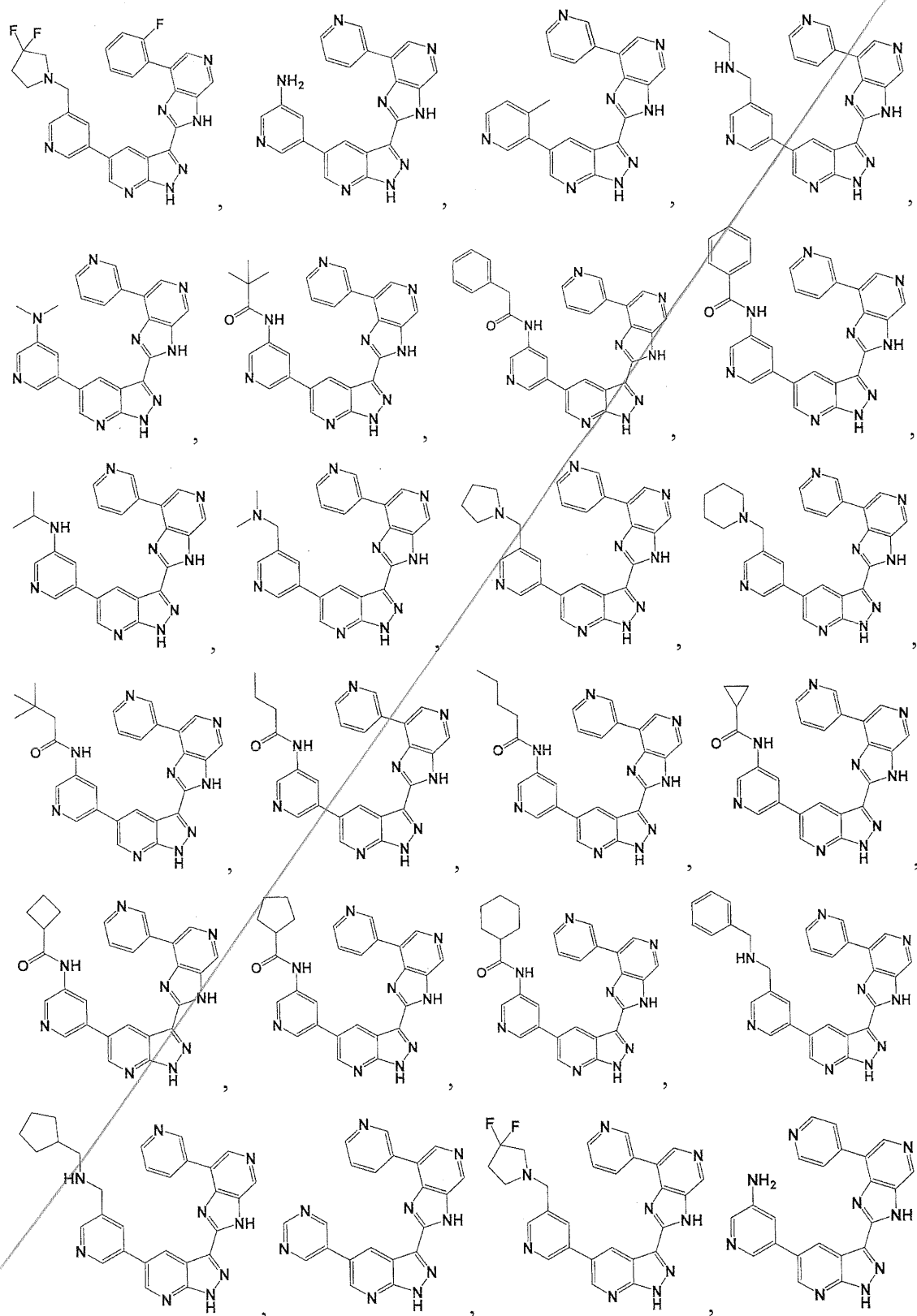


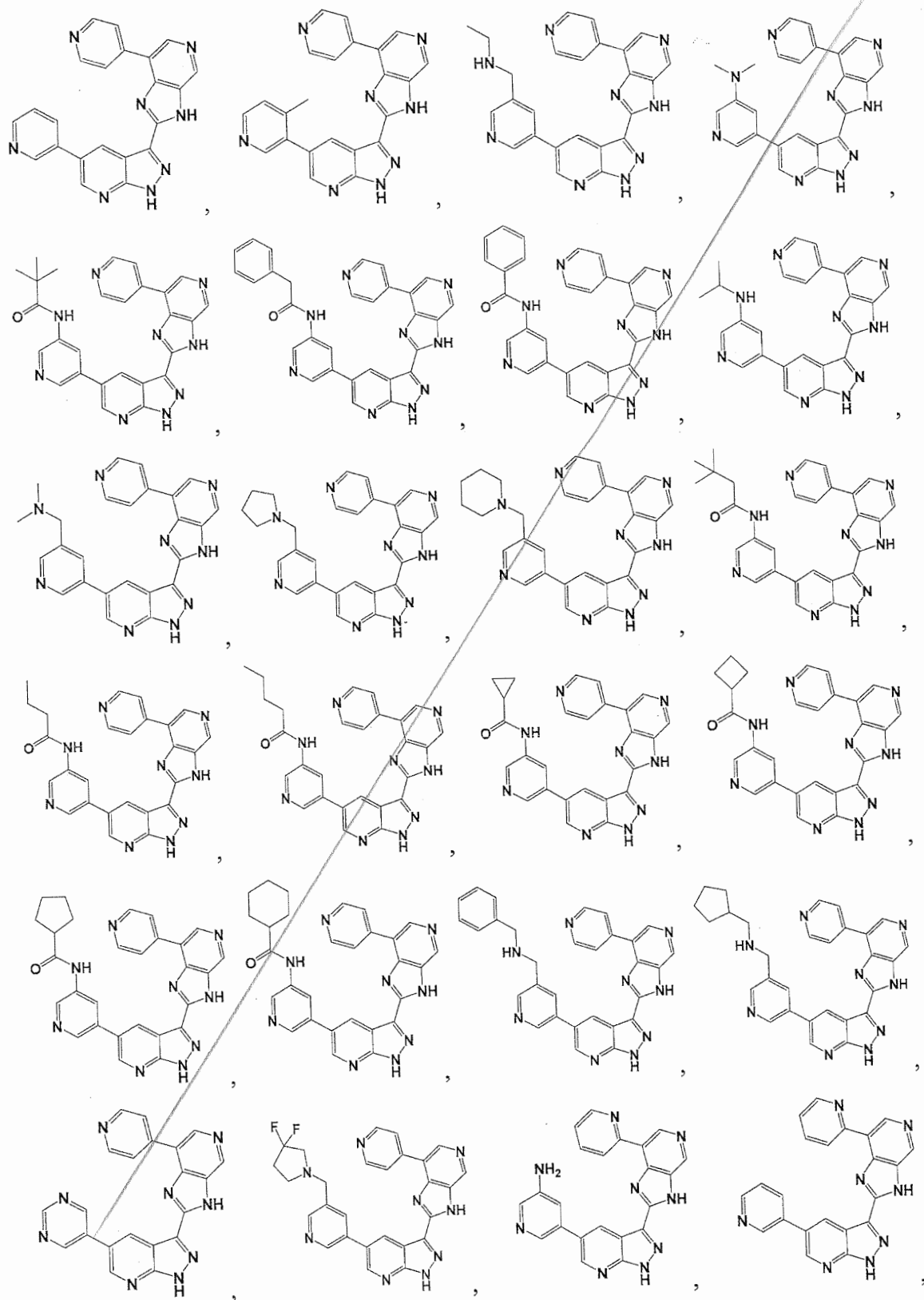


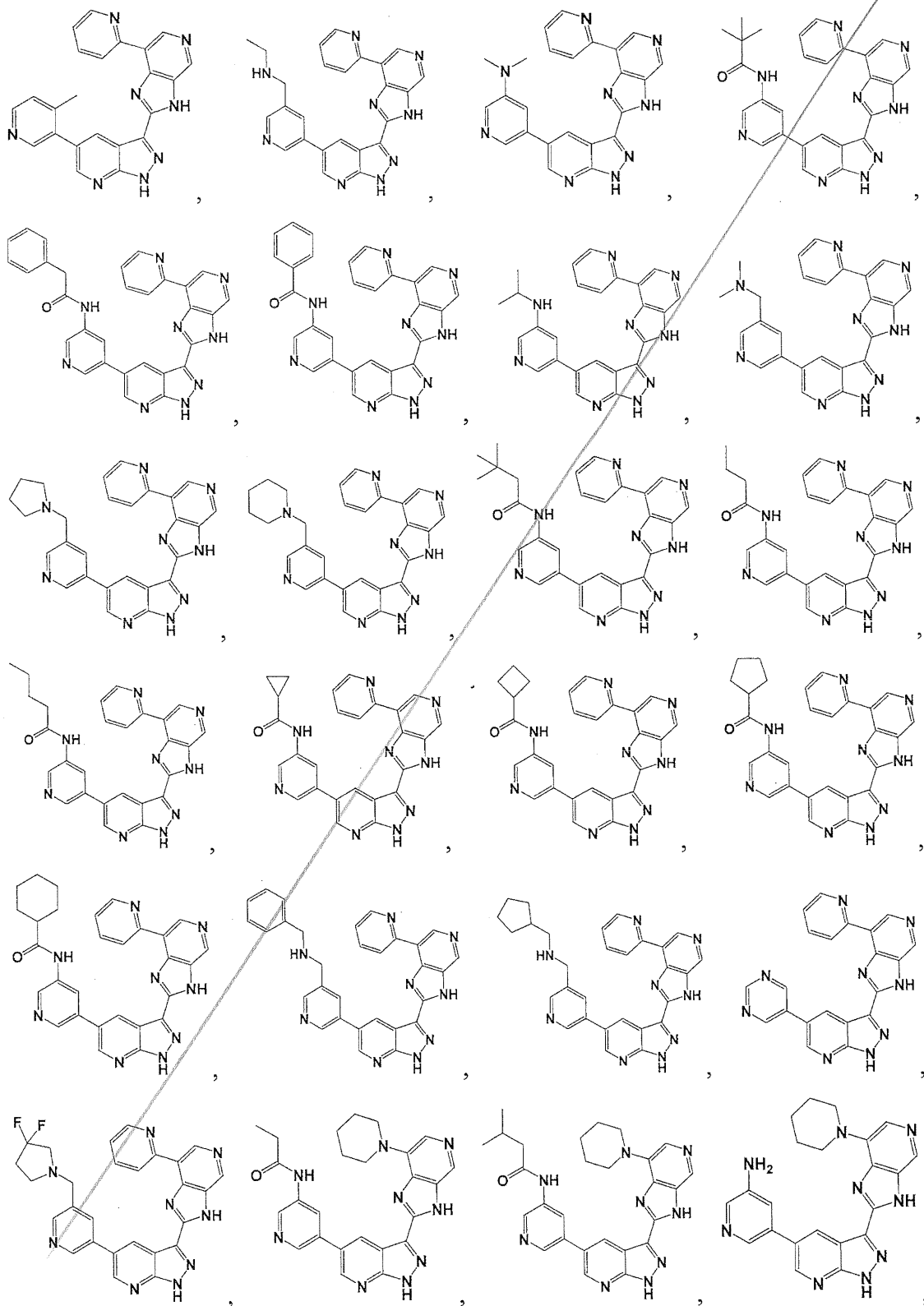


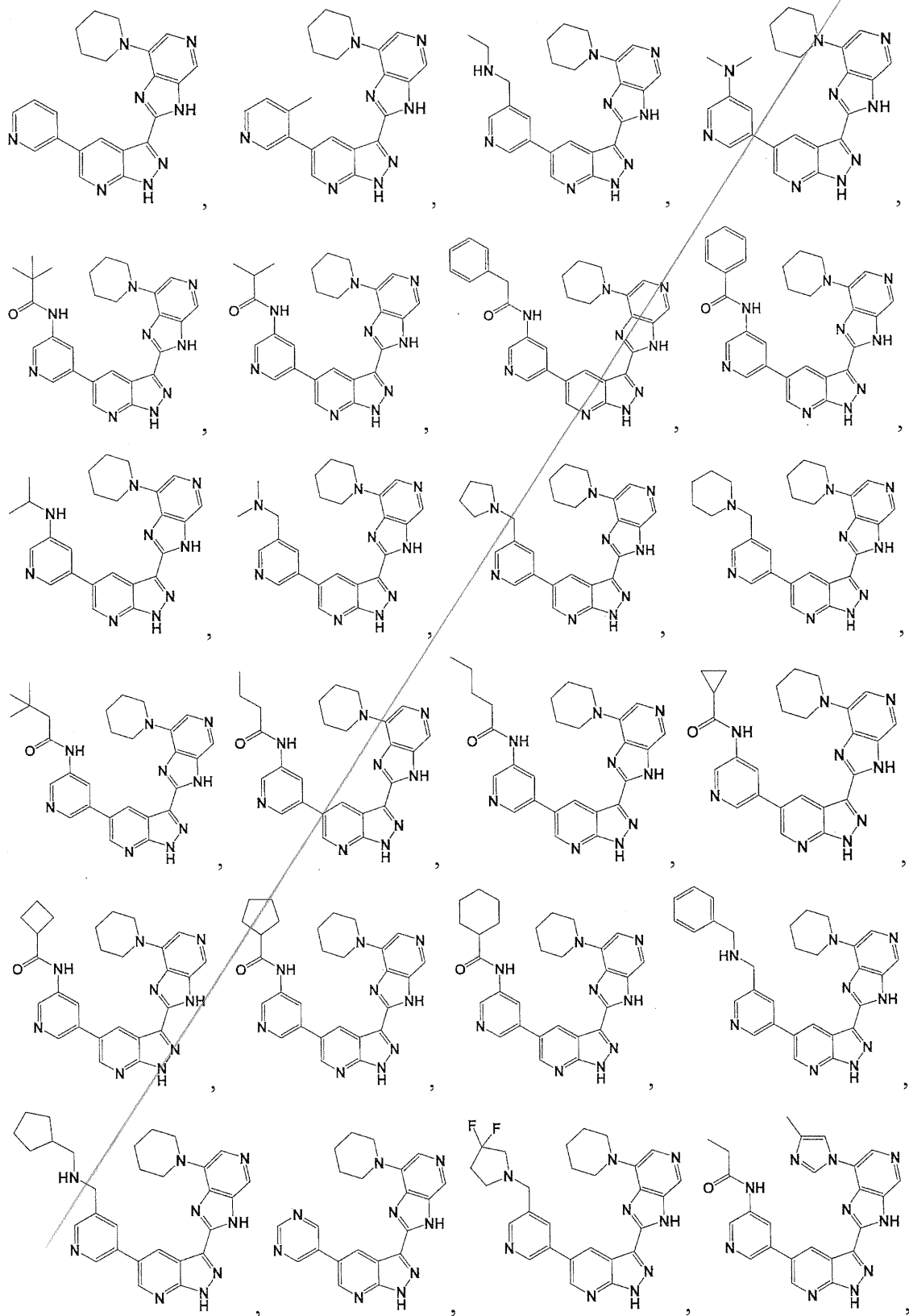


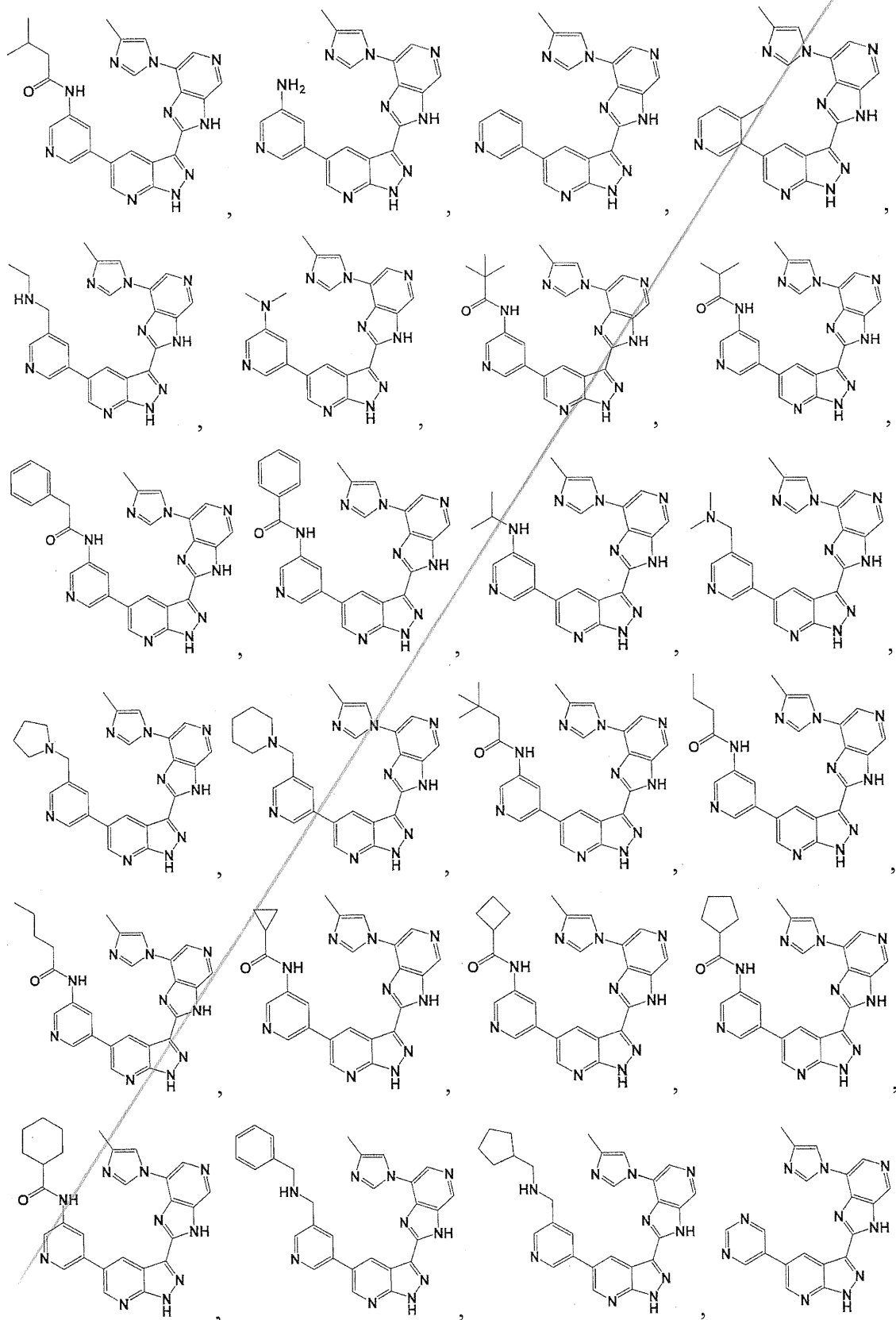


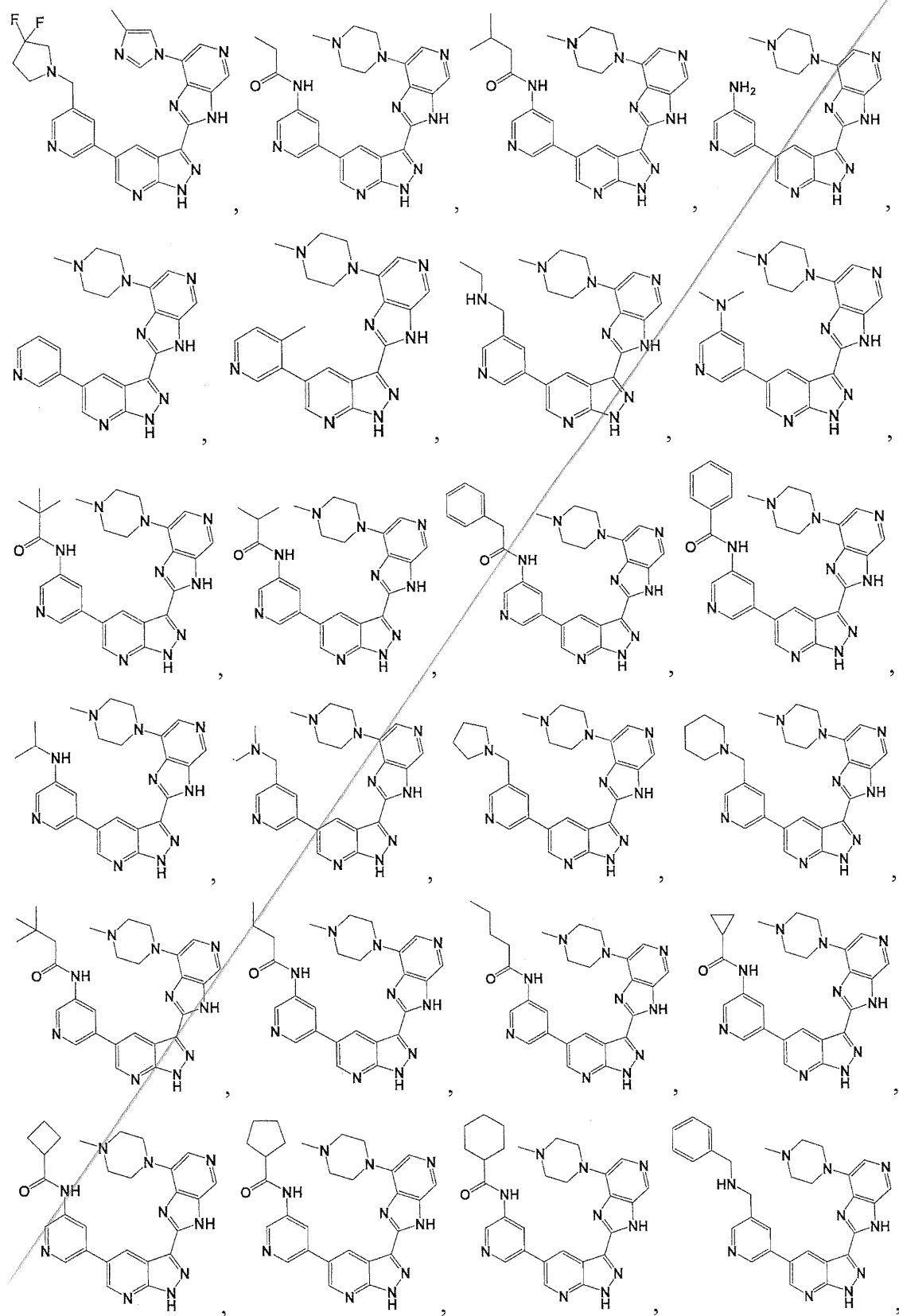


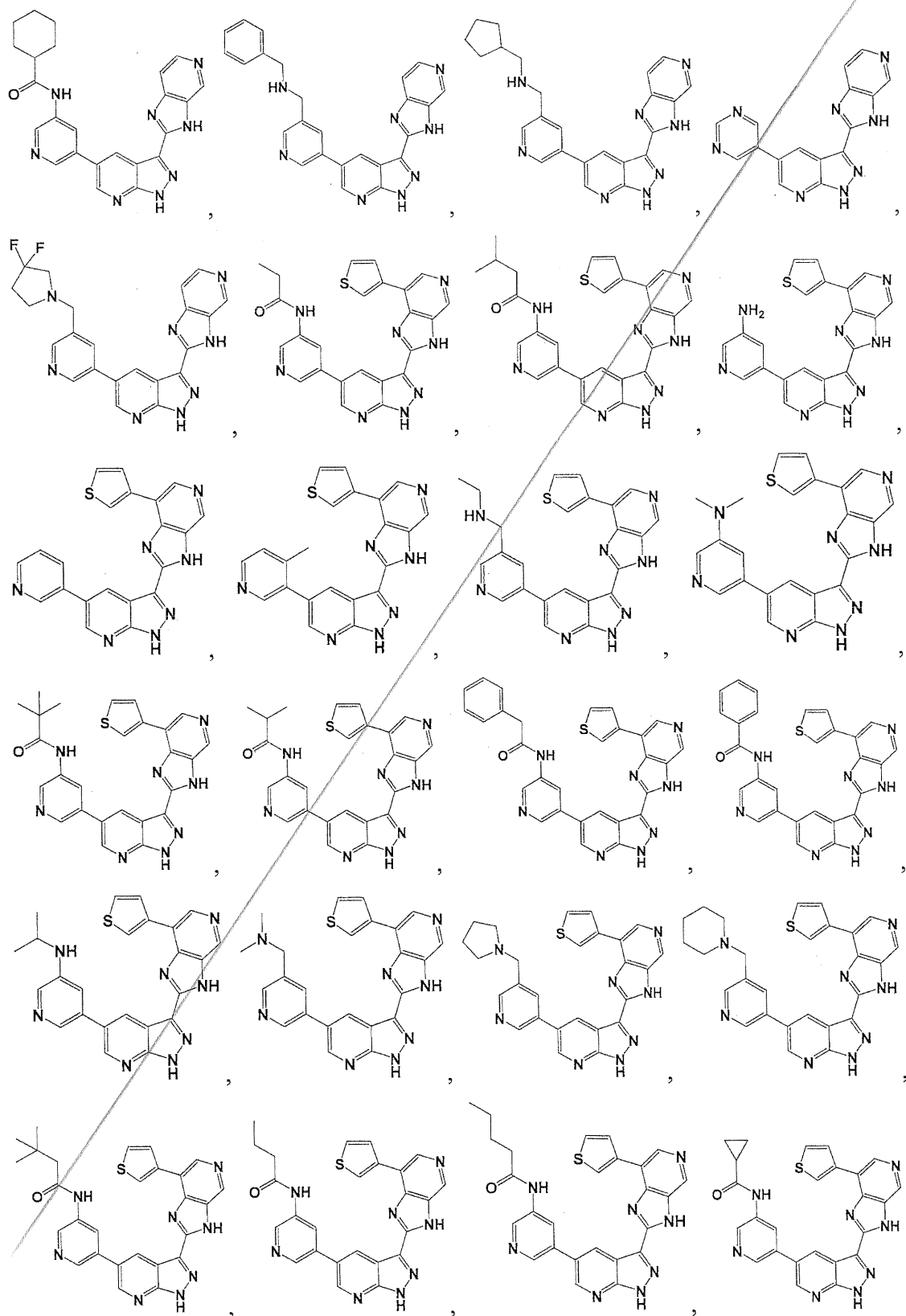


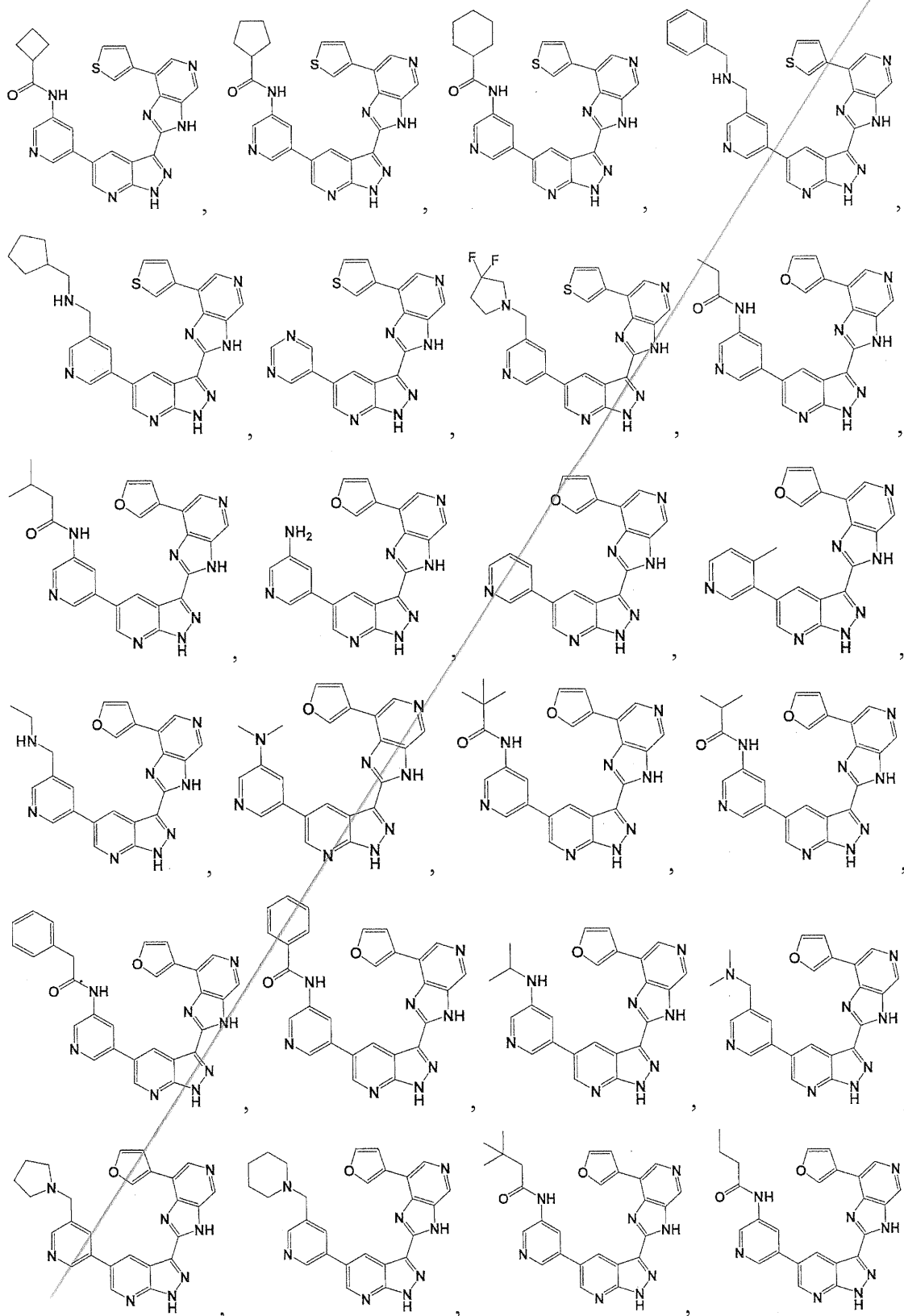


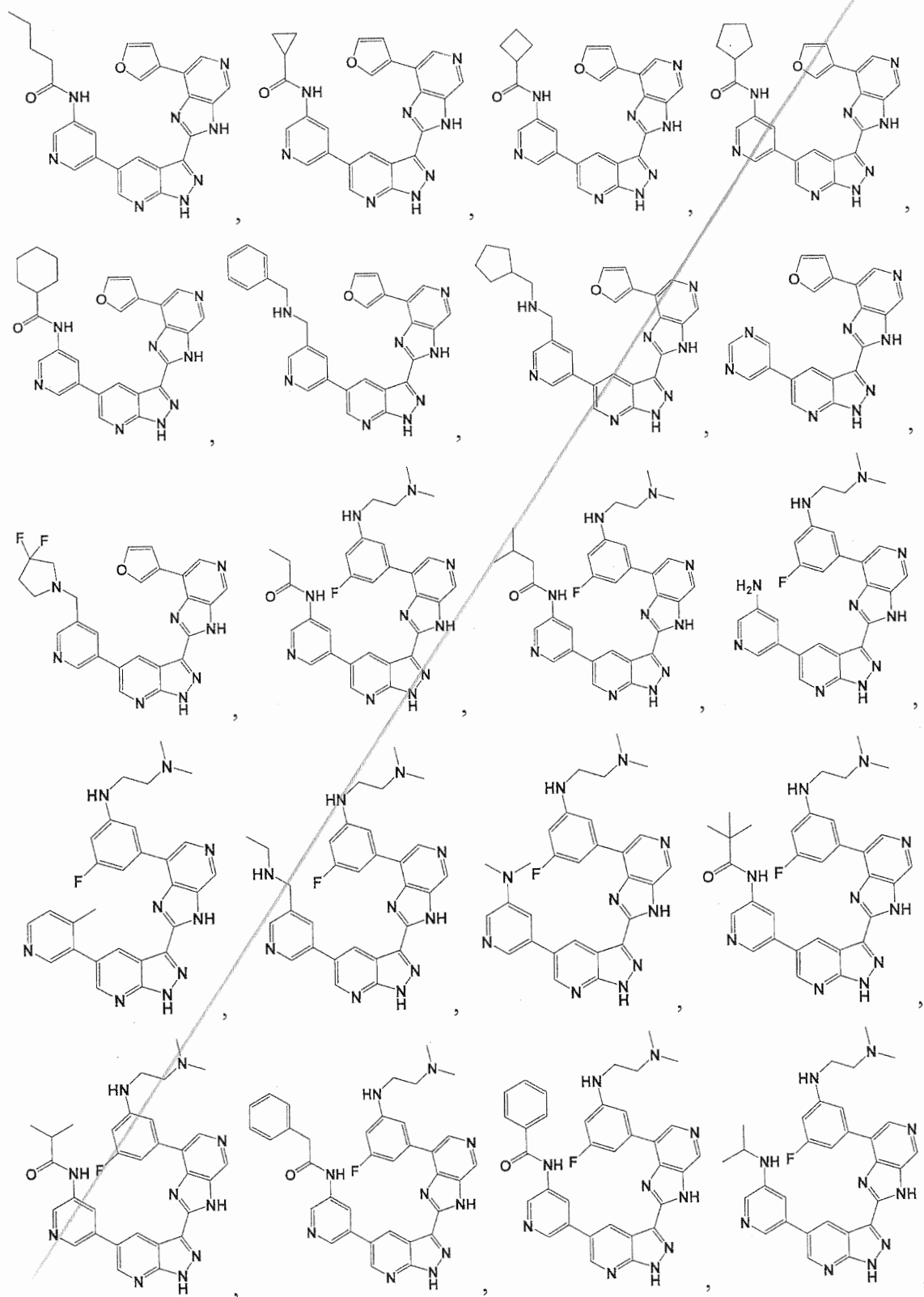


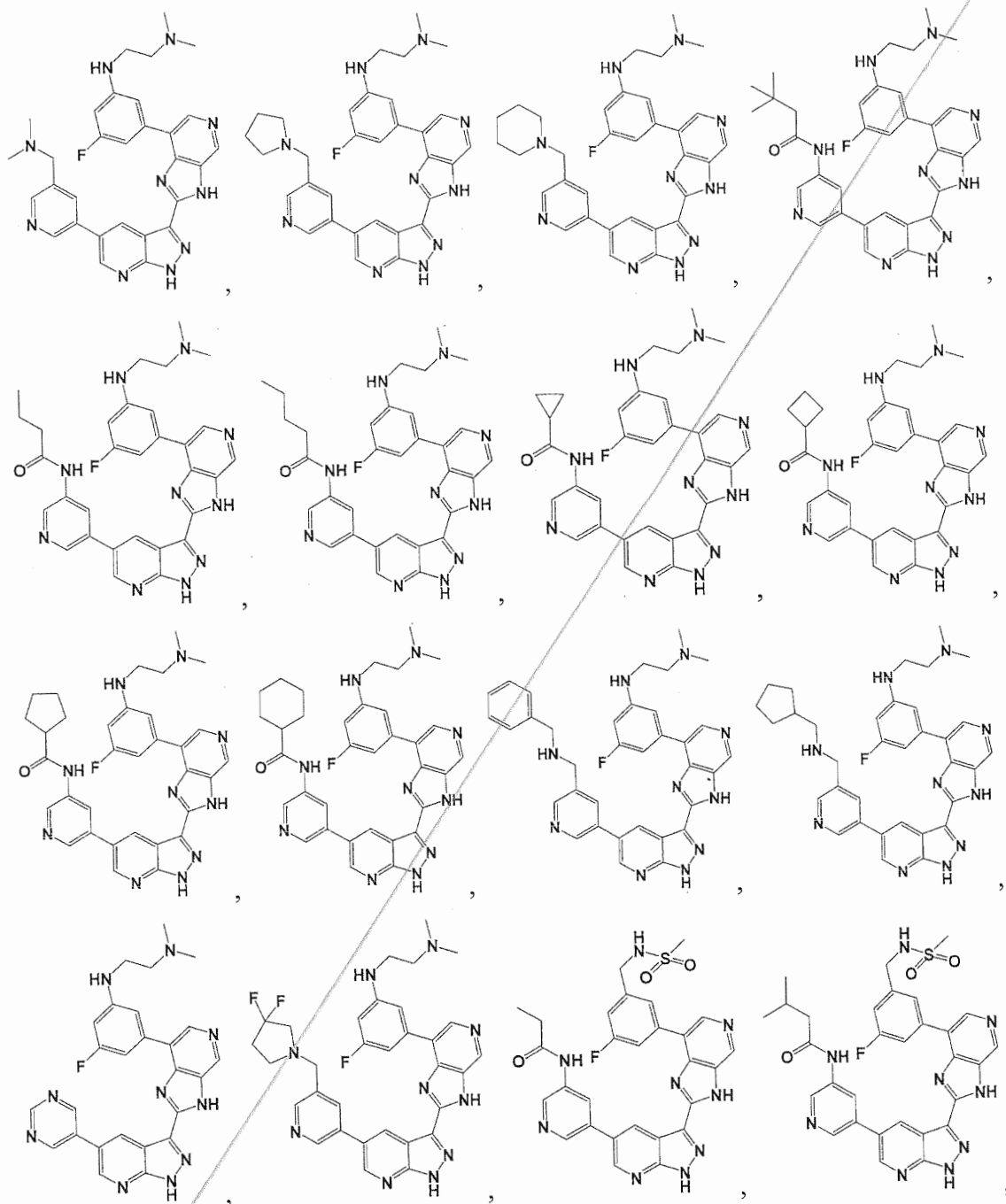


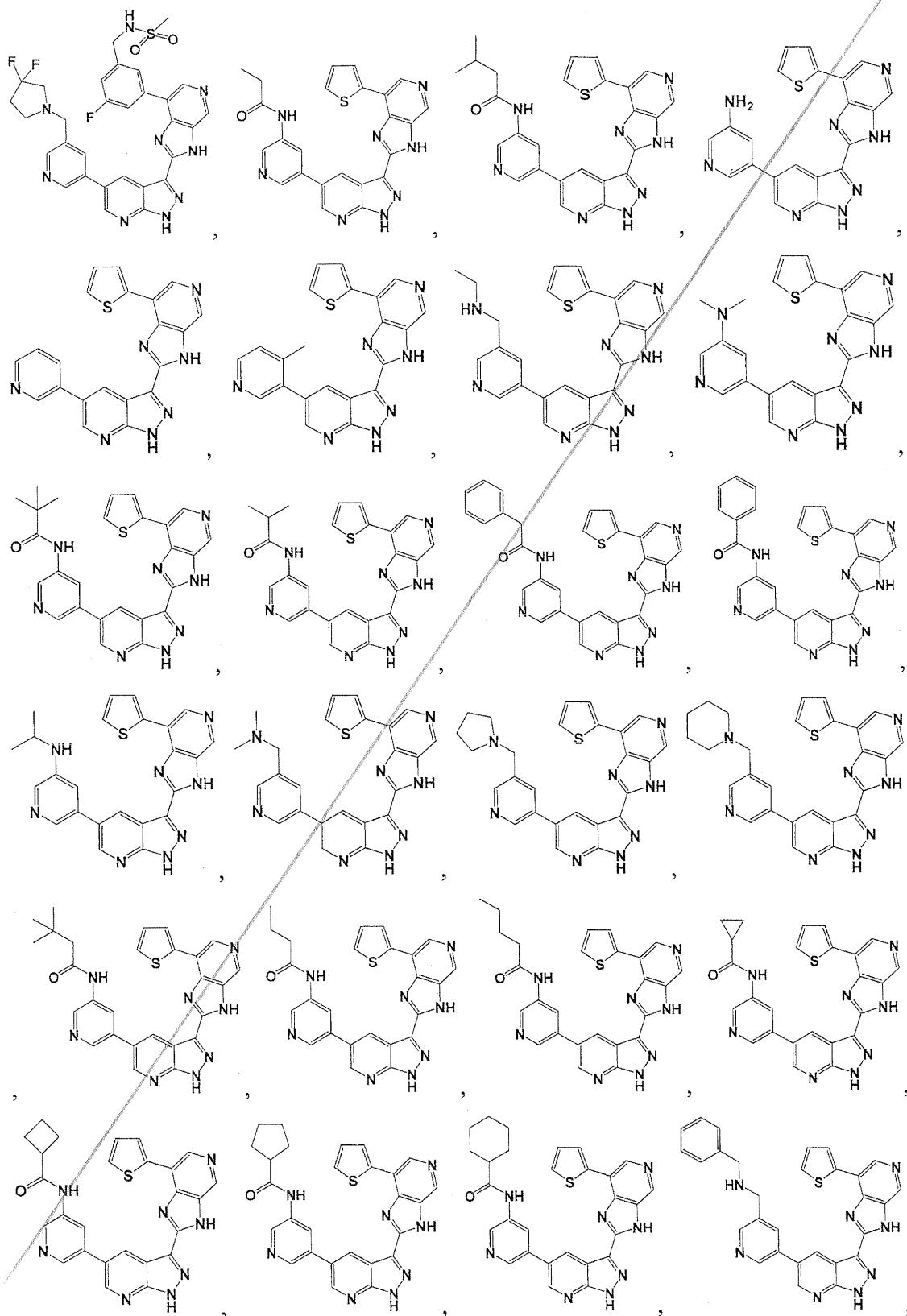


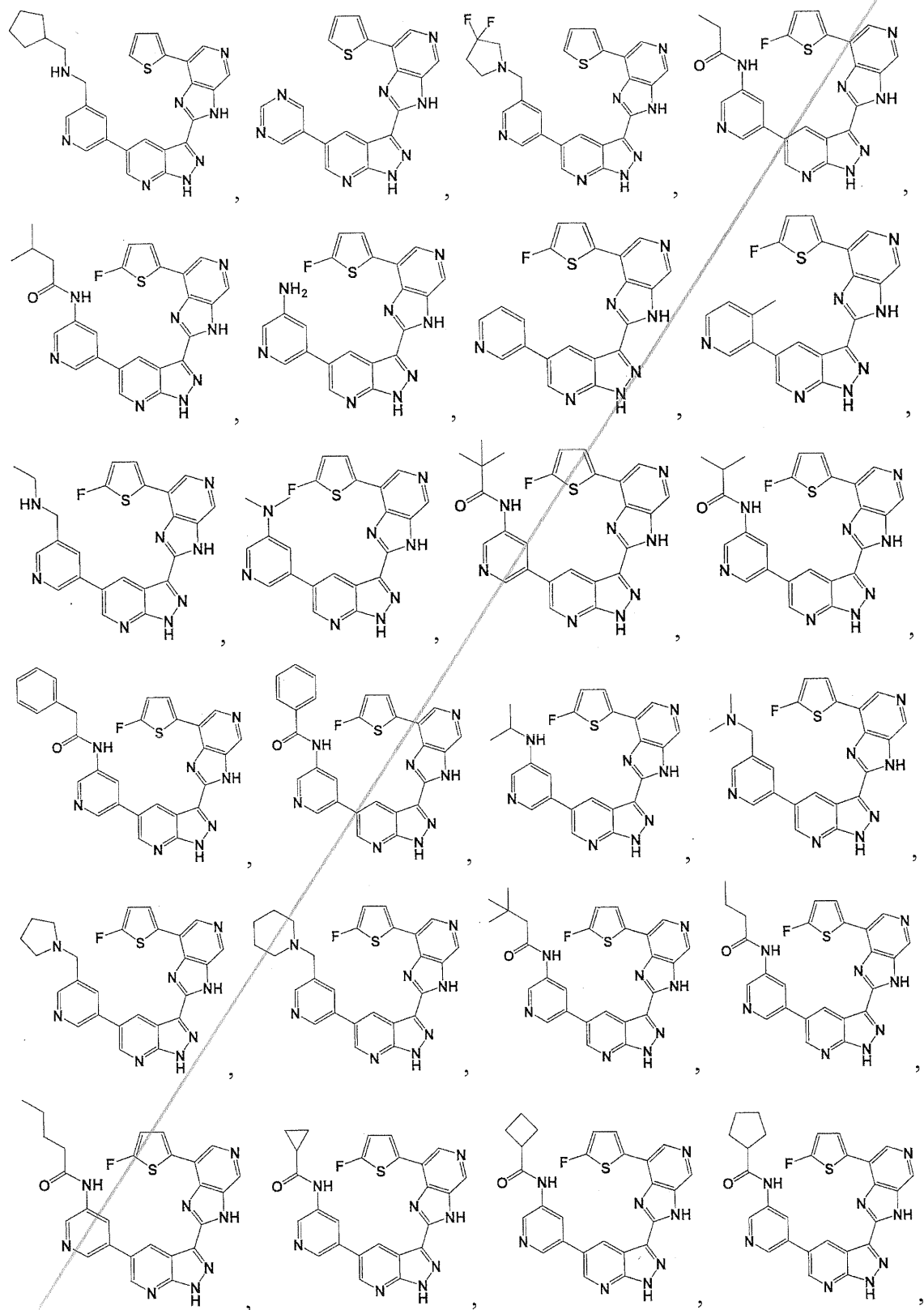


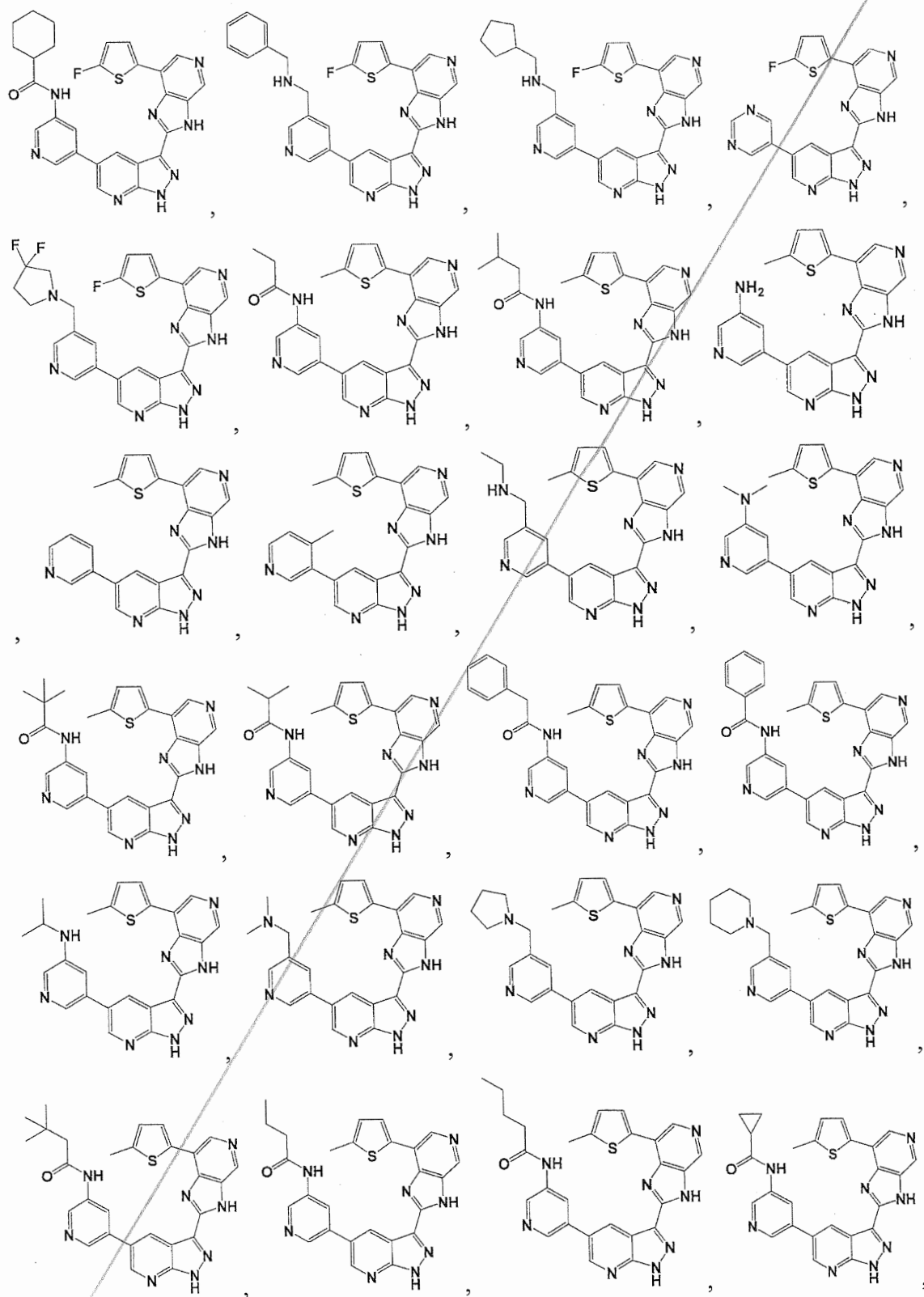


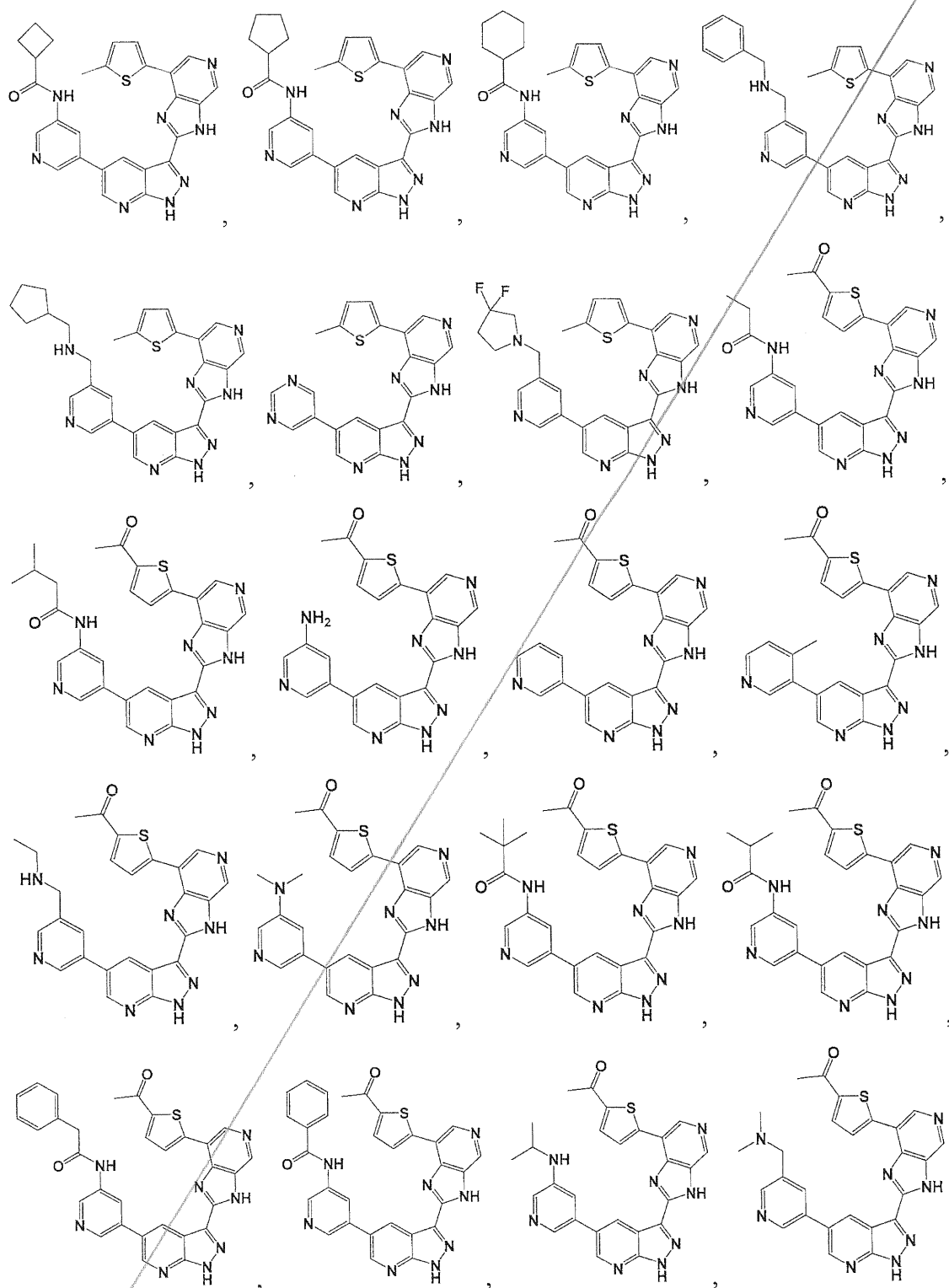


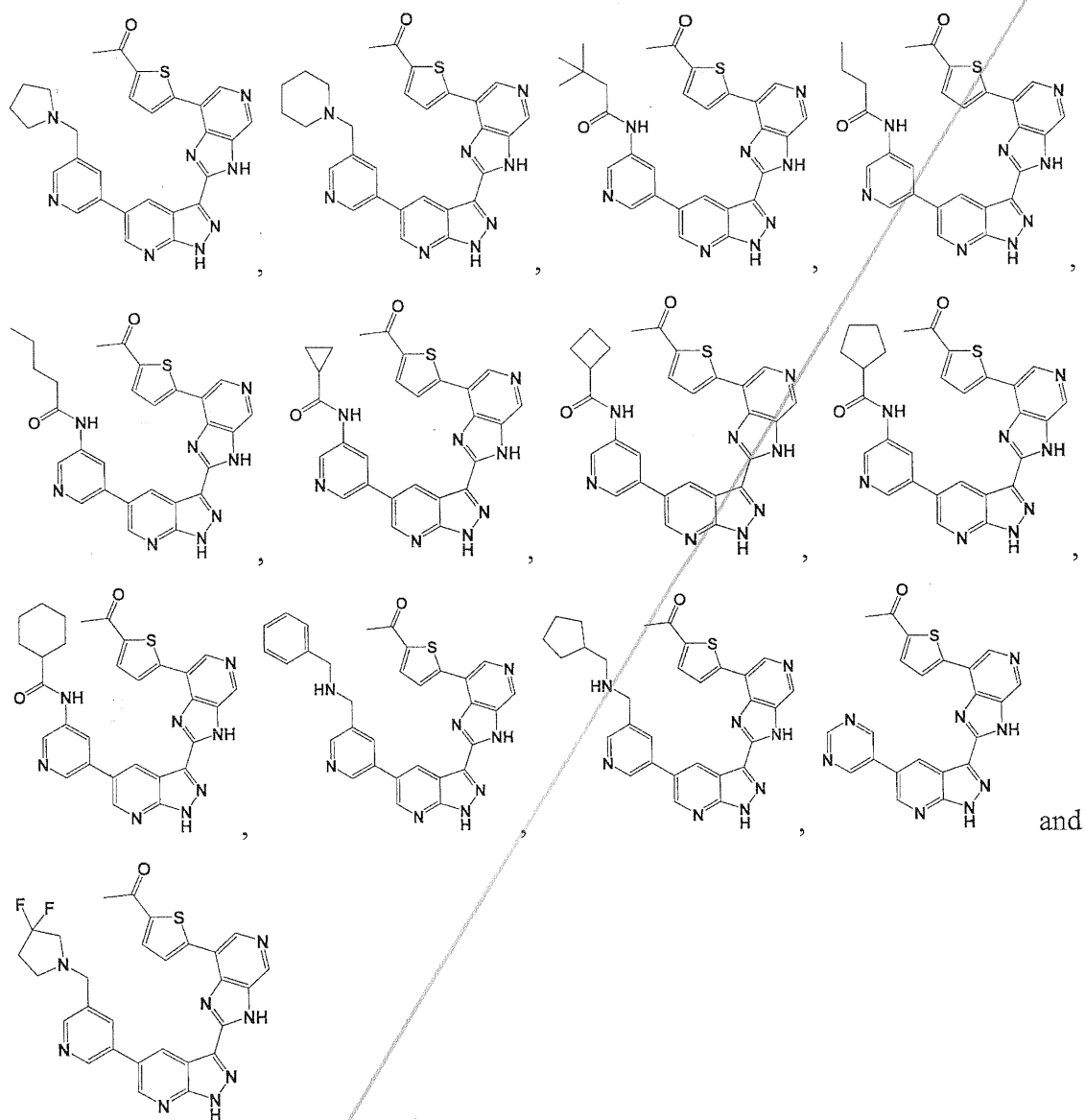






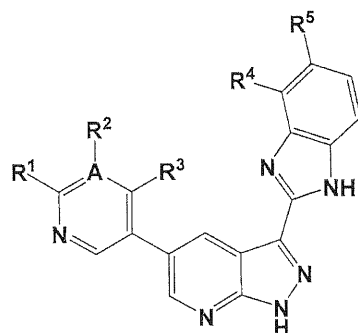






and

18. A compound or pharmaceutically acceptable salt or prodrug thereof having the structure of Formula II:



II

wherein:

R^1 and R^2 are independently selected from the group consisting of H, lower alkyl, halide, $-(C_{1-9} \text{ alkyl})_n \text{ aryl}(R^6)_q$, $-(C_{1-9} \text{ alkyl})_n \text{ heteroaryl}(R^7)_q$, $-(C_{1-9} \text{ alkyl})_n \text{ heterocyclyl}(R^8)_q$, $-(C_{1-9} \text{ alkyl})_n \text{ N}(R^9)_2$, $-\text{OR}^{10}$ and $-\text{NHC}(=\text{O})R^{11}$;

R^3 is selected from the group consisting of H, halide and lower alkyl;

with the proviso that at least two of R^1 , R^2 and R^3 are H;

R^4 and R^5 are independently selected from the group consisting of H, $-\text{C}(=\text{O})\text{N}(R^{12})_2$, $-\text{aryl}(R^{13})_q$, $-\text{heterocyclyl}(R^{14})_q$, and $-\text{heteroaryl}(R^{15})_q$;

with the proviso that at least one of R^4 and R^5 is H;

each R^6 is a substituent attached to the aryl ring and independently selected from the group consisting of H, $-\text{C}_{1-9} \text{ alkyl}$, halide, CF_3 and CN;

each R^7 is a substituent attached to the heteroaryl ring and independently selected from the group consisting of H, $-\text{C}_{1-9} \text{ alkyl}$, halide, CF_3 and CN;

each R^8 is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, halide, $-(C_{1-3} \text{ alkyl})_n \text{ aryl}(R^6)_q$, and $-\text{C}_{1-4} \text{ alkyl}$;

each R^9 is independently selected from the group consisting of H, $-\text{C}_{1-9} \text{ alkyl}$, $-(C_{1-3} \text{ alkyl})_n \text{ aryl}(R^6)_q$, $-(C_{1-3} \text{ alkyl})_n \text{ carbocyclyl}$ and $-(C_{1-9} \text{ alkyl})\text{N}(R^{16})_2$;

alternatively, two adjacent R^9 or two adjacent R^{12} , may be taken together with the atoms to which they are attached to form a heterocyclyl(R^{17})_q;

R^{10} is selected from the group consisting of H, $-\text{CF}_3$, $-(C_{1-3} \text{ alkyl})_n \text{ aryl}(R^6)_q$, and $-\text{C}_{1-9} \text{ alkyl}$;

R^{11} is selected from the group consisting of $-(C_{1-3} \text{ alkyl})_n \text{ aryl}(R^6)_q$, $-(C_{1-3} \text{ alkyl})_n \text{ carbocyclyl}$, $-\text{C}_{1-9} \text{ alkyl}$ and $-\text{CF}_3$;

each R^{12} is independently selected from the group consisting of H, $-(C_{1-9} \text{ alkyl})_n \text{ aryl}(R^6)_q$ and $-\text{C}_{1-9} \text{ alkyl}$;

each R^{13} is a substituent attached to the aryl ring and independently selected from the group consisting of H, halide, $-\text{CF}_3$, CN, $-(C_{1-3} \text{ alkyl})_n \text{ heterocyclyl}(R^8)_q$, $-(C_{1-9} \text{ alkyl})_n \text{ N}(R^9)_2$ and $-(C_{1-9} \text{ alkyl})_n \text{ NHSO}_2 R^{18}$;

each R^{14} is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, lower alkyl, halide, $-\text{CF}_3$ and CN;

each R^{15} is a substituent attached to the heteroaryl ring and independently selected from the group consisting of H, lower alkyl, halide, $-\text{CF}_3$, CN, $-\text{C}(=\text{O})(\text{C}_{1-3} \text{ alkyl})$, $-(\text{C}_{1-9} \text{ alkyl})_n\text{N}(\text{R}^9)_2$ and $-(\text{C}_{1-9} \text{ alkyl})_n\text{NHSO}_2\text{R}^{18}$;

each R^{16} is independently selected from the group consisting of H and lower alkyl;

each R^{17} is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, $-(\text{C}_{1-9} \text{ alkyl})_n\text{aryl}(\text{R}^6)_q$, and $-\text{C}_{1-9} \text{ alkyl}$;

each R^{18} is a lower alkyl;

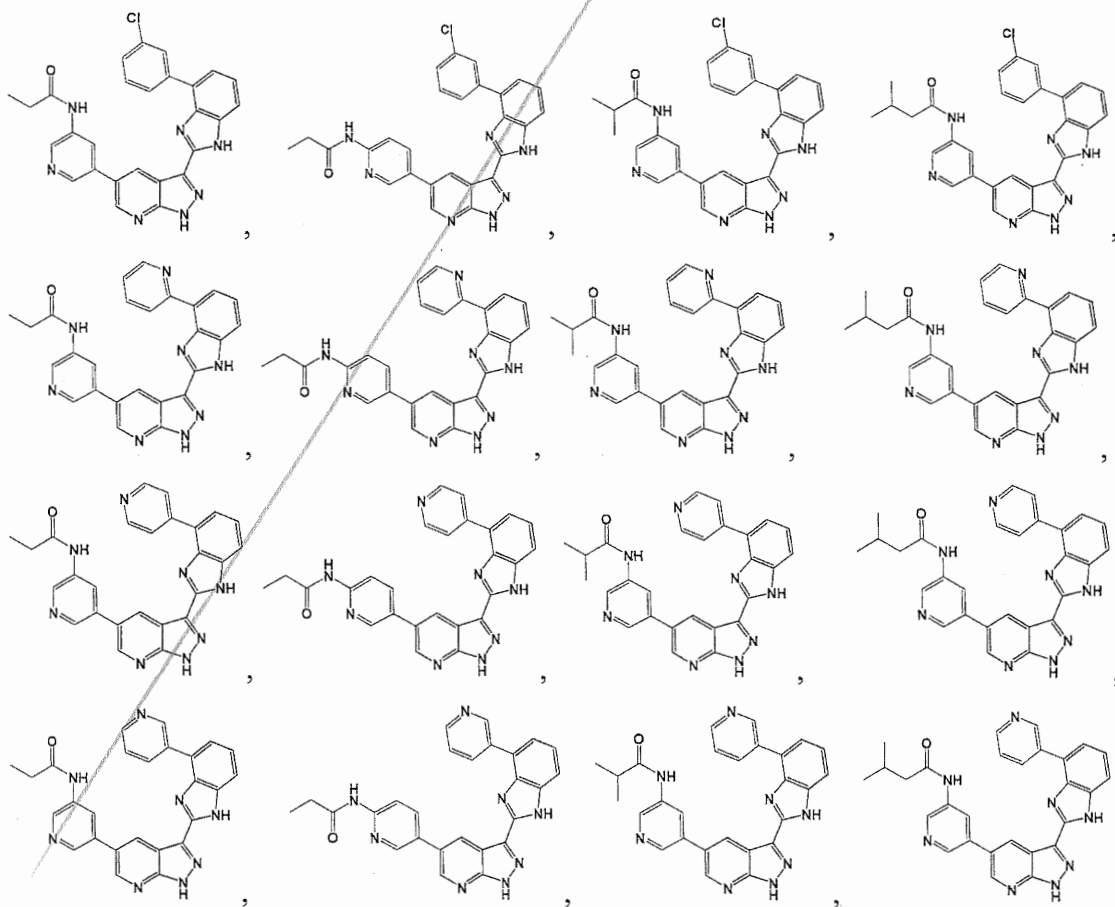
A is N or C;

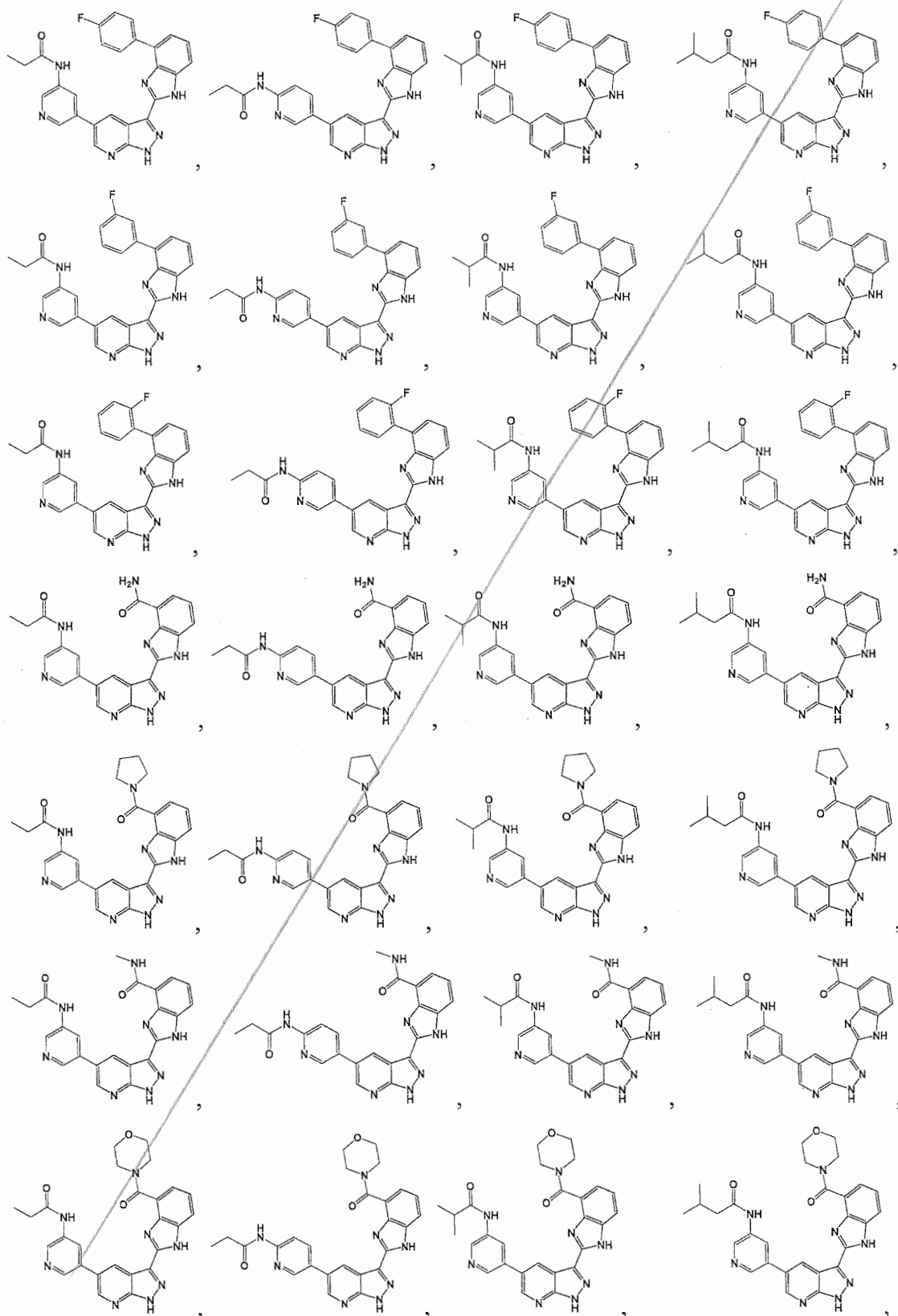
with the proviso that if A is N then R^2 is nil;

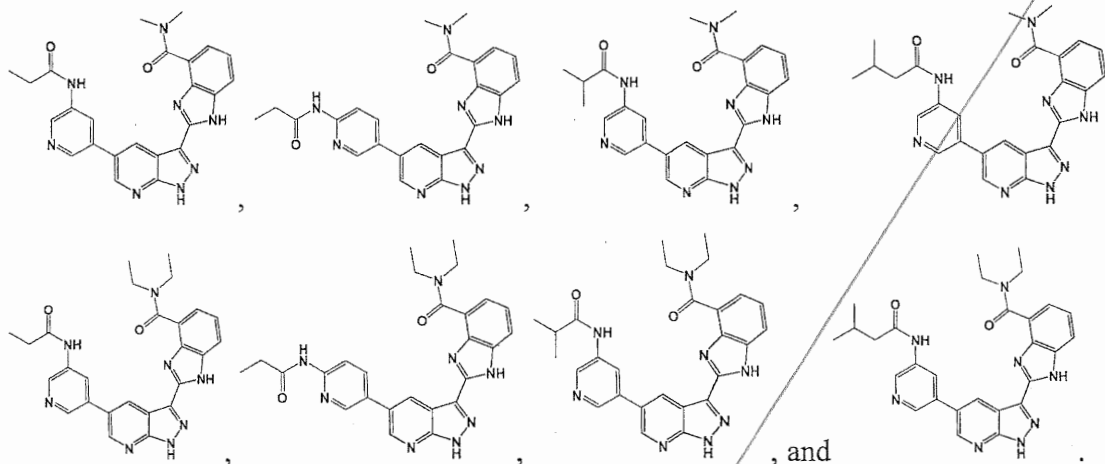
each q is an integer of 1 to 5;

each n is an integer of 0 or 1; and

with the proviso that Formula II is not a structure selected from the group consisting of:





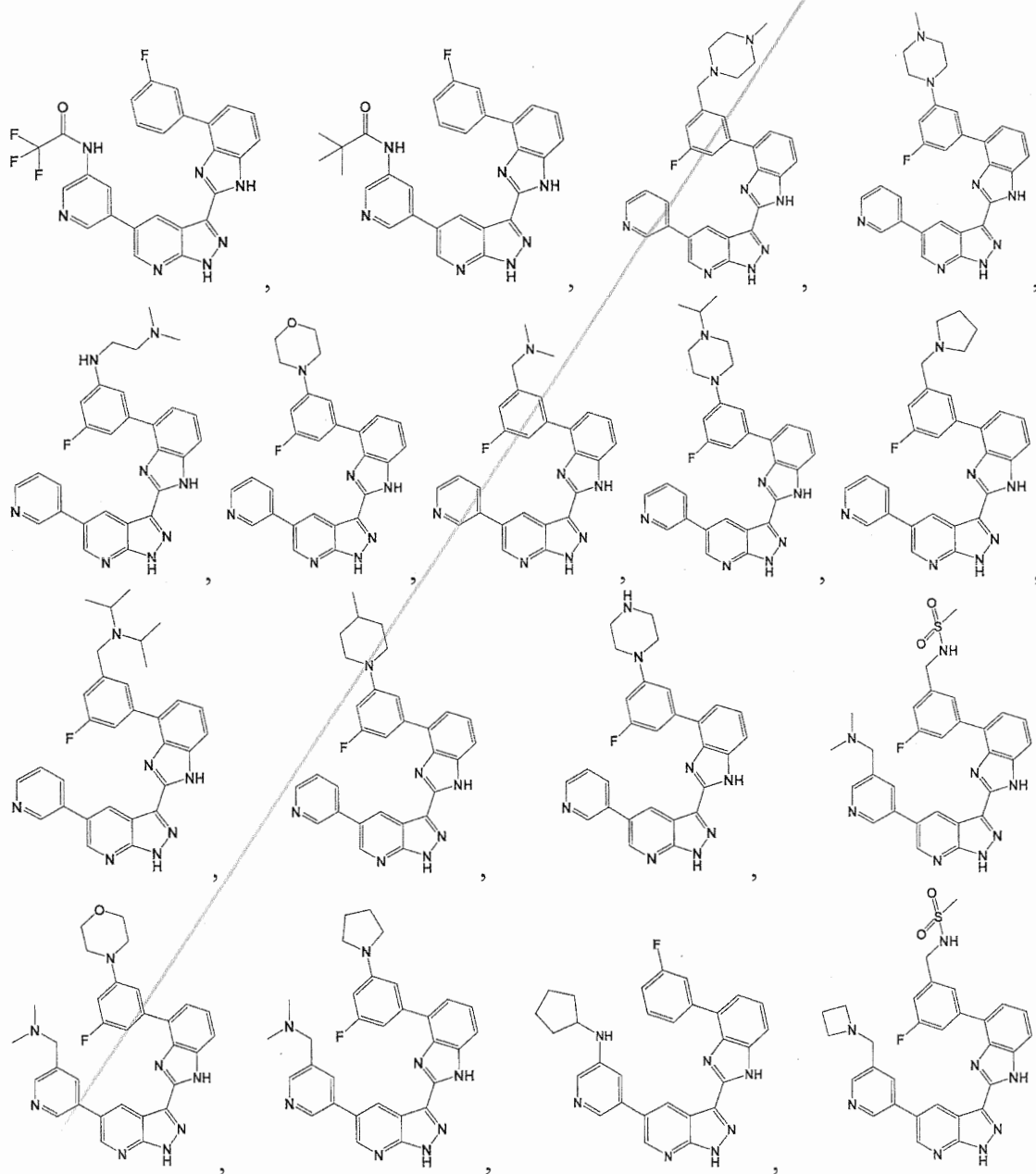


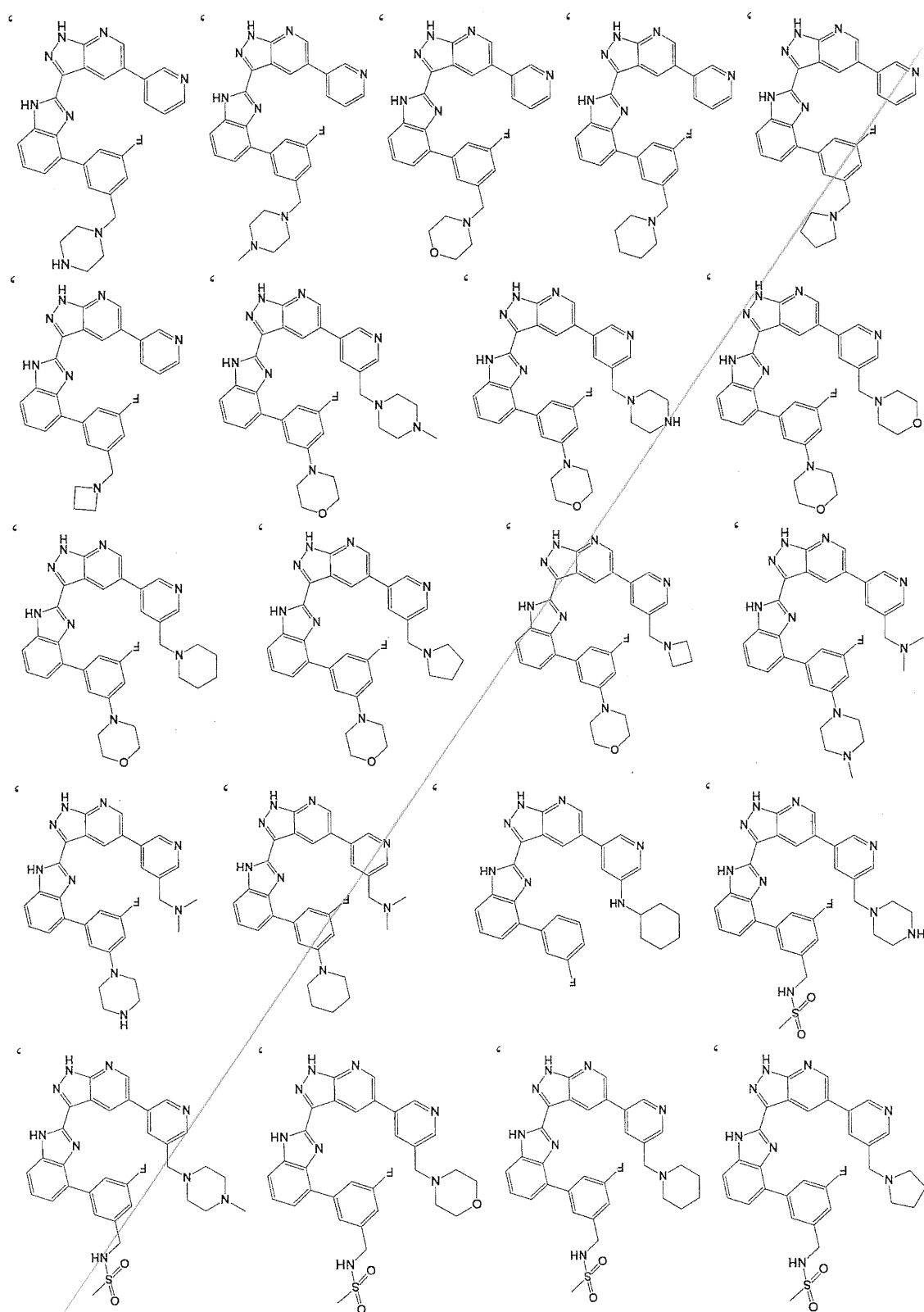
19. The compound of claim 18 wherein aryl is phenyl.
20. The compound of claim 18 wherein heteroaryl is pyridinyl.
21. The compound of claim 18 wherein heterocyclyl is selected from the group consisting of azetidiny, pyrrolidinyl, morpholinyl, piperazinyl and piperidinyl.
22. The compound of claim 18 wherein R^2 is selected from the group consisting of H, $-(C_{1-9} \text{ alkyl})_n\text{heterocyclyl}(R^8)_q$, $-NHC(=O)R^{11}$ and $-(C_{1-9} \text{ alkyl})_nN(R^9)_2$ and R^1 and R^3 are both H.
23. The compound of claim 22 wherein R^2 is $-\text{CH}_2N(R^9)_2$ or $-N(R^9)_2$.
24. The compound of claim 23 wherein R^9 is independently selected from the group consisting of H, Me, Et, $-\text{CH}_2\text{phenyl}$ and $-\text{CH}_2\text{carbocyclyl}$.
25. The compound of claim 22 wherein R^2 is $-NHC(=O)R^{11}$.
26. The compound of claim 25 wherein R^{11} is selected from the group consisting of $-C_{1-5} \text{ alkyl}$, carbocyclyl, $\text{phenyl}(R^6)_q$, and $-\text{CH}_2\text{phenyl}(R^6)_q$.
27. The compound as in any of claims 23-26, in which R^4 is $\text{phenyl}(R^{13})_q$.
28. The compound as in any of claims 23-26, in which R^4 is $-\text{heterocyclyl}(R^{14})_q$.
29. The compound as in any of claims 23-26, in which R^4 is $-\text{heteroaryl}(R^{15})_q$.
30. The compound of claim 27 wherein R^{13} is one substituent attached to the phenyl comprising a fluorine atom.
31. The compound of claim 27 wherein R^{13} is two substituents each attached to the phenyl comprising a fluorine atom and either a $-(\text{CH}_2)_nN(R^5)_2$ or a $-(\text{CH}_2)_n\text{NHSO}_2R^{18}$.

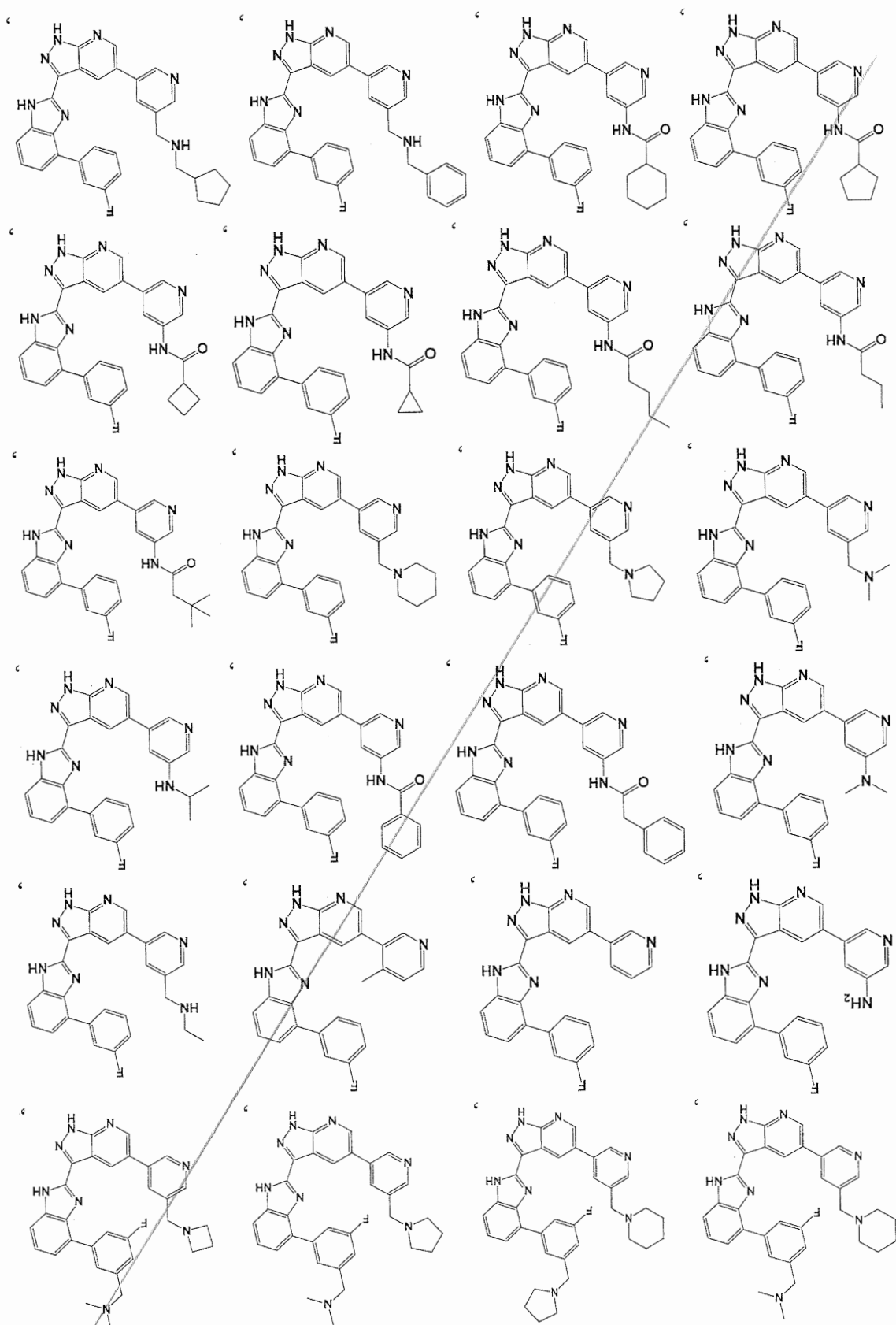
32. The compound of claim 28 wherein the heterocyclyl is selected from the group consisting of piperazinyl and piperidinyl; and the R¹⁴ is H or Me.

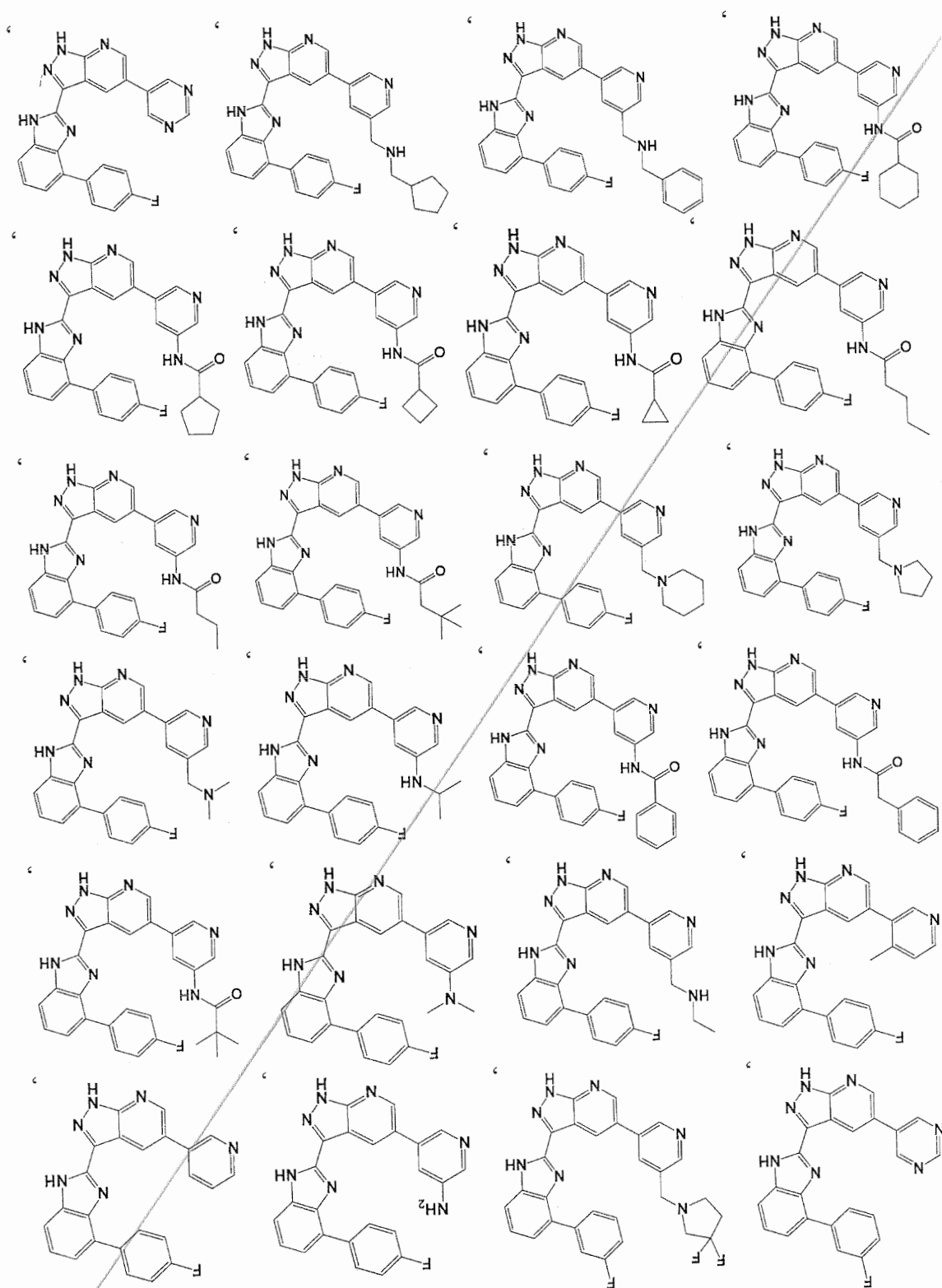
33. The compound of claim 29 wherein the heteroaryl is selected from the group consisting of pyridinyl, furyl, thiophenyl and imidazolyl; and R¹⁵ is lower alkyl or halide.

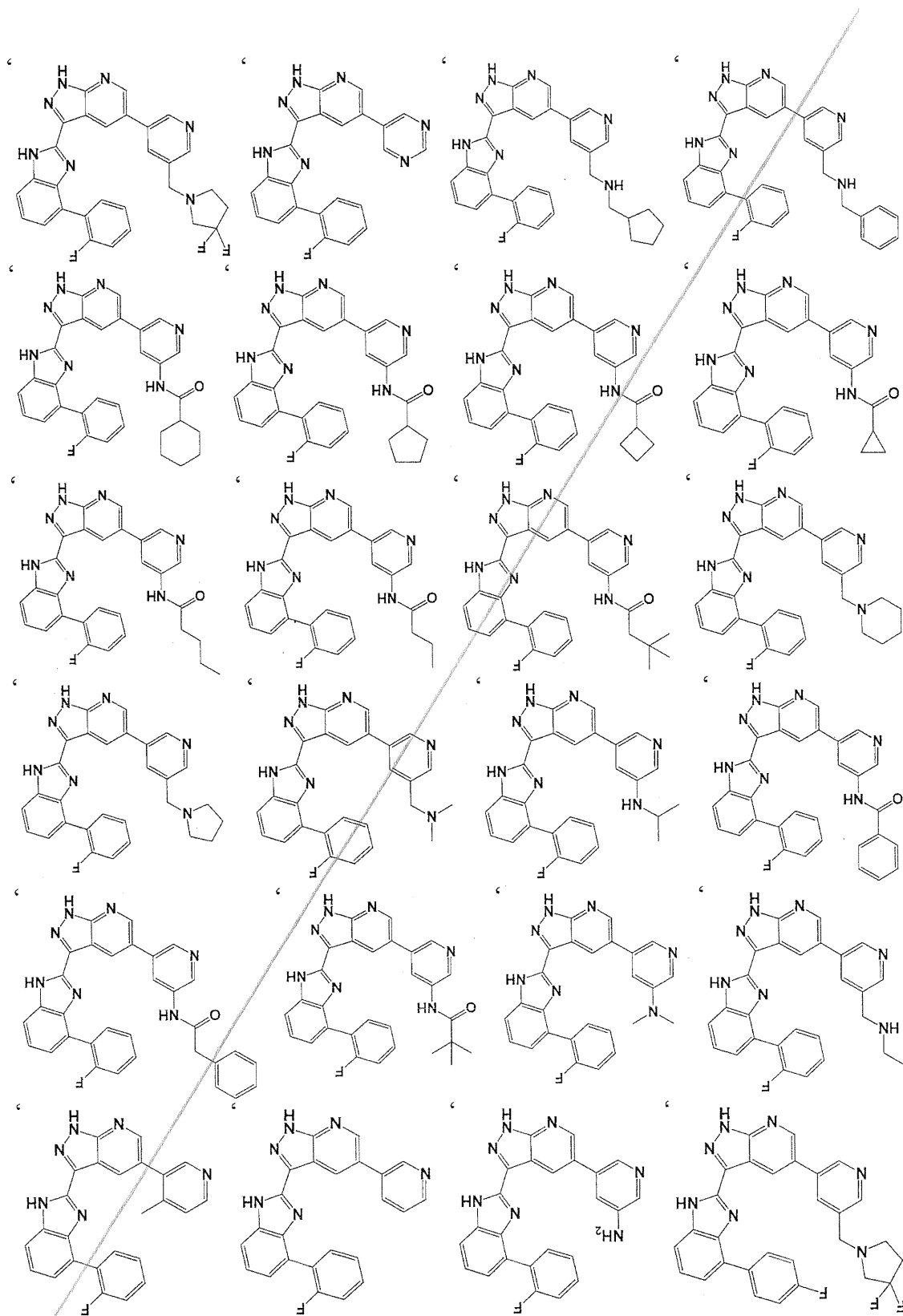
34. The compound of claim 18 having a structure selected from the group consisting of:

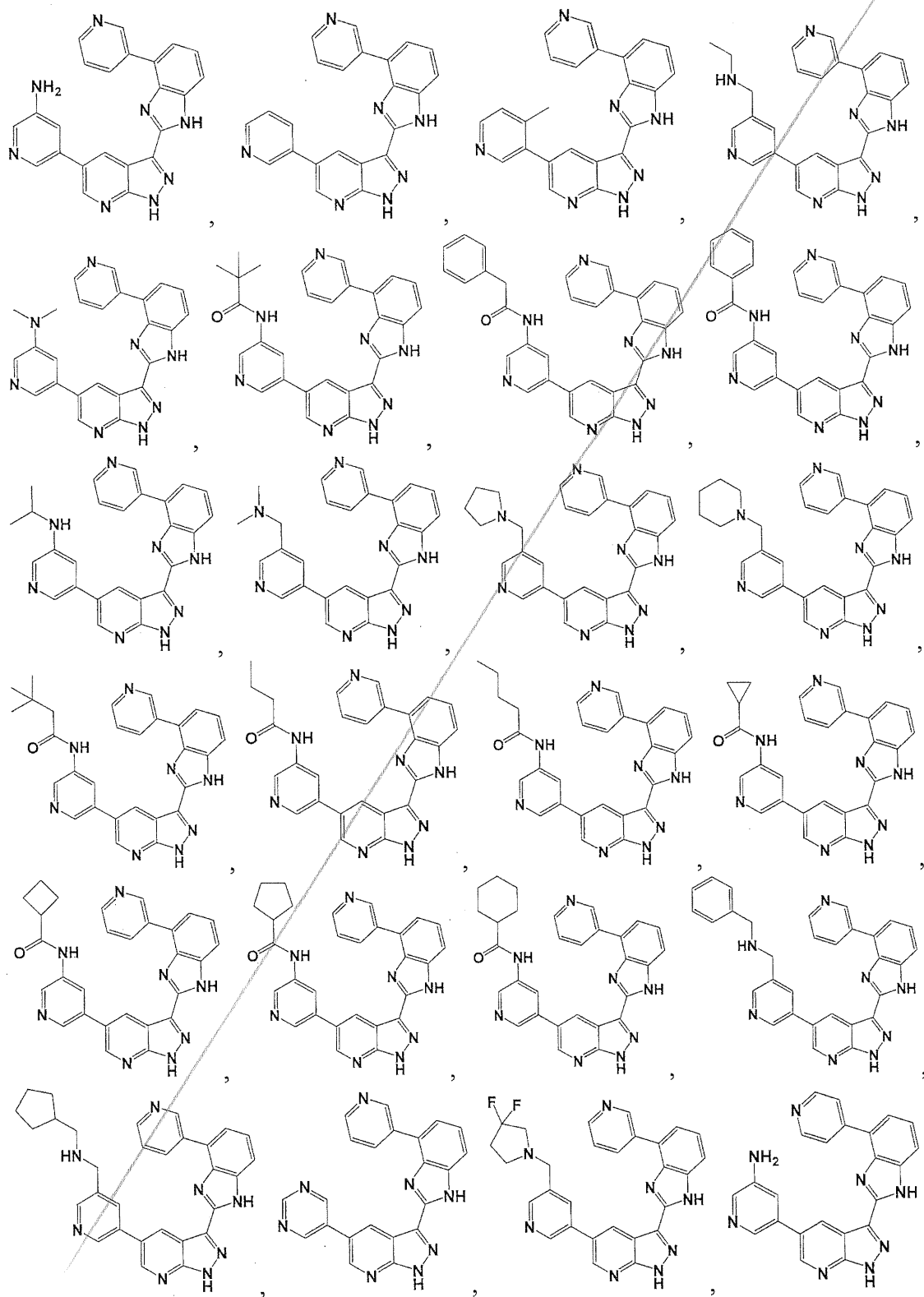


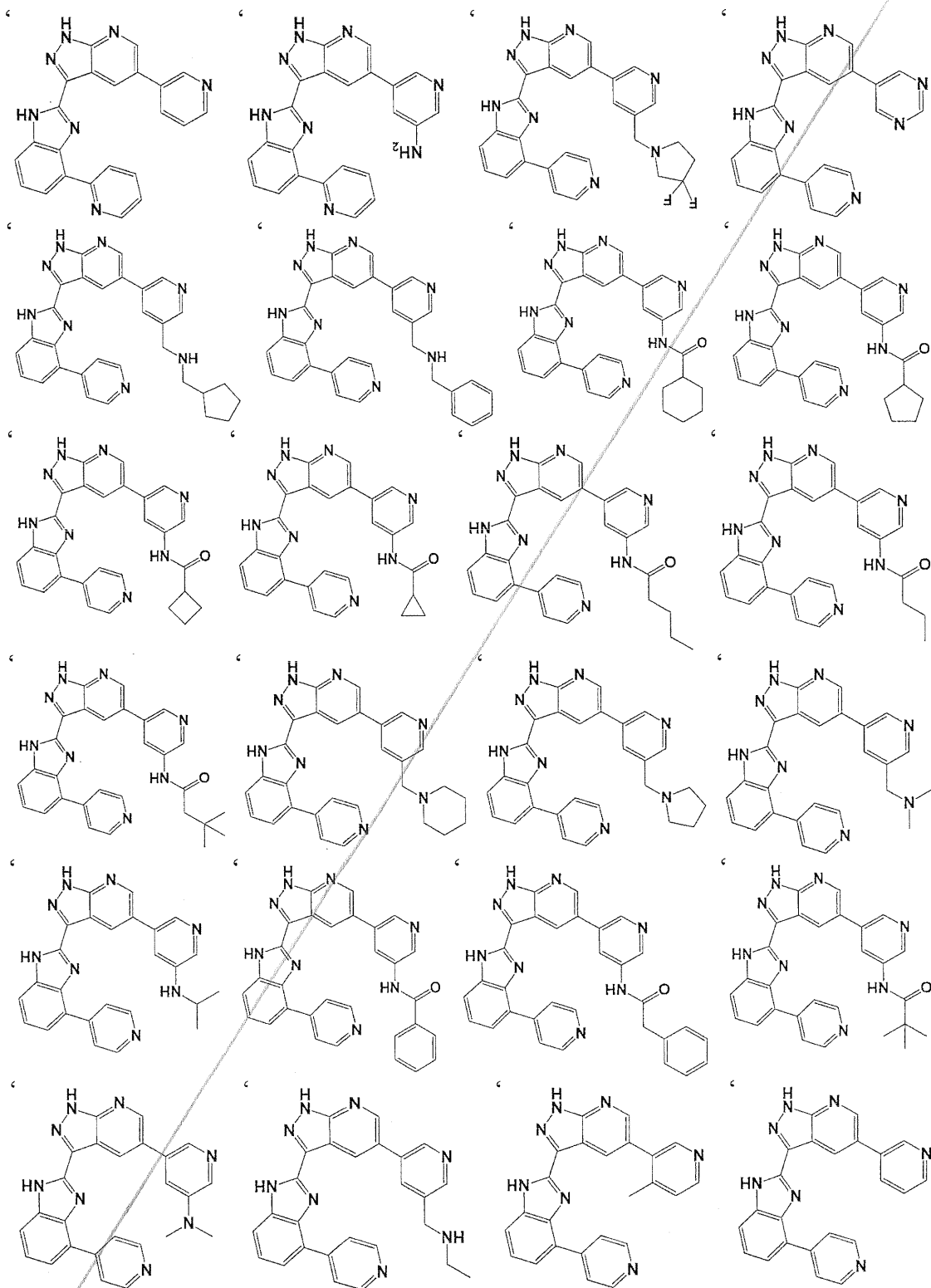


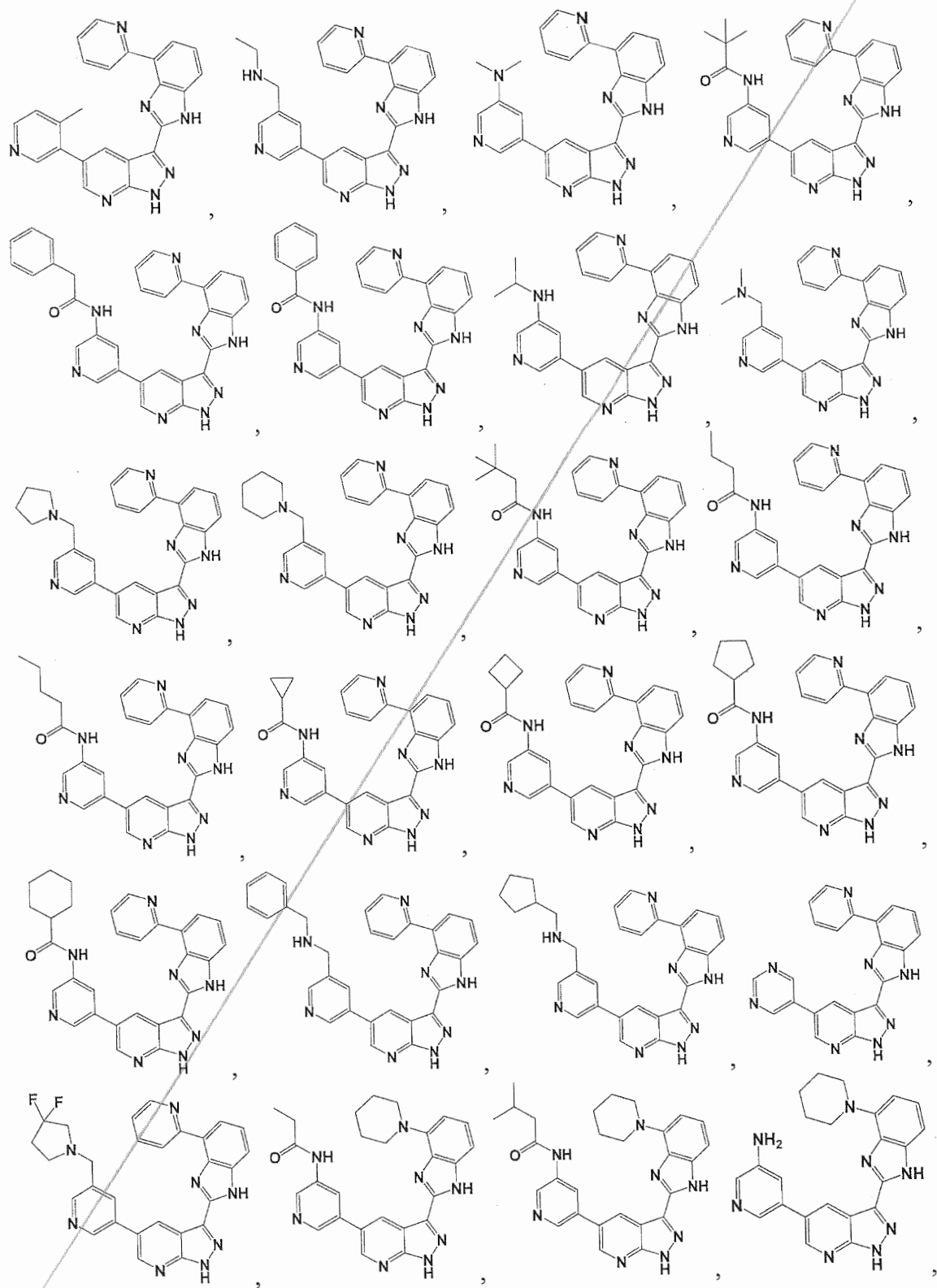


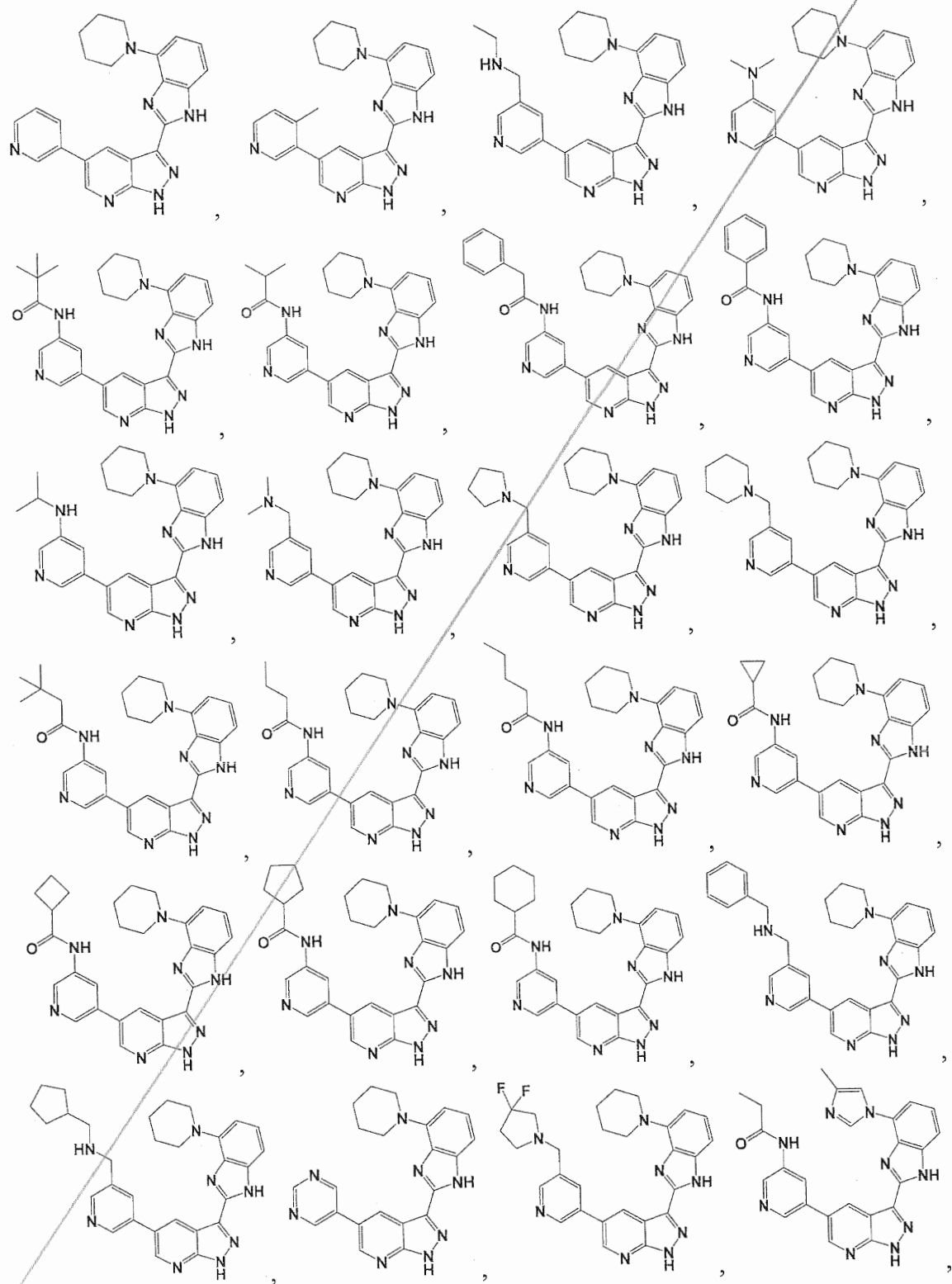


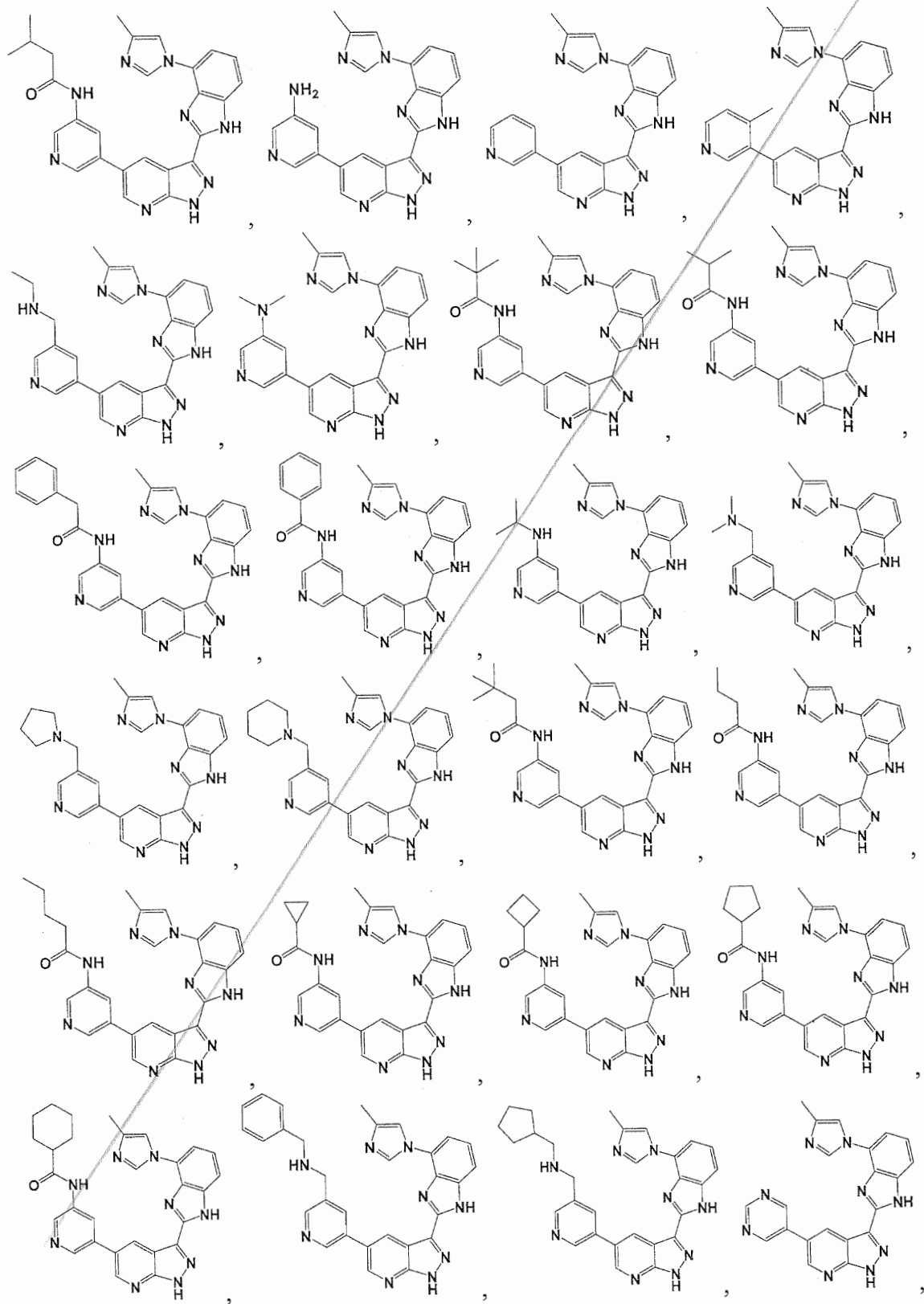


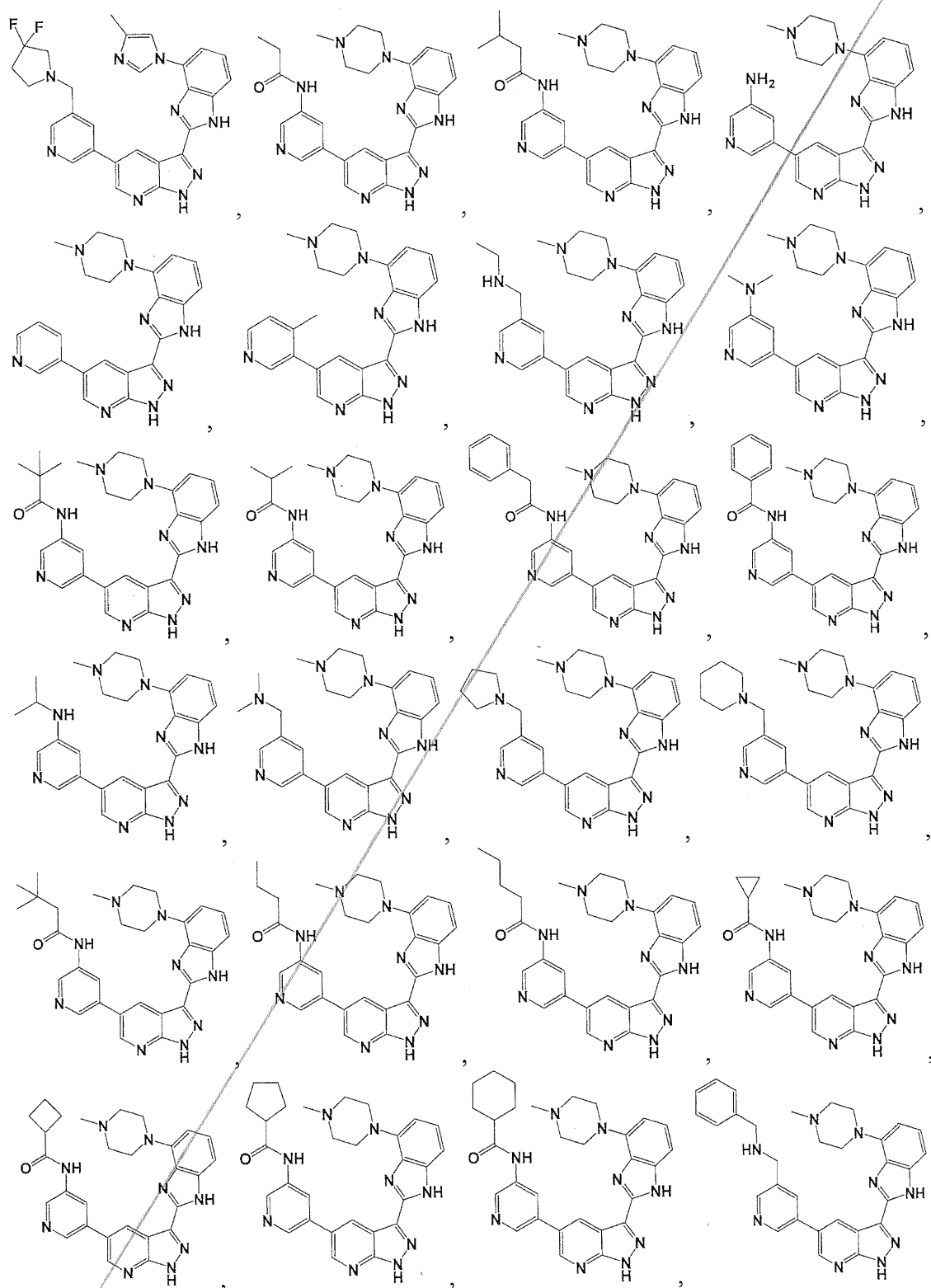


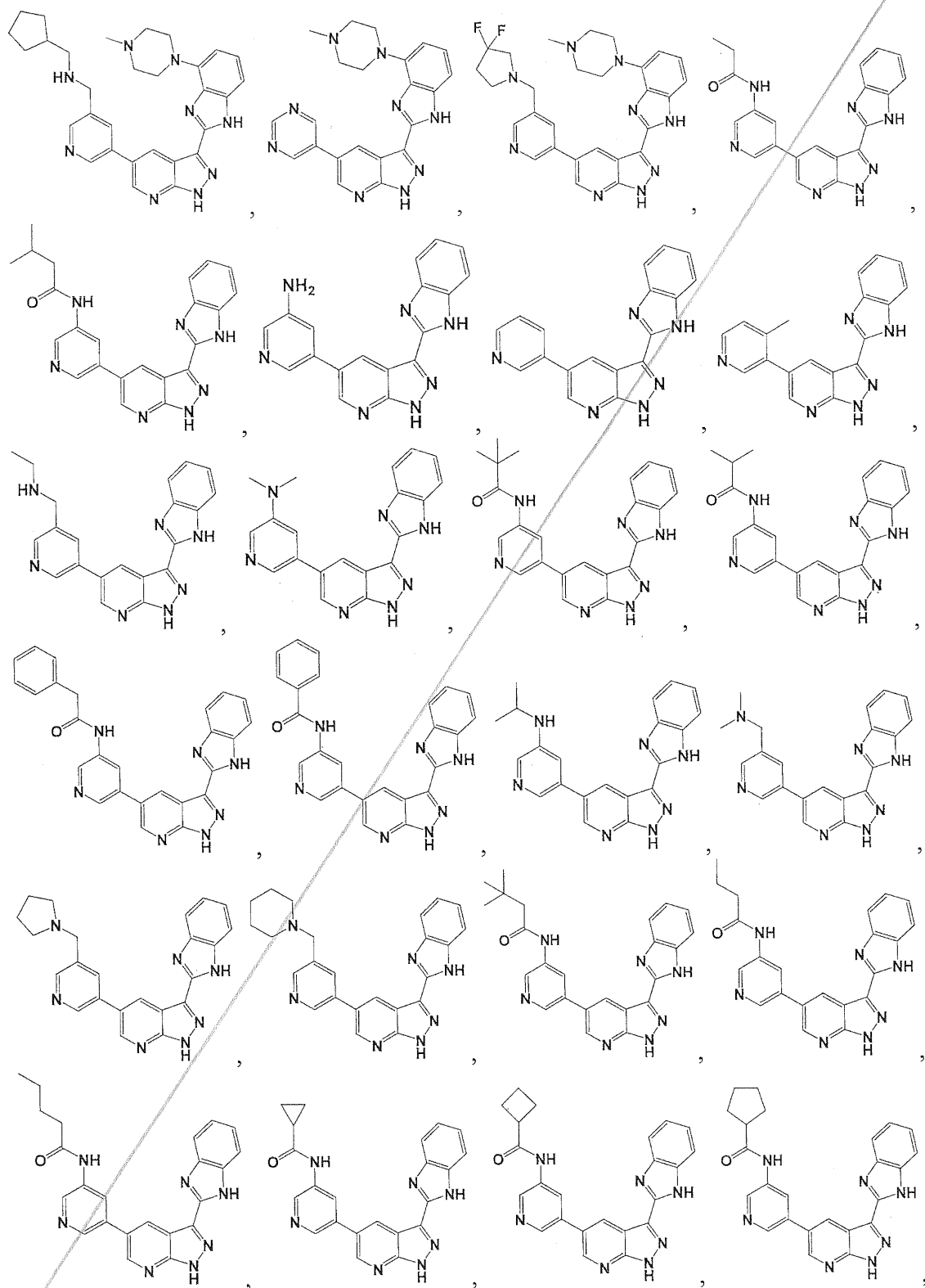


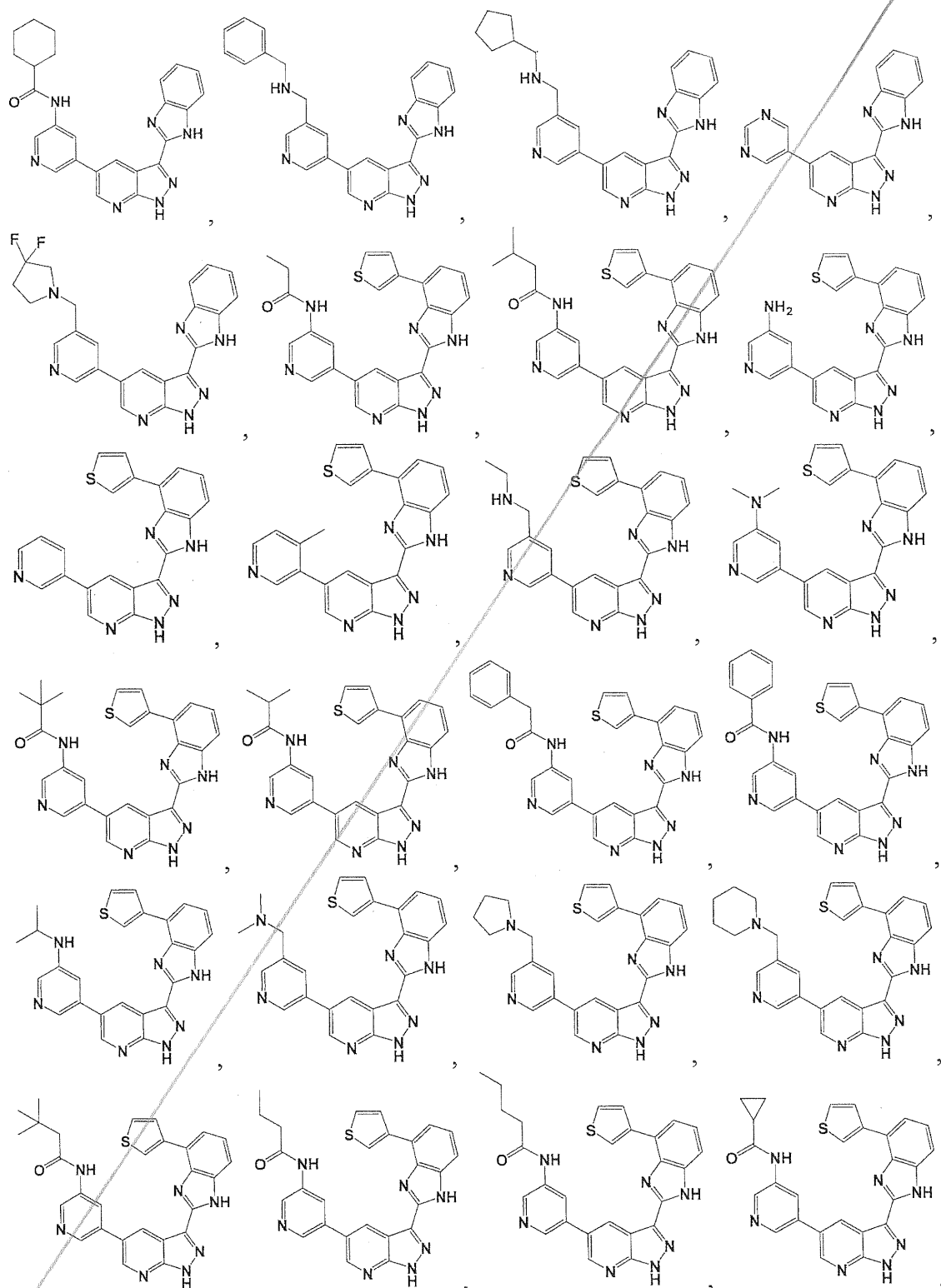


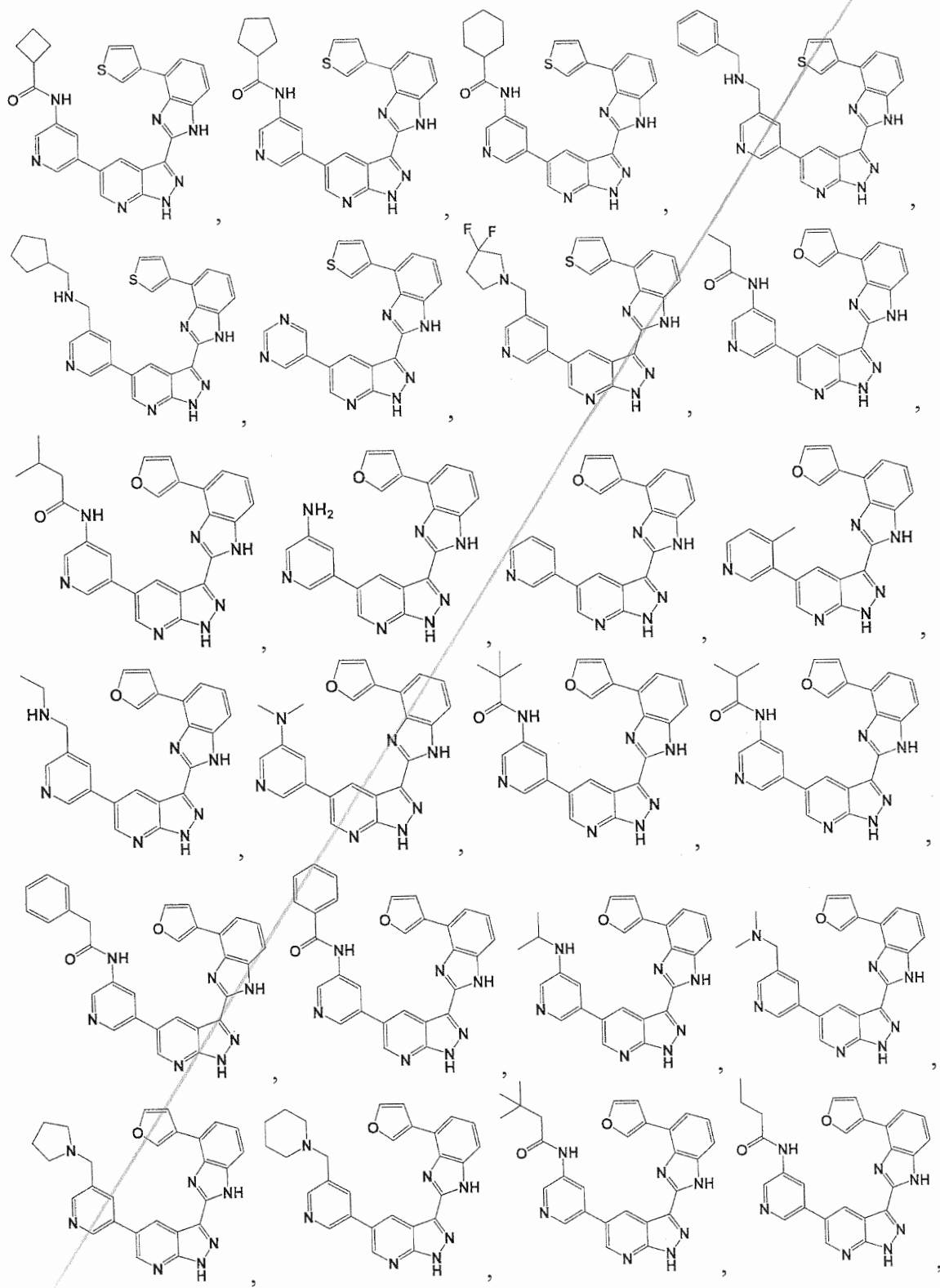


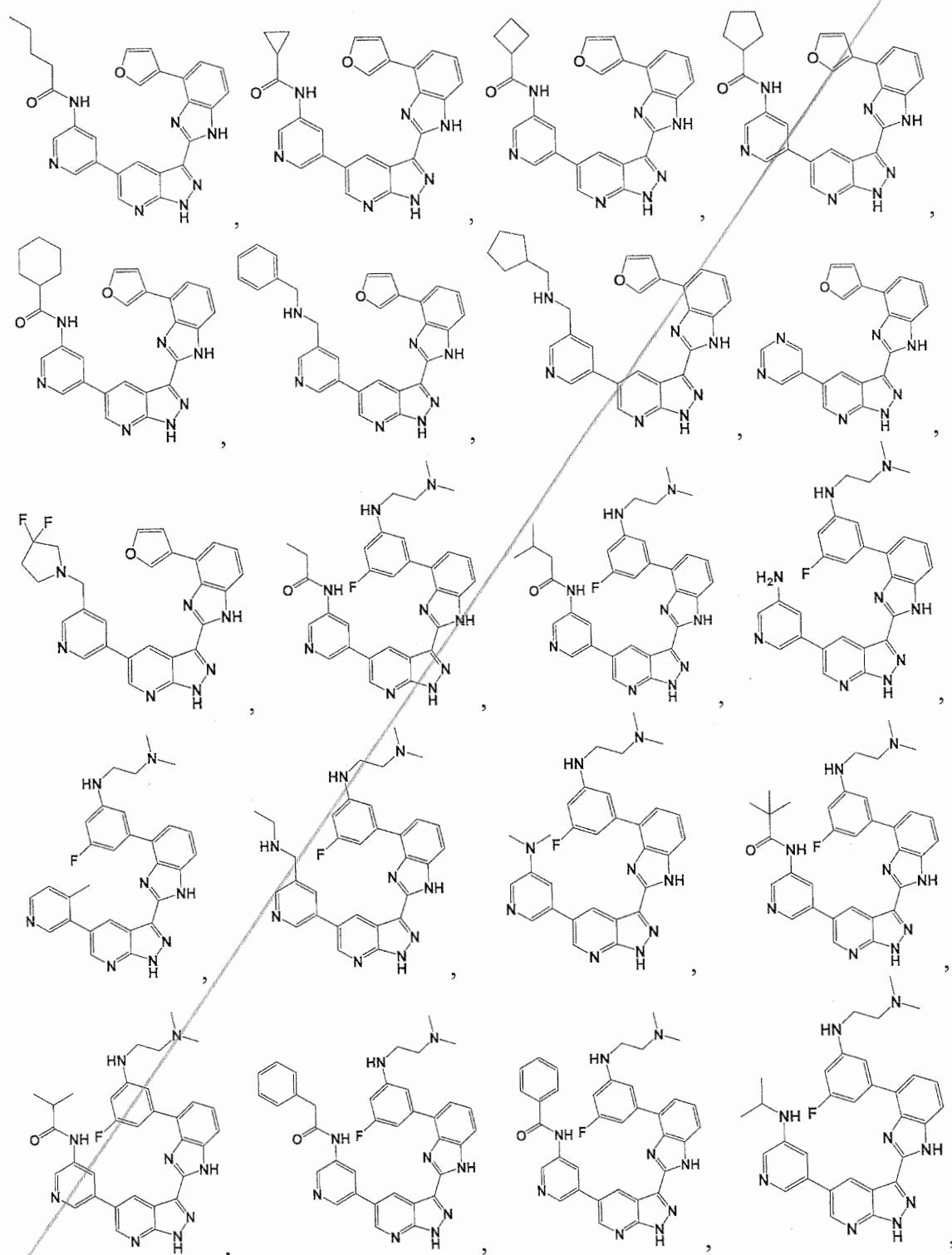


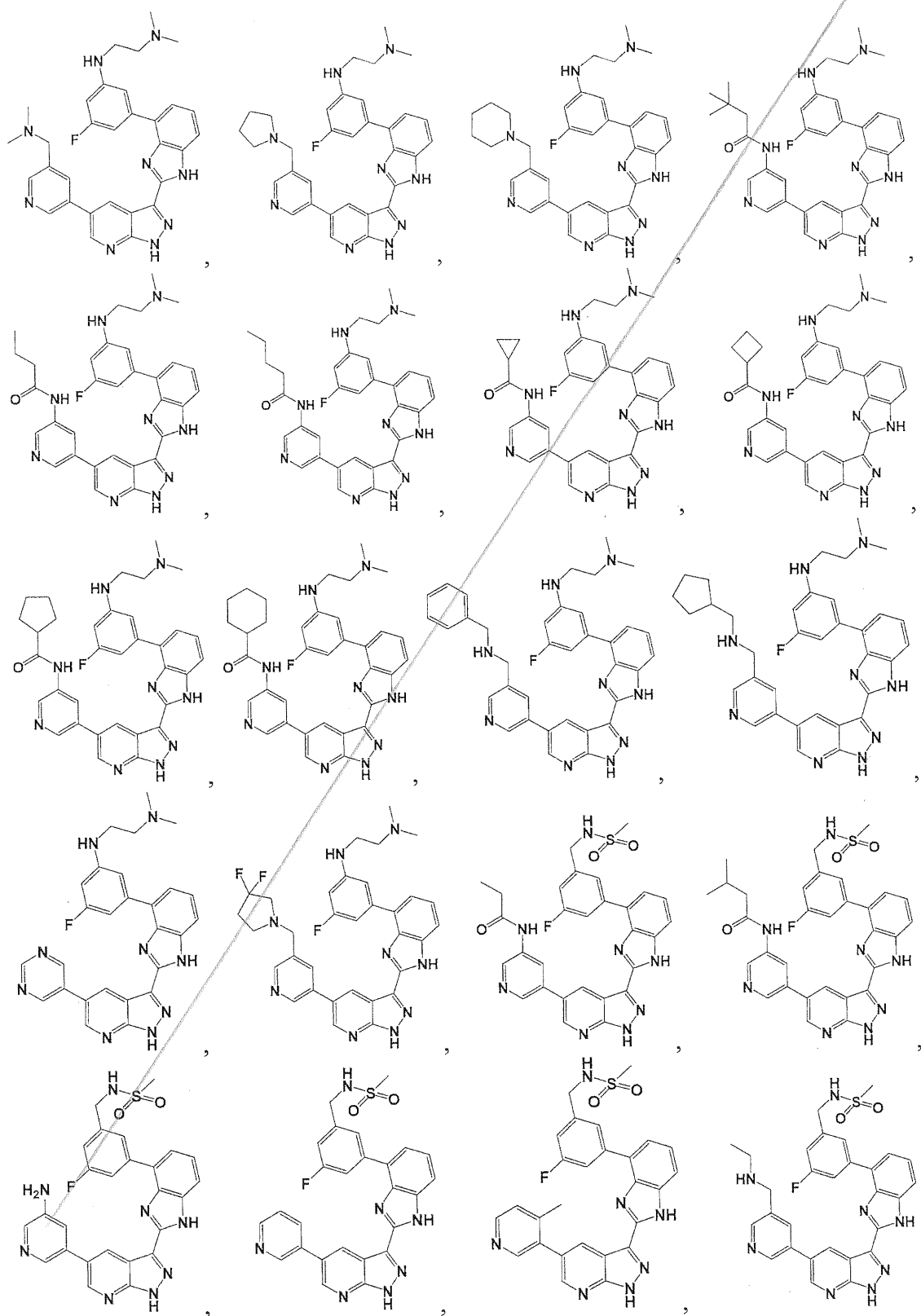


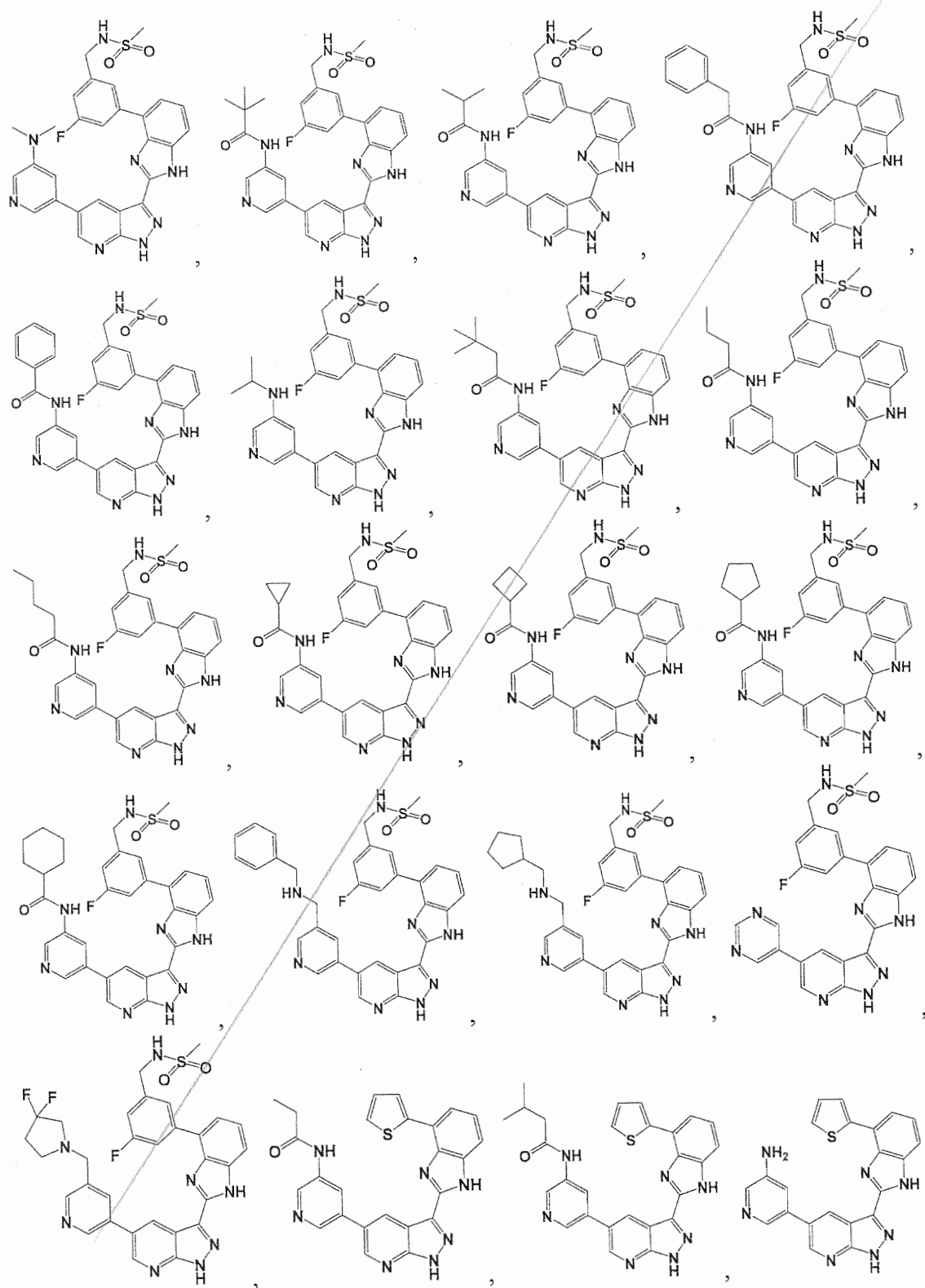


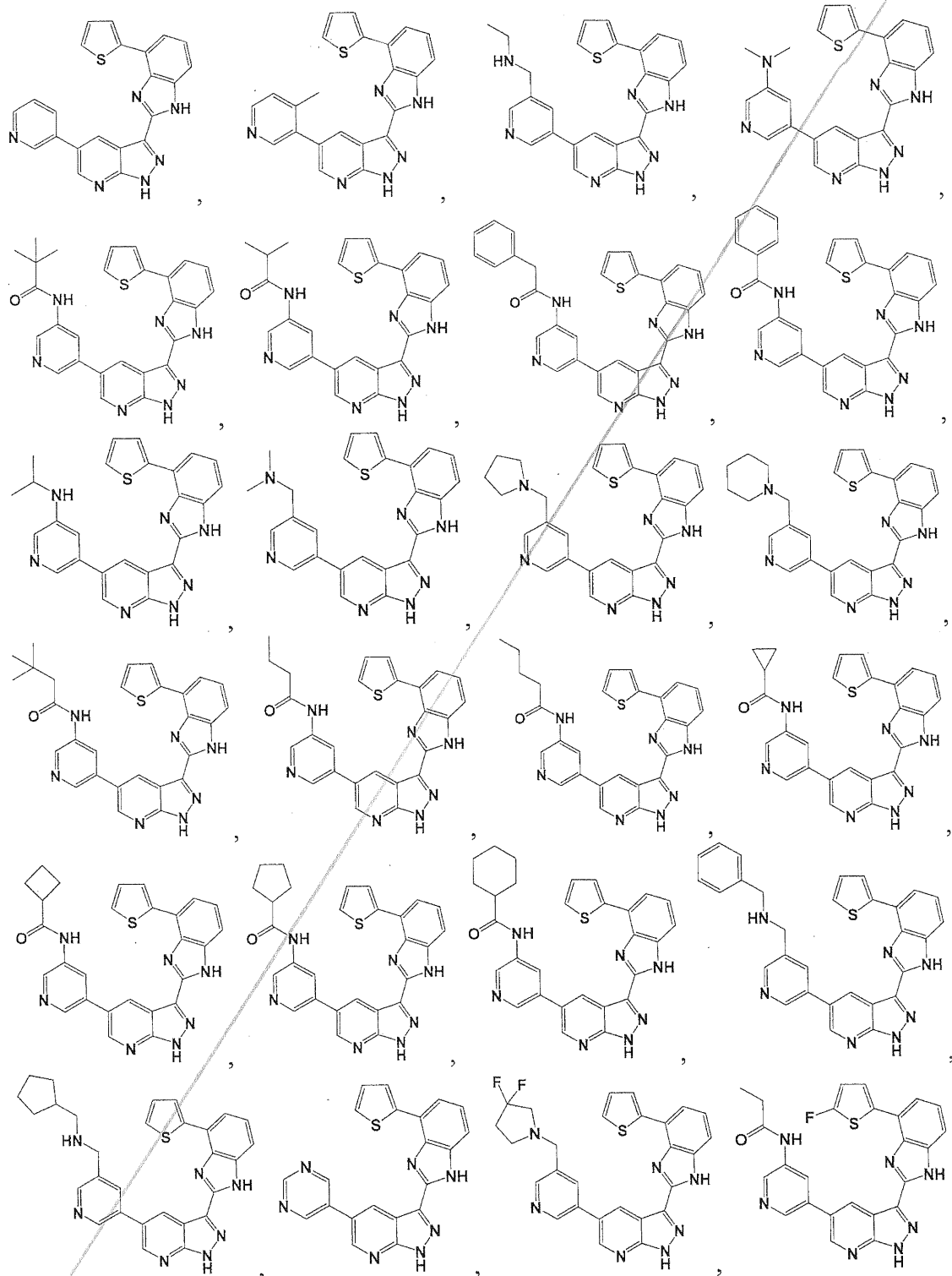


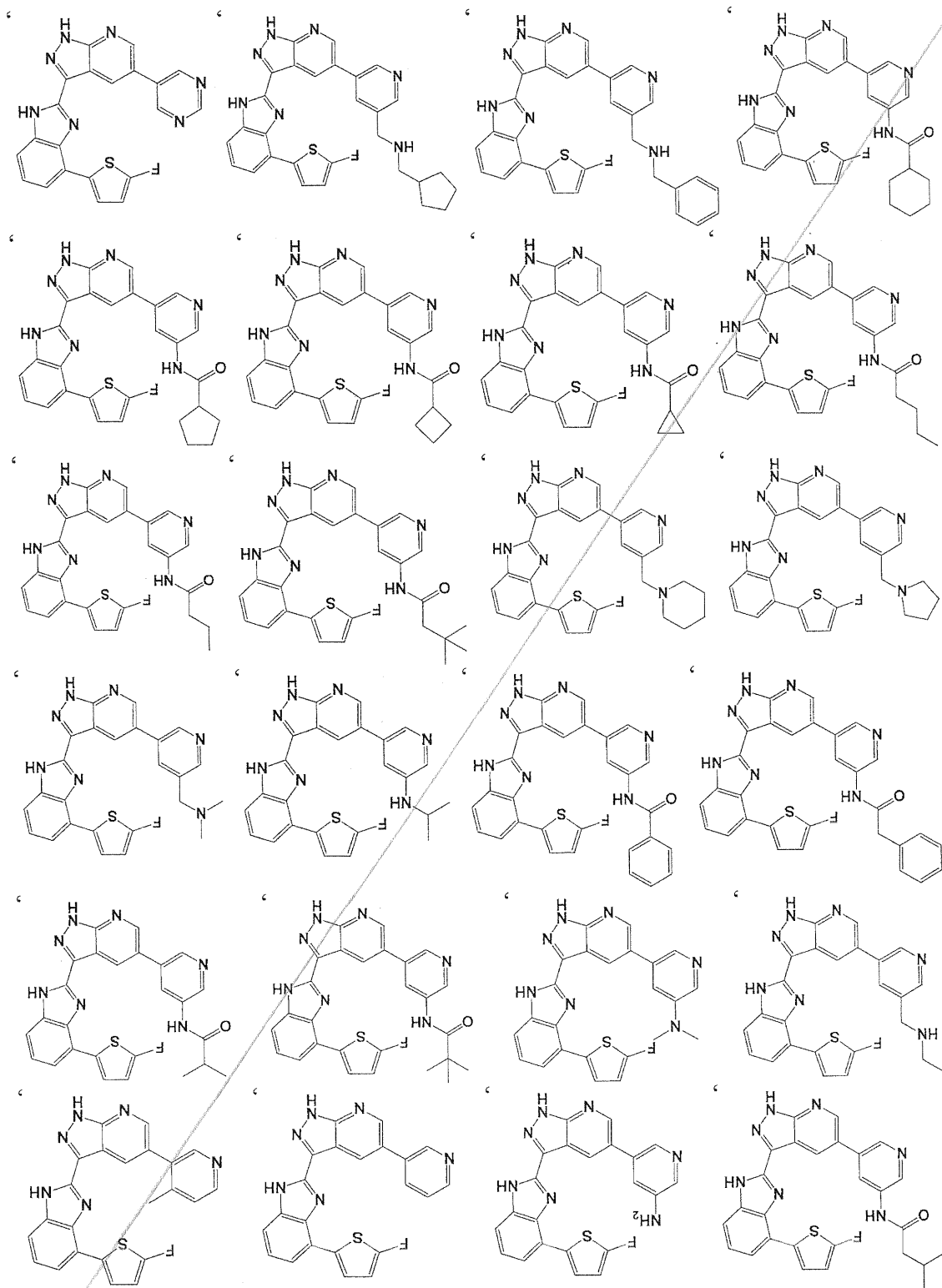


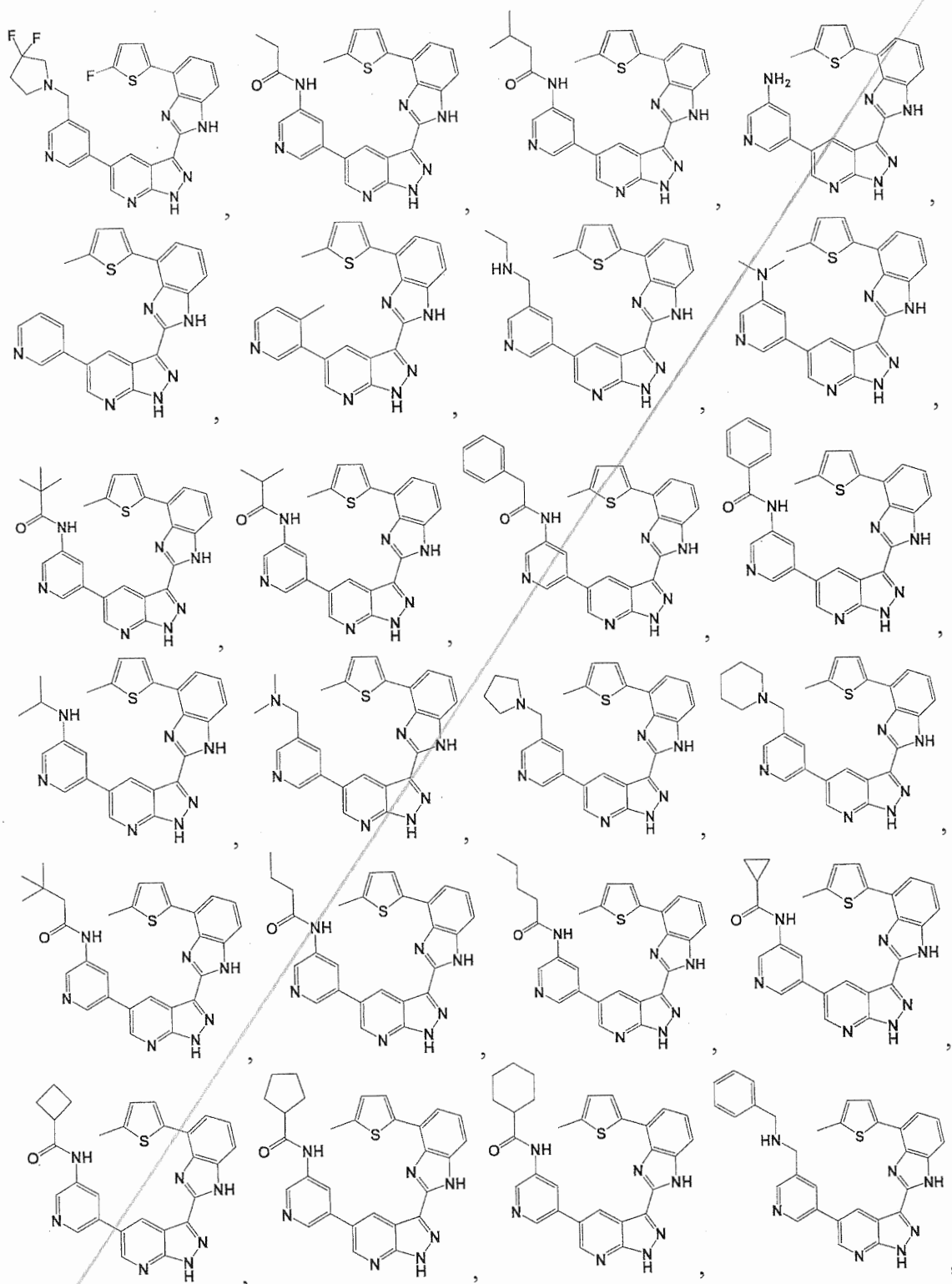


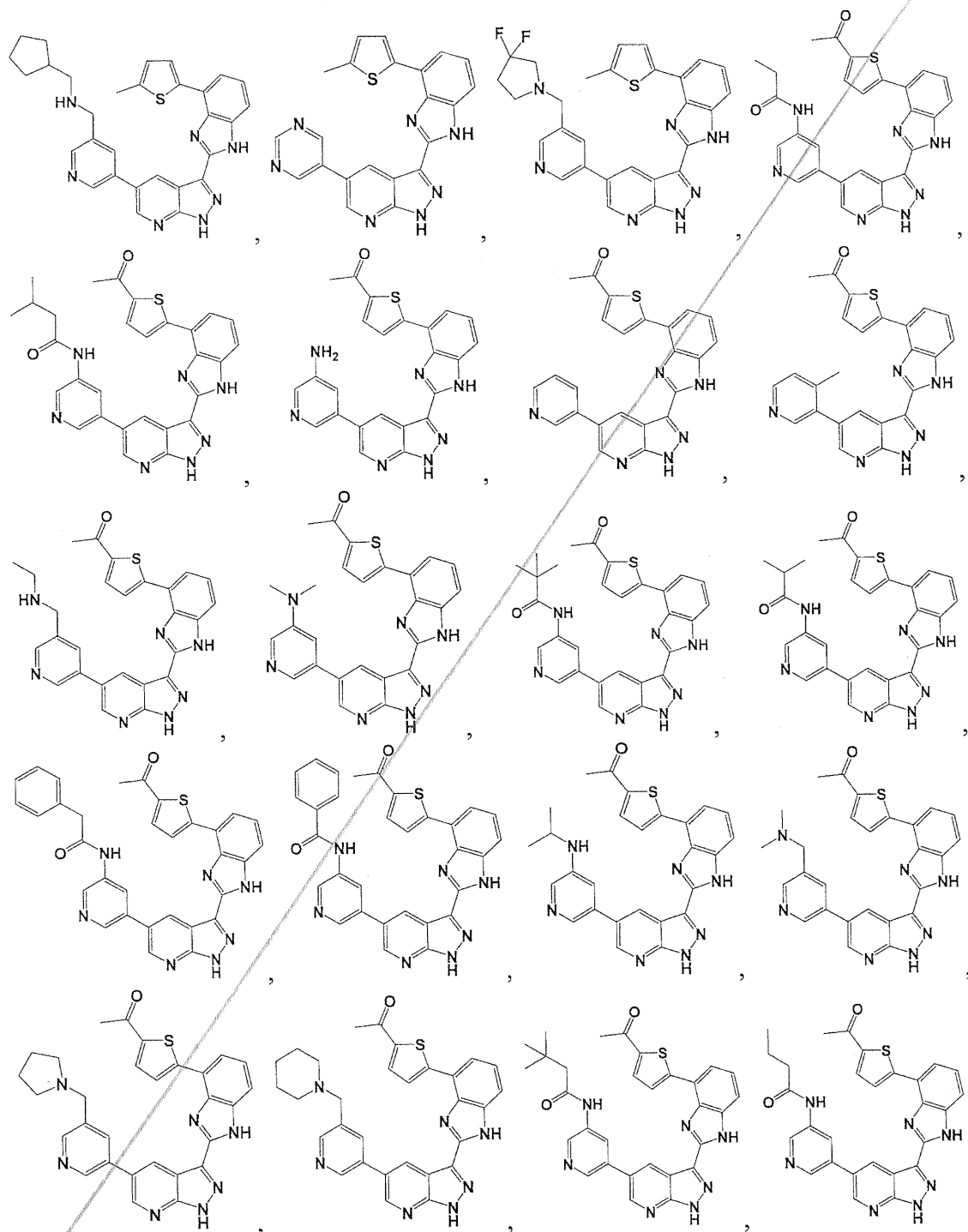


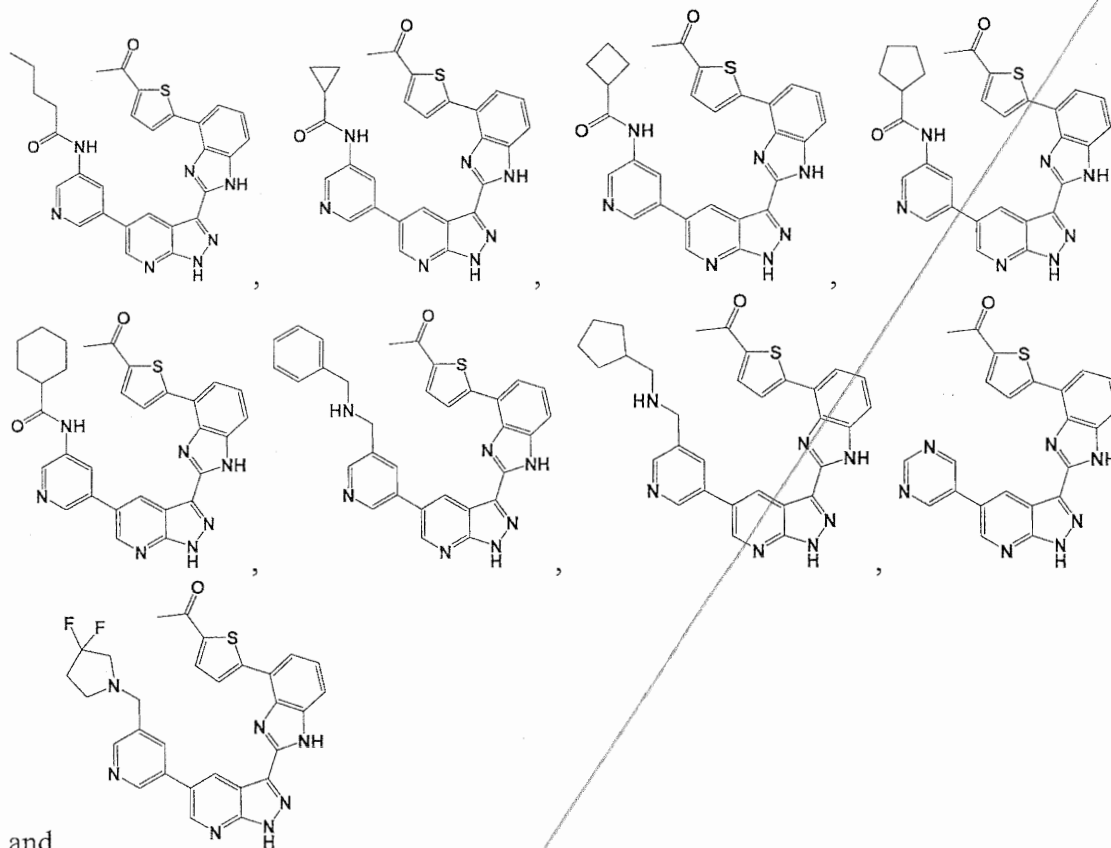












and

35. A pharmaceutical composition comprising a therapeutically effective amount of at least one compound according to any of the claims 1 or 18, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

36. A method of treating a disorder or disease in which aberrant Wnt signaling is implicated in a patient, the method comprising administering to the patient a therapeutically effective amount of at least one compound according to any of the claims 1 or 18, or a pharmaceutically acceptable salt thereof.

37. A method of claim 36, wherein the disorder or disease is cancer.

38. A method of claim 36, wherein the disorder or disease is diabetic retinopathy.

39. A method of claim 36, wherein the disorder or disease is pulmonary fibrosis.

40. A method of claim 36, wherein the disorder or disease is idiopathic pulmonary fibrosis (IPF).

41. A method of claim 36, wherein the disorder or disease is rheumatoid arthritis.

42. A method of claim 36, wherein the disorder or disease is scleroderma.
43. A method of claim 36, wherein the disorder or disease is a mycotic or viral infection.
44. A method of claim 36, wherein the disorder or disease is a bone or cartilage disease.
45. A method of claim 36, wherein the disorder or disease is Alzheimer's disease.
46. A method of claim 36, wherein the disorder or disease is dementia.
47. A method of claim 36, wherein the disorder or disease is Parkinson's disease.
48. A method of claim 36, wherein the disorder or disease is lung disease.
49. A method of claim 36, wherein the disorder or disease is osteoarthritis.
50. A method of claim 36, wherein the disorder or disease is a genetic disease caused by mutations in Wnt signaling components, wherein the genetic disease is selected from: polyposis coli, osteoporosis-pseudoglioma syndrome, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia syndrome, Müllerian-duct regression and virilization, SERKAL syndrome, diabetes mellitus type 2, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication syndrome, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease and Rett syndrome.
51. The method of claim 36, wherein the patient is a human.
52. The method of claim 37, wherein the cancer is chosen from: hepatocellular carcinoma, colon cancer, breast cancer, pancreatic cancer leukemia, lymphoma, sarcoma and ovarian cancer.
53. The method of claim 36, wherein the compound inhibits one or more proteins in the Wnt pathway.
54. The method of claim 51, wherein the compound inhibits signaling induced by one or more Wnt proteins.

55. The method of claim 52, wherein the Wnt proteins are chosen from: WNT1, WNT2, WNT2B, WNT3, WNT3A, WNT4, WNT5A, WNT5B, WNT6, WNT7A, WNT7B, WNT8A, WNT8B, WNT9A, WNT9B, WNT10A, WNT10B, WNT11, and WNT16.

56. The method of claim 36, wherein the compound inhibits a kinase activity.

57. A method of treating a disease or disorder mediated by the Wnt pathway in a patient, the method comprising administering to the patient a therapeutically effective amount of at least one compound according to any of the claims 1 or 18, or a pharmaceutically acceptable salt thereof.

58. The method of claim 55, wherein the compound inhibits one or more Wnt proteins.

59. A method of treating a disease or disorder mediated by kinase activity in a patient, the method comprising administering to the patient a therapeutically effective amount of at least one compound according to any of the claims 1 or 18, or a pharmaceutically acceptable salt thereof.

60. The method of claim 57, wherein the disease or disorder comprises tumor growth, cell proliferation, or angiogenesis.

61. A method of inhibiting the activity of a protein kinase receptor, the method comprising contacting the receptor with an effective amount of at least one compound according to any of the claims 1 or 18, or a pharmaceutically acceptable salt thereof.

62. A method of treating a disease or disorder associated with aberrant cellular proliferation in a patient, the method comprising administering to the patient a therapeutically effective amount of at least one compound according to any of the claims 1 or 18, or a pharmaceutically acceptable salt thereof.

63. A method of preventing or reducing angiogenesis in a patient, the method comprising administering to the patient a therapeutically effective amount of at least one compound according to any of the claims 1 or 18, or a pharmaceutically acceptable salt thereof.

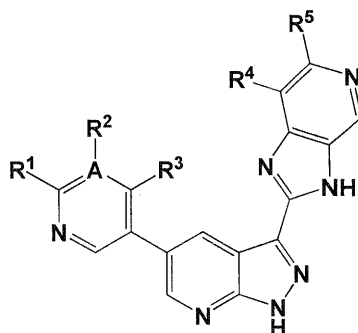
64. A method of preventing or reducing abnormal cellular proliferation in a patient, the method comprising administering to the patient a therapeutically effective

amount of at least one compound according to any of the claims 1 or 18, or a pharmaceutically acceptable salt thereof.

65. A method of treating a disease or disorder associated with aberrant cellular proliferation in a patient, the method comprising administering to the patient a pharmaceutical composition comprising one or more of the compounds of either claim 1 or 18 in combination with a pharmaceutically acceptable carrier and one or more other agents.

WHAT IS CLAIMED IS:

1. A compound or pharmaceutically acceptable salt or prodrug thereof having the structure of Formula I:



I

wherein:

R^1 and R^2 are independently selected from the group consisting of H, lower alkyl, halide, $-(C_{1-9} \text{ alkyl})_n\text{aryl}(R^6)_q$, $-(C_{1-9} \text{ alkyl})_n\text{heteroaryl}(R^7)_q$, $-(C_{1-9} \text{ alkyl})_n\text{heterocyclyl}(R^8)_q$, $-(C_{1-9} \text{ alkyl})_nN(R^9)_2$, $-OR^{10}$ and $-NHC(=O)R^{11}$;

R^3 is selected from the group consisting of H, halide and lower alkyl;

with the proviso that at least two of R^1 , R^2 and R^3 are H;

R^4 and R^5 are independently selected from the group consisting of H, $-C(=O)N(R^{12})_2$, $-\text{aryl}(R^{13})_q$, $-\text{heterocyclyl}(R^{14})_q$, and $-\text{heteroaryl}(R^{15})_q$;

with the proviso that at least one of R^4 and R^5 is H;

each R^6 is a substituent attached to the aryl ring and independently selected from the group consisting of H, $-C_{1-9}$ alkyl, halide, CF_3 and CN;

each R^7 is a substituent attached to the heteroaryl ring and independently selected from the group consisting of H, $-C_{1-9}$ alkyl, halide, CF_3 and CN;

each R^8 is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, halide, $-(C_{1-3} \text{ alkyl})_n\text{aryl}(R^6)_q$, and $-C_{1-4}$ alkyl;

each R^9 is independently selected from the group consisting of H, $-C_{1-9}$ alkyl, $-(C_{1-3} \text{ alkyl})_n\text{aryl}(R^6)_q$, $-(C_{1-3} \text{ alkyl})_n\text{carbocyclyl}$ and $-(C_{1-9} \text{ alkyl})N(R^{16})_2$;

alternatively, two adjacent R^9 or two adjacent R^{12} , may be taken together with the atoms to which they are attached to form a $\text{heterocyclyl}(R^{17})_q$;

R^{10} is selected from the group consisting of H, $-CF_3$, $-(C_{1-3} \text{ alkyl})_n \text{aryl}(R^6)_q$, and $-C_{1-9} \text{ alkyl}$;

R^{11} is selected from the group consisting of $-(C_{1-3} \text{ alkyl})_n \text{aryl}(R^6)_q$, $-(C_{1-3} \text{ alkyl})_n \text{carbocyclyl}$, $-C_{1-9} \text{ alkyl}$ and $-CF_3$;

each R^{12} is independently selected from the group consisting of H, $-(C_{1-9} \text{ alkyl})_n \text{aryl}(R^6)_q$ and $-C_{1-9} \text{ alkyl}$;

each R^{13} is a substituent attached to the aryl ring and independently selected from the group consisting of H, halide, $-CF_3$, CN, $-(C_{1-3} \text{ alkyl})_n \text{heterocyclyl}(R^8)_q$, $-(C_{1-9} \text{ alkyl})_n N(R^9)_2$ and $-(C_{1-9} \text{ alkyl})_n NHSO_2 R^{18}$;

each R^{14} is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, lower alkyl, halide, $-CF_3$ and CN;

each R^{15} is a substituent attached to the heteroaryl ring and independently selected from the group consisting of H, lower alkyl, halide, $-CF_3$, CN, $-C(=O)(C_{1-3} \text{ alkyl})$, $-(C_{1-9} \text{ alkyl})_n N(R^9)_2$ and $-(C_{1-9} \text{ alkyl})_n NHSO_2 R^{18}$;

each R^{16} is independently selected from the group consisting of H and lower alkyl;

each R^{17} is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, $-(C_{1-9} \text{ alkyl})_n \text{aryl}(R^6)_q$, and $-C_{1-9} \text{ alkyl}$;

each R^{18} is a lower alkyl;

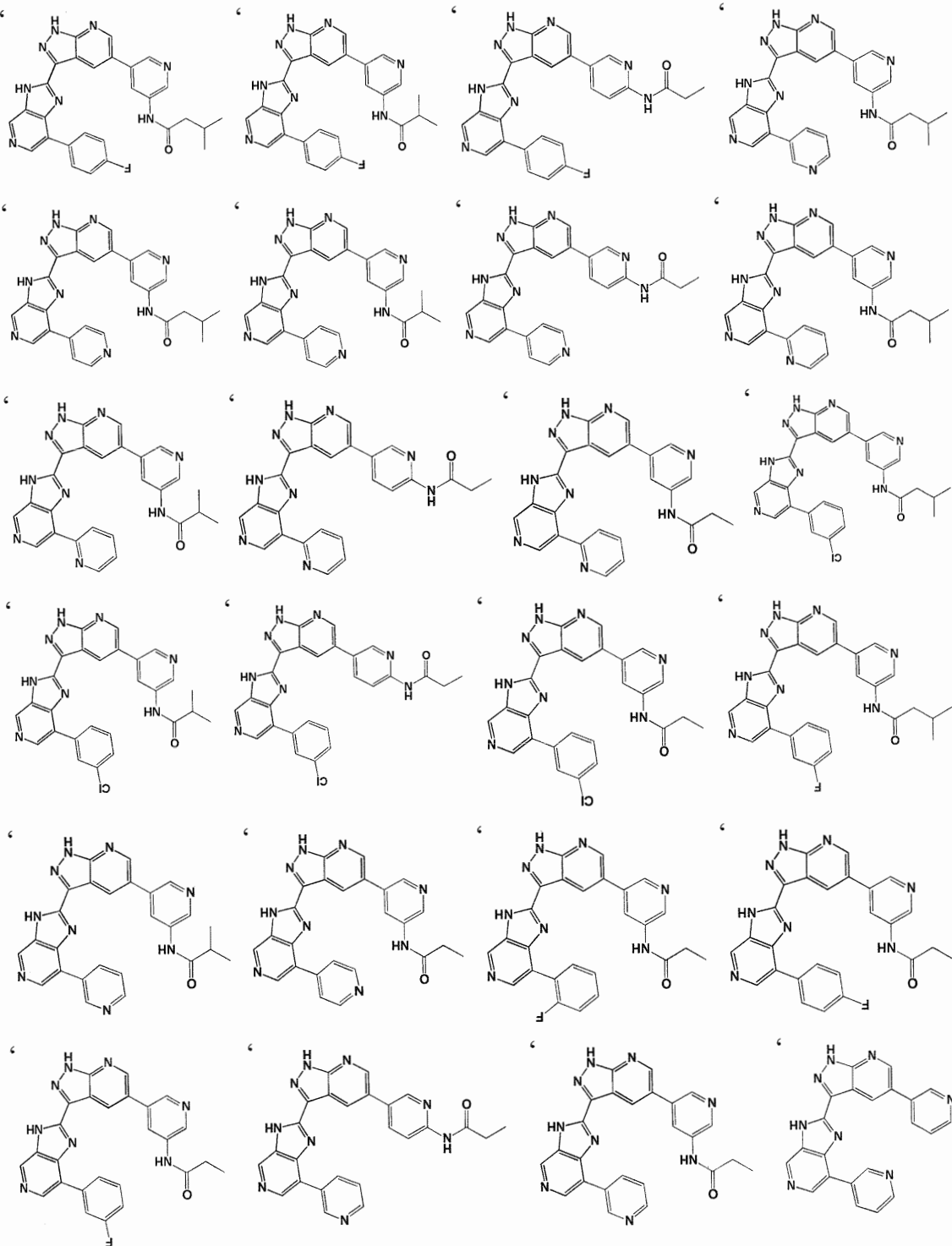
A is N or C;

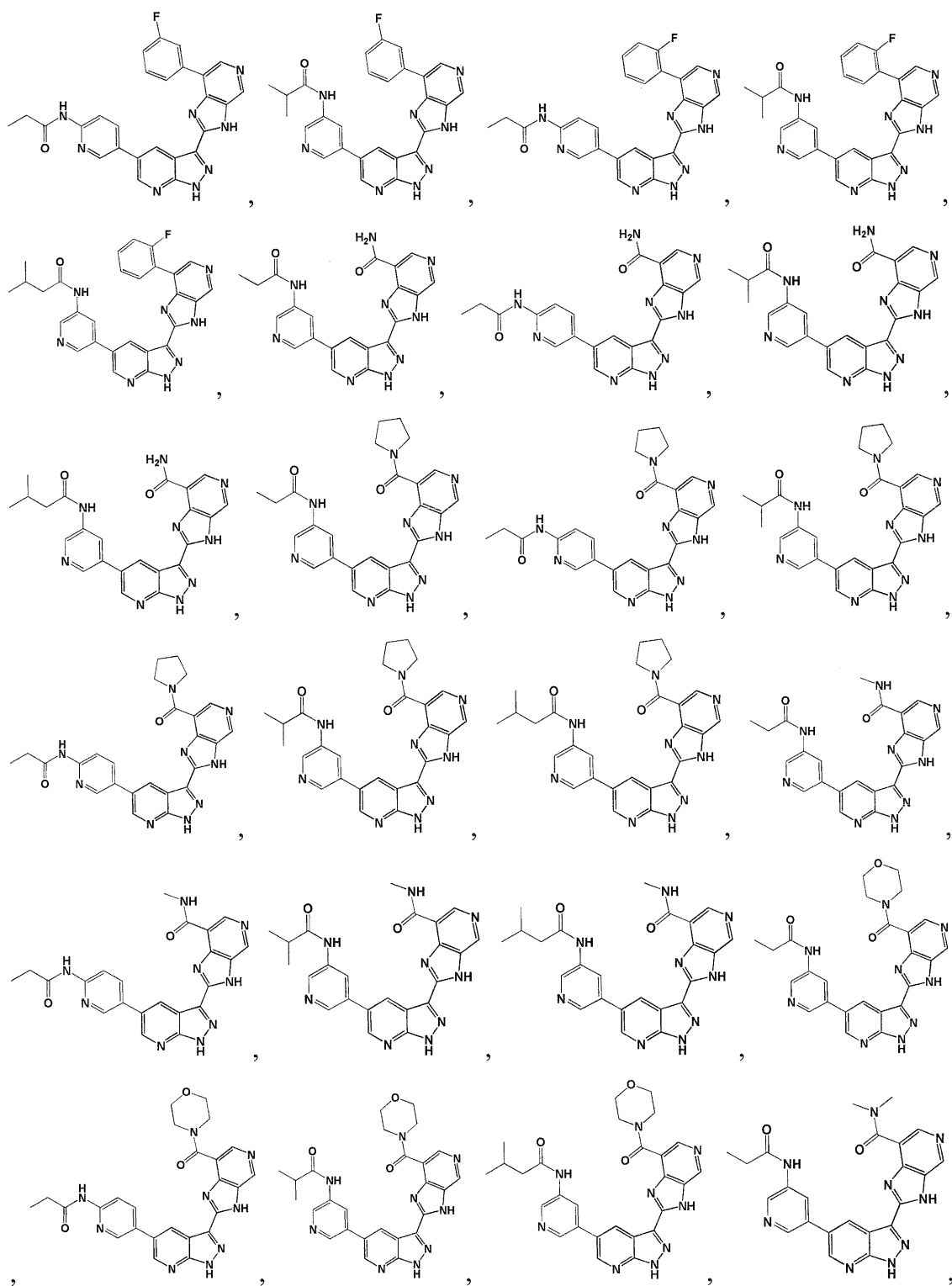
with the proviso that if A is N then R^2 is nil;

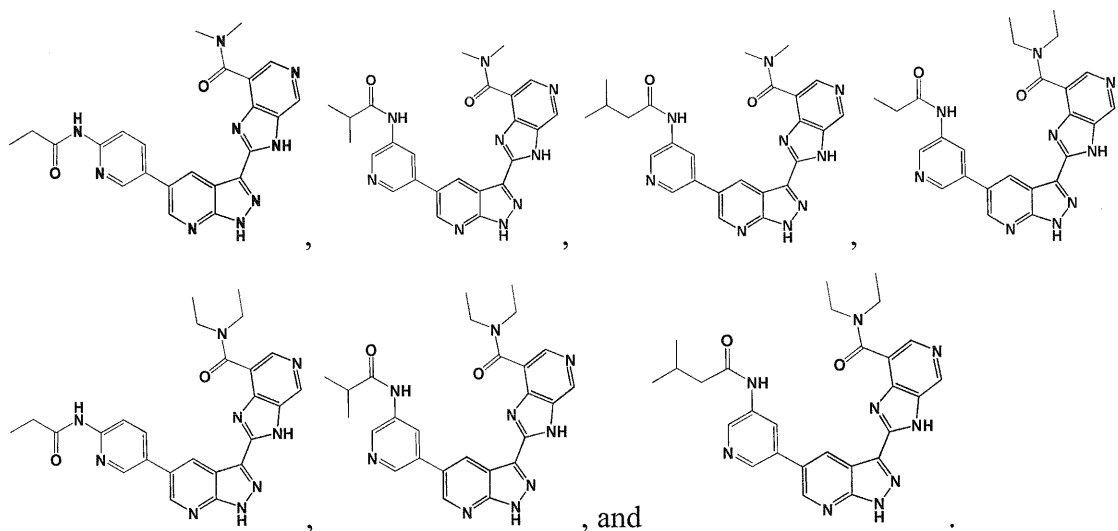
each q is an integer of 1 to 5;

each n is an integer of 0 or 1; and

with the proviso that Formula I is not a structure selected from the group consisting of:





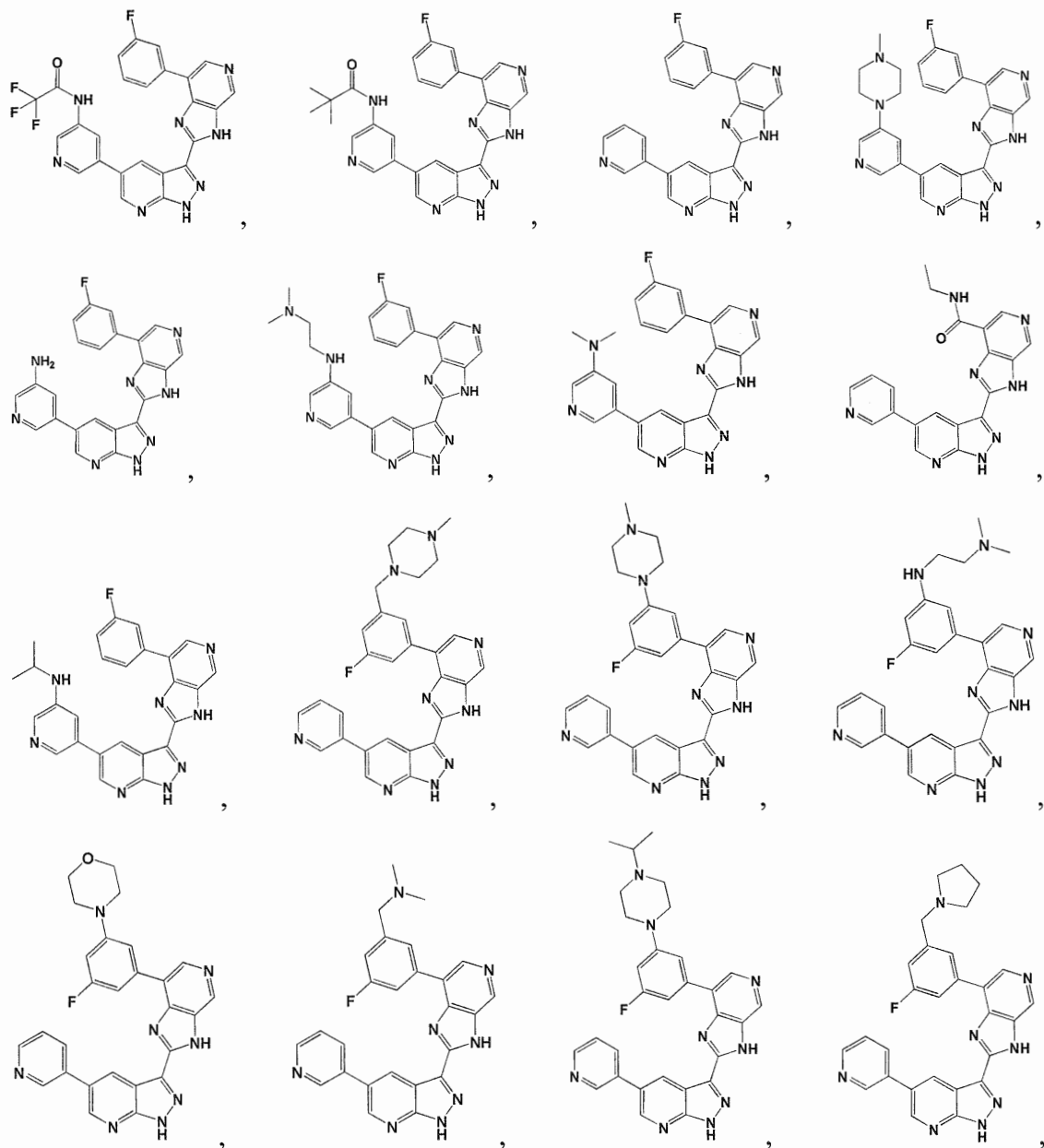


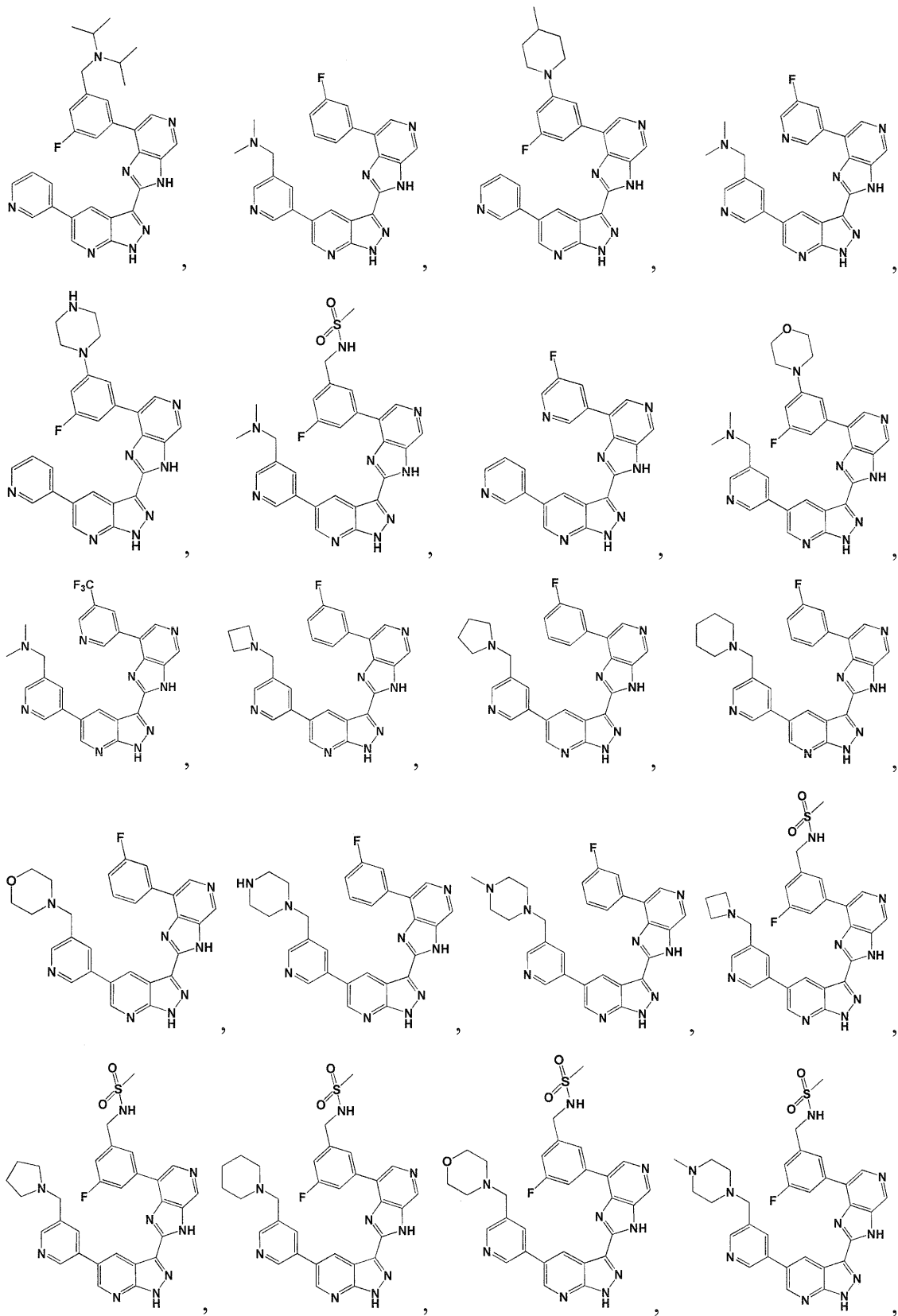
2. The compound of claim 1 wherein aryl is phenyl.
3. The compound of claim 1 wherein heteroaryl is pyridinyl.
4. The compound of claim 1 wherein heterocyclyl is selected from the group consisting of azetidiny, pyrrolidinyl, morpholinyl, piperazinyl and piperidinyl.
5. The compound of claim 1 wherein R^2 is selected from the group consisting of H, $-(C_{1-9} \text{ alkyl})_n \text{heterocyclyl}(R^8)_q$, $-NHC(=O)R^{11}$ and $-(C_{1-9} \text{ alkyl})_n N(R^9)_2$ and R^1 and R^3 are both H.
6. The compound of claim 5 wherein R^2 is $-\text{CH}_2 N(R^9)_2$ or $-N(R^9)_2$.
7. The compound of claim 6 wherein R^9 is independently selected from the group consisting of H, Me, Et, $-\text{CH}_2 \text{phenyl}$ and $-\text{CH}_2 \text{carbocyclyl}$.
8. The compound of claim 5 wherein R^2 is $-NHC(=O)R^{11}$.
9. The compound of claim 8 wherein R^{11} is selected from the group consisting of $-C_{1-5} \text{ alkyl}$, carbocyclyl, $\text{phenyl}(R^6)_q$, and $-\text{CH}_2 \text{phenyl}(R^6)_q$.
10. The compound as in any of claims 6-9, in which R^4 is $\text{phenyl}(R^{13})_q$.
11. The compound as in any of claims 6-9, in which R^4 is $-\text{heterocyclyl}(R^{14})_q$.
12. The compound as in any of claims 6-9, in which R^4 is $-\text{heteroaryl}(R^{15})_q$.
13. The compound of claim 10 wherein R^{13} is one substituent attached to the phenyl comprising a fluorine atom.
14. The compound of claim 10 wherein R^{13} is two substituents each attached to the phenyl comprising a fluorine atom and either a $-(\text{CH}_2)_n N(R^5)_2$ or a $-(\text{CH}_2)_n \text{NHSO}_2 R^{18}$.

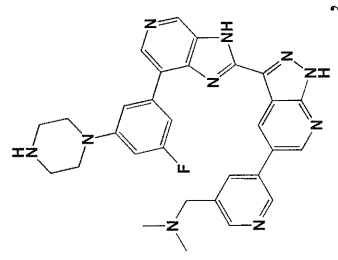
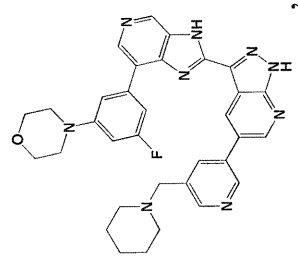
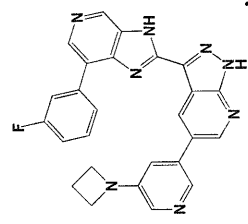
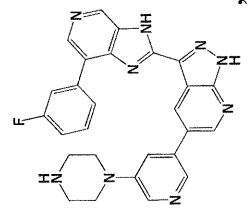
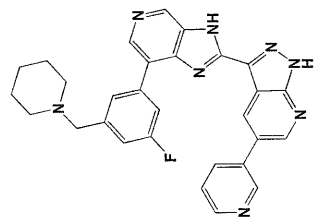
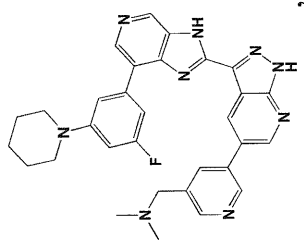
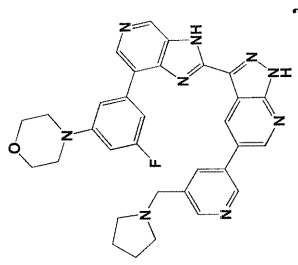
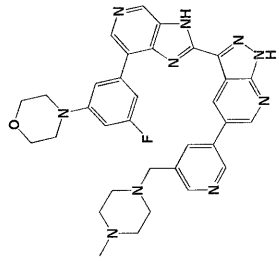
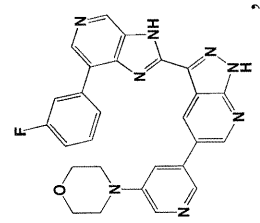
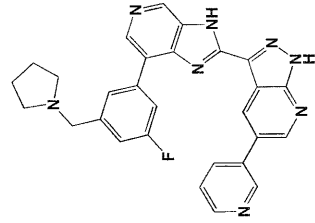
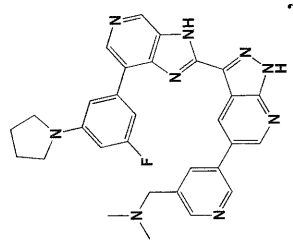
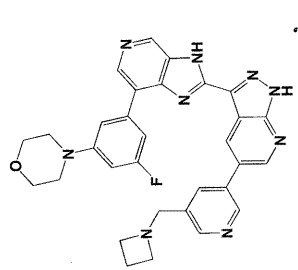
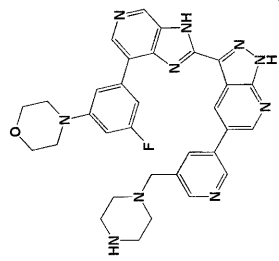
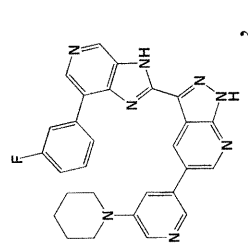
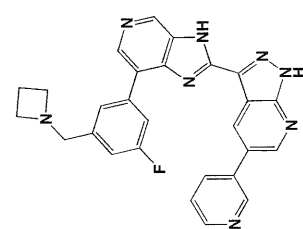
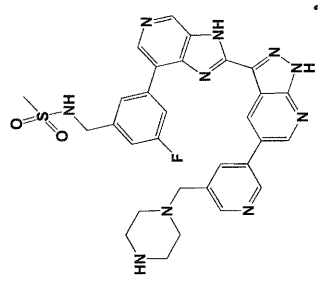
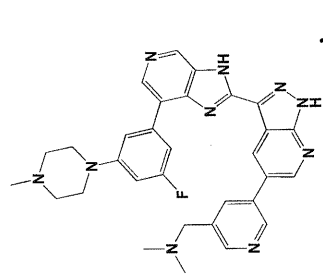
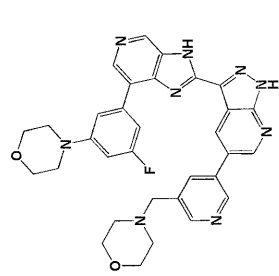
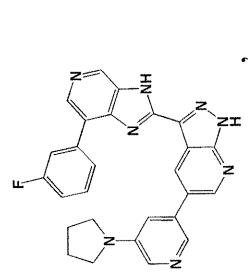
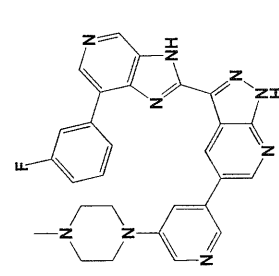
15. The compound of claim 11 wherein the heterocyclyl is selected from the group consisting of piperazinyl and piperidinyl; and the R¹⁴ is H or Me.

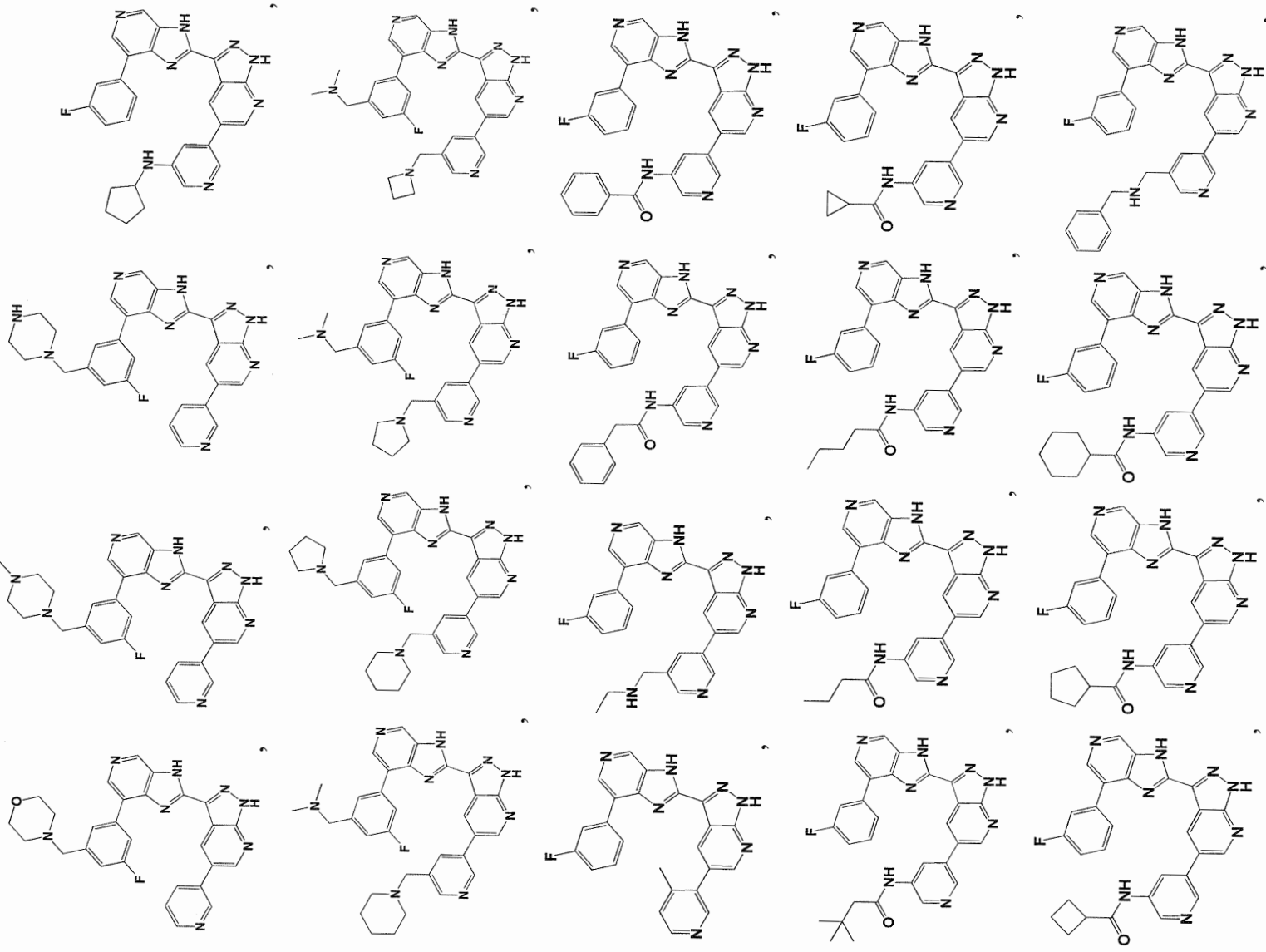
16. The compound of claim 12 wherein the heteroaryl is selected from the group consisting of pyridinyl, furyl, thiophenyl and imidazolyl; and R¹⁵ is lower alkyl or halide.

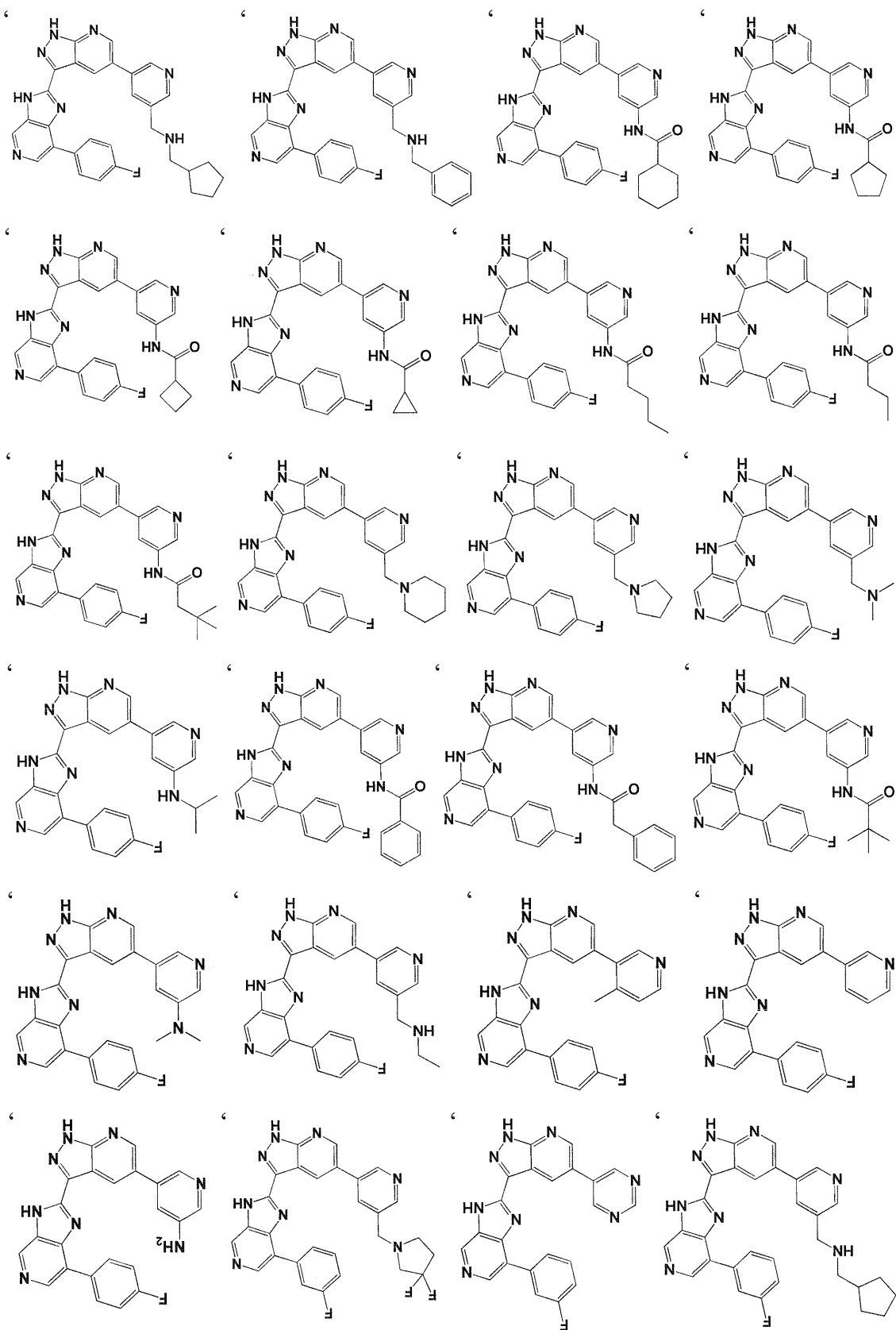
17. The compound of claim 1 having a structure selected from the group consisting of:

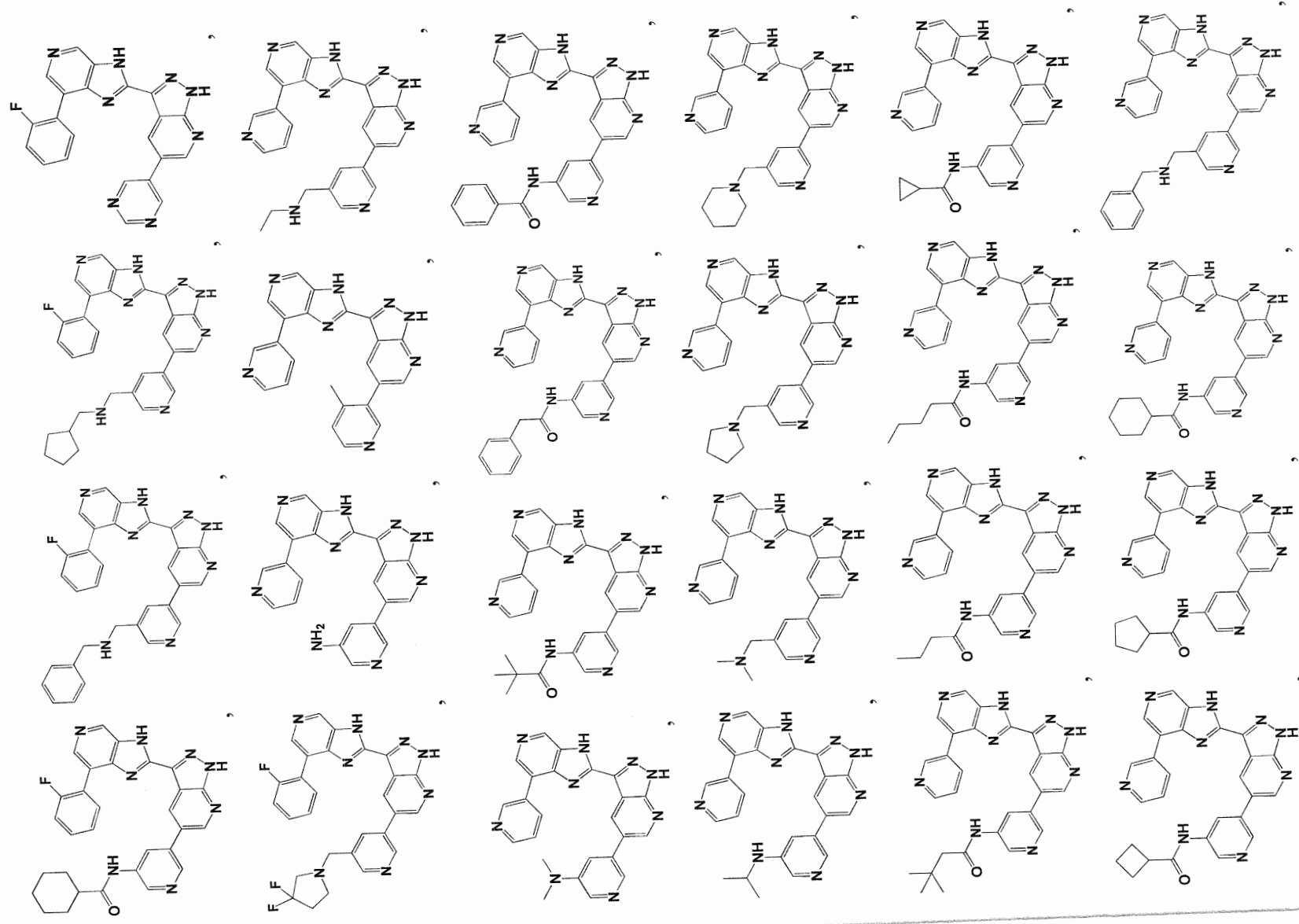


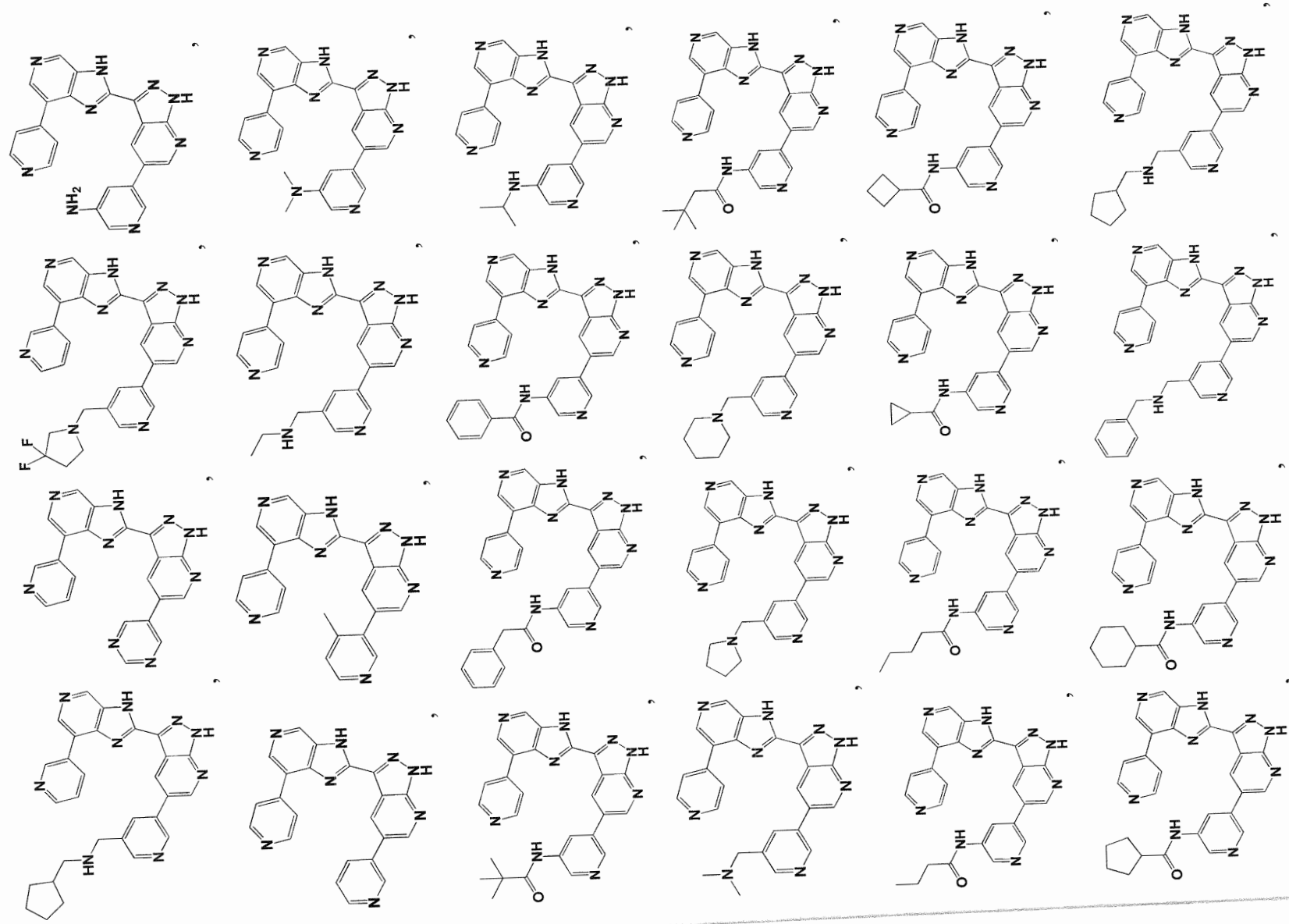


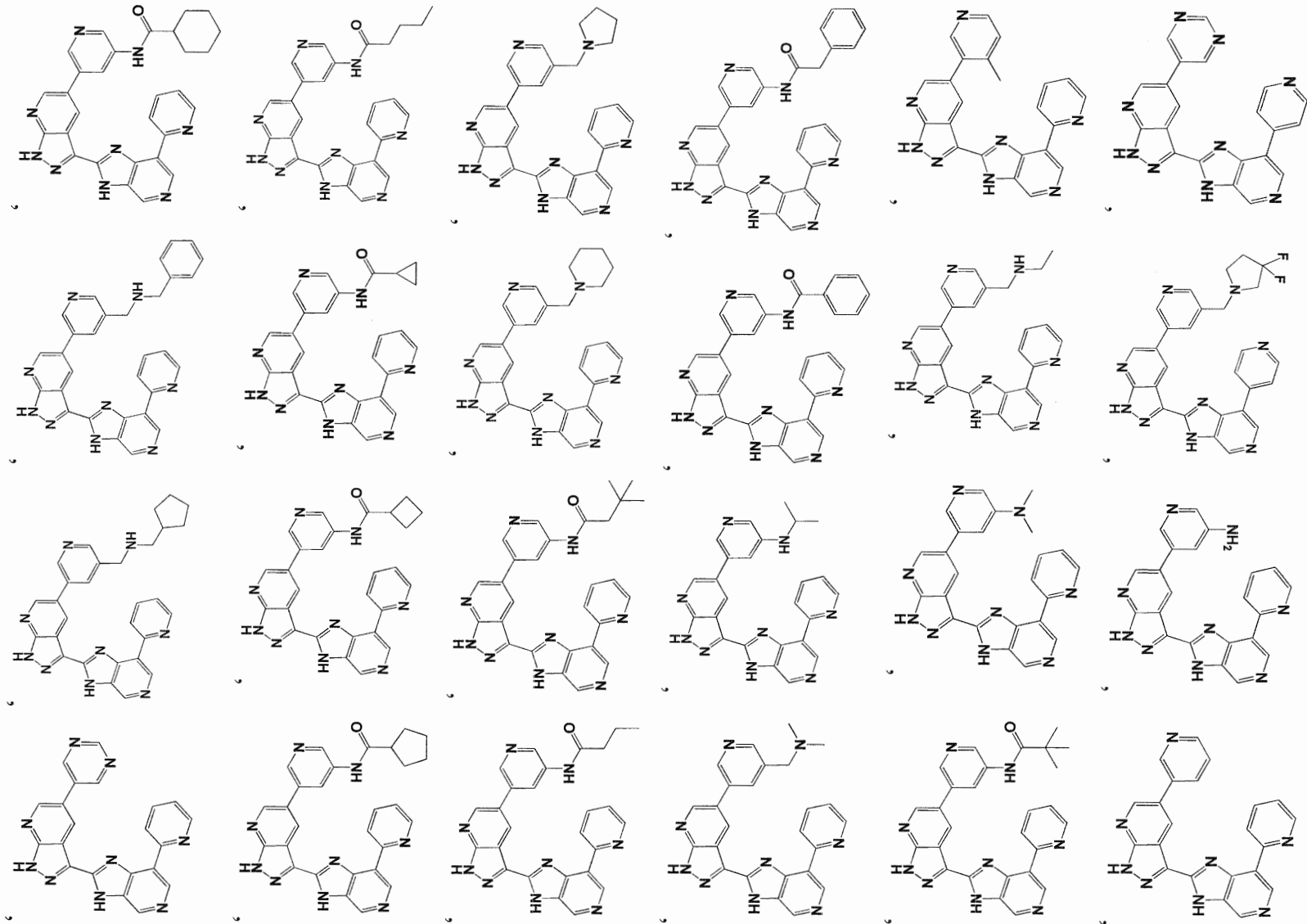




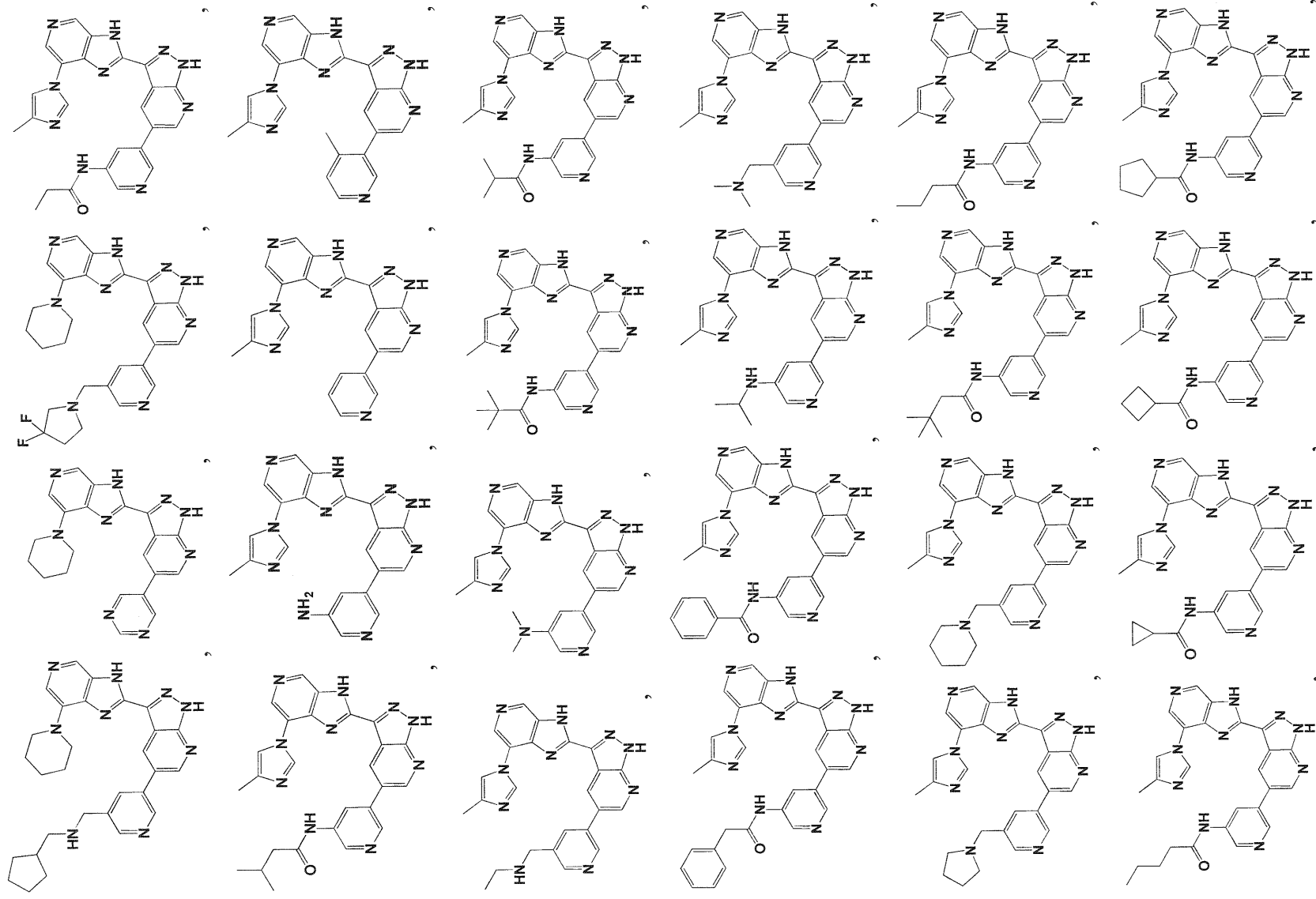


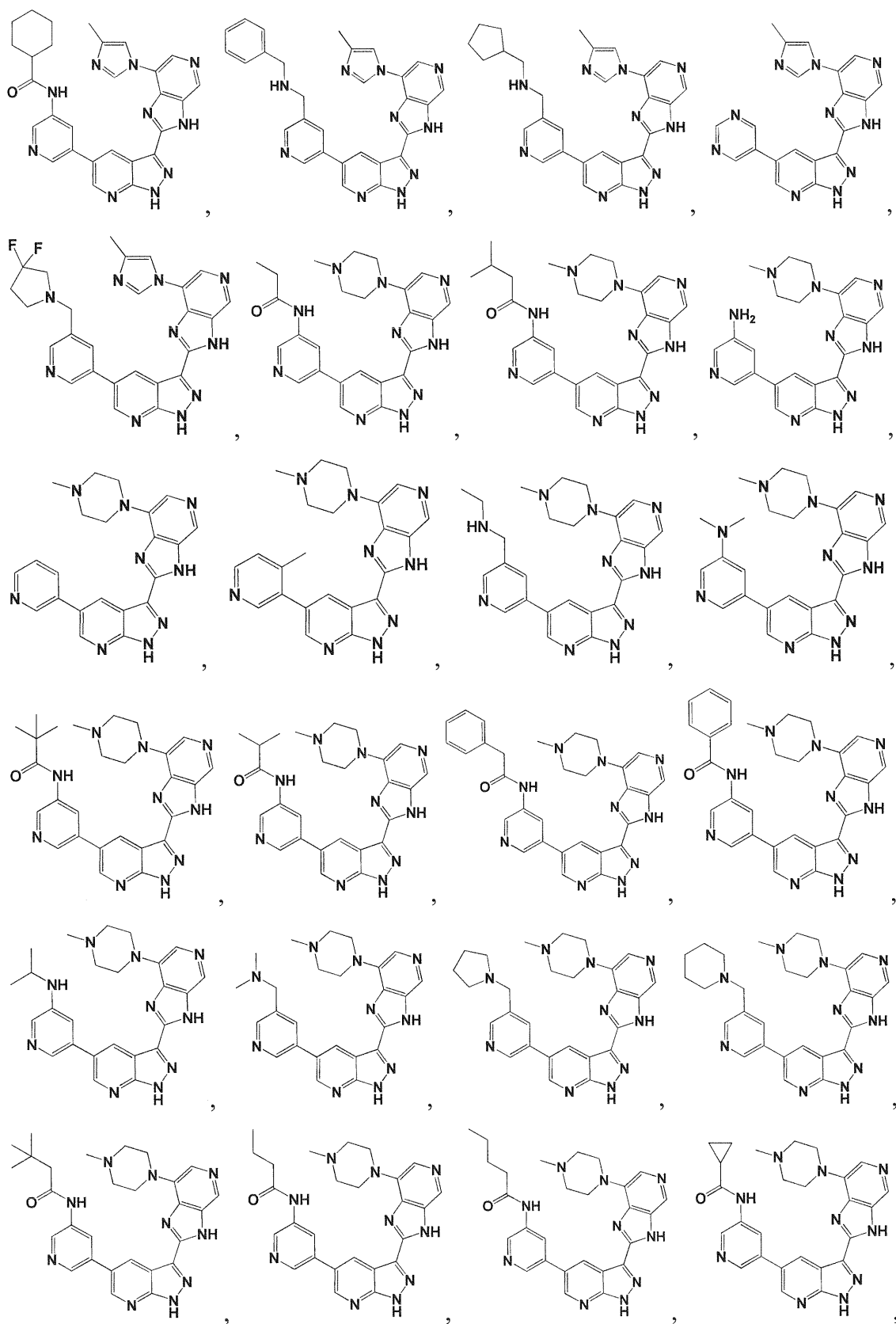


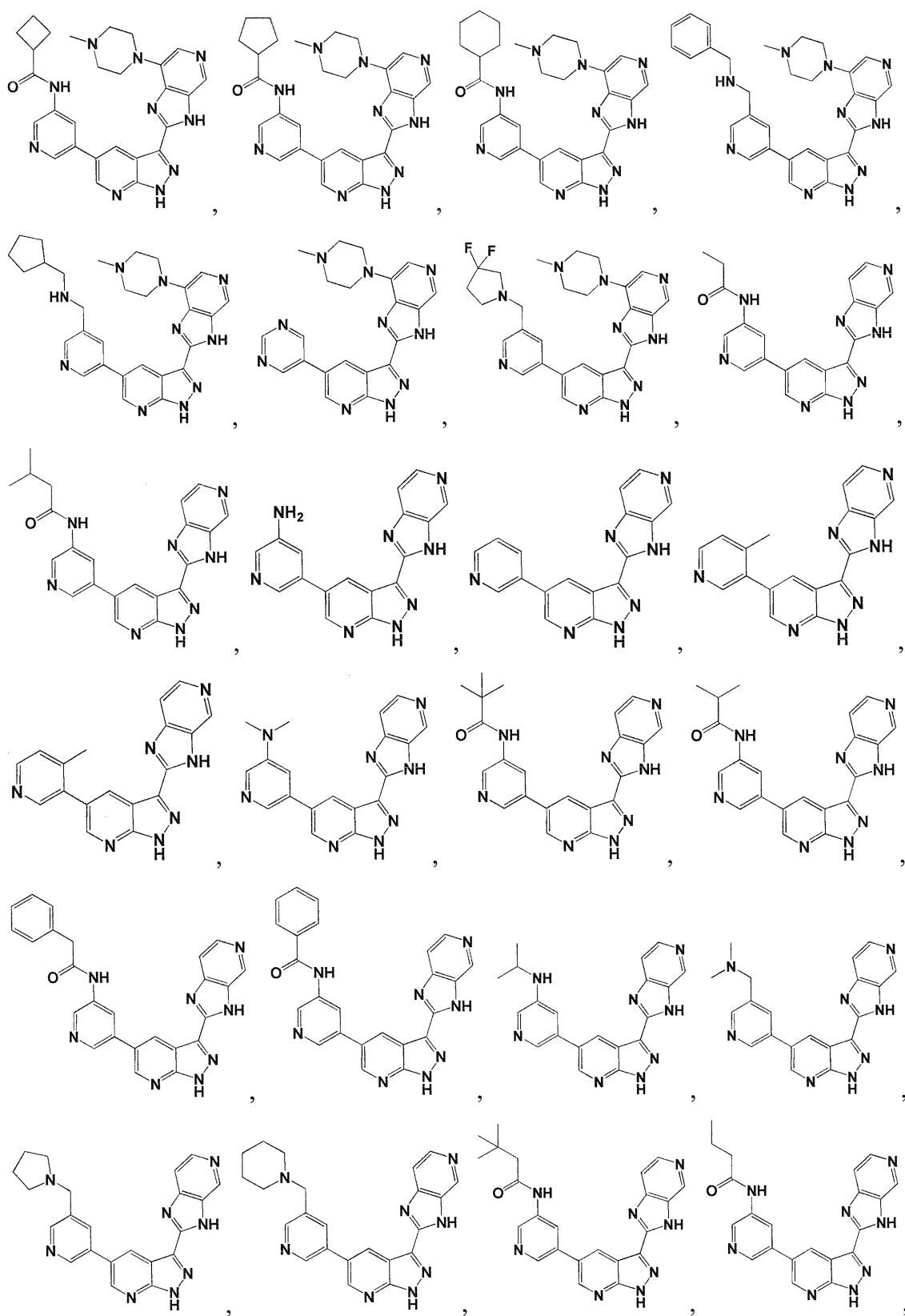


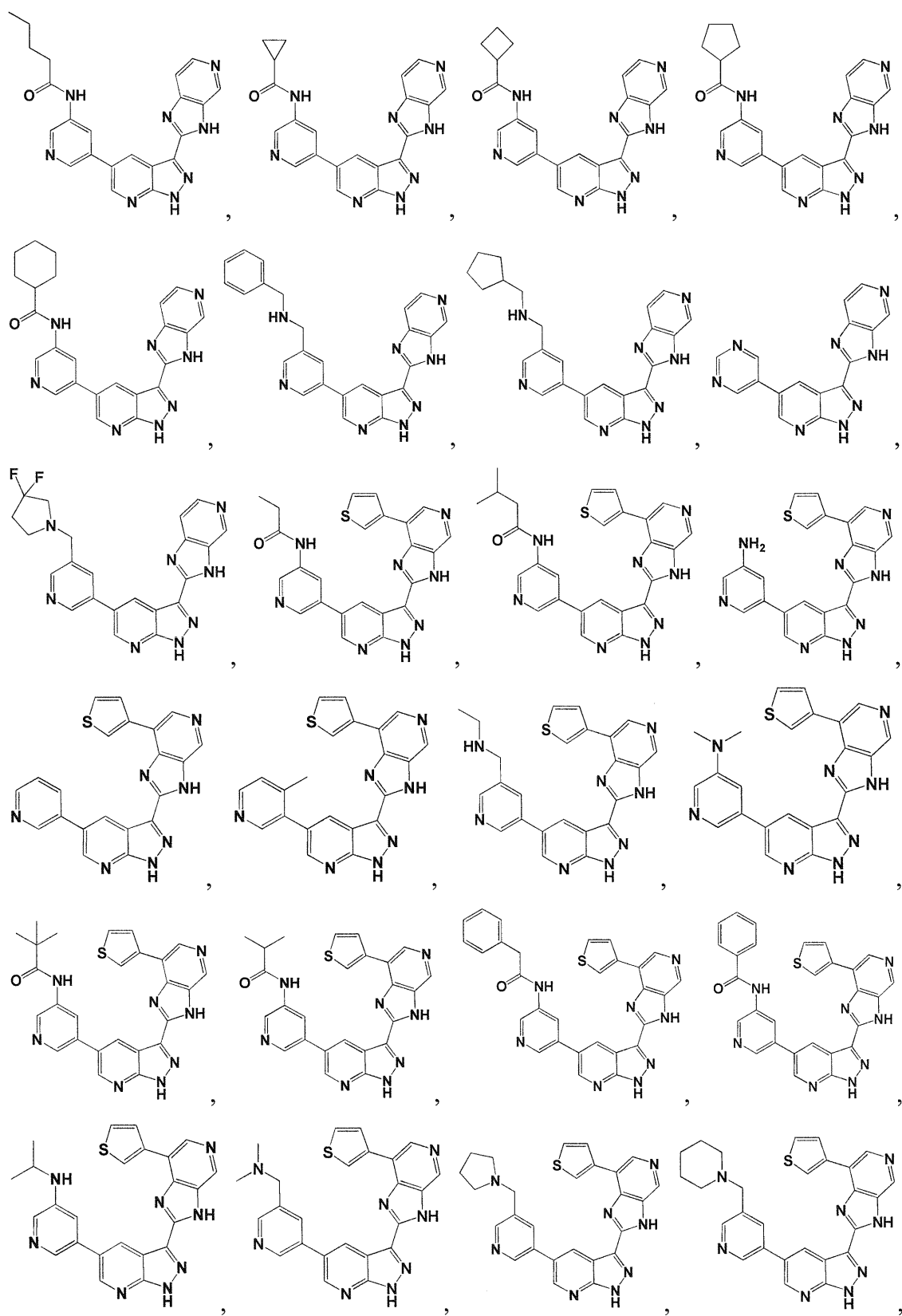


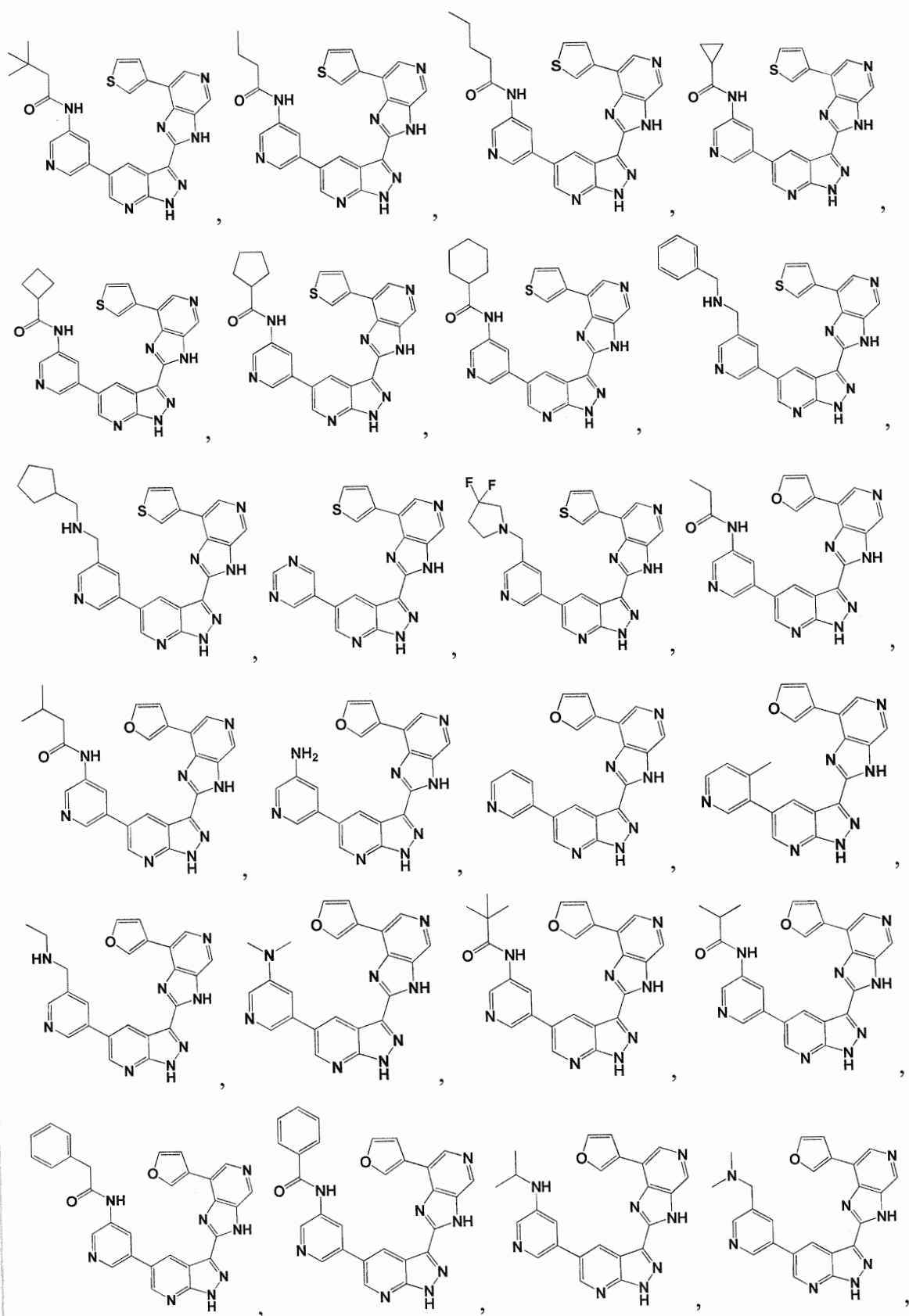


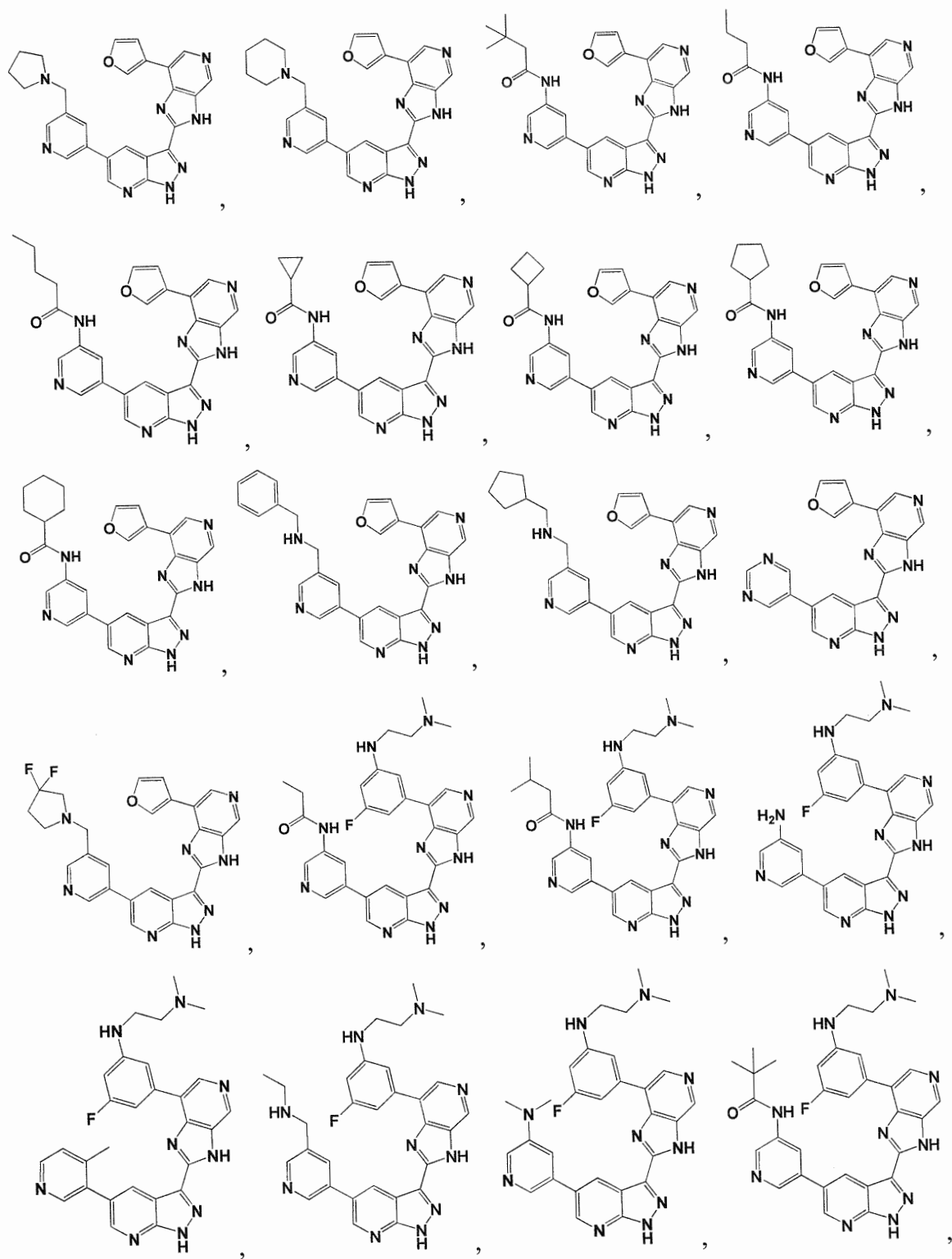


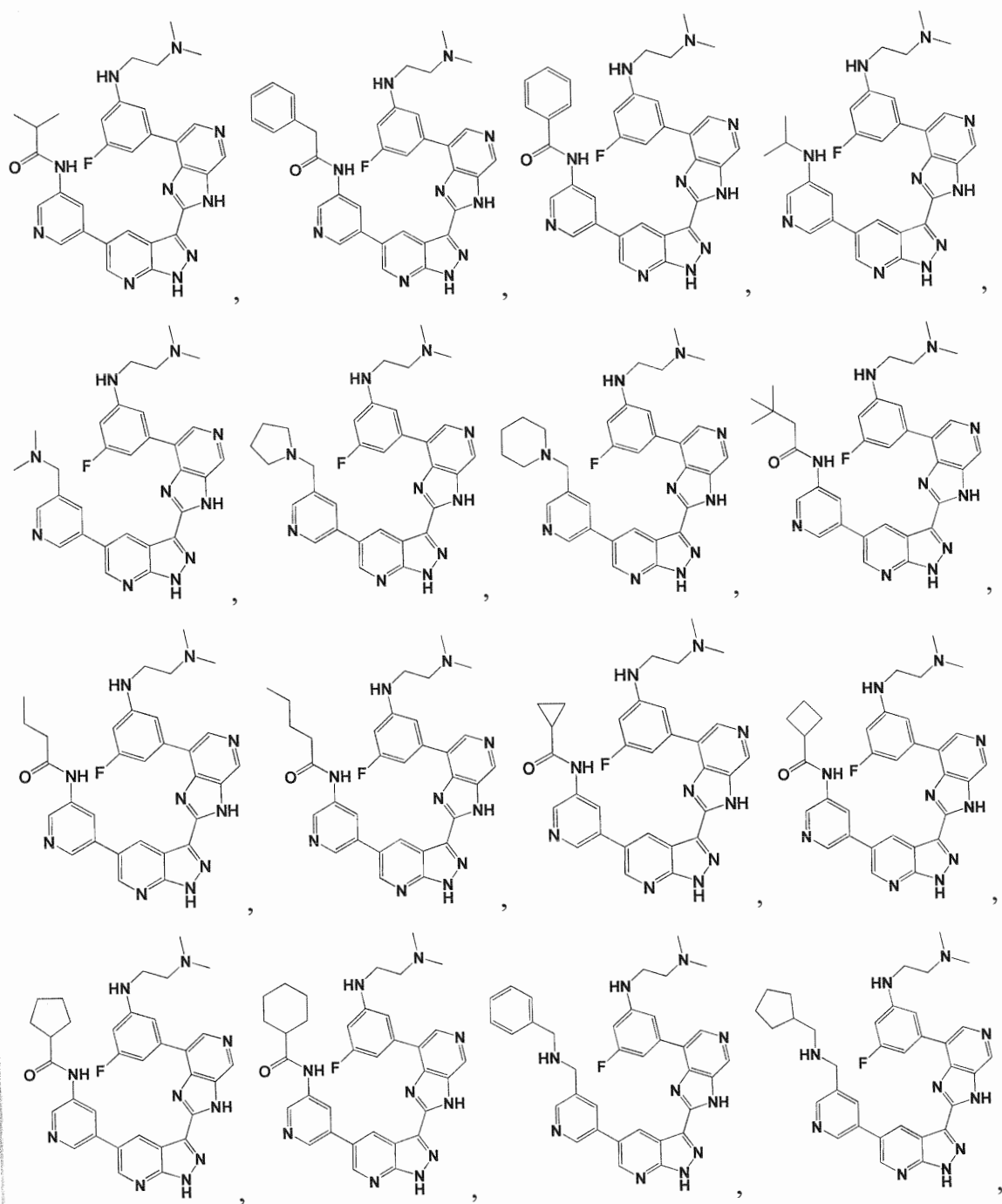


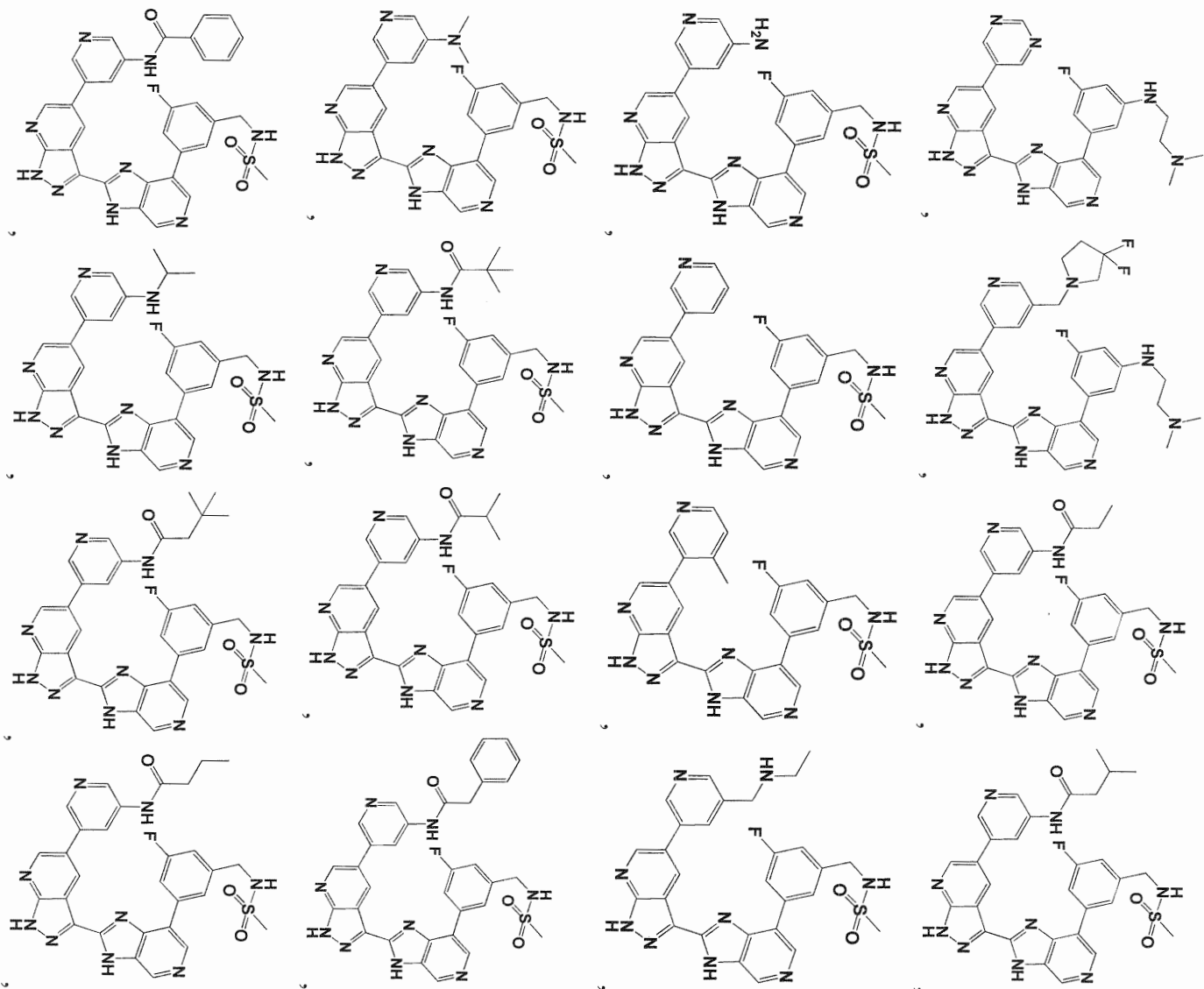




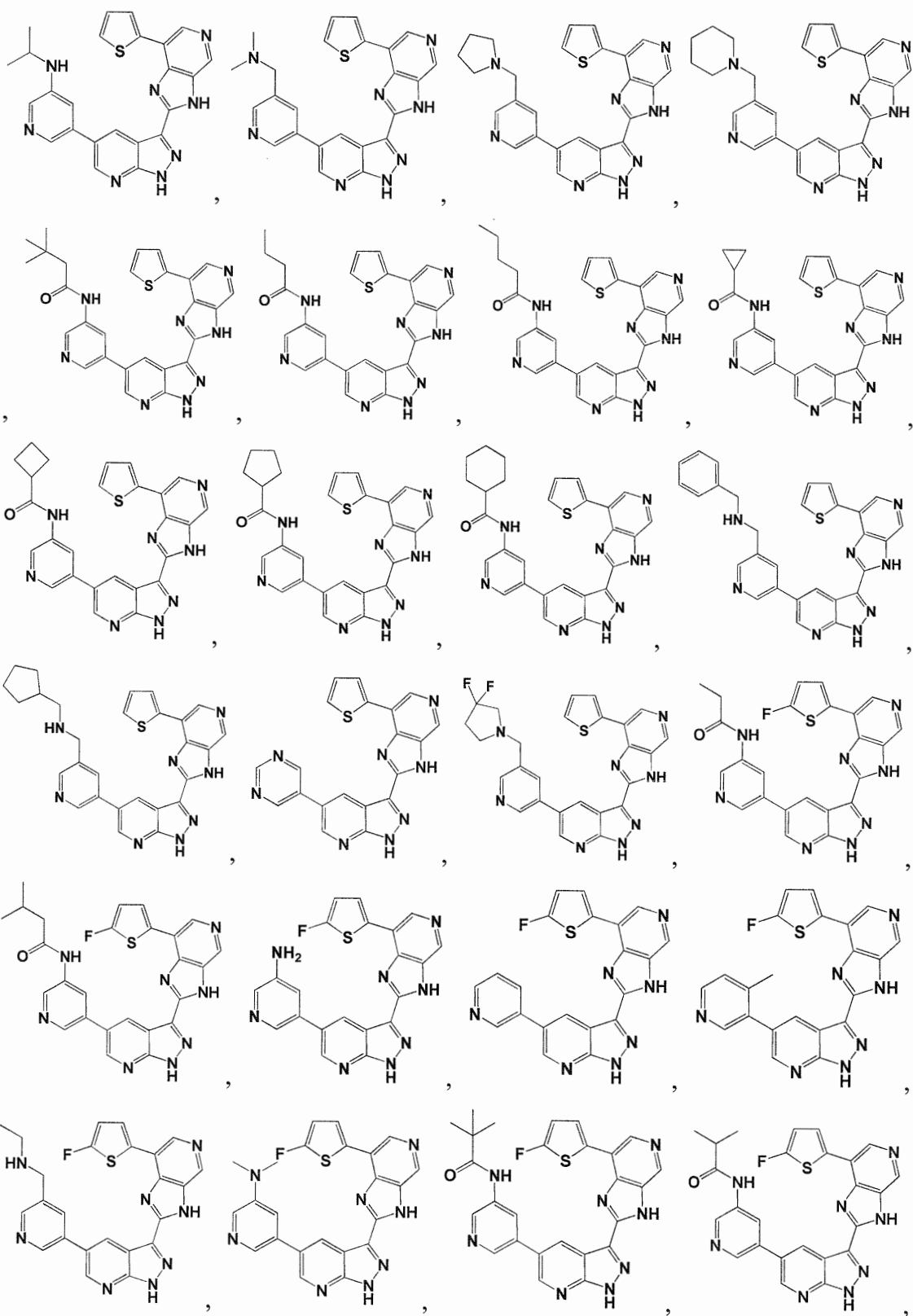


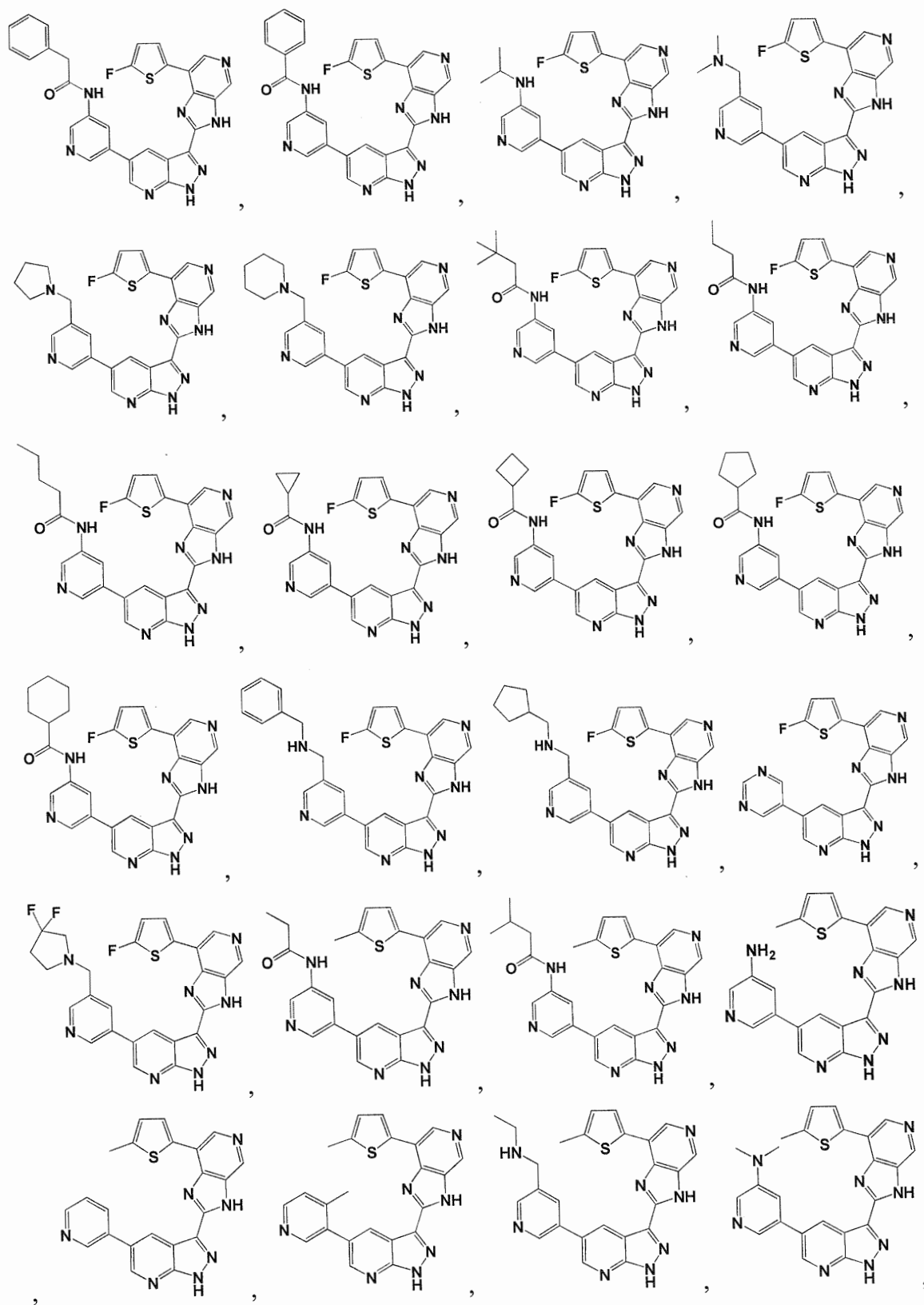


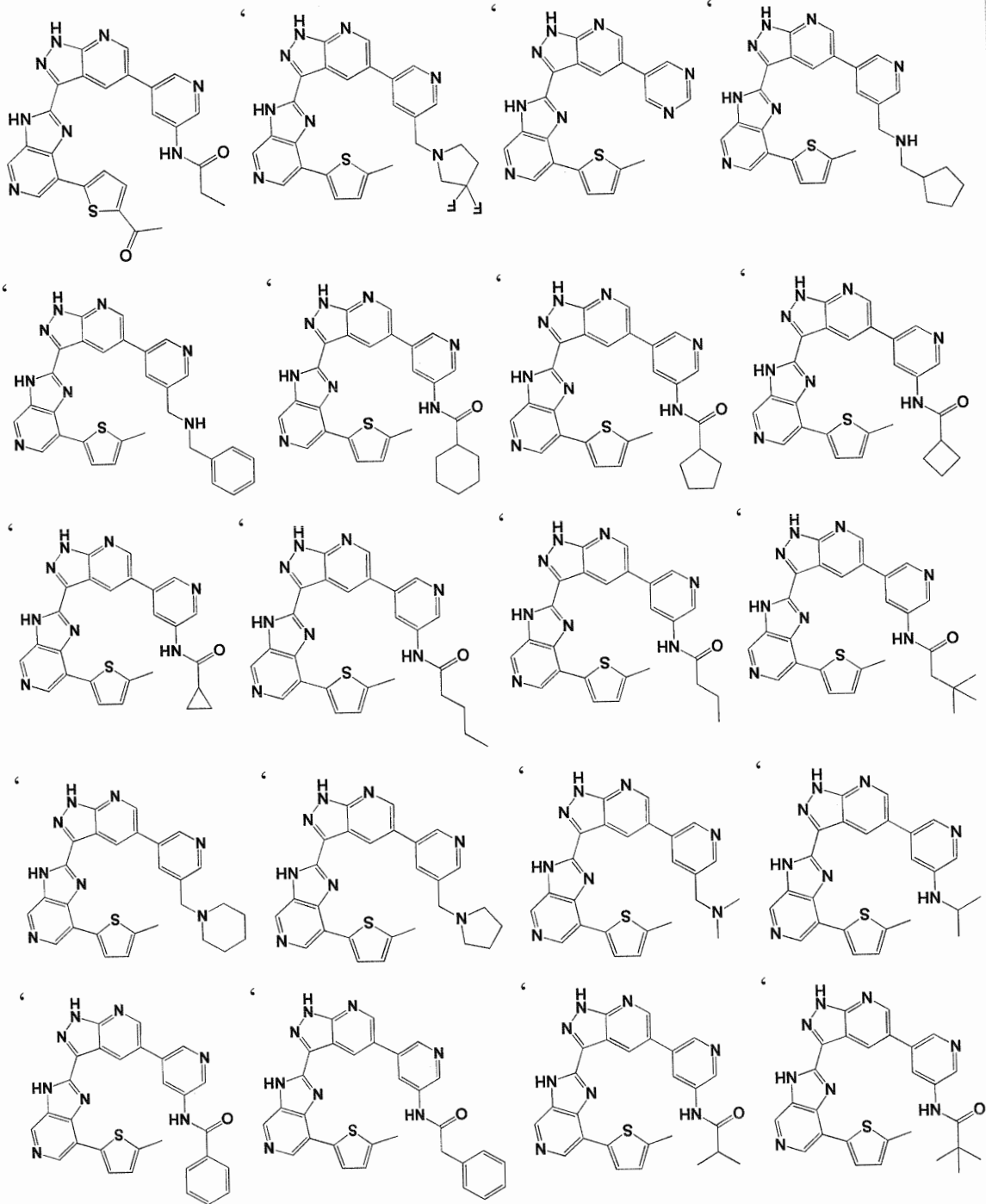


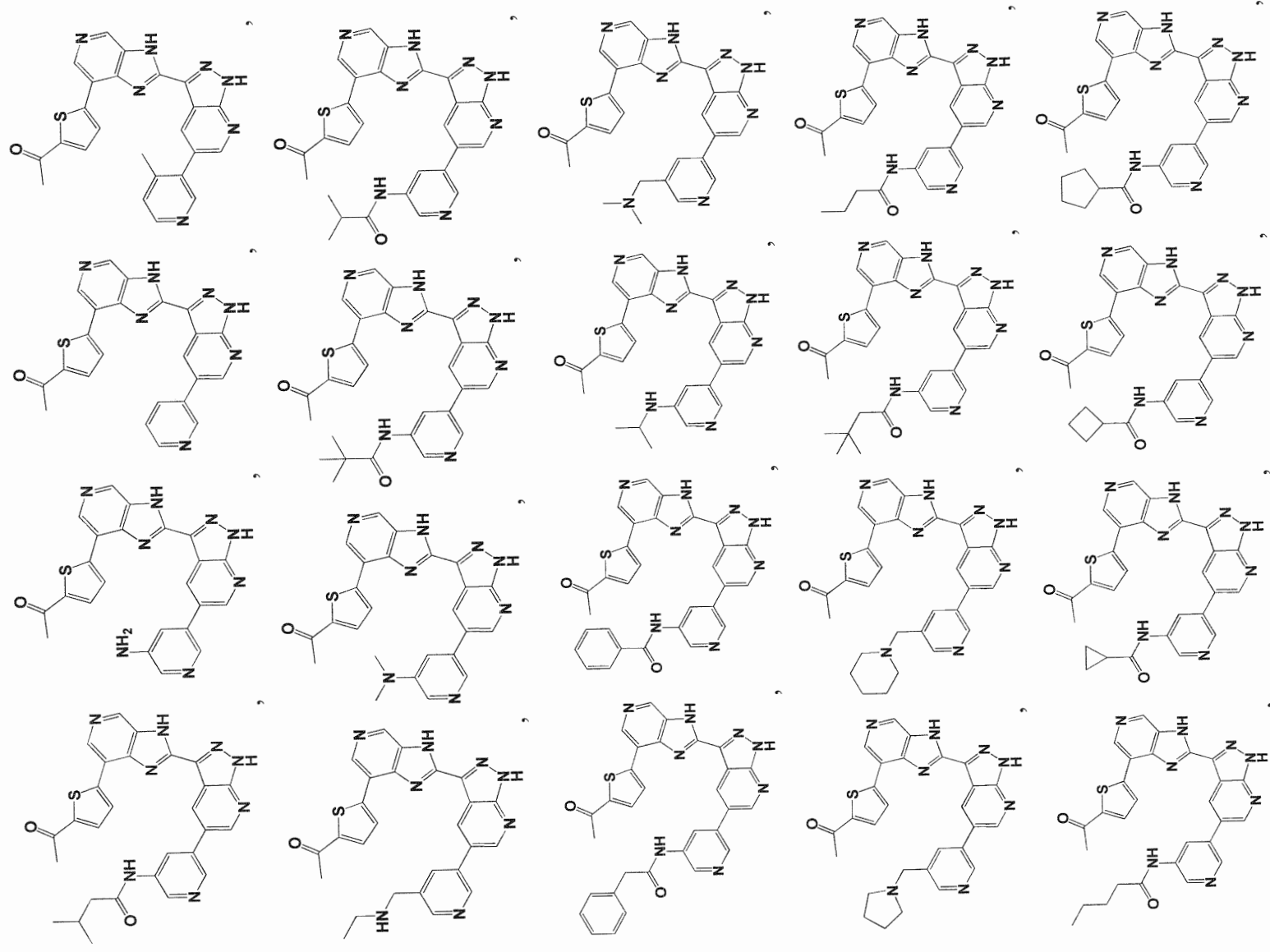


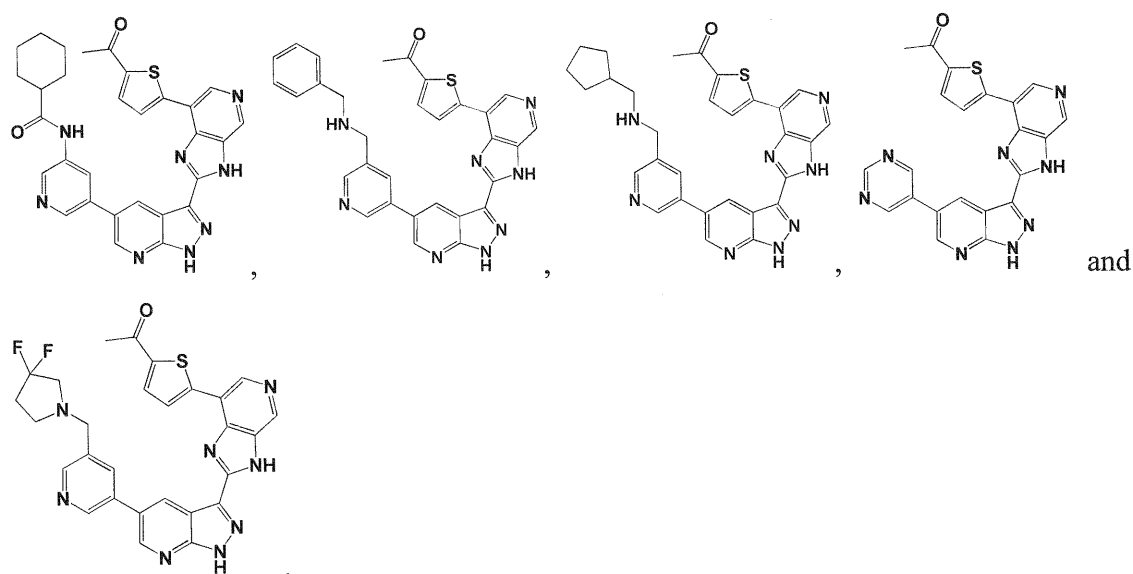




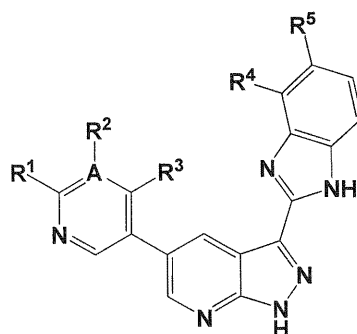








18. A compound or pharmaceutically acceptable salt or prodrug thereof having the structure of Formula II:



II

wherein:

R^1 and R^2 are independently selected from the group consisting of H, lower alkyl, halide, $-(C_{1-9} \text{ alkyl})_n \text{ aryl}(R^6)_q$, $-(C_{1-9} \text{ alkyl})_n \text{ heteroaryl}(R^7)_q$, $-(C_{1-9} \text{ alkyl})_n \text{ heterocyclyl}(R^8)_q$, $-(C_{1-9} \text{ alkyl})_n N(R^9)_2$, $-OR^{10}$ and $-NHC(=O)R^{11}$;

R^3 is selected from the group consisting of H, halide and lower alkyl;

with the proviso that at least two of R^1 , R^2 and R^3 are H;

R^4 and R^5 are independently selected from the group consisting of H, $-C(=O)N(R^{12})_2$, $-\text{aryl}(R^{13})_q$, $-\text{heterocyclyl}(R^{14})_q$, and $-\text{heteroaryl}(R^{15})_q$;

with the proviso that at least one of R^4 and R^5 is H;

each R^6 is a substituent attached to the aryl ring and independently selected from the group consisting of H, $-C_{1-9}$ alkyl, halide, CF_3 and CN;

each R^7 is a substituent attached to the heteroaryl ring and independently selected from the group consisting of H, $-C_{1-9}$ alkyl, halide, CF_3 and CN;

each R^8 is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, halide, $-(C_{1-3} \text{ alkyl})_n \text{ aryl}(R^6)_q$, and $-C_{1-4}$ alkyl;

each R^9 is independently selected from the group consisting of H, $-C_{1-9}$ alkyl, $-(C_{1-3} \text{ alkyl})_n \text{ aryl}(R^6)_q$, $-(C_{1-3} \text{ alkyl})_n \text{ carbocyclyl}$ and $-(C_{1-9} \text{ alkyl})N(R^{16})_2$;

alternatively, two adjacent R^9 or two adjacent R^{12} , may be taken together with the atoms to which they are attached to form a heterocyclyl(R^{17}) $_q$;

R^{10} is selected from the group consisting of H, $-CF_3$, $-(C_{1-3} \text{ alkyl})_n \text{ aryl}(R^6)_q$, and $-C_{1-9}$ alkyl;

R^{11} is selected from the group consisting of $-(C_{1-3} \text{ alkyl})_n \text{ aryl}(R^6)_q$, $-(C_{1-3} \text{ alkyl})_n \text{ carbocyclyl}$, $-C_{1-9}$ alkyl and $-CF_3$;

each R^{12} is independently selected from the group consisting of H, $-(C_{1-9} \text{ alkyl})_n \text{ aryl}(R^6)_q$ and $-C_{1-9}$ alkyl;

each R^{13} is a substituent attached to the aryl ring and independently selected from the group consisting of H, halide, $-CF_3$, CN, $-(C_{1-3} \text{ alkyl})_n \text{ heterocyclyl}(R^8)_q$, $-(C_{1-9} \text{ alkyl})_n N(R^9)_2$ and $-(C_{1-9} \text{ alkyl})_n NHSO_2 R^{18}$;

each R^{14} is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, lower alkyl, halide, $-CF_3$ and CN;

each R^{15} is a substituent attached to the heteroaryl ring and independently selected from the group consisting of H, lower alkyl, halide, $-CF_3$, CN, $-C(=O)(C_{1-3} \text{ alkyl})$, $-(C_{1-9} \text{ alkyl})_n N(R^9)_2$ and $-(C_{1-9} \text{ alkyl})_n NHSO_2 R^{18}$;

each R^{16} is independently selected from the group consisting of H and lower alkyl;

each R^{17} is a substituent attached to the heterocyclyl ring and independently selected from the group consisting of H, $-(C_{1-9} \text{ alkyl})_n \text{ aryl}(R^6)_q$, and $-C_{1-9}$ alkyl;

each R^{18} is a lower alkyl;

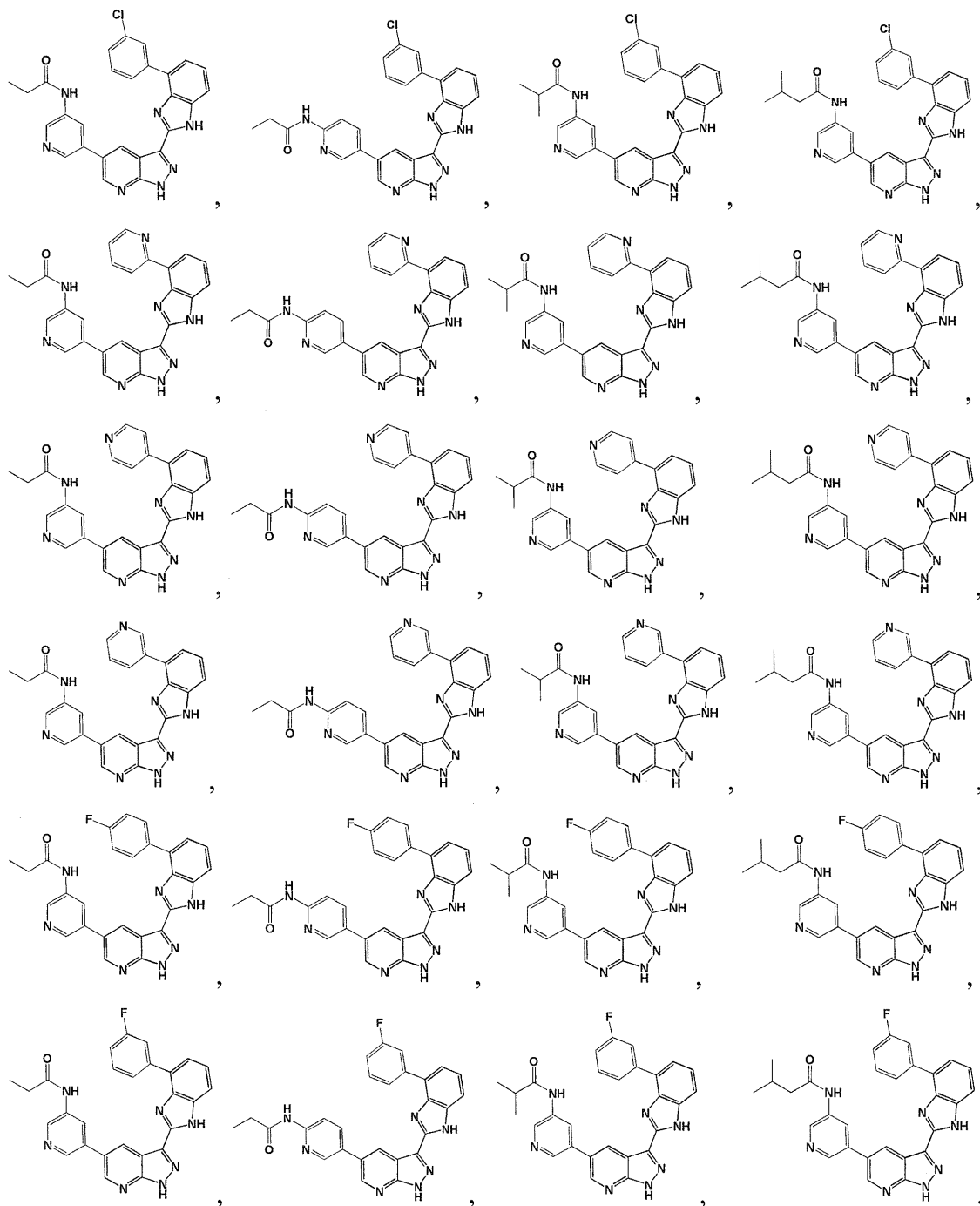
A is N or C;

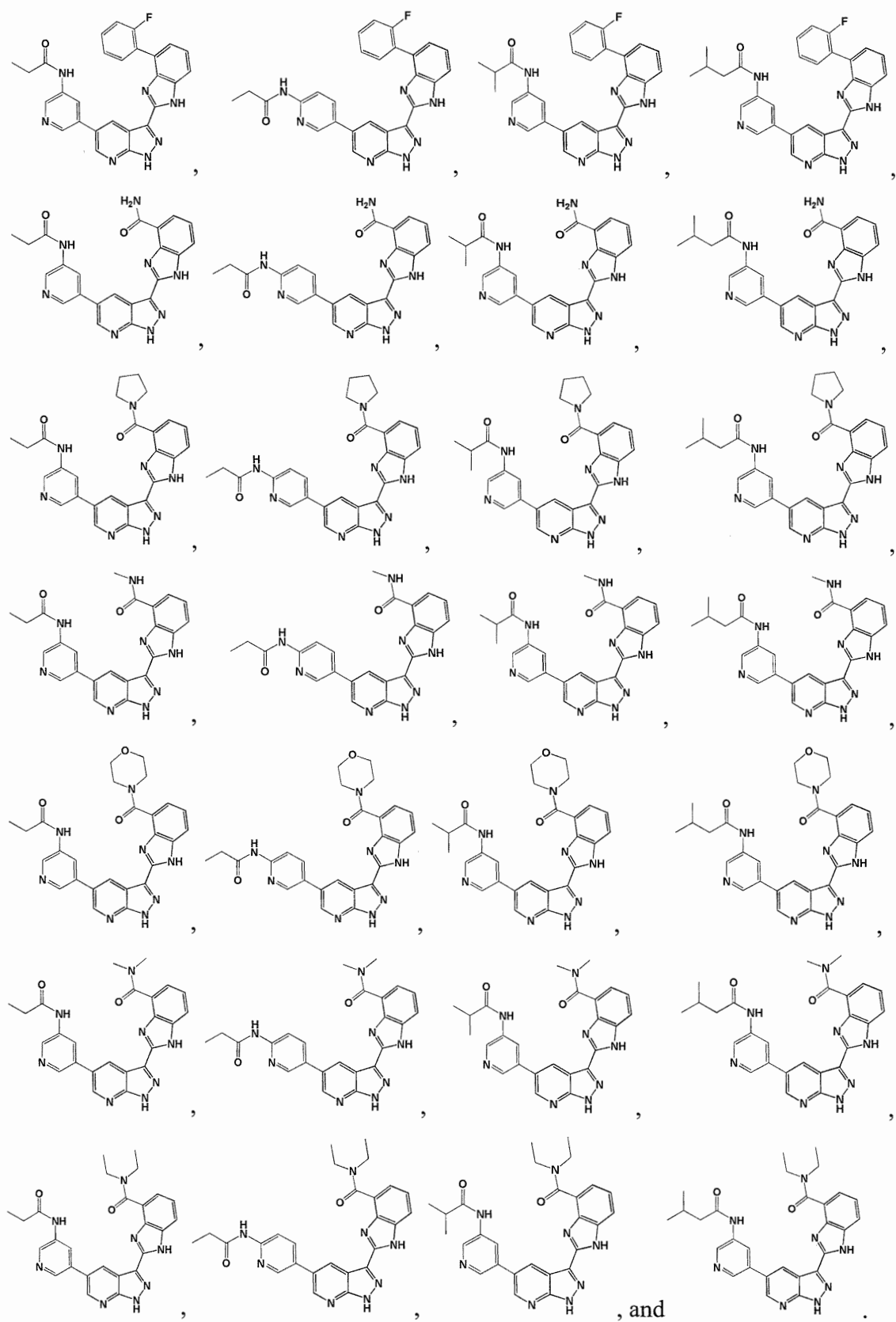
with the proviso that if A is N then R^2 is nil;

each q is an integer of 1 to 5;

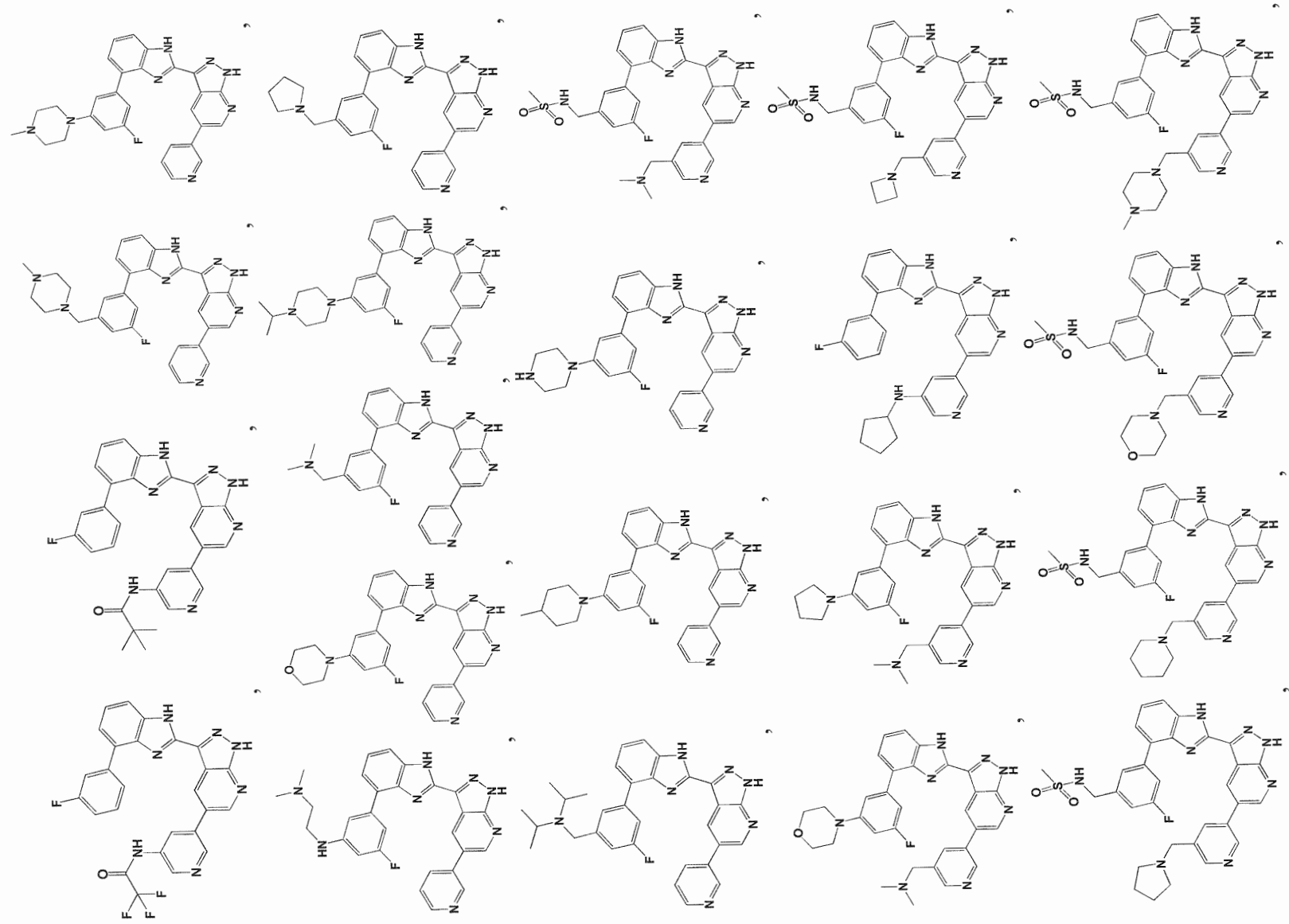
each n is an integer of 0 or 1; and

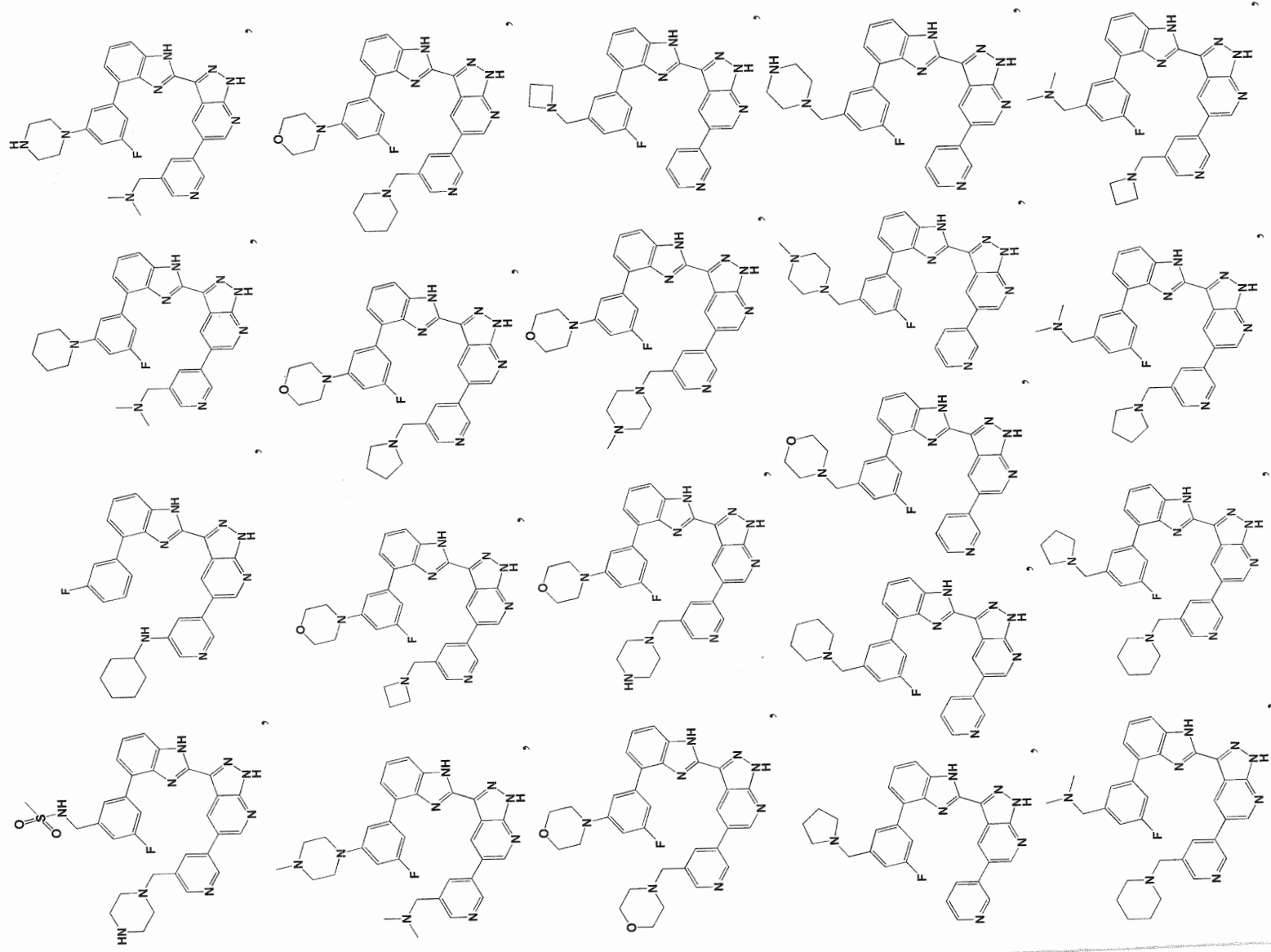
with the proviso that Formula II is not a structure selected from the group consisting of:

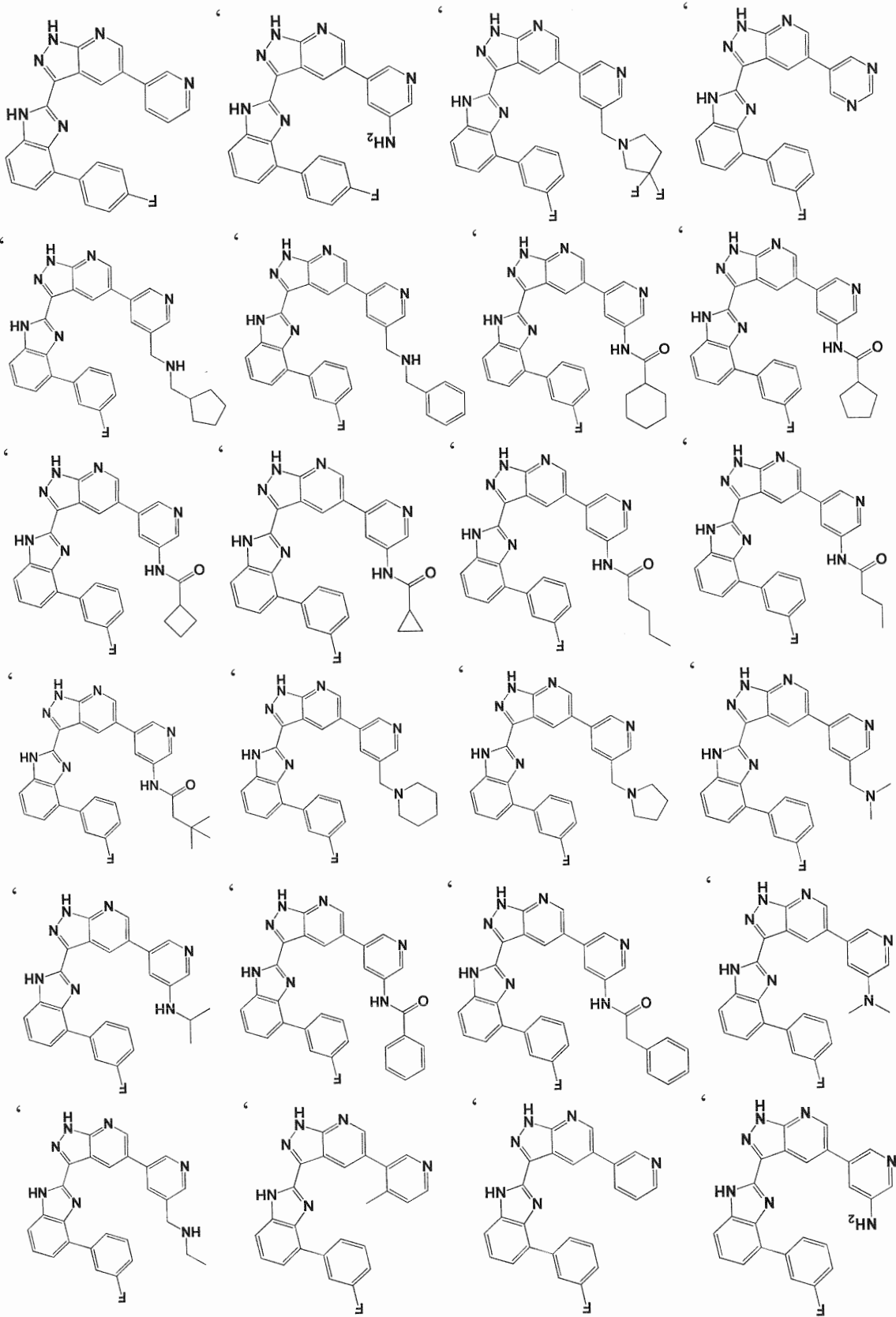


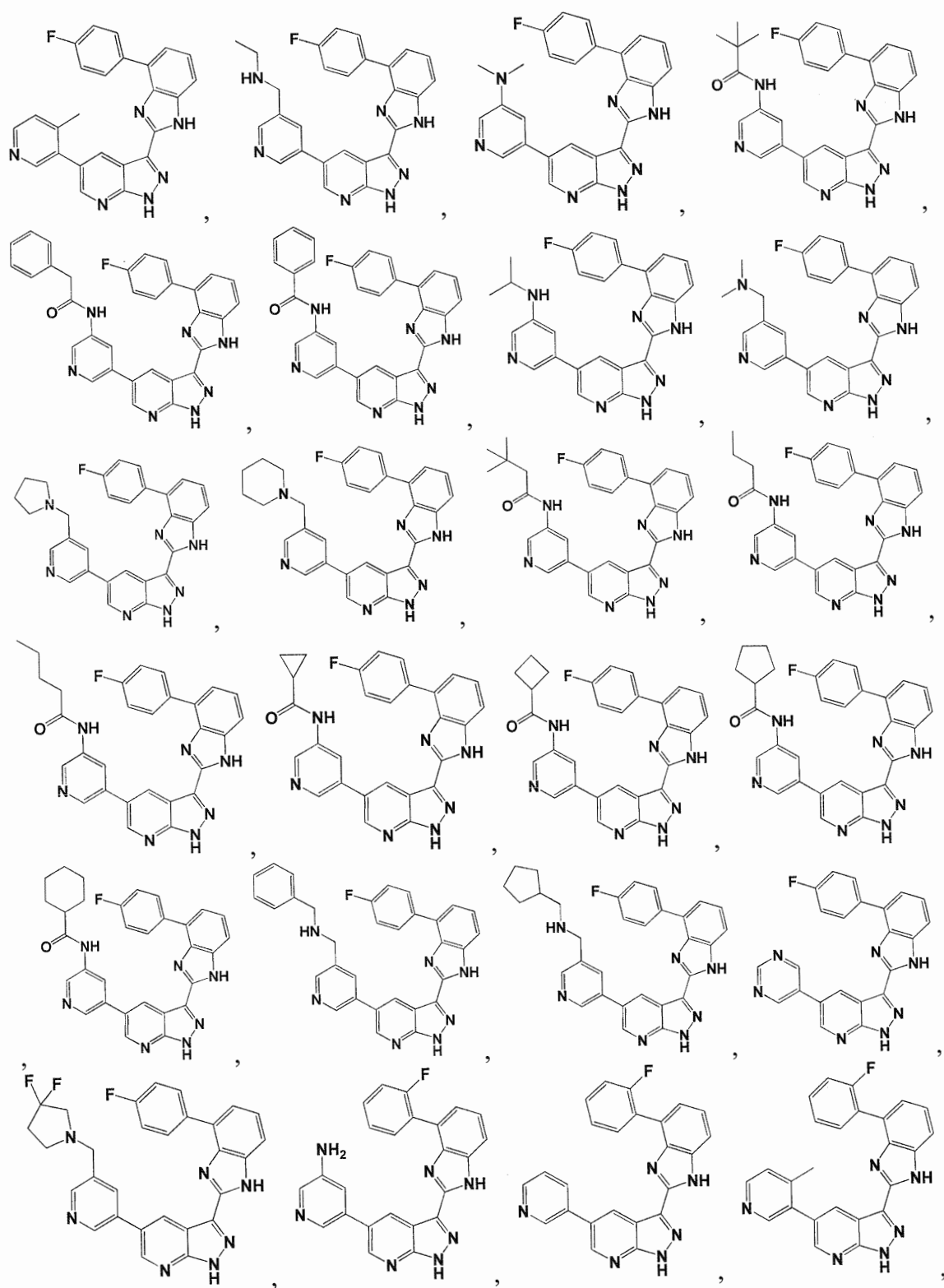


19. The compound of claim 18 wherein aryl is phenyl.
20. The compound of claim 18 wherein heteroaryl is pyridinyl.
21. The compound of claim 18 wherein heterocyclyl is selected from the group consisting of azetidiny, pyrrolidinyl, morpholinyl, piperazinyl and piperidinyl.
22. The compound of claim 18 wherein R^2 is selected from the group consisting of H, $-(C_{1-9} \text{ alkyl})_n \text{heterocyclyl}(R^8)_q$, $-NHC(=O)R^{11}$ and $-(C_{1-9} \text{ alkyl})_n N(R^9)_2$ and R^1 and R^3 are both H.
23. The compound of claim 22 wherein R^2 is $-\text{CH}_2 N(R^9)_2$ or $-N(R^9)_2$.
24. The compound of claim 23 wherein R^9 is independently selected from the group consisting of H, Me, Et, $-\text{CH}_2 \text{phenyl}$ and $-\text{CH}_2 \text{carbocyclyl}$.
25. The compound of claim 22 wherein R^2 is $-NHC(=O)R^{11}$.
26. The compound of claim 25 wherein R^{11} is selected from the group consisting of $-C_{1-5} \text{ alkyl}$, carbocyclyl, $\text{phenyl}(R^6)_q$, and $-\text{CH}_2 \text{phenyl}(R^6)_q$.
27. The compound as in any of claims 23-26, in which R^4 is $\text{phenyl}(R^{13})_q$.
28. The compound as in any of claims 23-26, in which R^4 is $-\text{heterocyclyl}(R^{14})_q$.
29. The compound as in any of claims 23-26, in which R^4 is $-\text{heteroaryl}(R^{15})_q$.
30. The compound of claim 27 wherein R^{13} is one substituent attached to the phenyl comprising a fluorine atom.
31. The compound of claim 27 wherein R^{13} is two substituents each attached to the phenyl comprising a fluorine atom and either a $-(\text{CH}_2)_n N(R^5)_2$ or a $-(\text{CH}_2)_n \text{NH}\text{SO}_2 R^{18}$.
32. The compound of claim 28 wherein the heterocyclyl is selected from the group consisting of piperazinyl and piperidinyl; and the R^{14} is H or Me.
33. The compound of claim 29 wherein the heteroaryl is selected from the group consisting of pyridinyl, furyl, thiophenyl and imidazolyl; and R^{15} is lower alkyl or halide.
34. The compound of claim 18 having a structure selected from the group consisting of:

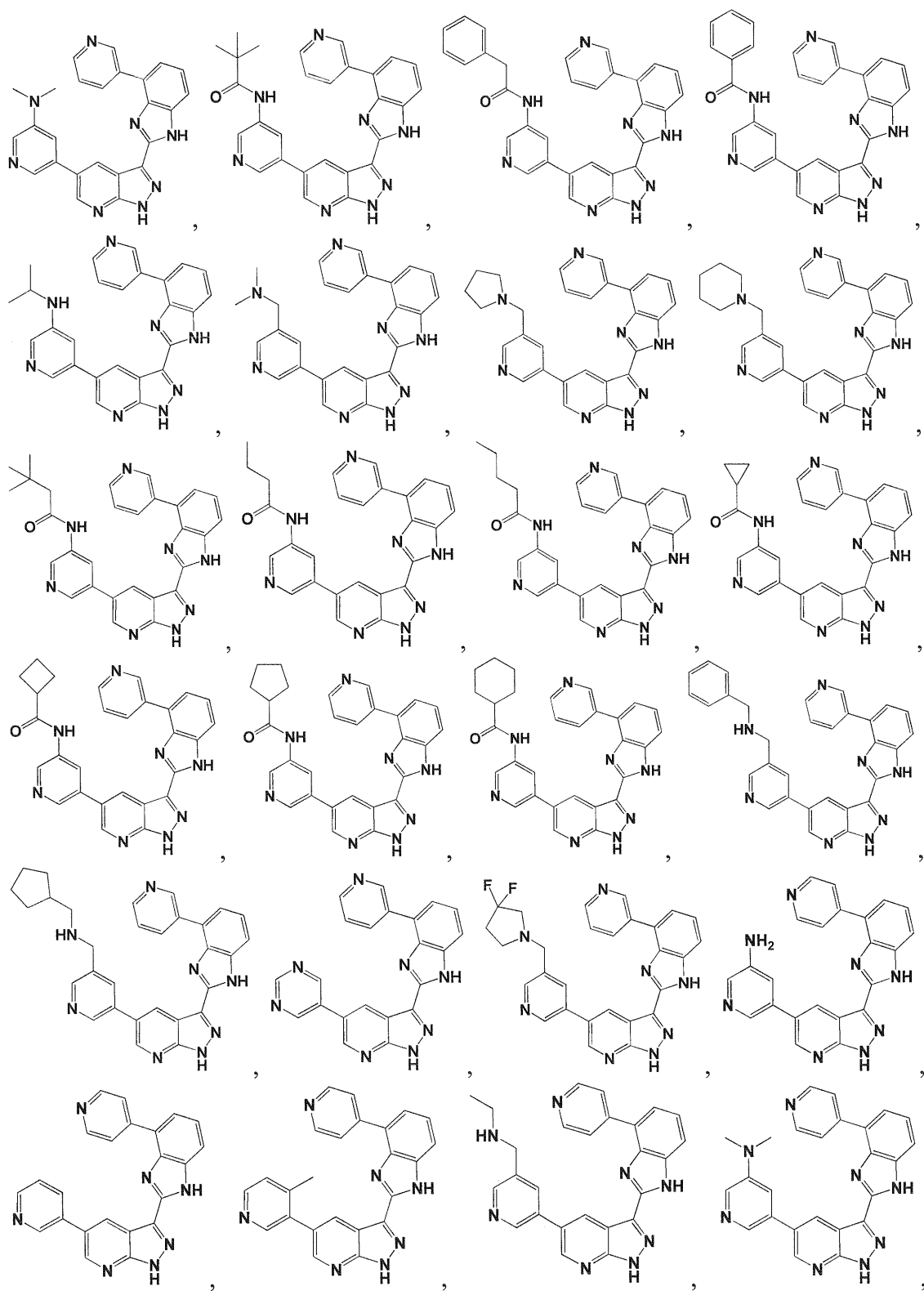


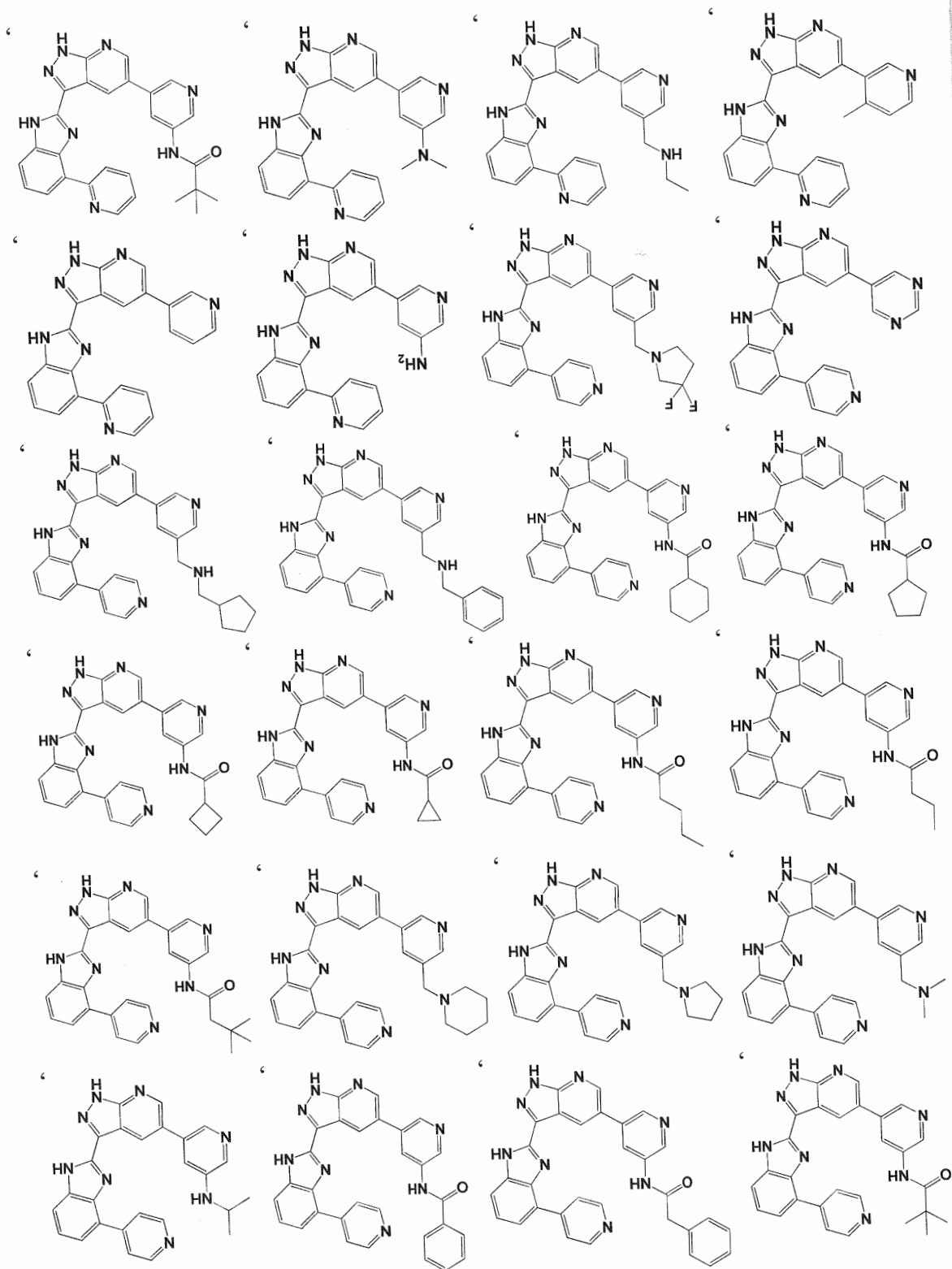


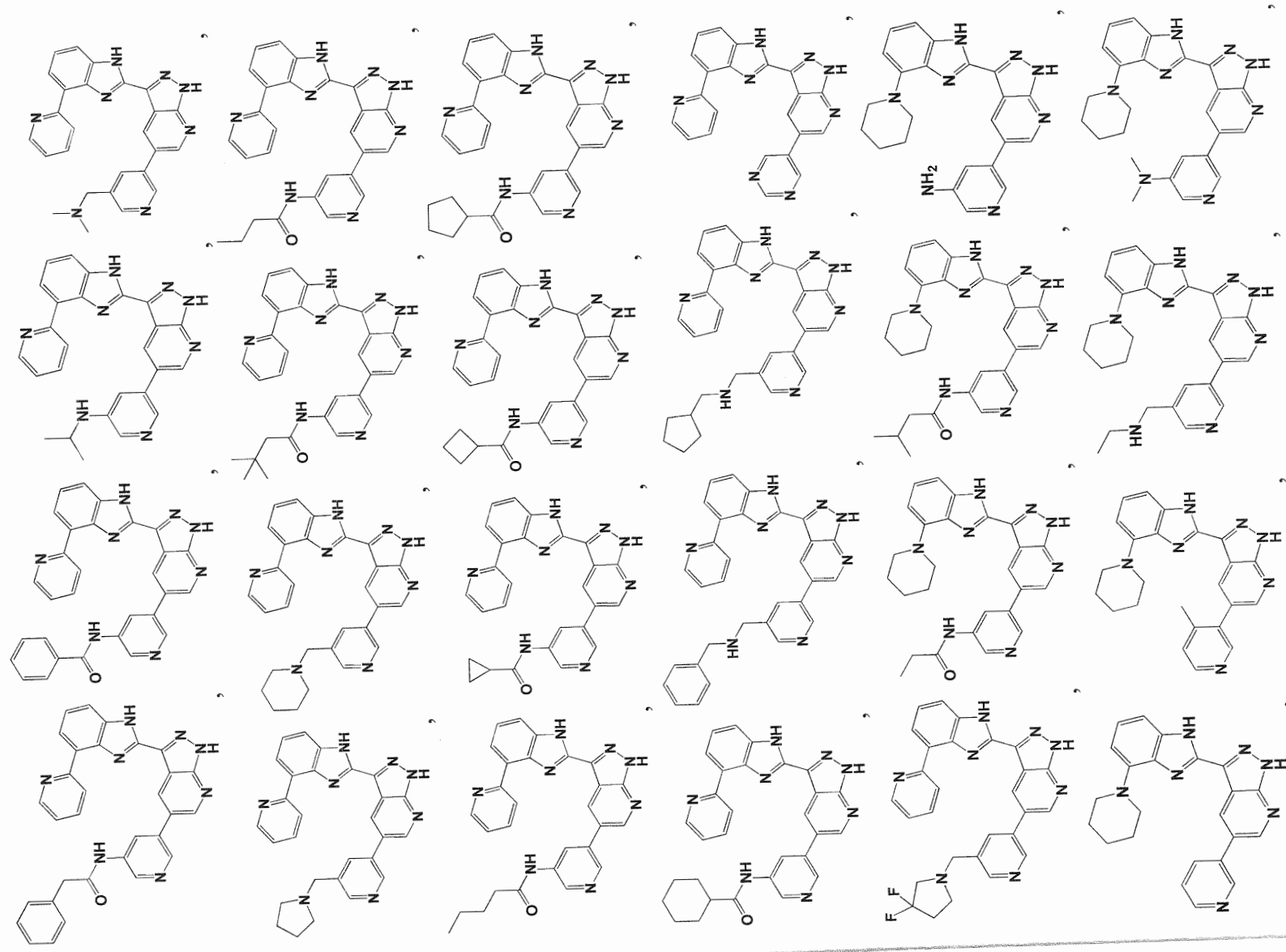


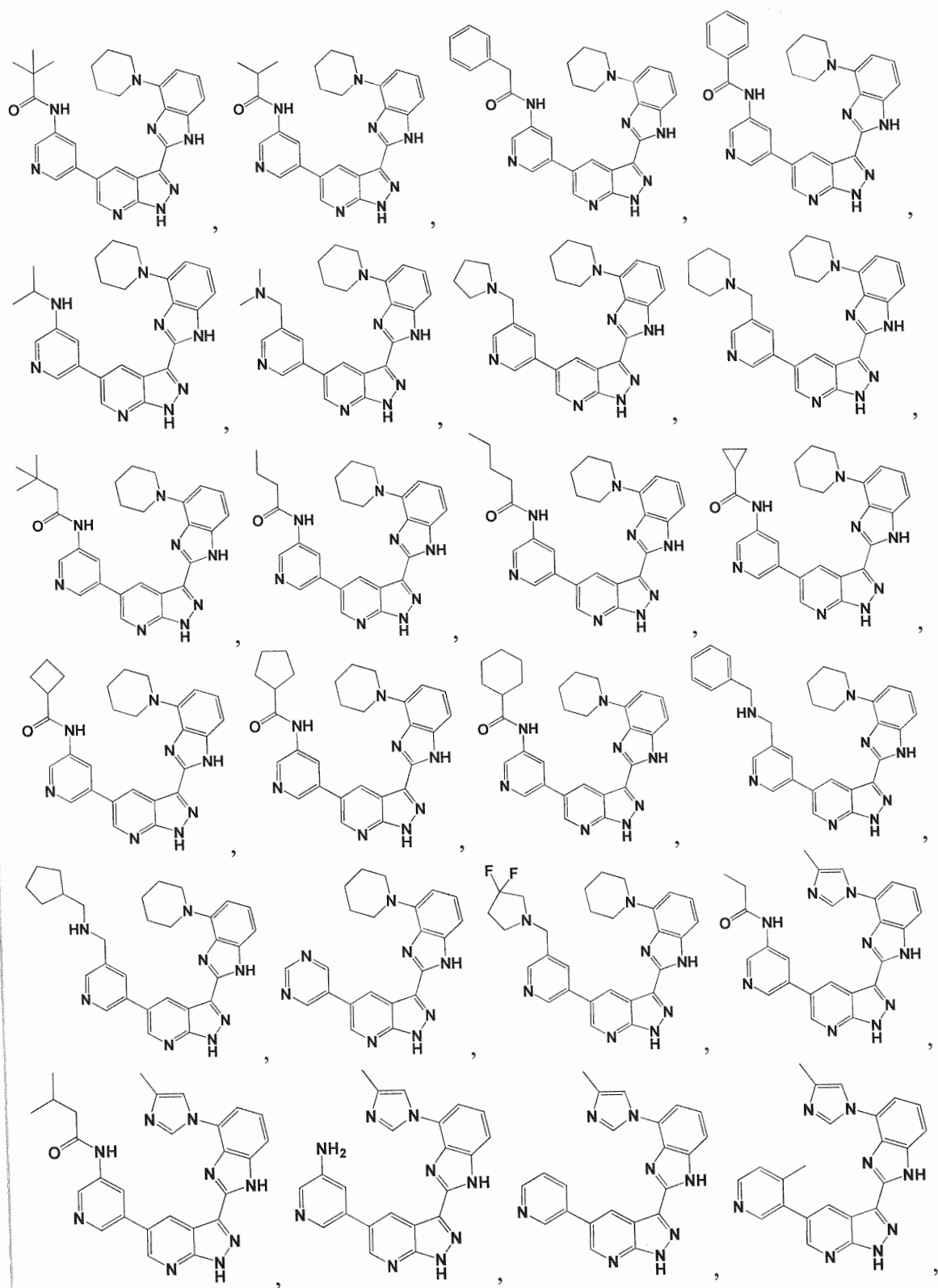


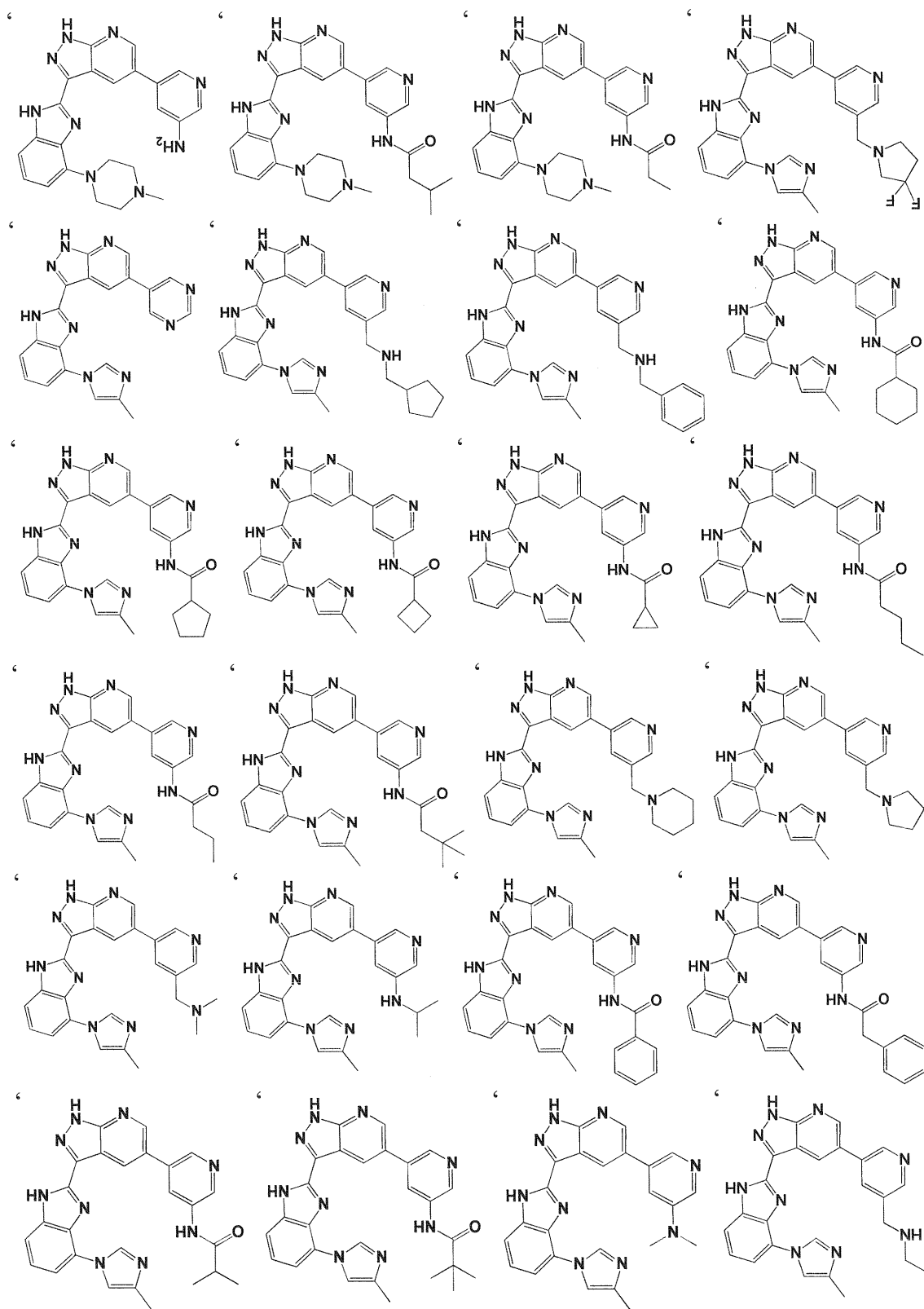


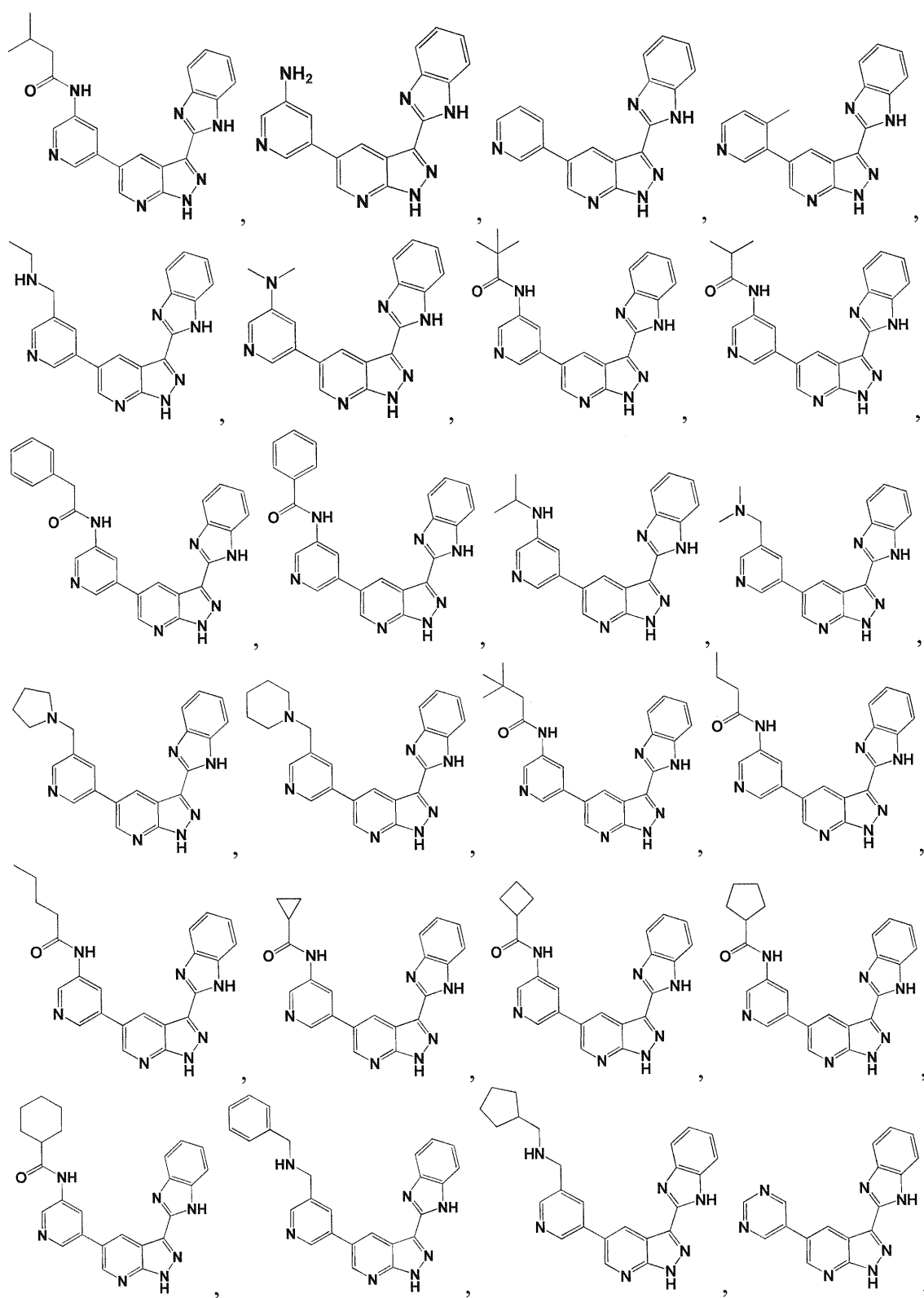


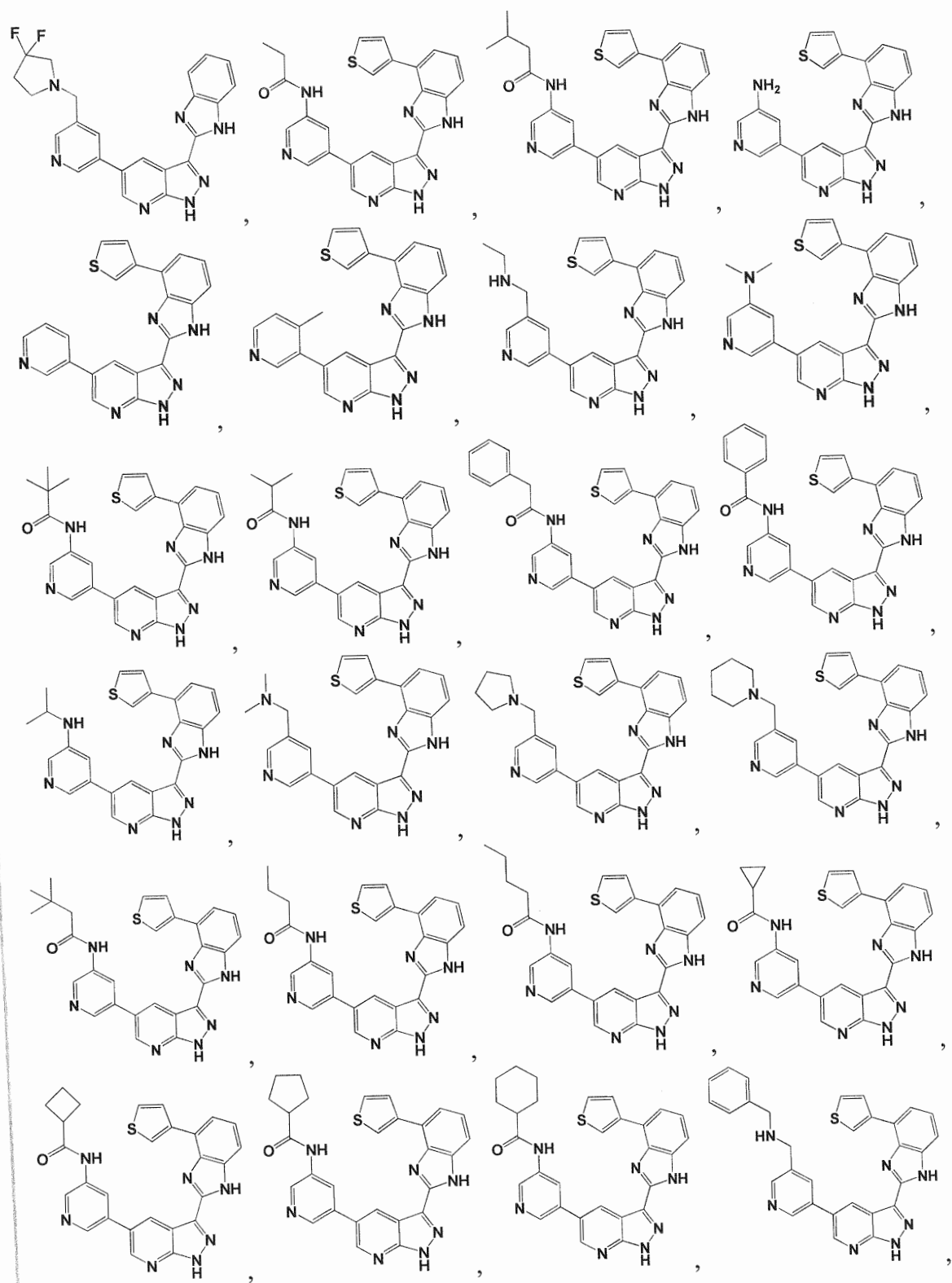


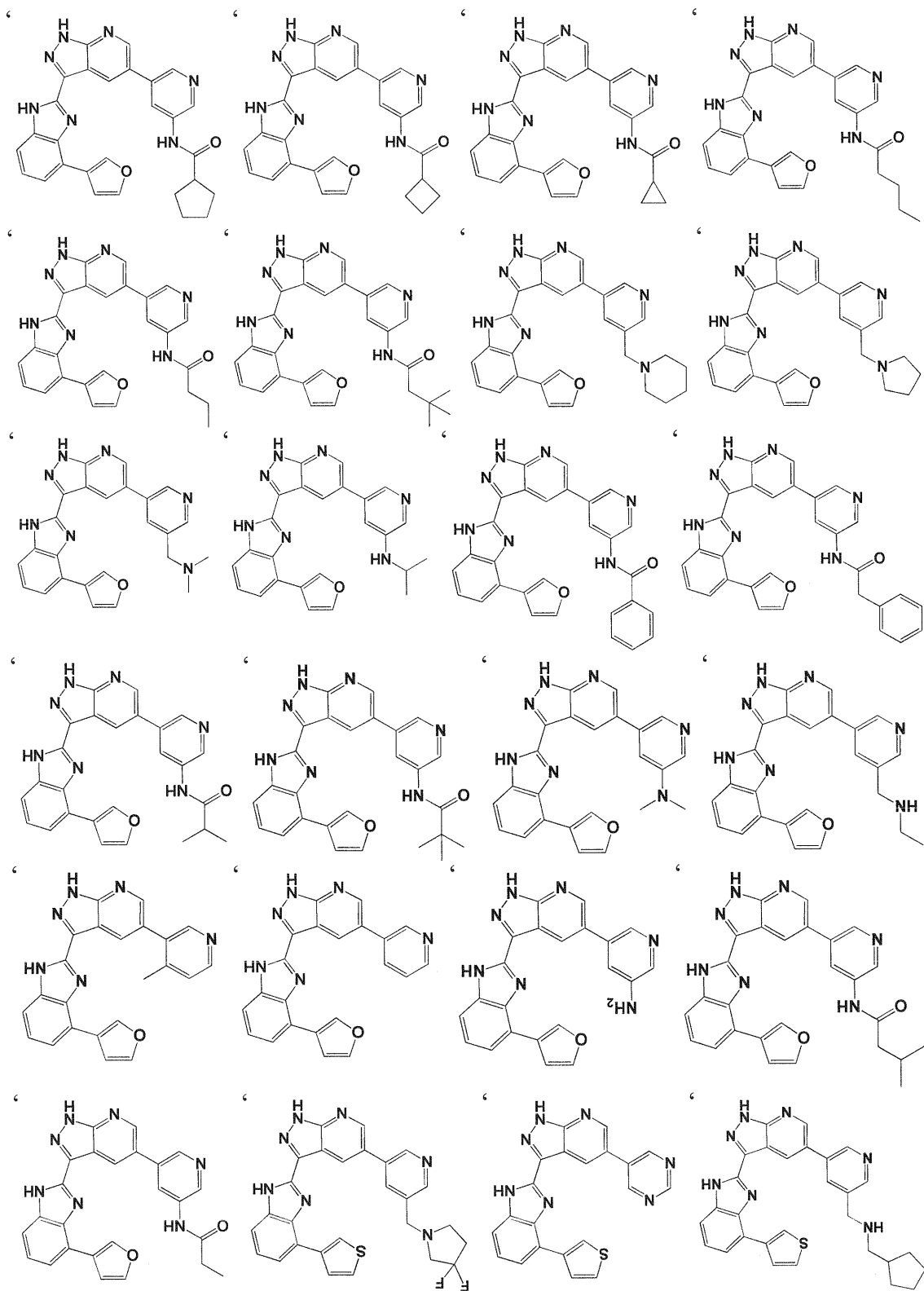


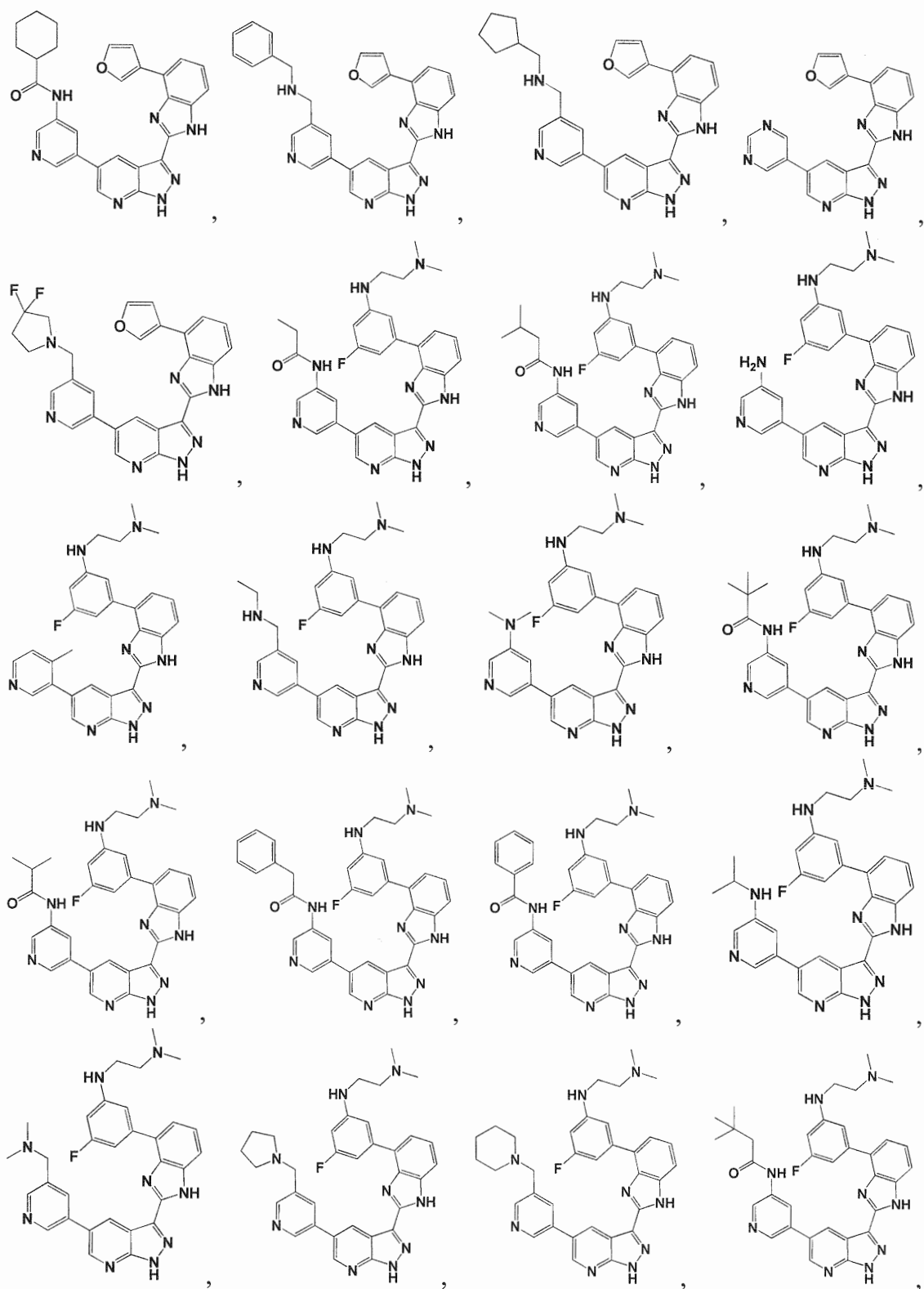


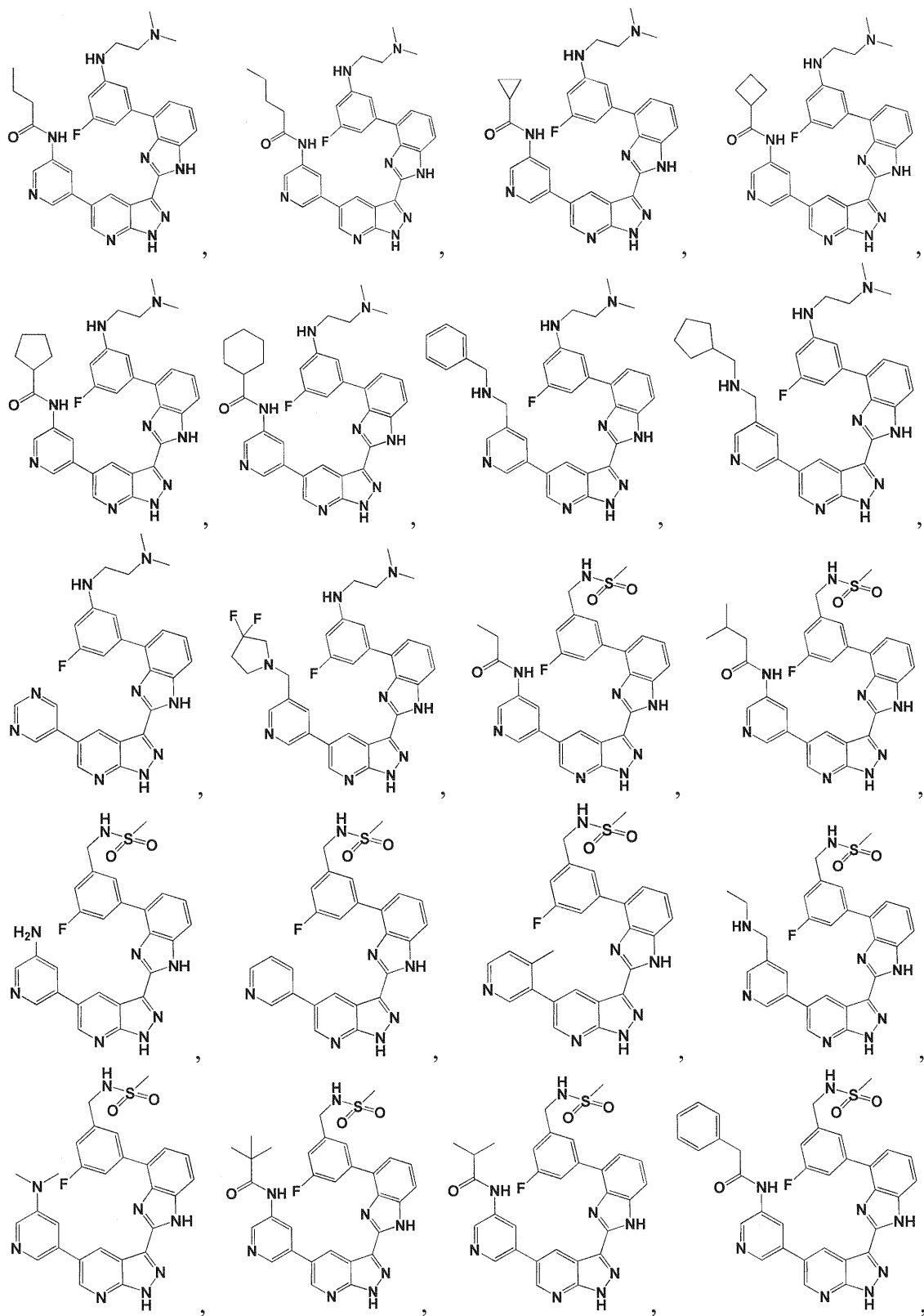


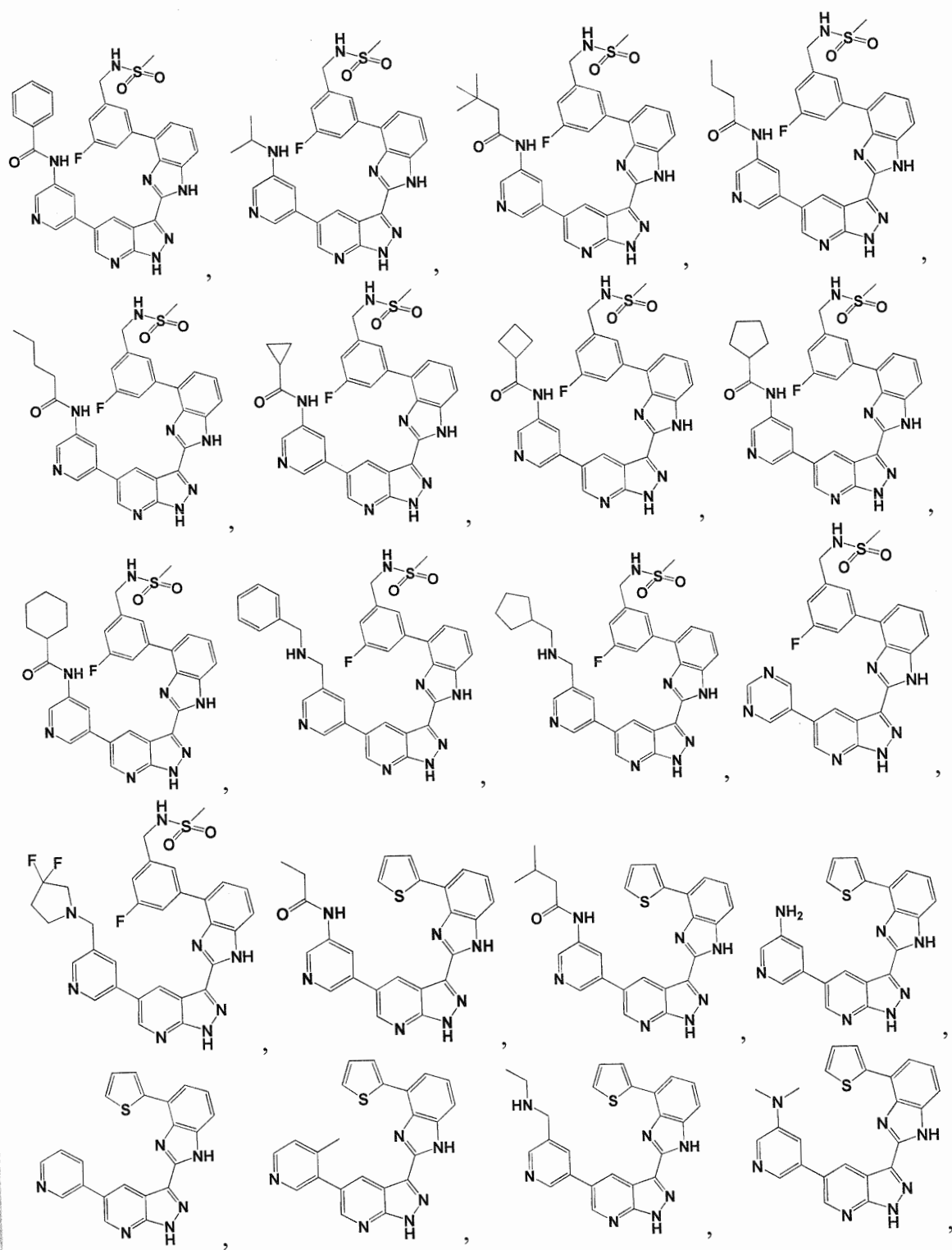




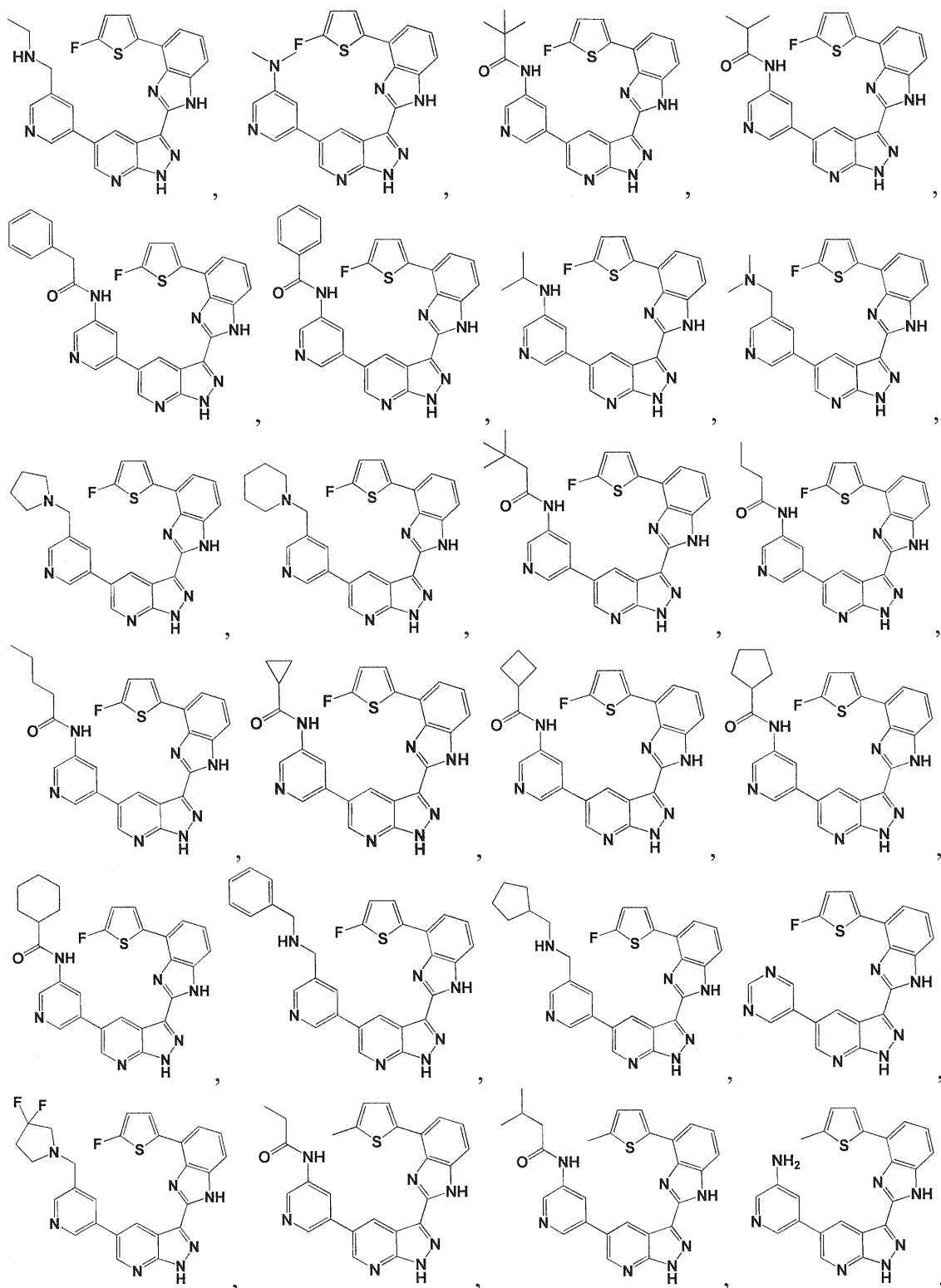


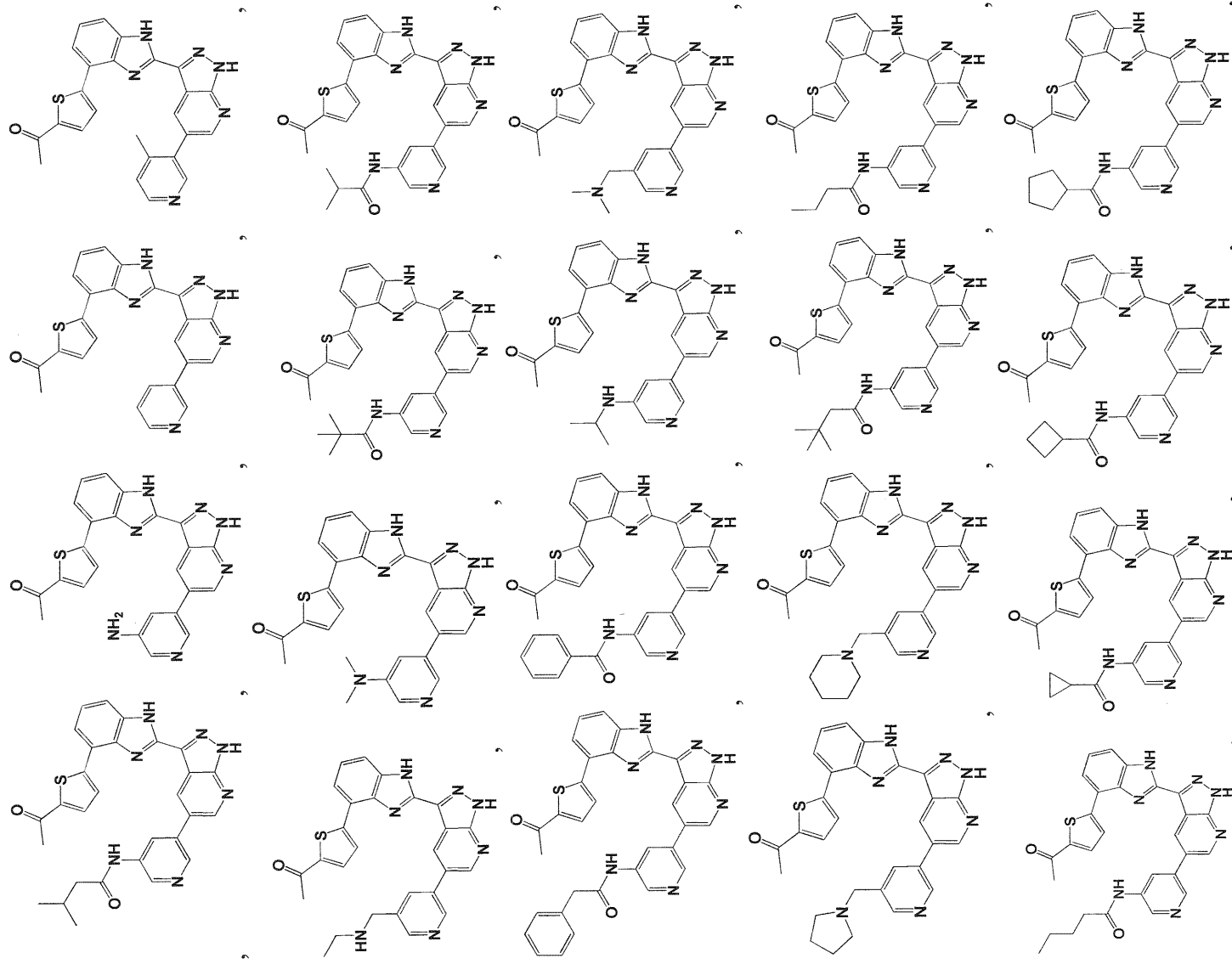


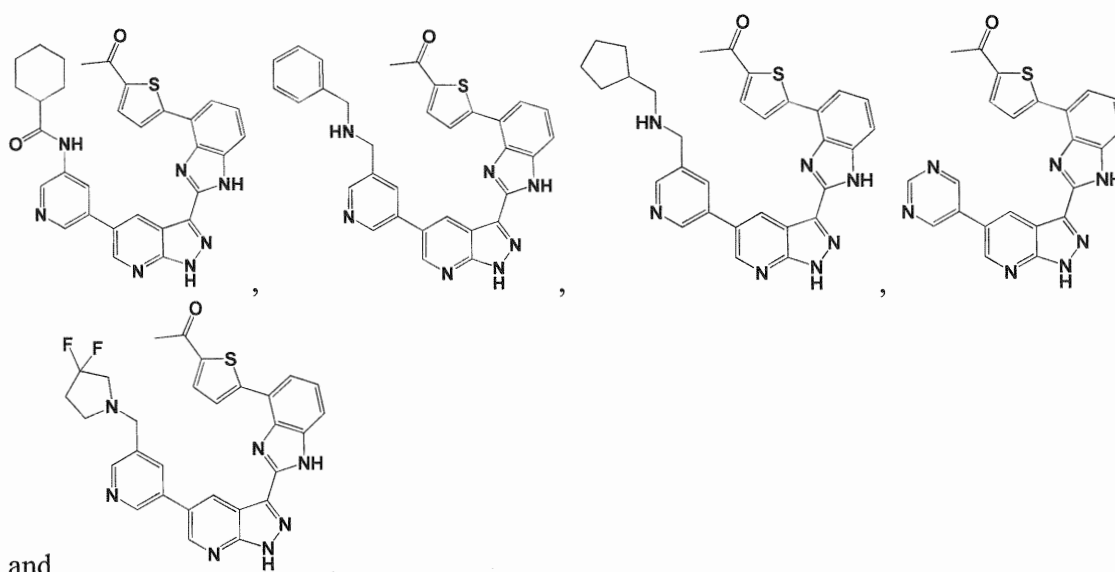












35. A pharmaceutical composition comprising a compound according to any one of the claims 1-34, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

36. A compound according to any one of claims 1-34, or a pharmaceutically acceptable salt thereof, for use in treating a disorder or disease in a patient, wherein the disorder or disease is selected from the group consisting of: diabetic retinopathy, pulmonary fibrosis, idiopathic pulmonary fibrosis (IPF), rheumatoid arthritis, scleroderma, a mycotic or viral infection, a bone or cartilage disease, Alzheimer's disease, dementia, Parkinson's disease, lung disease, and cancer.

37. The compound for use of claim 36, wherein the disorder or disease is cancer.

38. The compound for use of claim 36, wherein the disorder or disease is diabetic retinopathy.

39. The compound for use of claim 36, wherein the disorder or disease is pulmonary fibrosis.

40. The compound for use of claim 36, wherein the disorder or disease is idiopathic pulmonary fibrosis (IPF).

41. The compound for use of claim 36, wherein the disorder or disease is rheumatoid arthritis.

42. The compound for use of claim 36, wherein the disorder or disease is scleroderma.

43. The compound for use of claim 36, wherein the disorder or disease is a mycotic or viral infection.

44. The compound for use of claim 36, wherein the disorder or disease is a bone or cartilage disease.

45. The compound for use of claim 36, wherein the disorder or disease is Alzheimer's disease.

46. The compound for use of claim 36, wherein the disorder or disease is dementia.

47. The compound for use of claim 36, wherein the disorder or disease is Parkinson's disease.

48. The compound for use of claim 36, wherein the disorder or disease is lung disease.

49. The compound for use of either claim 36 or 44, wherein the bone or cartilage disease is osteoarthritis.

50. A compound according to any one of claims 1-34, or a pharmaceutically acceptable salt thereof, for use in treating a disorder or disease in a patient, wherein the disorder or disease is selected from the group consisting of: polyposis coli, osteoporosis-pseudoglioma syndrome, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia syndrome, Müllerian-duct regression and virilization, SERKAL syndrome, diabetes mellitus type 2, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication syndrome, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease, and Rett syndrome.

51. The compound for use of either claim 36 or 50, wherein the patient is a human.

52. The compound for use of claim 37, wherein the cancer is chosen from: hepatocellular carcinoma, colon cancer, breast cancer, pancreatic cancer leukemia, lymphoma, sarcoma, and ovarian cancer.

53. The compound for use of claim 36, wherein the compound inhibits one or more proteins in the Wnt pathway.

54. The compound for use of claim 36, wherein the compound inhibits signaling induced by one or more Wnt proteins.

55. The compound for use of claim 54, wherein the Wnt proteins are chosen from: WNT1, WNT2, WNT2B, WNT3, WNT3A, WNT4, WNT5A, WNT5B, WNT6, WNT7A, WNT7B, WNT8A, WNT8B, WNT9A, WNT9B, WNT10A, WNT10B, WNT11, and WNT16.

56. The compound for use of claim 36, wherein the compound inhibits a kinase activity.