

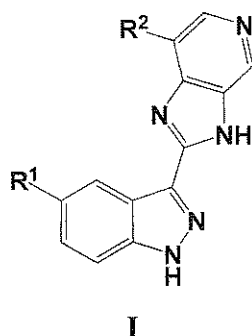
changes involving nuclear function. Recently, a link between neuronal activity, essential for the formation and refinement of neuronal connections, and Wnt signaling has been uncovered. Indeed, neuronal activity regulates the release of various Wnt proteins and the localization of their receptors. Wnt 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

[0009] The present disclosure makes available methods and reagents, involving contacting a cell with an agent, such as an aromatic compound, in a sufficient amount to antagonize a Wnt activity, e. g., to reverse or control an aberrant growth state or correct a genetic disorder due to mutations in Wnt signaling components.

[0010] Some embodiments disclosed herein include Wnt inhibitors containing an indazole core. Other embodiments disclosed herein include pharmaceutical compositions and methods of treatment using these compounds.

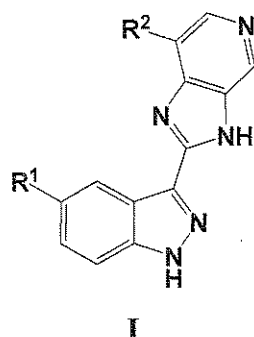
[0010a] In one ~~aspect~~embodiment, there is provided a compound or pharmaceutically acceptable salt thereof having the structure of Formula I:



wherein:

R¹ is –heteroarylR³R⁴;

[0010b] In one ~~aspect~~embodiment, there is provided a compound, or pharmaceutically acceptable salt thereof, having the structure of Formula I:



wherein:

R^1 is -heteroaryl R^3R^4 ;

R^2 is -aryl R^7 ;

R^3 is a -NHC(=O) R^9 ;

R^4 is H;

each R^7 is independently 1-2 substituents each selected from the group consisting of halide, -CF₃, -CN, -(C₁₋₆ alkyl)NHSO₂ R^{11} , -(C₁₋₆ alkyl)NR¹¹ R^{12} , and -NR¹²(C₁₋₆ alkyl)NR¹¹ R^{12} ;

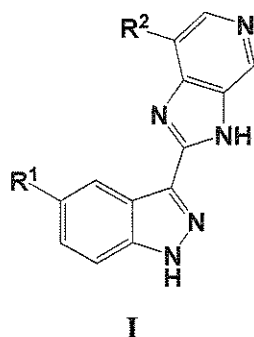
R^9 is selected from the group consisting of -(C₁₋₆ alkyl), -aryl, -carbocyclyl, and -CH₂carbocyclyl;

each R^{11} is independently selected from -(C₁₋₆ alkyl);

each R^{12} is independently selected from the group consisting of H and -(C₁₋₆ alkyl); and

each R^{11} and R^{12} are optionally linked to form a four to six membered heterocyclyl ring.

[0010c] In one ~~aspect~~embodiment, there is provided a compound, or pharmaceutically acceptable salt thereof, having the structure of Formula I:



wherein:

R^1 is $-\text{pyridin-3-ylR}^3R^4$;

R^2 is $-\text{phenylR}^7$;

R^3 is a $-\text{NHC}(=\text{O})R^9$;

R^4 is H;

each R^7 is independently 1-2 substituents each selected from the group consisting of fluorine, $-\text{CH}_2\text{NHSO}_2R^{11}$, $-(C_{1-6}\text{ alkyl})NR^{11}R^{12}$, and $-\text{NHCH}_2\text{CH}_2NR^{11}R^{12}$;

R^9 is selected from the group consisting of $-(C_{2-5}\text{ alkyl})$, $-\text{phenyl}$, $-\text{carbocyclyl}$, and $-\text{CH}_2\text{carbocyclyl}$;

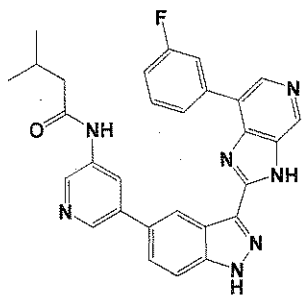
each R^{11} is independently selected from $-(C_{1-2}\text{ alkyl})$;

each R^{12} is independently selected from the group consisting of H and $-(C_{1-2}\text{ alkyl})$; and

each R^{11} and R^{12} are optionally linked to form a four to six membered heterocyclyl ring.

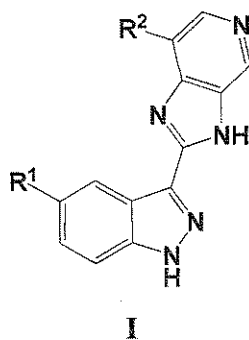
[0010d] In one ~~aspect~~embodiment, there is provided a compound having a structure selected from the group consisting of:

[0010e] In one aspect, there is provided a compound of formula:



or a pharmaceutically acceptable salt thereof.

[0011] One embodiment disclosed herein includes a compound having the structure of Formula I:



as well as prodrugs and pharmaceutically acceptable salts thereof.

[0012] In some embodiments of Formula (I):

R¹ is -heteroarylR³R⁴;

[0015] Some embodiments of the present disclosure include pharmaceutical compositions comprising a compound of general Formula (I) and a pharmaceutically acceptable carrier.

[0015a] In another ~~aspect~~embodiment, there is provided a compound as defined herein, or a pharmaceutically acceptable salt thereof, for use in treating a disorder or disease for preventing or reducing angiogenesis in a patient.

[0015b] In one aspect, there is provided a compound as defined 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, rheumatoid arthritis, scleroderma, a mycotic or viral infection, a bone or cartilage disease, Alzheimer's disease, osteoarthritis, and lung disease, and cancer.

[0015c] In one aspect, there is provided use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disorder or disease selected from: diabetic retinopathy, pulmonary fibrosis, rheumatoid arthritis, scleroderma, a mycotic or viral infection, a bone or cartilage disease, Alzheimer's disease, osteoarthritis, and lung disease.

[0016] 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 any of the above formulas. 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 an 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, 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-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 and Rett syndrome.

[0016a] In one aspect, there is provided a compound as defined herein, or a pharmaceutically acceptable salt thereof, for use in treating 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, and Rett syndrome.

[0016b] In one aspect, there is provided use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating 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, and Rett syndrome.

[0017] 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.

[0018] Some embodiments of the present disclosure include methods to prepare a compound of general Formula (I).

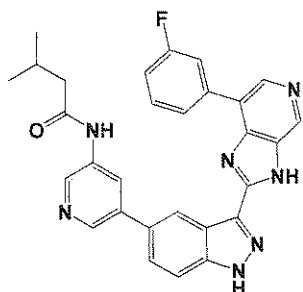
[0019] It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the invention, as claimed.

DETAILED DESCRIPTION OF THE INVENTION

[0020] 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

WHAT IS CLAIMED IS:

1. A compound of formula:



or a pharmaceutically acceptable salt thereof.

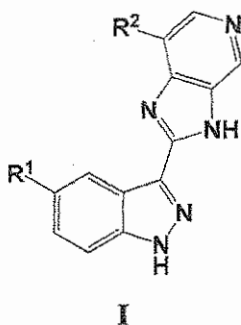
2. A pharmaceutical composition comprising a compound according to claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.
3. A compound according to claim 1, or a pharmaceutically acceptable salt thereof, for use in treating a disorder or disease selected from: diabetic retinopathy, pulmonary fibrosis, rheumatoid arthritis, scleroderma, a mycotic or viral infection, a bone or cartilage disease, Alzheimer's disease, osteoarthritis, and lung disease.
4. A compound according to claim 1, or a pharmaceutically acceptable salt thereof, for use in treating 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/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, and Rett syndrome.

5. The compound for use of claim 3, wherein the disorder or disease is osteoarthritis.
6. Use of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disorder or disease selected from: diabetic retinopathy, pulmonary fibrosis, rheumatoid arthritis, scleroderma, a mycotic or viral infection, a bone or cartilage disease, Alzheimer's disease, osteoarthritis, and lung disease.
7. Use of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating 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, and Rett syndrome.
8. The use of claim 6, wherein the disorder or disease is osteoarthritis.

WHAT IS CLAIMED IS:

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



wherein:

R^1 is -heteroaryl R^3R^4 ;

R^2 is selected from the group consisting of H, -pyridin-2-yl R^5 , -pyridin-4-yl R^5 , -thiophene R^5 , -furan R^5 , -imidazole R^5 , -heterocyclyl R^6 and -aryl R^7 ;

R^3 is selected from the group consisting of H, -heterocyclyl R^8 , -NHC(=O) R^9 , -NHSO₂ R^{10} , -NR¹¹ R^{12} and -(C₁₋₆ alkyl)NR¹¹ R^{12} ;

with the proviso that R^2 and R^3 are not both H;

R^4 is 1-3 substituents each selected from the group consisting of H, halide, -CF₃, -CN, OR¹³ and amino;

each R^5 is independently 1-4 substituents each selected from the group consisting of H, C₁₋₉ alkyl, halide, -CF₃, -CN, OR¹³, -C(=O) R^{11} , amino and -(C₁₋₆ alkyl)NR¹¹ R^{12} ;

each R^6 is independently 1-5 substituents each selected from the group consisting of H, C₁₋₉ alkyl, halide, -CF₃, -CN, OR¹³ and amino;

each R^7 is independently 1-5 substituents each selected from the group consisting of C₁₋₉ alkyl, halide, -CF₃, -CN, OR¹³, amino, -(C₁₋₆ alkyl)NHSO₂ R^{11} , -NR¹²(C₁₋₆ alkyl)NR¹¹ R^{12} and -(C₁₋₆ alkyl)NR¹¹ R^{12} ;

R^8 is 1-5 substituents each selected from the group consisting of H, C₁₋₉ alkyl, halide, -CF₃, -CN, OR¹³ and amino;

R^9 is selected from the group consisting of C₁₋₉ alkyl, -heteroaryl R^5 , -heterocyclyl R^6 , -aryl R^7 , -carbocyclyl, and -CH₂carbocyclyl;

- R^{10} is selected from the group consisting of C_{1-9} alkyl, -heteroaryl R^5 , -heterocyclyl R^6 , -aryl R^7 , and -carbocyclyl R^{14} ;
- each R^{11} is independently selected from C_{1-6} alkyl;
- each R^{12} is independently selected from the group consisting of H and C_{1-6} alkyl;
- each R^{11} and R^{12} are optionally linked to form a five or six membered heterocyclyl ring;
- each R^{13} is independently selected from the group consisting of H and C_{1-6} alkyl;
- R^{14} is 1-5 substituents each selected from the group consisting of H, C_{1-9} alkyl, halide, $-CF_3$, $-CN$, OR^{13} and amino.
2. The compound of claim 1, wherein R^1 is pyridine R^3R^4 .
 3. The compound according to any one of claims 1-2, wherein R^1 is pyridin-3-yl R^3R^4 .
 4. The compound according to any one of claims 1-3, wherein R^3 is $-(C_{1-6} \text{ alkyl})NR^{11}R^{12}$.
 5. The compound according to any one of claims 1-4, wherein R^3 is $-(C_{1-2} \text{ alkyl})NR^{11}R^{12}$, R^{11} is $-(C_{1-2} \text{ alkyl})$, R^{12} is $-(C_{1-2} \text{ alkyl})$ and R^4 is H.
 6. The compound according to any one of claims 1-4, wherein R^{11} and R^{12} are optionally linked to form a five or six membered heterocyclyl ring and R^4 is H.
 7. The compound according to any one of claims 1-4 and 6, wherein the five or six membered heterocyclyl ring is substituted with 1-2 fluorines.
 8. The compound according to any one of claims 1-3, wherein R^3 is $-NHC(=O)R^9$.
 9. The compound according to any one of claims 1-3 and 8, wherein R^4 is H and R^9 is selected from the group consisting of $-(C_{2-5} \text{ alkyl})$, phenyl, -carbocyclyl and $-CH_2\text{carbocyclyl}$.
 10. The compound according to any one of claims 1-3, wherein R^3 is $-NH\text{SO}_2R^{10}$.
 11. The compound according to any one of claims 1-3 and 10, wherein R^4 is H and R^{10} is selected from the group consisting of $-(C_{1-4} \text{ alkyl})$ and phenyl.
 12. The compound according to any one of claims 1-3, wherein R^3 is -heterocyclyl R^8 .

13. The compound according to any one of claims 1-3 and 12, wherein R^4 is H and heterocyclyl is selected from the group consisting of morpholine, piperazine and piperidine.

14. The compound according to any one of claims 1-3, wherein R^3 is H and R^4 is amino.

15. The compound according to any one of claims 3-14, in which R^2 is -pyridin-2-yl R^5 .

16. The compound according to any one of claims 3-14, in which R^2 is -pyridin-4-yl R^5 .

17. The compound according to any one of claims 3-14, in which R^2 is thiophene R^5 .

18. The compound according to any one of claims 3-14, in which R^2 is -heterocyclyl R^6 .

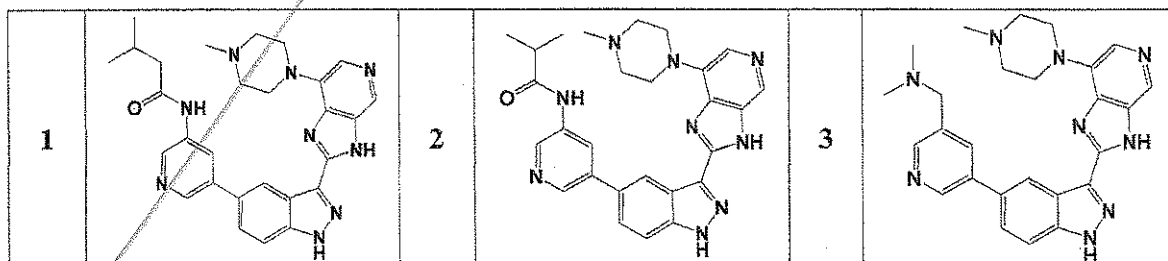
19. The compound according to any one of claims 3-14, in which R^2 is -heterocyclyl R^6 , in which R^6 is selected from the group consisting of H, F and $-(C_{1-4} \text{ alkyl})$, and heterocyclyl is selected from the group consisting of morpholine, piperazine and piperidine.

20. The compound according to any one of claims 3-14, in which R^2 is -aryl R^7 .

21. The compound according to any one of claims 3-14, in which R^2 is -phenyl R^7 and R^7 is 1-2 fluorine atoms.

22. The compound according to any one of claims 3-14, in which R^2 is -phenyl R^7 and R^7 is 2 substituents consisting of 1 fluorine atom and either $-NR^{12}(C_{1-6} \text{ alkyl})NR^{11}R^{12}$ or $-(C_{1-6} \text{ alkyl})NHSO_2R^{11}$.

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



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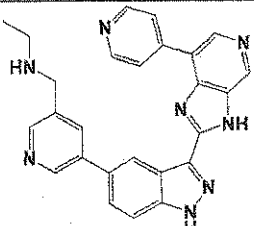
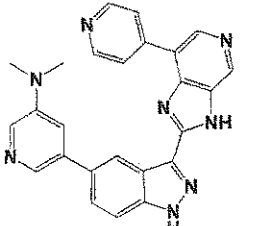
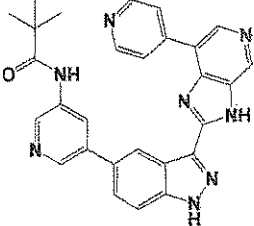
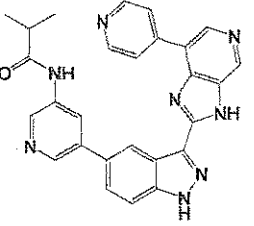
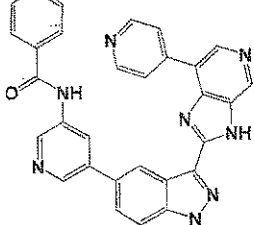
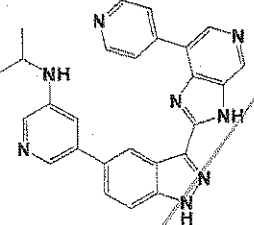
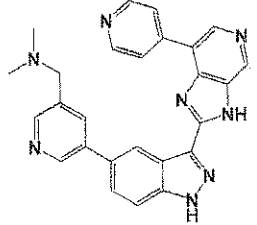
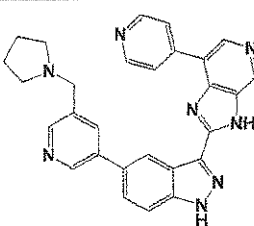
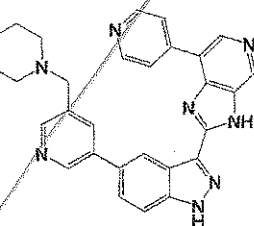
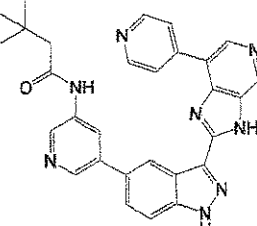
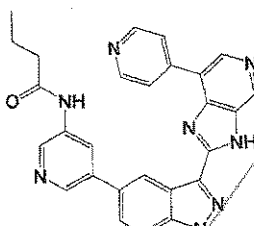
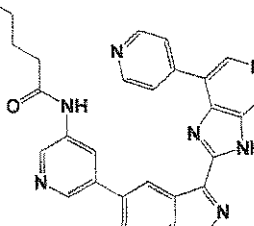
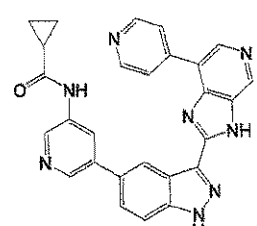
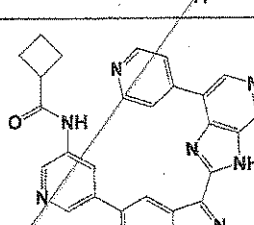
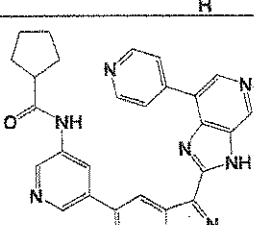
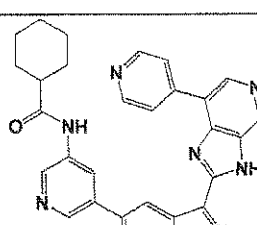
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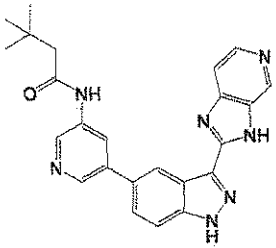
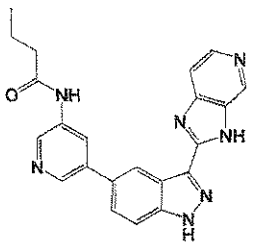
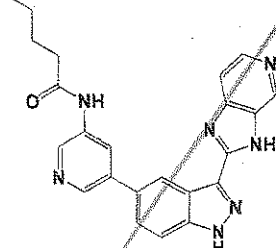
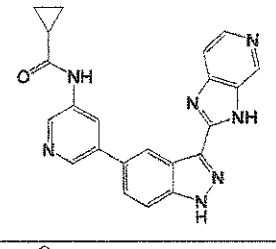
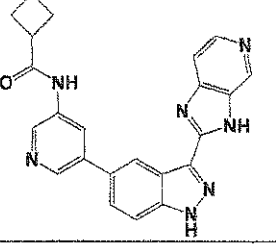
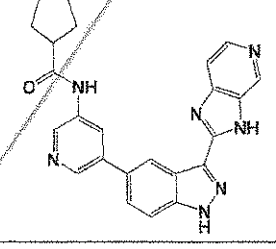
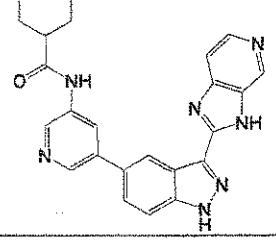
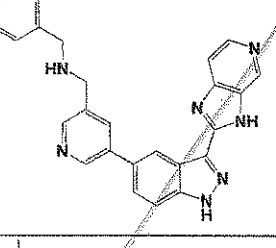
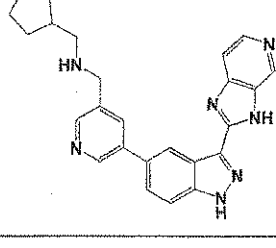
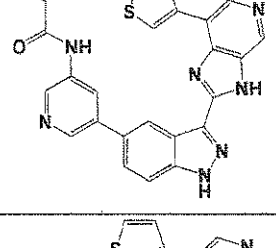
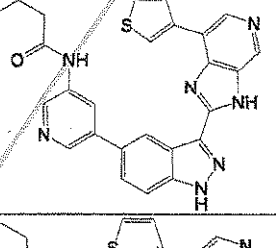
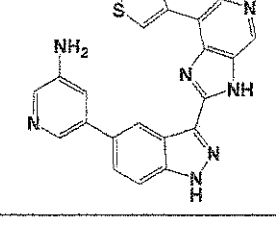
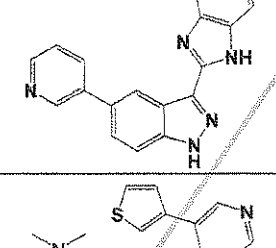
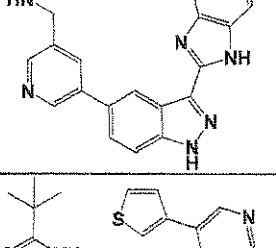
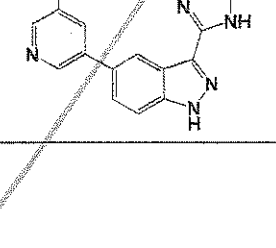
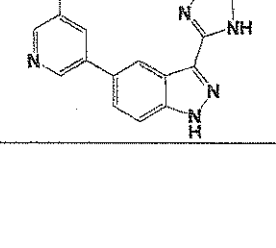
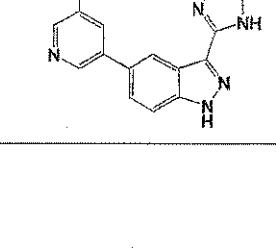
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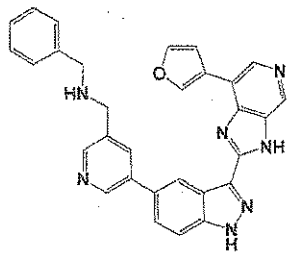
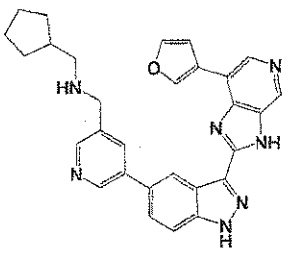
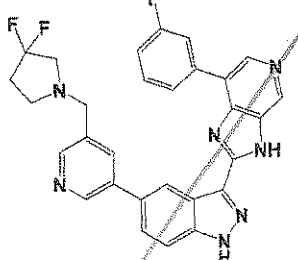
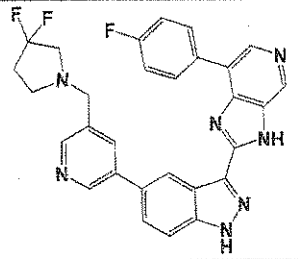
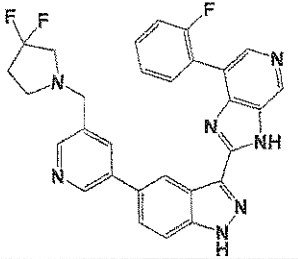
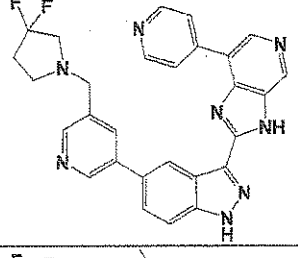
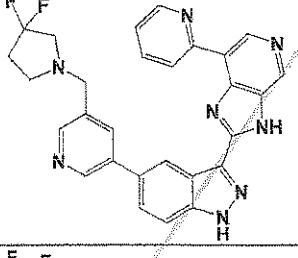
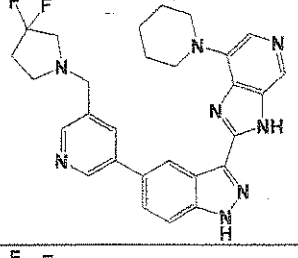
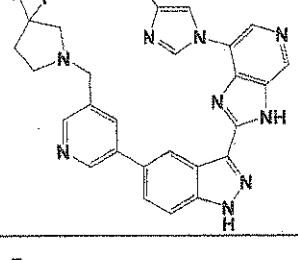
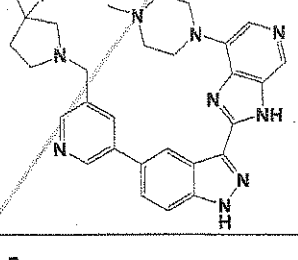
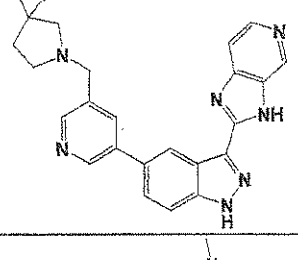
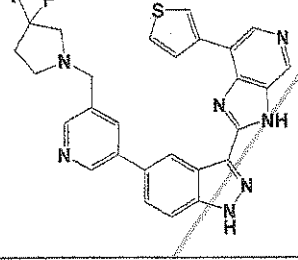
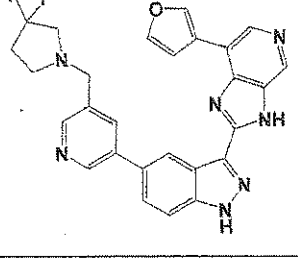
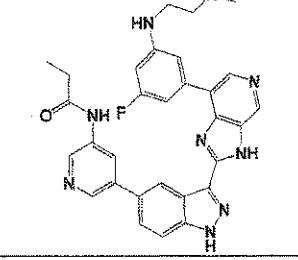
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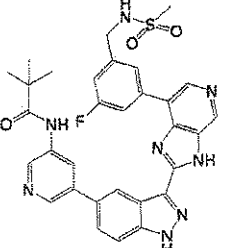
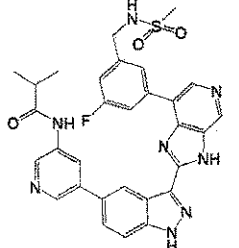
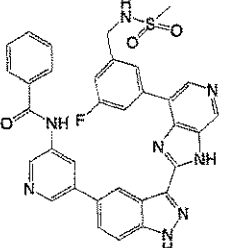
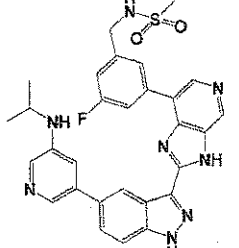
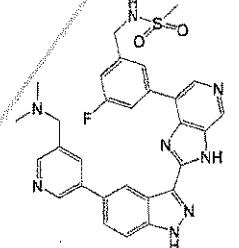
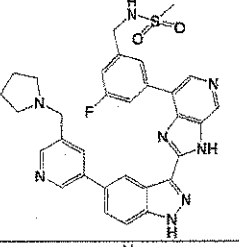
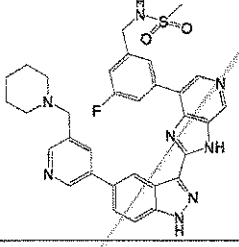
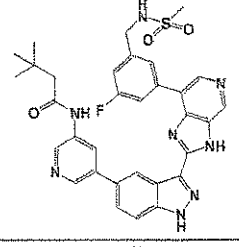
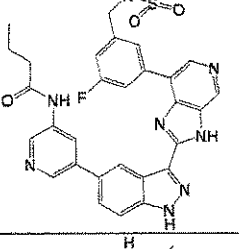
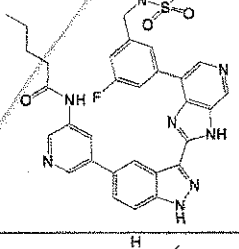
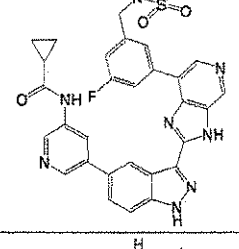
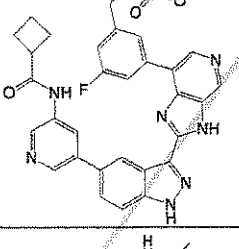
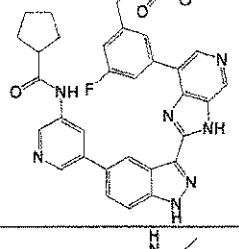
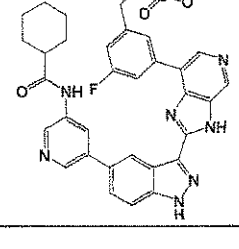
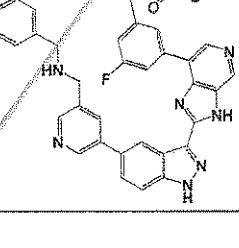
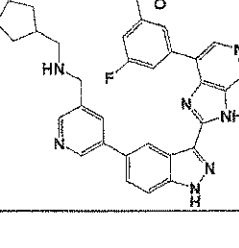
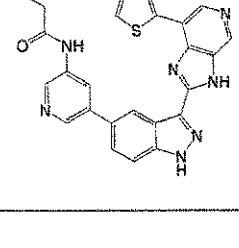
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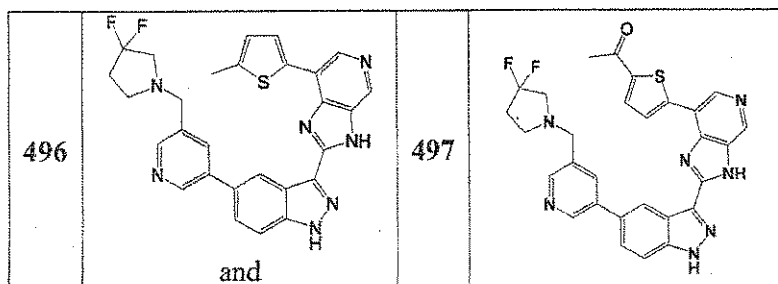
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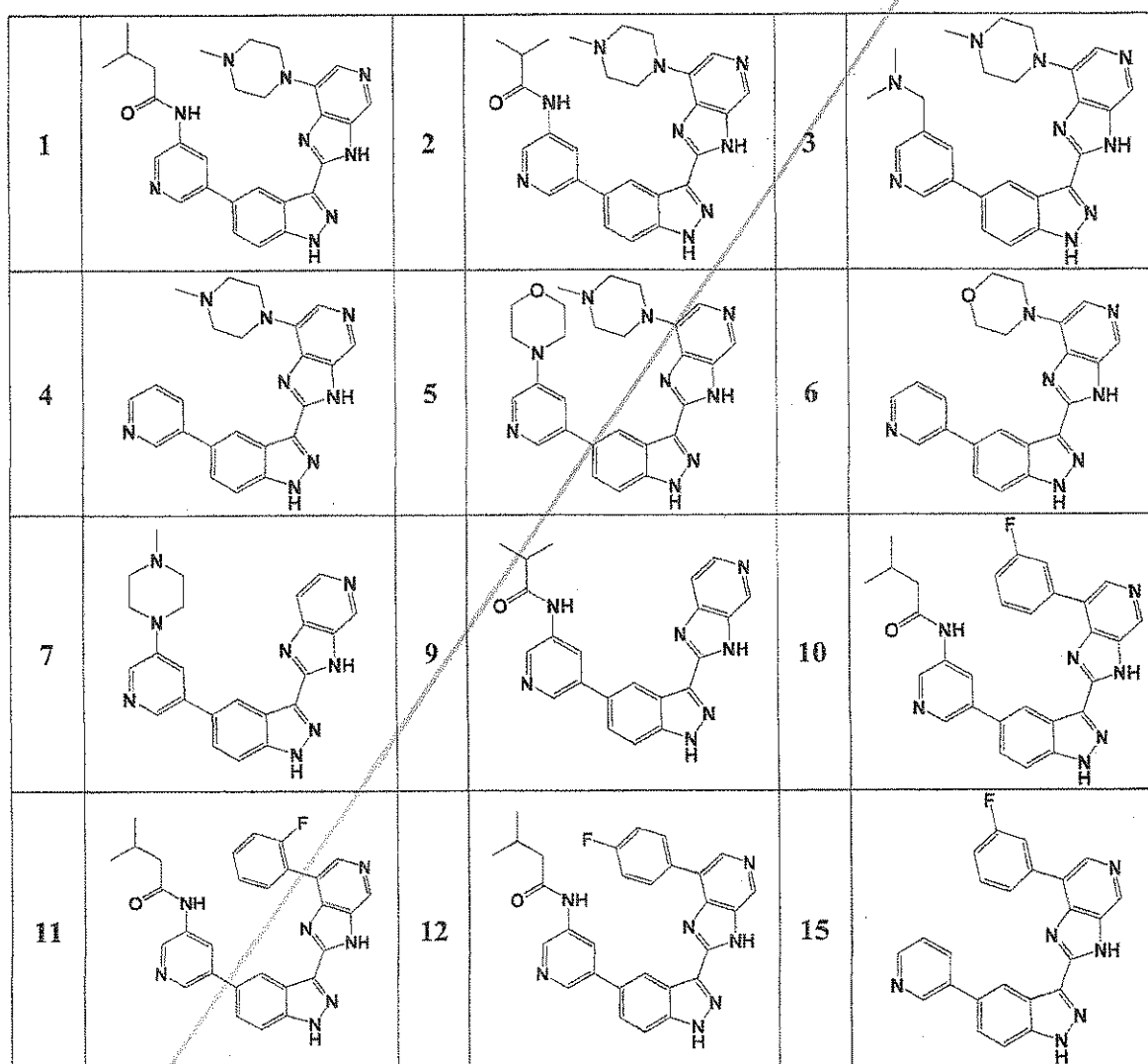
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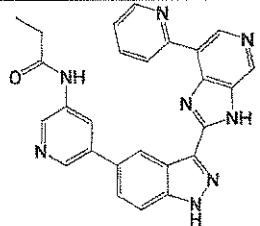
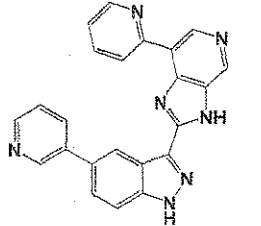
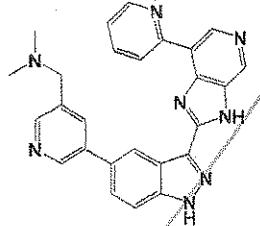
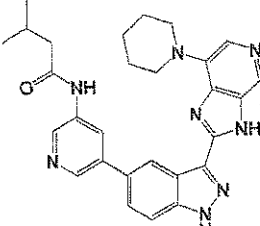
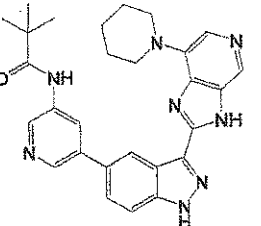
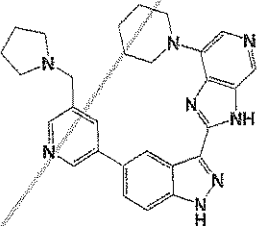
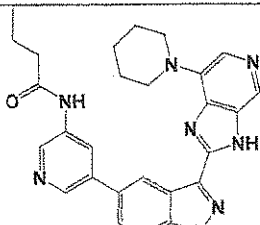
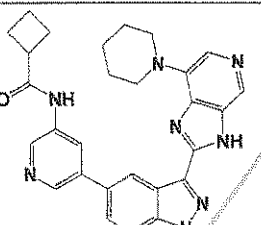
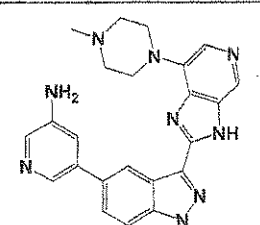
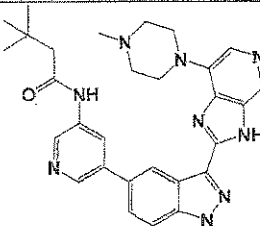
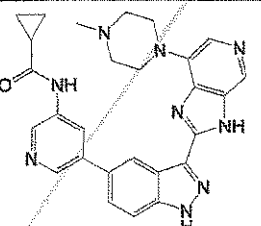
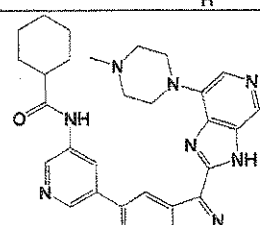
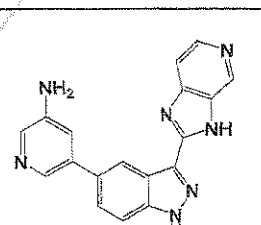
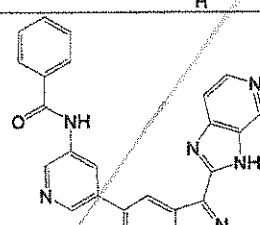
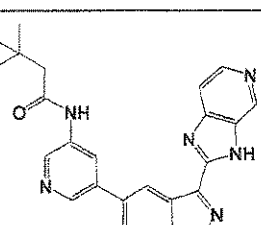
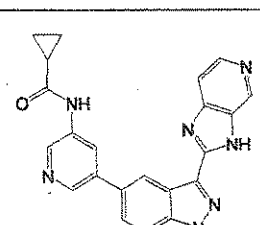


, or a pharmaceutically acceptable salt thereof.

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



24		31		86	
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104		107		111	
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164		170		173	

174		177		186	
199		205		211	
214		217		247	
257		260			
263		268			
275		280		283	

286		289		291	
295		301		303	
304		311		315	
319		329			
330		333		336	
342		346		349	

373		397	
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and

, or a pharmaceutically acceptable salt thereof.

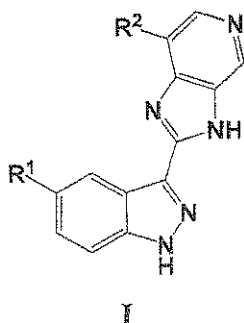
25. The compound of claim 1, having a structure selected from the group consisting of:

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12		31		90	
91		94		97	
102		104		111	

124		174		177	
247		283		289	
291		295		304	
319		329		346	
373		397			

, or a pharmaceutically acceptable salt thereof.

26. A compound, or pharmaceutically acceptable salt thereof, having the structure of Formula I:



wherein:

R^1 is -heteroaryl R^3R^4 ;

R^2 is -aryl R^7 ;

R^3 is a $-NHC(=O)R^9$;

R^4 is H;

each R^7 is independently 1-2 substituents each selected from the group consisting of halide, $-CF_3$, $-CN$, $-(C_{1-6} \text{ alkyl})NHSO_2R^{11}$, $-(C_{1-6} \text{ alkyl})NR^{11}R^{12}$, and $-NR^{12}(C_{1-6} \text{ alkyl})NR^{11}R^{12}$;

R^9 is selected from the group consisting of $-(C_{1-6} \text{ alkyl})$, -aryl, -carbocyclyl, and $-CH_2\text{carbocyclyl}$;

each R^{11} is independently selected from $-(C_{1-6} \text{ alkyl})$;

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

each R^{11} and R^{12} are optionally linked to form a four to six membered heterocyclyl ring.

27. The compound of claim 26, wherein R^1 is pyridinyl R^3R^4 .
28. The compound according to any one of claims 26-27, wherein R^1 is pyridin-3-yl R^3R^4 .
29. The compound of claim 26, wherein R^9 is $-(C_{1-6} \text{ alkyl})$.
30. The compound of claim 26, wherein R^9 is $-(C_{2-5} \text{ alkyl})$.
31. The compound of claim 26, wherein R^9 is carbocyclyl.
32. The compound of claim 26, wherein R^9 is $-CH_2\text{carbocyclyl}$.
33. The compound of claim 26, wherein R^9 is phenyl R^7 .
34. The compound of claim 33, wherein R^7 is halide.
35. The compound according to any one of claims 33-34, wherein R^7 is fluorine.

36. The compound of claim 33, wherein R^7 is 2 substituents consisting of a fluorine atom and $-(C_{1-6} \text{ alkyl})NR^{11}R^{12}$.

37. The compound of claim 36, wherein R^{11} and R^{12} are both $-(C_{1-2} \text{ alkyl})$.

38. The compound of claim 36, wherein R^{11} and R^{12} are linked to form an azetidine ring.

39. The compound of claim 36, wherein R^{11} and R^{12} are linked to form a pyrrolidine ring.

40. The compound of claim 36, wherein R^{11} and R^{12} are linked to form a piperidine ring.

41. The compound of claim 33, wherein R^7 is 2 substituents consisting of a fluorine atom and $-NR^{12}(C_{1-6} \text{ alkyl})NR^{11}R^{12}$.

42. The compound of claim 41, wherein R^7 is 2 substituents consisting of a fluorine atom and $-NHCH_2CH_2NR^{11}R^{12}$.

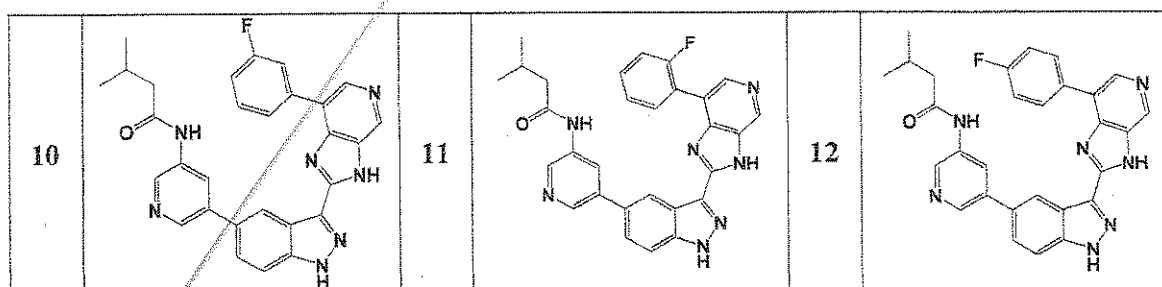
43. The compound according to any one of claims 41-42, wherein R^{11} and R^{12} are both $-(C_{1-2} \text{ alkyl})$.

44. The compound of claim 33, wherein R^7 is 2 substituents consisting of a fluorine atom and $-(C_{1-6} \text{ alkyl})NHSO_2R^{11}$.

45. The compound of claim 44, wherein R^7 is 2 substituents consisting of a fluorine atom and $-CH_2NHSO_2R^{11}$.

46. The compound according to any one of claims 44-45, wherein R^{11} is $-(C_{1-2} \text{ alkyl})$.

47. The compound of claim 26, having a structure selected from the group consisting of:



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70		71		72	

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130		131		132	
348		349		355	

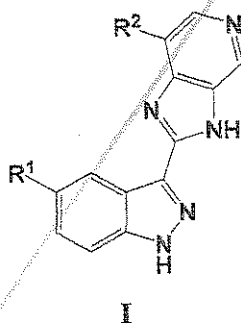
356		358		363	
364		365		366	
367		368		369	
372		373		379	
380		382		387	

388		389		390	
391		392		393	

and

, or a pharmaceutically acceptable salt thereof.

48. A compound, or pharmaceutically acceptable salt thereof, having the structure of Formula I:



wherein:

R^1 is -pyridin-3-yl R^3R^4 ;

R^2 is -phenyl R^7 ;

R^3 is a $-NHC(=O)R^9$;

R^4 is H;

each R^7 is independently 1-2 substituents each selected from the group consisting of fluorine, $-\text{CH}_2\text{NHSO}_2R^{11}$, $-(\text{C}_{1-6} \text{ alkyl})\text{NR}^{11}R^{12}$, and $-\text{NHCH}_2\text{CH}_2\text{NR}^{11}R^{12}$;

R^9 is selected from the group consisting of $-(\text{C}_{2-5} \text{ alkyl})$, -phenyl, -carbocyclyl, and $-\text{CH}_2\text{carbocyclyl}$;

each R^{11} is independently selected from $-(\text{C}_{1-2} \text{ alkyl})$;

each R^{12} is independently selected from the group consisting of H and $-(C_{1-2}$ alkyl); and

each R^{11} and R^{12} are optionally linked to form a four to six membered heterocyclyl ring.

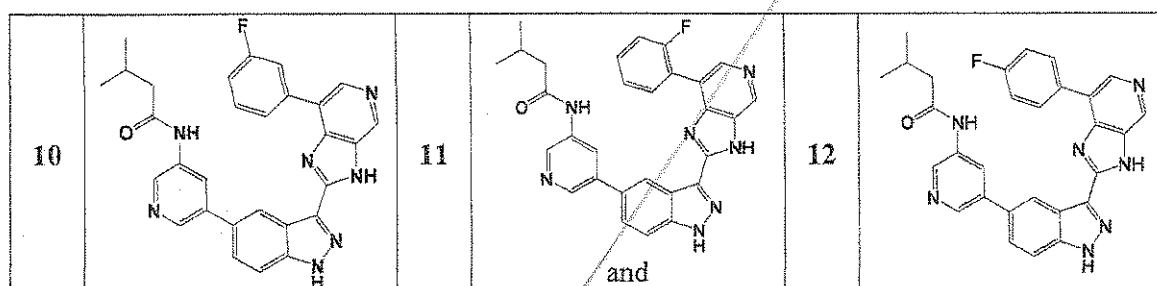
49. The compound of claim 48, wherein R^9 is $-(C_{2-5}$ alkyl).

50. The compound of claim 48, wherein R^9 is carbocyclyl.

51. The compound according to any one of claims 48-50, wherein R^7 is one fluorine.

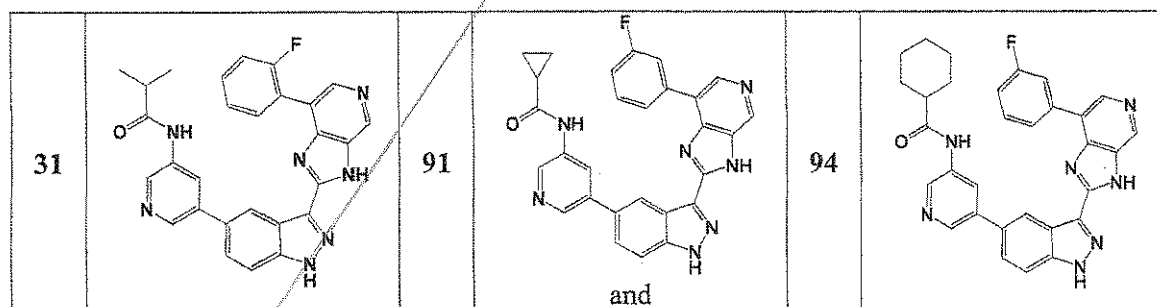
52. The compound according to any one of claims 48-50, wherein R^7 is 2 substituents consisting of a fluorine atom and $-\text{CH}_2\text{NHSO}_2R^{11}$, and R^{11} is $-(C_{1-2}$ alkyl).

53. The compound of claim 48, having a structure selected from the group consisting of:



, or a pharmaceutically acceptable salt thereof.

54. The compound of claim 48, having a structure selected from the group consisting of:



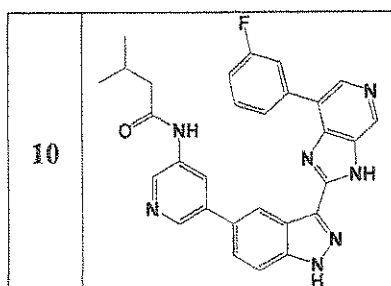
, or a pharmaceutically acceptable salt thereof.

55. The compound of claim 48, having a structure selected from the group consisting of:

102		104		373	
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, or a pharmaceutically acceptable salt thereof.

56. The compound of claim 48, having a structure of:



57. A compound having a structure selected from the group consisting of:

83		86		99	
103		118		122	
135		136		137	

138		139		140	
141		142		143	
144		145		146	
147		148		149	
154		159		178	
183		202		207	

226		231		248	
252		260		270	
274		283		293	
298		316		321	
352		357		376	
381		400		405	

424		429		448	
453		472		477	

, or a pharmaceutically acceptable salt thereof.

58. A compound according to any one of claims 1-57, 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, rheumatoid arthritis, scleroderma, a mycotic or viral infection, a bone or cartilage disease, Alzheimer's disease, lung disease, and cancer.

59. The compound of claim 58, wherein the bone or cartilage disease is osteoarthritis.

60. The compound of claim 58, wherein the disorder or disease is diabetic retinopathy.

61. The compound of claim 58, wherein the disorder or disease is pulmonary fibrosis.

62. The compound of claim 58, wherein the disorder or disease is rheumatoid arthritis.

63. The compound of claim 58, wherein the disorder or disease is scleroderma.

64. The compound of claim 58, wherein the disorder or disease is Alzheimer's disease.

65. The compound of claim 58, wherein the disorder or disease is lung disease.

66. The compound of claim 58, wherein the cancer is selected from the group consisting of: hepatocellular carcinoma, colorectal cancer, colon cancer, cancers of the

stomach, liver cancers, breast cancer, pancreatic cancer, leukemia, lymphoma, sarcoma, and ovarian cancer.

67. The compound of claim 66, wherein the cancer is hepatocellular carcinoma.
68. The compound of claim 66, wherein the cancer is colorectal cancer.
69. The compound of claim 66, wherein the cancer is colon cancer.
70. The compound of claim 66, wherein the cancer is a cancer of the stomach.
71. The compound of claim 66, wherein the cancer is a liver cancer.
72. The compound of claim 66, wherein the cancer is breast cancer.
73. The compound of claim 66, wherein the cancer is pancreatic cancer.
74. The compound of claim 66, wherein the cancer is leukemia.
75. The compound of claim 66, wherein the cancer is lymphoma.
76. The compound of claim 66, wherein the cancer is sarcoma.
77. The compound of claim 66, wherein the cancer is ovarian cancer.
78. The compound of claim 58, wherein the compound inhibits one or more proteins in the Wnt pathway.

79. The compound of claim 58, wherein the compound inhibits signaling induced by one or more Wnt proteins.

80. The compound of either claim 78 or 79, wherein the Wnt proteins are selected from the group consisting of: WNT1, WNT2, WNT2B, WNT3, WNT3A, WNT4, WNT5A, WNT5B, WNT6, WNT7A, WNT7B, WNT8A, WNT8B, WNT9A, WNT9B, WNT10A, WNT10B, WNT11, and WNT16.

81. The compound of claim 58, wherein the compound inhibits a kinase activity.

82. A compound of any one of claims 1-57, or a pharmaceutically acceptable salt thereof, for use in treating a disorder or disease for preventing or reducing angiogenesis in a patient.

83. The compound of claim 58 or 82, wherein the patient is human.

84. A pharmaceutical composition comprising a compound according to any one of the claims 1-57, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.