

Acknowledgement of receipt

We hereby acknowledge receipt of the following subsequently filed document(s):

PCT Application number	PCT/US2019/037543											
Date of receipt	15 April 2020											
Your reference	REAT.P0103WO											
Documents submitted	<table border="1"> <tr> <td>REATP0103WO_PCT-Demand.pdf</td> <td>Number of bytes (pages): 174,602 (4)</td> </tr> <tr> <td>REATP0103WO_PCT-Demand-Trans-Letter.pdf</td> <td>Number of bytes (pages): 68,106 (1)</td> </tr> <tr> <td>REATP0103WO_Letter-and-Article-34-Amdnts.pdf</td> <td>Number of bytes (pages): 944,708 (107)</td> </tr> <tr> <td>REATP0103WO_Resp-ISR-WO.pdf</td> <td>Number of bytes (pages): 81,161 (5)</td> </tr> <tr> <td>REATP0103WO_EPO-Fee-Payment-Receipt.pdf</td> <td>Number of bytes (pages): 58,323 (2)</td> </tr> </table>		REATP0103WO_PCT-Demand.pdf	Number of bytes (pages): 174,602 (4)	REATP0103WO_PCT-Demand-Trans-Letter.pdf	Number of bytes (pages): 68,106 (1)	REATP0103WO_Letter-and-Article-34-Amdnts.pdf	Number of bytes (pages): 944,708 (107)	REATP0103WO_Resp-ISR-WO.pdf	Number of bytes (pages): 81,161 (5)	REATP0103WO_EPO-Fee-Payment-Receipt.pdf	Number of bytes (pages): 58,323 (2)
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REATP0103WO_Resp-ISR-WO.pdf	Number of bytes (pages): 81,161 (5)											
REATP0103WO_EPO-Fee-Payment-Receipt.pdf	Number of bytes (pages): 58,323 (2)											
Submitted by	Mr. Reid Long, rlong@phiplaw.com											
Method of submission	Web form filing											
Date and time receipt generated	15 April 2020, 22:23:36 (CEST)											



S. Reid Long
Patent Agent

512-334-2926

rlong@phiplaw.com

April 15, 2020

BY ONLINE FILING ONLY

EUROPEAN PATENT OFFICE
International Preliminary Examination Authority
Bob-van-Benthem-Platz 1
80469 Munich
Germany

RE: PCT Application No. PCT/US2019/037543; Agent Docket No.: REAT.P0103WO

Dear Madam or Sir:

We submit a PCT Chapter II Demand for Preliminary Examination in connection with the above-referenced international application. The following documents are enclosed:

- PCT Chapter II Demand for Preliminary Examination (3 sheets);
- Fee Calculation Sheet;
- Formal Reply to Written Opinion (5 sheets);
- Letter Accompanying Article 34 Amendments; and
- Article 34 Amendments (106 sheets).

The prescribed fees in the amount of 2.013,00 EUR were paid via credit card on April 15, 2020 with the European Patent Office (Voucher Number 6022090). A copy of the credit card payment receipt is attached for your convenience.

Should this Authority have any questions concerning the Demand, please do not hesitate to contact the undersigned.

Sincerely,

S. Reid Long
Agent for Applicant
US Reg. No. 73,528

SRL/cmh/rao
Enclosures

{00777021}

The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/ EP

PCT

DEMAND

CHAPTER II

under Article 31 of the Patent Cooperation Treaty:
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty.

For International Preliminary Examining Authority use only

Identification of IPEA	Date of receipt of DEMAND
------------------------	---------------------------

Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION

Applicant's or agent's file reference REAT.P0103WO	International application No. PCT/US2019/037543
International filing date (day/month/year) June 17, 2019	(Earliest) Priority date (day/month/year) June 15, 2018
Title of invention PYRAZOLE AND IMIDAZOLE COMPOUNDS FOR INHIBITION OF IL-17 AND RORGAMMA	

Box No. II APPLICANT(S)

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) Reata Pharmaceuticals, Inc. 2801 Gateway Drive, Suite 150 Irving, TX 75063-2648 US	Telephone No.
	Facsimile No.
	Applicant's registration No. with the Office

E-mail authorization: Marking one of the check-boxes below authorizes the International Bureau and the International Preliminary Examining Authority to use the e-mail address indicated in this Box to send notifications issued in respect of this international application if those offices are willing to do so.

☐ as advance copies followed by paper notifications; or ☒ exclusively in electronic form (no paper notifications will be sent).
E-mail address: docket@phiplaw.com

State (that is, country) of nationality: US	State (that is, country) of residence: US
---	---

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

State (that is, country) of nationality:		State (that is, country) of residence:	

☐ Further applicants are indicated on a continuation sheet.

Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The following person is ☒ agent ☐ common representative
 and ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.
☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.
☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

Name and address: *(Family name followed by given name; for a legal entity, full official designation.
The address must include postal code and name of country.)*

LONG, S. Reid
 Parker Highlander PLLC
 1120 S. Capital of Texas Highway
 Building One, Suite 200
 Austin, TX 78746
 US

Telephone No.

512-334-2900

Facsimile No.

512-334-2999

Agent's registration No. with the Office

73,528

E-mail authorization: Marking one of the check-boxes below authorizes the International Bureau and the International Preliminary Examining Authority to use the e-mail address indicated in this Box to send notifications issued in respect of this international application if those offices are willing to do so.

☐ as advance copies followed by paper notifications; or ☒ exclusively in electronic form (no paper notifications will be sent).
 E-mail address: docket@phiplaw.com

☐ **Address for correspondence:** Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION**Statement concerning amendments:***

1. The applicant wishes the international preliminary examination to **start on the basis of:**

- the description ☒ as originally filed, or
☐ as amended under Article 34
- the sequence listing (if any) ☐ as originally filed, or
☐ as amended under Article 34:
☐ in the form of an Annex C/ST.25 text file
☐ on paper or in the form of an image file
- the claims ☐ as originally filed, or
☐ as amended under Article 19, and/or
☒ as amended under Article 34
- the drawings (if any) ☐ as originally filed, or
☐ as amended under Article 34

2. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.

3. ☐ Where the IPEA wishes to start the international preliminary examination at the same time as the international search in accordance with Rule 69.1(b), the applicant requests the IPEA to **postpone** the start of the international preliminary examination until the expiration of the applicable time limit under Rule 69.1(d).

4. ☐ The applicant expressly requests to **postpone** the start of the international preliminary examination until the expiration of the applicable time limit under Rule 54bis.1(a).

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: English

- ☒ which is the language in which the international application was filed.
☐ which is the language of a translation furnished for the purposes of international search.
☐ which is the language of publication of the international application.
☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.

Box No. V ELECTION OF STATES

The filing of this demand constitutes the election of all Contracting States which are designated and are bound by Chapter II of the PCT.

Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- | | | | |
|---|---|-----|--------|
| 1. translation of international application | : | | sheets |
| 2. amendments under Article 34 | : | 106 | sheets |
| 3. letter accompanying the amendments under Article 34 (Rule 66.8) | : | 1 | sheets |
| 4. copy (or, where required, translation) of amendments under Article 19 | : | | sheets |
| 5. copy of the letter accompanying the amendments under Article 19 (Rules 46.5(b) and 53.9) | : | | sheets |
| 6. copy (or, where applicable, translation) of any statement under Article 19 (Rule 62.1(ii)) | : | | sheets |
| 7. other (<i>specify</i>) Formal Reply to Written Opinion | : | 5 | sheets |

For International Preliminary Examining Authority use only

received	not received
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☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐
☐	☐

The demand is also accompanied by the item(s) marked below:

- | | |
|--|--|
| 1. ☒ fee calculation sheet | 5. ☐ sequence listing in the form of an Annex C/ST.25 text file |
| 2. ☐ original separate power of attorney | 6. ☐ other (<i>specify</i>): _____ |
| 3. ☐ original general power of attorney | _____ |
| 4. ☐ copy of general power of attorney; reference number, if any: | _____ |

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

/S. Reid Long/

S. Reid Long
US Reg. No. 73,528
Agent for Applicant

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply.

☐ The applicant has been informed accordingly.

4. ☐ The date of receipt of the demand is WITHIN the time limit of 19 months from the priority date as extended by virtue of Rule 80.5.

5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rules 82 or 82quater.

6. ☐ The date of receipt of the demand is AFTER the expiration of the time limit under Rule 54bis.1(a) and item 7 or 8, below, does not apply.

7. ☐ The date of receipt of the demand is WITHIN the time limit under Rule 54bis.1(a) as extended by virtue of Rule 80.5.

8. ☐ Although the date of receipt of the demand is after the expiration of the time limit under Rule 54bis.1(a), the delay in arrival is EXCUSED pursuant to Rules 82 or 82quater.

For International Bureau use only

Demand received from IPEA on:

PCT

FEE CALCULATION SHEET

Annex to the Demand

International application No. PCT/US2019/037543	For International Preliminary Examining Authority use only													
Applicant's or agent's file reference REAT.P0103WO	Date stamp of the IPEA													
Applicant Reata Pharmaceuticals, Inc.														
CALCULATION OF PRESCRIBED FEES <i>(Applicants may be entitled to a reduction of the preliminary examination fee and the handling fee as indicated in the PCT Fee Tables (www.wipo.int/pct/en/fees.pdf))</i> <table style="width: 100%;"> <tr> <td style="width: 60%;">1. PRELIMINARY EXAMINATION FEE</td> <td style="width: 20%; text-align: right;">1.830,00EUR</td> <td style="width: 20%; text-align: center; border: 1px solid black;">P</td> </tr> <tr> <td>2. HANDLING FEE</td> <td style="text-align: right;">183,00EUR</td> <td style="text-align: center; border: 1px solid black;">H</td> </tr> <tr> <td>3. TOTAL OF PRESCRIBED FEES Add the amounts entered at P and H and enter total in the TOTAL box</td> <td style="text-align: right; border: 1px solid black;">2.013,00EUR</td> <td></td> </tr> <tr> <td></td> <td style="text-align: center; border: 1px solid black;">TOTAL</td> <td></td> </tr> </table>			1. PRELIMINARY EXAMINATION FEE	1.830,00EUR	P	2. HANDLING FEE	183,00EUR	H	3. TOTAL OF PRESCRIBED FEES Add the amounts entered at P and H and enter total in the TOTAL box	2.013,00EUR			TOTAL	
1. PRELIMINARY EXAMINATION FEE	1.830,00EUR	P												
2. HANDLING FEE	183,00EUR	H												
3. TOTAL OF PRESCRIBED FEES Add the amounts entered at P and H and enter total in the TOTAL box	2.013,00EUR													
	TOTAL													
MODE OF PAYMENT <i>(Not all modes of payment may be available at all IPEAs)</i> ☐ credit card <i>(details should not be included on this sheet)</i> ☐ authorization to charge deposit or current account with the IPEA (see below) ☐ bank transfer ☐ cash ☐ postal money order ☐ check ☐ revenue stamps ☒ other (specify): <u>Credit Card Payment via EPO, Voucher No. 6022090</u>														
AUTHORIZATION TO CHARGE (OR CREDIT) DEPOSIT OR CURRENT ACCOUNT <i>(This mode of payment may not be available at all IPEAs)</i> ☐ Authorization to charge the total fees indicated above. ☐ <i>(This check-box may be marked only if the conditions for deposit or current accounts of the IPEA so permit)</i> Authorization to charge any deficiency or credit any overpayment in the total fees indicated above. IPEA/ _____ Deposit or Current Account No.: _____ Date: _____ Name: _____ Signature: _____														

PATENT

**IN THE EUROPEAN PATENT OFFICE ACTING AS THE INTERNATIONAL
SEARCH AUTHORITY**

In re Application of:

REATA PHARMACEUTICAL, INC.

Serial No.: PCT/US2019/037543

Filed: 10 July 2019

For: PYRAZOLE AND IMIDAZOLE
COMPOUNDS FOR INHIBITION OF IL-
17 AND RORgamma

Atty. Dkt. No.: REAT.P0103WO

**RESPONSE TO INTERNATIONAL SEARCH REPORT AND WRITTEN OPINION
AND DEMAND FOR PRELIMINARY EXAMINATION UNDER ARTICLE 31**

WIPO

34 Chemin des Colombettes
1211 Geneva 20, Switzerland

Attention: Examiner Daniela Gavrilu:

In response to the International Search Report and Written Opinion regarding the captioned application, Applicant hereby submits this response under Articles 31 and 34 and makes a demand for International Preliminary Examination under Chapter II of the Patent Cooperation Treaty.

A. Amendments to the Claims

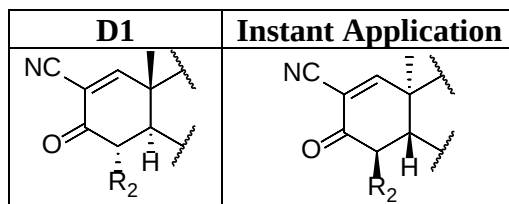
The Applicant has amended the claims herewith. The chemical groups hydrogen and $\text{alkyl}_{(C \leq 12)}$ has been removed as an option for the variable R_4 and R_5 , hydrogen has been removed from R_6 , and R_2' has been restricted to hydrogen in claims 1-10. Support for these amendments can be found in the claims as originally filed. Additionally, claims 31-34, 61-63, and 89 have been cancelled based upon the amendments to claim 1. Support for this amendment can be found in the claims as originally filed. Finally, claim 139 has been amended to remove those compounds which no longer fall within the scope of the amended claims. Support for this

amendment can be found in the claim as originally filed. All of these amendments are supported by the claims as originally filed and in light of the text of the application. A clean and marked up version of the claims have been attached.

B. Novelty

The Written Opinion of the International Search Authority contends that D1-D4 are novelty destroying for the instant claims. At least in view of the explanations below and the amended claims submitted herewith, Applicant submits that all of the amended claims are novel over D1-D4.

According to the Written Opinion, D1 is novelty destroying for the instant claims. The Applicant disagrees with this characterization of the instant claims. The Applicant notes that the compounds of D1 are drawn to compounds with the head group on the left while the instant compounds contain the head group on the right.

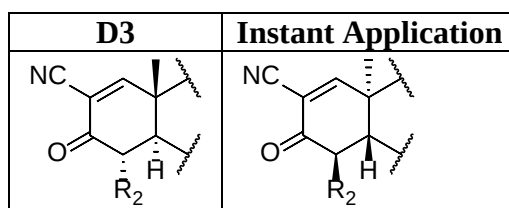


These two head groups as shown above have alternative stereochemical orientations. Based upon the differences between the head groups, the Applicant submits that a finding of anticipation is not well founded.

Turning to D2, the Applicant notes that the compounds included in D2 contain a methyl or methoxy group at the R5 position. Based upon the amendments to the claims, the Applicant submits that R5 is not allowed to be either an alkyl or alkoxy group. In view of this fact, the Applicant submits that D2 does not anticipate the instant claims.

Next, D3 is cited by the Written Opinion as novelty destroying for all claims. Again, the Applicant submits that the compounds of D3 contain a fixed headgroup with the following

stereochemistry as is shown on the left while the instant claims are limited to the head group on the right.



These two head groups as shown above have alternative stereochemical orientations. Based upon the differences in the headgroup, the Applicant submits that the amended claims submitted herewith are novel in view of D3.

Finally, the Applicant submits that D4 does not anticipate the instant claims. None of the compounds disclosed in D4 read upon the instant claims. In particular, most of the compounds in D4 contain a methyl group of the R₅ position which is not allowed by the instantly amended claims. In view of the amendments, the Applicant submits that the instant claims are not anticipated by D4.

C. Inventive Step

The Written Opinion contends that the problem to be solved is the provision of anti-inflammatory agents as the claims are not novel in view of D1-D4. This characterization misses an important mechanistic insight reported in the application. In particular, Applicants have reported a series of novel compounds that selectively inhibit the IL-17 pathway (*i.e.*, reduced activity in other anti-inflammatory pathways), which is a promising therapeutic property not shared by all or even most other previously reported anti-inflammatory agents.

Modulation of the IL-17 pathway is most directly implicated in treating inflammatory related autoimmune disorders such as psoriasis, multiple sclerosis, rheumatoid arthritis, and inflammatory bowel disease, or reactive disorders such as asthma. See, for example, Hu *et al.*, “The IL-17 pathway as a major therapeutic target in autoimmune diseases,” *Ann. N.Y. Acad. Sci.*, 1217(1):60-76, 2011; Ivanov *et al.*, “The orphan nuclear receptor ROR γ t directs the

differentiation program of proinflammatory IL-17+ T helper cells,” *Cells*, 126(6):1121-1133, 2006; Gaffen *et al.*, “IL-23-IL-17 immune axis: Discovery, Mechanistic Understanding, and Clinical Testing,” *Nat. Rev. Immunol.*, 14(9):585-600, 2014; Yan *et al.*, “CNS-specific therapy for ongoing EAE by silencing IL-17 pathway in astrocytes,” *Molecular Therapy*, 20(7):1338-1348, 2012 and Iwakura and Ishigame, “The IL-23/IL-17 axis in inflammation,” *J. Clinical Investigations*, 116(5):1218-1222, 2006. These references are all freely available.

In contrast, NO inhibition, which is described in D1-D4, is more directly implicated in the following indications: chronic obstructive pulmonary disease (COPD), cancer, asthma, hypertension, symptoms of diabetes, hypercholesterolemia, atherosclerosis, encephalomyelitis, and neurodegenerative diseases, such as Alzheimer’s disease (AD), Parkinson’s disease (PD), Huntington’s disease (HD), amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), and ischemia. See, for example, Li and Forstermann, “Nitric oxide in the pathogenesis of vascular disease,” *J. Pathology*, 190(3):244-254, 2000; Guix *et al.*, “The physiology and pathophysiology of nitric oxide in the brain,” *Progress in Neurobiology*, 76(2):126-152, 2005; and Ricciardolo *et al.*, “Nitric oxide in health and disease of the respiratory system,” *Physiological Reviews*, 84(3):731-765, 2004. These references are all freely available.

Furthermore, the Written Opinion’s assertion that anti-inflammatory compounds with varying pharmacologies are essentially interchangeable is also not well founded in scientific basis. For example, tumor necrosis factor (TNF- α) is a well known inflammatory cytokine and a variety of anti-TNF antibodies have been approved for the treatment of autoimmune diseases such as rheumatoid arthritis and Crohn’s disease. However, these agents are not approved for the treatment of systemic lupus erythematosus (SLE) or multiple sclerosis, both of which are also inflammatory autoimmune diseases. A recent survey of SLE patients reported that TNF- α was not elevated in these patients, although many other inflammatory cytokines were elevated. Given the underlying complexity of inflammatory diseases coupled with often

uncertain etiology, it may be true that any particular pharmacological approach will be more effective in certain indications than other indications or in certain patients relative to other patients.

Thus, the problem to be solved is not merely the identification of compounds with anti-inflammatory properties, rather, the problem is more precisely the identification of compounds with alternative pharmacological profiles, such as inhibition of IL-17 activity that may be useful therapeutic agents in one or more broad clinical settings.

In support of this conclusion, the Applicant points to Table 1 on page 328 of the instant Application. In particular, the instant compounds show low nanomolar activity inhibiting hIL17 which often show weak NRF2 activation. Compare compound T133 which shows IL17 activity of 247 nM compared to compound T69 which shows IL17 activity of 12 nM. For at least the above reasons, the Applicant submits that the amended claims submitted herewith possess an inventive step over the cited art.

D. Conclusions

The requisite fees for this demand have been paid via credit card directly to the International Search Authority, the European Patent Office. If there are any questions, please contact the undersigned agent.

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Telephone No.: (512) 334-2926
Facsimile No.: (512) 334-2999

Date: April 15, 2020

Respectfully submitted



S. Reid Long
U.S. Reg. No. 73,528
Agent for Applicant

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
AS RECEIVING OFFICE

In re Application of:

REATA PHARMACEUTICAL, INC.

Serial No.: PCT/US2019/037543

Filed: 10 July 2019

For: PYRAZOLE AND IMIDAZOLE
COMPOUNDS FOR INHIBITION OF IL-
17 AND RORgamma

Atty. Dkt. No.: REAT.P0103WO

LETTER ACCOMPANYING AMENDMENT UNDER ARTICLE 34

Applicant submits an Article 34 Amendment to amend the claims and enclose both a marked copy of the amended claims showing the difference between the original claims and the replacement claims. Replacement sheets of the amended claims (clean copy) also accompany the amendment.

Applicant also submits its formal reply to the Written Opinion filed concurrently herewith.

Should this Authority have any questions, please do not hesitate to contact the undersigned.

Respectfully submitted,



S. Reid Long
U.S. Reg. No. 73,528
Agent for Applicant

Parker Highlander PLLC
1120 S. Capital of Texas Highway
Building One, Suite 200
Austin, TX 78746
Telephone No.: 512.334.2926
Facsimile No.: 512.334.2999

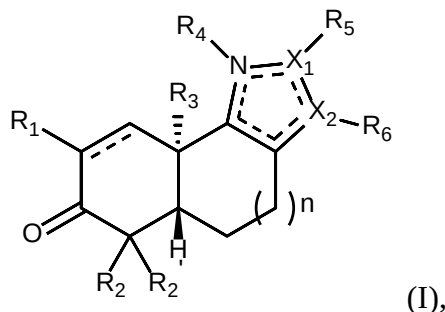
Date: April 15, 2020

AMENDMENT UNDER ARTICLE 34

Marked Copy of Amended Claims

CLAIMS

1. (Currently Amended) A compound of the formula:



wherein:

n is 0, 1, or 2;

R₁ is cyano, fluoro, -CF₃, or -C(O)R_a, wherein:

R_a is hydroxy or amino; or

alkoxy_(C≤6), alkylamino_(C≤6), dialkylamino_(C≤6), or a substituted version of any of these groups;

~~R₂ and R₂' are each independently~~ R₂ is hydrogen; or

alkyl_(C≤12), cycloalkyl_(C≤12), alkenyl_(C≤12), alkynyl_(C≤12), aryl_(C≤18), aralkyl_(C≤18), heteroaryl_(C≤18), heteroaralkyl_(C≤18), or a substituted version of any of these groups; ~~or~~

~~R₂ and R₂' are taken together and are alkanediyl_(C≤8), alkenediyl_(C≤8), or a substituted version of either of these groups;~~

R₂' is hydrogen;

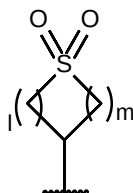
R₃ is alkyl_(C≤12), alkenyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12), or a substituted version of any of these groups;

R₄ and R₅ are each independently absent ~~or hydrogen;~~ or

~~alkyl_(C≤12), cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12), heteroaryl_(C≤12), heteroaralkyl_(C≤12), -arenediyl_(C≤12)-alkyl_(C≤12), -arenediyl_(C≤12)-aryl_(C≤12), -arenediyl_(C≤12)-heteroaryl_(C≤12), -arenediyl_(C≤12)-heterocycloalkyl_(C≤12), -arenediyl_(C≤12)-cycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-alkyl_(C≤12),~~

–heteroarenediyl_(C≤12)–aryl_(C≤12), –hetero-
arenediyl_(C≤12)–heteroaryl_(C≤12), –heteroarenediyl_(C≤12)–hetero-
cycloalkyl_(C≤12), –heteroarenediyl_(C≤12)–cycloalkyl_(C≤12),
–heterocycloalkanediyl_(C≤12)–aryl_(C≤12),
–heterocycloalkanediyl_(C≤12)–heteroaryl_(C≤12), or a substituted
version of any of these groups; or

a group of the formula:



wherein l and m are each 0, 1, 2, or 3;

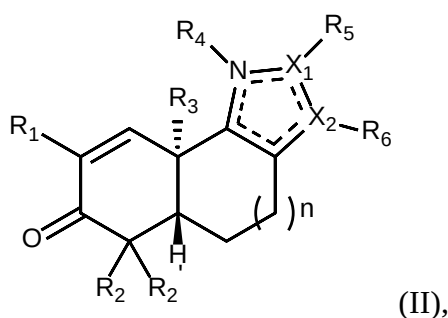
R₆ is absent, ~~hydrogen~~, or amino; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12),
–alkanediyl_(C≤12)–cycloalkyl_(C≤12), –alkanediyl_(C≤18)–aralkoxy_(C≤18),
heterocycloalkyl_(C≤12), aryl_(C≤18), –arenediyl_(C≤12)–alkyl_(C≤12),
aralkyl_(C≤18), –arenediyl_(C≤18)–heterocycloalkyl_(C≤12), heteroaryl_(C≤18),
–heteroarenediyl_(C≤12)–alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12),
alkoxy_(C≤12), or a substituted version of any of these groups; and

X₁ and X₂ are each independently C or N, provided that X₂ is C when R₆ is
amino, alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
or diarylamino_(C≤12);

or a pharmaceutically acceptable salt thereof.

2. (Currently Amended) The compound of claim 1 further defined as:



(II),

wherein:

n is 0, 1, or 2;

R₁ is cyano, fluoro, -CF₃, or -C(O)R_a, wherein

R_a is hydroxy or amino; or

alkoxy_(C≤6), alkylamino_(C≤6), dialkylamino_(C≤6), or a substituted version of any of these groups;

~~R₂ and R₂' are each independently~~ hydrogen; or

alkyl_(C≤12), cycloalkyl_(C≤12), alkenyl_(C≤12), alkynyl_(C≤12), aryl_(C≤18), aralkyl_(C≤18), heteroaryl_(C≤18), heteroaralkyl_(C≤18), or a substituted version of any of these groups; ~~or~~

~~R₂ and R₂' are taken together and are alkanediyl_(C≤8), alkenediyl_(C≤8), or a substituted version of either of these groups;~~

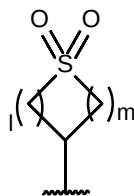
R₂' is hydrogen;

R₃ is alkyl_(C≤12), alkenyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12), or a substituted version of any of these groups;

R₄ and R₅ are each independently absent ~~or hydrogen~~; or

~~alkyl_(C≤12), cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12), heteroaryl_(C≤12), heteroaralkyl_(C≤12), -arenediyl_(C≤12)-alkyl_(C≤12), -arenediyl_(C≤12)-aryl_(C≤12), -arenediyl_(C≤12)-heteroaryl_(C≤12), -arenediyl_(C≤12)-heterocycloalkyl_(C≤12), -arenediyl_(C≤12)-cycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-alkyl_(C≤12), -heteroarenediyl_(C≤12)-aryl_(C≤12), -heteroarenediyl_(C≤12)-heteroaryl_(C≤12), -heteroarenediyl_(C≤12)-heterocycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-cycloalkyl_(C≤12), -heterocycloalkanediy_(C≤12)-aryl_(C≤12), -heterocycloalkanediy_(C≤12)-heteroaryl_(C≤12), or a substituted version of any of these groups; or~~

a group of the formula:



wherein l and m are each 0, 1, 2, or 3;

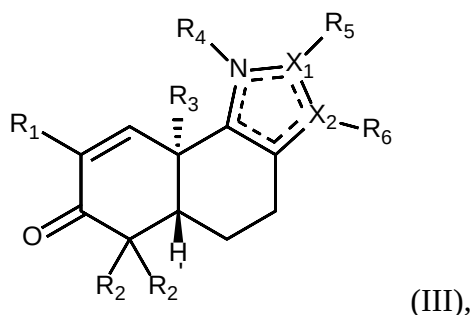
R₆ is absent, ~~hydrogen~~, or amino; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12), dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12), diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12),
 -alkanediyl_(C≤12)-cycloalkyl_(C≤12), -alkanediyl_(C≤18)-aralkoxy_(C≤18), heterocycloalkyl_(C≤12), aryl_(C≤18), -arenediyl_(C≤12)-alkyl_(C≤12), aralkyl_(C≤18), -arenediyl_(C≤18)-heterocycloalkyl_(C≤12), heteroaryl_(C≤18),
 -heteroarenediyl_(C≤12)-alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12), alkoxy_(C≤12), or a substituted version of any of these groups; and

X₁ and X₂ are each independently C or N, provided that X₂ is C when R₆ is amino, alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12), dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12), or diarylamino_(C≤12);

or a pharmaceutically acceptable salt thereof.

3. (Currently Amended) The compound of either claim 1 or claim 2 further defined as:



wherein:

R₁ is cyano, fluoro, -CF₃, or -C(O)R_a, wherein

R_a is hydroxy or amino; or

alkoxy_(C≤6), alkylamino_(C≤6), dialkylamino_(C≤6), or a substituted version of any of these groups;

~~R₂ and R₂' are each independently is~~ hydrogen; or

alkyl_(C≤12), cycloalkyl_(C≤12), alkenyl_(C≤12), alkynyl_(C≤12), aryl_(C≤18), aralkyl_(C≤18), heteroaryl_(C≤18), heteroaralkyl_(C≤18), or a substituted version of any of these groups; ~~or~~

~~R₂ and R₂' are taken together and are alkanediyl_(C≤8), alkenediyl_(C≤8), or a substituted version of either of these groups;~~

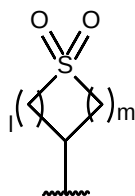
R₂' is hydrogen;

R₃ is alkyl_(C≤12), alkenyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12), or a substituted version of any of these groups;

R₄ and R₅ are each independently absent or hydrogen; or

~~alkyl_(C≤12), cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12),
aralkyl_(C≤12), heteroaryl_(C≤12), heteroaralkyl_(C≤12),
-arenediyl_(C≤12)-alkyl_(C≤12), -arenediyl_(C≤12)-aryl_(C≤12),
-arenediyl_(C≤12)-heteroaryl_(C≤12),
-arenediyl_(C≤12)-heterocycloalkyl_(C≤12), -arenediyl_(C≤12)-cyclo-
alkyl_(C≤12), -heteroarenediyl_(C≤12)-alkyl_(C≤12),
-heteroarenediyl_(C≤12)-aryl_(C≤12), -hetero-
arenediyl_(C≤12)-heteroaryl_(C≤12), -heteroarenediyl_(C≤12)-hetero-
cycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-cycloalkyl_(C≤12),
-heterocycloalkanediyl_(C≤12)-aryl_(C≤12),
-heterocycloalkanediyl_(C≤12)-heteroaryl_(C≤12), or a substituted
version of any of these groups; or~~

a group of the formula:



wherein l and m are each 0, 1, 2, or 3;

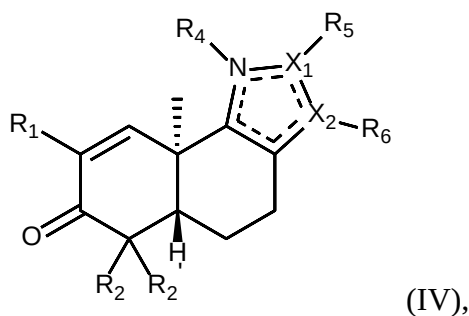
R₆ is absent, ~~hydrogen~~, or amino; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12),
-alkanediyl_(C≤12)-cycloalkyl_(C≤12), -alkanediyl_(C≤18)-aralkoxy_(C≤18),
heterocycloalkyl_(C≤12), aryl_(C≤18), -arenediyl_(C≤12)-alkyl_(C≤12),
aralkyl_(C≤18), -arenediyl_(C≤18)-heterocycloalkyl_(C≤12), heteroaryl_(C≤18),
-heteroarenediyl_(C≤12)-alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12),
alkoxy_(C≤12), or a substituted version of any of these groups; and

X₁ and X₂ are each independently C or N, provided that X₂ is C when R₆ is
amino, alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
or diarylamino_(C≤12);

or a pharmaceutically acceptable salt thereof.

4. (Currently Amended) The compound according to any one of claims 1-3 further defined as:



wherein:

R_1 is cyano, fluoro, $-CF_3$, or $-C(O)R_a$, wherein

R_a is hydroxy or amino; or

alkoxy_(C≤6), alkylamino_(C≤6), dialkylamino_(C≤6), or a substituted version of any of these groups;

~~R_2 and R_2' are each independently~~ is hydrogen; or

alkyl_(C≤12), cycloalkyl_(C≤12), alkenyl_(C≤12), alkynyl_(C≤12), aryl_(C≤18), aralkyl_(C≤18), heteroaryl_(C≤18), heteroaralkyl_(C≤18), or a substituted version of any of these groups; ~~or~~

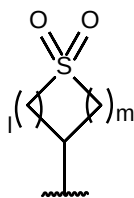
~~R_2 and R_2' are taken together and are~~ alkenediyl_(C≤8), or
~~a substituted version of either of these groups;~~

R_2' is hydrogen;

R_4 and R_5 are each independently absent ~~or hydrogen~~; or

~~alkyl_(C≤12), cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12),~~
aralkyl_(C≤12), heteroaryl_(C≤12), heteroaralkyl_(C≤12),
 $-\text{arenediyl}_{(C≤12)}-\text{alkyl}_{(C≤12)}$, $-\text{arenediyl}_{(C≤12)}-\text{aryl}_{(C≤12)}$,
 $-\text{arenediyl}_{(C≤12)}-\text{heteroaryl}_{(C≤12)}$,
 $-\text{arenediyl}_{(C≤18)}-\text{heterocycloalkyl}_{(C≤12)}$, $-\text{arenediyl}_{(C≤12)}-\text{cyclo-}$
 $\text{alkyl}_{(C≤12)}$, $-\text{heteroarenediyl}_{(C≤12)}-\text{alkyl}_{(C≤12)}$,
 $-\text{heteroarenediyl}_{(C≤12)}-\text{aryl}_{(C≤12)}$,
 $-\text{heteroarenediyl}_{(C≤12)}-\text{heteroaryl}_{(C≤12)}$,
 $-\text{heteroarenediyl}_{(C≤12)}-\text{heterocycloalkyl}_{(C≤12)}$,
 $-\text{heteroarenediyl}_{(C≤12)}-\text{cycloalkyl}_{(C≤12)}$,
 $-\text{heterocycloalkanediy}_{(C≤12)}-\text{aryl}_{(C≤12)}$,
 $-\text{heterocycloalkanediy}_{(C≤12)}-\text{heteroaryl}_{(C≤12)}$, or a substituted version of any of these groups; or

a group of the formula:



wherein l and m are each 0, 1, 2, or 3;

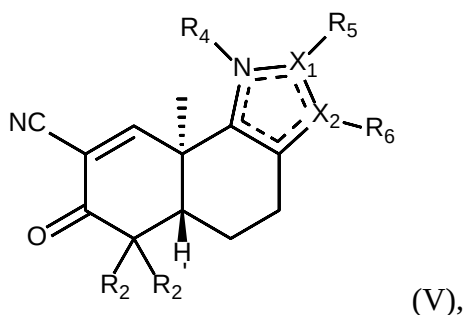
R₆ is absent, ~~hydrogen~~, or amino; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12),
-alkanediyl_(C≤12)-cycloalkyl_(C≤12), -alkanediyl_(C≤18)-aralkoxy_(C≤18),
heterocycloalkyl_(C≤12), aryl_(C≤18), -arenediyl_(C≤12)-alkyl_(C≤12),
aralkyl_(C≤18), -arenediyl_(C≤18)-heterocycloalkyl_(C≤12), heteroaryl_(C≤18),
-heteroarenediyl_(C≤12)-alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12),
alkoxy_(C≤12), or a substituted version of any of these groups; and

X₁ and X₂ are each independently C or N, provided that X₂ is C when R₆ is
amino, alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
or diarylamino_(C≤12);

or a pharmaceutically acceptable salt thereof.

5. (Currently Amended) The compound according to any one of claims 1-4, further defined as:



wherein:

R₂ and R_{2'} ~~are each independently~~ is hydrogen; or

alkyl_(C≤12), cycloalkyl_(C≤12), alkenyl_(C≤12), alkynyl_(C≤12), aryl_(C≤18),
aralkyl_(C≤18), heteroaryl_(C≤18), heteroaralkyl_(C≤18), or a substituted
version of any of these groups; ~~or~~

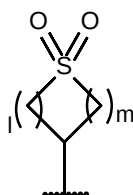
~~R₂ and R₂' are taken together and are alkanediyl_(C≤8), alkenediyl_(C≤8), or a substituted version of either of these groups;~~

R₂' is hydrogen;

R₄ and R₅ are each independently absent ~~or hydrogen;~~ or

~~alkyl_(C≤12), cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12), heteroaryl_(C≤12), heteroaralkyl_(C≤12), -arenediyl_(C≤12)-alkyl_(C≤12), -arenediyl_(C≤12)-aryl_(C≤12), -arenediyl_(C≤12)-heteroaryl_(C≤12), -arenediyl_(C≤12)-heterocycloalkyl_(C≤12), -arenediyl_(C≤12)-cycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-alkyl_(C≤12), -heteroarenediyl_(C≤12)-aryl_(C≤12), -heteroarenediyl_(C≤12)-heteroaryl_(C≤12), -heteroarenediyl_(C≤12)-heterocycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-cycloalkyl_(C≤12), -heterocycloalkanedyl_(C≤12)-aryl_(C≤12), -heterocycloalkanedyl_(C≤12)-heteroaryl_(C≤12), or a substituted version of any of these groups;~~ or

a group of the formula:



wherein l and m are each 0, 1, 2, or 3;

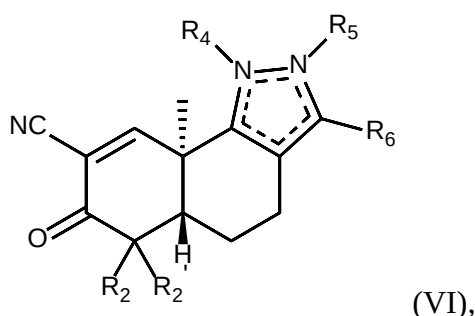
R₆ is absent, ~~hydrogen,~~ or amino; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12), dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12), diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12), -alkanediyl_(C≤12)-cycloalkyl_(C≤12), -alkanediyl_(C≤18)-aralkoxy_(C≤18), heterocycloalkyl_(C≤12), aryl_(C≤18), -arenediyl_(C≤12)-alkyl_(C≤12), aralkyl_(C≤18), -arenediyl_(C≤18)-heterocycloalkyl_(C≤12), heteroaryl_(C≤18), -heteroarenediyl_(C≤12)-alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12), alkoxy_(C≤12), or a substituted version of any of these groups; and

X₁ and X₂ are each independently C or N, provided that X₂ is C when R₆ is amino, alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12), dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12), or diarylamino_(C≤12);

or a pharmaceutically acceptable salt thereof.

6. (Currently Amended) The compound according to any one of claims 1-3, further defined as:



wherein:

~~R₂ and R₂' are each independently~~ is hydrogen; or

alkyl_(C≤12), cycloalkyl_(C≤12), alkenyl_(C≤12), alkynyl_(C≤12), aryl_(C≤18),
aralkyl_(C≤18), heteroaryl_(C≤18), heteroaralkyl_(C≤18), or a substituted
version of any of these groups; ~~or~~

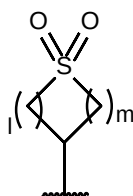
~~R₂ and R₂' are taken together and are~~ alkanedediyl_(C≤8), alkenedediyl_(C≤8), or
~~a substituted version of either of these groups;~~

R₂' is hydrogen;

~~R₄ and R₅ are each independently absent, hydrogen; or~~

~~alkyl_(C≤12), cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12),
aralkyl_(C≤12), heteroaryl_(C≤12), heteroaralkyl_(C≤12),
-arenediyl_(C≤12)-alkyl_(C≤12), -arenediyl_(C≤12)-aryl_(C≤12),
-arenediyl_(C≤12)-heteroaryl_(C≤12),
-arenediyl_(C≤12)-heterocycloalkyl_(C≤12), -arenediyl_(C≤12)-cyclo-
alkyl_(C≤12), -heteroarenediyl_(C≤12)-alkyl_(C≤12),
-heteroarenediyl_(C≤12)-aryl_(C≤12), -hetero-
arenediyl_(C≤12)-heteroaryl_(C≤12), -heteroarenediyl_(C≤12)-hetero-
cycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-cycloalkyl_(C≤12),
-heterocycloalkanediy_(C≤12)-aryl_(C≤12),
-heterocycloalkanediy_(C≤12)-heteroaryl_(C≤12), or a substituted
version of any of these groups; or~~

a group of the formula:



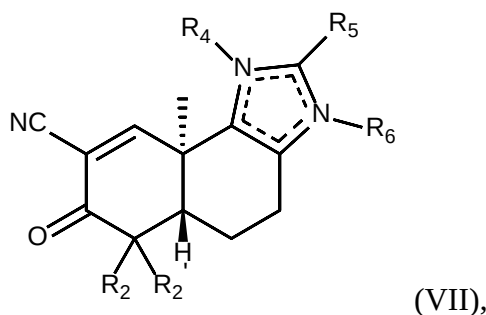
wherein l and m are each 0, 1, 2, or 3; and

R₆ is absent, ~~hydrogen~~; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
 dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
 diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12),
~~–alkanediyl_(C≤12)–cycloalkyl_(C≤12), –alkanediyl_(C≤18)–aralkoxy_(C≤18),
 heterocycloalkyl_(C≤12), aryl_(C≤18), –arenediyl_(C≤12)–alkyl_(C≤12),
 aralkyl_(C≤18), –arenediyl_(C≤18)–heterocycloalkyl_(C≤12), heteroaryl_(C≤18),
 –heteroarenediyl_(C≤12)–alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12),
 alkoxy_(C≤12), or a substituted version of any of these groups;~~

or a pharmaceutically acceptable salt thereof.

7. (Currently Amended) The compound according to any one of claims 1-3, further defined as:



wherein:

~~R₂ and R₂' are each independently~~ R₂ and R₂' are each independently is hydrogen; or

alkyl_(C≤12), cycloalkyl_(C≤12), alkenyl_(C≤12), alkynyl_(C≤12), aryl_(C≤18),
 aralkyl_(C≤18), heteroaryl_(C≤18), heteroaralkyl_(C≤18), or a substituted version
 of any of these groups; ~~or~~

~~R₂ and R₂' are taken together and are alkanediyl_(C≤8), alkenediyl_(C≤8), or a
 substituted version of either of these groups;~~

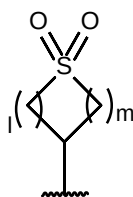
R₂' is hydrogen;

R₄ and R₅ are each independently absent, ~~hydrogen~~; or

~~alkyl_(C≤12), cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12),
 aralkyl_(C≤12), heteroaryl_(C≤12), heteroaralkyl_(C≤12),~~

$\text{--arenediyl}_{(C\leq 12)}\text{--alkyl}_{(C\leq 12)}$, $\text{--arenediyl}_{(C\leq 12)}\text{--aryl}_{(C\leq 12)}$,
 $\text{--arenediyl}_{(C\leq 12)}\text{--heteroaryl}_{(C\leq 12)}$,
 $\text{--arenediyl}_{(C\leq 12)}\text{--heterocycloalkyl}_{(C\leq 12)}$, $\text{--arenediyl}_{(C\leq 12)}\text{--cyclo-}$
 $\text{alkyl}_{(C\leq 12)}$, $\text{--heteroarenediyl}_{(C\leq 12)}\text{--alkyl}_{(C\leq 12)}$,
 $\text{--heteroarenediyl}_{(C\leq 12)}\text{--aryl}_{(C\leq 12)}$, --hetero-
 $\text{arenediyl}_{(C\leq 12)}\text{--heteroaryl}_{(C\leq 12)}$, $\text{--heteroarenediyl}_{(C\leq 12)}\text{--hetero-}$
 $\text{cycloalkyl}_{(C\leq 12)}$, $\text{--heteroarenediyl}_{(C\leq 12)}\text{--cycloalkyl}_{(C\leq 12)}$,
 $\text{--heterocycloalkanediy}_{(C\leq 12)}\text{--aryl}_{(C\leq 12)}$,
 $\text{--heterocycloalkanediy}_{(C\leq 12)}\text{--heteroaryl}_{(C\leq 12)}$, or a substituted
 version of any of these groups; or

a group of the formula:



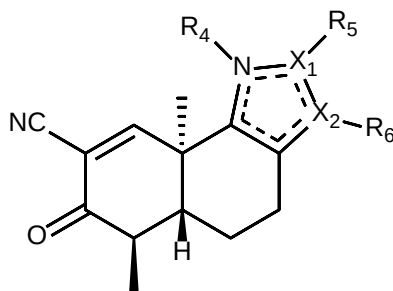
wherein l and m are each 0, 1, 2, or 3; and

R_6 is absent, ~~hydrogen~~; or

$\text{alkylamino}_{(C\leq 12)}$, $\text{dialkylamino}_{(C\leq 12)}$, $\text{cycloalkylamino}_{(C\leq 12)}$,
 $\text{dicycloalkylamino}_{(C\leq 12)}$, $\text{alkyl(cycloalkyl)amino}_{(C\leq 12)}$, $\text{arylamino}_{(C\leq 12)}$,
 $\text{diarylamino}_{(C\leq 12)}$, $\text{alkyl}_{(C\leq 12)}$, $\text{cycloalkyl}_{(C\leq 12)}$,
 $\text{--alkanediyl}_{(C\leq 12)}\text{--cycloalkyl}_{(C\leq 12)}$, $\text{--alkanediyl}_{(C\leq 18)}\text{--aralkoxy}_{(C\leq 18)}$,
 $\text{heterocycloalkyl}_{(C\leq 12)}$, $\text{aryl}_{(C\leq 18)}$, $\text{--arenediyl}_{(C\leq 12)}\text{--alkyl}_{(C\leq 12)}$,
 $\text{aralkyl}_{(C\leq 18)}$, $\text{--arenediyl}_{(C\leq 18)}\text{--heterocycloalkyl}_{(C\leq 12)}$, $\text{heteroaryl}_{(C\leq 18)}$,
 $\text{--heteroarenediyl}_{(C\leq 12)}\text{--alkyl}_{(C\leq 12)}$, $\text{heteroaralkyl}_{(C\leq 18)}$, $\text{acyl}_{(C\leq 12)}$,
 $\text{alkoxy}_{(C\leq 12)}$, or a substituted version of any of these groups;

or a pharmaceutically acceptable salt thereof.

8. (Currently Amended) The compound according to any one of claims 1-4, further defined as:



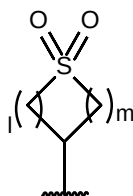
(VIII),

wherein:

R₄ and R₅ are each independently absent, ~~hydrogen~~; or

~~alkyl_(C≤12)~~, cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12),
aralkyl_(C≤12), heteroaryl_(C≤12), heteroaralkyl_(C≤12),
-arenediyl_(C≤12)-alkyl_(C≤12), -arenediyl_(C≤12)-aryl_(C≤12),
-arenediyl_(C≤12)-heteroaryl_(C≤12),
-arenediyl_(C≤12)-heterocycloalkyl_(C≤12), -arenediyl_(C≤12)-cyclo-
alkyl_(C≤12), -heteroarenediyl_(C≤12)-alkyl_(C≤12),
-heteroarenediyl_(C≤12)-aryl_(C≤12), -hetero-
arenediyl_(C≤12)-heteroaryl_(C≤12), -heteroarenediyl_(C≤12)-hetero-
cycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-cycloalkyl_(C≤12),
-heterocycloalkanediyl_(C≤12)-aryl_(C≤12),
-heterocycloalkanediyl_(C≤12)-heteroaryl_(C≤12), or a substituted
version of any of these groups; or

a group of the formula:



wherein l and m are each 0, 1, 2, or 3; and

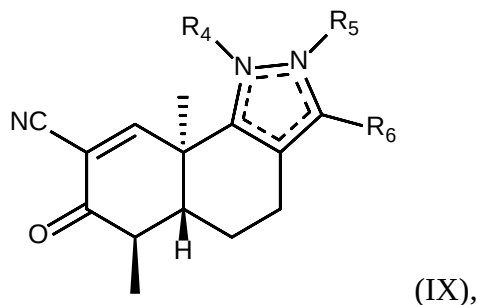
R₆ is absent, ~~hydrogen~~; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12),
-alkanediyl_(C≤12)-cycloalkyl_(C≤12), -alkanediyl_(C≤18)-aralkoxy_(C≤18),
heterocycloalkyl_(C≤12), aryl_(C≤18), -arenediyl_(C≤12)-alkyl_(C≤12),
aralkyl_(C≤18), -arenediyl_(C≤18)-heterocycloalkyl_(C≤12), heteroaryl_(C≤18),
-heteroarenediyl_(C≤12)-alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12),
alkoxy_(C≤12), or a substituted version of any of these groups; and

X₁ and X₂ are each independently C or N, provided that X₂ is C when R₆ is
amino, alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
or diarylamino_(C≤12);

or a pharmaceutically acceptable salt thereof.

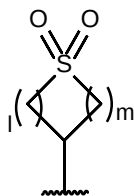
9. (Currently Amended) The compound according to any one of claims 1-4 and 8, further defined as:



wherein:

R₄ and R₅ are each independently absent, ~~hydrogen~~; or
~~alkyl_(C≤12)~~, cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12),
 aralkyl_(C≤12), heteroaryl_(C≤12), heteroaralkyl_(C≤12),
~~—arenediyl_(C≤12)—alkyl_(C≤12)~~, ~~—arenediyl_(C≤12)—aryl_(C≤12)~~,
~~—arenediyl_(C≤12)—heteroaryl_(C≤12)~~,
~~—arenediyl_(C≤12)—heterocycloalkyl_(C≤12)~~, ~~—arenediyl_(C≤12)—cyclo-~~
~~alkyl_(C≤12)~~, ~~—heteroarenediyl_(C≤12)—alkyl_(C≤12)~~,
~~—heteroarenediyl_(C≤12)—aryl_(C≤12)~~, ~~—hetero-~~
~~arenediyl_(C≤12)—heteroaryl_(C≤12)~~, ~~—heteroarenediyl_(C≤12)—hetero-~~
~~cycloalkyl_(C≤12)~~, ~~—heteroarenediyl_(C≤12)—cycloalkyl_(C≤12)~~,
~~—heterocycloalkanediyl_(C≤12)—aryl_(C≤12)~~,
~~—heterocycloalkanediyl_(C≤12)—heteroaryl_(C≤12)~~, or a substituted
 version of any of these groups; or

a group of the formula:



wherein l and m are each 0, 1, 2, or 3; and

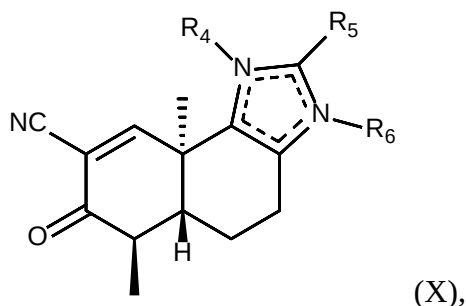
R₆ is absent, ~~hydrogen~~; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
 dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
 diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12),
~~—alkanediyl_(C≤12)—cycloalkyl_(C≤12)~~, ~~—alkanediyl_(C≤18)—aralkoxy_(C≤18)~~,
 heterocycloalkyl_(C≤12), aryl_(C≤18), ~~—arenediyl_(C≤12)—alkyl_(C≤12)~~,
 aralkyl_(C≤18), ~~—arenediyl_(C≤18)—heterocycloalkyl_(C≤12)~~, heteroaryl_(C≤18),

–heteroarenediyl_(C≤12)–alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12),
alkoxy_(C≤12), or a substituted version of any of these groups;

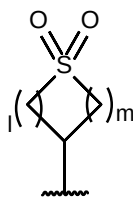
or a pharmaceutically acceptable salt thereof.

10. (Currently Amended) The compound according to any one of claims 1-4 and 8, further defined as:



wherein:

R₄ and R₅ are each independently absent, ~~hydrogen~~; or
~~alkyl_(C≤12)~~, cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12),
 aralkyl_(C≤12), heteroaryl_(C≤12), heteroaralkyl_(C≤12),
 –arenediyl_(C≤12)–alkyl_(C≤12), –arenediyl_(C≤12)–aryl_(C≤12),
 –arenediyl_(C≤12)–heteroaryl_(C≤12),
 –arenediyl_(C≤12)–heterocycloalkyl_(C≤12), –arenediyl_(C≤12)–cyclo-
 alkyl_(C≤12), –heteroarenediyl_(C≤12)–alkyl_(C≤12),
 –heteroarenediyl_(C≤12)–aryl_(C≤12), –hetero-
 arenediyl_(C≤12)–heteroaryl_(C≤12), –heteroarenediyl_(C≤12)–hetero-
 cycloalkyl_(C≤12), –heteroarenediyl_(C≤12)–cycloalkyl_(C≤12),
 –heterocycloalkanediyl_(C≤12)–aryl_(C≤12),
 –heterocycloalkanediyl_(C≤12)–heteroaryl_(C≤12), or a substituted
 version of any of these groups; or
 a group of the formula:



wherein l and m are each 0, 1, 2, or 3; and
 R₆ is absent, ~~hydrogen~~; or

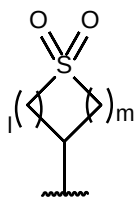
alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
 dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),

diarylaminoc_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12),
 -alkanediyl_(C≤12)-cycloalkyl_(C≤12), -alkanediyl_(C≤18)-aralkoxy_(C≤18),
 heterocycloalkyl_(C≤12), aryl_(C≤18), -arenediyl_(C≤12)-alkyl_(C≤12),
 aralkyl_(C≤18), -arenediyl_(C≤18)-heterocycloalkyl_(C≤12), heteroaryl_(C≤18),
 -heteroarenediyl_(C≤12)-alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12),
 alkoxy_(C≤12), or a substituted version of any of these groups;

or a pharmaceutically acceptable salt thereof.

11. The compound according to any one of claims 1-4 and 8, wherein X₁ and X₂ are both N.
12. The compound according to any one of claims 1-4 and 8, wherein X₁ and X₂ are not both N.
13. The compound according to any one of claims 1-4, 8, 11, and 12, wherein either X₁ or X₂ is N.
14. The compound according to any one of claims 1-4, 8, and 11-13, wherein X₁ is N.
15. The compound according to any one of claims 1-4, 8, and 11-13, wherein X₂ is N.
16. The compound according to any one of claims 1-3, wherein R₃ is alkyl_(C≤12) or substituted alkyl_(C≤12).
17. The compound of claim 16, wherein R₃ is alkyl_(C≤12).
18. The compound of claim 18, wherein R₃ is methyl.
19. The compound according to any one of claims 1-4 and 11-18, wherein R₁ is cyano.
20. The compound according to any one of claims 1-4 and 11-18, wherein R₁ is -C(O)R_a.
21. The compound of claim 20, wherein R_a is alkoxy_(C≤6).
22. The compound of claim 21, wherein R_a is methoxy.
23. The compound of claim 20, wherein R_a is amino.
24. The compound according to any one of claims 1-7 and 11-23, wherein R₂' is hydrogen.
25. The compound according to any one of claims 1-7 and 11-24, wherein R₂ is hydrogen.
26. The compound according to any one of claims 1-7 and 11-25, wherein R₂' and R₂ are both hydrogen.

27. The compound according to any one of claims 1-7 and 11-24, wherein R₂ is alkyl_(C≤12) or substituted alkyl_(C≤12).
28. The compound of claim 27, wherein R₂ is alkyl_(C≤12).
29. The compound of claim 28, wherein R₂ is methyl.
30. The compound according to any one of claims 1-29, wherein R₄ is absent.
- 31.-34. Cancelled
35. The compound according to any one of claims 1-29, wherein R₄ is cycloalkyl_(C≤12) or substituted cycloalkyl_(C≤12).
36. The compound of claim 35, wherein R₄ is cycloalkyl_(C≤12).
37. The compound of claim 36, wherein R₄ is cyclohexyl.
38. The compound according to any one of claims 1-29, wherein R₄ is heterocycloalkyl_(C≤12) or substituted heterocycloalkyl_(C≤12).
39. The compound of claim 38, wherein R₄ is heterocycloalkyl_(C≤12).
40. The compound of claim 39, wherein R₄ is tetrahydro-2H-pyran-4-yl or 1,1-dioxidotetrahydrothiophen-3-yl.
41. The compound according to any one of claims 1-29, wherein R₄ is:



wherein:

l and m are each 0, 1, 2, or 3.

42. The compound of claim 41, wherein l is 1 or 2.
43. The compound of either claim 41 or claim 42, wherein m is 1 or 2.
44. The compound according to any one of claims 1-29, wherein R₄ is aryl_(C≤18) or substituted aryl_(C≤18).
45. The compound of claim 44, wherein R₄ is aryl_(C≤18).
46. The compound of claim 45, wherein R₄ is phenyl, *o*-tolyl, *p*-tolyl, [1,1'-biphenyl]-4-yl, 4-isopropylphenyl, naphthalen-1-yl, 4'-methyl-[1,1'-biphenyl]-4-yl, or 2'-methyl-[1,1'-biphenyl]-4-yl.

47. The compound of claim 44, wherein R₄ is substituted aryl_(C≤18).
48. The compound of claim 47, wherein R₄ is 4-(trifluoromethyl)phenyl, 4-cyanophenyl, 2-fluorophenyl, 4-fluorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 4-methoxyphenyl, 4-(trifluoromethoxy)phenyl, 4-carboxyphenyl, 4'-methoxy-[1,1'-biphenyl]-4-yl, 4'-(dimethylamino)-[1,1'-biphenyl]-4-yl, 2'-fluoro-[1,1'-biphenyl]-4-yl, 3'-fluoro-[1,1'-biphenyl]-4-yl, 2'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl, 3'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl, 4'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl, or 5-(3-(hydroxymethyl)phenyl).
49. The compound according to any one of claims 1-29, wherein R₄ is aralkyl_(C≤18) or substituted aralkyl_(C≤18).
50. The compound of claim 49, wherein R₄ is aralkyl_(C≤18).
51. The compound of claim 50, wherein R₄ is benzyl.
52. The compound according to any one of claims 1-29, wherein R₄ is -arenediyl_(C≤12)-heterocycloalkyl_(C≤12) or substituted -arenediyl_(C≤12)-heterocycloalkyl_(C≤12).
53. The compound of claim 52, wherein R₄ is -arenediyl_(C≤12)-heterocycloalkyl_(C≤12).
54. The compound of claim 53, wherein R₄ is 4-morpholinophenyl.
55. The compound according to any one of claims 1-29, wherein R₄ is heteroaryl_(C≤18) or substituted heteroaryl_(C≤18).
56. The compound of claim 55, wherein R₄ is heteroaryl_(C≤18).
57. The compound of claim 56, wherein R₄ is pyridin-4-yl, quinolin-4-yl, 5-methylpyrindin-2-yl, 6-methylpyrindin-3-yl, (pyridin-3-yl)phenyl, (pyridin-4-yl)phenyl, 4-(3,5-dimethylisoxazol-4-yl)phenyl, 4-(pyrimidin-4-yl)phenyl, 4-(pyrimidin-5-yl)phenyl, 4-(pyridin-3-yl)phenyl, 4-(pyridin-4-yl)phenyl, 5-phenylpyridin-2-yl, [3,3'-bipyridin]-6-yl, 5-cyclopropylpyridin-2-yl, 6-phenylpyridin-3-yl, 4-(6-methylpyridazin-4-yl)phenyl, 5-methyl-1,2,4-oxadiazol-3-yl, 3-methyl-1,2,4-oxadiazol-5-yl, 4-methyl-5-phenyl-4*H*-1,2,4-triazol-3-yl, 1-phenylpiperidin-4-yl, 4-phenyloxazol-2-yl, 4-(6-methylpyridazin-4-yl)phenyl, 4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl, 4-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl, 4-(1,2,4-oxadiazol-3-yl)phenyl, 4-(pyridazin-3-yl)phenyl,

4-(5-methylpyridazin-3-yl)phenyl, 1-methyl-1*H*-benzo[*d*]imidazol-2-yl, or benzo[*d*]thiazol-2-yl.

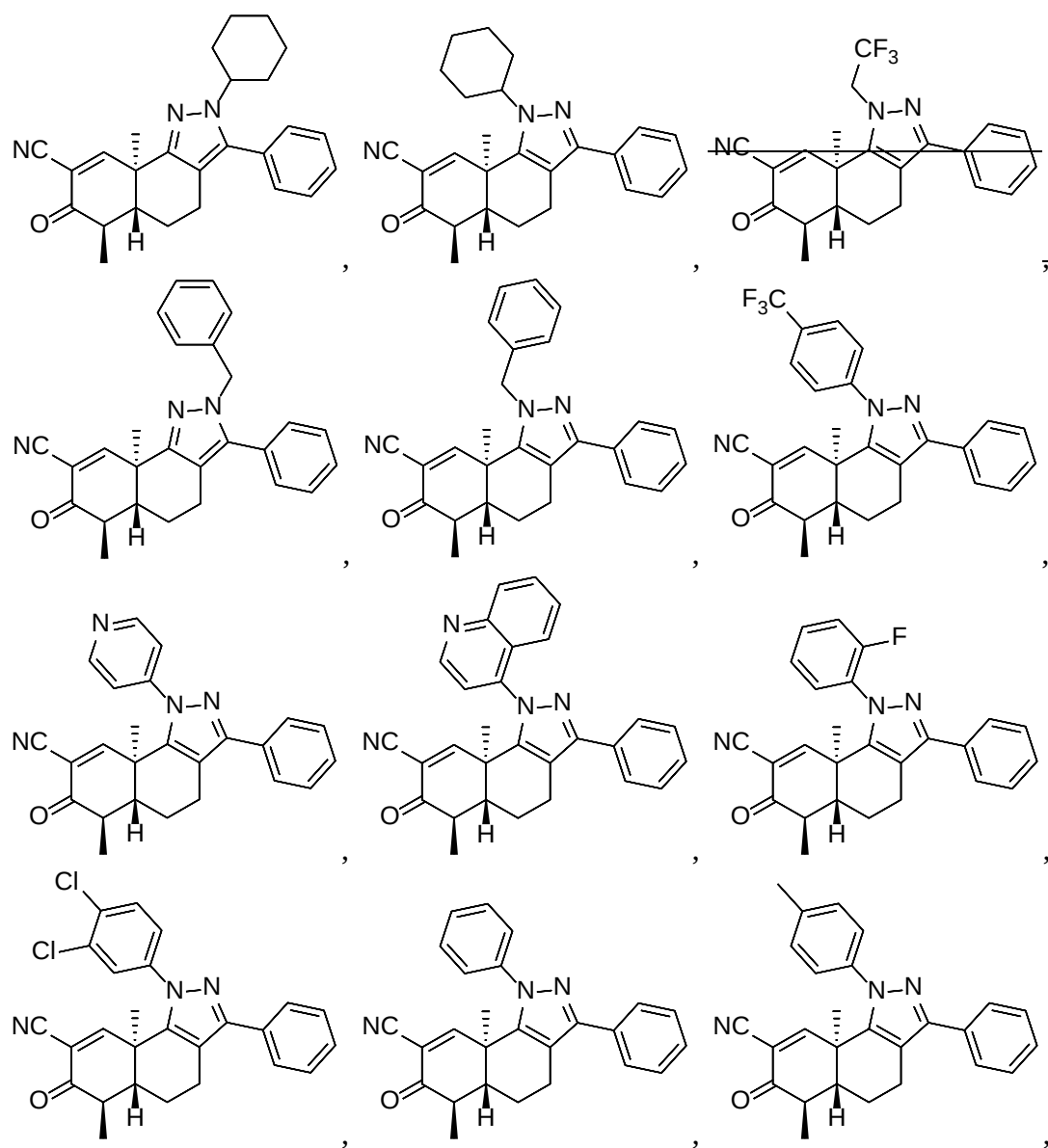
58. The compound of claim 55, wherein R₄ is substituted heteroaryl_(C≤18).
59. The compound of claim 58, wherein R₄ is 2-fluoro-4-(pyridin-3-yl)phenyl, 5-(trifluoromethyl)pyridin-2-yl, 5-(3-fluorophenyl)pyridin-2-yl, 5-(4-fluorophenyl)pyridin-2-yl, 4-(2-(hydroxymethyl)pyridine-4-yl)phenyl, 4-(2-(fluoromethyl)pyridine-4-yl)phenyl, 5-(trifluoromethyl)benzo[*d*]oxazol-2-yl, 6-chlorobenzo[*d*]thiazol-2-yl, or 4-(5-fluoropyridin-3-yl)phenyl.
- 60.-63. Cancelled
64. The compound according to any one of claims 1-59, wherein R₅ is cycloalkyl_(C≤12) or substituted cycloalkyl_(C≤12).
65. The compound of claim 64, wherein R₅ is cycloalkyl_(C≤12).
66. The compound of claim 65, wherein R₅ is cyclohexyl.
67. The compound according to any one of claims 1-59, wherein R₅ is heterocycloalkyl_(C≤12) or substituted heterocycloalkyl_(C≤12).
68. The compound of claim 67, wherein R₅ is heterocycloalkyl_(C≤12).
69. The compound of claim 68, wherein R₅ is tetrahydro-2*H*-pyran-4-yl.
70. The compound according to any one of claims 1-59, wherein R₅ is aryl_(C≤18) or substituted aryl_(C≤18).
71. The compound of claim 70, wherein R₅ is aryl_(C≤18).
72. The compound of claim 71, wherein R₅ is phenyl, *o*-tolyl, *p*-tolyl, [1,1'-biphenyl]-4-yl, 4-isopropylphenyl, naphthalen-1-yl, [1,1'-biphenyl]-3-yl, or 3-isopropylphenyl.
73. The compound of claim 72, wherein R₅ is substituted aryl_(C≤18).
74. The compound of claim 73, wherein R₅ is 4-chlorophenyl, 3,4-dichlorophenyl, 4-methoxyphenyl, 4-(trifluoromethoxy)phenyl, 3-bromophenyl, 3-chlorophenyl, 4-(dimethylamino)phenyl.
75. The compound according to any one of claims 1-59, wherein R₅ is aralkyl_(C≤18) or substituted aralkyl_(C≤18).
76. The compound of claim 75, wherein R₅ is aralkyl_(C≤18).

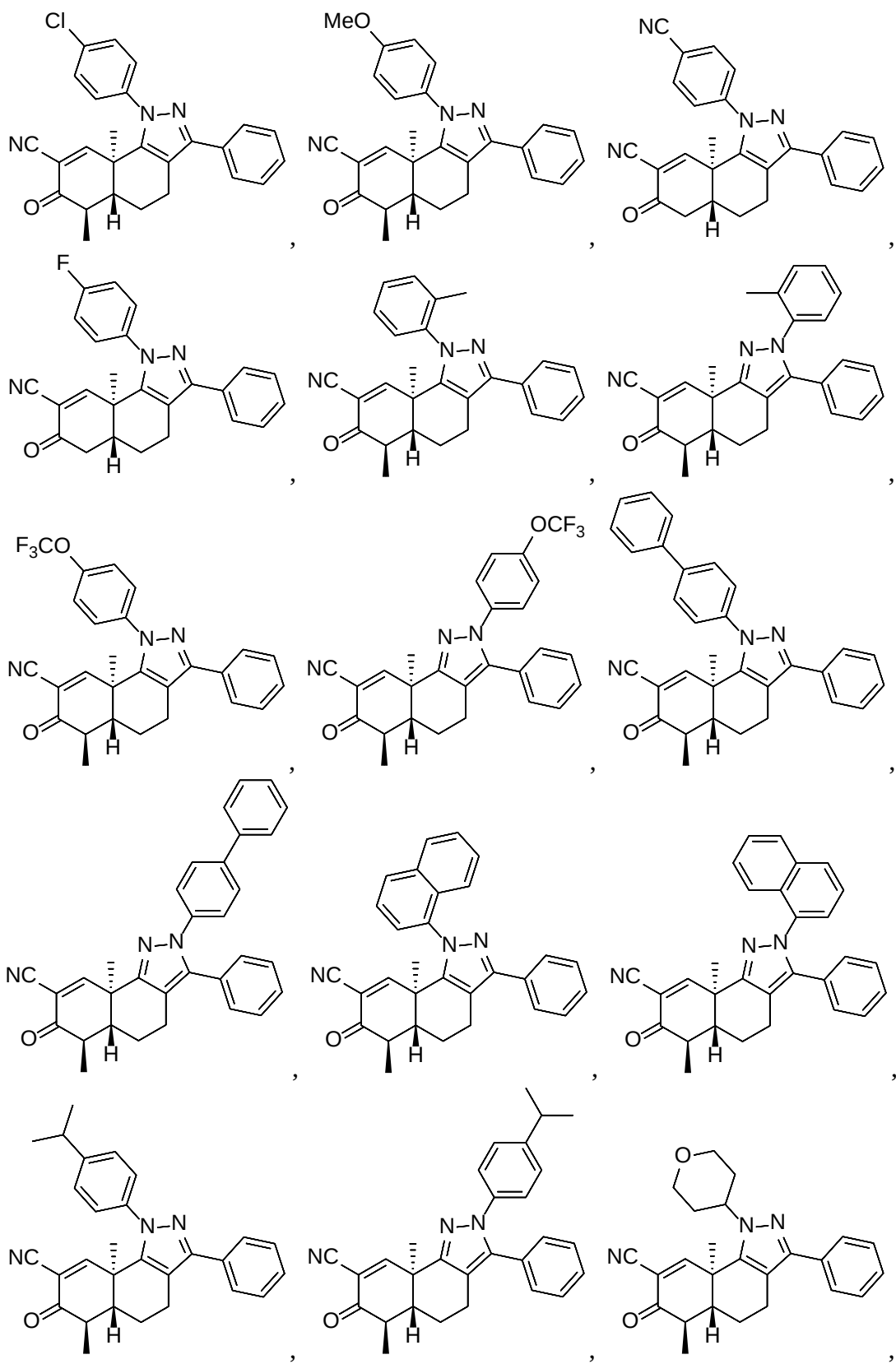
77. The compound of claim 76, wherein R₅ is benzyl.
78. The compound according to any one of claims 1-59, wherein R₅ is
–arenediyl_(C≤12)–heterocycloalkyl_(C≤12) or substituted
–arenediyl_(C≤12)–heterocycloalkyl_(C≤12).
79. The compound of claim 78, wherein R₅ is –arenediyl_(C≤12)–heterocycloalkyl_(C≤12).
80. The compound of claim 79, wherein R₅ is 3-morpholinophenyl.
81. The compound according to any one of claims 1-59, wherein R₅ is heteroaryl_(C≤18) or substituted heteroaryl_(C≤18).
82. The compound of claim 81, wherein R₅ is heteroaryl_(C≤18).
83. The compound of claim 82, wherein R₅ is pyridin-4-yl, quinolin-4-yl, quinolin-3-yl, quinolin-5-yl, 3-(pyridin-4-yl)phenyl, 3-(pyrimidin-5-yl)phenyl, 2-isopropylpyrimidin-5-yl, 6-cyclopropylpyridin-3-yl, 3-(1-methyl-1*H*-pyrazol-4-yl)phenyl, 1-methyl-1*H*-pyrazol-4-yl, 3-(3,5-dimethylisoxazol-4-yl)phenyl, 3-(1-methyl-1*H*-pyrazol-5-yl)phenyl, or 2-cyclopropylpyridin-4-yl.
84. The compound of claim 81, wherein R₅ is substituted heteroaryl_(C≤18).
85. The compound of claim 84, wherein R₅ is 2-(trifluoromethyl)pyridin-4-yl or 3-(5-fluoropyridin-3-yl)phenyl.
86. The compound according to any one of claims 1-59, wherein R₅ is
–heteroarenediyl_(C≤12)–heterocycloalkyl_(C≤12) or substituted
–heteroarenediyl_(C≤12)–heterocycloalkyl_(C≤12).
87. The compound of claim 86, wherein R₅ is –heteroarenediyl_(C≤12)–heterocycloalkyl_(C≤12).
88. The compound of claim 87, wherein R₅ is 2-morpholinopyridin-4-yl.
89. Cancelled
90. The compound according to any one of claims 1-88, wherein R₆ is amino.
91. The compound according to any one of claims 1-88, wherein R₆ is alkylamino_(C≤12) or substituted alkylamino_(C≤12).
92. The compound of claim 91, wherein R₆ is alkylamino_(C≤12).
93. The compound of claim 92, wherein R₆ is methylamino.

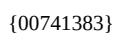
94. The compound according to any one of claims 1-88, wherein R₆ is cycloalkylamino_(C≤12) or substituted cycloalkylamino_(C≤12).
95. The compound of claim 94, wherein R₆ is cycloalkylamino_(C≤12).
96. The compound of claim 95, wherein R₆ is cyclobutylamino.
97. The compound according to any one of claims 1-88, wherein R₆ is alkyl(cycloalkyl)amino_(C≤12) or substituted alkyl(cycloalkyl)amino_(C≤12).
98. The compound of claim 97, wherein R₆ is alkyl(cycloalkyl)amino_(C≤12).
99. The compound of claim 98, wherein R₆ is methyl(cyclobutyl)amino.
100. The compound according to any one of claims 1-88, wherein R₆ is arylamino_(C≤12) or substituted arylamino_(C≤12).
101. The compound of claim 100, wherein R₆ is arylamino_(C≤12).
102. The compound of claim 101, wherein R₆ is phenylamino.
103. The compound according to any one of claims 1-88, wherein R₆ is alkyl_(C≤12) or substituted alkyl_(C≤12).
104. The compound of claim 103, wherein R₆ is alkyl_(C≤12).
105. The compound of claim 104, wherein R₆ is methyl.
106. The compound of claim 103, wherein R₆ is substituted alkyl_(C≤12).
107. The compound of claim 106, wherein R₆ is 2-hydroxyethyl or 2-methoxyethyl.
108. The compound according to any one of claims 1-88, wherein R₆ is acyl_(C≤6) or substituted acyl_(C≤6).
109. The compound of claim 108, wherein R₆ is acyl_(C≤6).
110. The compound of claim 109, wherein R₆ is -C(O)CH₃.
111. The compound according to any one of claims 1-88, wherein R₆ is cycloalkyl_(C≤12) or substituted cycloalkyl_(C≤12).
112. The compound of claim 111, wherein R₆ is cycloalkyl_(C≤12).
113. The compound of claim 112, wherein R₆ is cyclopropyl or cyclohexyl.
114. The compound according to any one of claims 1-88, wherein R₆ is -alkanediyl_(C≤18)-cycloalkyl_(C≤18) or substituted -alkanediyl_(C≤18)-cycloalkyl_(C≤18).

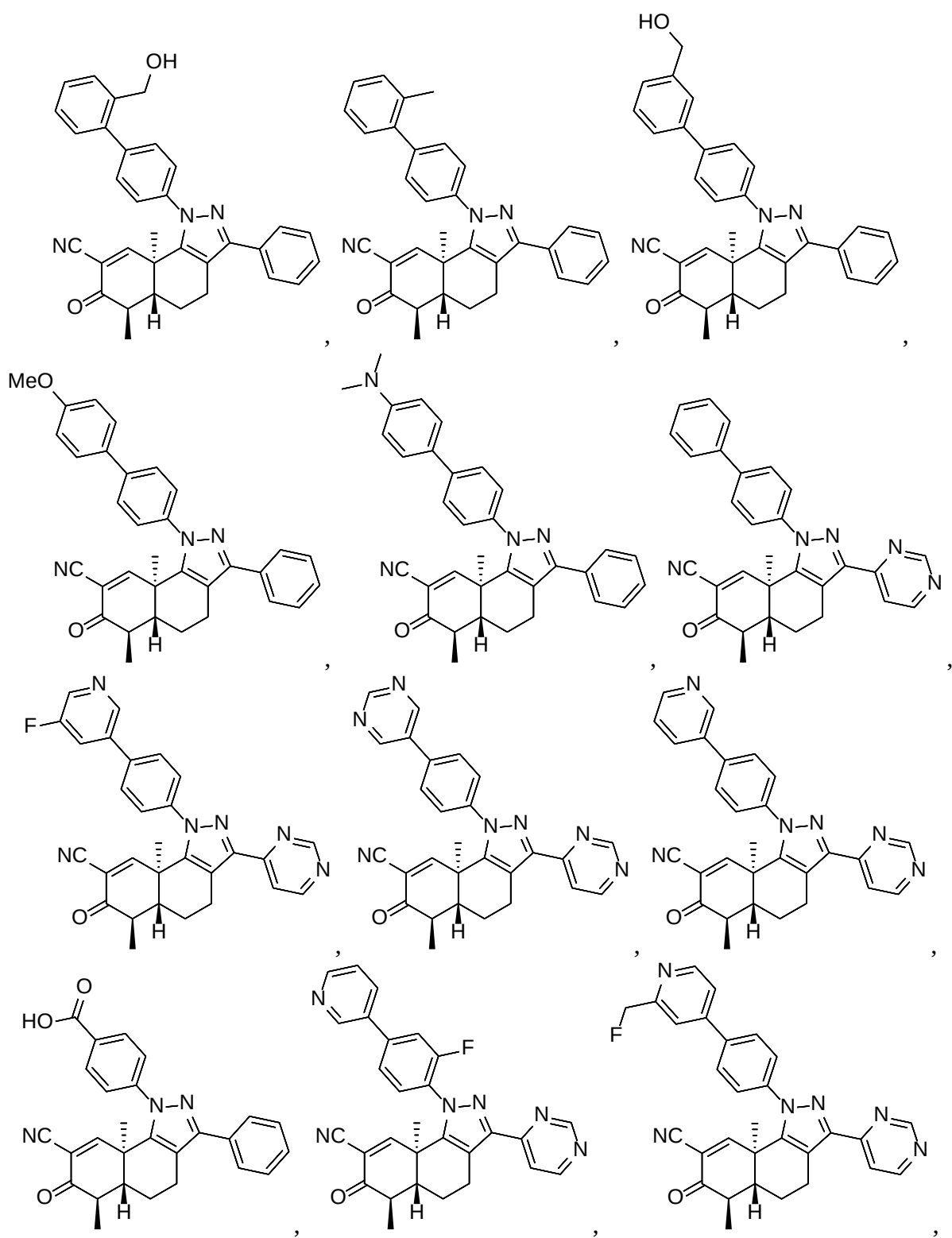
115. The compound of claim 114, wherein R₆ is $\text{-alkanediyl}_{(C\leq 18)\text{-cycloalkyl}_{(C\leq 18)}}$.
116. The compound of claim 115, wherein R₆ is cyclobutylmethyl.
117. The compound according to any one of claims 1-88, wherein R₆ is aryl_(C≤18) or substituted aryl_(C≤18).
118. The compound of claim 117, wherein R₆ is aryl_(C≤18).
119. The compound of claim 118, wherein R₆ is phenyl, *o*-tolyl, *p*-tolyl, or 3-isopropylphenyl.
120. The compound of claim 117, wherein R₆ is substituted aryl_(C≤18).
121. The compound of claim 120, wherein R₆ is 2-fluorophenyl, 4-fluorophenyl, 4-(hydroxymethyl)phenyl, 3-fluorophenyl, or 4-(fluoromethyl)phenyl.
122. The compound according to any one of claims 1-88, wherein R₆ is aralkyl_(C≤18) or substituted aralkyl_(C≤18).
123. The compound of claim 122, wherein R₆ is aralkyl_(C≤18).
124. The compound of claim 123, wherein R₆ is benzyl.
125. The compound of claim 122, wherein R₆ is substituted aralkyl_(C≤18).
126. The compound of claim 125, wherein R₆ is 2-fluorobenzyl, 4-fluorobenzyl, or 4-chlorobenzyl.
127. The compound according to any one of claims 1-88, wherein R₆ is $\text{-arenediyl}_{(C\leq 18)\text{-heterocycloalkyl}_{(C\leq 12)}}$ or substituted $\text{-arenediyl}_{(C\leq 18)\text{-heterocycloalkyl}_{(C\leq 12)}}$.
128. The compound of claim 127, wherein R₆ is $\text{-arenediyl}_{(C\leq 18)\text{-heterocycloalkyl}_{(C\leq 12)}}$.
129. The compound of claim 128, wherein R₆ is 4-morpholinophenyl.
130. The compound according to any one of claims 1-88, wherein R₆ is heteroaryl_(C≤18) or substituted heteroaryl_(C≤18).
131. The compound of claim 130, wherein R₆ is heteroaryl_(C≤18).
132. The compound of claim 131, wherein R₆ is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, 2-methyl-2*H*-tetrazol-5-yl, 1-methyl-1*H*-pyrazol-4-yl, pyrimidin-4-yl, pyrimidin-5-yl, 3-methyl-1,2,4-oxadiazol-5-yl)phenyl, pyridin-2-ylmethyl, 3-methyl-1,2,4-oxadiazol-5-yl, or 5-methyl-1,2,4-oxadiazol-3-yl.

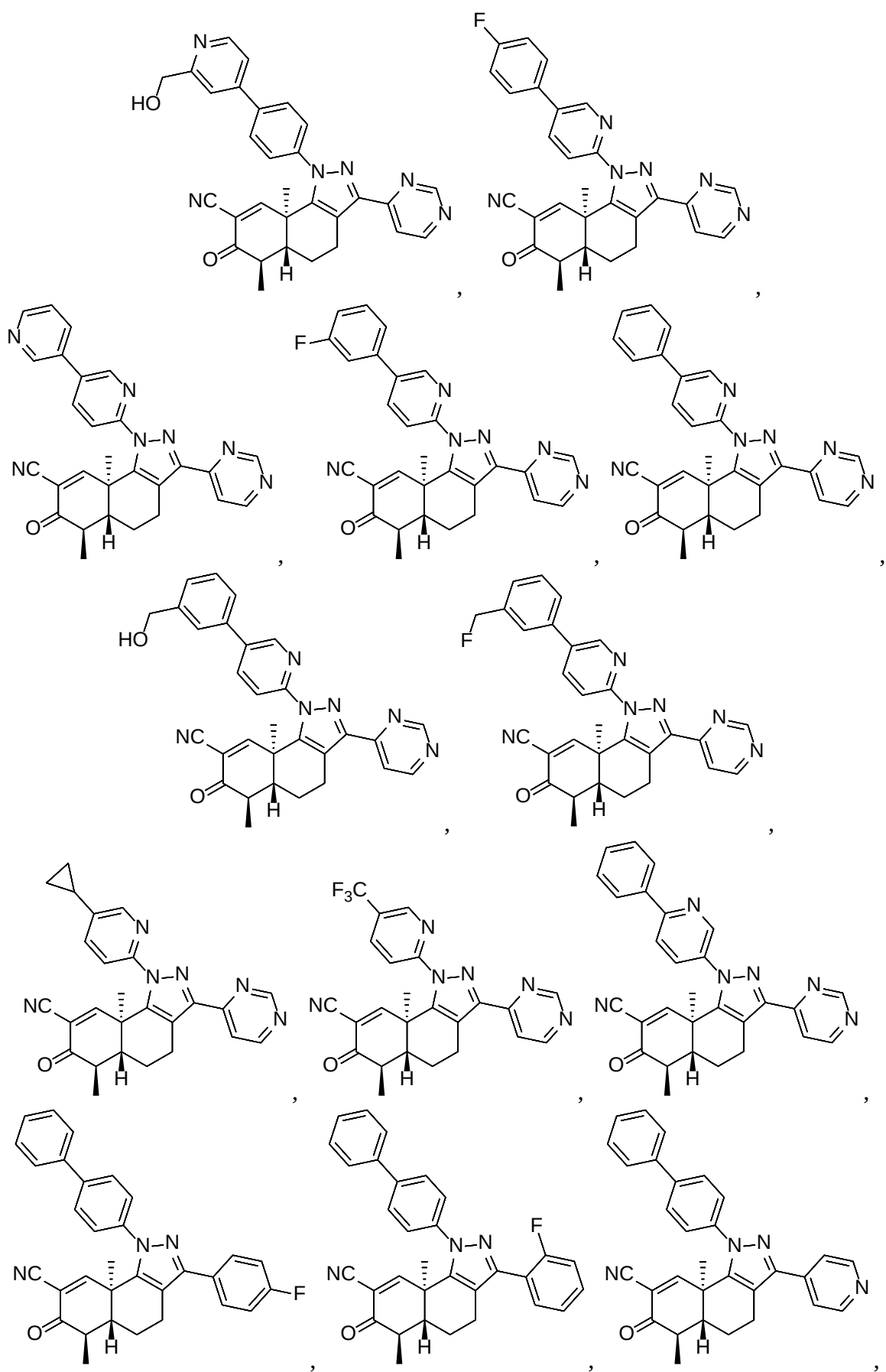
133. The compound according to any one of claims 1-88, wherein R₆ is heteroaralkyl_(C≤18) or heteroaralkyl_(C≤18).
134. The compound of claim 133, wherein R₆ is heteroaralkyl_(C≤18).
135. The compound of claim 134, wherein R₆ is 2-pyridinylmethyl or 4-pyridinylmethyl.
136. The compound according to any one of claims 1-88, wherein R₆ is -alkanediyl_(C≤18)-aralkoxy_(C≤18) or substituted -alkanediyl_(C≤18)-aralkoxy_(C≤18).
137. The compound of claim 136, wherein R₆ is -alkanediyl_(C≤18)-aralkoxy_(C≤18).
138. The compound of claim 137, wherein R₆ is 2-(benzyloxy)ethyl.
139. (Currently Amended) The compound according to any one of claims 1-138 further defined as:

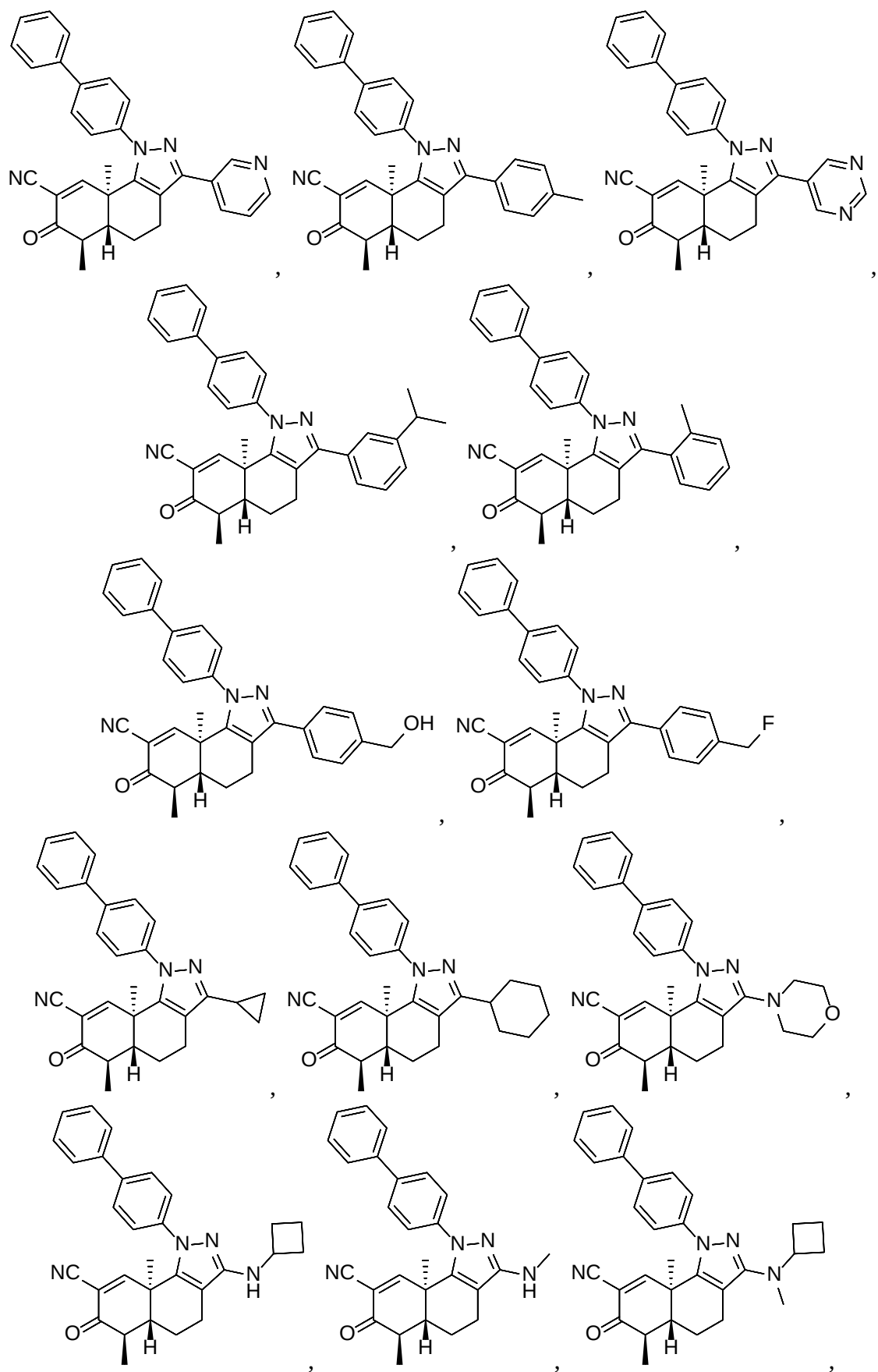


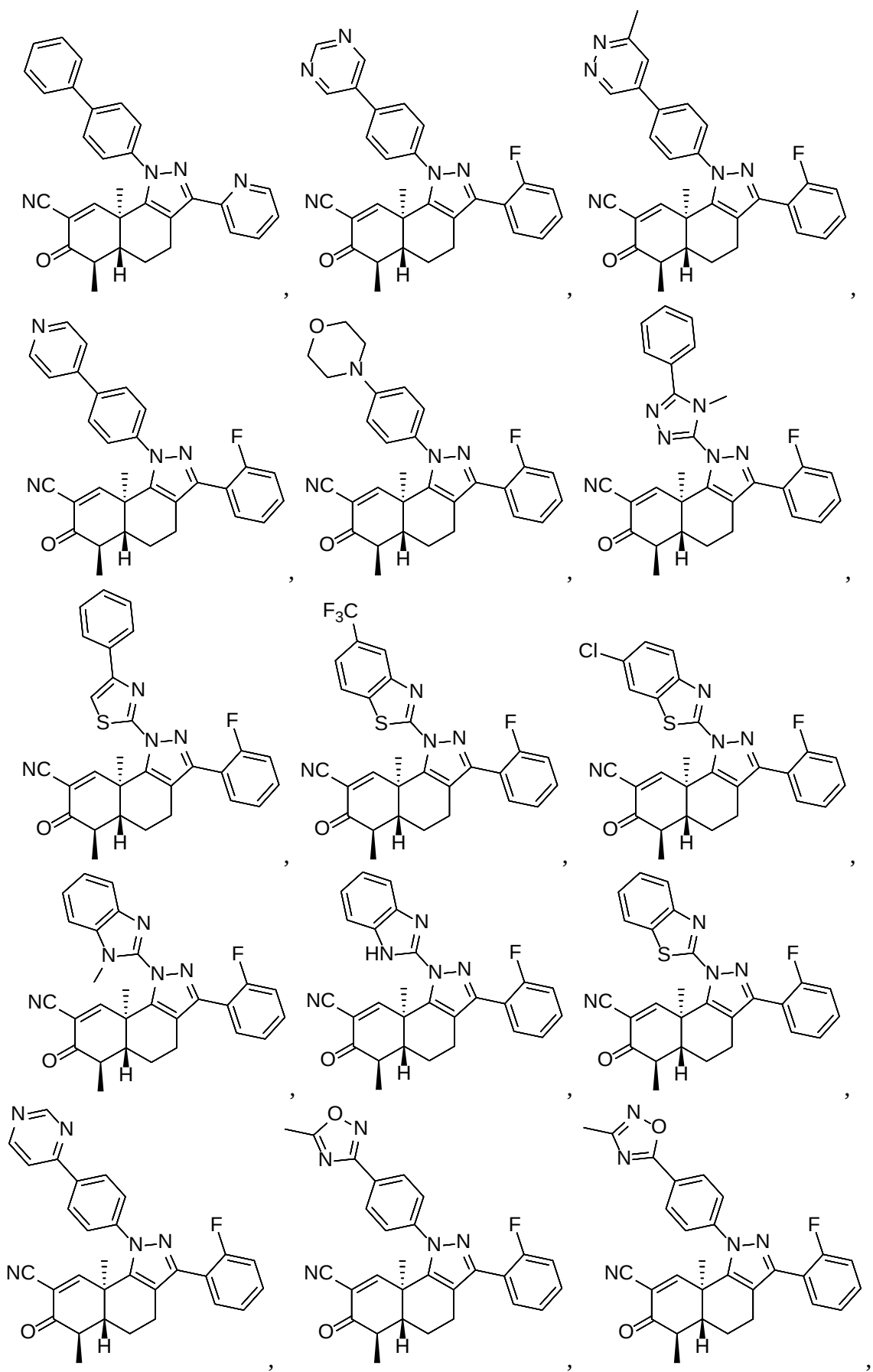


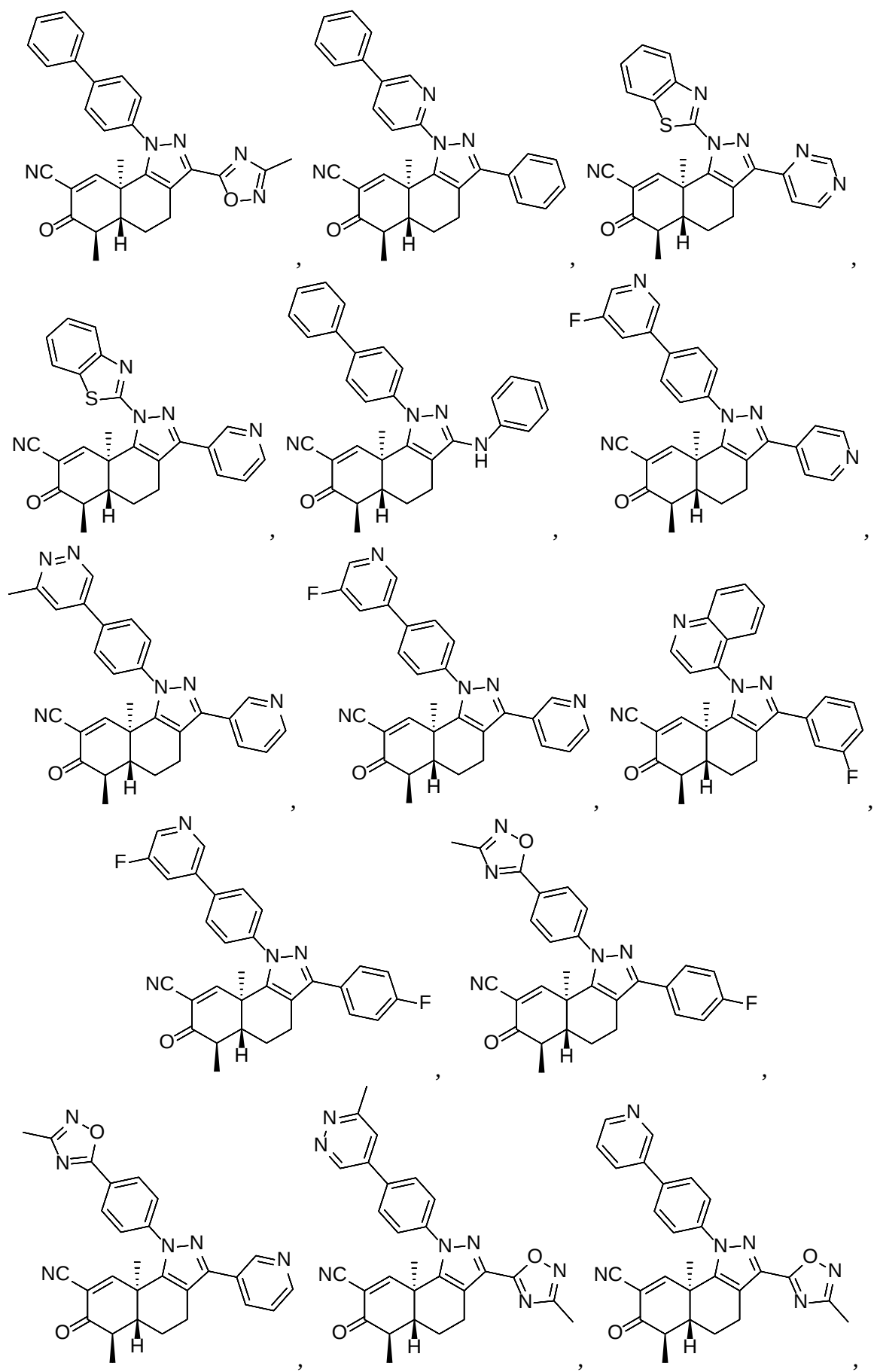


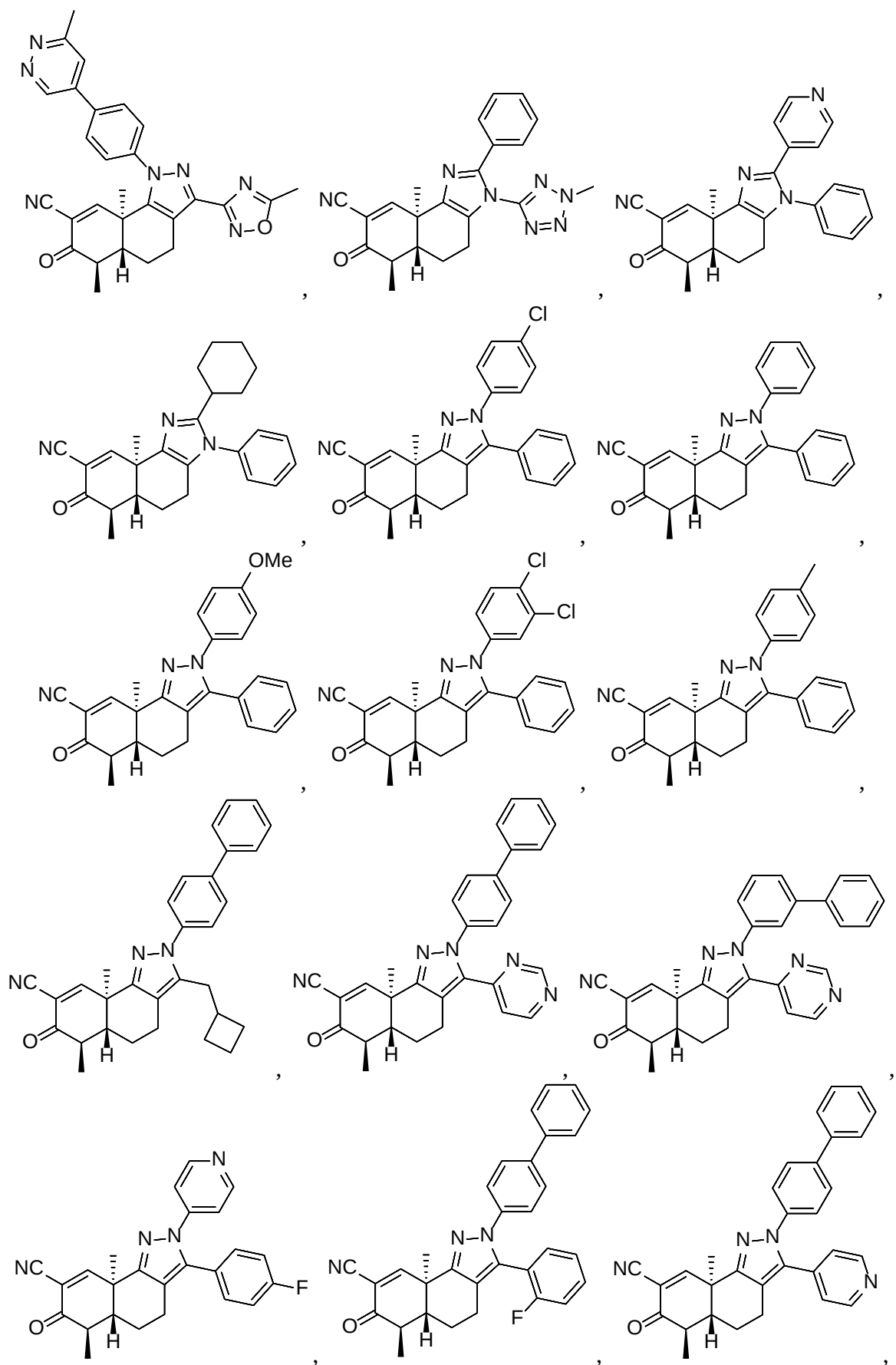


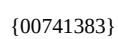


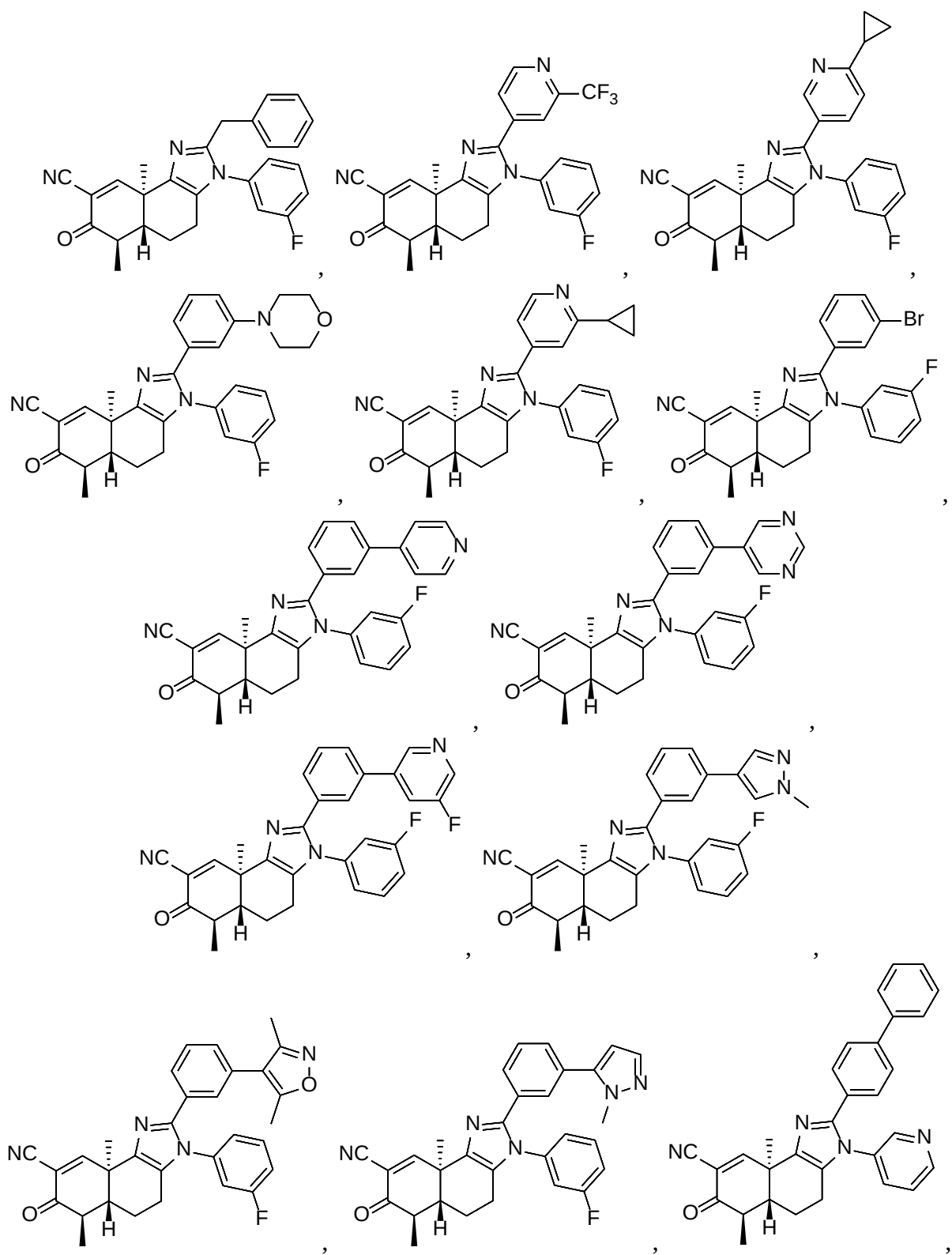


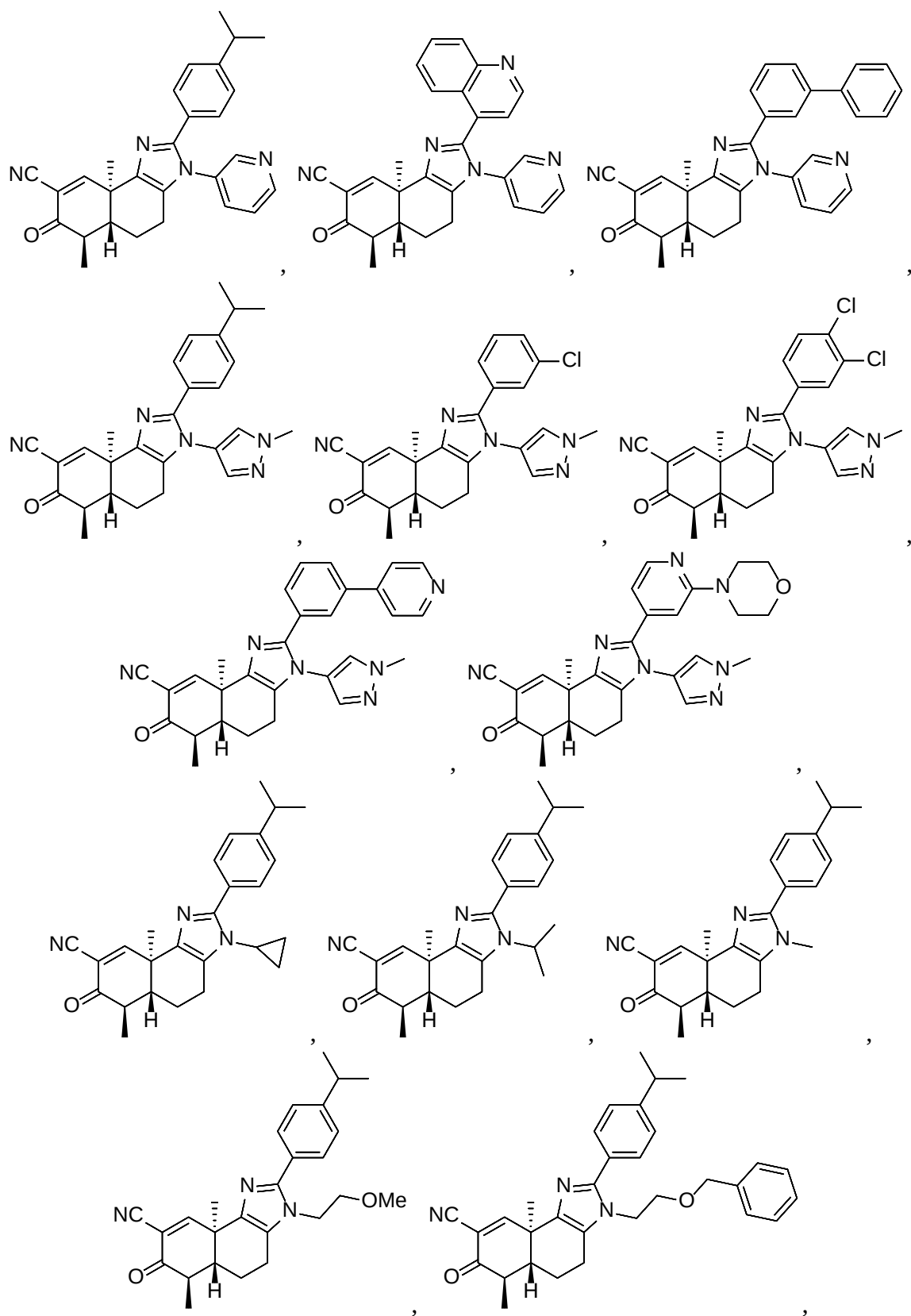


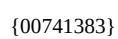


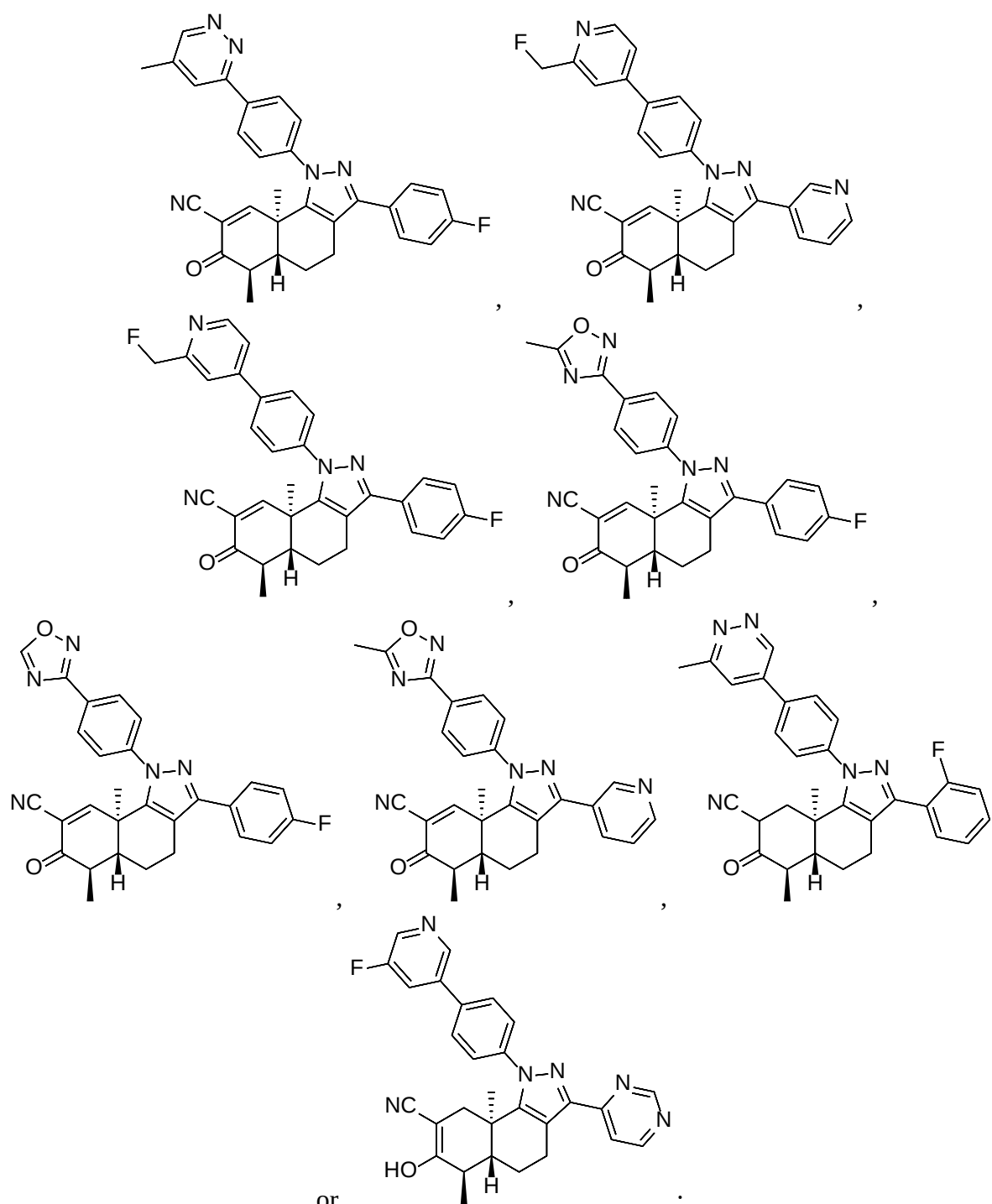






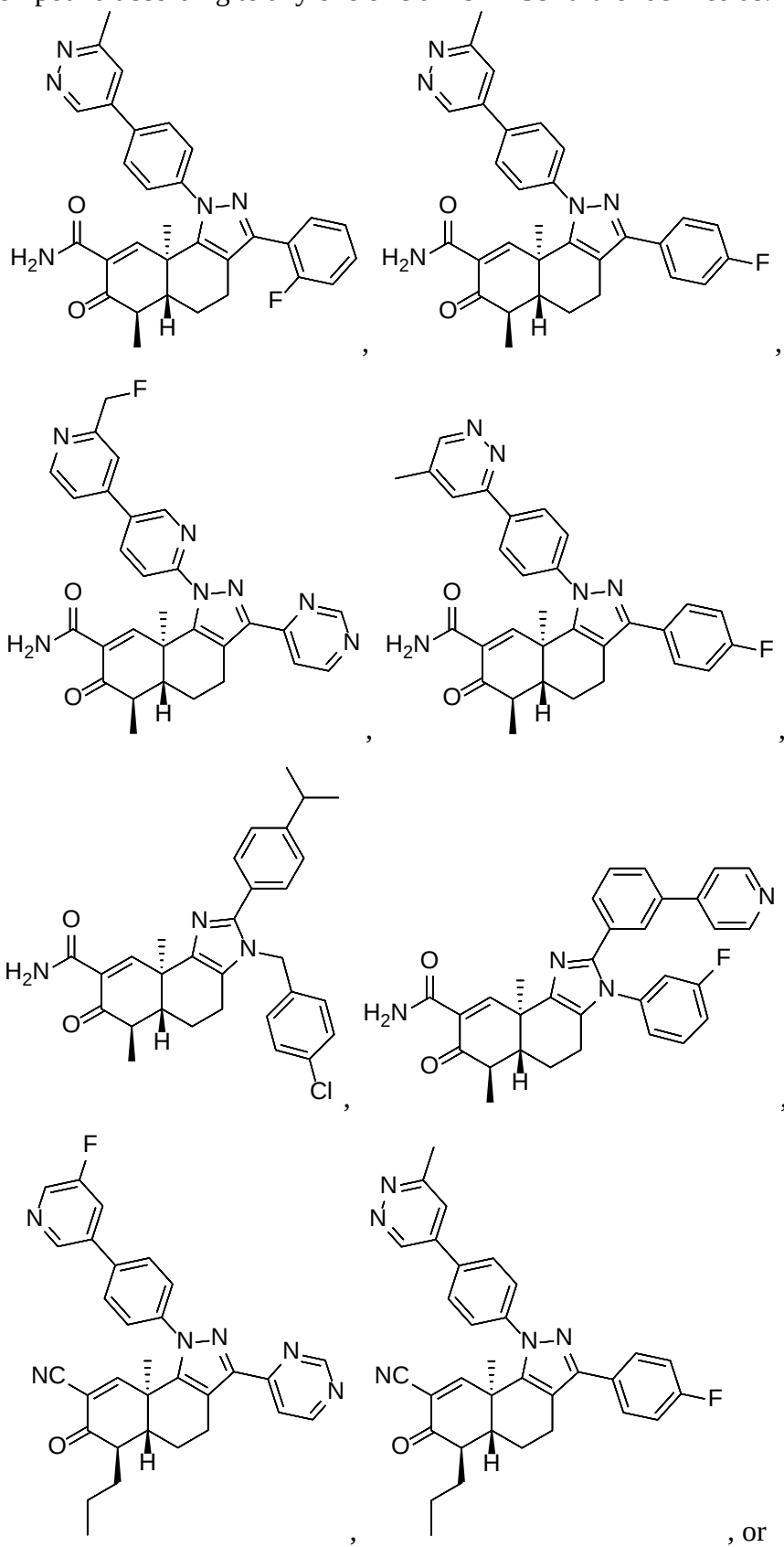


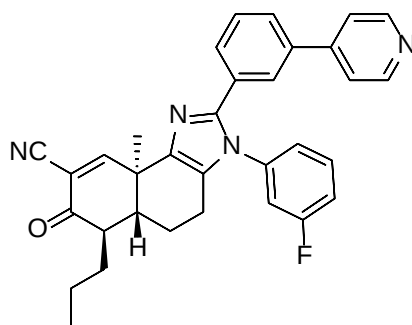




or a pharmaceutically acceptable salt of any of the above formulas.

140. The compound according to any one of claims 1-138 further defined as:





or a pharmaceutically acceptable salt of any of the above formulas.

141. A compound of the formula:

- (5a*R*,6*R*,9a*S*)-2-cyclohexyl-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;
- (5a*R*,6*R*,9a*S*)-1-cyclohexyl-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
- (5a*R*,6*R*,9a*S*)-6,9a-dimethyl-7-oxo-3-phenyl-1-(2,2,2-trifluoroethyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
- (5a*R*,6*R*,9a*S*)-2-benzyl-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;
- (5a*R*,6*R*,9a*S*)-1-benzyl-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
- (5a*R*,6*R*,9a*S*)-6,9a-dimethyl-7-oxo-3-phenyl-1-(4-(trifluoromethyl)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
- (5a*R*,6*R*,9a*S*)-6,9a-dimethyl-7-oxo-3-phenyl-1-(pyridin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
- (5a*R*,6*R*,9a*S*)-6,9a-dimethyl-7-oxo-3-phenyl-1-(quinolin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
- (5a*R*,6*R*,9a*S*)-1-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
- (5a*R*,6*R*,9a*S*)-1-(3,4-dichlorophenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
- (5a*R*,6*R*,9a*S*)-6,9a-dimethyl-7-oxo-1,3-diphenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
- (5a*R*,6*R*,9a*S*)-6,9a-dimethyl-7-oxo-3-phenyl-1-(*p*-tolyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-chlorophenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-methoxyphenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,9aS)-1-(4-cyanophenyl)-9a-methyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,9aS)-1-(4-fluorophenyl)-9a-methyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(*o*-tolyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-2-(*o*-tolyl)-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(4-(trifluoromethoxy)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-2-(4-(trifluoromethoxy)phenyl)-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-1-(naphthalen-1-yl)-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-2-(naphthalen-1-yl)-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(tetrahydro-2*H*-pyran-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-2-(tetrahydro-2*H*-pyran-4-yl)-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(1,1-dioxidotetrahydrothiophen-3-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-(1,1-dioxidotetrahydrothiophen-3-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-1-(5-methylpyridin-2-yl)-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-1-(6-methylpyridin-3-yl)-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(3-bromophenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(3-(pyridin-3-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-3-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(2'-fluoro-[1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(4-(pyridin-3-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(3,5-dimethylisoxazol-4-yl)phenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(4-(pyridin-4-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(3'-fluoro-[1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-1-(4'-methyl-[1,1'-biphenyl]-4-yl)-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(2'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-1-(2'-methyl-[1,1'-biphenyl]-4-yl)-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(3'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4'-methoxy-[1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4'-(dimethylamino)-[1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(5-fluoropyridin-3-yl)phenyl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-1-(4-(pyrimidin-5-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-1-(4-(pyridin-3-yl)phenyl)-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

4-((5aR,6R,9aS)-8-cyano-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazol-1-yl)benzoic acid;

(5aR,6R,9aS)-1-(2-fluoro-4-(pyridin-3-yl)phenyl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(2-(fluoromethyl)pyridin-4-yl)phenyl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(2-(hydroxymethyl)pyridin-4-yl)phenyl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(5-(4-fluorophenyl)pyridin-2-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([3,3'-bipyridin]-6-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(5-(3-fluorophenyl)pyridin-2-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-1-(5-phenylpyridin-2-yl)-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(5-(3-(hydroxymethyl)phenyl)pyridin-2-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(5-(3-(fluoromethyl)phenyl)pyridin-2-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(5-(cyclopropylpyridin-2-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-1-(5-(trifluoromethyl)pyridin-2-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-1-(6-phenylpyridin-3-yl)-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-(4-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyridin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(*p*-tolyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-5-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-(3-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(*o*-tolyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-(4-(hydroxymethyl)phenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-(4-(fluoromethyl)phenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-cyclopropyl-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-cyclohexyl-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-3-morpholino-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-(cyclobutylamino)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-3-(methylamino)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-(cyclobutyl(methyl)amino)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyridin-2-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-1-(4-(pyrimidin-5-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-1-(4-(6-methylpyridazin-4-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-1-(4-(pyridin-4-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-1-(4-morpholinophenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-1-(4-methyl-5-phenyl-4H-1,2,4-triazol-3-yl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-1-(4-phenylthiazol-2-yl)-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-1-(5-(trifluoromethyl)benzo[d]thiazol-2-yl)-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(6-chlorobenzo[d]thiazol-2-yl)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-1-(1-methyl-1H-benzo[d]imidazol-2-yl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(1H-benzo[d]imidazol-2-yl)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(benzo[d]thiazol-2-yl)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-1-(4-(pyrimidin-4-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-1-(4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-1-(4-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-3-(3-methyl-1,2,4-oxadiazol-5-yl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(5-phenylpyridin-2-yl)-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(benzo[d]thiazol-2-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(benzo[d]thiazol-2-yl)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(phenylamino)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(5-fluoropyridin-3-yl)phenyl)-6,9a-dimethyl-7-oxo-3-(pyridin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-1-(4-(6-methylpyridazin-4-yl)phenyl)-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(5-fluoropyridin-3-yl)phenyl)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-1-(quinolin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-fluorophenyl)-1-(4-(5-fluoropyridin-3-yl)phenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-fluorophenyl)-6,9a-dimethyl-1-(4-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-1-(4-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-3-(3-methyl-1,2,4-oxadiazol-5-yl)-1-(4-(6-methylpyridazin-4-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-3-(3-methyl-1,2,4-oxadiazol-5-yl)-7-oxo-1-(4-(pyridin-3-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-3-(5-methyl-1,2,4-oxadiazol-3-yl)-1-(4-(6-methylpyridazin-4-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-3-(2-methyl-2H-tetrazol-5-yl)-7-oxo-2-phenyl-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-2-(pyridin-4-yl)-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-cyclohexyl-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-chlorophenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-2,3-diphenyl-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-methoxyphenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-(3,4-dichlorophenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-2-(p-tolyl)-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-4-yl)-3-(cyclobutylmethyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-3-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(pyridin-4-yl)-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-4-yl)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyridin-4-yl)-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-3-yl)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-4-yl)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-3-yl)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(tetrahydro-2*H*-pyran-4-yl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-2-(2-isopropylpyrimidin-5-yl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-(dimethylamino)phenyl)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-2,6,9a-trimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-2-phenyl-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(quinolin-4-yl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(quinolin-5-yl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(quinolin-3-yl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-2-(3-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-2-(2-morpholinopyridin-4-yl)-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-benzyl-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(2-(trifluoromethyl)pyridin-4-yl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(6-cyclopropylpyridin-3-yl)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-2-(3-morpholinophenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(2-cyclopropylpyridin-4-yl)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(3-bromophenyl)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(3-(pyridin-4-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(3-(pyrimidin-5-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-2-(3-(5-fluoropyridin-3-yl)phenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-2-(3-(1-methyl-1*H*-pyrazol-4-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(3-(3,5-dimethylisoxazol-4-yl)phenyl)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-2-(3-(1-methyl-1*H*-pyrazol-5-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-2-(quinolin-4-yl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-3-yl)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-isopropylphenyl)-6,9a-dimethyl-3-(1-methyl-1*H*-pyrazol-4-yl)-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(3-chlorophenyl)-6,9a-dimethyl-3-(1-methyl-1*H*-pyrazol-4-yl)-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(3,4-dichlorophenyl)-6,9a-dimethyl-3-(1-methyl-1*H*-pyrazol-4-yl)-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-3-(1-methyl-1*H*-pyrazol-4-yl)-7-oxo-2-(3-(pyridin-4-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-3-(1-methyl-1*H*-pyrazol-4-yl)-2-(2-morpholinopyridin-4-yl)-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-cyclopropyl-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-isopropyl-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-isopropylphenyl)-3,6,9a-trimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-isopropylphenyl)-3-(2-methoxyethyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-(benzyloxy)ethyl)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-benzyl-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-fluorobenzyl)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorobenzyl)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-chlorobenzyl)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-3-(pyridin-2-ylmethyl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-3-(pyridin-4-ylmethyl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-hydroxyethyl)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-acetyl-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-1-(1-phenylpiperidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(1-phenylpiperidin-4-yl)-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-1-(4-(6-methylpyridazin-4-yl)phenyl)-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-fluorophenyl)-6,9a-dimethyl-1-(4-(6-methylpyridazin-4-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-fluorophenyl)-6,9a-dimethyl-7-oxo-1-(4-(pyridazin-3-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-fluorophenyl)-6,9a-dimethyl-1-(4-(5-methylpyridazin-3-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(2-(fluoromethyl)pyridin-4-yl)phenyl)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(2-(fluoromethyl)pyridin-4-yl)phenyl)-3-(4-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-fluorophenyl)-6,9a-dimethyl-1-(4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(1,2,4-oxadiazol-3-yl)phenyl)-3-(4-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-1-(4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(5-fluoropyridin-3-yl)phenyl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,8,9,9a-octahydro-1*H*-benzo[*g*]indazole-8-carbonitrile; or

(5aR,6R,9aR)-3-(2-fluorophenyl)-6,9a-dimethyl-1-(4-(6-methylpyridazin-4-yl)phenyl)-7-oxo-4,5,5a,6,7,8,9,9a-octahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

or a pharmaceutically acceptable salt thereof.

142. A pharmaceutical composition comprising:
 - (a) a compound according to any one of claims 1-141; and
 - (b) an excipient.
143. The pharmaceutical composition of claim 142, wherein the pharmaceutical composition is formulated for administration: orally, intraadiposally, intraarterially, intraarticularly, intracranially, intradermally, intralesionally, intramuscularly, intranasally, intraocularly, intrapericardially, intraperitoneally, intrapleurally, intraprostatically, intrarectally, intrathecally, intratracheally, intratumorally, intraumbilically,

intravaginally, intravenously, intravesicularly, intravitreally, liposomally, locally, mucosally, parenterally, rectally, subconjunctival, subcutaneously, sublingually, topically, transbuccally, transdermally, vaginally, in crèmes, in lipid compositions, via a catheter, via a lavage, via continuous infusion, via infusion, via inhalation, via injection, via local delivery, or via localized perfusion.

144. The pharmaceutical composition of claim 143, wherein the pharmaceutical composition is formulated for oral administration.
145. The pharmaceutical composition of claim 143, wherein the pharmaceutical composition is formulated for administration via injection.
146. The pharmaceutical composition of claim 145, wherein the pharmaceutical composition is formulated for intraarterial administration, intramuscular administration, intraperitoneal administration, or intravenous administration.
147. The pharmaceutical composition of claim 143, wherein the pharmaceutical composition is formulated for administration topically.
148. The pharmaceutical composition of claim 147, wherein the pharmaceutical composition is formulated for topical administration to the skin or to the eye.
149. The pharmaceutical composition according to any one of claims 142-148, wherein the pharmaceutical composition is formulated as a unit dose.
150. A method of treating or preventing a disease or disorder in a patient in need thereof comprising administering to the patient a pharmaceutically effective amount of a compound or composition according to any one of claims 1-149.
151. The method of claim 150, wherein the patient is a mammal.
152. The method of claim 151, wherein the patient is a human.
153. The method according to any one of claims 150-152, wherein the disease or disorder is associated with increased production of cytokine IL-17.
154. The method according to any one of claims 150-153, wherein the disease or disorder is associated with dysregulated angiogenesis.
155. The method according to any one of claims 150-154, wherein the disease or disorder is an autoimmune disease, organ rejection, asthma, cancer, a neurological disorder, a

psychiatric disorder, a neuropsychiatric disorder, chronic pain syndrome, an inflammatory condition, a retinal disorder, or a cardiovascular disease.

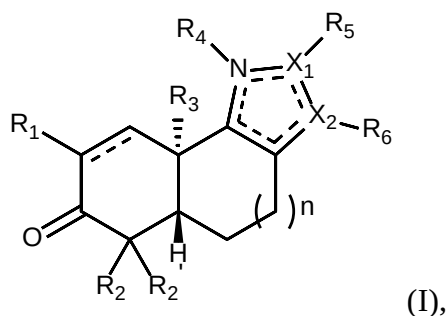
156. The method of claim 155, wherein the disease or disorder is cancer.
157. The method of claim 155, wherein the autoimmune disease is psoriasis, multiple sclerosis, scleroderma, rheumatoid arthritis, lupus, psoriatic arthritis, ankylosing spondylitis, Sjögren syndrome, vitiligo, uveitis, dry eye syndrome, systemic sclerosis, type 1 diabetes, myasthenia gravis, and inflammatory bowel disease.
158. The method of claim 155, wherein the cardiovascular disease is vasculitis, atherosclerosis, myocardial infarction, myocarditis, heart failure, pulmonary hypertension, or stroke.
159. The method of claim 155, wherein the neurological disorder is epilepsy, multiple sclerosis, spinal cord injury, Guillain-Barre syndrome, or another neurological disorder involving dysregulated inflammatory signaling or oxidative stress.
160. The method of claim 159, wherein the neurodegenerative disorder is Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, or Huntington's disease.
161. The method of claim 155, wherein the inflammatory condition is pancreatitis, hepatitis, pulmonary fibrosis, cystic fibrosis, chronic obstructive pulmonary disease, asthma, dermatitis, gastritis, esophagitis, irritable bowel syndrome, inflammatory bowel disease, nephritis, muscle wasting, or osteoarthritis.
162. The method of claim 155, wherein the chronic pain syndrome is fibromyalgia or neuropathic pain.
163. The method of claim 155, wherein the disease or disorder is a severe inflammatory response to a pathogen.
164. The method of claim 163, wherein the severe inflammatory response to a pathogen is from encephalitis, meningitis, *H. pylori*, *Toxoplasma gondii*, or *Leishmania spp.*
165. The method of claim 155, wherein the disease or disorder is obesity, or a condition associated with obesity.
166. The method of claim 165, wherein the condition associated with obesity is insulin resistance or fatty liver disease.

167. The method of claim 155, wherein the retinal disorder is macular degeneration or another disorder of the retina.
168. The method of claim 150, wherein the disease or disorder is associated with inflammation.
169. The method of claim 168, wherein the disease or disorder associated with inflammation is obesity, Type 2 diabetes, or a complication of Type 1 or Type 2 diabetes.
170. The method of claim 169, wherein the complication of Type 1 or Type 2 diabetes is neuropathy, reduced kidney function or chronic kidney disease, retinopathy, diabetic ulcers, or cardiovascular disease.
171. The method of claim 168, wherein the disease or disorder associated with inflammation is chronic kidney disease.
172. The method of claim 171, wherein the chronic kidney disease is hereditary.
173. The method of claim 171, wherein the chronic kidney disease is due to a non-hereditary cause.
174. The method according to any one of claims 150-164, wherein the method comprises administering the compound once.
175. The method according to any one of claims 150-164, wherein the method comprises administering the compound two or more times.

Replacement Sheets

CLAIMS

1. A compound of the formula:



wherein:

n is 0, 1, or 2;

R₁ is cyano, fluoro, -CF₃, or -C(O)R_a, wherein:

R_a is hydroxy or amino; or

alkoxy_(C≤6), alkylamino_(C≤6), dialkylamino_(C≤6), or a substituted version of any of these groups;

R₂ is hydrogen; or

alkyl_(C≤12), cycloalkyl_(C≤12), alkenyl_(C≤12), alkynyl_(C≤12), aryl_(C≤18), aralkyl_(C≤18), heteroaryl_(C≤18), heteroaralkyl_(C≤18), or a substituted version of any of these groups;

R₂' is hydrogen;

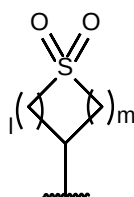
R₃ is alkyl_(C≤12), alkenyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12), or a substituted version of any of these groups;

R₄ and R₅ are each independently absent; or

cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12), heteroaryl_(C≤12), heteroaralkyl_(C≤12), -arenediyl_(C≤12)-alkyl_(C≤12), -arenediyl_(C≤12)-aryl_(C≤12), -arenediyl_(C≤12)-heteroaryl_(C≤12), -arenediyl_(C≤12)-heterocycloalkyl_(C≤12), -arenediyl_(C≤12)-cycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-alkyl_(C≤12), -heteroarenediyl_(C≤12)-aryl_(C≤12), -heteroarenediyl_(C≤12)-heteroaryl_(C≤12), -heteroarenediyl_(C≤12)-heterocycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-cycloalkyl_(C≤12), -heterocycloalkanediyl_(C≤12)-aryl_(C≤12),

–heterocycloalkanediy_(C≤12)–heteroaryl_(C≤12), or a substituted version of any of these groups; or

a group of the formula:



wherein l and m are each 0, 1, 2, or 3;

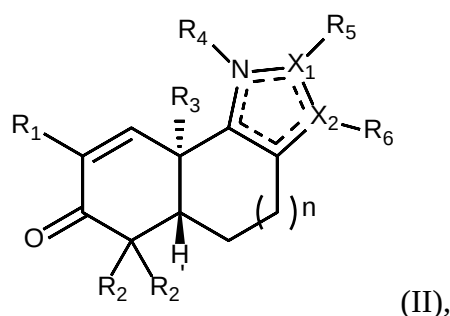
R₆ is absent or amino; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12), dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12), diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12), –alkanediyl_(C≤12)–cycloalkyl_(C≤12), –alkanediyl_(C≤18)–aralkoxy_(C≤18), heterocycloalkyl_(C≤12), aryl_(C≤18), –arenediyl_(C≤12)–alkyl_(C≤12), aralkyl_(C≤18), –arenediyl_(C≤18)–heterocycloalkyl_(C≤12), heteroaryl_(C≤18), –heteroarenediyl_(C≤12)–alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12), alkoxy_(C≤12), or a substituted version of any of these groups; and

X₁ and X₂ are each independently C or N, provided that X₂ is C when R₆ is amino, alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12), dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12), or diarylamino_(C≤12);

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1 further defined as:



wherein:

n is 0, 1, or 2;

R₁ is cyano, fluoro, –CF₃, or –C(O)R_a, wherein

R_a is hydroxy or amino; or

alkoxy_(C≤6), alkylamino_(C≤6), dialkylamino_(C≤6), or a substituted version of any of these groups;

R₂ is hydrogen; or

alkyl_(C≤12), cycloalkyl_(C≤12), alkenyl_(C≤12), alkynyl_(C≤12), aryl_(C≤18), aralkyl_(C≤18), heteroaryl_(C≤18), heteroaralkyl_(C≤18), or a substituted version of any of these groups;

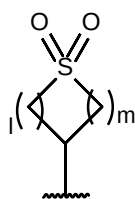
R₂' is hydrogen;

R₃ is alkyl_(C≤12), alkenyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12), or a substituted version of any of these groups;

R₄ and R₅ are each independently absent; or

cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12), heteroaryl_(C≤12), heteroaralkyl_(C≤12), -arenediyl_(C≤12)-alkyl_(C≤12), -arenediyl_(C≤12)-aryl_(C≤12), -arenediyl_(C≤12)-heteroaryl_(C≤12), -arenediyl_(C≤12)-heterocycloalkyl_(C≤12), -arenediyl_(C≤12)-cycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-alkyl_(C≤12), -heteroarenediyl_(C≤12)-aryl_(C≤12), -heteroarenediyl_(C≤12)-heteroaryl_(C≤12), -heteroarenediyl_(C≤12)-heterocycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-cycloalkyl_(C≤12), -heterocycloalkanediyl_(C≤12)-aryl_(C≤12), -heterocycloalkanediyl_(C≤12)-heteroaryl_(C≤12), or a substituted version of any of these groups; or

a group of the formula:



wherein l and m are each 0, 1, 2, or 3;

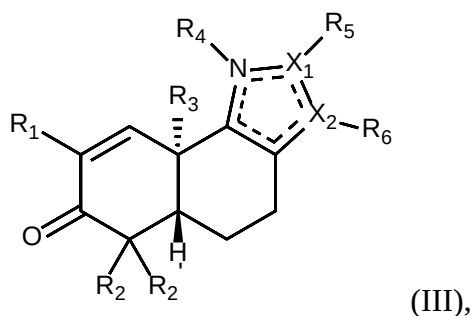
R₆ is absent or amino; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12), dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12), diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12), -alkanediyl_(C≤12)-cycloalkyl_(C≤12), -alkanediyl_(C≤18)-aralkoxy_(C≤18), heterocycloalkyl_(C≤12), aryl_(C≤18), -arenediyl_(C≤12)-alkyl_(C≤12), aralkyl_(C≤18), -arenediyl_(C≤18)-heterocycloalkyl_(C≤12), heteroaryl_(C≤18),

–heteroarenediyl_(C≤12)–alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12), alkoxy_(C≤12), or a substituted version of any of these groups; and X₁ and X₂ are each independently C or N, provided that X₂ is C when R₆ is amino, alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12), dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12), or diarylamino_(C≤12);

or a pharmaceutically acceptable salt thereof.

3. The compound of either claim 1 or claim 2 further defined as:



wherein:

R₁ is cyano, fluoro, –CF₃, or –C(O)R_a, wherein

R_a is hydroxy or amino; or

alkoxy_(C≤6), alkylamino_(C≤6), dialkylamino_(C≤6), or a substituted version of any of these groups;

R₂ is hydrogen; or

alkyl_(C≤12), cycloalkyl_(C≤12), alkenyl_(C≤12), alkynyl_(C≤12), aryl_(C≤18), aralkyl_(C≤18), heteroaryl_(C≤18), heteroaralkyl_(C≤18), or a substituted version of any of these groups;

R₂' is hydrogen;

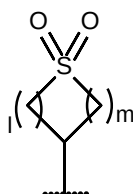
R₃ is alkyl_(C≤12), alkenyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12), or a substituted version of any of these groups;

R₄ and R₅ are each independently absent; or

cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12), heteroaryl_(C≤12), heteroaralkyl_(C≤12), –arenediyl_(C≤12)–alkyl_(C≤12), –arenediyl_(C≤12)–aryl_(C≤12), –arenediyl_(C≤12)–heteroaryl_(C≤12), –arenediyl_(C≤12)–heterocycloalkyl_(C≤12), –arenediyl_(C≤12)–cycloalkyl_(C≤12), –heteroarenediyl_(C≤12)–alkyl_(C≤12), –heteroarenediyl_(C≤12)–aryl_(C≤12), –hetero-

arenediyl_(C≤12)–heteroaryl_(C≤12), –heteroarenediyl_(C≤12)–hetero-
cycloalkyl_(C≤12), –heteroarenediyl_(C≤12)–cycloalkyl_(C≤12),
–heterocycloalkanediyl_(C≤12)–aryl_(C≤12),
–heterocycloalkanediyl_(C≤12)–heteroaryl_(C≤12), or a substituted
version of any of these groups; or

a group of the formula:



wherein l and m are each 0, 1, 2, or 3;

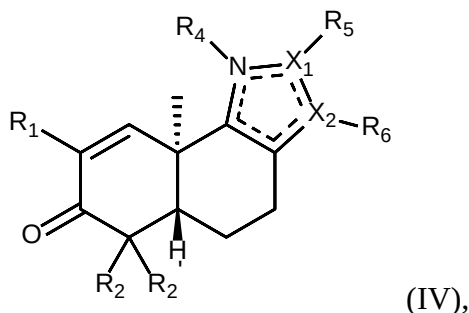
R₆ is absent or amino; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12),
–alkanediyl_(C≤12)–cycloalkyl_(C≤12), –alkanediyl_(C≤18)–aralkoxy_(C≤18),
heterocycloalkyl_(C≤12), aryl_(C≤18), –arenediyl_(C≤12)–alkyl_(C≤12),
aralkyl_(C≤18), –arenediyl_(C≤18)–heterocycloalkyl_(C≤12), heteroaryl_(C≤18),
–heteroarenediyl_(C≤12)–alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12),
alkoxy_(C≤12), or a substituted version of any of these groups; and

X₁ and X₂ are each independently C or N, provided that X₂ is C when R₆ is
amino, alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
or diarylamino_(C≤12);

or a pharmaceutically acceptable salt thereof.

4. The compound according to any one of claims 1-3 further defined as:



wherein:

R₁ is cyano, fluoro, –CF₃, or –C(O)R_a, wherein

R_a is hydroxy or amino; or

alkoxy_(C≤6), alkylamino_(C≤6), dialkylamino_(C≤6), or a substituted version of any of these groups;

R₂ is hydrogen; or

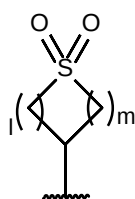
alkyl_(C≤12), cycloalkyl_(C≤12), alkenyl_(C≤12), alkynyl_(C≤12), aryl_(C≤18), aralkyl_(C≤18), heteroaryl_(C≤18), heteroaralkyl_(C≤18), or a substituted version of any of these groups;

R₂' is hydrogen;

R₄ and R₅ are each independently absent; or

cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12), heteroaryl_(C≤12), heteroaralkyl_(C≤12), -arenediyl_(C≤12)-alkyl_(C≤12), -arenediyl_(C≤12)-aryl_(C≤12), -arenediyl_(C≤12)-heteroaryl_(C≤12), -arenediyl_(C≤18)-heterocycloalkyl_(C≤12), -arenediyl_(C≤12)-cycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-alkyl_(C≤12), -heteroarenediyl_(C≤12)-aryl_(C≤12), -heteroarenediyl_(C≤12)-heteroaryl_(C≤12), -heteroarenediyl_(C≤12)-heterocycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-cycloalkyl_(C≤12), -heterocycloalkanediyl_(C≤12)-aryl_(C≤12), -heterocycloalkanediyl_(C≤12)-heteroaryl_(C≤12), or a substituted version of any of these groups; or

a group of the formula:



wherein l and m are each 0, 1, 2, or 3;

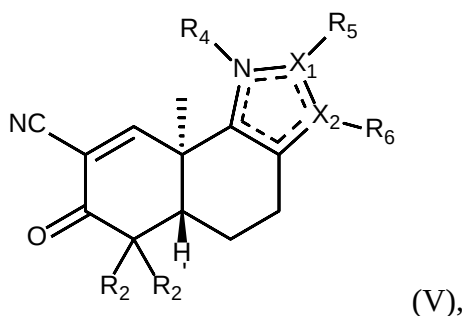
R₆ is absent or amino; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12), dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12), diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12), -alkanediyl_(C≤12)-cycloalkyl_(C≤12), -alkanediyl_(C≤18)-aralkoxy_(C≤18), heterocycloalkyl_(C≤12), aryl_(C≤18), -arenediyl_(C≤12)-alkyl_(C≤12), aralkyl_(C≤18), -arenediyl_(C≤18)-heterocycloalkyl_(C≤12), heteroaryl_(C≤18),

–heteroarenediyl_(C≤12)–alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12), alkoxy_(C≤12), or a substituted version of any of these groups; and X₁ and X₂ are each independently C or N, provided that X₂ is C when R₆ is amino, alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12), dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12), or diarylamino_(C≤12);

or a pharmaceutically acceptable salt thereof.

5. The compound according to any one of claims 1-4, further defined as:



wherein:

R₂ is hydrogen; or

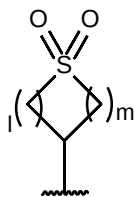
alkyl_(C≤12), cycloalkyl_(C≤12), alkenyl_(C≤12), alkynyl_(C≤12), aryl_(C≤18), aralkyl_(C≤18), heteroaryl_(C≤18), heteroaralkyl_(C≤18), or a substituted version of any of these groups;

R₂' is hydrogen;

R₄ and R₅ are each independently absent; or

cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12), heteroaryl_(C≤12), heteroaralkyl_(C≤12), –arenediyl_(C≤12)–alkyl_(C≤12), –arenediyl_(C≤12)–aryl_(C≤12), –arenediyl_(C≤12)–heteroaryl_(C≤12), –arenediyl_(C≤12)–heterocycloalkyl_(C≤12), –arenediyl_(C≤12)–cycloalkyl_(C≤12), –heteroarenediyl_(C≤12)–alkyl_(C≤12), –heteroarenediyl_(C≤12)–aryl_(C≤12), –heteroarenediyl_(C≤12)–heteroaryl_(C≤12), –heteroarenediyl_(C≤12)–heterocycloalkyl_(C≤12), –heteroarenediyl_(C≤12)–cycloalkyl_(C≤12), –heterocycloalkanediyl_(C≤12)–aryl_(C≤12), –heterocycloalkanediyl_(C≤12)–heteroaryl_(C≤12), or a substituted version of any of these groups; or

a group of the formula:



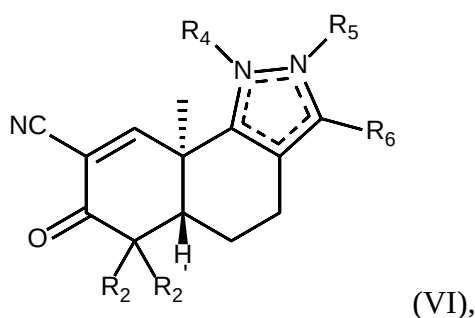
wherein l and m are each 0, 1, 2, or 3;
 R_6 is absent or amino; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
 dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
 diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12),
 -alkanediyl_(C≤12)-cycloalkyl_(C≤12), -alkanediyl_(C≤18)-aralkoxy_(C≤18),
 heterocycloalkyl_(C≤12), aryl_(C≤18), -arenediyl_(C≤12)-alkyl_(C≤12),
 aralkyl_(C≤18), -arenediyl_(C≤18)-heterocycloalkyl_(C≤12), heteroaryl_(C≤18),
 -heteroarenediyl_(C≤12)-alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12),
 alkoxy_(C≤12), or a substituted version of any of these groups; and

X_1 and X_2 are each independently C or N, provided that X_2 is C when R_6 is
 amino, alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
 dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
 or diarylamino_(C≤12);

or a pharmaceutically acceptable salt thereof.

6. The compound according to any one of claims 1-3, further defined as:



wherein:

R_2 is hydrogen; or

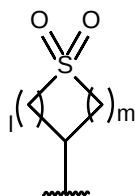
alkyl_(C≤12), cycloalkyl_(C≤12), alkenyl_(C≤12), alkynyl_(C≤12), aryl_(C≤18),
 aralkyl_(C≤18), heteroaryl_(C≤18), heteroaralkyl_(C≤18), or a substituted
 version of any of these groups;

R_2' is hydrogen;

R_4 and R_5 are each independently absent; or

cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12),
heteroaryl_(C≤12), heteroaralkyl_(C≤12), -arenediyl_(C≤12)-alkyl_(C≤12),
-arenediyl_(C≤12)-aryl_(C≤12), -arenediyl_(C≤12)-heteroaryl_(C≤12),
-arenediyl_(C≤12)-heterocycloalkyl_(C≤12), -arenediyl_(C≤12)-cyclo-
alkyl_(C≤12), -heteroarenediyl_(C≤12)-alkyl_(C≤12),
-heteroarenediyl_(C≤12)-aryl_(C≤12), -hetero-
arenediyl_(C≤12)-heteroaryl_(C≤12), -heteroarenediyl_(C≤12)-hetero-
cycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-cycloalkyl_(C≤12),
-heterocycloalkanediyl_(C≤12)-aryl_(C≤12),
-heterocycloalkanediyl_(C≤12)-heteroaryl_(C≤12), or a substituted
version of any of these groups; or

a group of the formula:



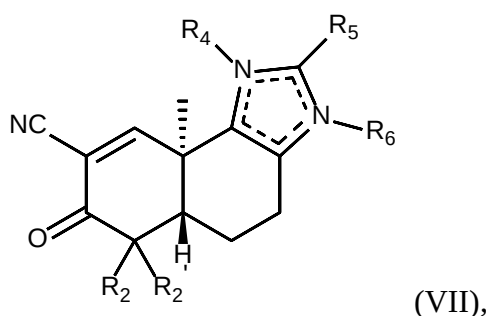
wherein l and m are each 0, 1, 2, or 3; and

R₆ is absent; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12),
-alkanediyl_(C≤12)-cycloalkyl_(C≤12), -alkanediyl_(C≤18)-aralkoxy_(C≤18),
heterocycloalkyl_(C≤12), aryl_(C≤18), -arenediyl_(C≤12)-alkyl_(C≤12),
aralkyl_(C≤18), -arenediyl_(C≤18)-heterocycloalkyl_(C≤12), heteroaryl_(C≤18),
-heteroarenediyl_(C≤12)-alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12),
alkoxy_(C≤12), or a substituted version of any of these groups;

or a pharmaceutically acceptable salt thereof.

7. The compound according to any one of claims 1-3, further defined as:



wherein:

R₂ is hydrogen; or

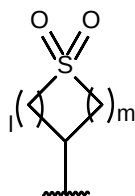
alkyl_(C≤12), cycloalkyl_(C≤12), alkenyl_(C≤12), alkynyl_(C≤12), aryl_(C≤18), aralkyl_(C≤18), heteroaryl_(C≤18), heteroaralkyl_(C≤18), or a substituted version of any of these groups;

R₂' is hydrogen;

R₄ and R₅ are each independently absent; or

cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12), heteroaryl_(C≤12), heteroaralkyl_(C≤12), -arenediyl_(C≤12)-alkyl_(C≤12), -arenediyl_(C≤12)-aryl_(C≤12), -arenediyl_(C≤12)-heteroaryl_(C≤12), -arenediyl_(C≤12)-heterocycloalkyl_(C≤12), -arenediyl_(C≤12)-cycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-alkyl_(C≤12), -heteroarenediyl_(C≤12)-aryl_(C≤12), -heteroarenediyl_(C≤12)-heteroaryl_(C≤12), -heteroarenediyl_(C≤12)-heterocycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-cycloalkyl_(C≤12), -heterocycloalkanediyl_(C≤12)-aryl_(C≤12), -heterocycloalkanediyl_(C≤12)-heteroaryl_(C≤12), or a substituted version of any of these groups; or

a group of the formula:



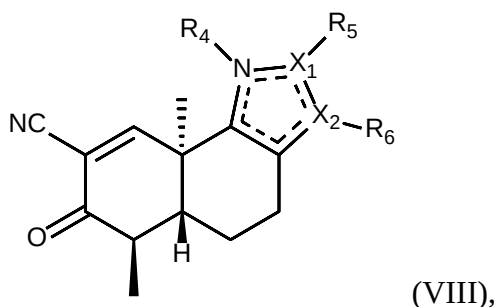
wherein l and m are each 0, 1, 2, or 3; and

R₆ is absent; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12), dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),

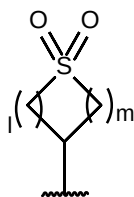
diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12),
 -alkanediyl_(C≤12)-cycloalkyl_(C≤12), -alkanediyl_(C≤18)-aralkoxy_(C≤18),
 heterocycloalkyl_(C≤12), aryl_(C≤18), -arenediyl_(C≤12)-alkyl_(C≤12),
 aralkyl_(C≤18), -arenediyl_(C≤18)-heterocycloalkyl_(C≤12), heteroaryl_(C≤18),
 -heteroarenediyl_(C≤12)-alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12),
 alkoxy_(C≤12), or a substituted version of any of these groups;
 or a pharmaceutically acceptable salt thereof.

8. The compound according to any one of claims 1-4, further defined as:



wherein:

R₄ and R₅ are each independently absent; or
 cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12),
 heteroaryl_(C≤12), heteroaralkyl_(C≤12), -arenediyl_(C≤12)-alkyl_(C≤12),
 -arenediyl_(C≤12)-aryl_(C≤12), -arenediyl_(C≤12)-heteroaryl_(C≤12),
 -arenediyl_(C≤12)-heterocycloalkyl_(C≤12), -arenediyl_(C≤12)-cyclo-
 alkyl_(C≤12), -heteroarenediyl_(C≤12)-alkyl_(C≤12),
 -heteroarenediyl_(C≤12)-aryl_(C≤12), -hetero-
 arenediyl_(C≤12)-heteroaryl_(C≤12), -heteroarenediyl_(C≤12)-hetero-
 cycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-cycloalkyl_(C≤12),
 -heterocycloalkanediyl_(C≤12)-aryl_(C≤12),
 -heterocycloalkanediyl_(C≤12)-heteroaryl_(C≤12), or a substituted
 version of any of these groups; or
 a group of the formula:



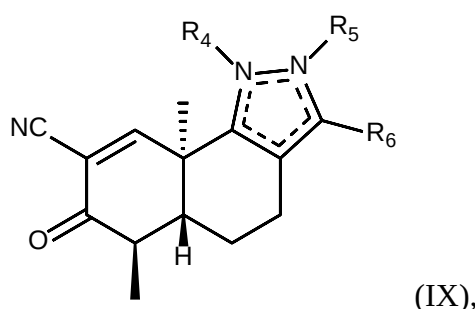
wherein l and m are each 0, 1, 2, or 3; and
 R₆ is absent; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12),
–alkanediyl_(C≤12)–cycloalkyl_(C≤12), –alkanediyl_(C≤18)–aralkoxy_(C≤18),
heterocycloalkyl_(C≤12), aryl_(C≤18), –arenediyl_(C≤12)–alkyl_(C≤12),
aralkyl_(C≤18), –arenediyl_(C≤18)–heterocycloalkyl_(C≤12), heteroaryl_(C≤18),
–heteroarenediyl_(C≤12)–alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12),
alkoxy_(C≤12), or a substituted version of any of these groups; and

X₁ and X₂ are each independently C or N, provided that X₂ is C when R₆ is
amino, alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
or diarylamino_(C≤12);

or a pharmaceutically acceptable salt thereof.

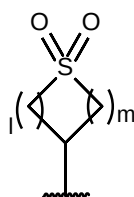
9. The compound according to any one of claims 1-4 and 8, further defined as:



wherein:

R₄ and R₅ are each independently absent; or
cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12),
heteroaryl_(C≤12), heteroaralkyl_(C≤12), –arenediyl_(C≤12)–alkyl_(C≤12),
–arenediyl_(C≤12)–aryl_(C≤12), –arenediyl_(C≤12)–heteroaryl_(C≤12),
–arenediyl_(C≤12)–heterocycloalkyl_(C≤12), –arenediyl_(C≤12)–cyclo-
alkyl_(C≤12), –heteroarenediyl_(C≤12)–alkyl_(C≤12),
–heteroarenediyl_(C≤12)–aryl_(C≤12), –hetero-
arenediyl_(C≤12)–heteroaryl_(C≤12), –heteroarenediyl_(C≤12)–hetero-
cycloalkyl_(C≤12), –heteroarenediyl_(C≤12)–cycloalkyl_(C≤12),
–heterocycloalkanediyl_(C≤12)–aryl_(C≤12),
–heterocycloalkanediyl_(C≤12)–heteroaryl_(C≤12), or a substituted
version of any of these groups; or

a group of the formula:

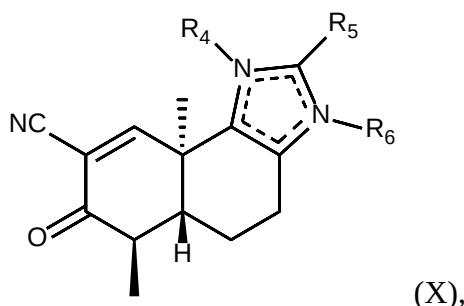


wherein l and m are each 0, 1, 2, or 3; and
R₆ is absent; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12),
-alkanediyl_(C≤12)-cycloalkyl_(C≤12), -alkanediyl_(C≤18)-aralkoxy_(C≤18),
heterocycloalkyl_(C≤12), aryl_(C≤18), -arenediyl_(C≤12)-alkyl_(C≤12),
aralkyl_(C≤18), -arenediyl_(C≤18)-heterocycloalkyl_(C≤12), heteroaryl_(C≤18),
-heteroarenediyl_(C≤12)-alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12),
alkoxy_(C≤12), or a substituted version of any of these groups;

or a pharmaceutically acceptable salt thereof.

10. The compound according to any one of claims 1-4 and 8, further defined as:



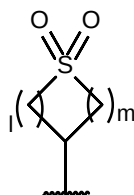
wherein:

R₄ and R₅ are each independently absent; or

cycloalkyl_(C≤12), heterocycloalkyl_(C≤12), aryl_(C≤12), aralkyl_(C≤12),
heteroaryl_(C≤12), heteroaralkyl_(C≤12), -arenediyl_(C≤12)-alkyl_(C≤12),
-arenediyl_(C≤12)-aryl_(C≤12), -arenediyl_(C≤12)-heteroaryl_(C≤12),
-arenediyl_(C≤12)-heterocycloalkyl_(C≤12), -arenediyl_(C≤12)-cyclo-
alkyl_(C≤12), -heteroarenediyl_(C≤12)-alkyl_(C≤12),
-heteroarenediyl_(C≤12)-aryl_(C≤12), -hetero-
arenediyl_(C≤12)-heteroaryl_(C≤12), -heteroarenediyl_(C≤12)-hetero-
cycloalkyl_(C≤12), -heteroarenediyl_(C≤12)-cycloalkyl_(C≤12),
-heterocycloalkanediyl_(C≤12)-aryl_(C≤12),

–heterocycloalkanediy_(C≤12)–heteroaryl_(C≤12), or a substituted version of any of these groups; or

a group of the formula:



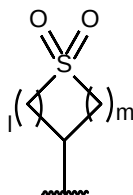
wherein l and m are each 0, 1, 2, or 3; and
R₆ is absent; or

alkylamino_(C≤12), dialkylamino_(C≤12), cycloalkylamino_(C≤12),
dicycloalkylamino_(C≤12), alkyl(cycloalkyl)amino_(C≤12), arylamino_(C≤12),
diarylamino_(C≤12), alkyl_(C≤12), cycloalkyl_(C≤12),
–alkanediyl_(C≤12)–cycloalkyl_(C≤12), –alkanediyl_(C≤18)–aralkoxy_(C≤18),
heterocycloalkyl_(C≤12), aryl_(C≤18), –arenediyl_(C≤12)–alkyl_(C≤12),
aralkyl_(C≤18), –arenediyl_(C≤18)–heterocycloalkyl_(C≤12), heteroaryl_(C≤18),
–heteroarenediyl_(C≤12)–alkyl_(C≤12), heteroaralkyl_(C≤18), acyl_(C≤12),
alkoxy_(C≤12), or a substituted version of any of these groups;

or a pharmaceutically acceptable salt thereof.

11. The compound according to any one of claims 1-4 and 8, wherein X₁ and X₂ are both N.
12. The compound according to any one of claims 1-4 and 8, wherein X₁ and X₂ are not both N.
13. The compound according to any one of claims 1-4, 8, 11, and 12, wherein either X₁ or X₂ is N.
14. The compound according to any one of claims 1-4, 8, and 11-13, wherein X₁ is N.
15. The compound according to any one of claims 1-4, 8, and 11-13, wherein X₂ is N.
16. The compound according to any one of claims 1-3, wherein R₃ is alkyl_(C≤12) or substituted alkyl_(C≤12).
17. The compound of claim 16, wherein R₃ is alkyl_(C≤12).
18. The compound of claim 18, wherein R₃ is methyl.
19. The compound according to any one of claims 1-4 and 11-18, wherein R₁ is cyano.

20. The compound according to any one of claims 1-4 and 11-18, wherein R_1 is $-C(O)R_a$.
21. The compound of claim 20, wherein R_a is alkoxy_(C≤6).
22. The compound of claim 21, wherein R_a is methoxy.
23. The compound of claim 20, wherein R_a is amino.
24. The compound according to any one of claims 1-7 and 11-23, wherein R_2' is hydrogen.
25. The compound according to any one of claims 1-7 and 11-24, wherein R_2 is hydrogen.
26. The compound according to any one of claims 1-7 and 11-25, wherein R_2' and R_2 are both hydrogen.
27. The compound according to any one of claims 1-7 and 11-24, wherein R_2 is alkyl_(C≤12) or substituted alkyl_(C≤12).
28. The compound of claim 27, wherein R_2 is alkyl_(C≤12).
29. The compound of claim 28, wherein R_2 is methyl.
30. The compound according to any one of claims 1-29, wherein R_4 is absent.
- 31.-34. Cancelled
35. The compound according to any one of claims 1-29, wherein R_4 is cycloalkyl_(C≤12) or substituted cycloalkyl_(C≤12).
36. The compound of claim 35, wherein R_4 is cycloalkyl_(C≤12).
37. The compound of claim 36, wherein R_4 is cyclohexyl.
38. The compound according to any one of claims 1-29, wherein R_4 is heterocycloalkyl_(C≤12) or substituted heterocycloalkyl_(C≤12).
39. The compound of claim 38, wherein R_4 is heterocycloalkyl_(C≤12).
40. The compound of claim 39, wherein R_4 is tetrahydro-2H-pyran-4-yl or 1,1-dioxidotetrahydrothiophen-3-yl.
41. The compound according to any one of claims 1-29, wherein R_4 is:



wherein:

l and m are each 0, 1, 2, or 3.

42. The compound of claim 41, wherein l is 1 or 2.
43. The compound of either claim 41 or claim 42, wherein m is 1 or 2.
44. The compound according to any one of claims 1-29, wherein R₄ is aryl_(C≤18) or substituted aryl_(C≤18).
45. The compound of claim 44, wherein R₄ is aryl_(C≤18).
46. The compound of claim 45, wherein R₄ is phenyl, *o*-tolyl, *p*-tolyl, [1,1'-biphenyl]-4-yl, 4-isopropylphenyl, naphthalen-1-yl, 4'-methyl-[1,1'-biphenyl]-4-yl, or 2'-methyl-[1,1'-biphenyl]-4-yl.
47. The compound of claim 44, wherein R₄ is substituted aryl_(C≤18).
48. The compound of claim 47, wherein R₄ is 4-(trifluoromethyl)phenyl, 4-cyanophenyl, 2-fluorophenyl, 4-fluorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 4-methoxyphenyl, 4-(trifluoromethoxy)phenyl, 4-carboxyphenyl, 4'-methoxy-[1,1'-biphenyl]-4-yl, 4'-(dimethylamino)-[1,1'-biphenyl]-4-yl, 2'-fluoro-[1,1'-biphenyl]-4-yl, 3'-fluoro-[1,1'-biphenyl]-4-yl, 2'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl, 3'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl, 4'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl, or 5-(3-(hydroxymethyl)phenyl).
49. The compound according to any one of claims 1-29, wherein R₄ is aralkyl_(C≤18) or substituted aralkyl_(C≤18).
50. The compound of claim 49, wherein R₄ is aralkyl_(C≤18).
51. The compound of claim 50, wherein R₄ is benzyl.
52. The compound according to any one of claims 1-29, wherein R₄ is -arenediyl_(C≤12)-heterocycloalkyl_(C≤12) or substituted -arenediyl_(C≤12)-heterocycloalkyl_(C≤12).
53. The compound of claim 52, wherein R₄ is -arenediyl_(C≤12)-heterocycloalkyl_(C≤12).
54. The compound of claim 53, wherein R₄ is 4-morpholinophenyl.
55. The compound according to any one of claims 1-29, wherein R₄ is heteroaryl_(C≤18) or substituted heteroaryl_(C≤18).
56. The compound of claim 55, wherein R₄ is heteroaryl_(C≤18).

57. The compound of claim 56, wherein R₄ is pyridin-4-yl, quinolin-4-yl, 5-methylpyridin-2-yl, 6-methylpyridin-3-yl, (pyridin-3-yl)phenyl, (pyridin-4-yl)phenyl, 4-(3,5-dimethylisoxazol-4-yl)phenyl, 4-(pyrimidin-4-yl)phenyl, 4-(pyrimidin-5-yl)phenyl, 4-(pyridin-3-yl)phenyl, 4-(pyridin-4-yl)phenyl, 5-phenylpyridin-2-yl, [3,3'-bipyridin]-6-yl, 5-cyclopropylpyridin-2-yl, 6-phenylpyridin-3-yl, 4-(6-methylpyridazin-4-yl)phenyl, 5-methyl-1,2,4-oxadiazol-3-yl, 3-methyl-1,2,4-oxadiazol-5-yl, 4-methyl-5-phenyl-4*H*-1,2,4-triazol-3-yl, 1-phenylpiperidin-4-yl, 4-phenyloxazol-2-yl, 4-(6-methylpyridazin-4-yl)phenyl, 4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl, 4-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl, 4-(1,2,4-oxadiazol-3-yl)phenyl, 4-(pyridazin-3-yl)phenyl, 4-(5-methylpyridazin-3-yl)phenyl, 1-methyl-1*H*-benzo[*d*]imidazol-2-yl, or benzo[*d*]thiazol-2-yl.
58. The compound of claim 55, wherein R₄ is substituted heteroaryl_(C≤18).
59. The compound of claim 58, wherein R₄ is 2-fluoro-4-(pyridin-3-yl)phenyl, 5-(trifluoromethyl)pyridin-2-yl, 5-(3-fluorophenyl)pyridin-2-yl, 5-(4-fluorophenyl)pyridin-2-yl, 4-(2-(hydroxymethyl)pyridine-4-yl)phenyl, 4-(2-(fluoromethyl)pyridine-4-yl)phenyl, 5-(trifluoromethyl)benzo[*d*]oxazol-2-yl, 6-chlorobenzo[*d*]thiazol-2-yl, or 4-(5-fluoropyridin-3-yl)phenyl.
- 60.-63. Cancelled
64. The compound according to any one of claims 1-59, wherein R₅ is cycloalkyl_(C≤12) or substituted cycloalkyl_(C≤12).
65. The compound of claim 64, wherein R₅ is cycloalkyl_(C≤12).
66. The compound of claim 65, wherein R₅ is cyclohexyl.
67. The compound according to any one of claims 1-59, wherein R₅ is heterocycloalkyl_(C≤12) or substituted heterocycloalkyl_(C≤12).
68. The compound of claim 67, wherein R₅ is heterocycloalkyl_(C≤12).
69. The compound of claim 68, wherein R₅ is tetrahydro-2*H*-pyran-4-yl.
70. The compound according to any one of claims 1-59, wherein R₅ is aryl_(C≤18) or substituted aryl_(C≤18).

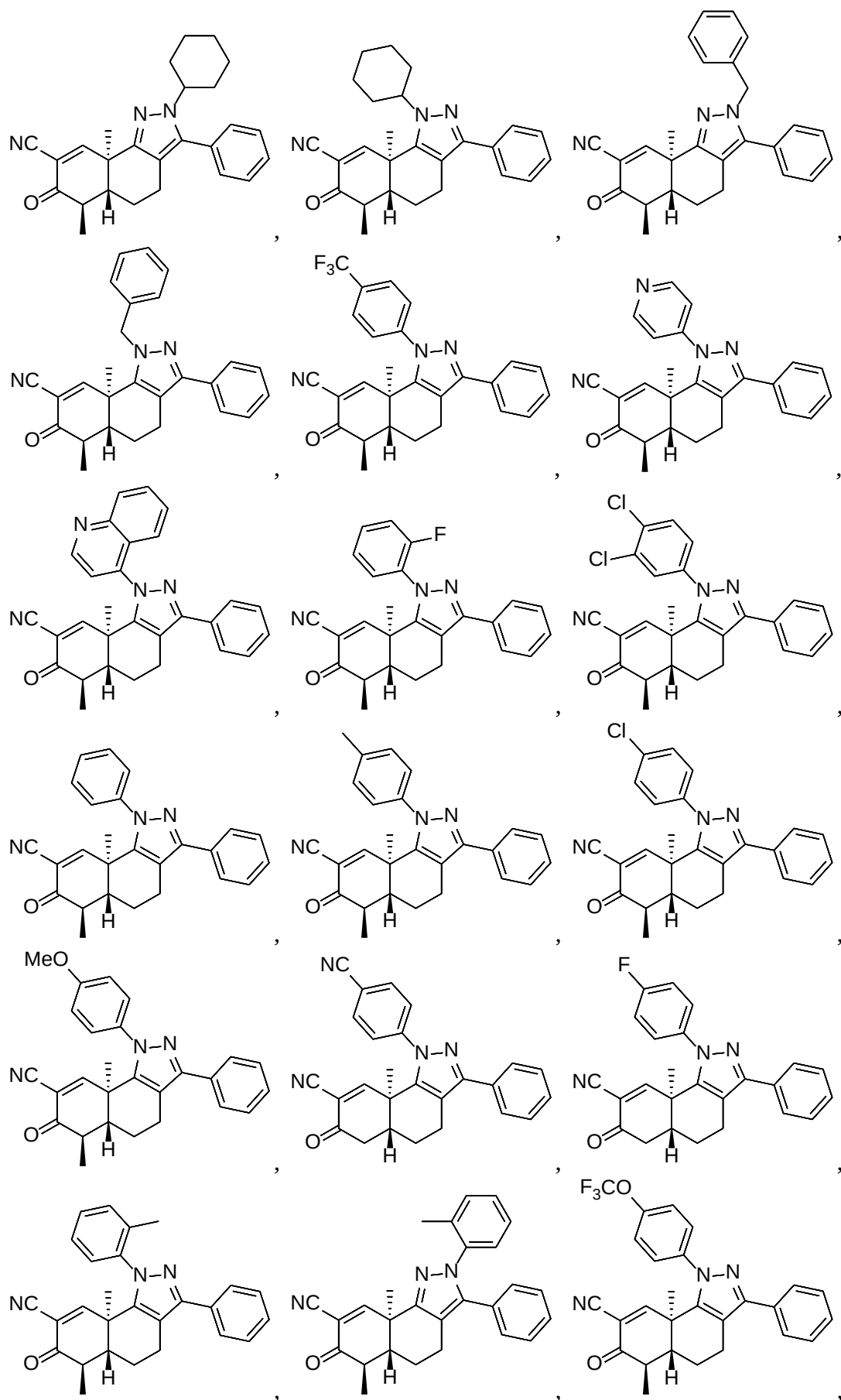
71. The compound of claim 70, wherein R₅ is aryl_(C≤18).
72. The compound of claim 71, wherein R₅ is phenyl, *o*-tolyl, *p*-tolyl, [1,1'-biphenyl]-4-yl, 4-isopropylphenyl, naphthalen-1-yl, [1,1'-biphenyl]-3-yl, or 3-isopropylphenyl.
73. The compound of claim 72, wherein R₅ is substituted aryl_(C≤18).
74. The compound of claim 73, wherein R₅ is 4-chlorophenyl, 3,4-dichlorophenyl, 4-methoxyphenyl, 4-(trifluoromethoxy)phenyl, 3-bromophenyl, 3-chlorophenyl, 4-(dimethylamino)phenyl.
75. The compound according to any one of claims 1-59, wherein R₅ is aralkyl_(C≤18) or substituted aralkyl_(C≤18).
76. The compound of claim 75, wherein R₅ is aralkyl_(C≤18).
77. The compound of claim 76, wherein R₅ is benzyl.
78. The compound according to any one of claims 1-59, wherein R₅ is
 -arenediyl_(C≤12)-heterocycloalkyl_(C≤12) or substituted
 -arenediyl_(C≤12)-heterocycloalkyl_(C≤12).
79. The compound of claim 78, wherein R₅ is -arenediyl_(C≤12)-heterocycloalkyl_(C≤12).
80. The compound of claim 79, wherein R₅ is 3-morpholinophenyl.
81. The compound according to any one of claims 1-59, wherein R₅ is heteroaryl_(C≤18) or substituted heteroaryl_(C≤18).
82. The compound of claim 81, wherein R₅ is heteroaryl_(C≤18).
83. The compound of claim 82, wherein R₅ is pyridin-4-yl, quinolin-4-yl, quinolin-3-yl, quinolin-5-yl, 3-(pyridin-4-yl)phenyl, 3-(pyrimidin-5-yl)phenyl, 2-isopropylpyrimidin-5-yl, 6-cyclopropylpyridin-3-yl, 3-(1-methyl-1*H*-pyrazol-4-yl)phenyl, 1-methyl-1*H*-pyrazol-4-yl, 3-(3,5-dimethylisoxazol-4-yl)phenyl, 3-(1-methyl-1*H*-pyrazol-5-yl)phenyl, or 2-cyclopropylpyridin-4-yl.
84. The compound of claim 81, wherein R₅ is substituted heteroaryl_(C≤18).
85. The compound of claim 84, wherein R₅ is 2-(trifluoromethyl)pyridin-4-yl or 3-(5-fluoropyridin-3-yl)phenyl.

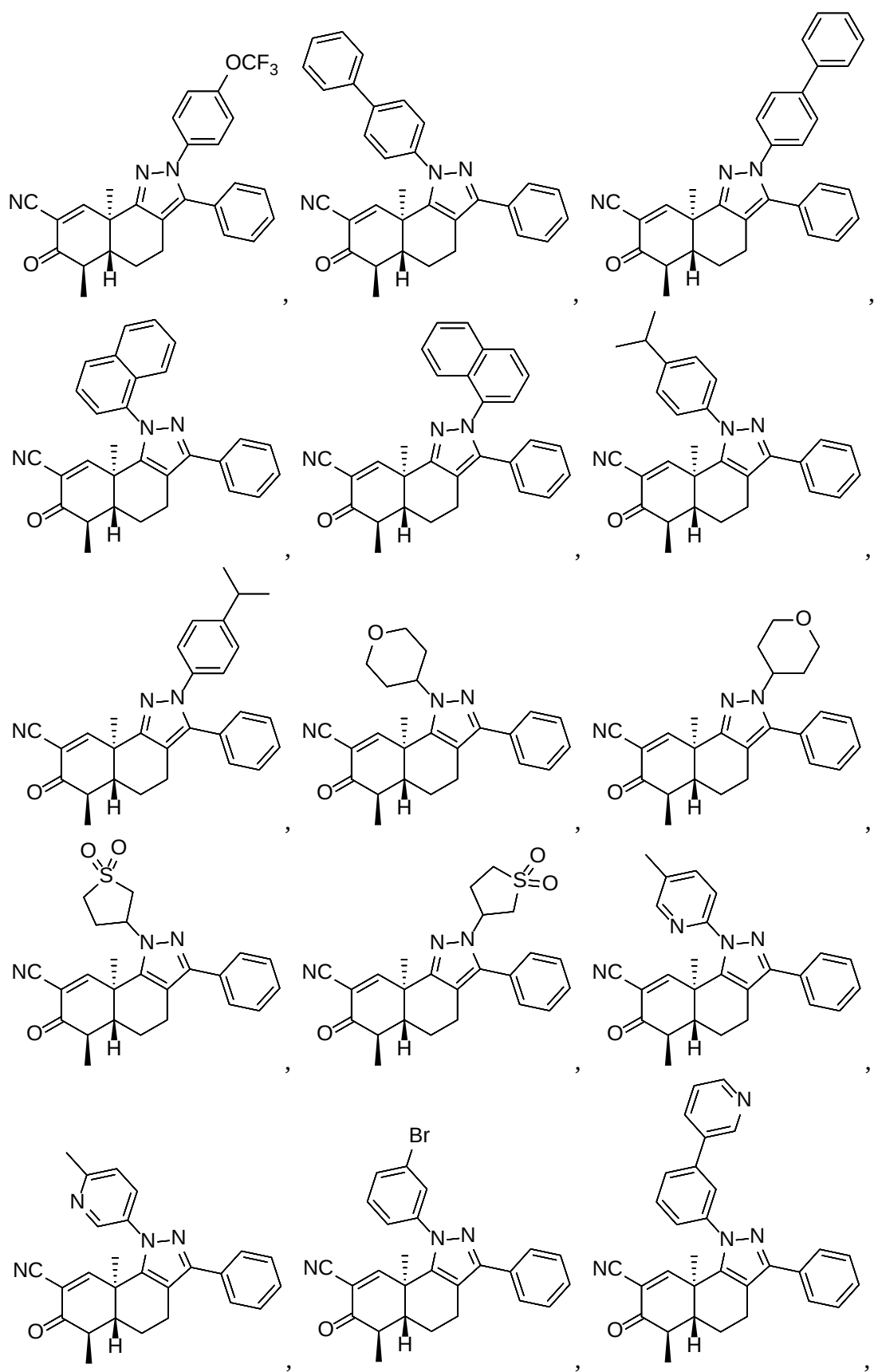
86. The compound according to any one of claims 1-59, wherein R₅ is
 –heteroarenediyl_(C≤12)–heterocycloalkyl_(C≤12) or substituted
 –heteroarenediyl_(C≤12)–heterocycloalkyl_(C≤12).
87. The compound of claim 86, wherein R₅ is –heteroarenediyl_(C≤12)–heterocycloalkyl_(C≤12).
88. The compound of claim 87, wherein R₅ is 2-morpholinopyridin-4-yl.
89. Cancelled
90. The compound according to any one of claims 1-88, wherein R₆ is amino.
91. The compound according to any one of claims 1-88, wherein R₆ is alkylamino_(C≤12) or
 substituted alkylamino_(C≤12).
92. The compound of claim 91, wherein R₆ is alkylamino_(C≤12).
93. The compound of claim 92, wherein R₆ is methylamino.
94. The compound according to any one of claims 1-88, wherein R₆ is
 cycloalkylamino_(C≤12) or substituted cycloalkylamino_(C≤12).
95. The compound of claim 94, wherein R₆ is cycloalkylamino_(C≤12).
96. The compound of claim 95, wherein R₆ is cyclobutylamino.
97. The compound according to any one of claims 1-88, wherein R₆ is
 alkyl(cycloalkyl)amino_(C≤12) or substituted alkyl(cycloalkyl)amino_(C≤12).
98. The compound of claim 97, wherein R₆ is alkyl(cycloalkyl)amino_(C≤12).
99. The compound of claim 98, wherein R₆ is methyl(cyclobutyl)amino.
100. The compound according to any one of claims 1-88, wherein R₆ is arylamino_(C≤12) or
 substituted arylamino_(C≤12).
101. The compound of claim 100, wherein R₆ is arylamino_(C≤12).
102. The compound of claim 101, wherein R₆ is phenylamino.
103. The compound according to any one of claims 1-88, wherein R₆ is alkyl_(C≤12) or
 substituted alkyl_(C≤12).
104. The compound of claim 103, wherein R₆ is alkyl_(C≤12).
105. The compound of claim 104, wherein R₆ is methyl.
106. The compound of claim 103, wherein R₆ is substituted alkyl_(C≤12).

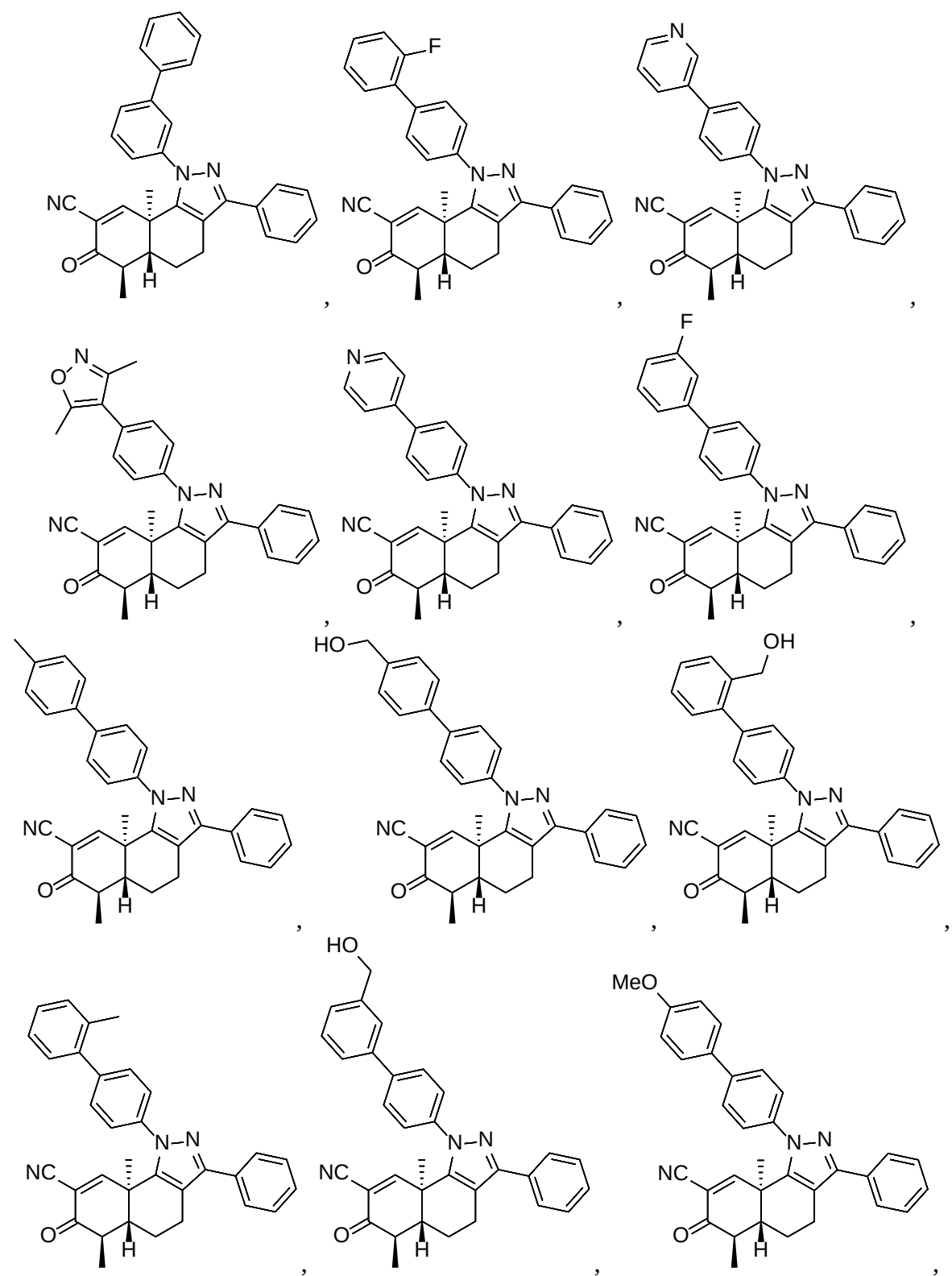
107. The compound of claim 106, wherein R₆ is 2-hydroxyethyl or 2-methoxyethyl.
108. The compound according to any one of claims 1-88, wherein R₆ is acyl_(C≤6) or substituted acyl_(C≤6).
109. The compound of claim 108, wherein R₆ is acyl_(C≤6).
110. The compound of claim 109, wherein R₆ is -C(O)CH₃.
111. The compound according to any one of claims 1-88, wherein R₆ is cycloalkyl_(C≤12) or substituted cycloalkyl_(C≤12).
112. The compound of claim 111, wherein R₆ is cycloalkyl_(C≤12).
113. The compound of claim 112, wherein R₆ is cyclopropyl or cyclohexyl.
114. The compound according to any one of claims 1-88, wherein R₆ is -alkanediyl_(C≤18)-cycloalkyl_(C≤18) or substituted -alkanediyl_(C≤18)-cycloalkyl_(C≤18).
115. The compound of claim 114, wherein R₆ is -alkanediyl_(C≤18)-cycloalkyl_(C≤18).
116. The compound of claim 115, wherein R₆ is cyclobutylmethyl.
117. The compound according to any one of claims 1-88, wherein R₆ is aryl_(C≤18) or substituted aryl_(C≤18).
118. The compound of claim 117, wherein R₆ is aryl_(C≤18).
119. The compound of claim 118, wherein R₆ is phenyl, *o*-tolyl, *p*-tolyl, or 3-isopropylphenyl.
120. The compound of claim 117, wherein R₆ is substituted aryl_(C≤18).
121. The compound of claim 120, wherein R₆ is 2-fluorophenyl, 4-fluorophenyl, 4-(hydroxymethyl)phenyl, 3-fluorophenyl, or 4-(fluoromethyl)phenyl.
122. The compound according to any one of claims 1-88, wherein R₆ is aralkyl_(C≤18) or substituted aralkyl_(C≤18).
123. The compound of claim 122, wherein R₆ is aralkyl_(C≤18).
124. The compound of claim 123, wherein R₆ is benzyl.
125. The compound of claim 122, wherein R₆ is substituted aralkyl_(C≤18).
126. The compound of claim 125, wherein R₆ is 2-fluorobenzyl, 4-fluorobenzyl, or 4-chlorobenzyl.

127. The compound according to any one of claims 1-88, wherein R₆ is
 –arenediyl_(C≤18)–heterocycloalkyl_(C≤12) or substituted
 –arenediyl_(C≤18)–heterocycloalkyl_(C≤12).
128. The compound of claim 127, wherein R₆ is –arenediyl_(C≤18)–heterocycloalkyl_(C≤12).
129. The compound of claim 128, wherein R₆ is 4-morpholinophenyl.
130. The compound according to any one of claims 1-88, wherein R₆ is heteroaryl_(C≤18) or
 substituted heteroaryl_(C≤18).
131. The compound of claim 130, wherein R₆ is heteroaryl_(C≤18).
132. The compound of claim 131, wherein R₆ is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl,
 2-methyl-2*H*-tetrazol-5-yl, 1-methyl-1*H*-pyrazol-4-yl, pyrimidin-4-yl, pyrimidin-5-yl,
 3-methyl-1,2,4-oxadiazol-5-yl)phenyl, pyridin-2-ylmethyl,
 3-methyl-1,2,4-oxadiazol-5-yl, or 5-methyl-1,2,4-oxadiazol-3-yl.
133. The compound according to any one of claims 1-88, wherein R₆ is heteroaralkyl_(C≤18)
 or heteroaralkyl_(C≤18).
134. The compound of claim 133, wherein R₆ is heteroaralkyl_(C≤18).
135. The compound of claim 134, wherein R₆ is 2-pyridinylmethyl or 4-pyridinylmethyl.
136. The compound according to any one of claims 1-88, wherein R₆ is
 –alkanediyl_(C≤18)–aralkoxy_(C≤18) or substituted –alkanediyl_(C≤18)–aralkoxy_(C≤18).
137. The compound of claim 136, wherein R₆ is –alkanediyl_(C≤18)–aralkoxy_(C≤18).
138. The compound of claim 137, wherein R₆ is 2-(benzyloxy)ethyl.

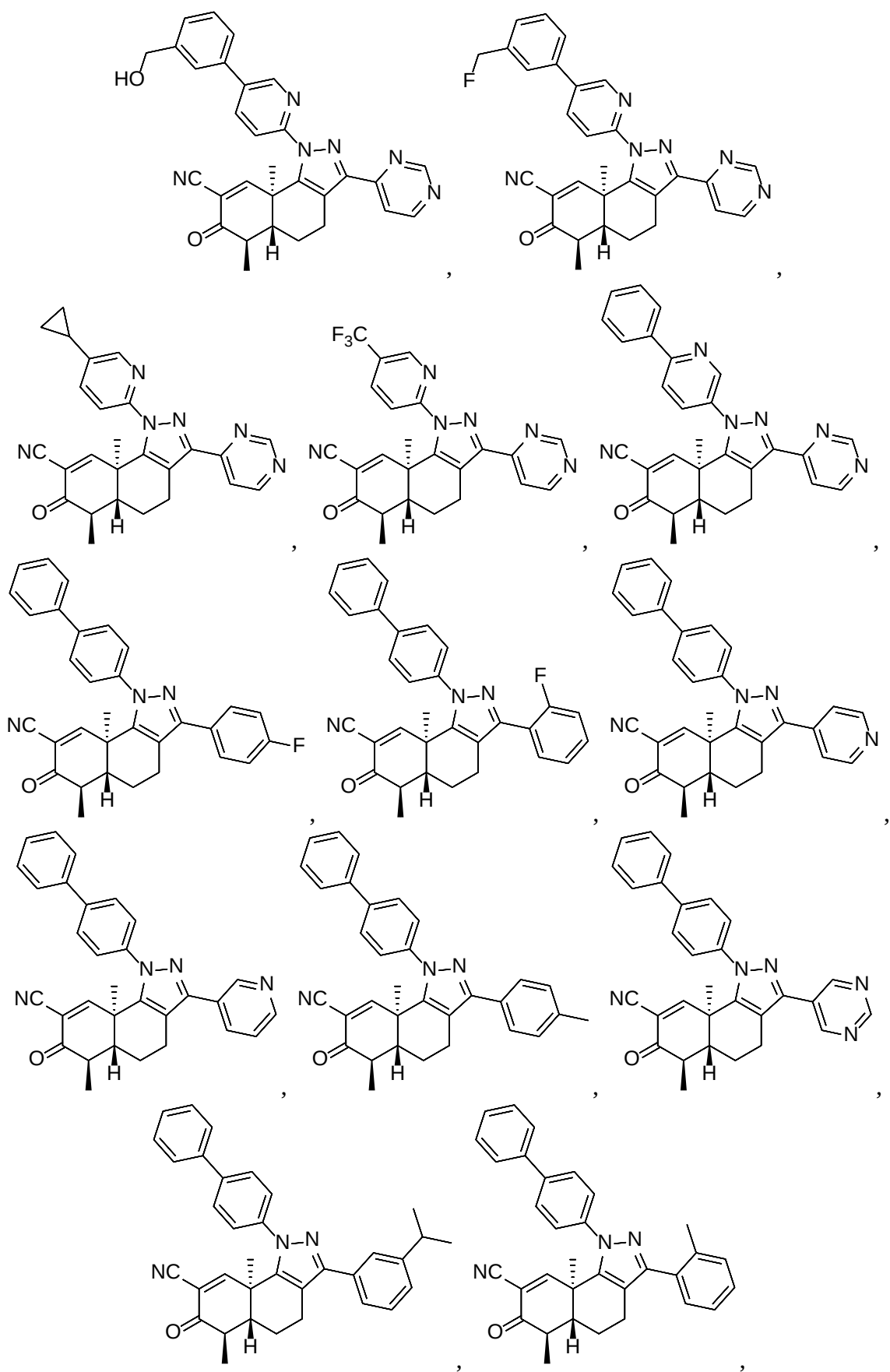
139. The compound according to any one of claims 1-138 further defined as:

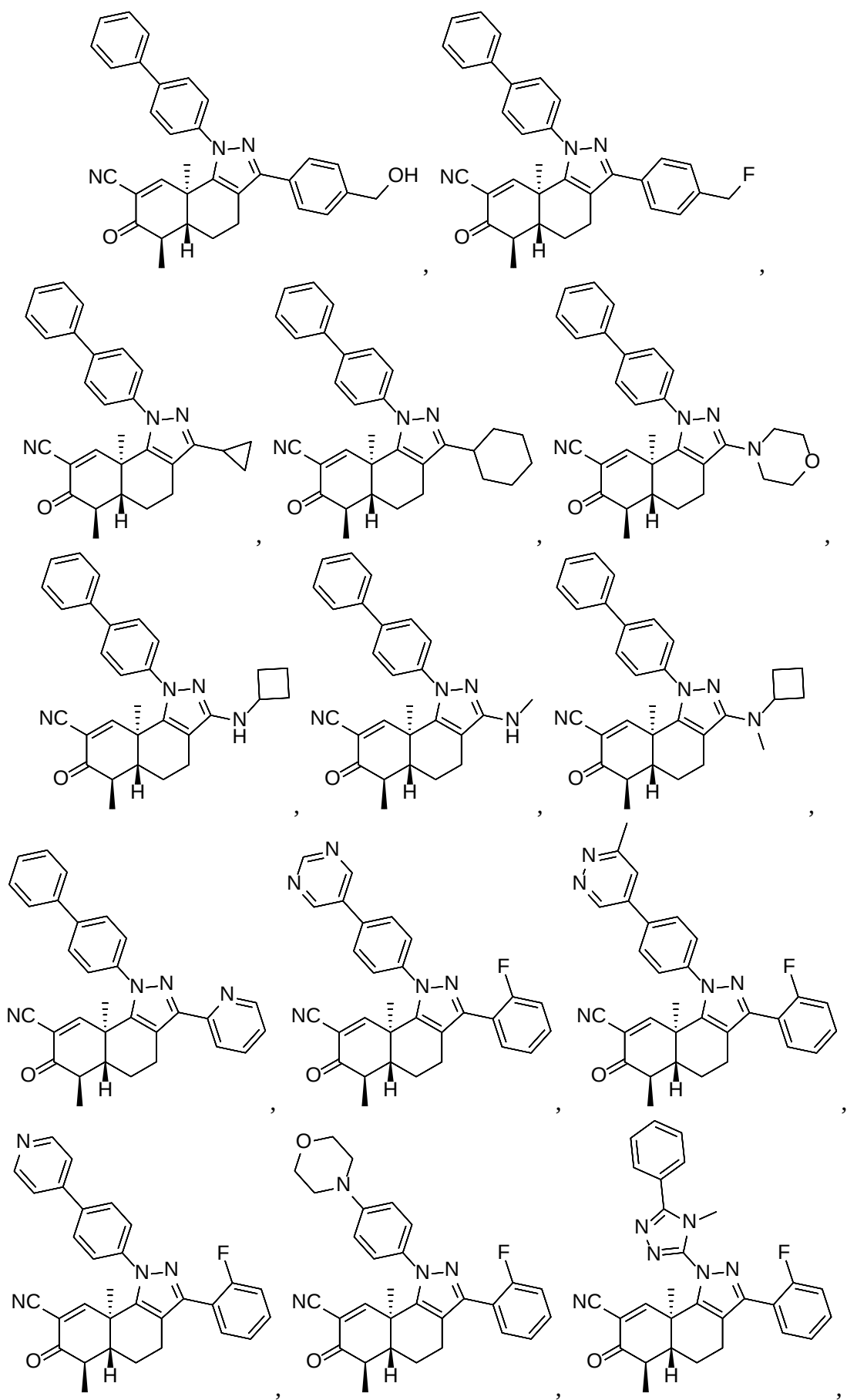


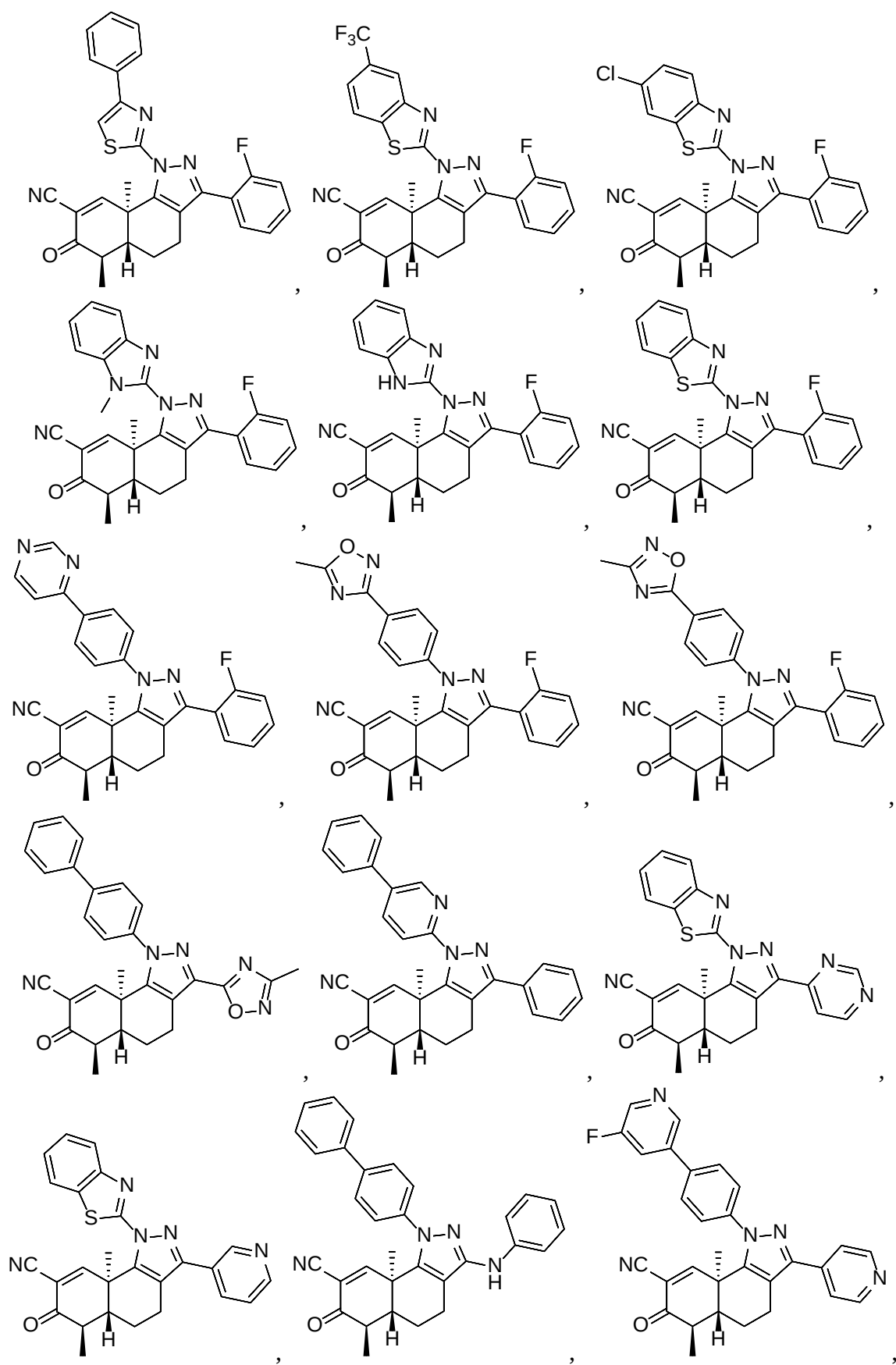


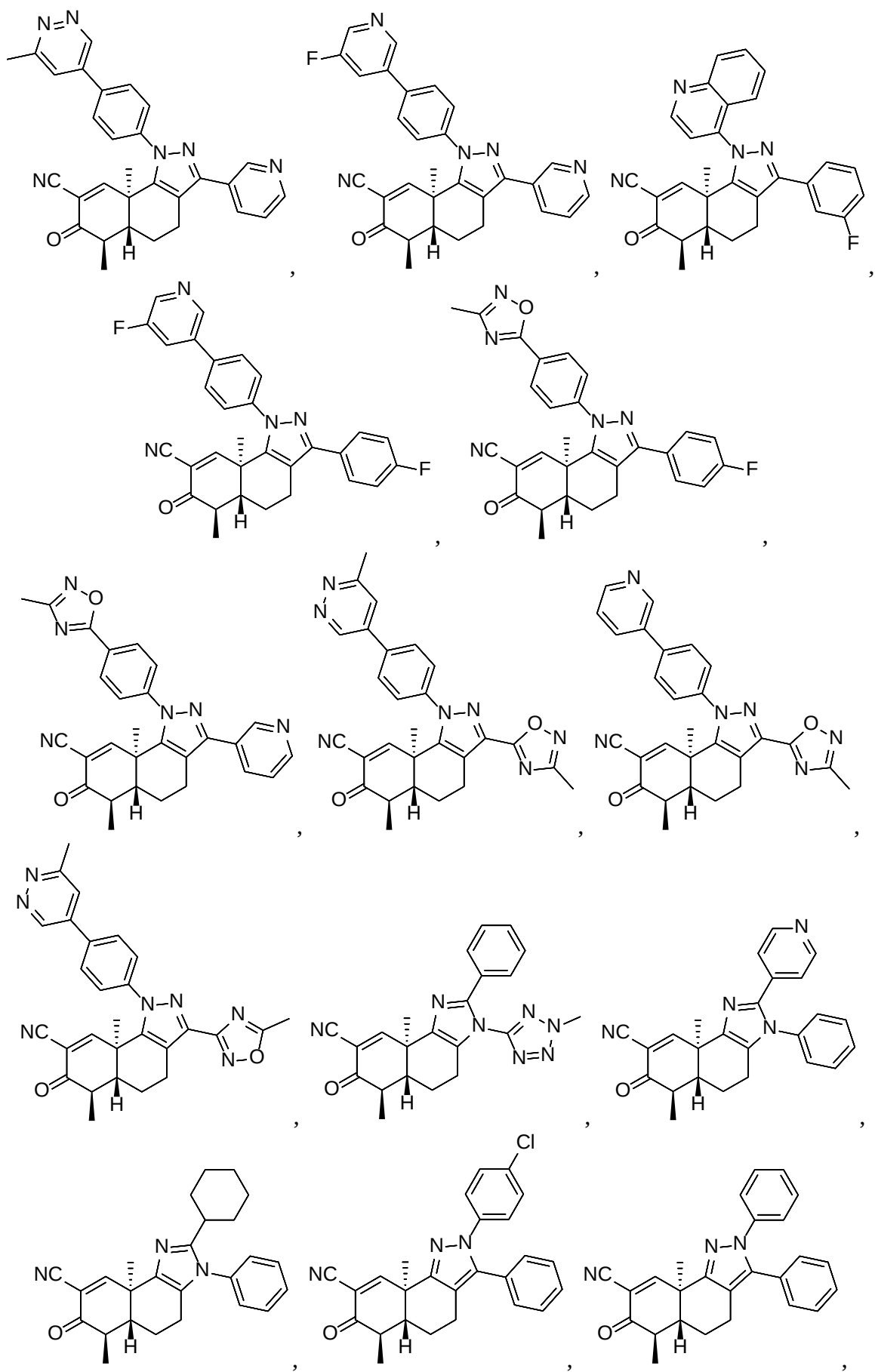


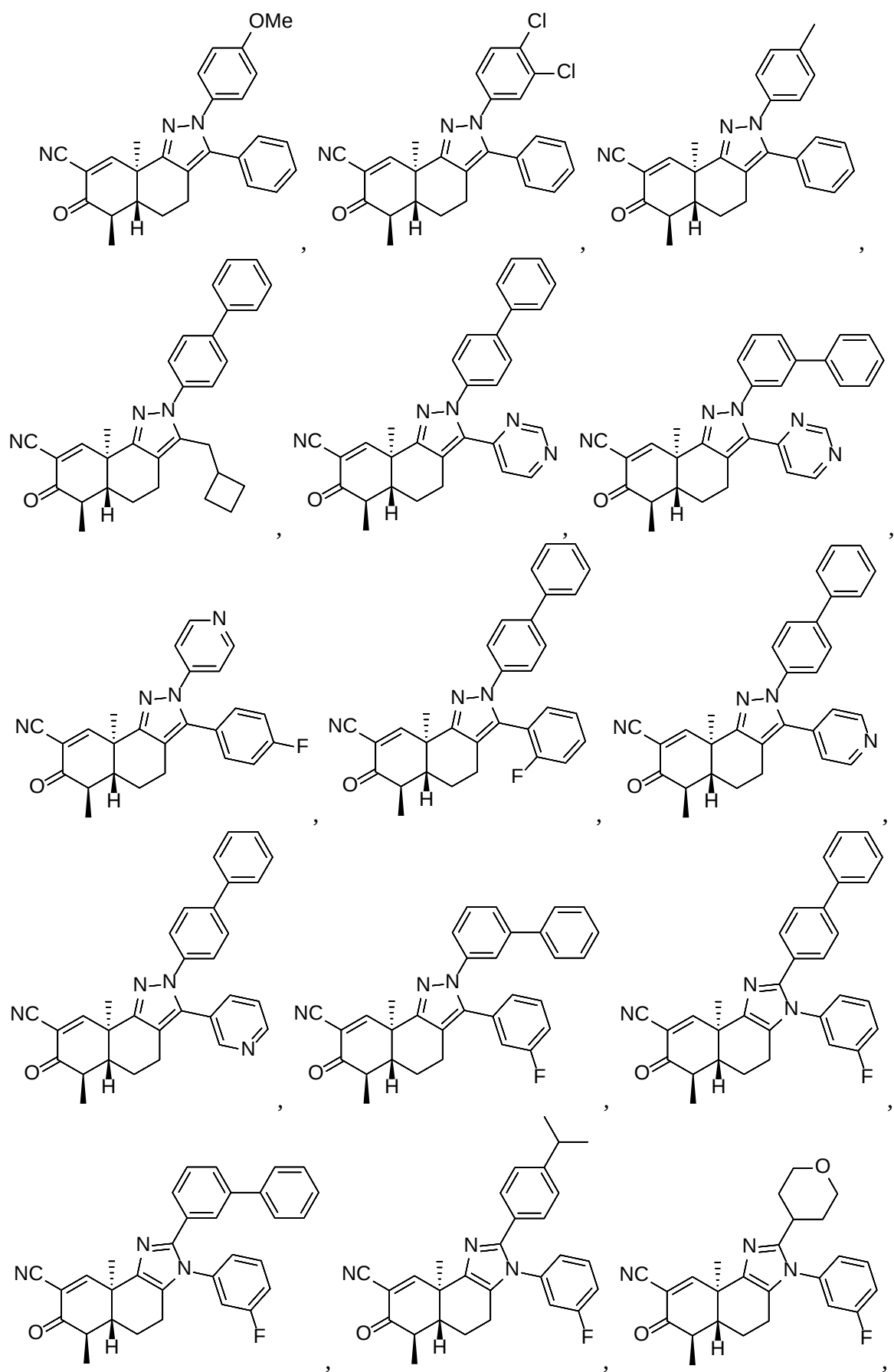


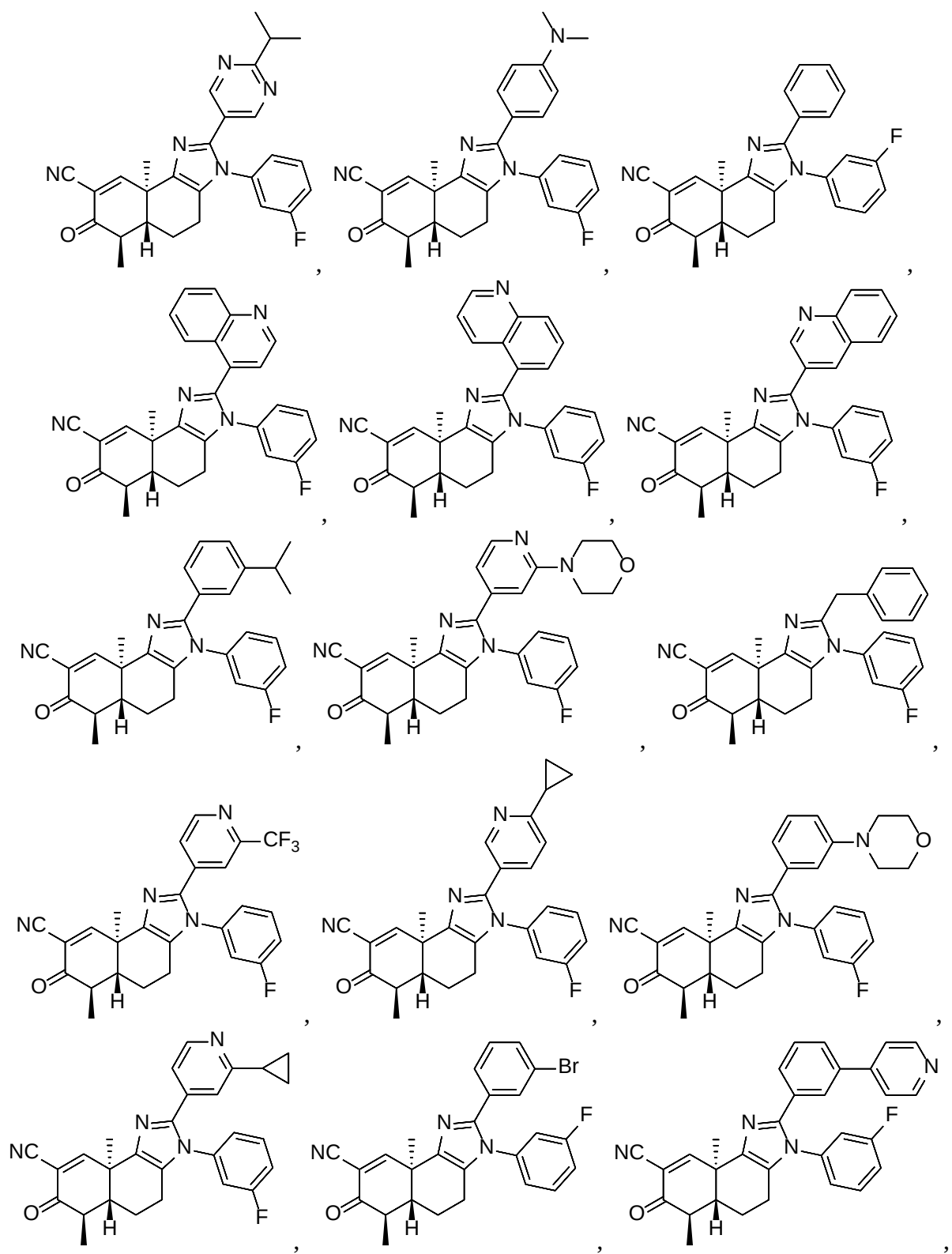


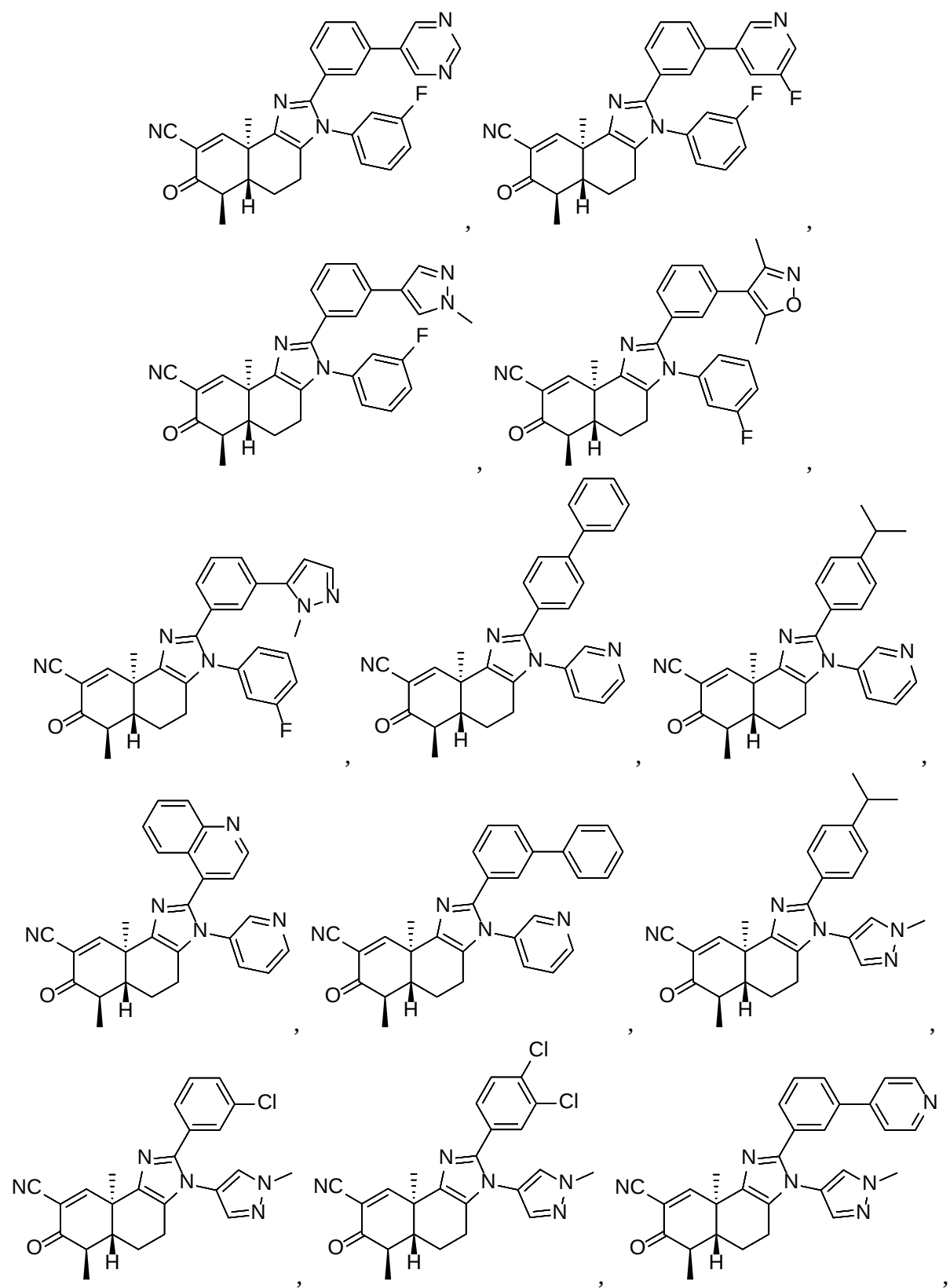


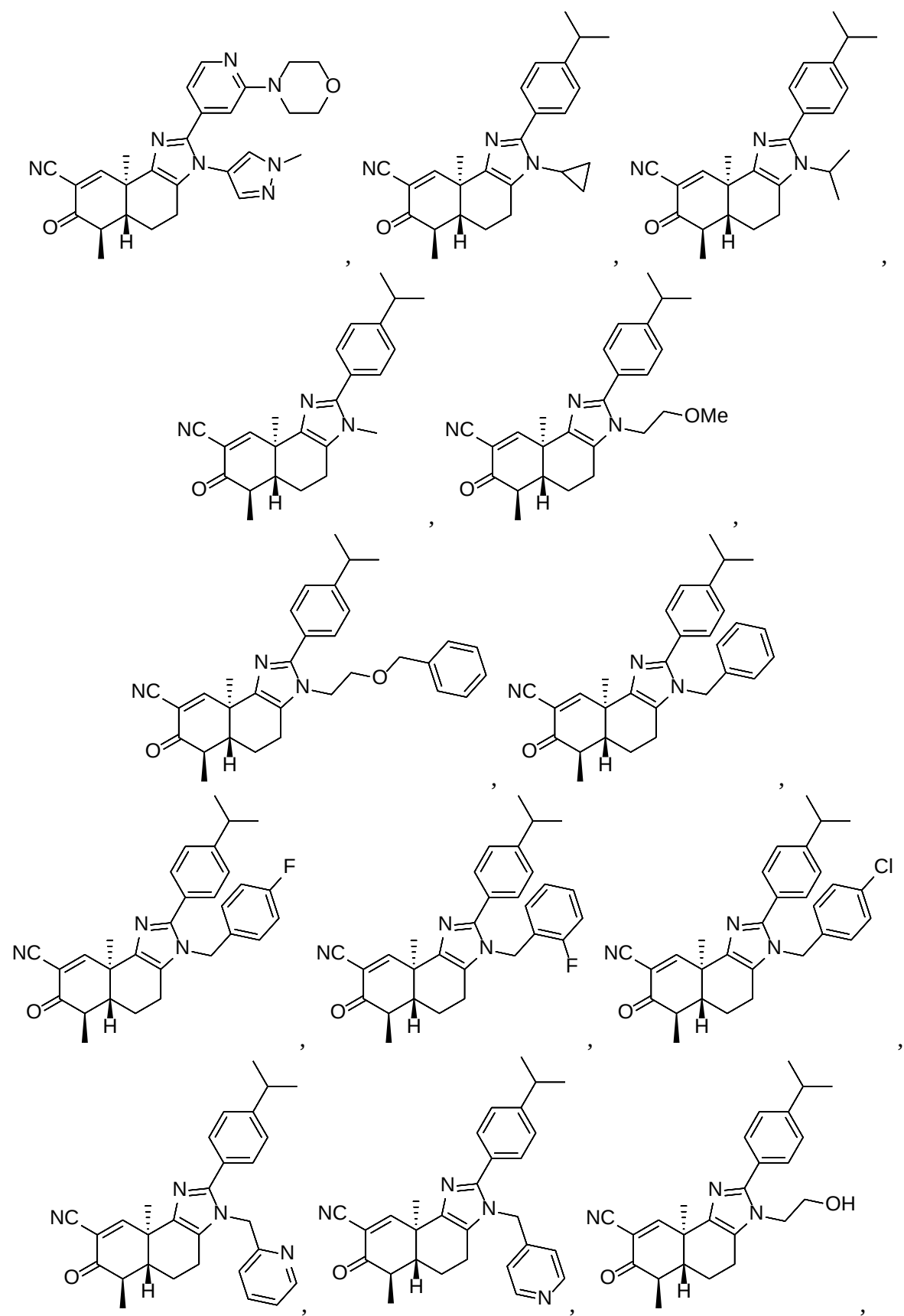


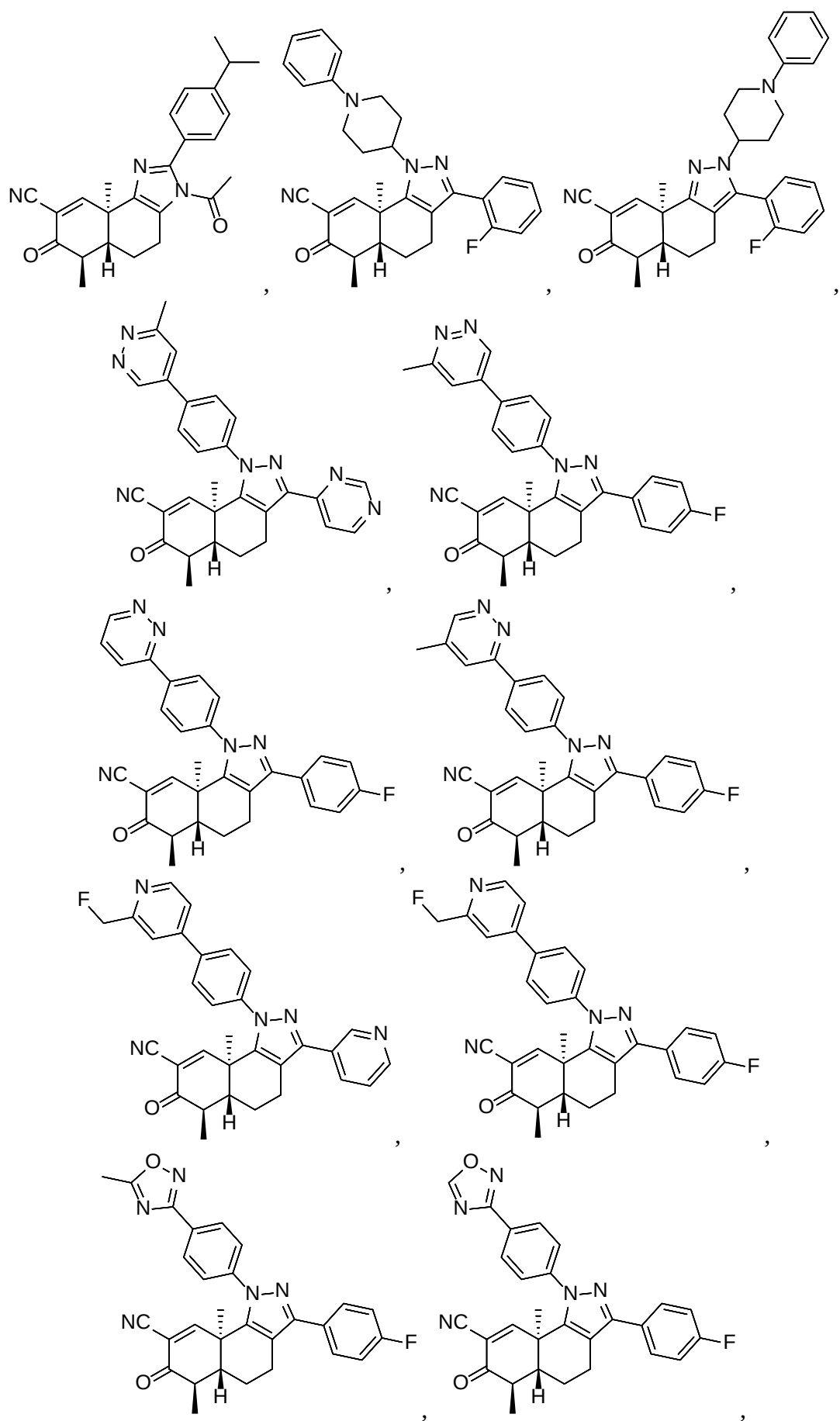


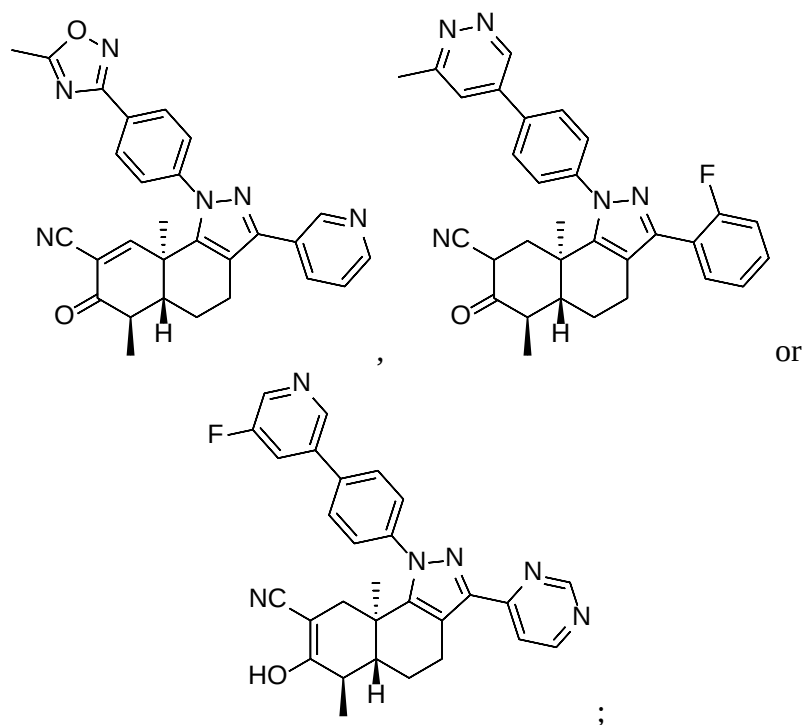






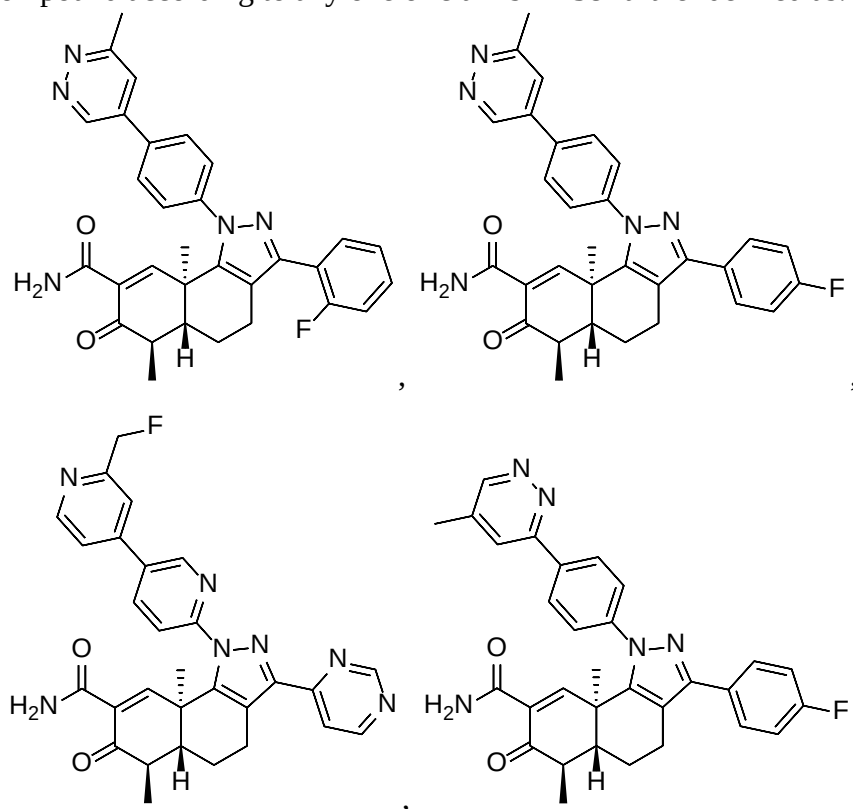


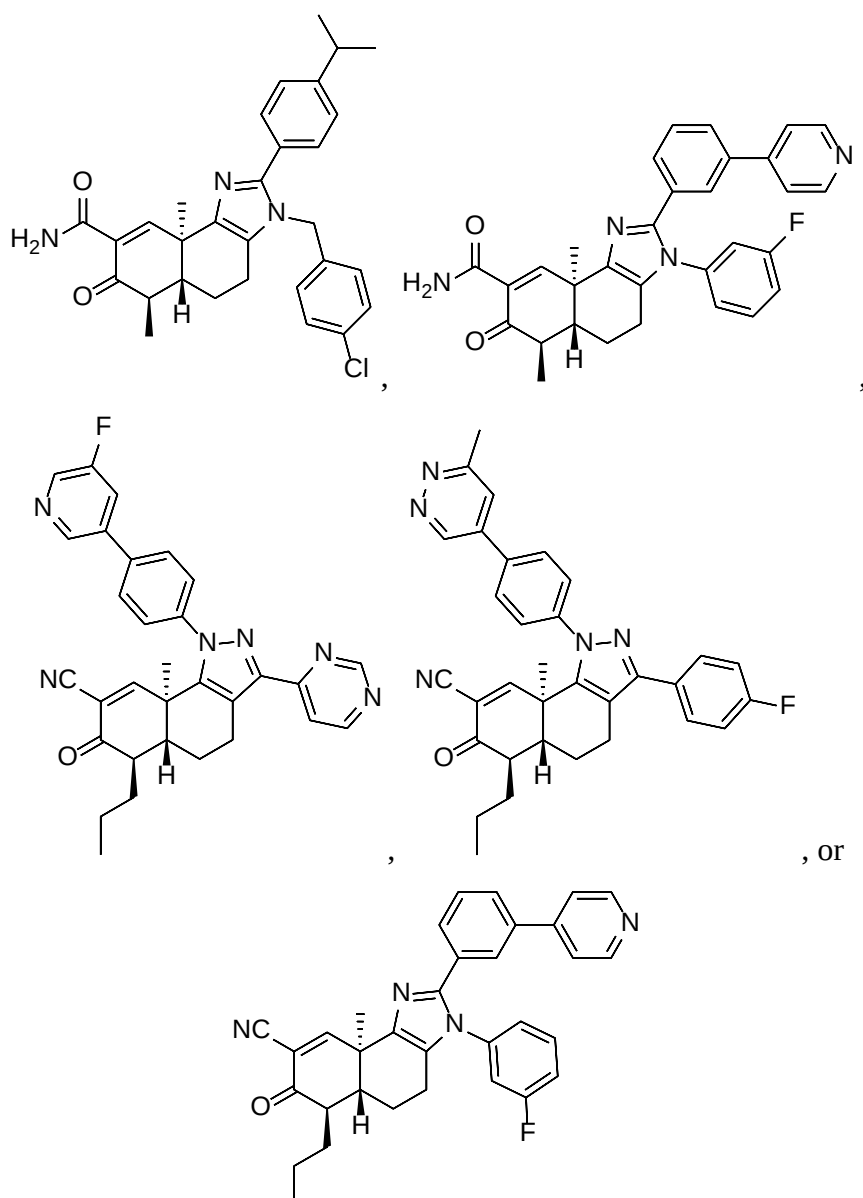




or a pharmaceutically acceptable salt of any of the above formulas.

140. The compound according to any one of claims 1-138 further defined as:





or a pharmaceutically acceptable salt of any of the above formulas.

141. A compound of the formula:

(5aR,6R,9aS)-2-cyclohexyl-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-cyclohexyl-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(2,2,2-trifluoroethyl)-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-benzyl-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-benzyl-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(4-(trifluoromethyl)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(pyridin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(quinolin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(3,4-dichlorophenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-1,3-diphenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(*p*-tolyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-chlorophenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-methoxyphenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,9aS)-1-(4-cyanophenyl)-9a-methyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,9aS)-1-(4-fluorophenyl)-9a-methyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(*o*-tolyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-2-(*o*-tolyl)-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(4-(trifluoromethoxy)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-2-(4-(trifluoromethoxy)phenyl)-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-
 4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;
 (5aR,6R,9aS)-6,9a-dimethyl-1-(naphthalen-1-yl)-7-oxo-3-phenyl-
 4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
 (5aR,6R,9aS)-6,9a-dimethyl-2-(naphthalen-1-yl)-7-oxo-3-phenyl-
 4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;
 (5aR,6R,9aS)-1-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-3-phenyl-
 4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
 (5aR,6R,9aS)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-3-phenyl-
 4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;
 (5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(tetrahydro-2*H*-pyran-4-yl)-
 4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
 (5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-2-(tetrahydro-2*H*-pyran-4-yl)-
 4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;
 (5aR,6R,9aS)-1-(1,1-dioxidotetrahydrothiophen-3-yl)-6,9a-dimethyl-7-oxo-3-
 phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
 (5aR,6R,9aS)-2-(1,1-dioxidotetrahydrothiophen-3-yl)-6,9a-dimethyl-7-oxo-3-
 phenyl-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;
 (5aR,6R,9aS)-6,9a-dimethyl-1-(5-methylpyridin-2-yl)-7-oxo-3-phenyl-
 4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
 (5aR,6R,9aS)-6,9a-dimethyl-1-(6-methylpyridin-3-yl)-7-oxo-3-phenyl-
 4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
 (5aR,6R,9aS)-1-(3-bromophenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-
 hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
 (5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(3-(pyridin-3-yl)phenyl)-
 4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
 (5aR,6R,9aS)-1-([1,1'-biphenyl]-3-yl)-6,9a-dimethyl-7-oxo-3-phenyl-
 4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
 (5aR,6R,9aS)-1-(2'-fluoro-[1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-
 4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
 (5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(4-(pyridin-3-yl)phenyl)-
 4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;
 (5aR,6R,9aS)-1-(4-(3,5-dimethylisoxazol-4-yl)phenyl)-6,9a-dimethyl-7-oxo-3-
 phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(4-(pyridin-4-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(3'-fluoro-[1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-1-(4'-methyl-[1,1'-biphenyl]-4-yl)-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(2'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-1-(2'-methyl-[1,1'-biphenyl]-4-yl)-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(3'-(hydroxymethyl)-[1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4'-methoxy-[1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4'-(dimethylamino)-[1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(5-fluoropyridin-3-yl)phenyl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-1-(4-(pyrimidin-5-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-1-(4-(pyridin-3-yl)phenyl)-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

4-((5aR,6R,9aS)-8-cyano-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazol-1-yl)benzoic acid;

(5aR,6R,9aS)-1-(2-fluoro-4-(pyridin-3-yl)phenyl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(2-(fluoromethyl)pyridin-4-yl)phenyl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(2-(hydroxymethyl)pyridin-4-yl)phenyl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(5-(4-fluorophenyl)pyridin-2-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([3,3'-bipyridin]-6-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(5-(3-fluorophenyl)pyridin-2-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-1-(5-phenylpyridin-2-yl)-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(5-(3-(hydroxymethyl)phenyl)pyridin-2-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(5-(3-(fluoromethyl)phenyl)pyridin-2-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(5-(cyclopropyl)pyridin-2-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-1-(5-(trifluoromethyl)pyridin-2-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-1-(6-phenylpyridin-3-yl)-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-(4-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyridin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(*p*-tolyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-5-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-(3-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(*o*-tolyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-(4-(hydroxymethyl)phenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-(4-(fluoromethyl)phenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-cyclopropyl-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-cyclohexyl-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-3-morpholino-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-(cyclobutylamino)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-3-(methylamino)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-3-(cyclobutyl(methyl)amino)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyridin-2-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-1-(4-(pyrimidin-5-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-1-(4-(6-methylpyridazin-4-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-1-(4-(pyridin-4-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-1-(4-morpholinophenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-1-(4-methyl-5-phenyl-4*H*-1,2,4-triazol-3-yl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-1-(4-phenylthiazol-2-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-1-(5-(trifluoromethyl)benzo[*d*]thiazol-2-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(6-chlorobenzo[*d*]thiazol-2-yl)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-1-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(1*H*-benzo[*d*]imidazol-2-yl)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(benzo[d]thiazol-2-yl)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-1-(4-(pyrimidin-4-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-1-(4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-1-(4-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-3-(3-methyl-1,2,4-oxadiazol-5-yl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-1-(5-phenylpyridin-2-yl)-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(benzo[d]thiazol-2-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(benzo[d]thiazol-2-yl)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(phenylamino)-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(5-fluoropyridin-3-yl)phenyl)-6,9a-dimethyl-7-oxo-3-(pyridin-4-yl)-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-1-(4-(6-methylpyridazin-4-yl)phenyl)-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(5-fluoropyridin-3-yl)phenyl)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-1-(quinolin-4-yl)-4,5,5a,6,7,9a-hexahydro-1H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-fluorophenyl)-1-(4-(5-fluoropyridin-3-yl)phenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-fluorophenyl)-6,9a-dimethyl-1-(4-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-1-(4-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl)-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-3-(3-methyl-1,2,4-oxadiazol-5-yl)-1-(4-(6-methylpyridazin-4-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-3-(3-methyl-1,2,4-oxadiazol-5-yl)-7-oxo-1-(4-(pyridin-3-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-3-(5-methyl-1,2,4-oxadiazol-3-yl)-1-(4-(6-methylpyridazin-4-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-3-(2-methyl-2*H*-tetrazol-5-yl)-7-oxo-2-phenyl-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-2-(pyridin-4-yl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-cyclohexyl-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-chlorophenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-2,3-diphenyl-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-methoxyphenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-(3,4-dichlorophenyl)-6,9a-dimethyl-7-oxo-3-phenyl-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-phenyl-2-(*p*-tolyl)-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-4-yl)-3-(cyclobutylmethyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-3-yl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(pyridin-4-yl)-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-4-yl)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyridin-4-yl)-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-3-yl)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-2H-benzo[g]indazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-4-yl)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-3-yl)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(tetrahydro-2H-pyran-4-yl)-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-2-(2-isopropylpyrimidin-5-yl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-(dimethylamino)phenyl)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-2,6,9a-trimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-2-phenyl-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(quinolin-4-yl)-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(quinolin-5-yl)-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(quinolin-3-yl)-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-2-(3-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-2-(2-morpholinopyridin-4-yl)-7-oxo-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-benzyl-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(2-(trifluoromethyl)pyridin-4-yl)-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(6-cyclopropylpyridin-3-yl)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-2-(3-morpholinophenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(2-cyclopropylpyridin-4-yl)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(3-bromophenyl)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(3-(pyridin-4-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-3H-naphtho[1,2-d]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(3-(pyrimidin-5-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-2-(3-(5-fluoropyridin-3-yl)phenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-2-(3-(1-methyl-1*H*-pyrazol-4-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(3-(3,5-dimethylisoxazol-4-yl)phenyl)-3-(3-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(3-fluorophenyl)-6,9a-dimethyl-2-(3-(1-methyl-1*H*-pyrazol-5-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-4-yl)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-2-(quinolin-4-yl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-([1,1'-biphenyl]-3-yl)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-isopropylphenyl)-6,9a-dimethyl-3-(1-methyl-1*H*-pyrazol-4-yl)-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(3-chlorophenyl)-6,9a-dimethyl-3-(1-methyl-1*H*-pyrazol-4-yl)-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(3,4-dichlorophenyl)-6,9a-dimethyl-3-(1-methyl-1*H*-pyrazol-4-yl)-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-3-(1-methyl-1*H*-pyrazol-4-yl)-7-oxo-2-(3-(pyridin-4-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-3-(1-methyl-1*H*-pyrazol-4-yl)-2-(2-morpholinopyridin-4-yl)-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-cyclopropyl-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-isopropyl-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-isopropylphenyl)-3,6,9a-trimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-isopropylphenyl)-3-(2-methoxyethyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-(benzyloxy)ethyl)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-benzyl-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-fluorobenzyl)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorobenzyl)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-chlorobenzyl)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-3-(pyridin-2-ylmethyl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-3-(pyridin-4-ylmethyl)-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-hydroxyethyl)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-acetyl-2-(4-isopropylphenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-3*H*-naphtho[1,2-*d*]imidazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-1-(1-phenylpiperidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(2-fluorophenyl)-6,9a-dimethyl-7-oxo-2-(1-phenylpiperidin-4-yl)-4,5,5a,6,7,9a-hexahydro-2*H*-benzo[*g*]indazole-8-carbonitrile

(5aR,6R,9aS)-6,9a-dimethyl-1-(4-(6-methylpyridazin-4-yl)phenyl)-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-fluorophenyl)-6,9a-dimethyl-1-(4-(6-methylpyridazin-4-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-fluorophenyl)-6,9a-dimethyl-7-oxo-1-(4-(pyridazin-3-yl)phenyl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-fluorophenyl)-6,9a-dimethyl-1-(4-(5-methylpyridazin-3-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(2-(fluoromethyl)pyridin-4-yl)phenyl)-6,9a-dimethyl-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(2-(fluoromethyl)pyridin-4-yl)phenyl)-3-(4-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-3-(4-fluorophenyl)-6,9a-dimethyl-1-(4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(1,2,4-oxadiazol-3-yl)phenyl)-3-(4-fluorophenyl)-6,9a-dimethyl-7-oxo-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-6,9a-dimethyl-1-(4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)-7-oxo-3-(pyridin-3-yl)-4,5,5a,6,7,9a-hexahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

(5aR,6R,9aS)-1-(4-(5-fluoropyridin-3-yl)phenyl)-6,9a-dimethyl-7-oxo-3-(pyrimidin-4-yl)-4,5,5a,6,7,8,9,9a-octahydro-1*H*-benzo[*g*]indazole-8-carbonitrile; or

(5aR,6R,9aR)-3-(2-fluorophenyl)-6,9a-dimethyl-1-(4-(6-methylpyridazin-4-yl)phenyl)-7-oxo-4,5,5a,6,7,8,9,9a-octahydro-1*H*-benzo[*g*]indazole-8-carbonitrile;

or a pharmaceutically acceptable salt thereof.

142. A pharmaceutical composition comprising:
- (a) a compound according to any one of claims 1-141; and
 - (b) an excipient.
143. The pharmaceutical composition of claim 142, wherein the pharmaceutical composition is formulated for administration: orally, intraadiposally, intraarterially, intraarticularly, intracranially, intradermally, intralesionally, intramuscularly, intranasally, intraocularly, intrapericardially, intraperitoneally, intrapleurally, intraprostatically, intrarectally, intrathecally, intratracheally, intratumorally, intraumbilically, intravaginally, intravenously, intravesicularly, intravitreally, liposomally, locally, mucosally, parenterally, rectally, subconjunctival, subcutaneously, sublingually, topically, transbuccally, transdermally, vaginally, in crèmes, in lipid compositions, via a catheter, via a lavage, via continuous infusion, via infusion, via inhalation, via injection, via local delivery, or via localized perfusion.
144. The pharmaceutical composition of claim 143, wherein the pharmaceutical composition is formulated for oral administration.
145. The pharmaceutical composition of claim 143, wherein the pharmaceutical composition is formulated for administration via injection.
146. The pharmaceutical composition of claim 145, wherein the pharmaceutical composition is formulated for intraarterial administration, intramuscular administration, intraperitoneal administration, or intravenous administration.
147. The pharmaceutical composition of claim 143, wherein the pharmaceutical composition is formulated for administration topically.

148. The pharmaceutical composition of claim 147, wherein the pharmaceutical composition is formulated for topical administration to the skin or to the eye.
149. The pharmaceutical composition according to any one of claims 142-148, wherein the pharmaceutical composition is formulated as a unit dose.
150. A method of treating or preventing a disease or disorder in a patient in need thereof comprising administering to the patient a pharmaceutically effective amount of a compound or composition according to any one of claims 1-149.
151. The method of claim 150, wherein the patient is a mammal.
152. The method of claim 151, wherein the patient is a human.
153. The method according to any one of claims 150-152, wherein the disease or disorder is associated with increased production of cytokine IL-17.
154. The method according to any one of claims 150-153, wherein the disease or disorder is associated with dysregulated angiogenesis.
155. The method according to any one of claims 150-154, wherein the disease or disorder is an autoimmune disease, organ rejection, asthma, cancer, a neurological disorder, a psychiatric disorder, a neuropsychiatric disorder, chronic pain syndrome, an inflammatory condition, a retinal disorder, or a cardiovascular disease.
156. The method of claim 155, wherein the disease or disorder is cancer.
157. The method of claim 155, wherein the autoimmune disease is psoriasis, multiple sclerosis, scleroderma, rheumatoid arthritis, lupus, psoriatic arthritis, ankylosing spondylitis, Sjögren syndrome, vitiligo, uveitis, dry eye syndrome, systemic sclerosis, type 1 diabetes, myasthenia gravis, and inflammatory bowel disease.
158. The method of claim 155, wherein the cardiovascular disease is vasculitis, atherosclerosis, myocardial infarction, myocarditis, heart failure, pulmonary hypertension, or stroke.
159. The method of claim 155, wherein the neurological disorder is epilepsy, multiple sclerosis, spinal cord injury, Guillain-Barre syndrome, or another neurological disorder involving dysregulated inflammatory signaling or oxidative stress.
160. The method of claim 159, wherein the neurodegenerative disorder is Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, or Huntington's disease.

161. The method of claim 155, wherein the inflammatory condition is pancreatitis, hepatitis, pulmonary fibrosis, cystic fibrosis, chronic obstructive pulmonary disease, asthma, dermatitis, gastritis, esophagitis, irritable bowel syndrome, inflammatory bowel disease, nephritis, muscle wasting, or osteoarthritis.
162. The method of claim 155, wherein the chronic pain syndrome is fibromyalgia or neuropathic pain.
163. The method of claim 155, wherein the disease or disorder is a severe inflammatory response to a pathogen.
164. The method of claim 163, wherein the severe inflammatory response to a pathogen is from encephalitis, meningitis, *H. pylori*, *Toxoplasma gondii*, or *Leishmania spp.*
165. The method of claim 155, wherein the disease or disorder is obesity, or a condition associated with obesity.
166. The method of claim 165, wherein the condition associated with obesity is insulin resistance or fatty liver disease.
167. The method of claim 155, wherein the retinal disorder is macular degeneration or another disorder of the retina.
168. The method of claim 150, wherein the disease or disorder is associated with inflammation.
169. The method of claim 168, wherein the disease or disorder associated with inflammation is obesity, Type 2 diabetes, or a complication of Type 1 or Type 2 diabetes.
170. The method of claim 169, wherein the complication of Type 1 or Type 2 diabetes is neuropathy, reduced kidney function or chronic kidney disease, retinopathy, diabetic ulcers, or cardiovascular disease.
171. The method of claim 168, wherein the disease or disorder associated with inflammation is chronic kidney disease.
172. The method of claim 171, wherein the chronic kidney disease is hereditary.
173. The method of claim 171, wherein the chronic kidney disease is due to a non-hereditary cause.
174. The method according to any one of claims 150-164, wherein the method comprises administering the compound once.

175. The method according to any one of claims 150-164, wherein the method comprises administering the compound two or more times.



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Application No. **US2019037543**

Procedure: PCT

Applicant name: Reata Pharmaceuticals, Inc.

Your reference: REAT.P0103WO

Selected group: PCT (EPO as Int. Preliminary Examining Authority)

021 - Fee for preliminary examination of int. application € 1.830,00

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