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Los abajo firmados,
QPEX Biopharma, Inc.

con domicilio en
**3013 Science Park Road, 1st Floor,
San Diego, California 92121, US**

nombramos por el presente a ALICIA LLOREDA y/o ANA MARIA CASTRO y/o TATIANA CARRILLO, domiciliadas en Bogotá, Colombia, con oficinas en dicha ciudad, Calle 72 No. 5-83, piso 6o., nuestras representantes legales y verdaderas en Bogotá, con facultades para recibir notificaciones y nombrar apoderados judiciales o extrajudiciales, con el fin de dar cumplimiento al parágrafo 1o. del artículo 543 del decreto 410 de 1971.

Las doctoras ALICIA LLOREDA y/o ANA MARIA CASTRO y/o TATIANA CARRILLO, o los apoderados que cualquiera de ellas designe, quedan especialmente facultados para representarnos ante las autoridades colombianas, administrativas, judiciales o de policía, en todos los trámites relativos a la propiedad industrial, a cuyo efecto les facultamos para dar ante dichas autoridades todos los pasos necesarios al objeto indicado; elevar solicitudes, declaraciones, reclamos, recursos y presentar desistimientos; formular descripciones, enmiendas, limitar el alcance de las solicitudes, presentar oposiciones y apelaciones; instaurar cancelaciones, renunciar total o parcialmente a los registros, abonar todos los impuestos y cuotas y efectuar todo otro pago determinado por la ley; recibir todos los documentos y valores, dando el descargo respectivo; llenar cualesquiera otros requisitos y tomar, en fin, todas las medidas que creyeran conducentes al resguardo de nuestros intereses; y en caso de producirse oposición, pasando los antecedentes a los tribunales, quedan facultados para tomar intervención como demandantes o demandados ante los jueces que sean competentes, pudiendo transar, someter a árbitros, desistir, percibir y apelar, con todas las demás facultades que resulten necesarias, y por el presente declaramos desde ahora válido y bueno cuanto dichos representantes y/o los apoderados que cualquiera de ellas nombre hicieren en nuestro beneficio.

Asimismo, facultamos a las doctoras ALICIA LLOREDA y/o ANA MARIA CASTRO y/o TATIANA CARRILLO, para solicitar en la Oficina de Propiedad Industrial la protocolización de este documento y de cualquier poder que cualquiera de ellos otorgue a nombre nuestro.

Dado y firmado,

The undersigned,
QPEX Biopharma, Inc.

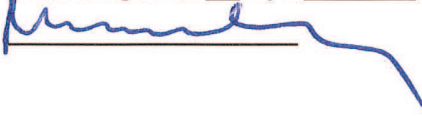
domiciled at
**3013 Science Park Road, 1st Floor,
San Diego, California 92121, US**

hereby appoint, ALICIA LLOREDA y/o ANA MARIA CASTRO y/o TATIANA CARRILLO, of Bogota, Colombia, with offices in said town, Calle 72 No. 5-83, Sixth Floor, our true and legal representatives in Bogotá, with power to receive notifications and to appoint judicial or extrajudicial agents, so as to comply with paragraph 1o. of article 543 of decree 410 of 1971.

ALICIA LLOREDA y/o ANA MARIA CASTRO y/o TATIANA CARRILLO, or the agents by any one of them appointed, are especially empowered to represent us before the administrative, judicial or police authorities of Colombia, in all proceedings pertaining to industrial property, for which purpose we authorize them to take before the said authorities all the necessary steps for the said end; to file petitions, declarations, claims, recourses and withdrawals, to draw up specifications; to file amendments, to limit the scope of applications, file oppositions; file cancellations total or partially waive registrations, to pay all installments and effect all other payments prescribed by law; to receive proper receipts, to comply with all other requirements and, in short, to take all those measures which they may deem fit for the protection of our interests; and in case of opposition, where the proceedings be passed over to the courts, we authorize said agents to act on our behalf, as complainants as well as defendants, before the competent judges, with full powers to make arrangements, to submit to arbitrators, to desist, to collect, to appeal and, in short, with all such further powers as may be required, and we hereby declare from now on as valid and good all that said representatives and/or the agents by any one of them appointed may do for our benefit.

We also authorize doctors ALICIA LLOREDA y/o ANA MARIA CASTRO y/o TATIANA CARRILLO, to apply for protocolization of this document and of any power of attorney by any one of them conferred in our name, before the Office of Industrial Property.

Given and signed this 17th day of DECEMBER, 2018



PATENT COOPERATION TREATY
PCT
INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference MDCO.127WO	FOR FURTHER ACTION See Form PCT/IPEA/416																	
International application No. PCT/US2017/039787	International filing date (<i>day/month/year</i>) 28 June 2017	Priority date (<i>day/month/year</i>) 30 June 2016																
International Patent Classification (IPC) or national classification and IPC See Supplemental Box																		
Applicant REMPEX PHARMACEUTICALS, INC.																		
1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of 7 sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: a. ☒ (<i>sent to the applicant and to the International Bureau</i>) a total of 64 sheets, as follows: ☒ sheets of the description, claims and/or drawings which have been amended and/or sheets containing rectifications authorized by this Authority, unless those sheets were superseded or cancelled, and any accompanying letters (see Rules 46.5, 66.8, 70.16, 91.2, and Section 607 of the Administrative Instructions). ☐ sheets containing rectifications not taken into account by this Authority because they were not available at the time when this Authority began to draw up this report, and any accompanying letters (Rules 66.4<i>bis</i>, 70.2(e), 70.16 and 91.2). ☐ Superseded sheets and any accompanying letters, where this Authority either considers that the superseding sheets contain an amendment that goes beyond the disclosure in the international application as filed, or the superseding sheets were not accompanied by a letter indicating the basis for the amendments in the application filed, as indicated in item 4 of Box No. I and the Supplemental Box (see Rule 70.16(b)). b. ☐ (<i>sent to the International Bureau only</i>) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see paragraph 3<i>bis</i> of Annex C of the Administrative Instructions). 4. This report contains indications relating to the following items: <table style="width: 100%; border: none;"> <tr><td>☒ Box No. I</td><td>Basis of the report</td></tr> <tr><td>☐ Box No. II</td><td>Priority</td></tr> <tr><td>☐ Box No. III</td><td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td></tr> <tr><td>☒ Box No. IV</td><td>Lack of unity of invention</td></tr> <tr><td>☒ Box No. V</td><td>Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement</td></tr> <tr><td>☐ Box No. VI</td><td>Certain documents cited</td></tr> <tr><td>☐ Box No. VII</td><td>Certain defects in the international application</td></tr> <tr><td>☒ Box No. VIII</td><td>Certain observations on the international application</td></tr> </table>			☒ Box No. I	Basis of the report	☐ Box No. II	Priority	☐ Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	☒ Box No. IV	Lack of unity of invention	☒ Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement	☐ Box No. VI	Certain documents cited	☐ Box No. VII	Certain defects in the international application	☒ Box No. VIII	Certain observations on the international application
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Date of submission of the demand 26 April 2018	Date of completion of this report 23 May 2018																	
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA Email address: pct@ipaaustralia.gov.au	Authorised officer Ross Heisey AUSTRALIAN PATENT OFFICE (ISO 9001 Quality Certified Service) Telephone No. +61262833185																	

Box No. I

Basis of the report

1. With regard to the **language**, this report has been established on the basis of:
- ☒ The international application in the language in which it was filed:
- ☐ A translation of the international application into , which is the language of a translation furnished for the purposes of :
- ☐ international search (under Rules 12.3(a) and 23.1 (b)).
- ☐ publication of the international application (under Rule 12.4(a)).
- ☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a) and (b)).
2. With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):
- ☐ the international application as originally filed/furnished, or
- ☒ the description: pages **1-135** , as originally filed/furnished
pages , received by this Authority on with the letter of
- ☒ the claims: pages , as originally filed/furnished
pages , as amended (together with any statement) under Article 19,
pages **136-165** , received by this Authority on **26 April 2018** with the letter of **24 April 2018**
- ☐ the drawings: pages , as originally filed/furnished
pages , received by this Authority on with the letter of
- ☐ a sequence listing - see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (specify):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since either they are considered to go beyond the disclosure as filed, or they were not accompanied by a letter indicating the basis for the amendments in the application as filed, as indicated in the Supplemental Box (Rules 70.2(c) and (c-bis)):
- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (specify):
5. ☐ This report has been established:
- ☐ taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rules 66.1(d-bis) and 70.2(e)).
- ☐ without taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rules 66.4bis and 70.2(e)).
6. With regard to top-up searches (Rules 66.1ter and 70.2(f)):
- ☒ A top-up search was carried out by this Authority on 22 May 2018.
- ☐ Additional relevant documents have been discovered during the top-up search.
- ☐ No top-up search was carried out by this Authority because it would serve no useful purpose.
7. ☐ Supplementary international search report(s) from Authority(ies)
has/have been received and taken into account in establishing this report (Rule 45bis.8(b) and (c)).

* If item 4 applies, some or all of those sheets may be marked "superseded."

Box No. IV

Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees the applicant has, within the applicable time limit:
- ☐ restricted the claims
 - ☐ paid additional fees
 - ☐ paid additional fees under protest and, where applicable, the protest fee
 - ☐ paid additional fees under protest but the applicable protest fee was not paid
 - ☒ neither restricted the claims nor paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:
- ☐ complied with.
 - ☒ not complied with for the following reasons:

See Supplemental Box

4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. **1-36 and 75 (in full) and 76-95 (in part).**

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 1-36, 75-95	YES
	Claims NONE	NO
Inventive step (IS)	Claims 1-36, 75-95	YES
	Claims NONE	NO
Industrial applicability (IA)	Claims 1-36, 75-95	YES
	Claims NONE	NO

The invention relates to boronic acid compounds of Formulae (I) and (II), and their use as antimicrobial agents.

2. CITATIONS AND EXPLANATIONS:**CITATIONS**

D1: CAS Registry Number 831209-98-4; Entered STN: 15 Feb 2005; 6H-Dibenz[c,e][1,2]oxaborin, 6a,10a-dihydro-6-hydroxy-

D2: CAS Registry Number 831210-03-8; Entered STN: 15 Feb 2005; 6H-Dibenz[c,e][1,2]oxaborin, 2,4-dibromo-6a,10a-dihydro-6-hydroxy-

D3: US 3686398 A (KOHN et al.) 22 August 1972

D4: US 4353807 A (BRAID) 12 October 1982

D5: WO 2010/130708 A9 (NOVARTIS INTERNATIONAL PHARMACEUTICAL LTD.) 18 November 2010

D6: WO 2012/021455 A1 (REMPEX PHARMACEUTICALS, INC.) 16 February 2012

D7: WO 2016/003929 A1 (REMPEX PHARMACEUTICALS, INC.) 07 January 2016

D8: SUMIDA, Y., et al., "Boron-Selective Biaryl Coupling Approach to Versatile Dibenzoxaborins and Application to Concise Synthesis of Defucogilvocarcin M", Organic Letters, 2014, vol. 16, pages 6240-6243

NOVELTY (N)

Both D1 and D2 are considered to be the closest prior art to the claimed compounds. D1 discloses the compound 6a,10a-dihydro-6-hydroxy-6H-dibenz[c,e][1,2]oxaborin (RN 831209-98-4). And D2 discloses the compound 2,4-dibromo-6a,10a-dihydro-6-hydroxy-6H-dibenz[c,e][1,2]oxaborin (RN 831210-03-8).

Each compound of D1 and D2 comprises a 1,3-cyclohexadiene ring which equates to the present formula I where R2 and R3 form a fused carbocyclic ring system. However the present R2 and R3 fused ring system is defined as a C3-C7 cycloalkyl or a 3-10 membered heterocycle. Since the present description defines cycloalkyl as a fully saturated carbocyclyl ring or ring system (at para. 0092), the claims are novel in light of each of D1 and D2.

Accordingly the subject matter of claims 1-36 and 75-95 meets the criteria set forth in PCT Article 33(2) for novelty. The prior art published before the priority date does not disclose compounds of Formulae (I) or (II) with the substitutions as defined in these claims.

INVENTIVE STEP (IS)

The subject matter of claims 1-36 and 75-95 meets the criteria set forth in PCT Article 33(3) for inventive step because the prior art does not obviously suggest to the person skilled in the art the compounds of Formulae (I) or (II) with the substitutions as defined in these claims.

INDUSTRIAL APPLICABILITY (IA)

The invention defined in claims 1-36 and 75-95 is considered to meet the requirements of Industrial Applicability under Article 33(4) of the PCT because it can be made by, or used in, industry.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International Application No.

Supplemental Box – IPC marks**PCT/US2017/039787***C07F 5/02 (2006.01)**C07F 5/04 (2006.01)**A61K 31/69 (2006.01)**A61P 31/00 (2006.01)**A61P 31/04 (2006.01)*

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Article 5

PCT Article 5 requires that the description shall disclose the invention in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art. The PCT Guidelines state that the disclosure of the claimed invention is considered sufficiently clear and complete if it provides information which is sufficient to allow the invention to be carried out by a person skilled in the art as of the international filing date, without undue experimentation.

Although a reasonable amount of trial and error is permissible, a person skilled in the art must, on the basis of the disclosure of the claimed invention and the general knowledge, be able to carry out the invention across the entire scope of the claim without undue experimentation.

The present application provides the synthetic routes and examples of compounds of Formulae (Ib)-(Id) and (IIb)-(IIc). While a person skilled in the art can ascertain the appropriate reactions to synthesise these compounds through routine trial and error, the broader Formulae (I) and (Ia) and Formulae (II) and (IIa) encompass embodiments wherein ring A is non-aromatic selected from C3-7 carbocyclyl or 3-10 membered heterocyclyl, and where Y1 is N. While there is disclosure of where ring A is phenyl or pyridinyl and Y1 is CR4, the other embodiments are not provided for. A person skilled in the art cannot rely on the synthetic routes of Formulae (Ib)-(Id) and (IIb)-(IIc) to synthesise such significantly different compounds, particularly where ring A is not aromatic or where Y1 is N.

It is noted that only substituted phenyl and pyridinyl are provided as starting materials and reactions that would produce 1,2-oxaborinane ring systems not containing additional heteroatoms, such as N for Y1 are provided in the description. No alternative synthesis is provided for other ring or substituent possibilities. While some alternative members of ring A and Y1 = N may be substituted for the reactants in the synthetic routes described, a person skilled in the art would be required to carry out extensive experimentation for appropriate reactions without any direction from the application to produce all the alternative embodiments. Given the large number of possible variations, the amount of experimentation required by a person skilled in the art to carry out the claimed invention would not be reasonable.

Therefore, the description does not meet the requirements of Article 5 of the PCT with regard to it being sufficiently complete for the invention to be carried out by a person skilled in the art.

Article 6

PCT Article 6 requires that the claims shall be fully supported by the description. The PCT Guidelines state that there must be a basis in the description for the subject matter of every claim and that the scope of the claims must not be broader than is justified by the description and drawings. This also means that the claims must be enabled across their entire scope.

Claims 1-10, 17-19, 22-35 and 76-95 relate to compounds of Formulae (I) and (II) wherein ring A is other than aryl or heteroaryl and Y1 is other than CR4. The claims cover all compounds having these characteristics whereas the description only provides support within the meaning of Article 6 for compounds where ring A is aryl or heteroaryl, and where Y1 = CR4.

The claims are considered to travel beyond the scope of the disclosure of the specification as it is not reasonable for a person skilled in the art to predict all possible synthetic routes for the compounds of Formulae (I) and (II) where ring A is not aryl or heteroaryl, or where Y1 = N. Only substituted aryl or heteroaryl as starting materials for ring A and reactions resulting in Y1 being CR4 are provided in the description and as exemplified.

As the claims are considered to lack enablement for all compounds thereby embraced, they are not fully supported across their entire scope as required by Article 6 of the PCT.

Continuation of: **Box IV**

This International Application does not comply with the requirements of unity of invention because it does not relate to one invention or to a group of inventions so linked as to form a single general inventive concept.

This Authority has found that there are different inventions based on the following features that separate the claims into distinct groups:

- I. Claims 1-36 and 75 (in full) and claims 76-95 (in part) are generally directed to tricyclic 6-membered 1,2-het-borinane and 7-membered 1,2-het-borepane compounds of formula (I), or ring-opened compounds of formula (II), the borinane or borepane being (i) ring-fused to cyclic ring system (A), and (ii) further ring-fused to form tricyclic systems including spirocyclic systems; and pharmaceutical compositions and methods of treating bacterial infections comprising same. The feature of the tricyclic 6-membered 1,2-het-borinane and 7-membered 1,2-het-borepane compounds of formula (I), and corresponding ring-opened formula (II), is specific to this group of claims.
- II. Claims 37-51 (in full) and claims 76-95 (in part) are generally directed to bicyclic unsaturated 6-membered 1,2-het-3-ene-borinane and 7-membered 1,2-het-3-ene-borepane compounds of formula (III), or ring-opened compounds of formula (IV), the unsaturated borinane or borepane being ring-fused to cyclic ring system (A), and optionally where the unsaturated borinane or borepane rings are further ring-fused to form tricyclic systems including spirocyclic ring-fused; and pharmaceutical compositions and methods of treating bacterial infections comprising same. The feature of the bicyclic unsaturated 6-membered 1,2-het-3-ene-borinane and 7-membered 1,2-het-3-ene-borepane compounds of formula (III), and corresponding ring-opened formula (IV), is specific to this group of claims.
- III. Claims 52-65 (in full) and claims 76-95 (in part) are generally directed to bicyclic 6-membered 1,2-het-borinane and 7-membered 1,2-het-borepane compounds of formula (V) absent the ring system (A) and having an (alkylene)-carboxylic acid adjacent to the "het" heteroatom, and wherein the borinane or borepane rings are further ring-fused to form bicyclic systems including spirocyclic systems; and pharmaceutical compositions and methods of treating bacterial infections comprising same. The feature of the bicyclic 6-membered 1,2-het-borinane and 7-membered 1,2-het-borepane compounds of formula (V) having an (alkylene)-carboxylic acid adjacent to the "het" heteroatom is specific to this group of claims.
- IV. Claims 66-74 (in full) and claims 76-95 (in part) are generally directed to monocyclic unsaturated 6-membered 1,2-het-borinane and 7-membered 1,2-het-borepane compounds of formula (VI) absent the ring system (A) and having an (alkylene)-carboxylic acid adjacent to the "het" heteroatom, and optionally where the unsaturated borinane or borepane rings are further ring-fused to form bicyclic systems including spirocyclic ring-fused; and pharmaceutical compositions and methods of treating bacterial infections comprising same. The feature of the monocyclic 6-membered 1,2-het-borinane and 7-membered 1,2-het-borepane compounds of formula (VI) having an (alkylene)-carboxylic acid adjacent to the "het" heteroatom is specific to this group of claims.

PCT Rule 13.2, first sentence, states that unity of invention is only fulfilled when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features. PCT Rule 13.2, second sentence, defines a special technical feature as a feature which makes a contribution over the prior art.

When there is no special technical feature common to all the claimed inventions there is no unity of invention.

In the above groups of claims, the identified features may have the potential to make a contribution over the prior art but are not common to all the claimed inventions and therefore cannot provide the required technical relationship. The only feature common to all of the claimed inventions and which provides a technical relationship among them is 6-membered 1,2-het-borinane or 7-membered 1,2-het-borepane compounds which are ring-fused and/or have an (alkylene)-carboxylic acid adjacent to the "het" heteroatom. However this feature does not make a contribution over the prior art because it is disclosed in many documents including:

- US 3,686,398 (KOHN et al.) 22 August 1972
- US 4,353,807 (BRAID) 12 October 1982
- WO 2012/021455 A1 (REMPEX PHARMACEUTICALS, INC.) 16 February 2012
- WO 2016/003929 A1 (REMPEX PHARMACEUTICALS, INC.) 7 January 2016

Therefore in the light of any of these documents this common feature cannot be a special technical feature. Therefore there is no special technical feature common to all the claimed inventions and the requirements for unity of invention are consequently not satisfied *a posteriori*.

24 April 2018

VIA IPA ESERVICES

Attention: Authorized Officer Ross Heisey

International Searching Authority

AUSTRALIAN PATENT OFFICE
PO BOX 200
WODEN ACT 2606
AUSTRALIA

Re: **RESPONSE TO WRITTEN OPINION AND AMENDMENTS UNDER ARTICLE 34 WITH DEMAND FOR PRELIMINARY EXAMINATION**
Title: BORONIC ACID DERIVATIVES AND THERAPEUTIC USES THEREOF
Int'l Application No.: PCT/US2017/039787
Int'l Filing Date: June 28, 2017
Applicant: REMPEX PHARMACEUTICALS, INC.
Our Reference No.: MDCO.127WO (Previously REMPEX.127WO)

Dear Officer Heisey:

In response to the Written Opinion of the International Searching Authority mailed October 12, 2017 in connection with the above-identified PCT application, Applicant respectfully submits the following remarks.

REMARKS

Claim Amendments

With this response, Applicant provides an amended claim set on Replacement Pages 136-165. Additionally, for the Examiner's convenience, a marked-up copy of the amended claim set is included in an Appendix showing the changes compared to the claims as filed. In the Appendix, deletions are shown in bold and strikethrough (**~~example~~**) and insertions are shown in bold and underline (**example**).

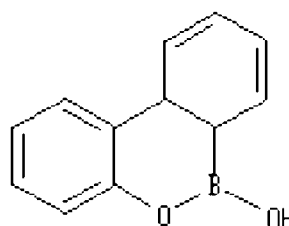
The marked-up amended claim set shows that Claim 1 has been amended to remove "C₆₋₁₀ aryl" and "5-10 membered heteroaryl" from the definition of R² and R³ in element (a) and also removed from the definition of R⁴ and R⁴ in element (e). In addition, "C₃₋₇ carbocyclyl" in the definition of R² and R³ in element (a) has been removed and replaced with "C₃₋₇ cycloalkyl." Claims 17-19 are also amended accordingly. One compound is deleted from Claim 36 and this canceled subject matter is incorporated in newly added Claim 75. Support and basis for the amendments can be found throughout the application as originally filed, for example, in paragraphs [0011] and [0090]. No new matter has been added.

Novelty

Applicant thanks the Examiner for acknowledging the novelty of Claims 2-9, 15, 16, 19-21, 24-30, 33-36, and 75-94. However, Claims 1, 10-14, 17, 18, 22, 23, 31 and 32 are rejected as allegedly being anticipated by D1 and D2.

D1 (CAS Registry Number 831209-98-4)

The Written Opinion takes the position that D1 is anticipatory on the basis that D1 discloses a compounds that fall within the scope of Formula I, element (a) of Claim 1. For the convenience of the



Examiner, the cited compound is reproduced as the following:

Applicant respectfully submits that independent Claim 1 as amended is novel over D1 at least because Claim 1 as amended, now exclude the possibility that R^2 and R^3 together with the atoms to which they are attached form a fused a carbocyclyl ring containing unsaturated bond(s). The term “cycloalkyl” as recited in Claim 1 requires the ring or ring system to be fully saturated. *See* paragraph [0092] of the application as filed. Thus, , Claim 1 does not encompass the compound of D1.

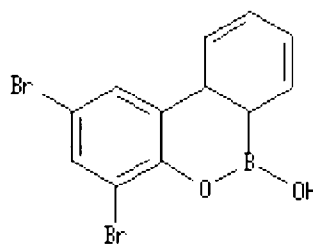
For at least this reason, Claim 1 and dependent claims thereof are novel over D1.

not include any A that would encompass such a carbocyclyl or heterocyclyl ring. A similar analysis applies to all of the specific compounds within D1.

Therefore, Claim 1 and its dependent claims are novel over D1.

D2 (CAS Registry Number 831210-03-8)

The Written Opinion takes the position that D2 is anticipatory on the basis that D2 discloses a compounds that fall within the scope of Formula I, element (a) of Claim 1. For the convenience of the



Examiner, the cited compound is reproduced as the following:

For at least the same reason as noted above with respect to D1, Applicant respectfully submits that independent Claim 1 as amended is novel over D2 because Claim 1 as amended, now exclude the

possibility that R^2 and R^3 together with the atoms to which they are attached form a fused carbocyclic ring containing unsaturated bond(s). For at least this reason, Claim 1 and dependent claims thereof are novel over D2.

Inventive Step

Applicant thanks the Examiner for acknowledging that Claims 2-9, 15, 16, 19-21, 24-30, 33-36, and 75-94 have met the criteria set forth in PCT Article 33(3) with regard to the requirements of inventive step. However, Claims 1, 10-14, 17, 18, 22, 23, 31 and 32 are rejected as allegedly lacking an inventive step in view of D1 and D2.

As discussed above, the cited references D1 and D2 fail to disclose any compounds that are encompassed by Formula I, element (a) recited in independent Claim 1. Each reference only discloses a single compound structure and provides no guidance to one of ordinary skill in the art to make any modification in order to arrive at the claimed compounds. For at least this reason, Claim 1 and dependent claims thereof are also inventive over D1 and D2.

Clarity

The Written Opinion states that the scope of Claim 1 is not clear for the following two reasons:

- i. When (a) R^2 and R^3 together with the atoms to which they are attached form a carbocyclic or heterocyclic aromatic ring system selected from C_{6-10} aryl and 5-10 membered heteroaryl, then R^1 and R^4 (when $Y^1 = CR^4$) would need to be absent; and
- ii. when (e) R^a and R^4 together with the atoms to which they are attached form a carbocyclic or heterocyclic aromatic ring system selected from C_{6-10} aryl and 5-10 membered heteroaryl, then R^3 would need to be absent.

The Written Opinion further states that if the definition of (a) R^2 and R^3 together [or (e) R^a and R^4 together] do included aromatic rings, then the relevant claims would not be novel or inventive in view of D3, D4 and D8.

Solely for expediting prosecution, “ C_{6-10} aryl” and “5-10 membered heteroaryl” have been deleted from the definition of R^2/R^3 and R^a/R^4 in elements (a) and (e) of Claim 1 respectively. For at least this reason, the scope of Claim 1 is clear and the proposed novelty and inventive rejection over D3, D4 and D8 are now moot.

Summary

In view of the amendments to the claims, Applicant respectfully submits that the claims are novel and inventive over the references cited in the International Search Report. In addition, the scope of the instant claims are clear. Accordingly, Applicant respectfully requests that the Examiner withdraw the

indicated rejections under PCT Article 33 and issue a favorable International Preliminary Examination Report on Patentability (Ch. II).

CONCLUSION

In view of the amendments and remarks set forth above, Applicant respectfully submits that all of the pending claims meet the patentability criteria set forth in Article 33(1), Article 33(2) and Article 33(3) PCT. Nevertheless, if any undeveloped issues remain or if any issues require clarification, **the Examiner is invited to contact the undersigned at 01-858-707-4136 in order to expedite the resolution of such issues.**

Respectfully submitted,



Jane Qian Dai
USPTO Reg. No. 61,569
Agent of Record

Enclosures

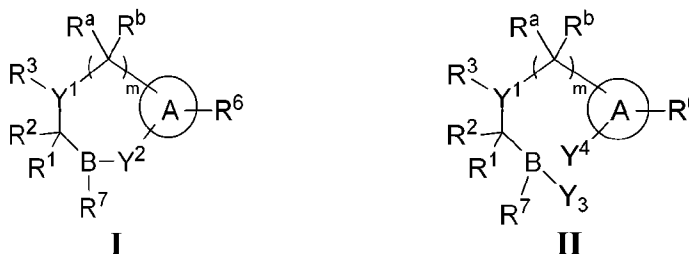
cc: Ryan E. Melnick

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Replacement Claims

WHAT IS CLAIMED IS:

1. A compound having the structure of the Formula I or II, or pharmaceutically acceptable salts thereof:



wherein

Y^1 is N or CR^4 ;

m is an integer of 0 or 1;

(a)

R^2 and R^3 together with the atoms to which they are attached form a fused ring or ring system selected from the group consisting of C_{3-7} cycloalkyl and 3-10 membered heterocyclyl, each optionally substituted with one or more R^5 , and

each of R^1 , R^4 , R^a , and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(C_{1-6} \text{ alkoxy})C_{1-6}$ alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted $(C_{3-7} \text{ carbocyclyl})C_{1-6}$ alkyl, optionally substituted $(3-10 \text{ membered heterocyclyl})C_{1-6}$ alkyl, optionally substituted $(C_{6-10} \text{ aryl})C_{1-6}$ alkyl, $(C_{6-10} \text{ aryl})C_{1-6}$ alkoxy, optionally substituted $(5-10 \text{ membered heteroaryl})C_{1-6}$ alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, and $-NR^fS(O)_2NR^fOR^d$;

or

(b)

R^3 and R^4 together with the atoms to which they are attached form a spirocyclic ring or ring system selected from the group consisting of C_3 -

7carbocyclyl and 3-10 membered heterocyclyl, each optionally substituted with one or more R⁵, and

each of R¹, R², R^a, and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d;

or

(c)

R¹ and R² together with the atoms to which they are attached form a spirocyclic ring or ring system selected from the group consisting of C₃₋₇carbocyclyl and 3-10 membered heterocyclyl, each optionally substituted with one or more R⁵, and

each of R³, R⁴, R^a, and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -

$\text{NR}^f\text{CR}^c(=\text{NR}^e)$, $-\text{NR}^f\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{S}(\text{O})(\text{CH}_2)_{1-3}\text{R}^c$, and $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{OR}^d$;
or

(d)

R^a and R^b together with the atoms to which they are attached form a spirocyclic ring or ring system selected from the group consisting of C_{3-7} carbocyclyl and 3-10 membered heterocyclyl, each optionally substituted with one or more R^5 , and

each of R^1 , R^2 , R^3 , and R^4 is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(\text{C}_{1-6} \text{ alkoxy})\text{C}_{1-6}$ alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted $(\text{C}_{3-7}\text{carbocyclyl})\text{C}_{1-6}$ alkyl, optionally substituted $(3-10 \text{ membered heterocyclyl})\text{C}_{1-6}$ alkyl, optionally substituted $(\text{C}_{6-10}\text{aryl})\text{C}_{1-6}$ alkyl, $(\text{C}_{6-10}\text{aryl})\text{C}_{1-6}$ alkoxy, optionally substituted $(5-10 \text{ membered heteroaryl})\text{C}_{1-6}$ alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-\text{SR}^c$, $-\text{C}(\text{O})(\text{CH}_2)_{0-3}\text{SR}^c$, $-\text{C}(\text{O})(\text{CH}_2)_{1-3}\text{R}^d$, $-\text{NR}^f\text{C}(\text{O})\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{R}^g$, $-\text{C}(=\text{NR}^e)\text{R}^c$, $-\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{CR}^c(=\text{NR}^e)$, $-\text{NR}^f\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{S}(\text{O})(\text{CH}_2)_{1-3}\text{R}^c$, and $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{OR}^d$;
or

(e)

R^a and R^4 together with the atoms to which they are attached form a fused ring or ring system selected from the group consisting of C_{3-7} carbocyclyl and 3-10 membered heterocyclyl, each optionally substituted with one or more R^5 , and

each of R^1 , R^2 , R^3 , and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(\text{C}_{1-6} \text{ alkoxy})\text{C}_{1-6}$ alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted $(\text{C}_{3-7}\text{carbocyclyl})\text{C}_{1-6}$ alkyl, optionally substituted $(3-10 \text{ membered heterocyclyl})\text{C}_{1-6}$ alkyl, optionally

substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d; R⁵ is -Y⁵-(CH₂)_t-G; t is an integer of 0 or 1;

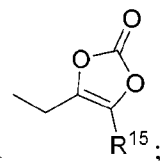
G is selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d;

A is selected from the group consisting of C₃₋₇ carbocyclyl, 3-10 membered heterocyclyl, C₆₋₁₀aryl, and 5-10 membered heteroaryl, each optionally substituted by one or more R¹²;

R⁶ is selected from the group consisting of H, halogen, optionally substituted C₁₋₆ alkyl, OH, -C(O)OR, optionally substituted C₁₋₆ alkoxy, amino, -N(OR⁸)R⁹, optionally substituted C₁₋₆ alkylthiol, C-amido, S-sulfonamido, CN, sulfinyl, sulfonyl, and a carboxylic acid isostere;

R is selected from the group consisting of H, C₁₋₉ alkyl, -CR¹⁰R¹¹OC(O)C₁₋₉alkyl, -CR¹⁰R¹¹OC(O)C₃₋₇carbocyclyl, -CR¹⁰R¹¹OC(O)(3 to 7 membered heterocyclyl), -CR¹⁰R¹¹OC(O)C₂₋₈alkoxyalkyl, -CR¹⁰R¹¹OC(O)OC₁₋₉alkyl, -CR¹⁰R¹¹OC(O)OC₃₋₇carbocyclyl, -CR¹⁰R¹¹OC(O)O(3 to 7 membered heterocyclyl), -CR¹⁰R¹¹OC(O)OC₂₋₈alkoxyalkyl, -CR¹⁰R¹¹OC(O)C₆₋₁₀aryl, -CR¹⁰R¹¹OC(O)OC₆₋₁₀aryl, -CR¹⁰R¹¹C(O)NR¹³R¹⁴, -CR¹⁰R¹¹OC(O)O(CH₂)₁₋

${}^3\text{C}(\text{O})\text{NR}^{13}\text{R}^{14}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{O}(\text{CH}_2)_{2-3}\text{OC}(\text{O})\text{C}_{1-4}$ alkyl, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{O}(\text{CH}_2)_1$



${}^3\text{C}(\text{O})\text{OC}_{1-4}$ alkyl, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})(\text{CH}_2)_{1-3}\text{OC}(\text{O})\text{C}_{1-4}$ alkyl, and

R^7 is selected from the group consisting of $-\text{OH}$, optionally substituted C_{1-6} alkoxy, amino, and $-\text{N}(\text{OR}^8)\text{R}^9$;

each R^8 and R^9 is independently selected from the group consisting of H, halogen, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

each R^{10} and R^{11} is independently selected from the group consisting of H, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

R^{12} is selected from the group consisting of hydrogen, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(\text{C}_{1-6}$ alkoxy) C_{1-6} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted $(\text{C}_{3-7}\text{carbocyclyl})\text{C}_{1-6}$ alkyl, optionally substituted $(3-10 \text{ membered heterocyclyl})\text{C}_{1-6}$ alkyl, optionally substituted $(\text{C}_{6-10}\text{aryl})\text{C}_{1-6}$ alkyl, $(\text{C}_{6-10}\text{aryl})\text{C}_{1-6}$ alkoxy, optionally substituted $(5-10 \text{ membered heteroaryl})\text{C}_{1-6}$ alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, sulfhydryl, $-\text{C}(\text{O})(\text{CH}_2)_{0-3}\text{SR}^c$, $-\text{C}(\text{O})(\text{CH}_2)_{1-3}\text{R}^d$, $-\text{NR}^f\text{C}(\text{O})\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{R}^g$, $-\text{C}(=\text{NR}^e)\text{R}^c$, $-\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{CR}^e(=\text{NR}^e)$, $-\text{NR}^f\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{S}(\text{O})(\text{CH}_2)_{1-3}\text{R}^c$, $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{OR}^d$, and $-(\text{CH}_2)_p\text{-Y}^6\text{-(CH}_2)_q\text{K}$;

each R^{13} and R^{14} is independently selected from the group consisting of H, optionally substituted C_{1-6} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

R^{15} is optionally substituted C_{1-6} alkyl;

Y^2 is selected from the group consisting of $-\text{O}-$, $-\text{S}-$, and $-\text{NR}^9$;

Y^3 is selected from the group consisting of $-\text{OH}$, $-\text{SH}$, and $-\text{NHR}^9$;

Y^4 is selected from the group consisting of -OH, optionally substituted C_{1-6} alkoxy, amino, and $-N(OR^8)R^9$; and

Y^5 is selected from the group consisting of -S-, $-S(O)-$, $-S(O)_2-$, -O-, $-CR^fR^g$ -, and $-NR^g$ -, or Y^5 is absent;

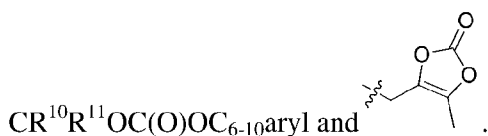
Y^6 is selected from the group consisting of -S-, $-S(O)-$, $-S(O)_2-$, -O-, $-CR^fR^g$ -, and $-NR^f$ -;

K is selected from the group consisting of C-amido; N-amido; S-sulfonamido; N-sulfonamido; $-NR^fC(O)NR^fR^g$; $-NR^fS(O)_2NR^fR^g$; $-C(=NR^e)R^e$; $-C(=NR^e)NR^fR^g$; $-NR^fCR^e(=NR^e)$; $-NR^fC(=NR^e)NR^fR^g$; C_{1-4} alkyl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; C_{6-10} aryl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; C_{3-7} carbocyclyl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; 5-10 membered heteroaryl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; and 3-10 membered heterocyclyl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido;

each R^c , R^d , R^e , R^f , and R^g are independently selected from the group consisting of H, halogen, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl; and

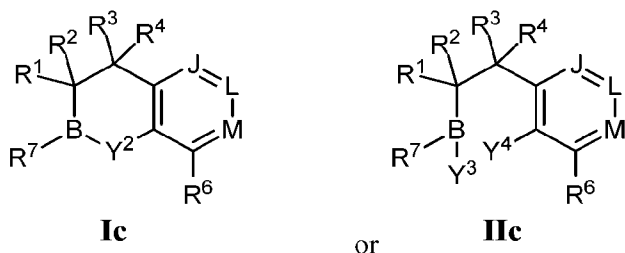
each p and q is independently 0 or 1.

2. The compound of claim 1, wherein R is selected from H, C_{1-9} alkyl, $-CR^{10}R^{11}OC(O)C_{1-9}$ alkyl, $-CR^{10}R^{11}OC(O)OC_{1-9}$ alkyl, $-CR^{10}R^{11}OC(O)C_{6-10}$ aryl, -

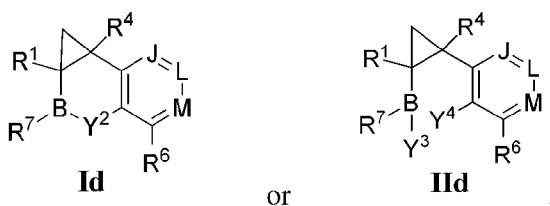


3. The compound of claim 1, wherein R is $-CR^{10}R^{11}OC(O)C_{1-9}$ alkyl, $-CR^{10}R^{11}OC(O)C_{3-7}$ carbocyclyl, $-CR^{10}R^{11}OC(O)$ (3 to 7 membered heterocyclyl), or $-CR^{10}R^{11}OC(O)C_{2-8}$ alkoxyalkyl.

pharmaceutically acceptable salts thereof:



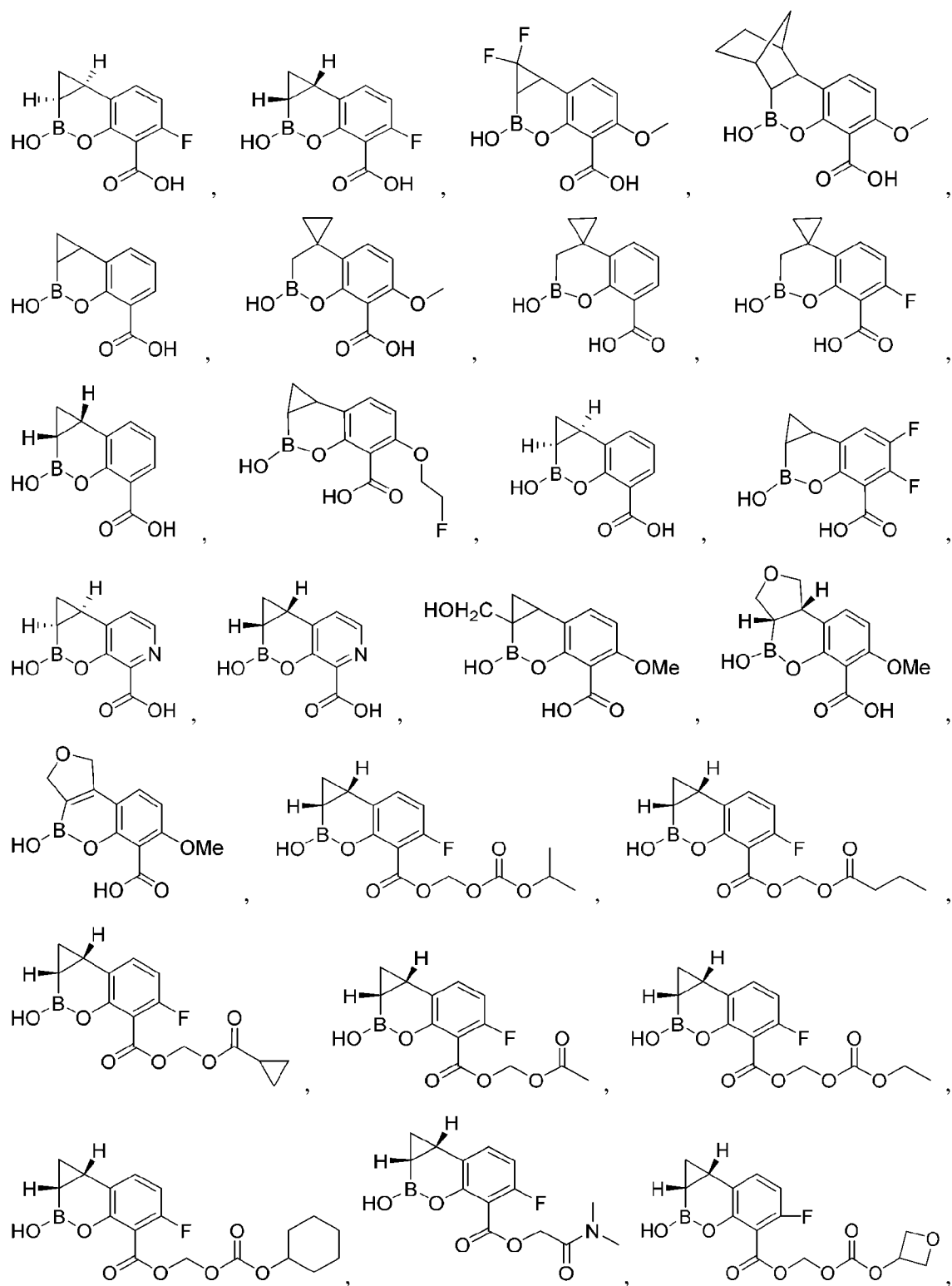
13. The compound of any claim 11 or 12, wherein each J, L and M is CR¹².
14. The compound of claim 13, wherein R¹² is hydrogen, halogen, C₁₋₆ alkoxy, or C₁₋₆ haloalkoxy.
15. The compound of claim 11 or 12, wherein at least one of J, L and M is N.
16. The compound of claim 15, wherein M is N.
17. The compound of any one of claims 1 to 16, wherein R² and R³ together with the atoms to which they are attached form a ring or ring system selected from the group consisting of C₃₋₇ cycloalkyl, and 3-10 membered heterocyclyl, each optionally substituted with one or more R⁵.
18. The compound of claim 17, wherein R² and R³ together with the atoms to which they are attached form C₃₋₇ cycloalkyl optionally substituted with one or more R⁵.
19. The compound of claim 18, wherein R² and R³ together with the atoms to which they are attached form cyclopropyl, bicyclo[2.2.1]heptyl, tetrahydrofuranyl, or dihydrofuranyl, each optionally substituted with one or more R⁵.
20. The compound of claim 18 or 19, having the structure of Formula Id or IId, or pharmaceutically acceptable salts thereof:

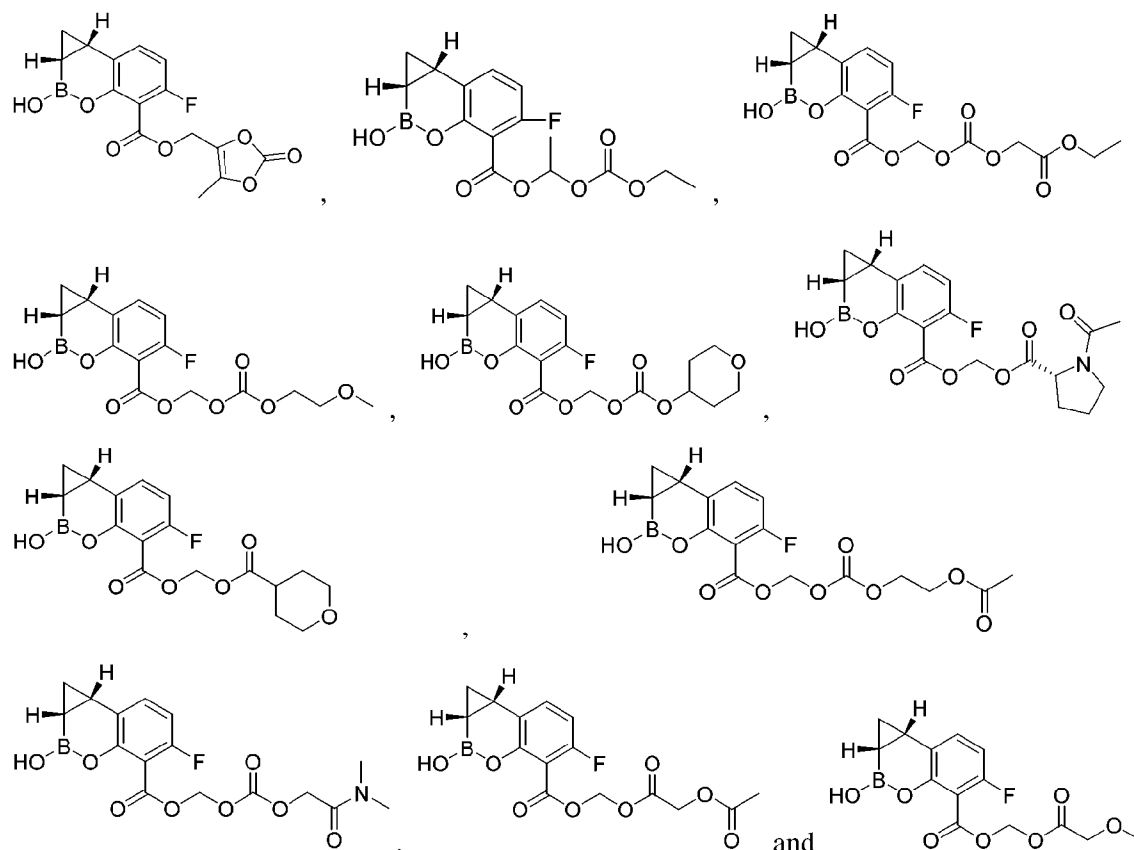


wherein the cyclopropyl moiety is optionally substituted with one or more R⁵.

21. The compound of claim 20, having the structure of Formula Id-1, Id-2, IId-1 or IId-2, or pharmaceutically acceptable salts thereof:

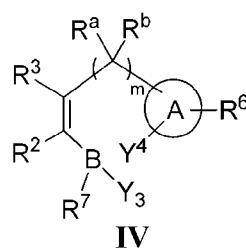
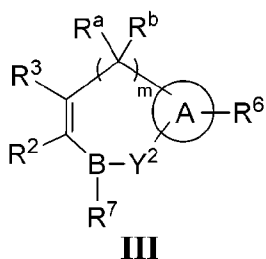
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or pharmaceutically acceptable salts thereof.

37. A compound having the structure of the Formula III or IV, or pharmaceutically acceptable salts thereof:



wherein

(a)

each of R² and R³ is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl,

optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d, or R² and R³ together with the atoms to which they are attached form a fused ring or ring system selected from the group consisting of C₃₋₇carbocyclyl, 3-10 membered heterocyclyl, C₆₋₁₀ aryl, and 5-10 membered heteroaryl, each optionally substituted with one or more R⁵;

m is an integer of 0 or 1; and

each R^a and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d, or R^a and R^b together with the atoms to which they are attached form a ring or ring system selected from the group consisting of C₃₋₇carbocyclyl and 3-10 membered heterocyclyl, each optionally substituted with one or more R⁵; or

(b)

m is 1;

R^a and R³ together with the atoms to which they are attached form a ring or ring system selected from the group consisting of C₃₋₇carbocyclyl and 3-10 membered heterocyclyl, each optionally substituted with one or more R⁵; and

each R² and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally

substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d;

R⁵ is -Y⁵-(CH₂)_t-G;

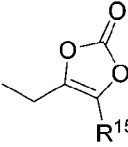
t is an integer of 0 or 1;

G is selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d;

A is a ring system selected from the group consisting of C₃₋₇ carbocyclyl, 3-10 membered heterocyclyl, C₆₋₁₀aryl, and 5-10 membered heteroaryl, each optionally substituted with one or more R¹²;

R⁶ is selected from the group consisting of H, halogen, optionally substituted C₁₋₆ alkyl, OH, -C(O)OR, optionally substituted C₁₋₆ alkoxy, amino, -N(OR⁸)R⁹, optionally substituted C₁₋₆ alkylthiol, C-amido, S-sulfonamido, CN, sulfinyl, sulfonyl, and a carboxylic acid isostere;

R is selected from the group consisting of H, C₁₋₉ alkyl, -CR¹⁰R¹¹OC(O)C₁₋₉alkyl, -CR¹⁰R¹¹OC(O)C₃₋₇carbocyclyl, -CR¹⁰R¹¹OC(O)(3 to 7 membered heterocyclyl), -CR¹⁰R¹¹OC(O)C₂₋₈alkoxyalkyl, -CR¹⁰R¹¹OC(O)OC₁₋₉alkyl, -CR¹⁰R¹¹OC(O)OC₃₋₇carbocyclyl, -CR¹⁰R¹¹OC(O)O(3 to 7 membered heterocyclyl), -CR¹⁰R¹¹OC(O)OC₂₋₈alkoxyalkyl, -CR¹⁰R¹¹OC(O)C₆₋₁₀aryl, -CR¹⁰R¹¹OC(O)OC₆₋₁₀aryl, -CR¹⁰R¹¹C(O)NR¹³R¹⁴, -CR¹⁰R¹¹OC(O)O(CH₂)₁₋₃C(O)NR¹³R¹⁴, -CR¹⁰R¹¹OC(O)O(CH₂)₂₋₃OC(O)C₁₋₄ alkyl, -CR¹⁰R¹¹OC(O)O(CH₂)₁₋

₃C(O)OC₁₋₄ alkyl, -CR¹⁰R¹¹OC(O)(CH₂)₁₋₃OC(O)C₁₋₄ alkyl, and  R¹⁵;

R⁷ is selected from the group consisting of -OH, optionally substituted C₁₋₆ alkoxy, amino, and -N(OR⁸)R⁹;

each R⁸ and R⁹ is independently selected from the group consisting of H, halogen, optionally substituted C₁₋₄alkyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, and optionally substituted 5-10 membered heteroaryl;

each R¹⁰ and R¹¹ is independently selected from the group consisting of H, optionally substituted C₁₋₄alkyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, and optionally substituted 5-10 membered heteroaryl;

R¹² is selected from the group consisting of hydrogen, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted C₁₋₆ alkylthiol, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, sulfhydryl, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^e(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, -NR^fS(O)₂NR^fOR^d, and -(CH₂)_p-Y⁶-(CH₂)_qK;

each R^{13} and R^{14} is independently selected from the group consisting of H, optionally substituted C_{1-6} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

R^{15} is optionally substituted C_{1-6} alkyl;

Y^2 is selected from the group consisting of -O-, -S-, and $-NR^9$;

Y^3 is selected from the group consisting of -OH, -SH, and $-NHR^9$;

Y^4 is selected from the group consisting of -OH, optionally substituted C_{1-6} alkoxy, amino, and $-N(OR^8)R^9$;

Y^5 is selected from the group consisting of -S-, $-S(O)$ -, $-S(O)_2$ -, -O-, $-CR^fR^g$ -, and $-NR^g$ -, or Y^5 is absent;

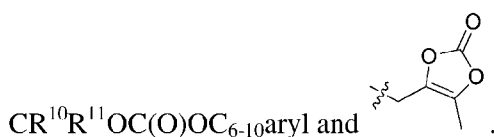
Y^6 is selected from the group consisting of -S-, $-S(O)$ -, $-S(O)_2$ -, -O-, $-CR^fR^g$ -, and $-NR^f$;

K is selected from the group consisting of C-amido; N-amido; S-sulfonamido; N-sulfonamido; $-NR^fC(O)NR^fR^g$; $-NR^fS(O)_2NR^fR^g$; $-C(=NR^e)R^e$; $-C(=NR^e)NR^fR^g$; $-NR^fCR^e(=NR^e)$; $-NR^fC(=NR^e)NR^fR^g$; C_{1-4} alkyl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; C_{6-10} aryl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; C_{3-7} carbocyclyl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; 5-10 membered heteroaryl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; and 3-10 membered heterocyclyl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido;

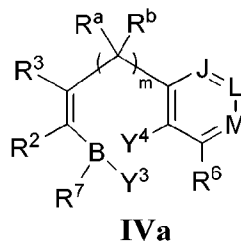
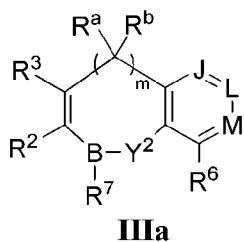
each R^c , R^d , R^e , R^f , and R^g are independently selected from the group consisting of H, halogen, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl; and

each p and q is independently 0 or 1.

38. The compound of claim 37, wherein R is selected from H, C_{1-9} alkyl, $-CR^{10}R^{11}OC(O)C_{1-9}$ alkyl, $-CR^{10}R^{11}OC(O)OC_{1-9}$ alkyl, $-CR^{10}R^{11}OC(O)C_{6-10}$ aryl, -

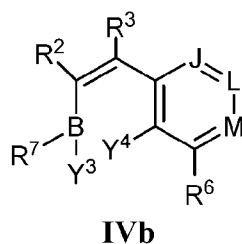
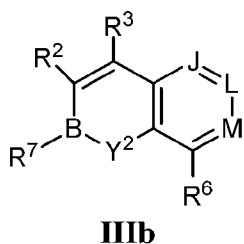


39. The compound of claim 37 or 38, having the structure Formula IIIa or IVa, or pharmaceutically acceptable salts thereof:



wherein each J, L, M is independently CR¹² or N.

40. The compound of claim 39, having the structure of Formula IIIb or IVb, or pharmaceutically acceptable salts thereof:



41. The compound of claim 39 or 40, wherein each J, L and M is CR¹².

42. The compound of any one of claims 37 to 41, wherein R² is hydrogen, halogen, or C₁₋₆ alkyl.

43. The compound of any one of claims 37 to 42, wherein R³ is hydrogen.

44. The compound of any one of claims 37 to 43, wherein R⁶ is -C(O)OR.

45. The compound of claim 44, wherein R is H.

46. The compound of any one of claims 37 to 45, wherein R⁷ is -OH.

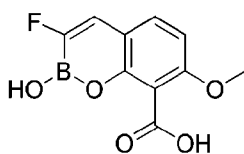
47. The compound of any one of claims 37 to 46, wherein Y² is -O-.

48. The compound of any one of claims 37 to 47, wherein Y³ is -OH.

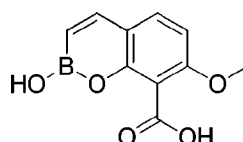
49. The compound of any one of claims 37 to 48, wherein Y⁴ is -OH.

50. The compound of any one of claims 37 to 49, wherein R¹² is hydrogen, halogen or C₁₋₆ alkoxy.

51. The compound of claim 37, selected from the group consisting of

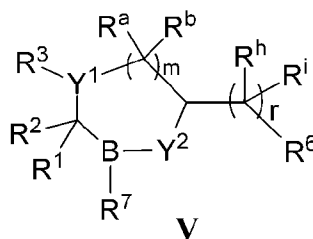


and



, or pharmaceutically acceptable salts thereof.

52. A compound having the structure of Formula V, or pharmaceutically acceptable salts thereof:



wherein

Y^1 is N or CR^4 ;

m is an integer of 0 or 1;

r is an integer of 0 or 1;

(a)

R^2 and R^3 together with the atoms to which they are attached form a fused ring or ring system selected from the group consisting of C_{3-7} carbocyclyl, 3-10 membered heterocyclyl, C_{6-10} aryl, and 5-10 membered heteroaryl, each optionally substituted with one or more R^5 , and

each of R^1 , R^4 , R^a , and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(C_{1-6}$ alkoxy) C_{1-6} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted $(C_{3-7}$ carbocyclyl) C_{1-6} alkyl, optionally substituted (3-10 membered heterocyclyl) C_{1-6} alkyl, optionally substituted $(C_{6-10}$ aryl) C_{1-6} alkyl, $(C_{6-10}$ aryl) C_{1-6} alkoxy, optionally substituted (5-10 membered heteroaryl) C_{1-6} alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, and $-NR^fS(O)_2NR^fOR^d$;

or

(b)

R^3 and R^4 together with the atoms to which they are attached form a spirocyclic ring or ring system selected from the group consisting of C_3 -

7carbocyclyl, and 3-10 membered heterocyclyl, each optionally substituted with one or more R⁵, and

each of R¹, R², R^a, and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d;

or

(c)

R¹ and R² together with the atoms to which they are attached form a spirocyclic ring or ring system selected from the group consisting of C₃₋₇carbocyclyl, and 3-10 membered heterocyclyl, each optionally substituted with one or more R⁵, and

each of R³, R⁴, R^a, and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -

$\text{NR}^f\text{CR}^c(=\text{NR}^e)$, $-\text{NR}^f\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{S}(\text{O})(\text{CH}_2)_{1-3}\text{R}^c$, and $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{OR}^d$;
or

(d)

R^a and R^b together with the atoms to which they are attached form a spirocyclic ring or ring system selected from the group consisting of C_{3-7} carbocyclyl, and 3-10 membered heterocyclyl, each optionally substituted with one or more R^5 , and

each of R^1 , R^2 , R^3 , and R^4 is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(\text{C}_{1-6} \text{ alkoxy})\text{C}_{1-6}$ alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted $(\text{C}_{3-7}\text{carbocyclyl})\text{C}_{1-6}$ alkyl, optionally substituted $(3-10 \text{ membered heterocyclyl})\text{C}_{1-6}$ alkyl, optionally substituted $(\text{C}_{6-10}\text{aryl})\text{C}_{1-6}$ alkyl, $(\text{C}_{6-10}\text{aryl})\text{C}_{1-6}$ alkoxy, optionally substituted $(5-10 \text{ membered heteroaryl})\text{C}_{1-6}$ alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-\text{SR}^c$, $-\text{C}(\text{O})(\text{CH}_2)_{0-3}\text{SR}^c$, $-\text{C}(\text{O})(\text{CH}_2)_{1-3}\text{R}^d$, $-\text{NR}^f\text{C}(\text{O})\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{R}^g$, $-\text{C}(=\text{NR}^e)\text{R}^c$, $-\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{CR}^c(=\text{NR}^e)$, $-\text{NR}^f\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{S}(\text{O})(\text{CH}_2)_{1-3}\text{R}^c$, and $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{OR}^d$;
or

(e)

R^a and R^4 together with the atoms to which they are attached form a fused ring or ring system selected from the group consisting of C_{3-7} carbocyclyl, 3-10 membered heterocyclyl, C_{6-10} aryl, and 5-10 membered heteroaryl, each optionally substituted with one or more R^5 , and

each of R^1 , R^2 , R^3 , and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(\text{C}_{1-6} \text{ alkoxy})\text{C}_{1-6}$ alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted $(\text{C}_{3-7}\text{carbocyclyl})\text{C}_{1-6}$ alkyl,

optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d; R⁵ is -Y⁵-(CH₂)_t-G;

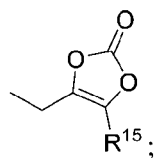
t is an integer of 0 or 1;

G is selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d;

R⁶ is selected from the group consisting of optionally substituted -(CH₂)_nC(O)OR and a carboxylic acid isostere;

n is an integer selected from 0 to 6;

R is selected from the group consisting of H, C₁₋₉ alkyl, -CR¹⁰R¹¹OC(O)C₁₋₉alkyl, -CR¹⁰R¹¹OC(O)C₃₋₇carbocyclyl, -CR¹⁰R¹¹OC(O)(3 to 7 membered heterocyclyl), -CR¹⁰R¹¹OC(O)C₂₋₈alkoxyalkyl, -CR¹⁰R¹¹OC(O)OC₁₋₉alkyl, -CR¹⁰R¹¹OC(O)OC₃₋₇carbocyclyl, -CR¹⁰R¹¹OC(O)O(3 to 7 membered heterocyclyl), -CR¹⁰R¹¹OC(O)OC₂₋₈alkoxyalkyl, -CR¹⁰R¹¹OC(O)C₆₋₁₀aryl, -CR¹⁰R¹¹OC(O)OC₆₋₁₀aryl, -CR¹⁰R¹¹C(O)NR¹³R¹⁴, -CR¹⁰R¹¹OC(O)O(CH₂)₁₋₃C(O)NR¹³R¹⁴, -CR¹⁰R¹¹OC(O)O(CH₂)₂₋₃OC(O)C₁₋₄ alkyl, -CR¹⁰R¹¹OC(O)O(CH₂)₁₋

₃C(O)OC₁₋₄ alkyl, -CR¹⁰R¹¹OC(O)(CH₂)₁₋₃OC(O)C₁₋₄ alkyl, and ; R¹⁵;

R^7 is selected from the group consisting of -OH, optionally substituted C_{1-6} alkoxy, amino, and $-N(OR^8)R^9$;

each R^8 and R^9 is independently selected from the group consisting of H, halogen, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

each R^{10} and R^{11} is independently selected from the group consisting of H, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

each R^{13} and R^{14} is independently selected from the group consisting of H, optionally substituted C_{1-6} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

R^{15} is optionally substituted C_{1-6} alkyl;

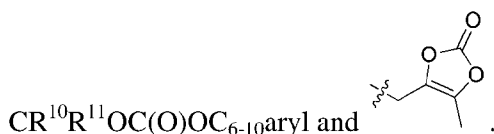
Y^2 is selected from the group consisting of -O-, -S-, and $-NR^9$ -;

Y^5 is selected from the group consisting of -S-, $-S(O)$ -, $-S(O)_2$ -, -O-, $-CR^fR^g$ -, and $-NR^g$ -, or Y^5 is absent;

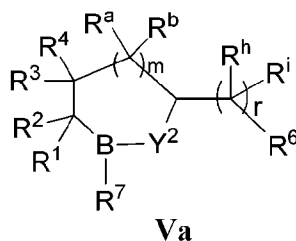
each R^c , R^d , R^e , R^f , and R^g are independently selected from the group consisting of H, halogen, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl; and

each R^h and R^i is independently selected from the group consisting of H, halogen, cyano, amino, C-amido, N-amido, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl; or R^h and R^i together with the atoms to which they are attached form a spirocyclic ring or ring system selected from the group consisting of C_{3-7} carbocyclyl, 3-10 membered heterocyclyl, C_{6-10} aryl, and 5-10 membered heteroaryl, each optionally substituted with one or more R^5 .

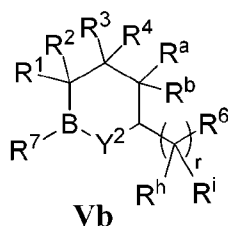
53. The compound of claim 52, wherein R is selected from H, C_{1-9} alkyl, $-CR^{10}R^{11}OC(O)C_{1-9}$ alkyl, $-CR^{10}R^{11}OC(O)OC_{1-9}$ alkyl, $-CR^{10}R^{11}OC(O)C_{6-10}$ aryl, -



54. The compound of claim 52 or 53, having the structure of Formula Va, or pharmaceutically acceptable salts thereof:



55. The compound of claim 54, having the structure of Formula Vb, or pharmaceutically acceptable salts thereof:



56. The compound of any one of claims 52 to 55, wherein both R^a and R^b are H.

57. The compound of any one of claims 52 to 56, wherein R² and R³ together with the atoms to which they are attached form a ring or ring system selected from the group consisting of C₃₋₇ carbocyclyl, 3-10 membered heterocyclyl, C₆₋₁₀ aryl, and 5-10 membered heteroaryl, each optionally substituted with one or more R⁵.

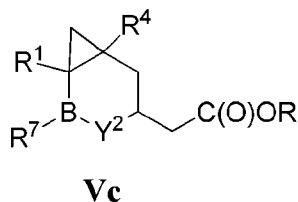
58. The compound of claim 57, wherein R² and R³ together with the atoms to which they are attached form C₃₋₇carbocyclyl optionally substituted with one or more R⁵.

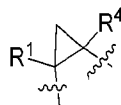
59. The compound of claim 58, wherein R² and R³ together with the atoms to which they are attached form cyclopropyl optionally substituted with one or more R⁵.

60. The compound of any one of claims 52 to 59, wherein r is 1, and both R^h and Rⁱ are H.

61. The compound of any one of claims 52 to 60, wherein R⁶ is -(CH₂)_nC(O)OR and n is 0.

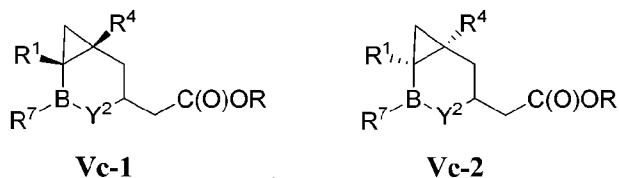
62. The compound of claim 61, having the structure of Formula Vc, or pharmaceutically acceptable salts thereof:





wherein the cyclopropyl moiety is optionally substituted with one or more R^5 .

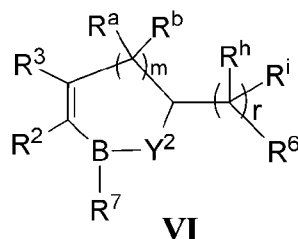
63. The compound of claim 62, having the structure of Formula Vc-1 or Vc-2, or pharmaceutically acceptable salts thereof:



64. The compound of any one of any one of claims 52 to 63, wherein Y^2 is -O-.

65. The compound of any one of claims 52 to 64, wherein R^7 is -OH.

66. A compound having the structure of Formula VI, or pharmaceutically acceptable salts thereof:



wherein

r is an integer of 0 or 1;

(a)

each of R^2 and R^3 is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(C_{1-6} \text{ alkoxy})C_{1-6}$ alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted $(C_{3-7}\text{carbocyclyl})C_{1-6}$ alkyl, optionally substituted (3-10 membered heterocyclyl) C_{1-6} alkyl, optionally substituted $(C_{6-10}\text{aryl})C_{1-6}$ alkyl, $(C_{6-10}\text{aryl})C_{1-6}$ alkoxy, optionally substituted (5-10 membered heteroaryl) C_{1-6} alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, and $-NR^fS(O)_2NR^fOR^d$, or R^2 and R^3 together with the atoms to

which they are attached form a fused ring or ring system selected from the group consisting of C₃₋₇carbocyclyl and 3-10 membered heterocyclyl, each optionally substituted with one or more R⁵;

m is an integer of 0 or 1;

each R^a and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d, or R^a and R^b together with the atoms to which they are attached form a ring or ring system selected from the group consisting of C₃₋₇carbocyclyl, and 3-10 membered heterocyclyl, each optionally substituted with one or more R⁵; or

(b)

m is 1;

R^a and R³ together with the atoms to which they are attached form a ring or ring system selected from the group consisting of C₃₋₇carbocyclyl, and 3-10 membered heterocyclyl, each optionally substituted with one or more R⁵; and

each R² and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋

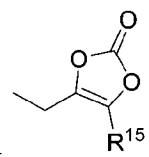
$_{10}\text{aryl})\text{C}_{1-6}\text{alkoxy}$, optionally substituted (5-10 membered heteroaryl) $\text{C}_{1-6}\text{alkyl}$, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-\text{SR}^c$, $-\text{C}(\text{O})(\text{CH}_2)_{0-3}\text{SR}^c$, $-\text{C}(\text{O})(\text{CH}_2)_{1-3}\text{R}^d$, $-\text{NR}^f\text{C}(\text{O})\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{R}^g$, $-\text{C}(=\text{NR}^e)\text{R}^c$, $-\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{CR}^c(=\text{NR}^e)$, $-\text{NR}^f\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{S}(\text{O})(\text{CH}_2)_{1-3}\text{R}^c$, and $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{OR}^d$;
 R^5 is $-\text{Y}^5-(\text{CH}_2)_t-\text{G}$;
 t is an integer of 0 or 1;

G is selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted (C_{1-6} alkoxy) C_{1-6} alkyl, optionally substituted $\text{C}_{2-10}\text{alkenyl}$, optionally substituted $\text{C}_{2-10}\text{alkynyl}$, optionally substituted $\text{C}_{3-7}\text{carbocyclyl}$, optionally substituted 3-10 membered heterocyclyl, optionally substituted $\text{C}_{6-10}\text{aryl}$, optionally substituted 5-10 membered heteroaryl, optionally substituted ($\text{C}_{3-7}\text{carbocyclyl})\text{C}_{1-6}\text{alkyl}$, optionally substituted (3-10 membered heterocyclyl) $\text{C}_{1-6}\text{alkyl}$, optionally substituted ($\text{C}_{6-10}\text{aryl})\text{C}_{1-6}\text{alkyl}$, ($\text{C}_{6-10}\text{aryl})\text{C}_{1-6}\text{alkoxy}$, optionally substituted (5-10 membered heteroaryl) $\text{C}_{1-6}\text{alkyl}$, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-\text{SR}^c$, $-\text{C}(\text{O})(\text{CH}_2)_{0-3}\text{SR}^c$, $-\text{C}(\text{O})(\text{CH}_2)_{1-3}\text{R}^d$, $-\text{NR}^f\text{C}(\text{O})\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{R}^g$, $-\text{C}(=\text{NR}^e)\text{R}^c$, $-\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{CR}^c(=\text{NR}^e)$, $-\text{NR}^f\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{S}(\text{O})(\text{CH}_2)_{1-3}\text{R}^c$, and $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{OR}^d$;

R^6 is selected from the group consisting of optionally substituted $-(\text{CH}_2)_n\text{C}(\text{O})\text{OR}$ and a carboxylic acid isostere;

n is an integer selected from 0 to 6;

R is selected from the group consisting of H, C_{1-9} alkyl, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{C}_{1-9}\text{alkyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{C}_{3-7}\text{carbocyclyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})(3 \text{ to } 7 \text{ membered heterocyclyl})$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{C}_{2-8}\text{alkoxyalkyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{OC}_{1-9}\text{alkyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{OC}_{3-7}\text{carbocyclyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{O}(3 \text{ to } 7 \text{ membered heterocyclyl})$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{OC}_{2-8}\text{alkoxyalkyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{C}_{6-10}\text{aryl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{OC}_{6-10}\text{aryl}$, $-\text{CR}^{10}\text{R}^{11}\text{C}(\text{O})\text{NR}^{13}\text{R}^{14}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{O}(\text{CH}_2)_{1-3}\text{C}(\text{O})\text{NR}^{13}\text{R}^{14}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{O}(\text{CH}_2)_{2-3}\text{OC}(\text{O})\text{C}_{1-4} \text{ alkyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{O}(\text{CH}_2)_{1-3}\text{C}(\text{O})\text{OC}_{1-4} \text{ alkyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})(\text{CH}_2)_{1-3}\text{OC}(\text{O})\text{C}_{1-4} \text{ alkyl}$, and



$-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})(\text{CH}_2)_{1-3}\text{OC}(\text{O})\text{C}_{1-4} \text{ alkyl}$, and

R^7 is selected from the group consisting of -OH, optionally substituted C_{1-6} alkoxy, amino, and $-N(OR^8)R^9$;

each R^8 and R^9 is independently selected from the group consisting of H, halogen, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

each R^{10} and R^{11} is independently selected from the group consisting of H, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

each R^{13} and R^{14} is independently selected from the group consisting of H, optionally substituted C_{1-6} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

R^{15} is optionally substituted C_{1-6} alkyl;

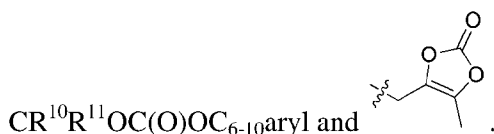
Y^2 is selected from the group consisting of -O-, -S-, and $-NR^9$ -;

Y^5 is selected from the group consisting of -S-, $-S(O)$ -, $-S(O)_2$ -, -O-, $-CR^fR^g$ -, and $-NR^g$ -, or Y^5 is absent;

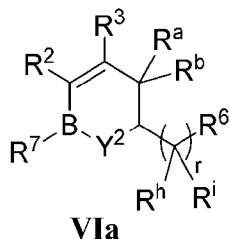
each R^c , R^d , R^e , R^f , and R^g are independently selected from the group consisting of H, halogen, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl; and

each R^h and R^i is independently selected from the group consisting of H, halogen, cyano, amino, C-amido, N-amido, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl; or R^h and R^i together with the atoms to which they are attached form a spirocyclic ring or ring system selected from the group consisting of C_{3-7} carbocyclyl, 3-10 membered heterocyclyl, C_{6-10} aryl, and 5-10 membered heteroaryl, each optionally substituted with one or more R^5 .

67. The compound of claim 66, wherein R is selected from H, C_{1-9} alkyl, $-CR^{10}R^{11}OC(O)C_{1-9}$ alkyl, $-CR^{10}R^{11}OC(O)OC_{1-9}$ alkyl, $-CR^{10}R^{11}OC(O)C_{6-10}$ aryl, -



68. The compound of claim 66 or 67, having the structure of Formula VIa, or pharmaceutically acceptable salts thereof:

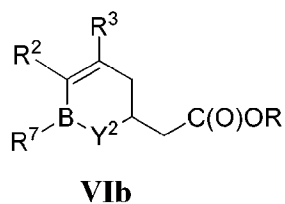


69. The compound of any one of claims 66 to 68, wherein both R^a and R^b are H.

70. The compound of any one of claims 66 to 69, wherein r is 1, and both R^h and R^i are H.

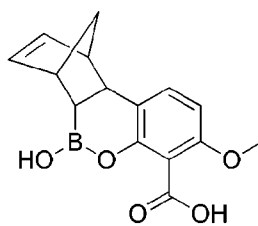
71. The compound of any one of claims 66 to 70, wherein R^6 is $-(CH_2)_nC(O)OR$ and n is 0.

72. The compound of claim 71, having the structure of Formula VIb, or pharmaceutically acceptable salts thereof:



73. The compound of any one of any one of claims 66 to 72, wherein Y^2 is $-O-$.

74. The compound of any one of claims 66 to 73, wherein R^7 is $-OH$.



75. A compound of structure , or pharmaceutically acceptable salts thereof.

76. The compound of any one of claims 1 to 75, wherein the pharmaceutically acceptable salt is an alkaline metal salt or an ammonium salt.

77. The compound of claim 76, wherein the pharmaceutically acceptable salt is a sodium salt.

78. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1 to 77, and a pharmaceutically acceptable excipient.

79. The pharmaceutical composition of claim 78, further comprising an additional medicament.

80. The pharmaceutical composition of claim 79, wherein the additional medicament is selected from the group consisting of an antibacterial agent, an antifungal agent, an antiviral agent, an anti-inflammatory agent, and an anti-allergic agent.

81. The pharmaceutical composition of claim 80, wherein the additional medicament is a β -lactam antibacterial agent.

82. The pharmaceutical composition of claim 81, wherein the β -lactam antibacterial agent is selected from the group consisting of Amoxicillin, Ampicillin (Pivampicillin, Hetacillin, Bacampicillin, Metampicillin, Talampicillin), Epicillin, Carbenicillin (Carindacillin), Ticarcillin, Temocillin, Azlocillin, Piperacillin, Mezlocillin, Mecillinam (Pivmecillinam), Sulbenicillin, Benzylpenicillin (G), Clometocillin, Benzathine benzylpenicillin, Procaine benzylpenicillin, Azidocillin, Penamecillin, Phenoxymethylpenicillin (V), Propicillin, Benzathine phenoxymethylpenicillin, Pheneticillin, Cloxacillin (Dicloxacillin, Flucloxacillin), Oxacillin, Meticillin, Nafcillin, Faropenem, Tomopenem, Razupenem, Cefazolin, Cefacetrile, Cefadroxil, Cefalexin, Cefaloglycin, Cefalonium, Cefaloridine, Cefalotin, Cefapirin, Cefatrizine, Cefazedone, Cefazaflur, Cefradine, Cefroxadine, Ceftezole, Cefaclor, Cefamandole, Cefminox, Cefonicid, Ceforanide, Cefotiam, Cefprozil, Cefbuperazone, Cefuroxime, Cefuzonam, Cefoxitin, Cefotetan, Cefmetazole, Loracarbef, Cefixime, Ceftriaxone, Cefcapene, Cefdaloxime, Cefdinir, Cefditoren, Cefetamet, Cefmenoxime, Cefodizime, Cefoperazone, Cefotaxime, Cefpimizole, Cefpiramide, Cefpodoxime, Cefsulodin, Cefteram, Ceftributen, Ceftiolene, Ceftizoxime, Flomoxef, Latamoxef, Cefepime, Cefozopran, Cefpirome, Cefquinome, Ceftobiprole, Ceftaroline, CXA- 101, RWJ-54428, MC-04,546, ME1036, Ceftiofur, Cefquinome, Cefovecin, RWJ-442831, RWJ-333441, and RWJ-333442.

83. The pharmaceutical composition of claim 81, wherein the β -lactam antibacterial agent is selected from the group consisting of Ceftazidime, Biapenem, Doripenem, Ertapenem, Imipenem, Meropenem, Tebipenem, Tebipenem pivoxil, Apapenem, and Panipenem.

84. The pharmaceutical composition of claim 81, wherein the β -lactam antibacterial agent is selected from the group consisting of Aztreonam, Tigemonam, BAL30072, SYN 2416, and Carumonam.

85. A method of treating a bacterial infection, comprising administering a compound according any one of claims 1 to 77 to a subject in need thereof.

86. The method of claim 85, further comprising administering to the subject an additional medicament.

87. The method of claim 86, wherein the additional medicament is an antibacterial agent, an antifungal agent, an antiviral agent, an anti-inflammatory agent, or an antiallergic agent.

88. The method of claim 87, wherein the additional medicament is a β -lactam antibacterial agent.

89. The method of claim 88, wherein the β -lactam antibacterial agent is selected from the group consisting of Amoxicillin, Ampicillin (Pivampicillin, Hetacillin, Bacampicillin, Metampicillin, Talampicillin), Epicillin, Carbenicillin (Carindacillin), Ticarcillin, Temocillin, Azlocillin, Piperacillin, Mezlocillin, Mecillinam (Pivmecillinam), Sulbenicillin, Benzylpenicillin (G), Clometocillin, Benzathine benzylpenicillin, Procaine benzylpenicillin, Azidocillin, Penamecillin, Phenoxymethylpenicillin (V), Propicillin, Benzathine phenoxymethylpenicillin, Pheneticillin, Cloxacillin (Dicloxacillin, Flucloxacillin), Oxacillin, Meticillin, Nafcillin, Faropenem, Tomopenem, Razupenem, Cefazolin, Cefacetile, Cefadroxil, Cefalexin, Cefaloglycin, Cefalonium, Cefaloridine, Cefalotin, Cefapirin, Cefatrizine, Cefazedone, Cefazaflur, Cefradine, Cefroxadine, Ceftezole, Cefaclor, Cefamandole, Cefminox, Cefonicid, Ceforanide, Cefotiam, Cefprozil, Cefbuperazone, Cefuroxime, Cefuzonam, Cefoxitin, Cefotetan, Cefmetazole, Loracarbef, Cefixime, Ceftriaxone, Cefcapene, Cefdaloxime, Cefdinir, Cefditoren, Cefetamet, Cefmenoxime, Cefodizime, Cefoperazone, Cefotaxime, Cefpimizole, Cefpiramide, Cefpodoxime, Cefsulodin, Cefteram, Ceftibuten, Ceftiolene, Ceftizoxime, Flomoxef, Latamoxef, Cefepime, Cefozopran, Cefpirome, Cefquinome, Ceftobiprole, Ceftaroline, CXA-101, RWJ-54428, MC-04,546, ME1036, Ceftiofur, Cefquinome, Cefovecin, RWJ-442831, RWJ-333441, and RWJ-333442.

90. The method of claim 88, wherein the β -lactam antibacterial agent is selected from the group consisting of Ceftazidime, Biapenem, Doripenem, Ertapenem, Imipenem, Meropenem, Tebipenem, Tebipenem pivoxil, Apapenem, and Panipenem.

91. The method of claim 88, wherein the β -lactam antibacterial agent is selected from the group consisting of Aztreonam, Tigemonam, BAL30072, SYN 2416, and Carumonam.

92. The method of any one of claims 85 to 91, wherein the subject is a mammal.

93. The method of claim 92, wherein the mammal is a human.

94. The method of any one of claims 85 to 93, wherein the infection comprises a bacteria selected from the group consisting of *Pseudomonas acidovorans*, *Pseudomonas alcaligenes*, *Pseudomonas putida*, *Burkholderia cepacia*, *Aeromonas hydrophilia*, *Francisella tularensis*, *Morganella morganii*, *Proteus mirabilis*, *Proteus vulgaris*, *Providencia alcalifaciens*, *Providencia rettgeri*, *Providencia stuartii*, *Acinetobacter baumannii*, *Bordetella pertussis*,

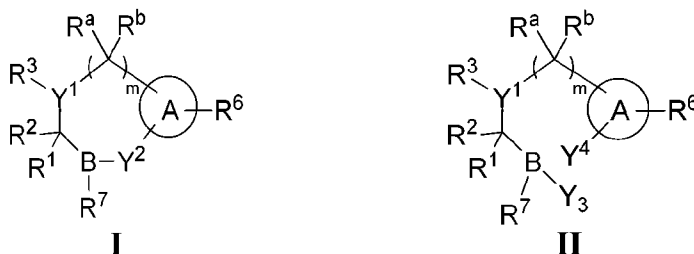
Bordetella pertussis, *Bordetella bronchiseptica*, *Haemophilus ducreyi*, *Pasteurella multocida*, *Pasteurella haemolytica*, *Branhamella catarrhalis*, *Borrelia burgdorferi*, *Kingella*, *Gardnerella vaginalis*, *Bacteroides distasonis*, *Bacteroides 3452A* homology group, *Clostridium difficile*, *Mycobacterium tuberculosis*, *Mycobacterium avium*, *Mycobacterium intracellulare*, *Mycobacterium leprae*, *Corynebacterium diphtheriae*, *Corynebacterium ulcerans*, *Streptococcus pneumoniae*, *Streptococcus agalactiae*, *Streptococcus pyogenes*, *Enterococcus faecalis*, *Enterococcus faecium*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus saprophyticus*, *Staphylococcus intermedius*, *Staphylococcus hyicus* subsp. *hyicus*, *Staphylococcus haemolyticus*, *Staphylococcus hominis*, and *Staphylococcus saccharolyticus*.

95. The method of any one of claims 85 to 93, wherein the infection comprises a bacteria selected from the group consisting of *Pseudomonas aeruginosa*, *Pseudomonas fluorescens*, *Stenotrophomonas maltophilia*, *Escherichia coli*, *Citrobacter freundii*, *Salmonella typhimurium*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella enteritidis*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Enterobacter cloacae*, *Enterobacter aerogenes*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Serratia marcescens*, *Acinetobacter calcoaceticus*, *Acinetobacter haemolyticus*, *Yersinia enterocolitica*, *Yersinia pestis*, *Yersinia pseudotuberculosis*, *Yersinia intermedia*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Haemophilus haemolyticus*, *Haemophilus parahaemolyticus*, *Helicobacter pylori*, *Campylobacter fetus*, *Campylobacter jejuni*, *Campylobacter coli*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Legionella pneumophila*, *Listeria monocytogenes*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Moraxella*, *Bacteroides fragilis*, *Bacteroides vulgatus*, *Bacteroides ovalus*, *Bacteroides thetaiotaomicron*, *Bacteroides uniformis*, *Bacteroides eggerthii*, and *Bacteroides splanchnicus*.

April 25, 2018 Marked up Article 34 Amendment

WHAT IS CLAIMED IS:

1. A compound having the structure of the Formula I or II, or pharmaceutically acceptable salts thereof:



wherein

Y^1 is N or CR^4 ;

m is an integer of 0 or 1;

(a)

R^2 and R^3 together with the atoms to which they are attached form a fused ring or ring system selected from the group consisting of C₃₋₇ cycloalkyl-C₃₋₇ carbocyclyl, and 3-10 membered heterocyclyl, C₆₋₁₀ aryl, and 5-10 membered heteroaryl, each optionally substituted with one or more R^5 , and

each of R^1 , R^4 , R^a , and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀ alkenyl, optionally substituted C₂₋₁₀ alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀ aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇ carbocyclyl)C₁₋₆ alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆ alkyl, optionally substituted (C₆₋₁₀ aryl)C₁₋₆ alkyl, (C₆₋₁₀ aryl)C₁₋₆ alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆ alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, and $-NR^fS(O)_2NR^fOR^d$;

or

(b)

R^3 and R^4 together with the atoms to which they are attached form a spirocyclic ring or ring system selected from the group consisting of C₃₋₇carbocyclyl and 3-10 membered heterocyclyl, each optionally substituted with one or more R^5 , and

each of R^1 , R^2 , R^a , and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, and $-NR^fS(O)_2NR^fOR^d$; or

(c)

R^1 and R^2 together with the atoms to which they are attached form a spirocyclic ring or ring system selected from the group consisting of C₃₋₇carbocyclyl and 3-10 membered heterocyclyl, each optionally substituted with one or more R^5 , and

each of R^3 , R^4 , R^a , and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido,

S-sulfonamido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, and $-NR^fS(O)_2NR^fOR^d$;
or

(d)

R^a and R^b together with the atoms to which they are attached form a spirocyclic ring or ring system selected from the group consisting of C_{3-7} carbocyclyl and 3-10 membered heterocyclyl, each optionally substituted with one or more R^5 , and

each of R^1 , R^2 , R^3 , and R^4 is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(C_{1-6} \text{ alkoxy})C_{1-6}$ alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted $(C_{3-7} \text{ carbocyclyl})C_{1-6}$ alkyl, optionally substituted $(3-10 \text{ membered heterocyclyl})C_{1-6}$ alkyl, optionally substituted $(C_{6-10} \text{ aryl})C_{1-6}$ alkyl, $(C_{6-10} \text{ aryl})C_{1-6}$ alkoxy, optionally substituted $(5-10 \text{ membered heteroaryl})C_{1-6}$ alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, and $-NR^fS(O)_2NR^fOR^d$;
or

(e)

R^a and R^4 together with the atoms to which they are attached form a fused ring or ring system selected from the group consisting of C_{3-7} carbocyclyl and 3-10 membered heterocyclyl, ~~C_{6-10} aryl, and 5-10 membered heteroaryl~~, each optionally substituted with one or more R^5 , and

each of R^1 , R^2 , R^3 , and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(C_{1-6} \text{ alkoxy})C_{1-6}$ alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered

heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d; R⁵ is -Y⁵-(CH₂)_t-G;

t is an integer of 0 or 1;

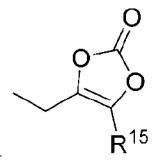
G is selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d;

A is selected from the group consisting of C₃₋₇ carbocyclyl, 3-10 membered heterocyclyl, C₆₋₁₀aryl, and 5-10 membered heteroaryl, each optionally substituted by one or more R¹²;

R⁶ is selected from the group consisting of H, halogen, optionally substituted C₁₋₆ alkyl, OH, -C(O)OR, optionally substituted C₁₋₆ alkoxy, amino, -N(OR⁸)R⁹, optionally substituted C₁₋₆ alkylthiol, C-amido, S-sulfonamido, CN, sulfinyl, sulfonyl, and a carboxylic acid isostere;

R is selected from the group consisting of H, C₁₋₉ alkyl, -CR¹⁰R¹¹OC(O)C₁₋₉alkyl, -CR¹⁰R¹¹OC(O)C₃₋₇carbocyclyl, -CR¹⁰R¹¹OC(O)(3 to 7 membered heterocyclyl), -CR¹⁰R¹¹OC(O)C₂₋₈alkoxyalkyl, -CR¹⁰R¹¹OC(O)OC₁₋₉alkyl, -CR¹⁰R¹¹OC(O)OC₃₋₇carbocyclyl, -CR¹⁰R¹¹OC(O)O(3 to 7 membered heterocyclyl), -CR¹⁰R¹¹OC(O)OC₂₋₈alkoxyalkyl, -CR¹⁰R¹¹OC(O)C₆₋₁₀aryl, -

$\text{CR}^{10}\text{R}^{11}\text{OC(O)OC}_{6-10}\text{aryl}$, $-\text{CR}^{10}\text{R}^{11}\text{C(O)NR}^{13}\text{R}^{14}$, $-\text{CR}^{10}\text{R}^{11}\text{OC(O)O(CH}_2)_1$
 $3\text{C(O)NR}^{13}\text{R}^{14}$, $-\text{CR}^{10}\text{R}^{11}\text{OC(O)O(CH}_2)_{2-3}\text{OC(O)C}_{1-4}\text{ alkyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC(O)O(CH}_2)_1$



$3\text{C(O)OC}_{1-4}\text{ alkyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC(O)(CH}_2)_{1-3}\text{OC(O)C}_{1-4}\text{ alkyl}$, and

R^7 is selected from the group consisting of $-\text{OH}$, optionally substituted C_{1-6} alkoxy, amino, and $-\text{N(OR}^8)\text{R}^9$;

each R^8 and R^9 is independently selected from the group consisting of H, halogen, optionally substituted $\text{C}_{1-4}\text{alkyl}$, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted $\text{C}_{6-10}\text{aryl}$, and optionally substituted 5-10 membered heteroaryl;

each R^{10} and R^{11} is independently selected from the group consisting of H, optionally substituted $\text{C}_{1-4}\text{alkyl}$, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted $\text{C}_{6-10}\text{aryl}$, and optionally substituted 5-10 membered heteroaryl;

R^{12} is selected from the group consisting of hydrogen, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(\text{C}_{1-6}\text{ alkoxy})\text{C}_{1-6}\text{ alkyl}$, optionally substituted $\text{C}_{2-10}\text{alkenyl}$, optionally substituted $\text{C}_{2-10}\text{alkynyl}$, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted $\text{C}_{6-10}\text{aryl}$, optionally substituted 5-10 membered heteroaryl, optionally substituted $(\text{C}_{3-7}\text{carbocyclyl})\text{C}_{1-6}\text{alkyl}$, optionally substituted $(3-10\text{ membered heterocyclyl})\text{C}_{1-6}\text{alkyl}$, optionally substituted $(\text{C}_{6-10}\text{aryl})\text{C}_{1-6}\text{alkyl}$, $(\text{C}_{6-10}\text{aryl})\text{C}_{1-6}\text{alkoxy}$, optionally substituted $(5-10\text{ membered heteroaryl})\text{C}_{1-6}\text{alkyl}$, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, sulfhydryl, $-\text{C(O)(CH}_2)_{0-3}\text{SR}^c$, $-\text{C(O)(CH}_2)_{1-3}\text{R}^d$, $-\text{NR}^f\text{C(O)NR}^f\text{R}^g$, $-\text{NR}^f\text{S(O)}_2\text{NR}^f\text{R}^g$, $-\text{C(=NR}^e)\text{R}^c$, $-\text{C(=NR}^e)\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{CR}^c(\text{=NR}^e)$, $-\text{NR}^f\text{C(=NR}^e)\text{NR}^f\text{R}^g$, $-\text{S(O)(CH}_2)_{1-3}\text{R}^c$, $-\text{NR}^f\text{S(O)}_2\text{NR}^f\text{OR}^d$, and $-(\text{CH}_2)_p\text{-Y}^6\text{-(CH}_2)_q\text{K}$;

each R^{13} and R^{14} is independently selected from the group consisting of H, optionally substituted $\text{C}_{1-6}\text{alkyl}$, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted $\text{C}_{6-10}\text{aryl}$, and optionally substituted 5-10 membered heteroaryl;

R^{15} is optionally substituted C_{1-6} alkyl;

Y^2 is selected from the group consisting of $-\text{O}-$, $-\text{S}-$, and $-\text{NR}^9-$;

Y^3 is selected from the group consisting of -OH, -SH, and -NHR⁹;

Y^4 is selected from the group consisting of -OH, optionally substituted C₁₋₆ alkoxy, amino, and -N(OR⁸)R⁹; and

Y^5 is selected from the group consisting of -S-, -S(O)-, -S(O)₂-, -O-, -CR^fR^g-, and -NR^g-, or Y^5 is absent;

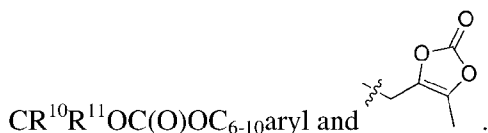
Y^6 is selected from the group consisting of -S-, -S(O)-, -S(O)₂-, -O-, -CR^fR^g-, and -NR^f-;

K is selected from the group consisting of C-amido; N-amido; S-sulfonamido; N-sulfonamido; -NR^fC(O)NR^fR^g; -NR^fS(O)₂NR^fR^g; -C(=NR^e)R^c; -C(=NR^e)NR^fR^g; -NR^fCR^c(=NR^e); -NR^fC(=NR^e)NR^fR^g; C₁₋₄ alkyl optionally substituted with 0-2 substituents selected from the group consisting of C₁₋₄ alkoxy, amino, halogen, C-amido, and N-amido; C₆₋₁₀ aryl optionally substituted with 0-2 substituents selected from the group consisting of C₁₋₄ alkyl, C₁₋₄ alkoxy, amino, halogen, C-amido, and N-amido; C₃₋₇ carbocyclyl optionally substituted with 0-2 substituents selected from the group consisting of C₁₋₄ alkyl, C₁₋₄ alkoxy, amino, halogen, C-amido, and N-amido; 5-10 membered heteroaryl optionally substituted with 0-2 substituents selected from the group consisting of C₁₋₄ alkyl, C₁₋₄ alkoxy, amino, halogen, C-amido, and N-amido; and 3-10 membered heterocyclyl optionally substituted with 0-2 substituents selected from the group consisting of C₁₋₄ alkyl, C₁₋₄ alkoxy, amino, halogen, C-amido, and N-amido;

each R^c, R^d, R^e, R^f, and R^g are independently selected from the group consisting of H, halogen, optionally substituted C₁₋₄alkyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, and optionally substituted 5-10 membered heteroaryl; and

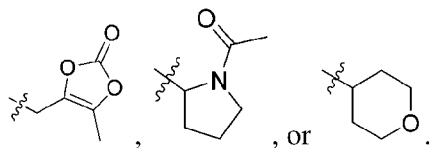
each p and q is independently 0 or 1.

2. The compound of claim 1, wherein R is selected from H, C₁₋₉ alkyl, -CR¹⁰R¹¹OC(O)C₁₋₉alkyl, -CR¹⁰R¹¹OC(O)OC₁₋₉alkyl, -CR¹⁰R¹¹OC(O)C₆₋₁₀aryl, -



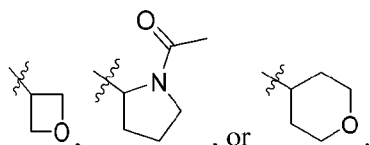
3. The compound of claim 1, wherein R is -CR¹⁰R¹¹OC(O)C₁₋₉alkyl, -CR¹⁰R¹¹OC(O)C₃₋₇carbocyclyl, -CR¹⁰R¹¹OC(O)(3 to 7 membered heterocyclyl), or -CR¹⁰R¹¹OC(O)C₂₋₈alkoxyalkyl.

4. The compound of claim 3, wherein the 3 to 7 membered heterocyclyl of R is



5. The compound of claim 1, wherein R is $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{OC}_{1-9}\text{alkyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{OC}_{3-7}\text{carbocyclyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{O}(3 \text{ to } 7 \text{ membered heterocyclyl})$, or $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{OC}_{2-8}\text{alkoxyalkyl}$.

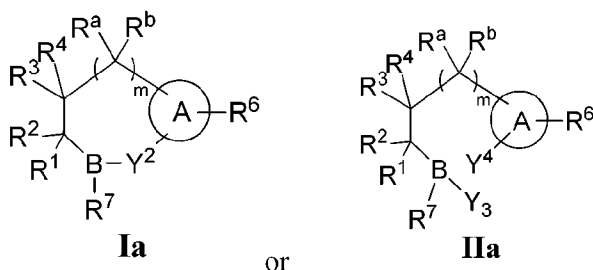
6. The compound of claim 5, wherein the 3 to 7 membered heterocyclyl of R is



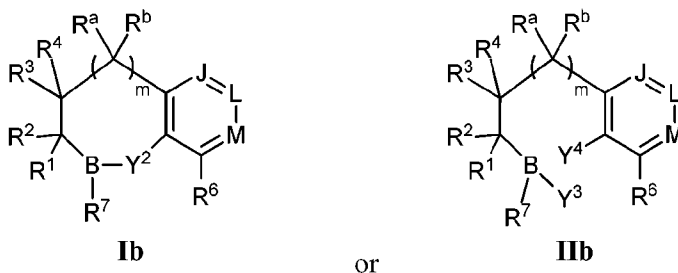
7. The compound of claim 1, wherein R is $-\text{CR}^{10}\text{R}^{11}\text{C}(\text{O})\text{NR}^{13}\text{R}^{14}$.
8. The compound of claim 1, wherein R is $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{O}(\text{CH}_2)_{1-3}\text{C}(\text{O})\text{NR}^{13}\text{R}^{14}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{O}(\text{CH}_2)_{2-3}\text{OC}(\text{O})\text{C}_{1-4}\text{alkyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})(\text{CH}_2)_{1-3}\text{OC}(\text{O})\text{C}_{1-4}\text{alkyl}$, or $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{O}(\text{CH}_2)_{1-3}\text{C}(\text{O})\text{OC}_{1-4}\text{alkyl}$.

9. The compound of any one of claims 3 to 8, wherein each R^{10} and R^{11} is independently hydrogen or C_{1-6} alkyl.

10. The compound of any one of claims 1 to 9, having the structure of Formula Ia or IIa, or pharmaceutically acceptable salts thereof:



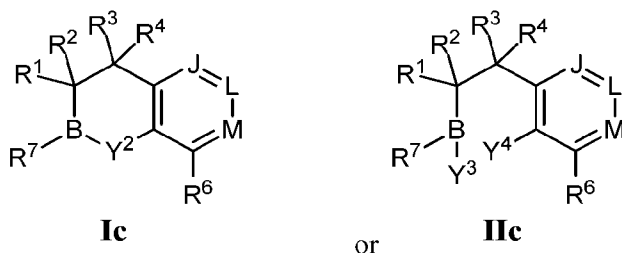
11. The compound of claim 10, having the structure of Formula Ib or IIb, or pharmaceutically acceptable salts thereof:



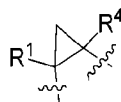
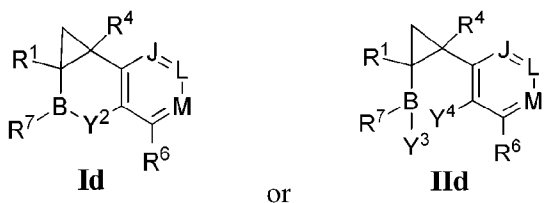
wherein each J, L, M is independently CR^{12} or N (nitrogen).

12. The compound of claim 11, having the structure of Formula Ic or IIc, or

pharmaceutically acceptable salts thereof:

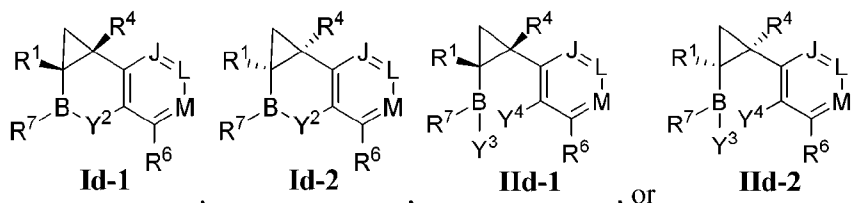


13. The compound of any claim 11 or 12, wherein each J, L and M is CR¹².
14. The compound of claim 13, wherein R¹² is hydrogen, halogen, C₁₋₆ alkoxy, or C₁₋₆ haloalkoxy.
15. The compound of claim 11 or 12, wherein at least one of J, L and M is N.
16. The compound of claim 15, wherein M is N.
17. The compound of any one of claims 1 to 16, wherein R² and R³ together with the atoms to which they are attached form a ring or ring system selected from the group consisting of ~~C₃₋₇ carbocyclyl~~, C₃₋₇ cycloalkyl, and 3-10 membered heterocyclyl, ~~C₆₋₁₀ aryl~~, and ~~5-10 membered heteroaryl~~, each optionally substituted with one or more R⁵.
18. The compound of claim 17, wherein R² and R³ together with the atoms to which they are attached form C₃₋₇ cycloalkyl~~C₃₋₇ carbocyclyl~~ optionally substituted with one or more R⁵.
19. The compound of claim 18, wherein R² and R³ together with the atoms to which they are attached form cyclopropyl, bicyclo[2.2.1]heptyl, bicyclo[2.2.1]heptenyl, tetrahydrofuranyl, or dihydrofuranyl, each optionally substituted with one or more R⁵.
20. The compound of claim 18 or 19, having the structure of Formula Id or IId, or pharmaceutically acceptable salts thereof:



wherein the cyclopropyl moiety is optionally substituted with one or more R⁵.

21. The compound of claim 20, having the structure of Formula Id-1, Id-2, IId-1 or IId-2, or pharmaceutically acceptable salts thereof:



22. The compound of any one of claims 1 to 21, wherein R^1 is hydrogen or C_{1-6} hydroxyalkyl.

23. The compound of any one of claims 1 to 22, wherein R^4 is hydrogen.

24. The compound of any one of claims 1 to 16, wherein R^3 and R^4 together with the atoms to which they are attached form a ring or ring system selected from the group consisting of C_{3-7} carbocyclyl and 3-10 membered heterocyclyl, each optionally substituted with one or more R^5 .

25. The compound of claim 24, wherein R^3 and R^4 together with the atoms to which they are attached form C_{3-7} carbocyclyl, optionally substituted with one or more R^5 .

26. The compound of claim 25, wherein R^3 and R^4 together with the atoms to which they are attached form cyclopropyl optionally substituted with one or more R^5 .

27. The compound of any one of claims 24 to 26, wherein R^1 is hydrogen.

28. The compound of any one of claims 24 to 27, wherein R^2 is hydrogen.

29. The compound of any one of claims 1 to 28, wherein R^6 is $-C(O)OR$.

30. The compound of claim 29, wherein R is H.

31. The compound of any one of claims 1 to 30, wherein R^7 is $-OH$.

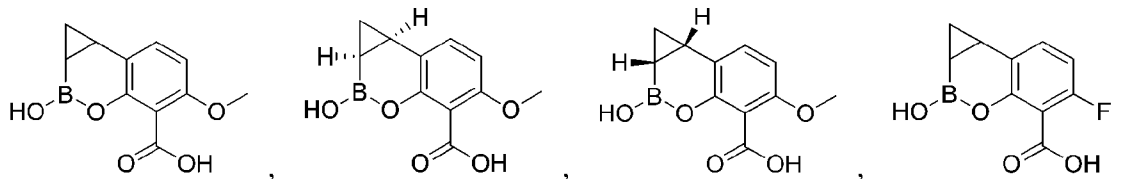
32. The compound of any one of claims 1 to 31, wherein Y^2 is $-O-$.

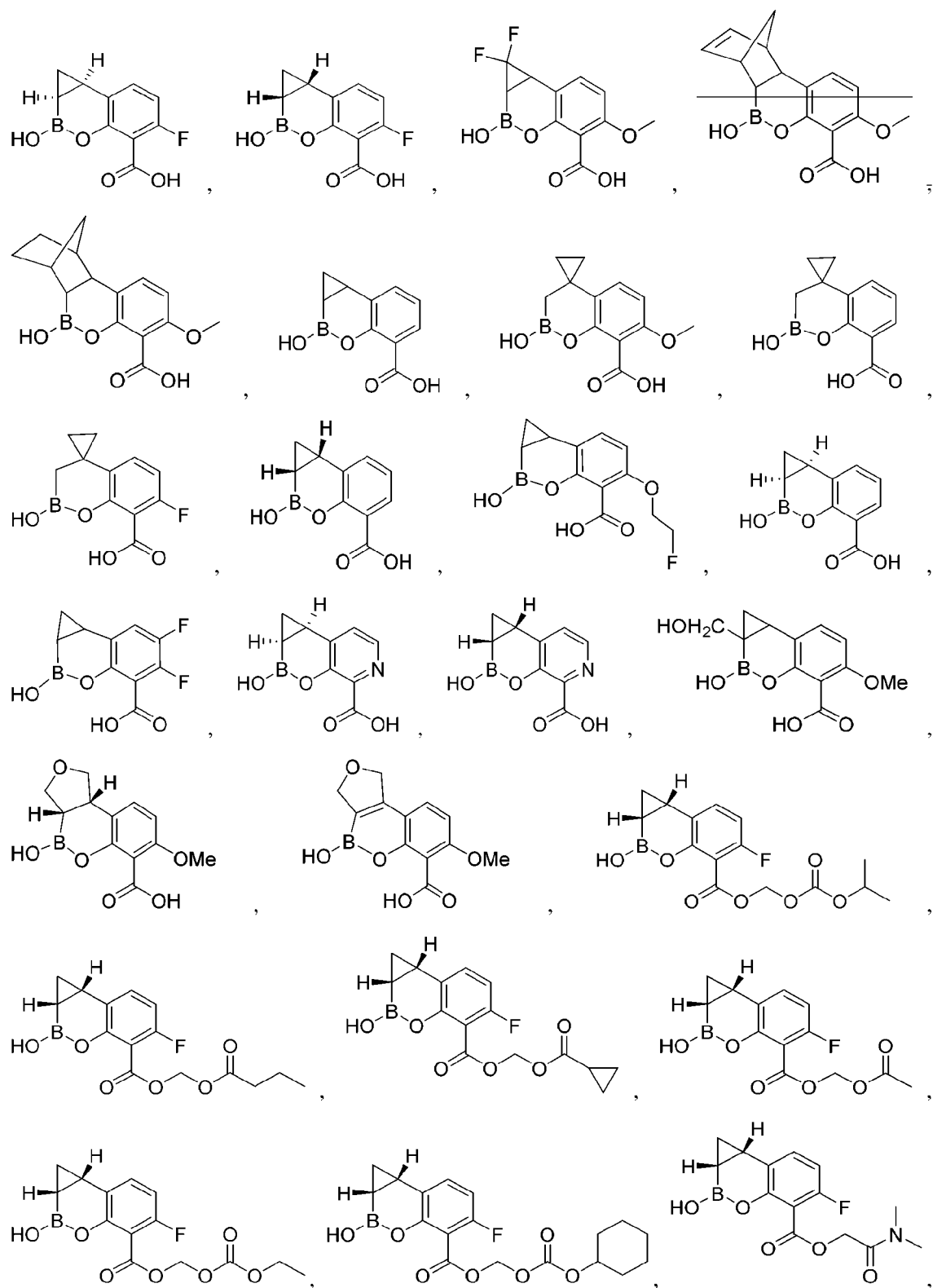
33. The compound of any one of claims 1 to 32, wherein Y^3 is $-OH$.

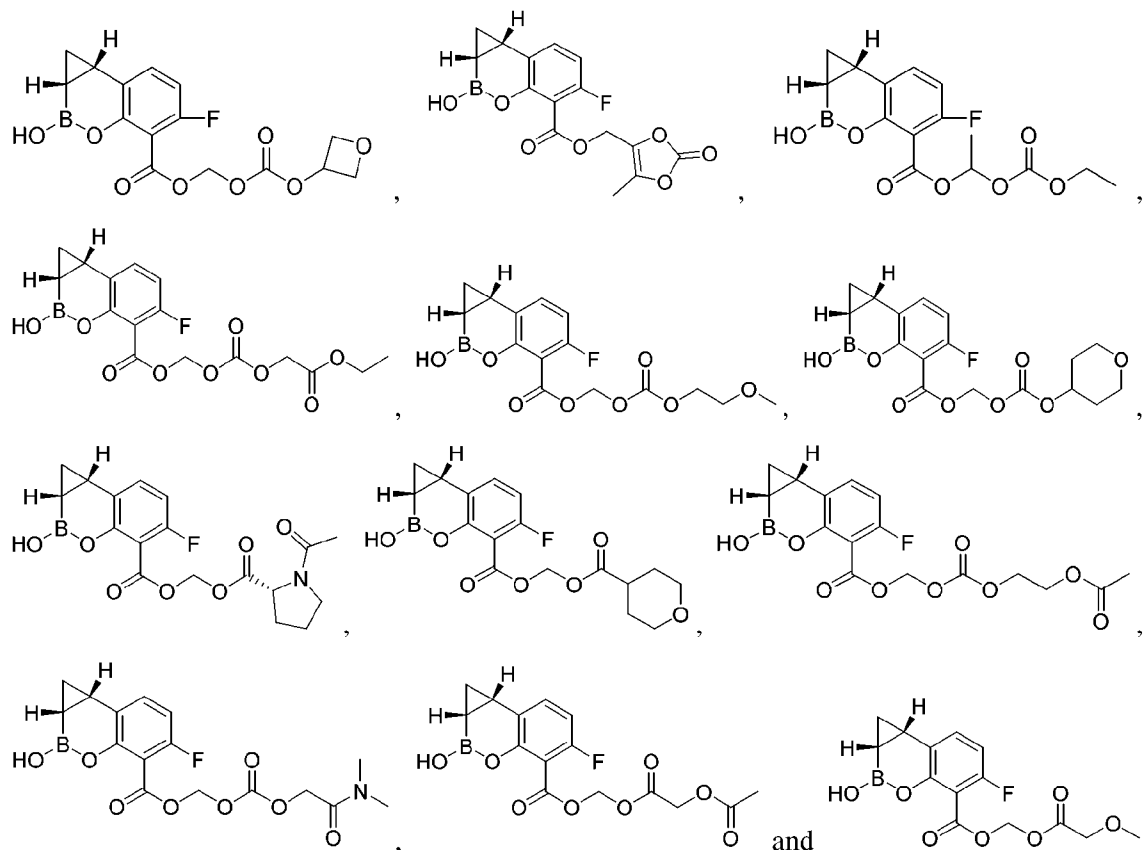
34. The compound of any one of claims 1 to 33, wherein Y^4 is $-OH$.

35. The compound of any one of claims 1 to 34, wherein Y^5 is absent and t is 0, and R^5 is selected from the group consisting of amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkoxy, acyl, C-carboxy, C-amido, N-amido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, and $-NR^fS(O)_2NR^fOR^d$.

36. The compound of claim 1, selected from the group consisting of

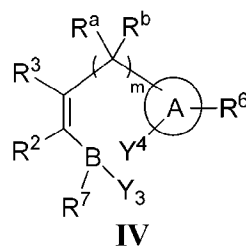
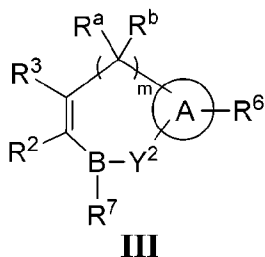






or pharmaceutically acceptable salts thereof.

37. A compound having the structure of the Formula III or IV, or pharmaceutically acceptable salts thereof:



wherein

(a)

each of R^2 and R^3 is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(C_{1-6} \text{ alkoxy})C_{1-6}$ alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl,

optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d, or R² and R³ together with the atoms to which they are attached form a fused ring or ring system selected from the group consisting of C₃₋₇carbocyclyl, 3-10 membered heterocyclyl, C₆₋₁₀ aryl, and 5-10 membered heteroaryl, each optionally substituted with one or more R⁵;

m is an integer of 0 or 1; and

each R^a and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d, or R^a and R^b together with the atoms to which they are attached form a ring or ring system selected from the group consisting of C₃₋₇carbocyclyl and 3-10 membered heterocyclyl, each optionally substituted with one or more R⁵; or

(b)

m is 1;

R^a and R³ together with the atoms to which they are attached form a ring or ring system selected from the group consisting of C₃₋₇carbocyclyl and 3-10 membered heterocyclyl, each optionally substituted with one or more R⁵; and

each R² and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally

substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d;

R⁵ is -Y⁵-(CH₂)_t-G;

t is an integer of 0 or 1;

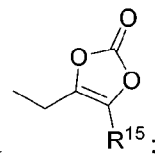
G is selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d;

A is a ring system selected from the group consisting of C₃₋₇ carbocyclyl, 3-10 membered heterocyclyl, C₆₋₁₀aryl, and 5-10 membered heteroaryl, each optionally substituted with one or more R¹²;

R⁶ is selected from the group consisting of H, halogen, optionally substituted C₁₋₆ alkyl, OH, -C(O)OR, optionally substituted C₁₋₆ alkoxy, amino, -N(OR⁸)R⁹, optionally substituted C₁₋₆ alkylthiol, C-amido, S-sulfonamido, CN, sulfinyl, sulfonyl, and a carboxylic acid isostere;

R is selected from the group consisting of H, C₁₋₉ alkyl, -CR¹⁰R¹¹OC(O)C₁₋₉alkyl, -CR¹⁰R¹¹OC(O)C₃₋₇carbocyclyl, -CR¹⁰R¹¹OC(O)(3 to 7 membered heterocyclyl), -CR¹⁰R¹¹OC(O)C₂₋₈alkoxyalkyl, -CR¹⁰R¹¹OC(O)OC₁₋₉alkyl, -CR¹⁰R¹¹OC(O)OC₃₋₇carbocyclyl, -CR¹⁰R¹¹OC(O)O(3 to 7 membered heterocyclyl), -CR¹⁰R¹¹OC(O)OC₂₋₈alkoxyalkyl, -CR¹⁰R¹¹OC(O)C₆₋₁₀aryl, -CR¹⁰R¹¹OC(O)OC₆₋₁₀aryl, -CR¹⁰R¹¹C(O)NR¹³R¹⁴, -CR¹⁰R¹¹OC(O)O(CH₂)₁₋₃C(O)NR¹³R¹⁴, -CR¹⁰R¹¹OC(O)O(CH₂)₂₋₃OC(O)C₁₋₄alkyl, -CR¹⁰R¹¹OC(O)O(CH₂)₁₋

₃C(O)OC₁₋₄alkyl, -CR¹⁰R¹¹OC(O)(CH₂)₁₋₃OC(O)C₁₋₄alkyl, and



R⁷ is selected from the group consisting of -OH, optionally substituted C₁₋₆alkoxy, amino, and -N(OR⁸)R⁹;

each R⁸ and R⁹ is independently selected from the group consisting of H, halogen, optionally substituted C₁₋₄alkyl, optionally substituted C₃₋₇carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, and optionally substituted 5-10 membered heteroaryl;

each R¹⁰ and R¹¹ is independently selected from the group consisting of H, optionally substituted C₁₋₄alkyl, optionally substituted C₃₋₇carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, and optionally substituted 5-10 membered heteroaryl;

R¹² is selected from the group consisting of hydrogen, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆alkyl, optionally substituted C₁₋₆haloalkyl, optionally substituted C₁₋₆alkoxy, optionally substituted C₁₋₆haloalkoxy, optionally substituted C₁₋₆alkylthiol, optionally substituted (C₁₋₆alkoxy)C₁₋₆alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, sulfhydryl, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^e(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, -NR^fS(O)₂NR^fOR^d, and -(CH₂)_p-Y⁶-(CH₂)_qK;

each R^{13} and R^{14} is independently selected from the group consisting of H, optionally substituted C_{1-6} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

R^{15} is optionally substituted C_{1-6} alkyl;

Y^2 is selected from the group consisting of -O-, -S-, and -NR⁹-;

Y^3 is selected from the group consisting of -OH, -SH, and -NHR⁹;

Y^4 is selected from the group consisting of -OH, optionally substituted C_{1-6} alkoxy, amino, and -N(OR⁸)R⁹;

Y^5 is selected from the group consisting of -S-, -S(O)-, -S(O)₂-, -O-, -CR^fR^g-, and -NR^g-, or Y^5 is absent;

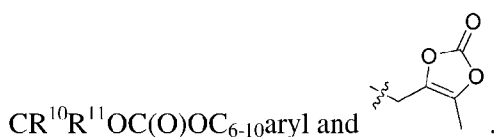
Y^6 is selected from the group consisting of -S-, -S(O)-, -S(O)₂-, -O-, -CR^fR^g-, and -NR^f-;

K is selected from the group consisting of C-amido; N-amido; S-sulfonamido; N-sulfonamido; -NR^fC(O)NR^fR^g; -NR^fS(O)₂NR^fR^g; -C(=NR^e)R^c; -C(=NR^e)NR^fR^g; -NR^fCR^c(=NR^e); -NR^fC(=NR^e)NR^fR^g; C_{1-4} alkyl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; C_{6-10} aryl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; C_{3-7} carbocyclyl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; 5-10 membered heteroaryl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; and 3-10 membered heterocyclyl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido;

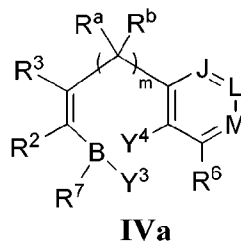
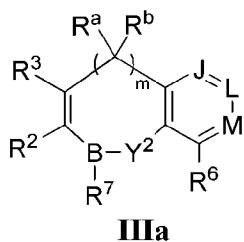
each R^c, R^d, R^e, R^f, and R^g are independently selected from the group consisting of H, halogen, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl; and

each p and q is independently 0 or 1.

38. The compound of claim 37, wherein R is selected from H, C_{1-9} alkyl, -CR¹⁰R¹¹OC(O) C_{1-9} alkyl, -CR¹⁰R¹¹OC(O)OC₁₋₉alkyl, -CR¹⁰R¹¹OC(O) C_{6-10} aryl, -

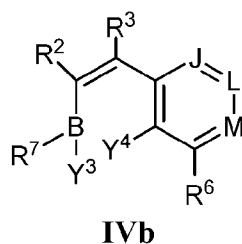
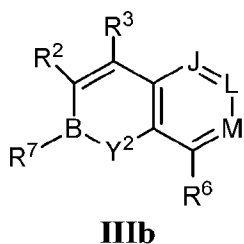


39. The compound of claim 37 or 38, having the structure Formula IIIa or IVa, or pharmaceutically acceptable salts thereof:



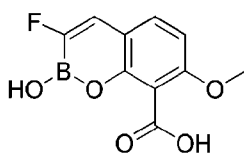
wherein each J, L, M is independently CR¹² or N.

40. The compound of claim 39, having the structure of Formula IIIb or IVb, or pharmaceutically acceptable salts thereof:

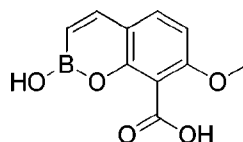


41. The compound of claim 39 or 40, wherein each J, L and M is CR¹².
42. The compound of any one of claims 37 to 41, wherein R² is hydrogen, halogen, or C₁₋₆ alkyl.
43. The compound of any one of claims 37 to 42, wherein R³ is hydrogen.
44. The compound of any one of claims 37 to 43, wherein R⁶ is -C(O)OR.
45. The compound of claim 44, wherein R is H.
46. The compound of any one of claims 37 to 45, wherein R⁷ is -OH.
47. The compound of any one of claims 37 to 46, wherein Y² is -O-.
48. The compound of any one of claims 37 to 47, wherein Y³ is -OH.
49. The compound of any one of claims 37 to 48, wherein Y⁴ is -OH.
50. The compound of any one of claims 37 to 49, wherein R¹² is hydrogen, halogen or C₁₋₆ alkoxy.

51. The compound of claim 37, selected from the group consisting of

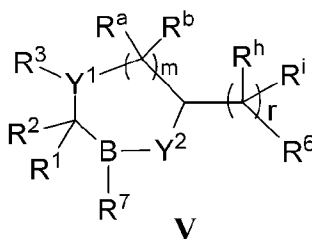


and



, or pharmaceutically acceptable salts thereof.

52. A compound having the structure of Formula V, or pharmaceutically acceptable salts thereof:



wherein

Y^1 is N or CR^4 ;

m is an integer of 0 or 1;

r is an integer of 0 or 1;

(a)

R^2 and R^3 together with the atoms to which they are attached form a fused ring or ring system selected from the group consisting of C_{3-7} carbocyclyl, 3-10 membered heterocyclyl, C_{6-10} aryl, and 5-10 membered heteroaryl, each optionally substituted with one or more R^5 , and

each of R^1 , R^4 , R^a , and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(C_{1-6}$ alkoxy) C_{1-6} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted $(C_{3-7}$ carbocyclyl) C_{1-6} alkyl, optionally substituted (3-10 membered heterocyclyl) C_{1-6} alkyl, optionally substituted $(C_{6-10}$ aryl) C_{1-6} alkyl, $(C_{6-10}$ aryl) C_{1-6} alkoxy, optionally substituted (5-10 membered heteroaryl) C_{1-6} alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, and $-NR^fS(O)_2NR^fOR^d$;

or

(b)

R^3 and R^4 together with the atoms to which they are attached form a spirocyclic ring or ring system selected from the group consisting of C_3 -

γ carbocyclyl, and 3-10 membered heterocyclyl, each optionally substituted with one or more R^5 , and

each of R^1 , R^2 , R^a , and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(C_{1-6} \text{ alkoxy})C_{1-6}$ alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted $(C_{3-7}\text{carbocyclyl})C_{1-6}$ alkyl, optionally substituted $(3-10 \text{ membered heterocyclyl})C_{1-6}$ alkyl, optionally substituted $(C_{6-10}\text{aryl})C_{1-6}$ alkyl, $(C_{6-10}\text{aryl})C_{1-6}$ alkoxy, optionally substituted $(5-10 \text{ membered heteroaryl})C_{1-6}$ alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, and $-NR^fS(O)_2NR^fOR^d$;

or

(c)

R^1 and R^2 together with the atoms to which they are attached form a spirocyclic ring or ring system selected from the group consisting of C_{3-7} carbocyclyl, and 3-10 membered heterocyclyl, each optionally substituted with one or more R^5 , and

each of R^3 , R^4 , R^a , and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(C_{1-6} \text{ alkoxy})C_{1-6}$ alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted $(C_{3-7}\text{carbocyclyl})C_{1-6}$ alkyl, optionally substituted $(3-10 \text{ membered heterocyclyl})C_{1-6}$ alkyl, optionally substituted $(C_{6-10}\text{aryl})C_{1-6}$ alkyl, $(C_{6-10}\text{aryl})C_{1-6}$ alkoxy, optionally substituted $(5-10 \text{ membered heteroaryl})C_{1-6}$ alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, -

$\text{NR}^f\text{CR}^e(=\text{NR}^e)$, $-\text{NR}^f\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{S}(\text{O})(\text{CH}_2)_{1-3}\text{R}^c$, and $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{OR}^d$;
or

(d)

R^a and R^b together with the atoms to which they are attached form a spirocyclic ring or ring system selected from the group consisting of C_{3-7} carbocyclyl, and 3-10 membered heterocyclyl, each optionally substituted with one or more R^5 , and

each of R^1 , R^2 , R^3 , and R^4 is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(\text{C}_{1-6} \text{ alkoxy})\text{C}_{1-6}$ alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted $(\text{C}_{3-7}\text{carbocyclyl})\text{C}_{1-6}$ alkyl, optionally substituted $(3-10 \text{ membered heterocyclyl})\text{C}_{1-6}$ alkyl, optionally substituted $(\text{C}_{6-10}\text{aryl})\text{C}_{1-6}$ alkyl, $(\text{C}_{6-10}\text{aryl})\text{C}_{1-6}$ alkoxy, optionally substituted $(5-10 \text{ membered heteroaryl})\text{C}_{1-6}$ alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-\text{SR}^c$, $-\text{C}(\text{O})(\text{CH}_2)_{0-3}\text{SR}^c$, $-\text{C}(\text{O})(\text{CH}_2)_{1-3}\text{R}^d$, $-\text{NR}^f\text{C}(\text{O})\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{R}^g$, $-\text{C}(=\text{NR}^e)\text{R}^c$, $-\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{CR}^e(=\text{NR}^e)$, $-\text{NR}^f\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{S}(\text{O})(\text{CH}_2)_{1-3}\text{R}^c$, and $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{OR}^d$;
or

(e)

R^a and R^4 together with the atoms to which they are attached form a fused ring or ring system selected from the group consisting of C_{3-7} carbocyclyl, 3-10 membered heterocyclyl, C_{6-10} aryl, and 5-10 membered heteroaryl, each optionally substituted with one or more R^5 , and

each of R^1 , R^2 , R^3 , and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(\text{C}_{1-6} \text{ alkoxy})\text{C}_{1-6}$ alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted $(\text{C}_{3-7}\text{carbocyclyl})\text{C}_{1-6}$ alkyl,

optionally substituted (3-10 membered heterocyclyl) C_{1-6} alkyl, optionally substituted (C_{6-10} aryl) C_{1-6} alkyl, (C_{6-10} aryl) C_{1-6} alkoxy, optionally substituted (5-10 membered heteroaryl) C_{1-6} alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, and $-NR^fS(O)_2NR^fOR^d$; R^5 is $-Y^5-(CH_2)_t-G$;

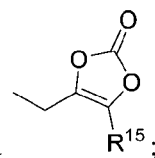
t is an integer of 0 or 1;

G is selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted (C_{1-6} alkoxy) C_{1-6} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C_{3-7} carbocyclyl) C_{1-6} alkyl, optionally substituted (3-10 membered heterocyclyl) C_{1-6} alkyl, optionally substituted (C_{6-10} aryl) C_{1-6} alkyl, (C_{6-10} aryl) C_{1-6} alkoxy, optionally substituted (5-10 membered heteroaryl) C_{1-6} alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, and $-NR^fS(O)_2NR^fOR^d$;

R^6 is selected from the group consisting of optionally substituted $-(CH_2)_nC(O)OR$ and a carboxylic acid isostere;

n is an integer selected from 0 to 6;

R is selected from the group consisting of H, C_{1-9} alkyl, $-CR^{10}R^{11}OC(O)C_{1-9}$ alkyl, $-CR^{10}R^{11}OC(O)C_{3-7}$ carbocyclyl, $-CR^{10}R^{11}OC(O)(3$ to 7 membered heterocyclyl), $-CR^{10}R^{11}OC(O)C_{2-8}$ alkoxyalkyl, $-CR^{10}R^{11}OC(O)OC_{1-9}$ alkyl, $-CR^{10}R^{11}OC(O)OC_{3-7}$ carbocyclyl, $-CR^{10}R^{11}OC(O)O(3$ to 7 membered heterocyclyl), $-CR^{10}R^{11}OC(O)OC_{2-8}$ alkoxyalkyl, $-CR^{10}R^{11}OC(O)C_{6-10}$ aryl, $-CR^{10}R^{11}OC(O)OC_{6-10}$ aryl, $-CR^{10}R^{11}C(O)NR^{13}R^{14}$, $-CR^{10}R^{11}OC(O)O(CH_2)_{1-3}C(O)NR^{13}R^{14}$, $-CR^{10}R^{11}OC(O)O(CH_2)_{2-3}OC(O)C_{1-4}$ alkyl, $-CR^{10}R^{11}OC(O)O(CH_2)_{1-3}C(O)OC_{1-4}$ alkyl, $-CR^{10}R^{11}OC(O)(CH_2)_{1-3}OC(O)C_{1-4}$ alkyl, and



$-CR^{10}R^{11}OC(O)(CH_2)_{1-3}OC(O)C_{1-4}$ alkyl, and

R^7 is selected from the group consisting of -OH, optionally substituted C_{1-6} alkoxy, amino, and $-N(OR^8)R^9$;

each R^8 and R^9 is independently selected from the group consisting of H, halogen, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

each R^{10} and R^{11} is independently selected from the group consisting of H, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

each R^{13} and R^{14} is independently selected from the group consisting of H, optionally substituted C_{1-6} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

R^{15} is optionally substituted C_{1-6} alkyl;

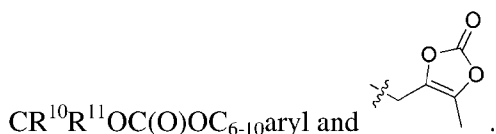
Y^2 is selected from the group consisting of -O-, -S-, and $-NR^9$ -;

Y^5 is selected from the group consisting of -S-, $-S(O)-$, $-S(O)_2-$, -O-, $-CR^fR^g$ -, and $-NR^g$ -, or Y^5 is absent;

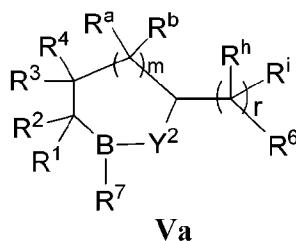
each R^c , R^d , R^e , R^f , and R^g are independently selected from the group consisting of H, halogen, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl; and

each R^h and R^i is independently selected from the group consisting of H, halogen, cyano, amino, C-amido, N-amido, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl; or R^h and R^i together with the atoms to which they are attached form a spirocyclic ring or ring system selected from the group consisting of C_{3-7} carbocyclyl, 3-10 membered heterocyclyl, C_{6-10} aryl, and 5-10 membered heteroaryl, each optionally substituted with one or more R^5 .

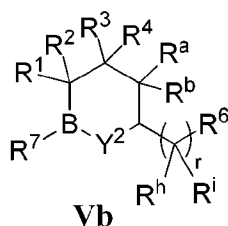
53. The compound of claim 52, wherein R is selected from H, C_{1-9} alkyl, $-CR^{10}R^{11}OC(O)C_{1-9}$ alkyl, $-CR^{10}R^{11}OC(O)OC_{1-9}$ alkyl, $-CR^{10}R^{11}OC(O)C_{6-10}$ aryl, -



54. The compound of claim 52 or 53, having the structure of Formula Va, or pharmaceutically acceptable salts thereof:



55. The compound of claim 54, having the structure of Formula Vb, or pharmaceutically acceptable salts thereof:



56. The compound of any one of claims 52 to 55, wherein both R^a and R^b are H.

57. The compound of any one of claims 52 to 56, wherein R² and R³ together with the atoms to which they are attached form a ring or ring system selected from the group consisting of C₃₋₇ carbocyclyl, 3-10 membered heterocyclyl, C₆₋₁₀ aryl, and 5-10 membered heteroaryl, each optionally substituted with one or more R⁵.

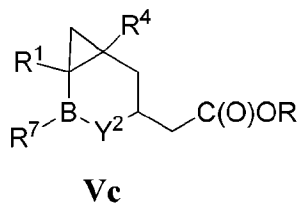
58. The compound of claim 57, wherein R² and R³ together with the atoms to which they are attached form C₃₋₇carbocyclyl optionally substituted with one or more R⁵.

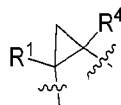
59. The compound of claim 58, wherein R² and R³ together with the atoms to which they are attached form cyclopropyl optionally substituted with one or more R⁵.

60. The compound of any one of claims 52 to 59, wherein r is 1, and both R^h and Rⁱ are H.

61. The compound of any one of claims 52 to 60, wherein R⁶ is -(CH₂)_nC(O)OR and n is 0.

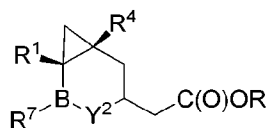
62. The compound of claim 61, having the structure of Formula Vc, or pharmaceutically acceptable salts thereof:



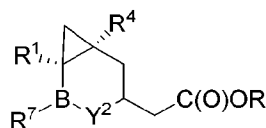


wherein the cyclopropyl moiety is optionally substituted with one or more R^5 .

63. The compound of claim 62, having the structure of Formula Vc-1 or Vc-2, or pharmaceutically acceptable salts thereof:



Vc-1

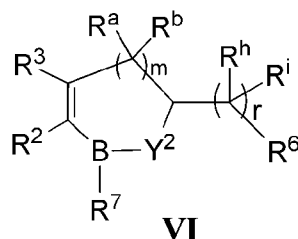


Vc-2

64. The compound of any one of any one of claims 52 to 63, wherein Y^2 is -O-.

65. The compound of any one of claims 52 to 64, wherein R^7 is -OH.

66. A compound having the structure of Formula VI, or pharmaceutically acceptable salts thereof:



VI

wherein

r is an integer of 0 or 1;

(a)

each of R^2 and R^3 is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted $(C_{1-6} \text{ alkoxy})C_{1-6}$ alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10} alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted $(C_{3-7}\text{carbocyclyl})C_{1-6}$ alkyl, optionally substituted (3-10 membered heterocyclyl) C_{1-6} alkyl, optionally substituted $(C_{6-10}\text{aryl})C_{1-6}$ alkyl, $(C_{6-10}\text{aryl})C_{1-6}$ alkoxy, optionally substituted (5-10 membered heteroaryl) C_{1-6} alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, and $-NR^fS(O)_2NR^fOR^d$, or R^2 and R^3 together with the atoms to

which they are attached form a fused ring or ring system selected from the group consisting of C₃₋₇carbocyclyl and 3-10 membered heterocyclyl, each optionally substituted with one or more R⁵;

m is an integer of 0 or 1;

each R^a and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋₁₀aryl)C₁₋₆alkoxy, optionally substituted (5-10 membered heteroaryl)C₁₋₆alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, -SR^c, -C(O)(CH₂)₀₋₃SR^c, -C(O)(CH₂)₁₋₃R^d, -NR^fC(O)NR^fR^g, -NR^fS(O)₂NR^fR^g, -C(=NR^e)R^c, -C(=NR^e)NR^fR^g, -NR^fCR^c(=NR^e), -NR^fC(=NR^e)NR^fR^g, -S(O)(CH₂)₁₋₃R^c, and -NR^fS(O)₂NR^fOR^d, or R^a and R^b together with the atoms to which they are attached form a ring or ring system selected from the group consisting of C₃₋₇carbocyclyl, and 3-10 membered heterocyclyl, each optionally substituted with one or more R⁵; or

(b)

m is 1;

R^a and R³ together with the atoms to which they are attached form a ring or ring system selected from the group consisting of C₃₋₇carbocyclyl, and 3-10 membered heterocyclyl, each optionally substituted with one or more R⁵; and

each R² and R^b is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C₁₋₆ alkyl, optionally substituted C₁₋₆ haloalkyl, optionally substituted C₁₋₆ alkoxy, optionally substituted C₁₋₆ haloalkoxy, optionally substituted (C₁₋₆ alkoxy)C₁₋₆ alkyl, optionally substituted C₂₋₁₀alkenyl, optionally substituted C₂₋₁₀alkynyl, optionally substituted C₃₋₇ carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C₆₋₁₀aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C₃₋₇carbocyclyl)C₁₋₆alkyl, optionally substituted (3-10 membered heterocyclyl)C₁₋₆alkyl, optionally substituted (C₆₋₁₀aryl)C₁₋₆alkyl, (C₆₋

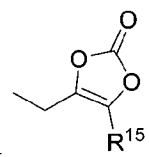
$_{10}\text{aryl})\text{C}_{1-6}\text{alkoxy}$, optionally substituted (5-10 membered heteroaryl) $\text{C}_{1-6}\text{alkyl}$, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-\text{SR}^c$, $-\text{C}(\text{O})(\text{CH}_2)_{0-3}\text{SR}^c$, $-\text{C}(\text{O})(\text{CH}_2)_{1-3}\text{R}^d$, $-\text{NR}^f\text{C}(\text{O})\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{R}^g$, $-\text{C}(=\text{NR}^e)\text{R}^c$, $-\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{CR}^c(=\text{NR}^e)$, $-\text{NR}^f\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{S}(\text{O})(\text{CH}_2)_{1-3}\text{R}^c$, and $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{OR}^d$;
 R^5 is $-\text{Y}^5-(\text{CH}_2)_t-\text{G}$;
 t is an integer of 0 or 1;

G is selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted (C_{1-6} alkoxy) C_{1-6} alkyl, optionally substituted $\text{C}_{2-10}\text{alkenyl}$, optionally substituted $\text{C}_{2-10}\text{alkynyl}$, optionally substituted $\text{C}_{3-7}\text{carbocyclyl}$, optionally substituted 3-10 membered heterocyclyl, optionally substituted $\text{C}_{6-10}\text{aryl}$, optionally substituted 5-10 membered heteroaryl, optionally substituted ($\text{C}_{3-7}\text{carbocyclyl})\text{C}_{1-6}\text{alkyl}$, optionally substituted (3-10 membered heterocyclyl) $\text{C}_{1-6}\text{alkyl}$, optionally substituted ($\text{C}_{6-10}\text{aryl})\text{C}_{1-6}\text{alkyl}$, ($\text{C}_{6-10}\text{aryl})\text{C}_{1-6}\text{alkoxy}$, optionally substituted (5-10 membered heteroaryl) $\text{C}_{1-6}\text{alkyl}$, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-\text{SR}^c$, $-\text{C}(\text{O})(\text{CH}_2)_{0-3}\text{SR}^c$, $-\text{C}(\text{O})(\text{CH}_2)_{1-3}\text{R}^d$, $-\text{NR}^f\text{C}(\text{O})\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{R}^g$, $-\text{C}(=\text{NR}^e)\text{R}^c$, $-\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{CR}^c(=\text{NR}^e)$, $-\text{NR}^f\text{C}(=\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{S}(\text{O})(\text{CH}_2)_{1-3}\text{R}^c$, and $-\text{NR}^f\text{S}(\text{O})_2\text{NR}^f\text{OR}^d$;

R^6 is selected from the group consisting of optionally substituted $-(\text{CH}_2)_n\text{C}(\text{O})\text{OR}$ and a carboxylic acid isostere;

n is an integer selected from 0 to 6;

R is selected from the group consisting of H, C_{1-9} alkyl, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{C}_{1-9}\text{alkyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{C}_{3-7}\text{carbocyclyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})(3 \text{ to } 7 \text{ membered heterocyclyl})$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{C}_{2-8}\text{alkoxyalkyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{OC}_{1-9}\text{alkyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{OC}_{3-7}\text{carbocyclyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{O}(3 \text{ to } 7 \text{ membered heterocyclyl})$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{OC}_{2-8}\text{alkoxyalkyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{C}_{6-10}\text{aryl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{OC}_{6-10}\text{aryl}$, $-\text{CR}^{10}\text{R}^{11}\text{C}(\text{O})\text{NR}^{13}\text{R}^{14}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{O}(\text{CH}_2)_{1-3}\text{C}(\text{O})\text{NR}^{13}\text{R}^{14}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{O}(\text{CH}_2)_{2-3}\text{OC}(\text{O})\text{C}_{1-4} \text{ alkyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})\text{O}(\text{CH}_2)_{1-3}\text{C}(\text{O})\text{OC}_{1-4} \text{ alkyl}$, $-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})(\text{CH}_2)_{1-3}\text{OC}(\text{O})\text{C}_{1-4} \text{ alkyl}$, and



$-\text{CR}^{10}\text{R}^{11}\text{OC}(\text{O})(\text{CH}_2)_{1-3}\text{OC}(\text{O})\text{C}_{1-4} \text{ alkyl}$, and

R^7 is selected from the group consisting of -OH, optionally substituted C_{1-6} alkoxy, amino, and $-N(OR^8)R^9$;

each R^8 and R^9 is independently selected from the group consisting of H, halogen, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

each R^{10} and R^{11} is independently selected from the group consisting of H, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

each R^{13} and R^{14} is independently selected from the group consisting of H, optionally substituted C_{1-6} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl;

R^{15} is optionally substituted C_{1-6} alkyl;

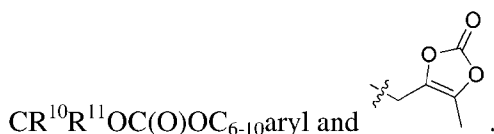
Y^2 is selected from the group consisting of -O-, -S-, and $-NR^9$ -;

Y^5 is selected from the group consisting of -S-, $-S(O)-$, $-S(O)_2-$, -O-, $-CR^fR^g$ -, and $-NR^g$ -, or Y^5 is absent;

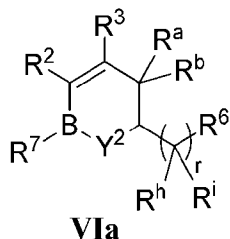
each R^c , R^d , R^e , R^f , and R^g are independently selected from the group consisting of H, halogen, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl; and

each R^h and R^i is independently selected from the group consisting of H, halogen, cyano, amino, C-amido, N-amido, optionally substituted C_{1-4} alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10} aryl, and optionally substituted 5-10 membered heteroaryl; or R^h and R^i together with the atoms to which they are attached form a spirocyclic ring or ring system selected from the group consisting of C_{3-7} carbocyclyl, 3-10 membered heterocyclyl, C_{6-10} aryl, and 5-10 membered heteroaryl, each optionally substituted with one or more R^5 .

67. The compound of claim 66, wherein R is selected from H, C_{1-9} alkyl, $-CR^{10}R^{11}OC(O)C_{1-9}$ alkyl, $-CR^{10}R^{11}OC(O)OC_{1-9}$ alkyl, $-CR^{10}R^{11}OC(O)C_{6-10}$ aryl, -



68. The compound of claim 66 or 67, having the structure of Formula VIa, or pharmaceutically acceptable salts thereof:

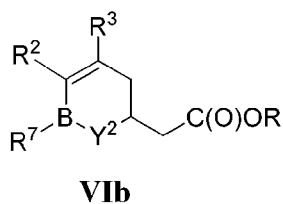


69. The compound of any one of claims 66 to 68, wherein both R^a and R^b are H.

70. The compound of any one of claims 66 to 69, wherein r is 1, and both Rⁿ and Rⁱ are H.

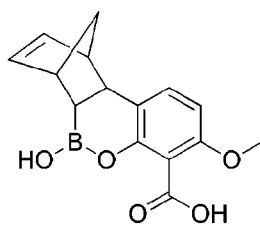
71. The compound of any one of claims 66 to 70, wherein R⁶ is -(CH₂)_nC(O)OR and n is 0.

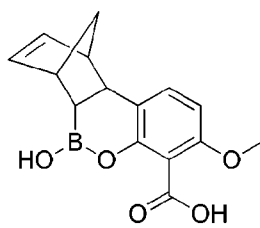
72. The compound of claim 71, having the structure of Formula VIb, or pharmaceutically acceptable salts thereof:



73. The compound of any one of any one of claims 66 to 72, wherein Y² is -O-.

74. The compound of any one of claims 66 to 73, wherein R⁷ is -OH.



75. A compound of structure , or pharmaceutically acceptable salts thereof.

~~75.~~76. The compound of any one of claims 1 to 7574, wherein the pharmaceutically acceptable salt is an alkaline metal salt or an ammonium salt.

~~76.~~77. The compound of claim 7675, wherein the pharmaceutically acceptable salt is a sodium salt.

~~77.~~78. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1 to 77, and a pharmaceutically acceptable excipient.

~~78.~~79. The pharmaceutical composition of claim 78, further comprising an additional medicament.

79.80. The pharmaceutical composition of claim 79, wherein the additional medicament is selected from the group consisting of an antibacterial agent, an antifungal agent, an antiviral agent, an anti-inflammatory agent, and an anti-allergic agent.

80.81. The pharmaceutical composition of claim 80, wherein the additional medicament is a β -lactam antibacterial agent.

81.82. The pharmaceutical composition of claim 81, wherein the β -lactam antibacterial agent is selected from the group consisting of Amoxicillin, Ampicillin (Pivampicillin, Hetacillin, Bacampicillin, Metampicillin, Talampicillin), Epicillin, Carbenicillin (Carindacillin), Ticarcillin, Temocillin, Azlocillin, Piperacillin, Mezlocillin, Mecillinam (Pivmecillinam), Sulbenicillin, Benzylpenicillin (G), Clometocillin, Benzathine benzylpenicillin, Procaine benzylpenicillin, Azidocillin, Penamecillin, Phenoxymethylpenicillin (V), Propicillin, Benzathine phenoxymethylpenicillin, Pheneticillin, Cloxacillin (Dicloxacillin, Flucloxacillin), Oxacillin, Meticillin, Nafcillin, Faropenem, Tomopenem, Razupenem, Cefazolin, Cefacetrile, Cefadroxil, Cefalexin, Cefaloglycin, Cefalonium, Cefaloridine, Cefalotin, Cefapirin, Cefatrizine, Cefazedone, Cefazaflur, Cefradine, Cefroxadine, Ceftezole, Cefaclor, Cefamandole, Cefminox, Cefonicid, Ceforanide, Cefotiam, Cefprozil, Cefbuperazone, Cefuroxime, Cefuzonam, Cefoxitin, Cefotetan, Cefmetazole, Loracarbef, Cefixime, Ceftriaxone, Cefcapene, Cefdaloxime, Cefdinir, Cefditoren, Cefetamet, Cefmenoxime, Cefodizime, Cefoperazone, Cefotaxime, Cefpimizole, Cefpiramide, Cefpodoxime, Cefsulodin, Cefteram, Ceftibuten, Ceftiolene, Ceftizoxime, Flomoxef, Latamoxef, Cefepime, Cefozopran, Cefpirome, Cefquinome, Ceftobiprole, Ceftaroline, CXA- 101, RWJ-54428, MC-04,546, ME1036, Ceftiofur, Cefquinome, Cefovecin, RWJ-442831, RWJ-333441, and RWJ-333442.

82.83. The pharmaceutical composition of claim 81, wherein the β -lactam antibacterial agent is selected from the group consisting of Ceftazidime, Biapenem, Doripenem, Ertapenem, Imipenem, Meropenem, Tebipenem, Tebipenem pivoxil, Apapenem, and Panipenem.

83.84. The pharmaceutical composition of claim 81, wherein the β -lactam antibacterial agent is selected from the group consisting of Aztreonam, Tigemonam, BAL30072, SYN 2416, and Carumonam.

84.85. A method of treating a bacterial infection, comprising administering a compound according any one of claims 1 to 77 to a subject in need thereof.

85.86. The method of claim 85, further comprising administering to the subject an additional medicament.

~~86.87.~~ The method of claim 86, wherein the additional medicament is an antibacterial agent, an antifungal agent, an antiviral agent, an anti-inflammatory agent, or an antiallergic agent.

~~87.88.~~ The method of claim 87, wherein the additional medicament is a β -lactam antibacterial agent.

~~88.89.~~ The method of claim 88, wherein the β -lactam antibacterial agent is selected from the group consisting of Amoxicillin, Ampicillin (Pivampicillin, Hetacillin, Bacampicillin, Metampicillin, Talampicillin), Epicillin, Carbenicillin (Carindacillin), Ticarcillin, Temocillin, Azlocillin, Piperacillin, Mezlocillin, Mecillinam (Pivmecillinam), Sulbenicillin, Benzylpenicillin (G), Clometocillin, Benzathine benzylpenicillin, Procaine benzylpenicillin, Azidocillin, Penamecillin, Phenoxymethylpenicillin (V), Propicillin, Benzathine phenoxymethylpenicillin, Pheneticillin, Cloxacillin (Dicloxacillin, Flucloxacillin), Oxacillin, Meticillin, Nafcillin, Faropenem, Tomopenem, Razupenem, Cefazolin, Cefacetile, Cefadroxil, Cefalexin, Cefaloglycin, Cefalonium, Cefaloridine, Cefalotin, Cefapirin, Cefatrizine, Cefazedone, Cefazaflur, Cefradine, Cefroxadine, Ceftezole, Cefaclor, Cefamandole, Cefminox, Cefonicid, Ceforanide, Cefotiam, Cefprozil, Cefbuperazone, Cefuroxime, Cefuzonam, Cefoxitin, Cefotetan, Cefmetazole, Loracarbef, Cefixime, Ceftriaxone, Cefcapene, Cefdaloxime, Cefdinir, Cefditoren, Cefetamet, Cefmenoxime, Cefodizime, Cefoperazone, Cefotaxime, Cefpimizole, Cefpiramide, Cefpodoxime, Cefsulodin, Cefteram, Ceftibuten, Ceftiolene, Ceftizoxime, Flomoxef, Latamoxef, Cefepime, Cefozopran, Cefpirome, Cefquinome, Ceftobiprole, Ceftaroline, CXA-101, RWJ-54428, MC-04,546, ME1036, Ceftiofur, Cefquinome, Cefovecin, RWJ-442831, RWJ-333441, and RWJ-333442.

~~89.90.~~ The method of claim 88, wherein the β -lactam antibacterial agent is selected from the group consisting of Ceftazidime, Biapenem, Doripenem, Ertapenem, Imipenem, Meropenem, Tebipenem, Tebipenem pivoxil, Apapenem, and Panipenem.

~~90.91.~~ The method of claim 88, wherein the β -lactam antibacterial agent is selected from the group consisting of Aztreonam, Tigemonam, BAL30072, SYN 2416, and Carumonam.

~~91.92.~~ The method of any one of claims 85 to 91, wherein the subject is a mammal.

~~92.93.~~ The method of claim 92, wherein the mammal is a human.

~~93.94.~~ The method of any one of claims 85 to 93, wherein the infection comprises a bacteria selected from the group consisting of *Pseudomonas acidovorans*, *Pseudomonas alcaligenes*, *Pseudomonas putida*, *Burkholderia cepacia*, *Aeromonas hydrophilia*, *Francisella tularensis*, *Morganella morganii*, *Proteus mirabilis*, *Proteus vulgaris*, *Providencia alcalifaciens*, *Providencia rettgeri*, *Providencia stuartii*, *Acinetobacter baumannii*, *Bordetella pertussis*,

Bordetella pertussis, *Bordetella bronchiseptica*, *Haemophilus ducreyi*, *Pasteurella multocida*, *Pasteurella haemolytica*, *Branhamella catarrhalis*, *Borrelia burgdorferi*, *Kingella*, *Gardnerella vaginalis*, *Bacteroides distasonis*, *Bacteroides* 3452A homology group, *Clostridium difficile*, *Mycobacterium tuberculosis*, *Mycobacterium avium*, *Mycobacterium intracellulare*, *Mycobacterium leprae*, *Corynebacterium diphtheriae*, *Corynebacterium ulcerans*, *Streptococcus pneumoniae*, *Streptococcus agalactiae*, *Streptococcus pyogenes*, *Enterococcus faecalis*, *Enterococcus faecium*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus saprophyticus*, *Staphylococcus intermedius*, *Staphylococcus hyicus* subsp. *hyicus*, *Staphylococcus haemolyticus*, *Staphylococcus hominis*, and *Staphylococcus saccharolyticus*.

94.95. The method of any one of claims 85 to 93, wherein the infection comprises a bacteria selected from the group consisting of *Pseudomonas aeruginosa*, *Pseudomonas fluorescens*, *Stenotrophomonas maltophilia*, *Escherichia coli*, *Citrobacter freundii*, *Salmonella typhimurium*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella enteritidis*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Enterobacter cloacae*, *Enterobacter aerogenes*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Serratia marcescens*, *Acinetobacter calcoaceticus*, *Acinetobacter haemolyticus*, *Yersinia enterocolitica*, *Yersinia pestis*, *Yersinia pseudotuberculosis*, *Yersinia intermedia*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Haemophilus haemolyticus*, *Haemophilus parahaemolyticus*, *Helicobacter pylori*, *Campylobacter fetus*, *Campylobacter jejuni*, *Campylobacter coli*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Legionella pneumophila*, *Listeria monocytogenes*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Moraxella*, *Bacteroides fragilis*, *Bacteroides vulgatus*, *Bacteroides ovalus*, *Bacteroides thetaiotaomicron*, *Bacteroides uniformis*, *Bacteroides eggerthii*, and *Bacteroides splanchnicus*.

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Los abajo firmados,
QPEX Biopharma, Inc.

con domicilio en
**3013 Science Park Road, 1st Floor,
San Diego, California 92121, US**

nombramos por el presente a ALICIA LLOREDA y/o ANA MARIA CASTRO y/o TATIANA CARRILLO, domiciliadas en Bogotá, Colombia, con oficinas en dicha ciudad, Calle 72 No. 5-83, piso 6o., nuestras representantes legales y verdaderas en Bogotá, con facultades para recibir notificaciones y nombrar apoderados judiciales o extrajudiciales, con el fin de dar cumplimiento al parágrafo 1o. del artículo 543 del decreto 410 de 1971.

Las doctoras ALICIA LLOREDA y/o ANA MARIA CASTRO y/o TATIANA CARRILLO, o los apoderados que cualquiera de ellas designe, quedan especialmente facultados para representarnos ante las autoridades colombianas, administrativas, judiciales o de policía, en todos los trámites relativos a la propiedad industrial, a cuyo efecto les facultamos para dar ante dichas autoridades todos los pasos necesarios al objeto indicado; elevar solicitudes, declaraciones, reclamos, recursos y presentar desistimientos; formular descripciones, enmiendas, limitar el alcance de las solicitudes, presentar oposiciones y apelaciones; instaurar cancelaciones, renunciar total o parcialmente a los registros, abonar todos los impuestos y cuotas y efectuar todo otro pago determinado por la ley; recibir todos los documentos y valores, dando el descargo respectivo; llenar cualesquiera otros requisitos y tomar, en fin, todas las medidas que creyeren conducentes al resguardo de nuestros intereses; y en caso de producirse oposición, pasando los antecedentes a los tribunales, quedan facultados para tomar intervención como demandantes o demandados ante los jueces que sean competentes, pudiendo transar, someter a árbitros, desistir, percibir y apelar, con todas las demás facultades que resulten necesarias, y por el presente declaramos desde ahora válido y bueno cuanto dichos representantes y/o los apoderados que cualquiera de ellas nombre hicieren en nuestro beneficio.

Asimismo, facultamos a las doctoras ALICIA LLOREDA y/o ANA MARIA CASTRO y/o TATIANA CARRILLO, para solicitar en la Oficina de Propiedad Industrial la protocolización de este documento y de cualquier poder que cualquiera de ellos otorgue a nombre nuestro.

Dado y firmado,

The undersigned,
QPEX Biopharma, Inc.

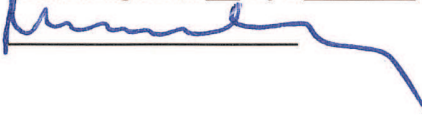
domiciled at
**3013 Science Park Road, 1st Floor,
San Diego, California 92121, US**

hereby appoint, ALICIA LLOREDA y/o ANA MARIA CASTRO y/o TATIANA CARRILLO, of Bogota, Colombia, with offices in said town, Calle 72 No. 5-83, Sixth Floor, our true and legal representatives in Bogotá, with power to receive notifications and to appoint judicial or extrajudicial agents, so as to comply with paragraph 1o. of article 543 of decree 410 of 1971.

ALICIA LLOREDA y/o ANA MARIA CASTRO y/o TATIANA CARRILLO, or the agents by any one of them appointed, are especially empowered to represent us before the administrative, judicial or police authorities of Colombia, in all proceedings pertaining to industrial property, for which purpose we authorize them to take before the said authorities all the necessary steps for the said end; to file petitions, declarations, claims, recourses and withdrawals, to draw up specifications; to file amendments, to limit the scope of applications, file oppositions; file cancellations total or partially waive registrations, to pay all installments and effect all other payments prescribed by law; to receive proper receipts, to comply with all other requirements and, in short, to take all those measures which they may deem fit for the protection of our interests; and in case of opposition, where the proceedings be passed over to the courts, we authorize said agents to act on our behalf, as complainants as well as defendants, before the competent judges, with full powers to make arrangements, to submit to arbitrators, to desist, to collect, to appeal and, in short, with all such further powers as may be required, and we hereby declare from now on as valid and good all that said representatives and/or the agents by any one of them appointed may do for our benefit.

We also authorize doctors ALICIA LLOREDA y/o ANA MARIA CASTRO y/o TATIANA CARRILLO, to apply for protocolization of this document and of any power of attorney by any one of them conferred in our name, before the Office of Industrial Property.

Given and signed this 17th day of DECEMBER, 2018



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(54) Title (EN): BORONIC ACID DERIVATIVES AND THERAPEUTIC USES THEREOF

(54) Title (FR): DÉRIVÉS D'ACIDE BORONIQUE ET LEURS UTILISATIONS THÉRAPEUTIQUES

(57) Abstract:

(EN): Disclosed herein are antimicrobial compounds compositions, pharmaceutical compositions, the method of use and preparation thereof. Some embodiments relate to boronic acid derivatives and their use as therapeutic agents, for example, β -lactamase inhibitors (BLIs).

(FR): L'invention concerne des compositions de composés antimicrobiens, des compositions pharmaceutiques, leur méthodes utilisation et leur préparation. Certaines réalisations liées à au dérivés de l'acide boronique et leur utilisation en tant qu'agents thérapeutiques, par exemple: des inhibiteurs β -lactamase (BLIs).

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European Patent Office (EPO) : AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR

African Intellectual Property Organization (OAPI) : BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG

African Regional Intellectual Property Organization (ARIPO) : BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW

Eurasian Patent Organization (EAPO) : AM, AZ, BY, KG, KZ, RU, TJ, TM

Declarations:

Declaration made as applicant's entitlement, as at the international filing date, to apply for and be granted a patent (Rules 4.17(ii) and 51bis.1(a)(ii)), in a case where the declaration under Rule 4.17(iv) is not appropriate

Declaration made as applicant's entitlement, as at the international filing date, to claim the priority of the earlier application, where the applicant is not the applicant who filed the earlier application or where the applicant's name has changed since the filing of the earlier application (Rules 4.17(iii) and 51bis.1(a)(iii))

Señor

SUPERINTENDENTE DE INDUSTRIA Y COMERCIO

DIVISIÓN DE NUEVAS CREACIONES

E. _____ S. _____ D. _____

Re: PI.- **OPEX BIOPHARMA, INC.**-Solicitud de Patente de Invención en Fase Nacional PCT para "**DERIVADOS DE ÁCIDO BORÓNICO Y USOS TERAPÉUTICOS DE LOS MISMOS.**".-Clase **C07F 5/02.** - Expediente número **NC2018/0013978.**

Por medio del presente, hago referencia al Auto No. 75 dictado por este Despacho y notificado por fijación en lista del 02 de enero de 2019. Con el fin de dar respuesta al Auto emitido por la División de Nuevas Creaciones, a continuación expongo lo siguiente:

1. Capítulo I o II (PCT)

En respuesta al requerimiento emitido por el examinador, es de aclarar que la solicitud de patente radicada el 21 de diciembre de 2018 se presentó bajo **Capítulo II**, toda vez que el 26 de abril de 2018, durante la Fase Internacional, se solicitó la práctica de un Examen Internacional Preliminar y se presentó un capítulo reivindicatorio modificado. Lo anterior se puede verificar al consultar la solicitud internacional en la plataforma Patentscope de la OMPI, vigente al momento de la presentación de esta respuesta.

Adicionalmente, amablemente solicito se tenga en cuenta que el 24 de mayo de 2018 la autoridad internacional emitió el Informe Preliminar Internacional IPEA/409 sobre Patentabilidad Capítulo II del PCT.

2. Poder

En cuanto al segundo punto mencionado en el Auto de Forma, me permito allegar a este Despacho copia del documento que acredita a la SUSCRITA (ALICIA LLOREDA) y/o a las doctoras ANA MARIA CASTRO y/o TATIANA CARRILLO, de conformidad con las normas legales aplicables en Colombia-, como Representantes Legales en Colombia para todos los asuntos relacionados con asuntos de

propiedad industrial de la sociedad **QPEX BIOPHARMA, INC.**, domiciliada en San Diego, California, Estados Unidos de América.

En vista de lo anterior, atentamente solicito a este Despacho reconocermé personería en este asunto de la sociedad QPEX BIOPHARMA, INC., de acuerdo con la copia que adjunto al presente expediente y según lo dispuesto en los Artículos 26 y 39 de la Decisión 486 de la Comunidad Andina.

3. Anexos

Anexo a la presente respuesta, presento los siguientes documentos:

- Copia del Informe Preliminar Internacional IPEA/409 sobre Patentabilidad Capítulo II del PCT
- Informe sobre la Situación de la Solicitud Internacional, en el cual queda constancia de la fecha en la cual se solicitó el IPIP y se presentó capítulo reivindicatorio modificado en Fase Internacional
- Poder de representación del Solicitante

Superadas las objeciones formuladas, ruego a usted tomar atenta nota de lo anterior y continuar con el trámite de conformidad.

Mi dirección es Calle 72 No. 5-83, Piso 6º, Bogotá D.C., Colombia.

Señor Superintendente,



ALICIA LLOREDA RICAURTE

T.P. 53.215

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