

Señora

Directora de la Dirección de Nuevas Creaciones

Superintendencia de Industria y Comercio

Ministerio de Comercio, Industria y Turismo

E. S. D.

Re.: Expediente No. **NC2019/0006455**

Solicitud de Patente PCT entrada en Fase Nacional, para: **“CONJUGADOS ANTICUERPO-FÁRMACO PARA ABLACIÓN DE CÉLULAS MADRE HEMATOPOYÉTICAS”**

Solicitante: **NOVARTIS AG**

RESPUESTA A EXAMEN DE FONDO

MARGARITA CASTELLANOS ABONDANO, mayor de edad, identificada y domiciliada como aparece al pie de mi firma, obrando en mi calidad de apoderada de la sociedad solicitante del asunto citado en la referencia, en atención a su oficio No. **2316** notificado electrónicamente el 24 de febrero de 2022, me permito dar respuesta al mismo de la siguiente manera:

1. Modificación a las Reivindicaciones

De acuerdo con lo establecido en el Artículo 34 de la Decisión 486 y en vista de las observaciones realizadas por el examinador, se presenta en esta oportunidad un nuevo pliego reivindicatorio conformado por quince (15) reivindicaciones, en donde se han realizado las siguientes modificaciones:

- No se incluyen las anteriores reivindicaciones 8 a 13, 15 y 20 a 23.
- Se modificó la anterior reivindicación 8 con el fin de definir claramente las opciones entre las cuales es seleccionada la Fórmula (I).
- Las reivindicaciones restantes y sus dependencias fueron reenumeradas de acuerdo con las modificaciones anteriores.

Se pone de presente que la materia recitada se encuentra debidamente soportada en la descripción tal como fue originalmente presentada, así como en las reivindicaciones originales.

En este sentido el pliego reivindicatorio ha sido modificado con el fin de aclarar la materia reivindicada y para responder a los requerimientos elevados por su Despacho.

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2. Claridad y Concisión de las Reivindicaciones

Con respecto a la reivindicación 1, el solicitante señala que en la misma se mantiene la expresión “*el conjugado no induce desgranulación de mastocitos*” ya que respetuosamente considera que una persona experta en la materia reconocería el efecto técnico reivindicado basado en la estructura definida del conjugado en la reivindicación 1.

Teniendo en cuenta las modificaciones realizadas, es claro que la presente invención cumple con los requerimientos del artículo 30 de la Decisión 486 de la Comisión de la Comunidad Andina.

3. Descripción

En relación con la objeción realizada a la descripción, el solicitante respetuosamente señala que no está de acuerdo con la afirmación de que las reivindicaciones dirigidas a las Fórmulas C, D y E no se divulgan en la solicitud de manera suficiente como para que una persona normalmente versada en la materia técnica correspondiente pueda ejecutarla (o reproducirla). Sin embargo, sin aceptar dicha objeción y con el único efecto de dar continuidad con el trámite, las reivindicaciones 8-13, 15, y 20-23 dirigidas a las Fórmulas C, D y E no han sido incluidas en el nuevo capítulo reivindicatorio. Asimismo, sostiene respetuosamente que la nueva reivindicación 8 está soportada por la memoria descriptiva y define además las estructuras potenciales de $(L_B-(D)_n)$ de Fórmula (I). Por estas razones, se afirma respetuosamente que las reivindicaciones están plenamente respaldadas por la memoria descriptiva.

4. Nivel inventivo

El examinador ha determinado el arte previo con base en la fecha de la presentación de la solicitud de la cual se invoca prioridad, siendo ésta 21 de diciembre de 2016.

En esta oportunidad se han citado los documentos WO2015/138615 (D1), WO2014/150937 (D2) y WO2016/020791 (D3).

Teniendo en cuenta el nuevo pliego reivindicatorio y los argumentos que se ponen de presente a continuación, es claro que la materia objeto de protección es inventiva frente a los documentos citados, tal como se muestra a continuación:

Tal como fue reconocido en el oficio que se contesta, ninguna de las combinaciones VH/VL reivindicadas presenta una identidad del 100 % con respecto a D3. El solicitante señala además que las secuencias de anticuerpos reivindicadas son inesperadas en el estado de la técnica y no se enseñan ni se sugieren en D1, D2 y D3, de manera individual o en combinación.

Cabe destacar que la reivindicación 1 está dirigida a conjugados que comprenden fragmentos de anticuerpos Fab o Fab' que no provocan la degranulación de mastocitos en presencia del entrecruzante. D1 no hace referencia alguna sobre los anticuerpos, fragmentos de anticuerpos o conjugados de los mismos que no inducen la degranulación de mastocitos y no divulga ninguna de las secuencias de anticuerpos reivindicadas. NEG085 y 20376 son los únicos anticuerpos anti-cKit que se enseñan en D2 y D3 como no inductores de la degranulación de los mastocitos (véase el Ejemplo 20 en D2 y el Ejemplo 13 en D3). D2 y D3 no enseñan ni sugieren ninguna otra secuencia de anticuerpos, similar en secuencia o de otro modo, que tenga esta característica. Como se ha argumentado anteriormente, no se reivindica ninguna de las secuencias de NEG085 o 20376. En el oficio que se contesta se admite incluso que ninguna de las combinaciones VH/VL presenta una identidad del 100% con los documentos del estado de la técnica. Las combinaciones de secuencias VH/VL reivindicadas también comprenden CDRs diferentes a las de NEG085 y 20376. En consecuencia, a pesar de la similitud general de la secuencia, el solicitante afirma respetuosamente que las diferencias estructurales por sí solas son suficientes, por lo que existe actividad inventiva en la presente solicitud.

Además, es importante señalar que en los ejemplos de D2 y D3, NEG085 y 20376 se utilizan como anticuerpos IgG humanos no conjugados. Ni D2 ni D3 enseñan o sugieren que un fragmento de anticuerpo Fab o Fab' de NEG085 o 20376 tampoco induciría la degranulación de los mastocitos. Tampoco D2 o D3 enseñan o sugieren que esta característica se mantenga en presencia de un entrecruzante.

La presente invención muestra que incluso si la falta de degranulación se observó con ciertos anticuerpos IgG de longitud completa para la condición de “*cero entrecruzamiento*”, cuando se añade el entrecruzante a estos anticuerpos de longitud completa, se desencadena la degranulación de los mastocitos en el ensayo. No se esperaba que dicha característica pudiera mantenerse utilizando diferentes fragmentos de anticuerpos o en presencia de un entrecruzante. En consecuencia, en vista de D2 y/o D3, no se esperaba que los anticuerpos NEG085 y 20376 IgG en presencia de un entrecruzante mantuvieran la capacidad de no inducir la degranulación de los mastocitos. Tampoco se esperaba que los fragmentos Fab o Fab' de NEG085 y 20376 mantuvieran la capacidad de no inducir la degranulación de los mastocitos en presencia o ausencia de un entrecruzante. Por lo tanto, no habría sido obvio para un experto en la materia utilizar cualquiera de los fragmentos D1-D3 para identificar las secuencias de anticuerpos Fab o Fab' reivindicadas con este efecto.

Se alega respetuosamente que un experto no se habría dejado llevar directamente por una cuestión de rutina, en vista de las enseñanzas de D1, D2 y D3, para probar los conjugados reivindicados actualmente con la expectativa de que los fragmentos Fab/Fab' serían inactivos en un mastocito con ensayo de entrecruzamiento, proporcionando así un perfil único de los conjugados reivindicados para el desarrollo clínico. Así, la presente invención ha identificado inesperadamente secuencias CDR, VH/VL, HC/LC de fragmentos de anticuerpos Fab y Fab' que tienen este efecto incluso cuando se

entrecruzan y/o se multimerizan en compuestos más grandes. En consecuencia, se sostiene respetuosamente que las presentes reivindicaciones y las secuencias de fragmentos de anticuerpos reivindicadas son inventivas con respecto a D1, D2 o D3, solos o en combinación.

Finalmente, si bien entendemos y aceptamos que cada país es autónomo en la concesión o negación de los privilegios de patente, queremos resaltar el hecho que el análisis de los requisitos para el otorgamiento de esos derechos es prácticamente universal. La presente solicitud con reivindicaciones similares fue concedida en Australia, Argelia y Estados Unidos de América, por lo tanto la presente solicitud cumple con los requisitos de patentabilidad. En el caso de la solicitud equivalente de Estados Unidos, las reivindicaciones concedidas tienen un alcance similar a las presentadas actualmente (es decir, las reivindicaciones contienen, entre otras, las secuencias CDR, VH/VL y HC/LC de Ab1, Ab2, Ab4 y Ab5). Adjunto se acompaña copia de las reivindicaciones concedidas y la notificación de concesión emitida por la USPTO, que detalla las enmiendas permitidas.

Por estas razones, respetuosamente se considera que la reivindicación 1 es inventiva respecto a D1, D2 y D3.

Teniendo en cuenta lo anterior, es claro entonces que la persona normalmente versada en la materia, de acuerdo con las enseñanzas de D1, D2 y D3, no llegaría a la presente invención, tal como se reclama en las nuevas reivindicaciones 1 a 15 presentadas junto con este memorial.

Solicito al Despacho que en este caso acepte el nuevo pliego reivindicatorio y los argumentos aquí presentados.

Dado que el capítulo reivindicatorio ha sido modificado, se anexa el comprobante de pago de tasa oficial correspondiente a dicha modificación.

5. Conclusión

Teniendo en cuenta las modificaciones introducidas en esta oportunidad y los argumentos que se presentan, es posible establecer que las reivindicaciones cumplen con los requerimientos de la Decisión 486.

6. Anexos

- Nuevo pliego reivindicatorio conformado quince (15) reivindicaciones.
- Comprobante de pago en línea por concepto de modificación a la solicitud.

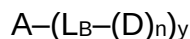
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REIVINDICACIONES

1. Un conjugado de Fórmula (I) o una sal farmacéuticamente aceptable del mismo;



Fórmula (I)

donde:

A es un fragmento de anticuerpo que específicamente se une a cKIT humano, donde el fragmento de anticuerpo se selecciona entre cualquiera de los siguientes:

- (1) un Fab o Fab' que comprende (i) una región variable de cadena pesada que comprende (a) una HCDR1 (Región Determinante de Complementariedad de Cadena Pesada 1) de SEQ ID NO: 1, (b) una HCDR2 (Región Determinante de Complementariedad de Cadena Pesada 2) de SEQ ID NO: 2, y (c) una HCDR3 (Región Determinante de Complementariedad de Cadena Pesada 3) de SEQ ID NO: 3; y (ii) una región variable de cadena liviana que comprende: (d) una LCDR1 (Región Determinante de Complementariedad de Cadena Liviana 1) de SEQ ID NO: 16, (e) una LCDR2 (Región Determinante de Complementariedad de Cadena Liviana 2) de SEQ ID NO: 17, y (f) una LCDR3 (Región Determinante de Complementariedad de Cadena Liviana 3) de SEQ ID NO: 18;
- (2) un Fab o Fab' que comprende (i) una región variable de cadena pesada que comprende (a) una HCDR1 de SEQ ID NO: 4, (b) una HCDR2 de SEQ ID NO: 5, (c) una HCDR3 de SEQ ID NO: 3; y (ii) una región variable de cadena liviana que comprende: (d) una LCDR1 de SEQ ID NO: 19, (e) una LCDR2 de SEQ ID NO: 20, y (f) una LCDR3 de SEQ ID NO: 21;
- (3) un Fab o Fab' que comprende (i) una región variable de cadena pesada que comprende (a) una HCDR1 de SEQ ID NO: 6, (b) una HCDR2 de SEQ ID NO: 2, (c) una HCDR3 de SEQ ID NO: 3; y (ii) una región variable de cadena liviana que comprende: (d) una LCDR1 de SEQ ID

NO: 16, (e) una LCDR2 de SEQ ID NO: 17, y (f) una LCDR3 de SEQ ID NO: 18;

- (4) un Fab o Fab' que comprende (i) una región variable de cadena pesada que comprende (a) una HCDR1 de SEQ ID NO: 7, (b) una HCDR2 de SEQ ID NO: 8, (c) una HCDR3 de SEQ ID NO: 9; y (ii) una región variable de cadena liviana que comprende: (d) una LCDR1 de SEQ ID NO: 22, (e) una LCDR2 de SEQ ID NO: 20, y (f) una LCDR3 de SEQ ID NO: 18;
- (5) un Fab o Fab' que comprende (i) una región variable de cadena pesada que comprende (a) una HCDR1 de SEQ ID NO: 27, (b) una HCDR2 de SEQ ID NO: 28, (c) una HCDR3 de SEQ ID NO: 29; y (ii) una región variable de cadena liviana que comprende: (d) una LCDR1 de SEQ ID NO: 42, (e) una LCDR2 de SEQ ID NO: 17, y (f) una LCDR3 de SEQ ID NO: 43;
- (6) un Fab o Fab' que comprende (i) una región variable de cadena pesada que comprende (a) una HCDR1 de SEQ ID NO: 30, (b) una HCDR2 de SEQ ID NO: 31, (c) una HCDR3 de SEQ ID NO: 29; y (ii) una región variable de cadena liviana que comprende: (d) una LCDR1 de SEQ ID NO: 44, (e) una LCDR2 de SEQ ID NO: 20, y (f) una LCDR3 de SEQ ID NO: 45;
- (7) un Fab o Fab' que comprende (i) una región variable de cadena pesada que comprende (a) una HCDR1 de SEQ ID NO: 32, (b) una HCDR2 de SEQ ID NO: 28, (c) una HCDR3 de SEQ ID NO: 29; y (ii) una región variable de cadena liviana que comprende: (d) una LCDR1 de SEQ ID NO: 42, (e) una LCDR2 de SEQ ID NO: 17, y (f) una LCDR3 de SEQ ID NO: 43;
- (8) un Fab o Fab' que comprende (i) una región variable de cadena pesada que comprende (a) una HCDR1 de SEQ ID NO: 33, (b) una HCDR2 de SEQ ID NO: 34, (c) una HCDR3 de SEQ ID NO: 35; y (ii) una región variable de cadena liviana que comprende: (d) una LCDR1 de SEQ ID

NO: 46, (e) una LCDR2 de SEQ ID NO: 20, y (f) una LCDR3 de SEQ ID NO: 43;

(9) un Fab o Fab' que comprende (i) una región variable de cadena pesada que comprende (a) una HCDR1 de SEQ ID NO: 60, (b) una HCDR2 de SEQ ID NO: 61, (c) una HCDR3 de SEQ ID NO: 62; y (ii) una región variable de cadena liviana que comprende: (d) una LCDR1 de SEQ ID NO: 75, (e) una LCDR2 de SEQ ID NO: 76, y (f) una LCDR3 de SEQ ID NO: 77;

(10) un Fab o Fab' que comprende (i) una región variable de cadena pesada que comprende (a) una HCDR1 de SEQ ID NO: 63, (b) una HCDR2 de SEQ ID NO: 64, (c) una HCDR3 de SEQ ID NO: 62; y (ii) una región variable de cadena liviana que comprende: (d) una LCDR1 de SEQ ID NO: 78, (e) una LCDR2 de SEQ ID NO: 79, y (f) una LCDR3 de SEQ ID NO: 80;

(11) un Fab o Fab' que comprende (i) una región variable de cadena pesada que comprende (a) una HCDR1 de SEQ ID NO: 65, (b) una HCDR2 de SEQ ID NO: 61, (c) una HCDR3 de SEQ ID NO: 62; y (ii) una región variable de cadena liviana que comprende: (d) una LCDR1 de SEQ ID NO: 75, (e) una LCDR2 de SEQ ID NO: 76, y (f) una LCDR3 de SEQ ID NO: 77;

(12) un Fab o Fab' que comprende (i) una región variable de cadena pesada que comprende (a) una HCDR1 de SEQ ID NO: 66, (b) una HCDR2 de SEQ ID NO: 67, (c) una HCDR3 de SEQ ID NO: 68; y (ii) una región variable de cadena liviana que comprende: (d) una LCDR1 de SEQ ID NO: 81, (e) una LCDR2 de SEQ ID NO: 79, y (f) una LCDR3 de SEQ ID NO: 77;

(13) un Fab o Fab' que comprende (i) una región variable de cadena pesada que comprende (a) una HCDR1 de SEQ ID NO: 86, (b) una HCDR2 de SEQ ID NO: 87, (c) una HCDR3 de SEQ ID NO: 88; y (ii) una región variable de cadena liviana que comprende: (d) una LCDR1 de SEQ ID

- NO: 101, (e) una LCDR2 de SEQ ID NO: 102, y (f) una LCDR3 de SEQ ID NO: 103;
- (14) un Fab o Fab' que comprende (i) una región variable de cadena pesada que comprende (a) una HCDR1 de SEQ ID NO: 89, (b) una HCDR2 de SEQ ID NO: 90, (c) una HCDR3 de SEQ ID NO: 88; y (ii) una región variable de cadena liviana que comprende: (d) una LCDR1 de SEQ ID NO: 104, (e) una LCDR2 de SEQ ID NO: 105, y (f) una LCDR3 de SEQ ID NO: 106;
- (15) un Fab o Fab' que comprende (i) una región variable de cadena pesada que comprende (a) una HCDR1 de SEQ ID NO: 91, (b) una HCDR2 de SEQ ID NO: 87, (c) una HCDR3 de SEQ ID NO: 88; y (ii) una región variable de cadena liviana que comprende: (d) una LCDR1 de SEQ ID NO: 101, (e) una LCDR2 de SEQ ID NO: 102, y (f) una LCDR3 de SEQ ID NO: 103;
- (16) un Fab o Fab' que comprende (i) una región variable de cadena pesada que comprende (a) una HCDR1 de SEQ ID NO: 92, (b) una HCDR2 de SEQ ID NO: 93, (c) una HCDR3 de SEQ ID NO: 94; y (ii) una región variable de cadena liviana que comprende: (d) una LCDR1 de SEQ ID NO: 107, (e) una LCDR2 de SEQ ID NO: 105, y (f) una LCDR3 de SEQ ID NO: 103;
- (17) un Fab o Fab' que comprende una región variable de cadena pesada (VH) que comprende SEQ ID NO: 10, y una región variable de cadena liviana (VL) que comprende SEQ ID NO: 23;
- (18) un Fab o Fab' que comprende una VH que comprende SEQ ID NO: 36, y una VL que comprende SEQ ID NO: 47;
- (19) un Fab o Fab' que comprende una VH que comprende SEQ ID NO: 69, y una VL que comprende SEQ ID NO: 82;
- (20) un Fab o Fab' que comprende una VH que comprende SEQ ID NO: 95, y una VL que comprende SEQ ID NO: 108;
- (21) un Fab' que comprende una cadena pesada que comprende SEQ ID NO: 14, y una cadena liviana que comprende SEQ ID NO: 25;

- (22) un Fab' que comprende una cadena pesada que comprende SEQ ID NO: 40, y una cadena liviana que comprende SEQ ID NO: 49;
- (23) un Fab' que comprende una cadena pesada que comprende SEQ ID NO: 73, y una cadena liviana que comprende SEQ ID NO: 84;
- (24) un Fab' que comprende una cadena pesada que comprende SEQ ID NO: 99, y una cadena liviana que comprende SEQ ID NO: 110;
- (25) un Fab que comprende una cadena pesada que comprende SEQ ID NO: 118, y una cadena liviana que comprende SEQ ID NO: 122;
- (26) un Fab que comprende una cadena pesada que comprende SEQ ID NO: 118, y una cadena liviana que comprende SEQ ID NO: 123;
- (27) un Fab que comprende una cadena pesada que comprende SEQ ID NO: 124, y una cadena liviana que comprende SEQ ID NO: 128;
- (28) un Fab que comprende una cadena pesada que comprende SEQ ID NO: 124, y una cadena liviana que comprende SEQ ID NO: 129;
- (29) un Fab que comprende una cadena pesada que comprende SEQ ID NO: 130, y una cadena liviana que comprende SEQ ID NO: 134;
- (30) un Fab que comprende una cadena pesada que comprende SEQ ID NO: 130, y una cadena liviana que comprende SEQ ID NO: 135;
- (31) un Fab que comprende una cadena pesada que comprende SEQ ID NO: 136, y una cadena liviana que comprende SEQ ID NO: 140;
- (32) un Fab que comprende una cadena pesada que comprende SEQ ID NO: 141, y una cadena liviana que comprende SEQ ID NO: 145;
- (33) un Fab que comprende una cadena pesada que comprende una secuencia de aminoácidos seleccionada entre SEQ ID NO: 119, 120 o 121, y una cadena liviana que comprende la secuencia de aminoácidos de SEQ ID NO: 25;
- (34) un Fab que comprende una cadena pesada que comprende una secuencia de aminoácidos seleccionada entre SEQ ID NO: 125, 126, o 127, y una cadena liviana que comprende la secuencia de aminoácidos de SEQ ID NO: 49;

(35) un Fab que comprende una cadena pesada que comprende una secuencia de aminoácidos seleccionada entre SEQ ID NO: 137, 138, o 139, y una cadena liviana que comprende la secuencia de aminoácidos de SEQ ID NO: 84; o

(36) un Fab que comprende una cadena pesada que comprende una secuencia de aminoácidos seleccionada entre SEQ ID NO: 142, 143, o 144, y una cadena liviana que comprende la secuencia de aminoácidos de SEQ ID NO: 110;

L_B es un enlazador, donde cada L_B se selecciona independientemente de un enlazador escindible o un enlazador no-escindible;

D es un agente citotóxico, donde cada D es un agente citotóxico seleccionado independientemente entre una auristatina, una amanitina, un maitansinoide o una saporina;

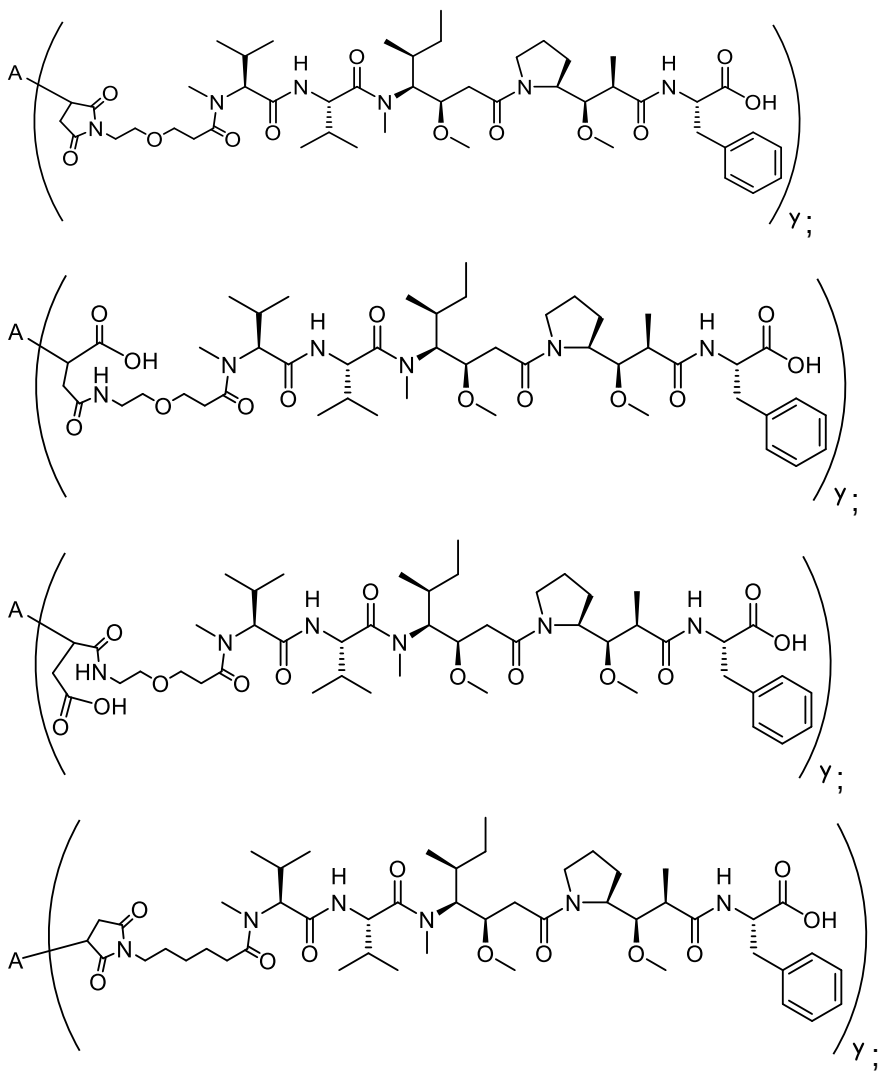
n es un número entero que va desde 1 hasta 10; y

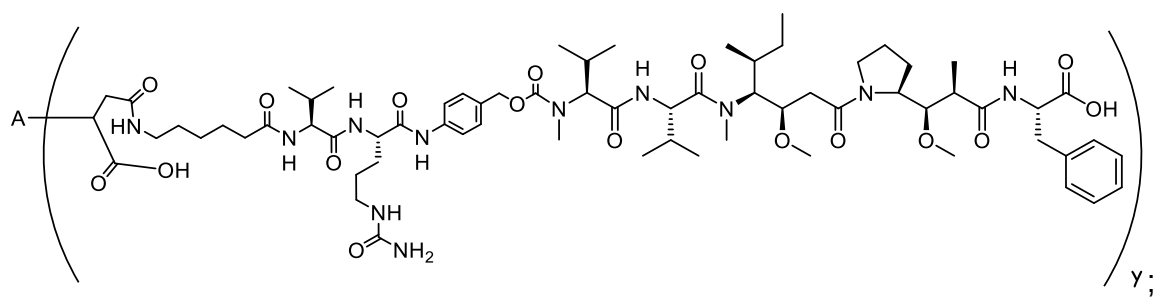
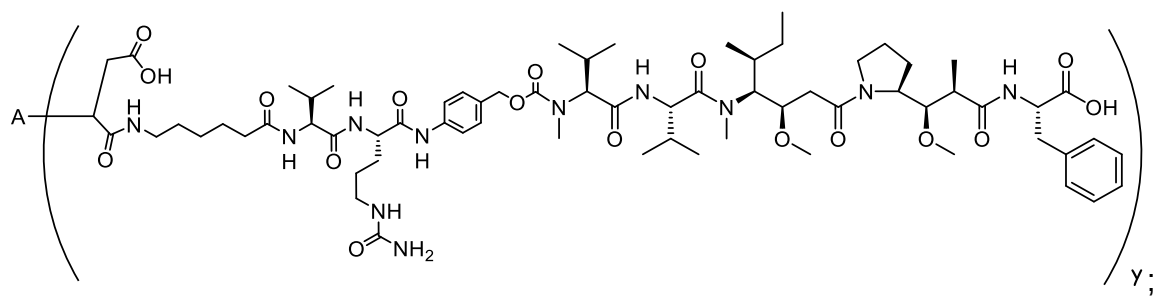
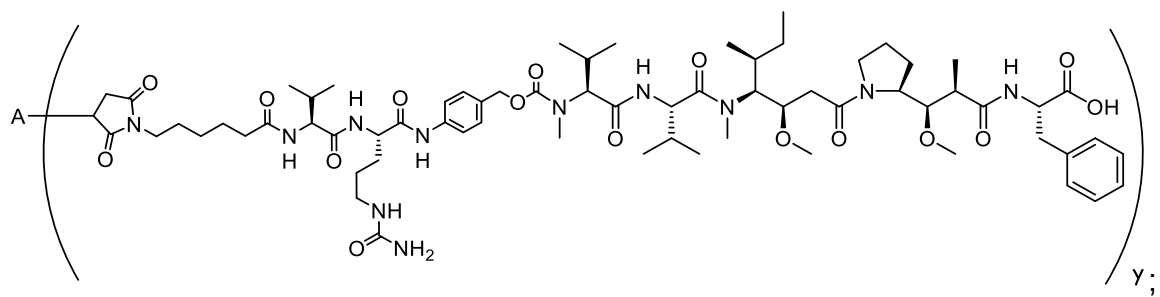
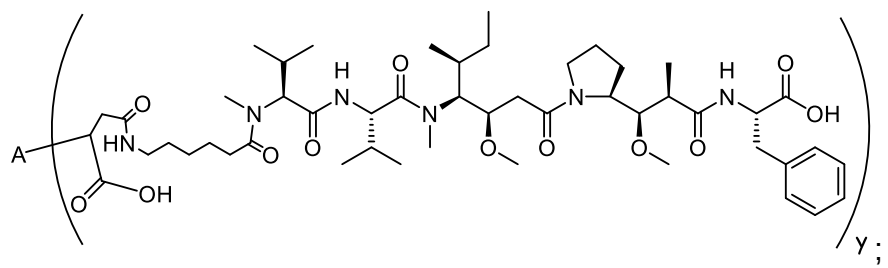
y es un número entero que va desde 1 hasta 10; y

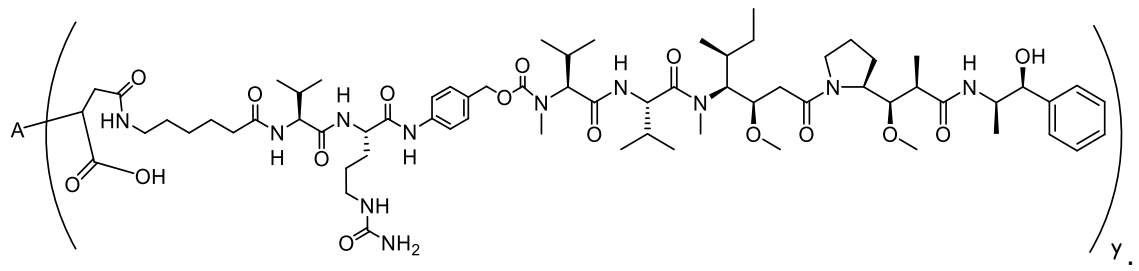
donde el conjugado no induce degranulación de mastocitos.

2. El conjugado de la reivindicación 1, donde n es 1, 2, 3, 4, 5, 6, 7 o 8.
3. El conjugado de la reivindicación 1, donde y es 1, 2, 3 o 4.
4. El conjugado de cualquiera de las reivindicaciones 1 a 3, donde cada D es un agente citotóxico seleccionado independientemente entre una auristatina, una amanitina o un maitansinoide.
5. El conjugado de cualquiera de las reivindicaciones 1 a 4, donde cada D es un agente citotóxico seleccionado independientemente entre una auristatina o una amanitina.

6. El conjugado de cualquiera de las reivindicaciones 1 a 5, donde cada L_B es un enlazador escindible.
7. El conjugado de cualquiera de las reivindicaciones 1 a 5, donde cada L_B es un enlazador no-escindible.
8. El conjugado de cualquiera de las reivindicaciones 1 a 7, donde la Fórmula (I) se selecciona entre:







9. El conjugado de cualquiera de las reivindicaciones 1 a 8, donde el fragmento de anticuerpo se une específicamente al dominio extracelular de cKIT humano (SEQ ID NO: 112).
10. El conjugado de cualquiera de las reivindicaciones 1 a 8, donde el fragmento de anticuerpo se une específicamente a un epítipo en dominios 1–3 de cKIT humano (SEQ ID NO: 113).
11. El conjugado de cualquiera de las reivindicaciones 1 a 7, donde el fragmento de anticuerpo es un Fab' y el enlazador (L_B) se adhiere a un residuo cisteína nativo en la región bisagra del Fab'.
12. El conjugado de cualquiera de las reivindicaciones 1 a 7, donde el fragmento de anticuerpo comprende una cisteína no nativa introducida dentro de una región constante, y el enlazador (L_B) se adhiere a la cisteína no–nativa.
13. El conjugado de cualquiera de las reivindicaciones 1 a 12, donde la semi–vida del conjugado es entre 0 y 48 horas.
14. Una composición farmacéutica que comprende el conjugado de cualquiera de las reivindicaciones 1 a 13 y un portador farmacéuticamente aceptable.
15. La composición farmacéutica de la reivindicación 14, donde la composición es un liofilizado.



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Cambridge, MA 02139

EXAMINER

HADDAD, MAHER M

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 02/03/2022

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/470,897	06/18/2019	Ben WEN	PAT057400-US-PCT	4370

TITLE OF INVENTION: ANTIBODY DRUG CONJUGATES FOR ABLATING HEMATOPOIETIC STEM CELLS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1200	\$0.00	\$0.00	\$1200	05/03/2022

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via EFS-Web.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

29490 7590 02/03/2022
GENOMICS INSTITUTE OF THE
NOVARTIS RESEARCH FOUNDATION
250 Massachusetts Avenue
Cambridge, MA 02139

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via EFS-Web or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/470,897	06/18/2019	Ben WEN	PAT057400-US-PCT	4370

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nonprovisional	UNDISCOUNTED	\$1200	\$0.00	\$0.00	\$1200	05/03/2022

EXAMINER	ART UNIT	CLASS-SUBCLASS
HADDAD, MAHER M	1644	424-133100

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,

1 _____

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☐ Corporation or other private group entity ☐ Government4a. Fees submitted: ☐ Issue Fee ☐ Publication Fee (if required) ☐ Advance Order - # of Copies _____

4b. Method of Payment: (Please first reapply any previously paid fee shown above)

☐ Electronic Payment via EFS-Web ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. Change in Entity Status (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29☐ Applicant asserting small entity status. See 37 CFR 1.27☐ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____

Date _____

Typed or printed name _____

Registration No. _____



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/470,897	06/18/2019	Ben WEN	PAT057400-US-PCT	4370
29490 7590 02/03/2022 GENOMICS INSTITUTE OF THE NOVARTIS RESEARCH FOUNDATION 250 Massachusetts Avenue Cambridge, MA 02139			EXAMINER HADDAD, MAHER M	
			ART UNIT 1644	PAPER NUMBER
DATE MAILED: 02/03/2022				

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 16/470,897	Applicant(s) WEN et al.	
	Examiner MAHER M HADDAD	Art Unit 1644	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 11/24/2021.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on ____.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.

3. ☒ The allowed claim(s) is/are 1,3-4,7,16,18-20,23,30-32,35-43 and 46-47. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a) ☐ All b) ☐ Some* c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. ____.

3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: ____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date ____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892) 2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date ____. 3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material ____. 4. ☒ Interview Summary (PTO-413), Paper No./Mail Date _____.	5. ☒ Examiner's Amendment/Comment 6. ☒ Examiner's Statement of Reasons for Allowance 7. ☐ Other _____.
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/MAHER M HADDAD/
Primary Examiner, Art Unit 1644

DETAILED ACTION

1. Applicant's amendment, filed 11/24/2021, is acknowledged.
2. Applicant IDS, filed 11/24/2021 and 12/15/2021, is acknowledged.
3. Claims 1, 3-4, 7, 16, 18-20, 23, 30-32, 46 are allowable. Claims 35-43 and 47, previously withdrawn from consideration as a result of a restriction requirement, are all the limitations of an allowable claim. Pursuant to the procedures set forth in MPEP § 821.04(a), **the restriction requirement between inventions I-III, as set forth in the Office action mailed on 05/28/2021, is hereby withdrawn** and claims 35-43 and 47 hereby rejoined and fully examined for patentability under 37 CFR 1.104. In view of the withdrawal of the restriction requirement, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.
4. In view of the Applicant's amendment all the previous NS-ODP rejections are hereby withdrawn.

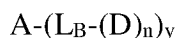
EXAMINER'S AMENDMENT

5. An Examiner's Amendment to the record appears below. Should the changes and/or additions be unacceptable to Applicant, an amendment may be filed as provided by 37 C.F.R. § 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the Issue Fee.
6. Authorization for this Examiner's Amendment was given in a telephone interview with Jana E. Harris on January 20, 2022.

In the Claims:

7. Amend claim 1 as follows:

-- 1. **(Currently Amended)** A conjugate of Formula (I) or a pharmaceutically acceptable salt thereof;



Formula (I)

wherein:

A is an antibody fragment that specifically binds to human cKIT, wherein the antibody fragment is selected from any of the following:

(1) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 (Heavy Chain Complementarity Determining Region 1) of SEQ ID NO: 1, (b) a HCDR2 (Heavy Chain Complementarity Determining Region 2) of SEQ ID NO: 2, and (c) a HCDR3 (Heavy Chain Complementarity Determining Region 3) of SEQ ID NO: 3; and (ii) a light chain variable region that comprises: (d) a LCDR1 (Light Chain Complementarity Determining Region 1) of SEQ ID NO: 16, (e) a LCDR2 (Light Chain Complementarity Determining Region 2) of SEQ ID NO: 17, and (f) a LCDR3 (Light Chain Complementarity Determining Region 3) of SEQ ID NO: 18;

(2) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 4, (b) a HCDR2 of SEQ ID NO: 5, (c) a HCDR3 of SEQ ID NO: 3; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 19, (e) a LCDR2 of SEQ ID NO: 20, and (f) a LCDR3 of SEQ ID NO: 21;

(3) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 6, (b) a HCDR2 of SEQ ID NO: 2, (c) a HCDR3 of SEQ ID NO: 3; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 16, (e) a LCDR2 of SEQ ID NO: 17, and (f) a LCDR3 of SEQ ID NO: 18;

(4) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 7, (b) a HCDR2 of SEQ ID NO: 8, (c) a HCDR3 of SEQ ID NO: 9; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 22, (e) a LCDR2 of SEQ ID NO: 20, and (f) a LCDR3 of SEQ ID NO: 18;

(5) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 27, (b) a HCDR2 of SEQ ID NO: 28, (c) a HCDR3 of SEQ ID NO: 29; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 42, (e) a LCDR2 of SEQ ID NO: 17, and (f) a LCDR3 of SEQ ID NO: 43;

(6) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 30, (b) a HCDR2 of SEQ ID NO: 31, (c) a HCDR3 of SEQ ID NO: 29; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 44, (e) a LCDR2 of SEQ ID NO: 20, and (f) a LCDR3 of SEQ ID NO: 45;

(7) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 32, (b) a HCDR2 of SEQ ID NO: 28, (c) a HCDR3 of SEQ ID NO: 29; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 42, (e) a LCDR2 of SEQ ID NO: 17, and (f) a LCDR3 of SEQ ID NO: 43;

(8) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 33, (b) a HCDR2 of SEQ ID NO: 34, (c) a HCDR3 of SEQ ID NO: 35; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 46, (e) a LCDR2 of SEQ ID NO: 20, and (f) a LCDR3 of SEQ ID NO: 43;

~~(9) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 4, (b) a HCDR2 of SEQ ID NO: 52, (c) a HCDR3 of SEQ ID NO: 3; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 19, (e) a LCDR2 of SEQ ID NO: 20, and (f) a LCDR3 of SEQ ID NO: 21;~~

~~(10) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 6, (b) a HCDR2 of SEQ ID NO: 51, (c) a HCDR3 of SEQ ID NO: 3; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 16, (e) a LCDR2 of SEQ ID NO: 17, and (f) a LCDR3 of SEQ ID NO: 18;~~

~~(11) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 7, (b) a HCDR2 of SEQ ID NO: 53, (c) a HCDR3 of SEQ ID NO: 9; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 22, (e) a LCDR2 of SEQ ID NO: 20, and (f) a LCDR3 of SEQ ID NO: 18;~~

(9)[(12)] a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 60, (b) a HCDR2 of SEQ ID NO: 61, (c) a HCDR3 of SEQ ID NO: 62; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 75, (e) a LCDR2 of SEQ ID NO: 76, and (f) a LCDR3 of SEQ ID NO: 77;

(10)[(13)] a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 63, (b) a HCDR2 of SEQ ID NO: 64, (c) a HCDR3 of SEQ ID NO: 62; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 78, (e) a LCDR2 of SEQ ID NO: 79, and (f) a LCDR3 of SEQ ID NO: 80;

(11)[(14)] a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 65, (b) a HCDR2 of SEQ ID NO: 61, (c) a HCDR3 of SEQ ID NO:

62; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 75, (e) a LCDR2 of SEQ ID NO: 76, and (f) a LCDR3 of SEQ ID NO: 77;

(12)[(15)] a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 66, (b) a HCDR2 of SEQ ID NO: 67, (c) a HCDR3 of SEQ ID NO: 68; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 81, (e) a LCDR2 of SEQ ID NO: 79, and (f) a LCDR3 of SEQ ID NO: 77;

(13)[(16)] a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 86, (b) a HCDR2 of SEQ ID NO: 87, (c) a HCDR3 of SEQ ID NO: 88; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 101, (e) a LCDR2 of SEQ ID NO: 102, and (f) a LCDR3 of SEQ ID NO: 103;

(14)[(17)] a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 89, (b) a HCDR2 of SEQ ID NO: 90, (c) a HCDR3 of SEQ ID NO: 88; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 104, (e) a LCDR2 of SEQ ID NO: 105, and (f) a LCDR3 of SEQ ID NO: 106;

(15)[(18)] a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 91, (b) a HCDR2 of SEQ ID NO: 87, (c) a HCDR3 of SEQ ID NO: 88; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 101, (e) a LCDR2 of SEQ ID NO: 102, and (f) a LCDR3 of SEQ ID NO: 103;

(16)[(19)] a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 92, (b) a HCDR2 of SEQ ID NO: 93, (c) a HCDR3 of SEQ ID NO: 94; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 107, (e) a LCDR2 of SEQ ID NO: 105, and (f) a LCDR3 of SEQ ID NO: 103;

(17)[(20)] a Fab or Fab' comprising a heavy chain variable region (VH) that comprises SEQ ID NO: 10, and a light chain variable region (VL) that comprises SEQ ID NO: 23;

(18)[(21)] a Fab or Fab' comprising a VH that comprises SEQ ID NO: 36, and a VL that comprises SEQ ID NO: 47;

(19)[(22)] a Fab or Fab' comprising a VH that comprises SEQ ID NO: 69, and a VL that comprises SEQ ID NO: 82;

(20)[(23)] a Fab or Fab' comprising a VH that comprises SEQ ID NO: 95, and a VL that comprises SEQ ID NO: 108;

(21)[(24)] a Fab' comprising a heavy chain that that comprises SEQ ID NO: 14, and a light chain that comprises SEQ ID NO: 25;

(22)[(25)] a Fab' comprising a heavy chain that that comprises SEQ ID NO: 40, and a light chain that comprises SEQ ID NO: 49;

(23)[(26)] a Fab' comprising a heavy chain that that comprises SEQ ID NO: 73, and a light chain that comprises SEQ ID NO: 84;

(24)[(27)] a Fab' comprising a heavy chain that that comprises SEQ ID NO: 99, and a light chain that comprises SEQ ID NO: 110;

(25)[(28)] a Fab comprising a heavy chain that comprises SEQ ID NO: 118, and a light chain that comprises SEQ ID NO: 122;

(26)[(29)] a Fab comprising a heavy chain that comprises SEQ ID NO: 118, and a light chain that comprises SEQ ID NO: 123;

(27)[(30)] a Fab comprising a heavy chain that comprises SEQ ID NO: 124, and a light chain that comprises SEQ ID NO: 128;

(28)[(31)] a Fab comprising a heavy chain that comprises SEQ ID NO: 124, and a light chain that comprises SEQ ID NO: 129;

(29)[(32)] a Fab comprising a heavy chain that comprises SEQ ID NO: 130, and a light chain that comprises SEQ ID NO: 134;

(30)[(33)] a Fab comprising a heavy chain that comprises SEQ ID NO: 130, and a light chain that comprises SEQ ID NO: 135;

(31)[(34)] a Fab comprising a heavy chain that comprises SEQ ID NO: 136, and a light chain that comprises SEQ ID NO: 140;

(32)[(35)] a Fab comprising a heavy chain that comprises SEQ ID NO: 141, and a light chain that comprises SEQ ID NO: 145;

(33)[(36)] a Fab comprising a heavy chain that comprises an amino acid sequence selected from SEQ ID NO: 119, 120 or 121, and a light chain comprising the amino acid sequence of SEQ ID NO: 25;

(34)[(37)] a Fab comprising a heavy chain that comprises an amino acid sequence selected from SEQ ID NO: 125, 126, or 127, and a light chain comprising the amino acid sequence of SEQ ID NO: 49;

(35)[[(38)]] a Fab comprising a heavy chain that comprises an amino acid sequence selected from SEQ ID NO: 137, 138, or 139, and a light chain comprising the amino acid sequence of SEQ ID NO: 84; or

(36)[[(39)]] a Fab comprising a heavy chain that comprises an amino acid sequence selected from SEQ ID NO: 142, 143, or 144, and a light chain comprising the amino acid sequence of SEQ ID NO: 110;

L_B is a linker;

D is a cytotoxic agent;

n is an integer from 1 to 10[[],]; and

y is an integer from 1 to 10. --

8. In claim 16, the phrase “, wherein the Formula (I) is” has been inserted after “claim 1”.

REASONS FOR ALLOWANCE

9. The following is an Examiner's Statement of Reasons for Allowance:

The prior art does not teach or suggest the antibody or antibody fragment that specifically binds to human cKIT recited in claims 1 and 46 and dependent claims thereof.

10. Claims 1, 3, 4, 7, 16, 18-20, 23, 30-32, 35-43, 46-47 are allowable.

11. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Daniel E. Kolker can be reached on (571) 272-3181. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

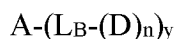
January 21, 2022

/MAHER M HADDAD/
Primary Examiner, Art Unit 1644

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. **(Currently Amended)** A conjugate of Formula (I) or a pharmaceutically acceptable salt thereof;



Formula (I)

wherein:

A is an antibody fragment that specifically binds to human cKIT, wherein the antibody fragment is selected from any of the following:

(1) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 (Heavy Chain Complementarity Determining Region 1) of SEQ ID NO: 1, (b) a HCDR2 (Heavy Chain Complementarity Determining Region 2) of SEQ ID NO: 2, and (c) a HCDR3 (Heavy Chain Complementarity Determining Region 3) of SEQ ID NO: 3; and (ii) a light chain variable region that comprises: (d) a LCDR1 (Light Chain Complementarity Determining Region 1) of SEQ ID NO: 16, (e) a LCDR2 (Light Chain Complementarity Determining Region 2) of SEQ ID NO: 17, and (f) a LCDR3 (Light Chain Complementarity Determining Region 3) of SEQ ID NO: 18;

(2) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 4, (b) a HCDR2 of SEQ ID NO: 5, (c) a HCDR3 of SEQ ID NO: 3; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 19, (e) a LCDR2 of SEQ ID NO: 20, and (f) a LCDR3 of SEQ ID NO: 21;

(3) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 6, (b) a HCDR2 of SEQ ID NO: 2, (c) a HCDR3 of SEQ ID NO: 3; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 16, (e) a LCDR2 of SEQ ID NO: 17, and (f) a LCDR3 of SEQ ID NO: 18;

(4) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 7, (b) a HCDR2 of SEQ ID NO: 8, (c) a HCDR3 of SEQ ID NO: 9; and

(ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 22, (e) a LCDR2 of SEQ ID NO: 20, and (f) a LCDR3 of SEQ ID NO: 18;

(5) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 27, (b) a HCDR2 of SEQ ID NO: 28, (c) a HCDR3 of SEQ ID NO: 29; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 42, (e) a LCDR2 of SEQ ID NO: 17, and (f) a LCDR3 of SEQ ID NO: 43;

(6) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 30, (b) a HCDR2 of SEQ ID NO: 31, (c) a HCDR3 of SEQ ID NO: 29; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 44, (e) a LCDR2 of SEQ ID NO: 20, and (f) a LCDR3 of SEQ ID NO: 45;

(7) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 32, (b) a HCDR2 of SEQ ID NO: 28, (c) a HCDR3 of SEQ ID NO: 29; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 42, (e) a LCDR2 of SEQ ID NO: 17, and (f) a LCDR3 of SEQ ID NO: 43;

(8) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 33, (b) a HCDR2 of SEQ ID NO: 34, (c) a HCDR3 of SEQ ID NO: 35; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 46, (e) a LCDR2 of SEQ ID NO: 20, and (f) a LCDR3 of SEQ ID NO: 43;

(9) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 4, (b) a HCDR2 of SEQ ID NO: 52, (c) a HCDR3 of SEQ ID NO: 3; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 19, (e) a LCDR2 of SEQ ID NO: 20, and (f) a LCDR3 of SEQ ID NO: 21;

(10) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 6, (b) a HCDR2 of SEQ ID NO: 51, (c) a HCDR3 of SEQ ID NO: 3; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 16, (e) a LCDR2 of SEQ ID NO: 17, and (f) a LCDR3 of SEQ ID NO: 18;

(11) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 7, (b) a HCDR2 of SEQ ID NO: 53, (c) a HCDR3 of SEQ ID NO: 9; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 22, (e) a LCDR2 of SEQ ID NO: 20, and (f) a LCDR3 of SEQ ID NO: 18;

(12) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 60, (b) a HCDR2 of SEQ ID NO: 61, (c) a HCDR3 of SEQ ID NO: 62; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 75, (e) a LCDR2 of SEQ ID NO: 76, and (f) a LCDR3 of SEQ ID NO: 77;

(13) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 63, (b) a HCDR2 of SEQ ID NO: 64, (c) a HCDR3 of SEQ ID NO: 62; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 78, (e) a LCDR2 of SEQ ID NO: 79, and (f) a LCDR3 of SEQ ID NO: 80;

(14) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 65, (b) a HCDR2 of SEQ ID NO: 61, (c) a HCDR3 of SEQ ID NO: 62; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 75, (e) a LCDR2 of SEQ ID NO: 76, and (f) a LCDR3 of SEQ ID NO: 77;

(15) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 66, (b) a HCDR2 of SEQ ID NO: 67, (c) a HCDR3 of SEQ ID NO: 68; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 81, (e) a LCDR2 of SEQ ID NO: 79, and (f) a LCDR3 of SEQ ID NO: 77;

(16) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 86, (b) a HCDR2 of SEQ ID NO: 87, (c) a HCDR3 of SEQ ID NO: 88; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 101, (e) a LCDR2 of SEQ ID NO: 102, and (f) a LCDR3 of SEQ ID NO: 103;

(17) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 89, (b) a HCDR2 of SEQ ID NO: 90, (c) a HCDR3 of SEQ ID NO: 88; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 104, (e) a LCDR2 of SEQ ID NO: 105, and (f) a LCDR3 of SEQ ID NO: 106;

(18) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 91, (b) a HCDR2 of SEQ ID NO: 87, (c) a HCDR3 of SEQ ID NO: 88; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 101, (e) a LCDR2 of SEQ ID NO: 102, and (f) a LCDR3 of SEQ ID NO: 103;

(19) a Fab or Fab' comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 92, (b) a HCDR2 of SEQ ID NO: 93, (c) a HCDR3 of SEQ ID NO: 94;

and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 107, (e) a LCDR2 of SEQ ID NO: 105, and (f) a LCDR3 of SEQ ID NO: 103;

(20) a Fab or Fab' comprising a heavy chain variable region (VH) that comprises SEQ ID NO: 10, and a light chain variable region (VL) that comprises SEQ ID NO: 23;

(21) a Fab or Fab' comprising a VH that comprises SEQ ID NO: 36, and a VL that comprises SEQ ID NO: 47;

(22) a Fab or Fab' comprising a VH that comprises SEQ ID NO: 69, and a VL that comprises SEQ ID NO: 82;

(23) a Fab or Fab' comprising a VH that comprises SEQ ID NO: 95, and a VL that comprises SEQ ID NO: 108;

(24) a Fab' comprising a heavy chain that that comprises SEQ ID NO: 14, and a light chain that comprises SEQ ID NO: 25;

(25) a Fab' comprising a heavy chain that that comprises SEQ ID NO: 40, and a light chain that comprises SEQ ID NO: 49;

(26) a Fab' comprising a heavy chain that that comprises SEQ ID NO: 73, and a light chain that comprises SEQ ID NO: 84;

(27) a Fab' comprising a heavy chain that that comprises SEQ ID NO: 99, and a light chain that comprises SEQ ID NO: 110;

(28) a Fab comprising a heavy chain that comprises SEQ ID NO: 118, and a light chain that comprises SEQ ID NO: 122;

(29) a Fab comprising a heavy chain that comprises SEQ ID NO: 118, and a light chain that comprises SEQ ID NO: 123;

(30) a Fab comprising a heavy chain that comprises SEQ ID NO: 124, and a light chain that comprises SEQ ID NO: 128;

(31) a Fab comprising a heavy chain that comprises SEQ ID NO: 124, and a light chain that comprises SEQ ID NO: 129;

(32) a Fab comprising a heavy chain that comprises SEQ ID NO: 130, and a light chain that comprises SEQ ID NO: 134;

(33) a Fab comprising a heavy chain that comprises SEQ ID NO: 130, and a light chain that comprises SEQ ID NO: 135;

(34) a Fab comprising a heavy chain that comprises SEQ ID NO: 136, and a light chain that comprises SEQ ID NO: 140;

(35) a Fab comprising a heavy chain that comprises SEQ ID NO: 141, and a light chain that comprises SEQ ID NO: 145;

(36) a Fab comprising a heavy chain that comprises an amino acid sequence selected from SEQ ID NO: 119, 120 or 121, and a light chain comprising the amino acid sequence of SEQ ID NO: 25;

(37) a Fab comprising a heavy chain that comprises an amino acid sequence selected from SEQ ID NO: 125, 126, or 127, and a light chain comprising the amino acid sequence of SEQ ID NO: 49;

(38) a Fab comprising a heavy chain that comprises an amino acid sequence selected from SEQ ID NO: 137, 138, or 139, and a light chain comprising the amino acid sequence of SEQ ID NO: 84; or

(39) a Fab comprising a heavy chain that comprises an amino acid sequence selected from SEQ ID NO: 142, 143, or 144, and a light chain comprising the amino acid sequence of SEQ ID NO: 110;

L_B is a linker;

D is a cytotoxic agent;

n is an integer from 1 to 10[[],]; and

y is an integer from 1 to 10.

2. **(Canceled)**

3. **(Original)** The conjugate of claim 1, wherein y is 1, 2, 3 or 4.

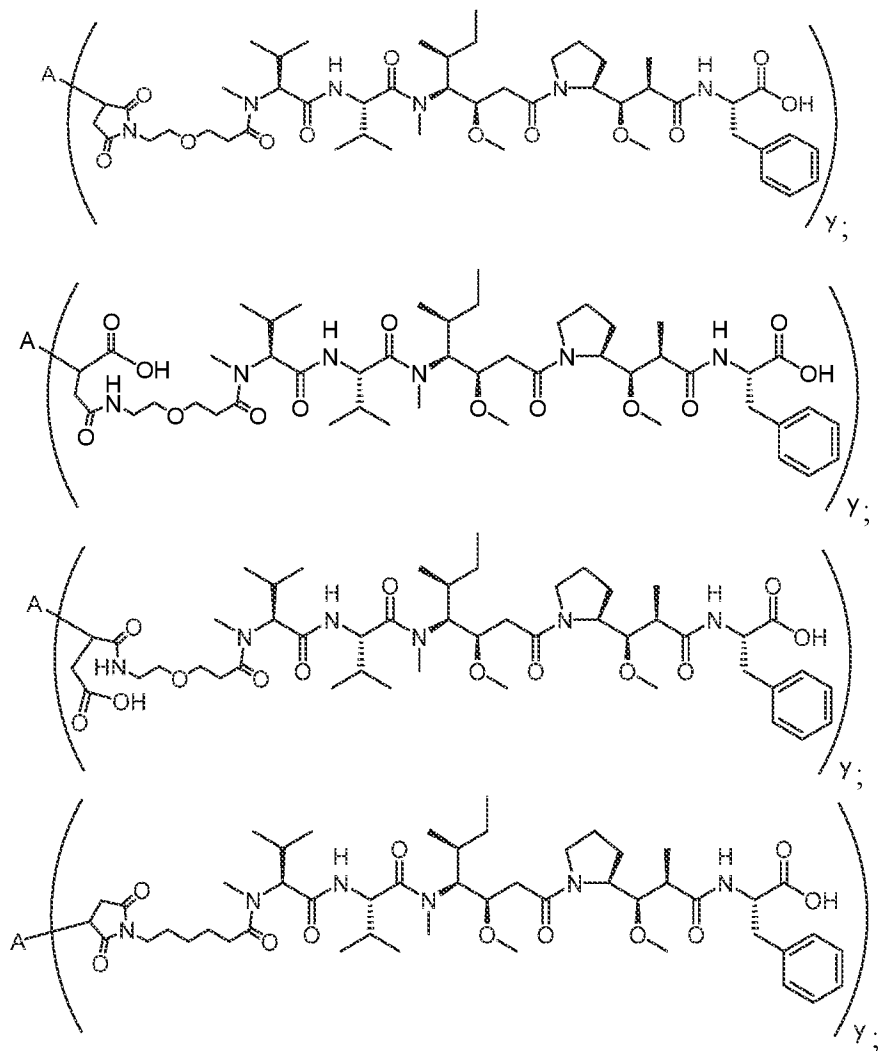
4. **(Previously Presented)** The conjugate of claim 1, wherein each D is a cytotoxic agent independently selected from an auristatin, an amanitin, a maytansinoid or a saporin.

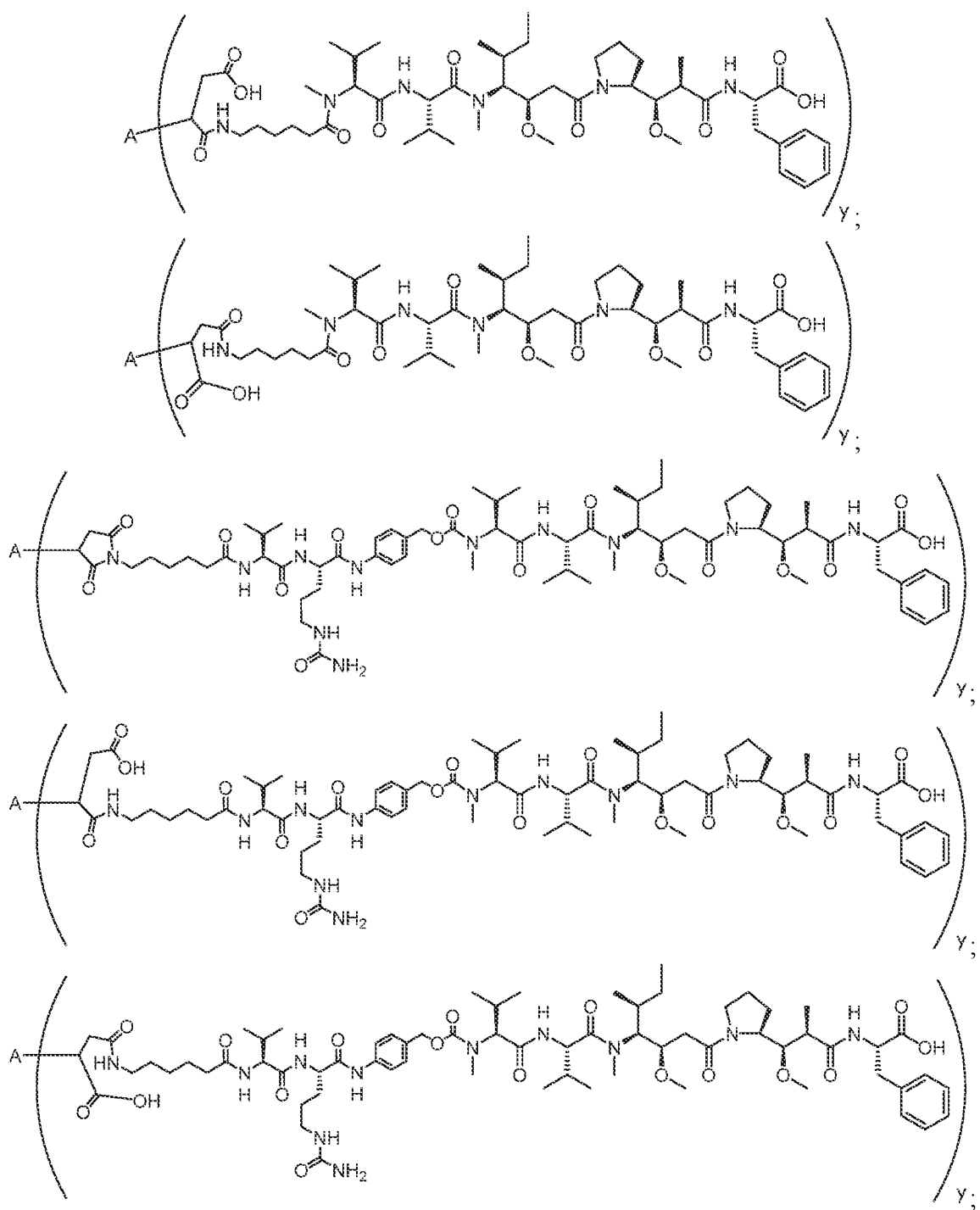
5-6. **(Canceled)**

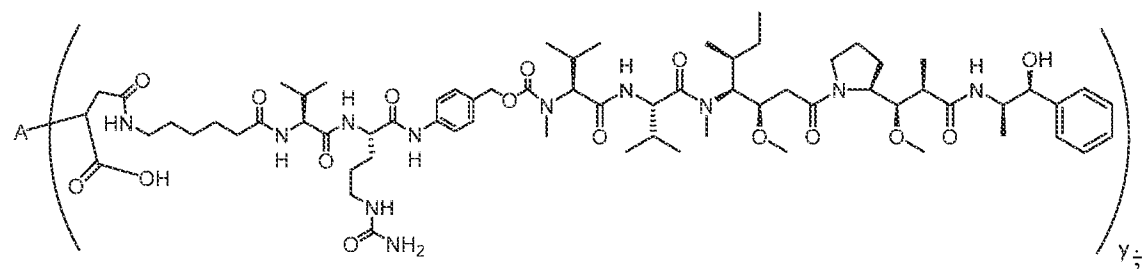
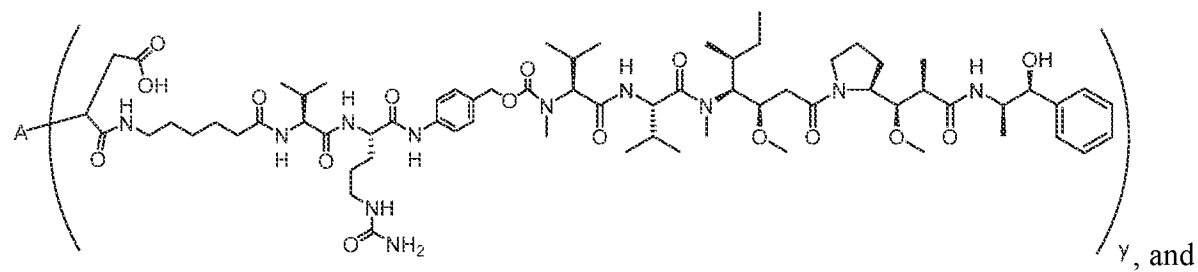
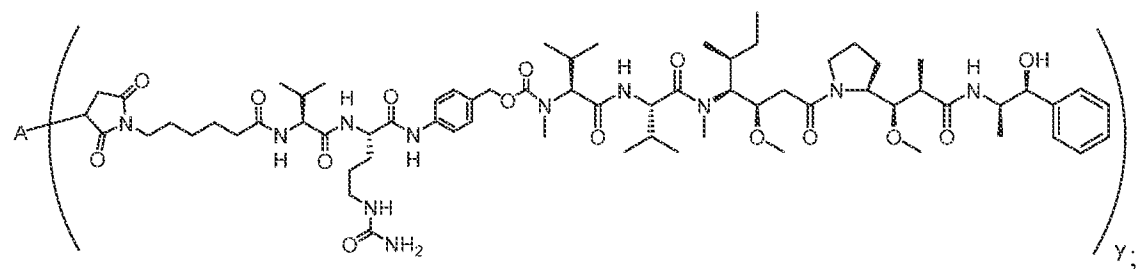
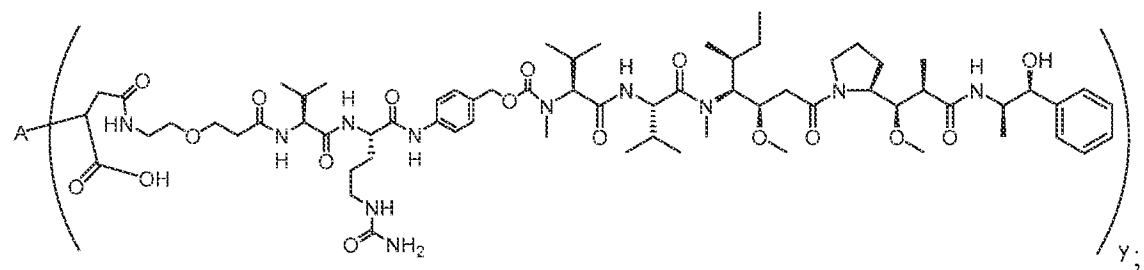
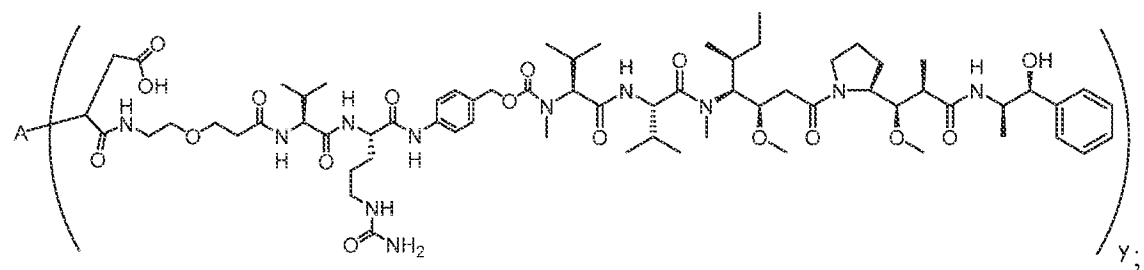
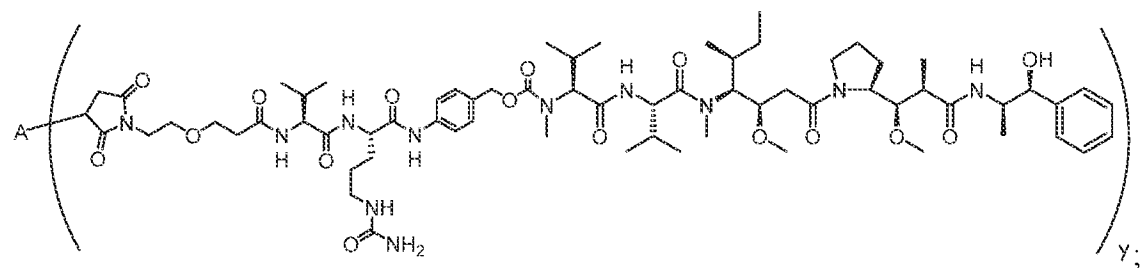
7. **(Previously Presented)** The conjugate of claim 1, wherein each L_B is independently selected from a cleavable linker or a non-cleavable linker.

8-15. **(Canceled)**

16. **(Currently Amended)** The conjugate of claim 1 selected from:







~~wherein:~~

~~A is an antibody fragment that specifically binds to human cKIT, and
y is an integer from 1 to 10.~~

17. **(Canceled)**

18. **(Previously Presented)** The conjugate of claim 1, wherein the antibody fragment specifically binds to the extracellular domain of human cKIT (SEQ ID NO: 112).

19. **(Previously Presented)** The conjugate of claim 1, wherein the antibody fragment specifically binds to an epitope in domains 1-3 of human cKIT (SEQ ID NO: 113).

20. **(Currently Amended)** The conjugate of claim 1, wherein the antibody fragment is a human or humanized Fab or Fab'.

21-22. (Canceled)

23. **(Previously Presented)** The conjugate of claim 1, wherein the antibody fragment is a Fab' and the linker (LB) is attached to a native cysteine residue in the hinge region of the Fab'.

24-29. (Canceled)

30. **(Currently Amended)** The conjugate of claim 1, wherein the conjugate has a half-life ~~of the conjugate~~ is less than about 24-48 hours.

31. **(Previously Presented)** The conjugate of claim 1, wherein the conjugate does not induce mast cell degranulation.

32. **(Previously Presented)** A pharmaceutical composition comprising the conjugate of claim 1 and a pharmaceutically acceptable carrier.

33-34. **(Canceled)**

35. **(Withdrawn)** A method of ablating hematopoietic stem cells in a patient in need thereof, the method comprising administering to the patient an effective amount of the pharmaceutical composition of claim 32.

36. **(Withdrawn)** The method of claim 35, wherein the patient is a hematopoietic stem cell transplantation recipient.

37. **(Withdrawn)** The method of claim 36, wherein the method is performed before hematopoietic stem cell transplantation to the patient.

38. **(Withdrawn)** A method of conditioning a hematopoietic stem cell transplantation patient, the method comprising: administering to the patient an effective amount of the pharmaceutical composition of claim 32, and allowing a sufficient period of time for the conjugates to clear from the patient's circulation before performing hematopoietic stem cell transplantation to the patient.

39. **(Withdrawn)** The method of claim 38, wherein the patient has an inherited immunodeficient disease, an autoimmune disorder, a hematopoietic disorder, or an inborn error of metabolism.

40. **(Withdrawn)** The method of claim 39, wherein the hematopoietic disorder is selected from: Acute myeloid leukemia (AML), Acute lymphoblastic leukemia (ALL), acute monocytic leukemia (AMoL), Chronic myeloid leukemia (CML), Chronic lymphocytic leukemia (CLL), Myeloproliferative disorders, Myelodysplastic syndromes, Multiple myeloma, Non-Hodgkin lymphoma, Hodgkin disease, Aplastic anemia, Pure red cell aplasia, Paroxysmal nocturnal hemoglobinuria, Fanconi anemi, Thalassemia major, Sickle cell anemia, Severe combined immunodeficiency, Wiskott-Aldrich syndrome, Hemophagocytic lymphohistiocytosis.

41. **(Withdrawn)** The method of claim 39, wherein the inborn error of metabolism is selected from mucopolysaccharidosis, Gaucher disease, metachromatic leukodystrophies, or adrenoleukodystrophies.

42. **(Withdrawn)** The method of claim 38, wherein the patient has a non-malignant disease or condition selected from Severe aplastic anemia (SAA), Wiskott Aldrich Syndrome, Hurlers Syndrome, FHL, CGD, Kostmanns syndrome, Severe immunodeficiency syndrome (SCID), other autoimmune disorders such as SLE, Multiple sclerosis, IBD, Crohns Disease, Sjogrens syndrome, vasculitis, Lupus, Myasthenia Gravis, Wegeners disease, inborn errors of metabolism and/or other immunodeficiencies.

43. **(Withdrawn)** The method of claim 38, wherein the patient has a malignant disease or condition selected from myelodysplastic syndromes (MDS), acute lymphoblastic leukemia (ALL), acute myelogenous leukemia (AML), acute monocytic leukemia (AMoL), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), hairy cell leukemia (HCL), T-cell prolymphocytic leukemia (T-PLL), large granular lymphocytic leukemia, adult T-cell leukemia, Precursor T-cell leukemia/lymphoma, Burkitt lymphoma, follicular lymphoma, diffuse large B cell lymphoma, mantle cell lymphoma, B-cell chronic lymphocytic leukemia/lymphoma, MALT lymphoma, Mycosis fungoides, Peripheral T-cell lymphoma not otherwise specified, Nodular sclerosis form of Hodgkin lymphoma Mixed-cellularity subtype of Hodgkin lymphoma.

44-45. **(Canceled)**

46. **(Original)** An antibody or antibody fragment that specifically binds to human cKIT, wherein the antibody or antibody fragment is selected from any of the following:

(1) an antibody or antibody fragment comprising (i) a heavy chain variable region that comprises (a) a HCDR1 (Heavy Chain Complementarity Determining Region 1) of SEQ ID NO: 1, (b) a HCDR2 (Heavy Chain Complementarity Determining Region 2) of SEQ ID NO: 2, and

(c) a HCDR3 (Heavy Chain Complementarity Determining Region 3) of SEQ ID NO: 3; and (ii) a light chain variable region that comprises: (d) a LCDR1 (Light Chain Complementarity Determining Region 1) of SEQ ID NO: 16, (e) a LCDR2 (Light Chain Complementarity Determining Region 2) of SEQ ID NO: 17, and (f) a LCDR3 (Light Chain Complementarity Determining Region 3) of SEQ ID NO: 18;

(2) an antibody or antibody fragment comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 4, (b) a HCDR2 of SEQ ID NO: 5, (c) a HCDR3 of SEQ ID NO: 3; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 19, (e) a LCDR2 of SEQ ID NO: 20, and (f) a LCDR3 of SEQ ID NO: 21;

(3) an antibody or antibody fragment comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 6, (b) a HCDR2 of SEQ ID NO: 2, (c) a HCDR3 of SEQ ID NO: 3; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 16, (e) a LCDR2 of SEQ ID NO: 17, and (f) a LCDR3 of SEQ ID NO: 18;

(4) an antibody or antibody fragment comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 7, (b) a HCDR2 of SEQ ID NO: 8, (c) a HCDR3 of SEQ ID NO: 9; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 22, (e) a LCDR2 of SEQ ID NO: 20, and (f) a LCDR3 of SEQ ID NO: 18;

(5) an antibody or antibody fragment comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 27, (b) a HCDR2 of SEQ ID NO: 28, (c) a HCDR3 of SEQ ID NO: 29; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 42, (e) a LCDR2 of SEQ ID NO: 17, and (f) a LCDR3 of SEQ ID NO: 43;

(6) an antibody or antibody fragment comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 30, (b) a HCDR2 of SEQ ID NO: 31, (c) a HCDR3 of SEQ ID NO: 29; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 44, (e) a LCDR2 of SEQ ID NO: 20, and (f) a LCDR3 of SEQ ID NO: 45;

(7) an antibody or antibody fragment comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 32, (b) a HCDR2 of SEQ ID NO: 28, (c) a HCDR3 of SEQ ID NO: 29; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 42, (e) a LCDR2 of SEQ ID NO: 17, and (f) a LCDR3 of SEQ ID NO: 43;

(8) an antibody or antibody fragment comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 33, (b) a HCDR2 of SEQ ID NO: 34, (c) a HCDR3 of SEQ ID NO: 35; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 46, (e) a LCDR2 of SEQ ID NO: 20, and (f) a LCDR3 of SEQ ID NO: 43;

(9) an antibody or antibody fragment comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 60, (b) a HCDR2 of SEQ ID NO: 61, (c) a HCDR3 of SEQ ID NO: 62; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 75, (e) a LCDR2 of SEQ ID NO: 76, and (f) a LCDR3 of SEQ ID NO: 77;

(10) an antibody or antibody fragment comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 63, (b) a HCDR2 of SEQ ID NO: 64, (c) a HCDR3 of SEQ ID NO: 62; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 78, (e) a LCDR2 of SEQ ID NO: 79, and (f) a LCDR3 of SEQ ID NO: 80;

(11) an antibody or antibody fragment comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 65, (b) a HCDR2 of SEQ ID NO: 61, (c) a HCDR3 of SEQ ID NO: 62; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 75, (e) a LCDR2 of SEQ ID NO: 76, and (f) a LCDR3 of SEQ ID NO: 77;

(12) an antibody or antibody fragment comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 66, (b) a HCDR2 of SEQ ID NO: 67, (c) a HCDR3 of SEQ ID NO: 68; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 81, (e) a LCDR2 of SEQ ID NO: 79, and (f) a LCDR3 of SEQ ID NO: 77;

(13) an antibody or antibody fragment comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 86, (b) a HCDR2 of SEQ ID NO: 87, (c) a HCDR3 of SEQ ID NO: 88; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 101, (e) a LCDR2 of SEQ ID NO: 102, and (f) a LCDR3 of SEQ ID NO: 103;

(14) an antibody or antibody fragment comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 89, (b) a HCDR2 of SEQ ID NO: 90, (c) a HCDR3 of SEQ ID NO: 88; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 104, (e) a LCDR2 of SEQ ID NO: 105, and (f) a LCDR3 of SEQ ID NO: 106;

(15) an antibody or antibody fragment comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 91, (b) a HCDR2 of SEQ ID NO: 87, (c) a HCDR3 of

SEQ ID NO: 88; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 101, (e) a LCDR2 of SEQ ID NO: 102, and (f) a LCDR3 of SEQ ID NO: 103;

(16) an antibody or antibody fragment comprising (i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 92, (b) a HCDR2 of SEQ ID NO: 93, (c) a HCDR3 of SEQ ID NO: 94; and (ii) a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 107, (e) a LCDR2 of SEQ ID NO: 105, and (f) a LCDR3 of SEQ ID NO: 103;

(17) an antibody or antibody fragment comprising a heavy chain variable region (VH) that comprises SEQ ID NO: 10, and a light chain variable region (VL) that comprises SEQ ID NO: 23;

(18) an antibody or antibody fragment comprising a VH that comprises SEQ ID NO: 36, and a VL that comprises SEQ ID NO: 47;

(19) an antibody or antibody fragment comprising a VH that comprises SEQ ID NO: 69, and a VL that comprises SEQ ID NO: 82;

(20) an antibody or antibody fragment comprising a VH that comprises SEQ ID NO: 95, and a VL that comprises SEQ ID NO: 108;

(21) an antibody or antibody fragment comprising a heavy chain that that comprises SEQ ID NO: 14, and a light chain that comprises SEQ ID NO: 25;

(22) an antibody or antibody fragment comprising a heavy chain that that comprises SEQ ID NO: 40, and a light chain that comprises SEQ ID NO: 49;

(23) an antibody or antibody fragment comprising a heavy chain that that comprises SEQ ID NO: 73, and a light chain that comprises SEQ ID NO: 84;

(24) an antibody or antibody fragment comprising a heavy chain that that comprises SEQ ID NO: 99, and a light chain that comprises SEQ ID NO: 110;

(25) an antibody or antibody fragment comprising a heavy chain that comprises SEQ ID NO: 118, and a light chain that comprises SEQ ID NO: 122;

(26) an antibody or antibody fragment comprising a heavy chain that comprises SEQ ID NO: 118, and a light chain that comprises SEQ ID NO: 123;

(27) an antibody or antibody fragment comprising a heavy chain that comprises SEQ ID NO: 124, and a light chain that comprises SEQ ID NO: 128;

(28) an antibody or antibody fragment comprising a heavy chain that comprises SEQ ID NO: 124, and a light chain that comprises SEQ ID NO: 129;

(29) an antibody or antibody fragment comprising a heavy chain that comprises SEQ ID NO: 130, and a light chain that comprises SEQ ID NO: 134;

(30) an antibody or antibody fragment comprising a heavy chain that comprises SEQ ID NO: 130, and a light chain that comprises SEQ ID NO: 135;

(31) an antibody or antibody fragment comprising a heavy chain that comprises SEQ ID NO: 136, and a light chain that comprises SEQ ID NO: 140;

(32) an antibody or antibody fragment comprising a heavy chain that comprises SEQ ID NO: 141, and a light chain that comprises SEQ ID NO: 145;

(33) an antibody comprising a heavy chain that that comprises SEQ ID NO: 12, and a light chain that comprises SEQ ID NO: 25;

(34) an antibody comprising a heavy chain that that comprises SEQ ID NO: 38, and a light chain that comprises SEQ ID NO: 49;

(35) an antibody comprising a heavy chain that that comprises SEQ ID NO: 71, and a light chain that comprises SEQ ID NO: 84; or

(36) an antibody comprising a heavy chain that that comprises SEQ ID NO: 97, and a light chain that comprises SEQ ID NO: 110.

47. **(Withdrawn)** A nucleic acid encoding an antibody or antibody fragment of claim 46.

48-50. **(Canceled)**



SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

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Detalle del pago

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