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| EXAMINER |
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CANELLA, KAREN A

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1643

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08/15/2017

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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|                              |                                      |                                         |                                                  |
|------------------------------|--------------------------------------|-----------------------------------------|--------------------------------------------------|
| <b>Office Action Summary</b> | <b>Application No.</b><br>14/432,073 | <b>Applicant(s)</b><br>ZHAO, R. YONGXIN |                                                  |
|                              | <b>Examiner</b><br>KAREN CANELLA     | <b>Art Unit</b><br>1643                 | <b>AIA (First Inventor to File) Status</b><br>No |

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

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 5/18/17.  
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ 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.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims\*

- 5) ☒ Claim(s) 1-12 and 14-20 is/are pending in the application.  
5a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 6) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 7) ☒ Claim(s) 1-12 and 14-20 is/are rejected.
- 8) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 9) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

\* If any claims have been determined allowable, 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](http://www.uspto.gov/patents/init_events/pph/index.jsp) or send an inquiry to [PPHfeedback@uspto.gov](mailto:PPHfeedback@uspto.gov).

### Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

### Priority under 35 U.S.C. § 119

- 12) ☐ 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)).

\*\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                                                                          |                                                                                         |
|------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                                              | 3) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b)<br>Paper No(s)/Mail Date ____. | 4) <input type="checkbox"/> Other: ____.                                                |

### **DETAILED ACTION**

The present application is being examined under the pre-AIA first to invent provisions.

Acknowledgement is made of applicant's election of the species -P(=O)(OM)-, and applicant's indication that claims 1-20 read on the elected species. Claim 13 has been canceled. Claims 1-12, 14-20 have been amended. Claims 1-12 and 14-20 are pending and examined to the extent that they read on the elected species.

#### ***Claim Objections***

Claim 13 is objected to for:

reciting "doxorubicin" twice: the first instance on page 9, line 6 from the bottom of the page, and the second instance being on page 10, line 6

reciting "dactinomycin" twice: the first instance on page 9, line 6 from the bottom and the second instance on page 10, line 5;

reciting spectinomycin twice: page 9, section 3a and page 10, section 3k;

reciting "f)" twice: page 7, last line and page 8, line 18;

reciting glycylicyclines twice: page 10, section 3f and page 11, section 3t;

reciting bacitracin twice; page 10, section 3o and page 11, section 3u;

reciting rifampicin three times; page 10, section 3k, page 11, section 3u and page 11, section 4f;

reciting diarylpyrimidines twice: page 11, section 4f and page 12, section 4h;

reciting hydroxyurea twice: page 7, section 1d and page 9, section 1f;

reciting ribavirin twice" page 7, section 1d and page 11, section 4e;

reciting tobramycin twice: page 8, section 3a;

reciting tacrolimus twice: page 9, section 2 and page 10, section 3k.

Claim 5 is objected to for the typographical error of "dimmers of pyrrolobenzodiazepine" rather than "dimers of pyrrolobenzodiazepine".

Appropriate correction is required.

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***Claim Rejections - 35 USC § 112***

The following is a quotation of 35 U.S.C. 112(b):

(b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12 and 14-20 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

(A) Claims 1-4 present a structure wherein the moiety represented as [T-R3] is associated with the moiety represented as [Q-R2], the moiety represented by R4 is associated with both the [T-R3] moiety and Z or Drug, and Y-R1 is associated with the [Q-R2] moiety. It is unclear if “T” is required to be directly bonded to R2, R3 is required to be directly bonded to R4, R1 is required to be directly bonded to Q, Y or Cb is directly bonded to R1 and Z is directly bonded to R4, and R5 and R6 are directly bonded to R4 because the claims permit R1 and R4 to be “H” which would not allow for further bonding to either “Z”, “Drug”, “Y” and “Cb”. The claims also permit R2 to be “H” which would not allow for further bonding to the [T-R3] moiety and thus elimination of the inclusion of the “Z” and “Drug” moieties. Likewise, the claims permit R3 to be “H” which would not allow for further bonding to R4 and exclusion of the “Z” and “Drug” moieties. Thus, it appears that inclusion of “H” for R1, R2, R3 and/or R4 is not consistent with the interpretation of the claims wherein Y or Cb is directly attached to R1, R1 is directly attached to Q which is directly attached to R2 which is directly attached to T which is directly attached to R3 which is directly attached to R4 which is directly attached to either Z or Drug.

(B ) Claim 1 recites "Z represents a functional group that enables linkage of the hydrophilic linker to a cytotoxic drug via a disulfide, thioether, thioester, peptide, hydrazone, ether, ester, carbamate, carbonate, secondary or tertiary or quaternary amine, imine, cycloheteroalkane, heteroaromatic, alkoximine or amide bond". It is unclear if the recited

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species of disulfide, thioether, thioester, peptide, hydrazone, ether, ester, carbamate, carbonate, secondary or tertiary or quaternary amine, imine, cycloheteroalkyane, heteroaromatic, alkoximine or amide bond are required as part of the “Z” moiety, or if the recited species are intended to be part of the cytotoxic drug.

Claim 3 recites “Z represents a functional group that is capable of reacting with a cytotoxic drug via a disulfide, thioether, thioester, peptide, hydrazone, ether, ester, carbamate, carbonate, secondary or tertiary or quaternary amine, imine, cycloheteroalkyane, heteroaromatic, alkoximine or amide bond”. It is unclear if the recited species of disulfide, thioether, thioester, peptide, hydrazone, ether, ester, carbamate, carbonate, secondary or tertiary or quaternary amine, imine, cycloheteroalkyane, heteroaromatic, alkoximine or amide bond are required as part of the “Z” moiety, or if the recited species are intended to be part of the cytotoxic drug.

For purpose of examination, the elected species will be examined within the context of the compounds described by the specification.

(C) A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by “such as” and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

In the present instance,

claims 1 and 3 recite the broad recitation that Z represents a functional group that enables linkage of the hydrophilic linker compound to a cytotoxic drug via an amide bond, and the claim also recites that Z represents a functional group that enables linkage of the hydrophilic linker compound to a cytotoxic drug via a peptide bond which is the narrower statement of the range/limitation;

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claim 5 recites the broad recitation “retinols” (page 7, 1c), and the claim also recites retinoic acids which is the narrower statement of the range/limitation;

claim 5 recites the broad recitation “retinols”, and the claim also recites CB1093, RB1089, KH1060, cholecalciferol and ergocalciferol (page 7, 1e) which is the narrower statement of the range/limitation;

claim 5 recites the broad recitation anti-EGFR/ErbB2, and the claim also recites BIBW 2992 (page 8, first line) which is the narrower statement of the range/limitation

claim 5 recites the broad recitation anti-VEGFR2, and the claim also recites E7080 (page 8, 3<sup>rd</sup> line) which is the narrower statement of the range/limitation;

claim 5 recites the broad recitation polyketides (page 8, section f), and the claim also recites acetogenins which is the narrower statement of the range/limitation;

claim 5 recites the broad recitation actinomycin on page 8, line 11, and the claim also recites actinomycin D on page 8, line 24 which are the narrower statements of the range/limitation;

claim 5 recites the broad recitation bleomycins on page 8, line 12, and the claim also recites bleomycin A2, bleomycin B2 and peplomycin on page 8, line 25 which are the narrower statements of the range/limitation;

claim 5 recites the broad recitation CA2+ ATPase inhibitors (page 8, line 27), and the claim also recites thapsigargin (page 9, line 1) which is the narrower statement of the range/limitation;

claim 5 recites the broad recitation bactoprenol inhibitors, and the claim also recites Bacitracin (page 11, line 8) which is the narrower statement of the range/limitation;

claim 5 recites the broad recitation DADAL/AR inhibitors, and the claim also recites cycloserine (page 11, line 8) which is the narrower statement of the range/limitation;

claim 5 recites the broad recitation diarylpyrimidines, and the claim also recites etravirine and rilpivirine (page 11, section f) which are the narrower statements of the range/limitation;

claim 8 recites the broad limitation of integrins, and the claim also recites  $\alpha v \beta 3$ ,  $\alpha 5 \beta 1$ ,  $\alpha 6 \beta 4$ ,  $\alpha 11 \beta 3$ ,  $\alpha 5 \beta 5$ ,  $\alpha v \beta$  which are the narrower statements of the range/limitation.

claim 15 recites the broad recitation benzodiazepine dimers, and the claim also recites dimers of pyrrolbenzodiazepine, tomaymycin, indolinbenzodiazepines,

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imidazobenzothiadiazepines, or oxazolidinobenzodiazepines which are the narrower statements of the range/limitation;

claim 15 recites the broad recitation dolastatins/auristatins and the claim also recites monomethyl auristatin E, MMAE, MMAF, auristatin PYE, auristatin TP, Auristatins 2-AQ, 6-AQ, EB (AEB), and EFP which are the narrower statement of the range/limitation.

(D) It is unclear how the subheadings a)-f) under “Chemotherapeutic agents in claim 5 limit the subject matter of the claim. For instance subsection e) “Hormonal Therapies” (starting on line 19 of page 7 continues until the bottom of the page) includes a multitude of diverse agents unrelated to “hormonal therapies” such as vitamin D3 analogs, photodynamic “therapies”, and cytokines.

(E) Claim 5 (page 11 section 4), recites “Anti-Viral drugs comprising a) Entry/fusion inhibitors” including gp41 and CD4. However, gp41 and CD4 are the targets of the entry/fusion inhibitors, not the inhibitors per se;

(F) Claim 5 recites various radioisotopes as drugs on page 12, and also recites “derivatives of any of the above drugs”. It is unclear what applicant is intending for a radioisotope derivative, as the radioisotopes are atomic species not compounds.

(G) Claim 15 recites “...esperamicins, and analogues and derivatives thereof”. It is unclear if applicant is claiming analogues and derivatives of the entire Markush group of claim 15, or if analogues and derivatives refers only to esperamicins. For purpose of examination, the claims will be read as encompassing analogues and derivatives of all the species of the Markush group of claim 15.

The following is a quotation of the first paragraph of 35 U.S.C. 112(a):

(a) IN GENERAL.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

The following is a quotation of the first paragraph of pre-AIA 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person

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skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 6 and 15 are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor or a joint inventor, or for pre-AIA the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 5 requires "derivatives of any of the above drugs". Claim 6 requires "derivatives of any of the above". Claim 15 requires "analogues and derivatives thereof". The instant specification has failed to describe any analog or derivative originating from the large genus of chemotherapeutic, anti-autoimmune, anti-infectious, or anti-viral compounds or radioisotopes recited in the specification to be analogs or derivatives. One of skill in the art would reasonably conclude that applicant was not in possession of the compounds of claim 2 requiring the large genus of analogs and derivatives of the recited drug species of claims 5, 6 and 15 at the time of filing.

Claims 13 and 30-32 are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re wands, 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(A) Claim 5 requires the compound of any one of claim 2 wherein the "Drug" is selected from the group consisting of a multitude of agents unrelated in structure. It is clear that the biological activity of the Drug incorporated into the compound must be preserved in order for the claimed compounds to be used by one of skill in the art.

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The specification has described conjugation the synthesis of bi-functional mono, bi, tri and tetraphosphinate linkers enabling conjugation to a drug via reaction of a thiol group on a drug moiety and conjugation of a protein or antibody via a maleimido group on the opposite end of the linker. The use of the maleimido group in protein and antibody conjugation is well known in the art. However, claim 5 is not limited to drugs or biologically active proteins having a free thiol group, but includes a plethora of drug molecules, nucleosides and nucleotides, siRNA and anti-sense drugs in addition to multi-component substances, such as Stimuvax (also known as BLP25, see Sangha and Butts, *Clinical Cancer Research*, 2007, Vol. 13, suppl. 15, pp. 4652s-4654s, see page 4653s, first paragraph under the heading "Liposomal MUC1 Vaccine BLP25"), Allovectin-7 (Stopeck et al, (*Clinical Cancer Research*, 2001, Vol. 7, pp. 2285-2291, see page 2286, first column, lines 1-6 of the second paragraph) and Provenge (Harzstark and Small, *Expert Opinion on Biological Therapy*, 2007, Vol. 7, pp. 1275-1280) which is an antigen-loaded antigen presenting cell. The specification provides no teaching or guidance on the modification of the multitude of drugs, including multi-component products and cells, to provide a free thiol group for conjugation to the linker such that the modification and/or the conjugation of the drug, products or cells preserves the required function of the drug, multicomponent products or cells. Thus, one of skill in the art would be required to determine how to modify all the drugs and multicomponent products required in claims 5 such that the expected biological functions of the drugs and products are maintained and if such modification was possible. Based on this requirement, one of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to make and use the broadly claimed compounds of claim 5.

(B) As drawn to the conjugates of the invention comprising anti-infectious disease agent and anti-viral drugs.

Claim 5 is drawn in part to the cell-binding agent drug conjugate of claim 2 wherein the "drug" includes an anti-infectious disease agent or an anti-viral agent. Claim 20 is included with this rejection because a pharmaceutical composition comprising a therapeutically effective amount of the conjugate of claim 2 and additionally, an anti-infectious agent is presumably used to treat an infectious disease. The specification does not teach any binding agent specific for the treatment of a patient with a viral or bacterial infection. The art teaches that the vast majority of therapeutic mAb are administered for a the treatment of cancer, autoimmune disorder and

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transplantation (Irani et al, Molecular Immunology, 2015, Vol. 67, pp. 171-182, see page 171, second column, lines 14-17) but that the development of monoclonal therapeutic antibodies against specific infectious diseases has been slow (page 171, first column, lines 5-8). Irani et al note that antibodies developed to HIV target HIV envelop glycoproteins, antibodies developed to West Nile virus target domain III of the virus, antibodies developed to gram positive Staph aureus target poly N-acetyl glucosamine, and antibodies targeting gram negative bacteria target Serogroup O6 LPS, and Shiga toxin 2 (Table 4). It is noted that antibodies targeting bacteria bind directly to the infectious agent, and that with the exception of lentivirus infected cells and retrovirus infected cells, antibodies which bind to viruses also bind directly to the virus rather than the cell infected with the virus (Pelegrin et al, Trends in Microbiology, 2015, Vol. 23, pp. 653-665, see page 653, lines 1-3 and page 654, lines 9-10). The conjugate of the instant invention requires a cell binding agent, but for recognition of non-retroviral or non-lentiviral viral infections, the virus itself will be bound, rather than the cell harboring the virus. As a free virus is not a cell per se, the targeting of a free virus cannot be carried out by a "cell-binding agent" required by the conjugate of instant claim 2. Further, there are no teachings in the specification of a "Drug" active against a free virus which is not capable of autonomous replication outside of a host cell.

Targeting of free bacteria by the conjugate of the invention could be carried out with a cell binding agent which is a monoclonal antibody recognizing the bacteria cells. Bacterial cells are in possession of a cell wall which is not a feature of a eukaryotic cell. The instant specification provides no guidance as to the ability of the a bacterial cell bound to an antibody to internalize the antibody through the cell wall in order that the Drug attached to the conjugate can be internalized and exert a toxic affect against the targeted bacterial cell. There is no art of record or teachings in the specification to support the notion that antibody-drug conjugates are effective at targeting bacterial cells to exert the effect of the drug on the bacterial cells.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of pre-AIA 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7 are rejected under pre-AIA 35 U.S.C. 102(b) as being anticipated by Brixner (U.S. 5,094,848).

Brixner discloses the compound of “A-bridge-targeting moiety” (column 2, lines 52-68) for targeting of an active agent in vitro or in vivo, wherein the bridging moiety is the diphosphate linker  $-L^1_n-DP-L^2-$ , wherein  $L^1$  is an optional spacer group between the active agent and the diphosphate and  $L^2$  is a linking group connecting the diphosphate with the targeting moiety (column 3, lines 1-14). Brixner discloses that the targeting moiety includes polypeptides such as antibodies and fragments thereof (column 10, lines 27-36). Brixner discloses radiolabeled molecules as the active agent (column 13, line 58 to column 15, line 45). Brixner discloses antitumor agents as the active agent, such as ARA-C, cyclophosphamide, diethylstilbestrol diphosphate, polyestradiol phosphate, estrmustine, cytarabine (column 16, lines 40-62) and active agents comprised within polymers, such as methotrexate, daunomycin, doxorubicin, mitomycin, bleomycin and mitoxantrone in addition to ribosomal inactivating toxins (column 17, lines 3-29). Brixner discloses that the polymeric substrate can be conventionally derivatized for conjugation to the targeting group using an HNS or other active ester (column 3, lines 61-67). Brixner disclose the targeting of tumor with a diagnostic or therapeutic agent using the targeting agent of NR-Lu-10 Fab conjugated to anti-breast cancer agents (column 17, lines 61-68). The compound of Brixner comprising the diphosphate meet the limitation of the instant claims 1-4 wherein Q and T are both  $-P=O(OM)-$ ,  $m=1$ ,  $n=1$ , wherein  $R_2$  is “O” that covalently connects the phosphinate group to the second phosphinate group. Brixner discloses the structure in example 1 wherein Y is the functional group enabling reaction of the linker with the cell binding agent and Z is the functional group enabling a link of the agent to the "cytotoxic drug" which is a radionuclide via a hydrogen bond with the amide nitrogen (column 13, lines 60-68). The structure of Brixner meets the limitation of claims 1-4 wherein  $R_5$  and  $R_6$  are “H”.

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAREN CANELLA whose telephone number is (571)272-0828. The examiner can normally be reached on 9:30-6:00 M-F.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at <http://www.uspto.gov/interviewpractice>.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu can be reached on (571)272-0839. The fax phone 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 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). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/KAREN CANELLA/  
Primary Examiner, Art Unit 1643

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