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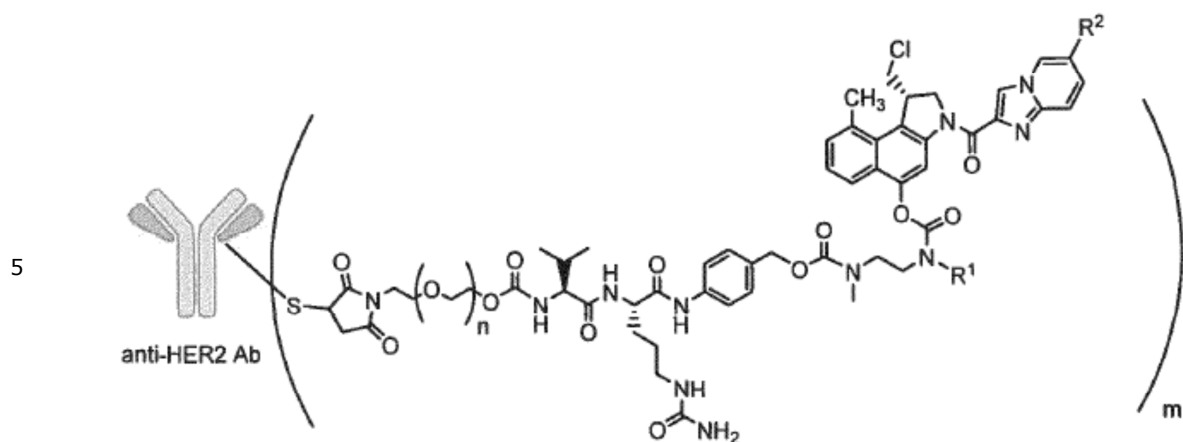
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(54)	Title	DUOCARMYCIN ADCS FOR USE IN THE TREATMENT OF BLADDER CANCER
(56)	References Cited:	EP-A1- 2 165 710, HIDEO SHIGEMATSU ET AL: "A case of HER-2-positive recurrent breast cancer showing a clinically complete response to trastuzumab-containing chemotherapy after primary treatment of triple-negative breast cancer", WORLD JOURNAL OF SURGICAL ONCOLOGY, BIOMED CENTRAL, LONDON, GB, vol. 9, no. 1, 7 November 2011 (2011-11-07), page 146, XP021113554, ISSN: 1477-7819, DOI: 10.1186/1477-7819-9-146, Dokter W et al: "Abstract 4329: Novel HER2 targeting antibody-drug conjugates based on DNA-interacting duocarmycin and an unique linker technology with great potential in breast cancer and NSCLC", 15 April 2013 (2013-04-15), XP002725434, Retrieved from the Internet:

URL:http://cancerres.aacrjournals.org/cgi/content/meeting_abstract/73/8_MeetingAbstracts/4329?sid=79046d57-942d-4258-9aed-2238d480704d [retrieved on 2014-06-05], EP-A1- 2 380 909, WO-A1-02/096910, WO-A1-2010/070117, WO-A1-2012/143523, WO-A2-03/026577, WO-A2-2004/032828, WO-A2-2011/133039, Synthon company. "Synthon Biopharmaceuticals reports positive early results with its second generation HER2-antibody-drug conjugate", 22 January 2013 (2013-01-22), XP002725428, Retrieved from the Internet: URL:<http://www.synthon.com/Corporate/News/PressReleases/Synthon-reports-positive-early-results-with-its-second-generation-HER2-antibody-drug-conjugate> [retrieved on 2014-06-05], RAJALETCHUMY VELOO KUTTY ET AL: "Cetuximab conjugated vitamin E TPGS micelles for targeted delivery of docetaxel for treatment of triple negative breast cancers", BIOMATERIALS, vol. 34, no. 38, 1 December 2013 (2013-12-01), pages 10160-10171, XP055122815, ISSN: 0142-9612, DOI: 10.1016/j.biomaterials.2013.09.043, TRAIL P A: "Antibody drug conjugates as cancer therapeutics", ANTIBODIES 20130227 MDPI AG CHE, vol. 2, no. 1, 27 February 2013 (2013-02-27), pages 113-129, XP002725437, NOLTING B: "Linker technologies for antibody-drug conjugates", METHODS IN MOLECULAR BIOLOGY - ANTIBODY-DRUG CONJUGATES 2013 HUMANA PRESS USA, vol. 1045, 2013, pages 71-100, XP008169796, ISSN: 1064-3745, JOHN A. FLYGARE ET AL: "Antibody-Drug Conjugates for the Treatment of Cancer", CHEMICAL BIOLOGY & DRUG DESIGN, vol. 81, no. 1, 17 January 2013 (2013-01-17), pages 113-121, XP055121985, ISSN: 1747-0277, DOI: 10.1111/cbdd.12085, REBECCA K KELLY ET AL: "An antibody cytotoxic conjugate, BIIB015, is a new targeted therapy for Cripot positive tumours", EUROPEAN JOURNAL OF CANCER, PERGAMON PRESS, OXFORD, GB, vol. 47, no. 11, 28 February 2011 (2011-02-28), pages 1736-1746, XP028323640, ISSN: 0959-8049, DOI: 10.1016/J.EJCA.2011.02.023 [retrieved on 2011-03-03], S. A. KAZANE ET AL: "Site-specific DNA-antibody conjugates for specific and sensitive immuno-PCR", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 109, no. 10, 6 March 2012 (2012-03-06), pages 3731-3736, XP055076255, ISSN: 0027-8424, DOI: 10.1073/pnas.1120682109, SHEN B - Q ET AL: "Conjugation site modulates the in vivo stability and therapeutic activity of antibody-drug conjugates", NATURE BIOTECHNOLOGY 2012 NATURE PUBLISHING GROUP USA, vol. 30, no. 2, February 2012 (2012-02), pages 184-189, XP055123129, ISSN: 1087-0156

Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters concerning the validity of the patent, language of the application/patent granted at the EPO will be used as the basis for the decision. The patent documents published by the EPO are available through Espacenet (<http://worldwide.espacenet.com>) or via the search engine on our website here: <https://search.patentstyret.no/>

Patentkrav**1.** Forbindelse av formel (I)

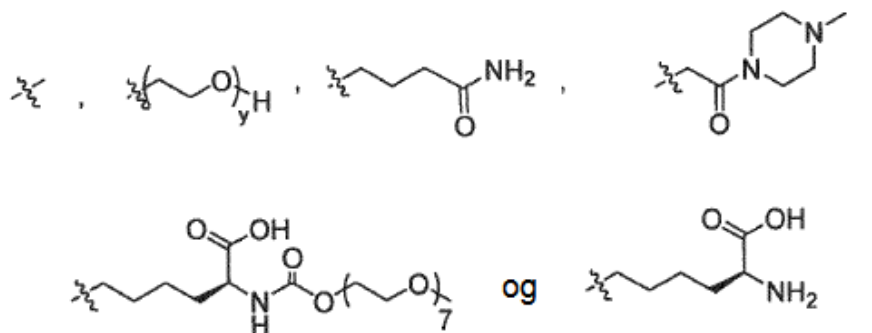
hvor

anti-HER2 Ab er et anti-HER2 antistoff eller antistoffragment,

10 n er 0-3,

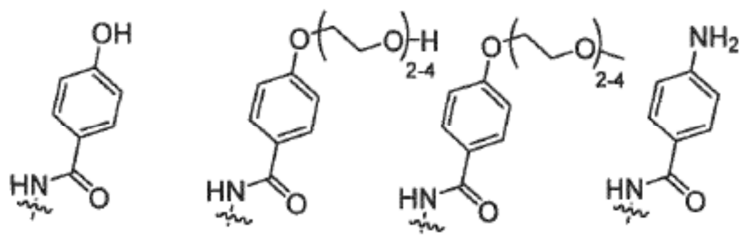
m representerer en gjennomsnittlig DAR på fra 1 til 4,

R¹ er valgt fra



y er 1-16, og

15 R² er valgt fra



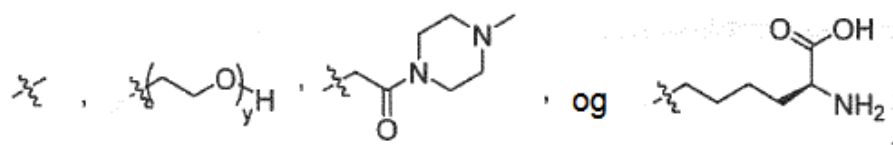
for anvendelse ved behandling av humane faste svulster som uttrykker HER2, hvor den humane faste svulst som uttrykker HER2 er blærekreft.

2. Forbindelse for anvendelse ifølge krav 1, hvor anti-HER2 Ab er et anti-HER2 antistoff eller antistofffragment,

5 n er 0-1,

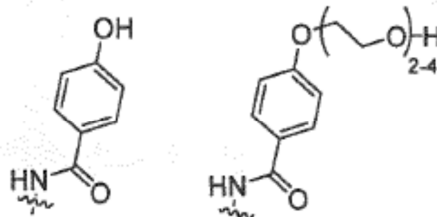
m representerer en gjennomsnittlig DAR på fra 1 til 4,

R¹ er valgt fra

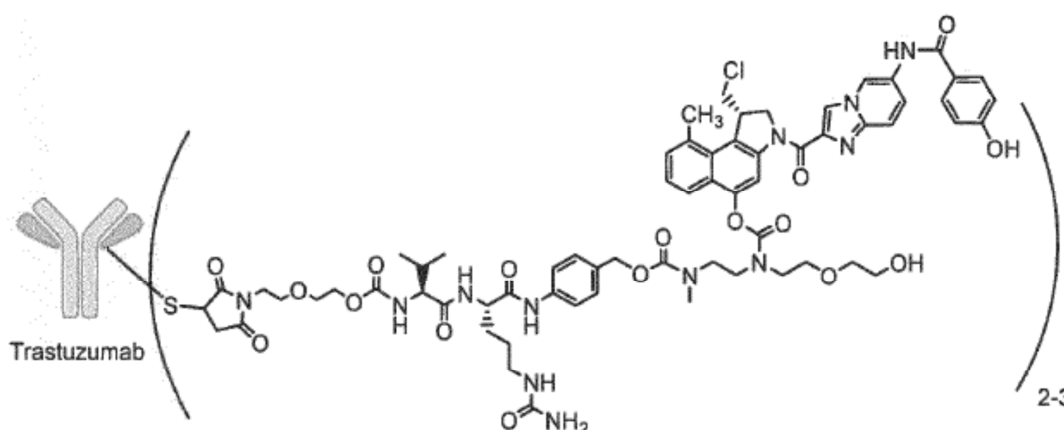


y er 1-16, og

10 R² er valgt fra



3. Forbindelse for anvendelse ifølge krav 1 eller 2 av formel (II)



- 4.** Forbindelse for anvendelse ifølge krav 3 av formel (II) som har en gjennomsnittlig DAR på fra 2,6 til 2,9.
- 5.** Forbindelse for anvendelse ifølge et hvilket som helst av kravene 1 til 4, hvor blærekreften er HER2 IHC 2+ eller 1+.
- 5 **6.** Forbindelse for anvendelse ifølge et hvilket som helst av kravene 1 til 5, hvor blærekreften er HER2 FISH-negativ.
- 7.** Kombinasjon av forbindelse for anvendelse ifølge et hvilket som helst av kravene 1 til 6 med et terapeutisk antistoff og/eller et kjemoterapeutisk middel, for anvendelse ved behandling av blærekreft.
- 10 **8.** Kombinasjon for anvendelse ifølge krav 7, hvor det terapeutiske antistoffet er pertuzumab og det kjemoterapeutiske middelet er taxan eller et antracyklin.
- 9.** Farmasøytisk sammensetning omfattende en forbindelse for anvendelse ifølge et hvilket som helst av kravene 1 til 6 eller en kombinasjon for anvendelse ifølge krav 7 eller 8, og én eller flere farmasøytisk akseptable eksipienter.
- 15 **10.** Farmasøytisk sammensetning ifølge krav 9 i form av et frysetørket pulver eller en frossen oppløsning.