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(73)	Proprietor	The Johns Hopkins University, 3400 North Charles Street, Baltimore, MD 21218, USA Institute of Organic Chemistry and Biochemistry AS CR, V.V.I., Flemingovo namesti 542/2, 166 10 Praha 6, Den tsjekkiske republikk
(72)	Inventor	SLUSHER, Barbara, 7424 Longfield Dr., Kingsville, Maryland 21087, USA RAIS, Rana, 12905 Vistaview Dr., West Friendship, Maryland 21794, USA TENORA, Lukas, Flemingovo Nám. 2, 166 10 Praha 6, Den tsjekkiske republikk MAJER, Pavel, 6201 Long Meadow Dr., Sykesville, Maryland 21784, USA JANCARIK, Andrej, Pod Moravii 1315, 74221 Koprivnice, Den tsjekkiske republikk
(74)	Agent or Attorney	Nordic Patent Service A/S, Bredgade 30, 1260 KØBENHAVN K, Danmark

(54) Title **PRODRUGS OF GLUTAMINE ANALOGS**

(56) References
Cited:

WO-A1-2014/138391
EP-A2- 0 123 170
US-A1- 2006 276 438
WO-A2-2004/113363
HAUSCH, FELIX ET AL.: 'Design, synthesis and evaluation of gluten peptide analogs as
selective inhibitors of human tissue transglutaminase' CHEMISTRY & BIOLOGY vol. 10, 2003,
pages 225 - 231, XP002293619
DEWALD, HORACE A. ET AL.: '6-Diazo-5-oxo-L-norleucine, a new tumor- inhibitory substance.
Preparation of L-, D-, and DL-forms' JOURNAL OF THE AMERICAN CHEMICAL SOCIETY vol.

80, 1958, pages 3941 - 3945, XP055440091

LEE, MAY D. ET AL.: 'New antitumor antibiotic, LL-D0513913 fermentation, isolation, structure determination and biological activities' THE JOURNAL OF ANTIBIOTICS vol. 40, no. 12, 1987, pages 1657 - 1663, XP009508285

JUDSON ENGLERT ET AL: "Abstract 1035: Targeting glutamine metabolism with the novel inhibitor JHU-083 inhibits tumor growth and alters the tumor immune microenvironment", PROCEEDINGS: AACR 107TH ANNUAL MEETING, 16 April 2016 (2016-04-16), pages 1-2, XP055545012,

LE MAUX, PAUL ET AL.: 'Chemical reactivity of 6-diazo-5-oxo-L-norleucine (DON) catalyzed by metalloporphyrins(Fe,Ru' TETRAHEDRON vol. 66, 2010, pages 4462 - 4468, XP055362317

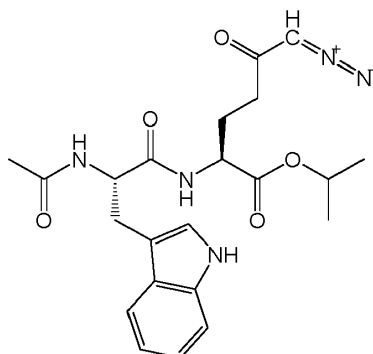
ABO-GHALIA M ET AL: "Synthesis of inhibitors of the meso-diaminopimelate-adding enzyme from Escherichia coli", INTERNATIONAL JOURNAL OF PEPTIDE AND PROTEIN RESEA, MUNKSGAARD, COPENHAGEN, DK, vol. 32, no. 3, 1 September 1998 (1998-09-01), pages 208-222, XP008167470, ISSN: 0367-8377, DOI: 10.1111/J.1399-3011.1988.TB00936.X

ANDREJ JANCARIK: "Novel lymphoid targeted prodrugs of the glutamine antagonist DON for the treatment of hematological malignancies", FASEB, 2 April 2016 (2016-04-02), pages 1-2, XP055545018, DOI: 10.1096/fasebj.30

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 som er:



5 2. Forbindelse som er isopropyl-2-(2-acetamido-3-(1H-indol-3-yl)propanamido)-6-diazo-5-oksoheksanoat, eller en stereoisomer derav.

3. Farmasøytisk sammensetning omfattende en forbindelse ifølge krav 1 eller 2, eller et farmasøytisk akseptabelt salt derav, og en farmasøytisk akseptabel bærer, fortynningsmiddel
10 eller eksipiens.

4. Forbindelsen ifølge krav 1 eller 2, eller et farmasøytisk akseptabelt salt derav, for anvendelse ved behandling av kreft hos et individ.

15 5. Forbindelsen for anvendelse ifølge krav 4, hvori kreften er akutt lymfoblastisk leukemi, akutt myelogen leukemi, fremskredet bløtvevssarkom, hjernekreft, metastatisk eller aggressiv brystkreft, brystkarsinom, bronkogen karsinom, koriokarsinom, kronisk myelocytisk leukemi, kolonkarsinom, kolorektalt karsinom, Ewings sarkom, mage-tarmkanalkarsinom, gliom, glioblastoma multiforme, plateepitelkarsinom i hode og nakke, hepatocellulært karsinom,
20 Hodgkins sykdom, intrakranielt ependymoblastom, tykktarmskreft, leukemi, leverkreft, lungekarsinom, Lewis lungekarsinom, lymfom, ondartet fibrøst histiocytt, melanom, mesoteliom, nevroblastom, osteosarkom, eggstokkreft, kreft i bukspyttkjertelen, en pontinsvulst, prostatakreft, rabdomyosarkom, retikulumcellesarkom, sarkom, småcellet lungekreft, magekreft, testikkelkreft eller karsinom i livmoren.

25 6. Forbindelsen for anvendelse ifølge krav 5, hvori kreften er kolorektalt karsinom, plateepitelkarsinom i hode og nakke, hepatocellulært karsinom, lungekarsinom, melanom eller prostatakreft.