



(51) International Patent Classification:

*A61K 51/04* (2006.01)      *A61P 35/00* (2006.01)  
*A61K 38/43* (2006.01)      *C07K 14/485* (2006.01)  
*A61K 39/395* (2006.01)      *C07K 14/79* (2006.01)

(21) International Application Number:

PCT/US2019/019090

(22) International Filing Date:

22 February 2019 (22.02.2019)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/633,849      22 February 2018 (22.02.2018)      US

(71) Applicant: **NORTH CAROLINA STATE UNIVERSITY** [US/US]; 1021 Main Campus Drive, 2nd Floor, Raleigh, North Carolina 27606 (US).

(72) Inventors: **LINDSEY, Jonathan S.**; 1236 Canterbury Road, Raleigh, North Carolina 27608 (US). **FUJITA, Hikaru**; 1800 Vienna Woods Drive, Apartment 307,

Raleigh, North Carolina 27606 (US). **ZHANG, Yunlong**; 3502 Ivy Commons Drive, Apartment 101, Raleigh, North Carolina 27606 (US).

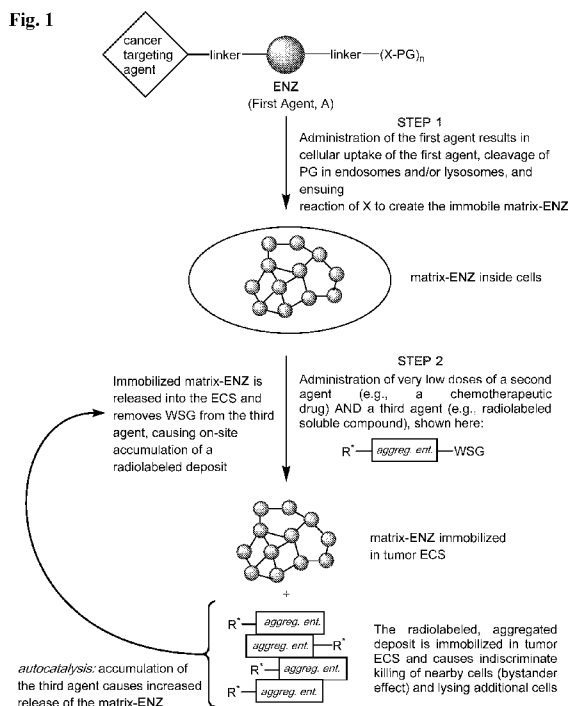
(74) Agent: **MYERS BIGEL, P.A.**; PO Box 37428, Raleigh, North Carolina 27627 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,

(54) Title: COMPOUNDS AND METHODS USEFUL IN BRACHYTHERAPY

Fig. 1



(57) Abstract: Compounds and methods are described herein that are useful in brachytherapy. A compound of the present invention may comprise: a cancer cell targeting agent (e.g., transferrin); a protecting group; a cross-linking moiety; and an enzyme (e.g., a protein, ribozyme, abzyme, or abiological catalyst). Compounds and methods of the present invention may be used for localizing a radioactive compound and/or for creating a self-amplifying response.



TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

**Published:**

— *with international search report (Art. 21(3))*

**(88) Date of publication of the international search report:**

07 May 2020 (07.05.2020)

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2019/019090

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC(8) - A61K 51/04; A61K 38/43; A61K 39/395; A61P 35/00; C07K 14/485; C07K 14/79 (2019.01)  
 CPC - A61K 39/395; A61K 38/43; A61K 51/04; A61P 35/00; C07K 14/485; C07K 14/79 (2019.02)

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
 See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
 USPC - 424/1.69; 424/1.65; 424/179.1 (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
 See Search History document

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011/0152252 A1 (JOHANNES et al) 23 June 2011 (23.06.2011) entire document	1-3
X	US 2011/0142756 A1 (MAYERS et al) 16 June 2011 (16.06.2011) entire document	20-22, 53, 54
A	US 7,615,221 B2 (MAYERS et al) 10 November 2009 (10.11.2009) entire document	1-3, 20-22, 53, 54
A	US 6,759,509 B1 (KING et al) 06 July 2004 (06.07.2004) entire document	1-3, 20-22, 53, 54

Further documents are listed in the continuation of Box C.  See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search  
03 April 2019

Date of mailing of the international search report  
**22 APR 2019**

Name and mailing address of the ISA/US  
 Mail Stop PCT, Attn: ISA/US, Commissioner for Patents  
 P.O. Box 1450, Alexandria, VA 22313-1450  
 Facsimile No. 571-273-8300

Authorized officer  
 Blaine R. Copenheaver  
 PCT Helpdesk: 571-272-4300  
 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2019/019090

**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  Claims Nos.: 4-19, 23-52  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

- Remark on Protest**
- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
  - The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
  - No protest accompanied the payment of additional search fees.