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- (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, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, 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.

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(54) **Title:** CARBONIC ANHYDRASE TARGETING AGENTS AND METHODS OF USING SAME

(57) **Abstract:** The invention provides agents that target carbonic anhydrase, which can be used as imaging agents or therapeutic agents. The agents can be used to image tumor hypoxia as well as other physiological processes in a subject.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/37166

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61P 35/00 (2012.01) USPC - 530/350 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) USPC - 530/350 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PubWEST (USPT,PGPB,JPAB,EPAB); Google Search Terms: Carbonic anhydrase targeting agent dye fluorescent sulfonamide sulfonate amine aryl alkyl hydrogen CAB naphto condensed benzo condensed		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6,747,159 B2 (Caputo et al.) 08 Jun 2004 (08.06.2004), entire document especially Abstract, col 7, ln 30 to col 8, ln 25, and col 11, ln 15	1, 3, 21 and 25
Y	WO 2006/137092 A1 (Supuran et al.) 28 Dec 2006 (28.12.2006), entire document especially Abstract, page 5-7	1, 3, 21 and 25
A	US 2008/0286207 A1 (Narayanan) 20 November 2008 (20.11.2008), entire document	1, 3, 21 and 25
A	US 2010/0323389 A1 (Xu et al.) 23 Dec 2010 (23.12.2010), entire document	1, 3, 21 and 25
A	US 2008/0317676 A1 (Rajopadhye et al.) 25 Dec 2008 (25.12.2008), entire document	1, 3, 21 and 25
A,P	US 2011/0165075 A1 (Rajopadhye et al.) 07 Jul 2011 (07.07.2011), entire document	1, 3, 21 and 25
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/>		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "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) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "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 "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 "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 "&" document member of the same patent family		
Date of the actual completion of the international search 8 November 2012 (08.11.2012)		Date of mailing of the international search report 11 DEC 2012
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201		Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/37166

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.: 4-18, 20, 23, 24, and 26-44
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:
----- See Extra Sheet -----

- 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.:
1, 3, 21, and 25. See description of claim groups I and II on extra sheet.
- 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.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

PCT/US 12/37166

Box III: Observations where unity of invention is lacking: (continuation)

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group I: claims 1 and 3, directed to an agent of Formula I comprising the Q-L1-CAB in the center of the structure along with the 4 L3-M moieties and wherein W represents a benzo-condensed ring.

Group II: claims 1, 3, 21, and 25 directed to an agent of Formulas I and IV comprising the Q-L1-CAB in the center of the structure along with the 4 L3-M moieties and wherein W represents a naphtho-condensed ring.

Group III: claims 1 and 3, directed to an agent of Formula I comprising the Q-L1-CAB in the center of the structure along with the 4 L3-M moieties and wherein W represents a pyrido-condensed ring.

Group IV: claims 2, 3, 21, 22, and 25, directed to an agent of Formula II comprising the SO₂N(R-Q-L1-CAB moiety on the right side as well as the possible alkene chain extension defined by n, and wherein W represents a benzo-condensed ring.

Group V: claims 2, 3, 21, 22, and 25, directed to an agent of Formula II comprising the SO₂N(R-Q-L1-CAB moiety on the right side as well as the possible alkene chain extension defined by n, and wherein W represents a naphtho-condensed ring.

Group VI: claims 2, 3, 21, 22, and 25, directed to an agent of Formula II comprising the SO₂N(R-Q-L1-CAB moiety on the right side as well as the possible alkene chain extension defined by n, and wherein W represents a naphtho-condensed ring.

Group VII: claims 19 and 25, directed to an agent of formula III, comprising F-L-CAB, wherein F is a near infrared fluorochrome.

The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Groups II-VII do not include the inventive concept of an agent of Formula I comprising the Q-L1-CAB in the center of the structure along with the 4 L3-M moieties and wherein W represents a benzo-condensed ring as required by Group I.

Groups I and III-VII do not include the inventive concept of an agent of Formula I comprising the Q-L1-CAB in the center of the structure along with the 4 L3-M moieties and wherein W represents a benzo-condensed ring as required by Group II.

Groups I, II, and IV-VII do not include the inventive concept of an agent of Formula I comprising the Q-L1-CAB in the center of the structure along with the 4 L3-M moieties and wherein W represents a pyrido-condensed ring as required by Group III.

Groups I-III and V-VII do not include the inventive concept of an agent of Formula II comprising the SO₂N(R-Q-L1-CAB moiety on the right side as well as the possible alkene chain extension defined by n, and wherein W represents a benzo-condensed ring as required by Group IV.

Groups I-IV, VI, and VII do not include the inventive concept of an agent of Formula II comprising the SO₂N(R-Q-L1-CAB moiety on the right side as well as the possible alkene chain extension defined by n, and wherein W represents a naphtho-condensed ring as required by Group V.

Groups I-V and VII do not include the inventive concept of agent of Formula II comprising the SO₂N(R-Q-L1-CAB moiety on the right side as well as the possible alkene chain extension defined by n, and wherein W represents a naphtho-condensed ring as required by Group VI.

Groups I-VI do not include the inventive concept of an agent of formula III, comprising F-L-CAB, wherein F is a near infrared fluorochrome as required by Group VII.

Groups I-VII share the technical feature of a chemical structure with substituted pyrrolidine and dihydropyrrole rings with a substituted polymethine bridge therebetween; and wherein the substituted pyrrolidine and dihydropyrrole rings may be benzo-condensed or naphtho-condensed, which is not a contribution over US 6,747,159 B2 to Caputo et al. (8 June 2004), see Abstract. As the core structural element of the claimed structures are were known, this cannot be considered a special technical feature that would otherwise unify the groups.

Groups I-VII therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

Claims 4-18, 20, 23, 24, and 26-44 are considered unsearchable because they are dependent claims that are not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).