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(54) Title: COMPOUNDS AND METHODS FOR MODULATING EXPRESSION OF PTP1B

(57) Abstract: The present disclosure describes short antisense compounds, including such compounds comprising chemically-modified high-affinity monomers 8-16 monomers in length. Certain such short antisense compound are useful for the reduction of target nucleic acids and/or proteins in cells, tissues, and animals with increased potency and improved therapeutic index. Thus, provided herein are short antisense compounds comprising high-affinity nucleotide modifications useful for reducing a target RNA in vivo. Such short antisense compounds are effective at lower doses than previously described antisense compounds, allowing for a reduction in toxicity and cost of treatment. In addition, the described short antisense compounds have greater potential for oral dosing.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 07/68402

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - C12Q 1/68; C12N 5/06, 5/16 (2008.04) USPC - 435/6, 333; 514/44 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: 435/6, 435/333; 514/44 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC: 435/91.51; 530/388.21 (see search terms below) Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) WEST (PGPB,USPT,EPAB,JPAB): antisense, monomer, deoxyribonucleotide, PTP1B, nucleotides, bridge, phosphorothioate, internucleoside; esp@cenet: isis, antisense, bhanot Google Scholar: PTP1B, antisense, deoxyribonucleotide, gap, monomer													
C. DOCUMENTS CONSIDERED TO BE RELEVANT													
<table border="1"> <thead> <tr> <th>Category*</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X --- Y</td> <td>US 2006/0025372 A1 (BHANOT et al.) 2 February 2006 (02.02.2006) abstract; para [0020]-[0022], [0024], [0061]-[0062], [0069], [0074], [0227]</td> <td>43-46 ----- 1-37</td> </tr> <tr> <td>Y</td> <td>US 2006/0063730 A1 (MONIA et al.) 23 March 2006 (23.03.2006) abstract; para [0004]-[0005], [0122]</td> <td>1-37</td> </tr> <tr> <td>Y</td> <td>US 2005/0261218 A1 (ESAU et al.) 24 November 2005 (24.11.2005) para [0053], [0088], [0204], [0277], [0284]</td> <td>1-37</td> </tr> </tbody> </table>	Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X --- Y	US 2006/0025372 A1 (BHANOT et al.) 2 February 2006 (02.02.2006) abstract; para [0020]-[0022], [0024], [0061]-[0062], [0069], [0074], [0227]	43-46 ----- 1-37	Y	US 2006/0063730 A1 (MONIA et al.) 23 March 2006 (23.03.2006) abstract; para [0004]-[0005], [0122]	1-37	Y	US 2005/0261218 A1 (ESAU et al.) 24 November 2005 (24.11.2005) para [0053], [0088], [0204], [0277], [0284]	1-37	
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<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/>													
<p>* Special categories of cited documents:</p> <table border="0"> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"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</td> </tr> <tr> <td>"E" earlier application or patent but published on or after the international filing date</td> <td>"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</td> </tr> <tr> <td>"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)</td> <td>"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</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td>"&" document member of the same patent family</td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>		"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			
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"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 10 September 2008 (10.09.2008)	Date of mailing of the international search report 15 SEP 2008												
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 07/68402

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.: 38-42 and 47-52
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.