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(54) Title: COMPOSITIONS AND METHODS FOR MODULATION OF SMN2 SPLICING

(57) Abstract: Disclosed herein are compounds, compositions and methods for modulating splicing of SMN2 mRNA in a cell, tissue or animal. Also provided are uses of disclosed compounds and compositions in the manufacture of a medicament for treatment of diseases and disorders, including spinal muscular atrophy.



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**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US06/24469

<p><b>A. CLASSIFICATION OF SUBJECT MATTER</b></p> <p>IPC: C07H 21/02( 2006.01),21/04( 2006.01);A61K 31/70( 2006.01);C12N 5/00( 2006.01) C12Q 1/68( 2006.01)</p> <p>USPC: 536/24.5;514/44;435/6,375,377</p> <p>According to International Patent Classification (IPC) or to both national classification and IPC</p>																	
<p><b>B. FIELDS SEARCHED</b></p> <p>Minimum documentation searched (classification system followed by classification symbols) U.S. : 536/24.5; 514/44; 435/6, 375, 377</p> <p>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched</p> <p>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) WEST, MEDLINE, CAPLUS, EMBASE</p>																	
<p><b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b></p> <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>Y</td> <td>US 6,376,508 B1 (LI et al) 23 April 2002 (23.04.2002), see entire document.</td> <td>1-23</td> </tr> <tr> <td>Y</td> <td>LIM et al. Modulation of Survival Motor Neuron Pre-mRNA Splicing by Inhibition of Alternative 3' Splice Site Pairing. The Journal of Biological Chemistry. 30 November 2001, Vol. 276, No. 48, pages 45476-454483, see entire document.</td> <td>1-23</td> </tr> <tr> <td>Y</td> <td>MIYASO et al. An Intronic Splicing Enhancer Element in Survival Motor Neuron (SMN) Pre-mRNA. The Journal of Biological Chemistry. 02 May 2003, Vol, 278, No. 18, pages 15825-15831, see entire document.</td> <td>1-23</td> </tr> <tr> <td>Y</td> <td>MIYAJIMA et al. Identification of a Cis-Acting Element For The Regulation of SMN Exon 7 Splicing. The Journal of Biological Chemistry. 28 June 2002, Vol. 277, No. 26, pages 23271-23277, see entire document.</td> <td>1-23</td> </tr> </tbody> </table>			Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	Y	US 6,376,508 B1 (LI et al) 23 April 2002 (23.04.2002), see entire document.	1-23	Y	LIM et al. Modulation of Survival Motor Neuron Pre-mRNA Splicing by Inhibition of Alternative 3' Splice Site Pairing. The Journal of Biological Chemistry. 30 November 2001, Vol. 276, No. 48, pages 45476-454483, see entire document.	1-23	Y	MIYASO et al. An Intronic Splicing Enhancer Element in Survival Motor Neuron (SMN) Pre-mRNA. The Journal of Biological Chemistry. 02 May 2003, Vol, 278, No. 18, pages 15825-15831, see entire document.	1-23	Y	MIYAJIMA et al. Identification of a Cis-Acting Element For The Regulation of SMN Exon 7 Splicing. The Journal of Biological Chemistry. 28 June 2002, Vol. 277, No. 26, pages 23271-23277, see entire document.	1-23
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<p>Date of the actual completion of the international search 06 August 2007 (06.08.2007)</p>		<p>Date of mailing of the international search report <b>13 SEP 2007</b></p>															
<p>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</p>		<p>Authorized officer <i>Maureen Watson</i> /Sean R. McGarry/ Telephone No. (571) 272 0763</p>															

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**C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

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Y	SKORDIS et al. Bifunctional Antisense Oligonucleotides Provide a Trans-Acting Splicing Enhancer That Stimulates SMN2 Gene Expression in Patient Fibroblasts. PNAS. 01 April 2003, Vol. 100, No. 7, pages 4114-4119,see entire document.	1-23