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(71) Applicant (for all designated States except US): AERIS THERAPEUTICS, INC. [US/US]; 10K Hill Street, Woburn, MA 01801 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): INGENITO, Ed [US/US]; 26 Tilden Circle, North Quincy, MA 02171 (US). SCHWARZ, Alexander [US/US]; 20 John Street #3, Brookline, MA 02446 (US). TSAI, Larry, W. [US/US]; 11 Durham Street, #5, Boston, MA 02115 (US).

(74) Agents: GORDON, Dana, M. et al.; FOLEY HOAG LLP, Patent Group, 155 Seaport Boulevard, Boston, MA 02210-2698 (US).

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(54) Title: POLYCATION-POLYANION COMPLEXES, COMPOSITIONS AND METHODS OF USE THEREOF

(57) Abstract: One aspect of the present invention relates to compositions and methods comprising polyelectrolyte molecules for treating patients who have certain diseases. Aspects of the invention relate to using certain polyelectrolyte compositions in therapy. According to the invention polyelectrolyte compositions may be used, for example, to slow or stop cell growth, kill cells (e.g., via necrotic or apoptotic pathways), promote fibrosis, or a combination thereof. In one aspect of the invention, certain toxic (e.g., cytotoxic) properties of polyelectrolytes are exploited for therapeutic purposes, hi certain embodiments, compositions and methods of the invention are used to target polyelectrolyte toxicity to predetermined regions within a subject, while minimizing undesirable toxicity at other regions with the subject. In certain embodiments, the present invention relates to lung-volume-reduction therapy using a polyelectrolyte composition.

International application No PCT/US2006/042338

A. CLASSIFICATION OF SUBJECT MATTER INV. A61K47/48 A61P43/00

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)

A61K

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 practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, EMBASE

	ENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where appropriate, of	the relevant passages	Relevant to claim No.		
X	WO 03/105676 A (BISTECH INC [IEDWARD M D [US]) 24 December 2003 (2003-12-24)	1,4-11, 15,16, 25, 28-34, 38,50, 51,53, 54, 69-73, 77-87, 90,94, 95,104, 107-113, 117,129, 130,132,			
X .	the whole document	-/	133, 148-156 160, 163-168, 176,177,		
X Furt	her documents are listed in the continuation of Box C.	X See patent family annex.			
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	actual completion of the international search	——————————————————————————————————————	Date of mailing of the international search report		
9	June 2008	19/06/2008			
Name and r	matling address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nt,	Authorized officer			

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C(Continua	tion). DOCUMENTS CONSIDERED TO BE RELEVANT	<u> </u>	 		
Category*	Citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.		
			186,189, 190, 192-195, 199,211, 212,214, 215, 230-234		
Y	page 25, lines 6-10 page 26, line 23 - page 29, line 28 page 32, lines 14-18; claims 1-11 page 5, line 30 - page 6, line 31 & US 2004/047855 A1 (INGENITO EDWARD [US]) 11 March 2004 (2004-03-11)		1-237 1,4-11, 15,16, 25, 28-34, 38,50, 51,53, 54, 69-73, 77-87, 90,94, 95,104, 107-113,		
	paragraphs [0011], [0058] — [0080], [0089]; claims 1—11		117,129, 130,132, 133, 148-156 160, 163-168, 176,177, 186,189, 190, 192-195, 199,211, 212,214, 215, 230-234		
	-/				
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International application No PCT/US2006/042338

C(Continua Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X .	WO 01/13908 A (INGENITO EDWARD P [US]) 1 March 2001 (2001-03-01) the whole document	1,4-11, 15,16, 25, 28-34, 38,50, 51,53, 54, 69-72, 77-87, 90,94, 95,104, 107-113, 117,129, 130,132, 133, 148-155
	page 11, line 25 - page 14, line 31; claims 1-54; figure 9; example 6	1-23/
X	INGENITO E P ET AL: "Bronchoscopic Lung Volume Reduction Using Tissue Engineering Principles" AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE, AMERICAN LUNG ASSOCIATION, NEW YORK, NY, US, vol. 167, 1 January 2003 (2003-01-01), pages 771-778, XP003009383 ISSN: 1073-449X cited in the application	1,4,5, 7-10,15, 25, 28-34, 38,50, 51,53, 54, 69-72, 77-81, 83-87, 90,104, 107-113, 117,129, 130,132, 133, 148-152,
Y	the whole document page 772, column 2, paragraph 3	148-152, 154,155 1-237

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PCT/US2006/042338

C(Continua	tion). DOCUMENTS CONSIDERED TO BE RELEVANT	
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	INGENITO E P ET AL: "Bronchoscopic Volume Reduction, A Safe and Effective Alternative to Surgical Therapy for Emphysema" AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE, AMERICAN LUNG ASSOCIATION, NEW YORK, NY, US, vol. 164, 1 January 2001 (2001-01-01), pages 295-301, XP003009382 ISSN: 1073-449X	1,4,5, 7-10,15, 25, 28-34, 38,50, 51,53, 54, 69-72, 77-81, 83-87, 90,104, 107-113, 117,129, 130,132,
Υ	the whole document	133, 148-152, 154,155 1-237
	page 295, column 2, paragraph 4	
X	BRENNER MATT ET AL: "Innovative approaches to lung volume reduction for emphysema" CHEST, vol. 126, no. 1, July 2004 (2004-07), pages 238-248, XP002483341 ISSN: 0012-3692	1,4,5, 7-10,15, 25, 28-34, 38,50, 51,53, 54, 69-72, 77-81, 83-87, 90,104, 107-113, 117,129, 130,132, 133, 148-152, 154,155
Υ	the whole document page 240, column 1, paragraph 2 - page 241, column 2, paragraph 1	1-237
P , X	WO 2006/066234 A (AERIS THERAPEUTICS INC [US]; INGENITO EDWARD P [US]) 22 June 2006 (2006-06-22) the whole document	1-237
Ρ,Χ	US 2005/244401 A1 (INGENITO EDWARD P [US]) 3 November 2005 (2005-11-03) the whole document	1-237
Ρ,Χ	WO 2006/009699 A (PNEUMRX INC [US]; GONG GLEN [US]; DIECK RONALD [US]) 26 January 2006 (2006-01-26) the whole document	1-159

International application No
PCT/US2006/042338

C(Continue	tion) DOCUMENTS CONCIDENTS TO BE BELEVANT	PC1/US2006/042338
	ILION). DOCUMENTS CONSIDERED TO BE RELEVANT	
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	US 2005/281802 A1 (GONG GLEN [US] ET AL) 22 December 2005 (2005-12-22) the whole document	1-159
A	WO 03/078579 A (BISTECH INC [US]; INGENITO: EDWARD [US] AERIS THERAPEUTICS INC [US]; IN) 25 September 2003 (2003-09-25)	
A	US 2002/086852 A1 (CANTOR JEROME O [US] ET AL) 4 July 2002 (2002-07-04)	
A	US 2003/228344 A1 (FIELDS ANTONY J [US] ET AL) 11 December 2003 (2003-12-11)	
A	INGENITO EDWARD P ET AL: "Respiratory impedance following bronchoscopic or surgical lung volume reduction for emphysema." RESPIRATION; INTERNATIONAL REVIEW OF THORACIC DISEASES 2005 JUL-AUG, vol. 72, no. 4, July 2005 (2005-07), pages 406-417, XP002483345 ISSN: 0025-7931	
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INTERNATIONAL: SEARCH REPORT

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. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Although claims 77-159 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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.: 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 an 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 reportcovers 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.

Information on patent family members

International application No PCT/US2006/042338

	Patent document ed in search report		Publication date		Patent family member(s)		Publication date	10 m 1 m 1 m 1 m 1 m 1 m 1 m 1 m 1 m 1 m
W	0 03105676	A	24-12-2003	AU CA	2003253664 / 2530042 /		31-12-2003 24-12-2003	,
Ū	S 2004047855	A1	11-03-2004	NONE				
W	0 0113908	A	01-03-2001	AT AU CA CN DE DE EP ES HK JP US US	279938 783750 6799300 2382817 1373670 60015152 1206276 2232483 1048586 2003507130 2308967 6610043 2004038868 2001051799	B2 A A1 A1 D1 T2 A2 T3 A1 TC2 B1 A1	15-11-2004 01-12-2005 19-03-2001 01-03-2001 09-10-2002 25-11-2004 02-02-2006 22-05-2002 01-06-2005 03-06-2005 25-02-2003 27-10-2007 26-08-2003 26-02-2004 13-12-2001	
W	0 2006066234	A	22-06-2006	NONE	andie die gegen die eeuwelke heer v ^{ege} n die proof vele	<u></u>	<u> </u>	
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W	0 2006009699	A	26-01-2006	EP JP	1776139 2008503465		25-04-2007 07-02-2008	
U	S 2005281802	A1,	22-12-2005	WO	2006009682	A2	26-01-2006	
<u> </u>	0 03078579	A	25-09-2003	AU CA CN EP JP	2003225755 2518794 1652795 1503766 2005522465	A1 A A2	29-09-2003 25-09-2003 10-08-2005 09-02-2005 28-07-2005	
U	S 2002086852	A1	04-07-2002	NONE			·	
. U	S 2003228344	A1	11-12-2003	US (US	2006283462 2008027343		21-12-2006 31-01-2008	,
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