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(71) Applicant: **GERON CORPORATION**
Menlo Park, CA 94025 (US)

(72) Inventors:
• **Halrley, Calvin B**
Palo Alto, CA 94301 (US)

- **Chin, Allison C.**
Stanford, CA 94305 (US)
- **Akama, Tsutomu**
Sunnyvale, CA 94087 (US)
- **Ip, Nancy Yuk-yu**
Kowloon (US)
- **Wong, Yung-hou, PhD**
Associate Professor, Dept of Biochemistry,
Clear Water Bay, Kowloon (US)
- **Miller-Martini, David M., Dr.**
Ridgway, PA 15853 (US)

(74) Representative: **Vossius & Partner**
Siebertstrasse 4
81675 München (DE)

(54) **Compositions for increasing telomerase activity**

(57) The present invention relates to compositions for increasing telomerase activity in cells. Such compositions include pharmaceutical, including topical, and nutraceutical formulations. The compositions are useful for treating diseases subject to treatment by an increase in telomerase activity in cells or tissue of a patient, such as,

for example, HIV infection, various degenerative diseases, and acute or chronic skin ailments. They are also useful for enhancing replicative capacity of cells in culture, as in ex vivo cell therapy and proliferation of stem cells.

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EUROPEAN SEARCH REPORT

Application Number
EP 12 18 0710

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X,D	WO 01/01996 A1 (UNIV WESTERN AUSTRALIA [AU]; GUANGZHOU UNIVERSITY OF TRADIT [CN]; PRIN) 11 January 2001 (2001-01-11) * claims 1,10, 18, 22 * * page 4, lines 1-5 * -----	1-6, 8-10, 12-14	INV. C07J1/00 A61K31/56 A61K31/7048 A61P31/12 A61P25/00
X	LI C-X ET AL: "Effects of Buyang Huanwu decoction and its active constituents on the fluidity of brain cell membrane in vitro", ZHONGGUO YAOXUE ZAZHI - CHINESE PHARMACEUTICAL JOURNAL, GAI KAN BIAN-WEI-HUI, BEIJING, CN, vol. 36, no. 8, 1 August 2001 (2001-08-01), pages 528-531, XP008119507, ISSN: 1001-2494 * abstract * * page 529, right-hand column, paragraph 3 * * table 1 *	1-5, 8-10,12, 13	A61P19/00 A61P27/02 A61P9/10 A61P7/06 A61P17/00 A61P17/02
X	LUO H M ET AL: "Nuclear cardiology study on effective ingredients of Astragalus membranaceus in treating heart failure", CHUNG-KUO CHUNG HSI I CHIEH HO TSA CHIH - ZHONGGUO ZHONGXIYIJIEHE ZAZHE - CHINESE JOURNAL OF INTEGRATED TRADITIONAL ANDWESTERN MEDICINE, BEIJING, CN, vol. 15, no. 12, 1 December 1995 (1995-12-01), pages 707-709, XP008119506, ISSN: 1003-5370 * abstract * ----- -/--	1-5,8,9, 12,13	TECHNICAL FIELDS SEARCHED (IPC) A61K
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 13 May 2013	Examiner Herdemann, Matthias
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</p>			

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EPO FORM 1503 03 82 (P04C01)



EUROPEAN SEARCH REPORT

Application Number
EP 12 18 0710

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X,D	US 5 770 578 A (BINDER BERND [AT] ET AL) 23 June 1998 (1998-06-23) * column 2, lines 35-47 * * column 2, line 50 - column 3, line 63 * * claims 1-2 * -----	1-5, 8-10,12, 13	TECHNICAL FIELDS SEARCHED (IPC)
X	PAN FEI YANG JUN-SHAN ET AL: "Studies on triterpenoids of Astragalus floridus", ACTA BOTANICA SINICA, ZHIWU XUEBAO, KEXUE CHUBANSHE, CN, vol. 38, no. 10, 1 January 1996 (1996-01-01), pages 836-838, XP008119504, ISSN: 0577-7496 * abstract * * compounds 2, 5 * * table 1 *	1-5,8,9, 12,13	
X	JP 62 012792 A (OSAKA CHEM LAB) 21 January 1987 (1987-01-21) * abstract * * page 7, left-hand column, line 18 - right-hand column, line 20 * * page 9, right-hand column, line 21 - page 10, right-hand column, last line; table *	1-5,8,9, 12-14	
X	CN 1 283 462 A (ZHONGSHAN HOSPITAL ATTACHED TO [CN]) 14 February 2001 (2001-02-14) * abstract * * page 1, line 10 - last line * ----- -/--	1-5,8,9, 12,13	
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 13 May 2013	Examiner Herdemann, Matthias
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

EPO FORM 1503 03.92 (P04C01)



EUROPEAN SEARCH REPORT

Application Number
EP 12 18 0710

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	CN 1 403 470 A (SHANGHAI TRADITIONAL CHINESE M [CN] SHANGHAI UNIVERSITY OF TRADITI [CN] 19 March 2003 (2003-03-19) * abstract * * page 1, line 1 - last line * -----	1-5,8,9,12,13	
X	KAO SHUNG-TE ET AL: "The Chinese medicine Bu-Zhong-Yi-Qi-Tang inhibited proliferation of hepatoma cell lines by inducing apoptosis via G0/G1 arrest", LIFE SCIENCES, vol. 69, no. 13, 17 August 2001 (2001-08-17), pages 1485-1496, XP055061975, ISSN: 0024-3205 * abstract * * page 1486, paragraph 1 * * table 1 * * figure 3 *	1-6,8,9,12-14	
X,D	BEDIR E ET AL: "Immunostimulatory Effects of Cycloartane-Type Triterpene Glycosides from Astragalus Species", BIOLOGICAL & PHARMACEUTICAL BULLETIN (OF JAPAN), PHARMACEUTICAL SOCIETY OF JAPAN, TOKYO, JP, vol. 32, no. 7, 1 January 2000 (2000-01-01), pages 834-837, XP007919860, ISSN: 0918-6158, DOI: 10.1248/BPB.23.834 * abstract * * page 834, left-hand column, paragraph 1 * * compounds 12, 17, 18 * * page 836, left-hand column, paragraph 1 * ----- -/--	4-6,8,9,11-14	
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 13 May 2013	Examiner Herdemann, Matthias
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</p>			

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EPO FORM 1503 03.82 (P44C01)



EUROPEAN SEARCH REPORT

Application Number
EP 12 18 0710

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	KITAGAWA I ET AL: "SAPONIN AND SAPOGENOL 34. CHEMICAL CONSTITUENTS OF ASTRAGALI RADIX THE ROOT OF ASTRAGALUS-MEMBRANACEUS 1. CYCLO ASTRAGENOL THE 9 19 CYCLO LANOSTANE TYPE AGLYCONE OF ASTRAGALOSIDES AND THE ARTIFACT AGLYCONE ASTRAGENOL", CHEMICAL AND PHARMACEUTICAL BULLETIN (TOKYO), vol. 31, no. 2, 1983, pages 689-697, XP055061283, ISSN: 0009-2363 * abstract * * compounds 1, 5 * * page 689, paragraph 1 * * page 689, last paragraph - page 690, paragraph 1 *	4-6,8,9, 12-14	
X,D	ZHANG WEI-JIAN ET AL: "Regulation of the fibrinolytic potential of cultured human umbilical vein endothelial cells: Astragaloside IV downregulates plasminogen activator inhibitor-1 and upregulates tissue-type plasminogen activator expression", JOURNAL OF VASCULAR RESEARCH, vol. 34, no. 4, 1997, pages 273-280, XP008162031, ISSN: 1018-1172 * abstract * * page 274, right-hand column, paragraph 3 *	4-6,8,9, 12-14	TECHNICAL FIELDS SEARCHED (IPC)
Y	* figures 2, 3 * * page 277, right-hand column, paragraph 4 - page 278, left-hand column, paragraph 1 * * page 279, left-hand column, paragraph 1 *	1-5,8,9, 11	
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 13 May 2013	Examiner Herdemann, Matthias
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EPO FORM 1503 (03.82 (P04C01))



EUROPEAN SEARCH REPORT

 Application Number
EP 12 18 0710

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	US 2002/164387 A1 (WEI KAIYUAN [US] ET AL WEI KAIYUAN [CN]) 7 November 2002 (2002-11-07) * paragraphs [0036], [0037] * * paragraphs [0046], [0047] * * paragraph [0053] *	4-6,8, 12-14	TECHNICAL FIELDS SEARCHED (IPC)
X	ABDALLAH R M ET AL: "ASTRAGALOSIDES FROM EGYPTIAN ASTRAGALUS SPINOSUS VAHL", DIE PHARMAZIE, GOVI VERLAG PHARMAZEUTISCHER VERLAG GMBH, ESCHBORN, DE, vol. 48, no. 6, 1 January 1993 (1993-01-01), pages 452-454, XP001160860, ISSN: 0031-7144 * abstract * * page 454, left-hand column, paragraph 2-3; figure * * compound 4 *	12,13	
Y	MORISAKI NOBUHIRO ET AL: "Mechanism of angiogenic effects of saponin from Ginseng Radix rubra in human umbilical vein endothelial cells", BRITISH JOURNAL OF PHARMACOLOGY, vol. 115, no. 7, 1995, pages 1188-1193, XP055062495, ISSN: 0007-1188 * abstract * * page 1189, left-hand column, last paragraph * * figures 3-5, 7 * * page 1192, left-hand column, paragraph 1 * ----- -/--	1-5,8,9, 11	
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 13 May 2013	Examiner Herdemann, Matthias
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

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EPO FORM 1503 03.82 (P04C01)



EUROPEAN SEARCH REPORT

 Application Number
EP 12 18 0710

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	IONKOVA I ET AL: "Cycloartane saponin production in hairy root cultures of Astragalus mongholicus", PHYTOCHEMISTRY, PERGAMON PRESS, GB, vol. 45, no. 8, 1 August 1997 (1997-08-01), pages 1597-1600, XP004293321, ISSN: 0031-9422 * page 1597, left-hand column, paragraph 1 * * compound 2 * * page 1599, left-hand column, paragraph 1 *	1-10, 12-14	
X,P	----- CN 1 470 241 A (ZHENGDA TIANQING PHARMACEUTICA [CN]) 28 January 2004 (2004-01-28) * claims 1-3 *	1-5,8-14	
E	----- WO 2004/096251 A1 (WESTLAKE PARTNERS [US]) 11 November 2004 (2004-11-11) * claims 1-6 *	12-14	
T	----- FAUCE STEVEN RUSSELL ET AL: "Telomerase-Based Pharmacologic Enhancement of Antiviral Function of Human CD8(+) T Lymphocytes", JOURNAL OF IMMUNOLOGY, vol. 181, no. 10, November 2008 (2008-11), pages 7400-7406, XP002570921, ISSN: 0022-1767 * the whole document * ----- -/--		TECHNICAL FIELDS SEARCHED (IPC)
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 13 May 2013	Examiner Herdemann, Matthias
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EPO FORM 1503 03.02 (P04C01)



EUROPEAN SEARCH REPORT

Application Number
EP 12 18 0710

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
T	YUNG LISA Y ET AL: "Astragaloside IV and Cycloastragenol Stimulate the Phosphorylation of Extracellular Signal-Regulated Protein Kinase in Multiple Cell Types", PLANTA MEDICA, vol. 78, no. 2, January 2012 (2012-01), pages 115-121, XP055062190, * the whole document *		
T	HARLEY CALVIN B ET AL: "A natural product telomerase activator as part of a health maintenance program.", REJUVENATION RESEARCH FEB 2011, vol. 14, no. 1, February 2011 (2011-02), pages 45-56, XP055062170, ISSN: 1557-8577 * abstract * * page 46, right-hand column, paragraph 2 * * figure 3 *		TECHNICAL FIELDS SEARCHED (IPC)
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 13 May 2013	Examiner Herdemann, Matthias
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EPO FORM 1503 (03.82 (P04C01))



Application Number

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CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing claims for which payment was due.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☒ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

☐ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

☐ The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).



LACK OF UNITY OF INVENTION
SHEET B

Application Number
EP 12 18 0710

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 10, 12-14(completely); 1-9(partially)

Use of an effective amount of an isolated compound which is selected from astragaloside IV, cycloastragenol, astragenol, cycloastragenol 6-beta-D- glucopyranoside, and cycloastragenol 3-beta-D-xylopyranoside or use of an effective amount of astragaloside IV 16-one for increasing telomerase activity in a cell or tissue for treating a degenerative disease. A nutraceutical composition comprising an effective amount of one of said compounds.

2. claims: 11(completely); 1-9(partially)

Use of an effective amount of an isolated compound which is selected from astragaloside IV, cycloastragenol, astragenol, cycloastragenol 6-beta-D- glucopyranoside, and cycloastragenol 3-beta-D-xylopyranoside or use of an effective amount of astragaloside IV 16-one for increasing telomerase activity in a cell or tissue for treating a chronic or acute condition of the epidermis.

3. claims: 1-8(partially)

Use of an effective amount of an isolated compound which is selected from astragaloside IV, cycloastragenol, astragenol, cycloastragenol 6-beta-D- glucopyranoside, and cycloastragenol 3-beta-D-xylopyranoside or use of an effective amount of astragaloside IV 16-one for increasing telomerase activity in a cell or tissue, as far as not comprised in inventions 1 or 2.

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 12 18 0710

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

13-05-2013

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0101996 A1	11-01-2001	NONE	
US 5770578 A	23-06-1998	AT 402890 B EP 0705103 A1 JP H08510474 A US 5770578 A WO 9524905 A1	25-09-1997 10-04-1996 05-11-1996 23-06-1998 21-09-1995
JP 62012792 A	21-01-1987	-----	
CN 1283462 A	14-02-2001	NONE	
CN 1403470 A	19-03-2003	NONE	
US 2002164387 A1	07-11-2002	CN 1369276 A US 2002164387 A1	18-09-2002 07-11-2002
CN 1470241 A	28-01-2004	NONE	
WO 2004096251 A1	11-11-2004	AU 2003228378 A1 WO 2004096251 A1	23-11-2004 11-11-2004