#### PATENT COOPERATION TREATY

## From the INTERNATIONAL SEARCHING AUTHORITY To: **PCT** COLEMAN, Henry D. 714 Colorado Avenue Bridgeport, Connecticut 06605-1601 WRITTEN OPINION OF THE United States of America INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1) Date of mailing (day/month/year) 18 March 2020 (18.03.2020) Applicant's or agent's file reference FOR FURTHER ACTION N 12-323PCT See paragraph 2 below International application No. International filing date (day/month/year) Priority date (day/month/year) PCT/US 2019/063602 27 November 2019 (27.11.2019) 29 November 2018 (29.11.2018) International Patent Classification (IPC) or both national classification and IPC A61K 31/05 (2006.01) A61K 36/28 (2006.01) **A61K 8/36** (2006.01) A61K 8/38 (2006.01) A61K 8/67 (2006.01) **A61P 17/12** (2006.01) **A61Q 19/00** (2006.01) Applicant STC. UNM et al. 1. This opinion contains indications relating to the following items: Box No. I Basis of the opinion Box No. II Priority Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability Box No. IV Lack of unity of invention Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement Box No. VI Certain documents cited Box No. VII Certain defects in the international application Box No. VIII Certain observations on the international application 2. FURTHER ACTION If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1 bis(b) that written opinions of this International Searching Authority will not be so considered. If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later. For further options, see Form PCT/ISA/220.

Date of completion of this opinion

04 February 2020 (04.02.2020)

Authorized officer

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International application No.

### PCT/US 2019/063602

Sox No. 1 Basis of this opinion						
1.	With regard to the <b>language</b> , this opinion has been established on the basis of:  X the international application in the language in which it was filed.					
	a translation of the international application into translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).					
2.	This opinion has been established taking into account the <b>rectification of an obvious mistake</b> authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))					
3.	With regard to any <b>nucleotide and/or amino acid sequence</b> disclosed in the international application, this opinion has been established on the basis of a sequence listing filed or furnished:					
	a. forming part of the international application as filed:					
	in the form of an Annex C/ST.25 text file.					
	on paper or in the form of an image file.					
	b furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.					
	c. furnished subsequent to the international filing date for the purposes of international search only:					
in the form of an Annex C/ST.25 text file (Rule 13 <i>ter</i> .1(a)).						
	on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).					
4.	In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.					
5.	Additional comments:					

International application No.

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability						
The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:						
the entire international application.						
X claims Nos. 5-18, 22-31, 34-35						
because:						
the said international application, or the said claims Nos. relate to the following						
subject matter which does not require an international search (specify):						
the description, claims or drawings (indicate particular elements below) or said claims Nos.  are so unclear that no meaningful opinion could be formed (specify):						
the claims, or said claims Nos.  by the description that no meaningful opinion could be formed (specify):  are so inadequately supported						
X no international search report has been established for said claims Nos. 5-18, 22-31, 34-35						
a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:						
furnish a sequence listing in the form of an Annex C/ST.25 text file, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply the standard provided for in Annex C of the Administrative Instructions.  [International Searching Authority in the form of an image file complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in the form and man acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administra Instructions.  [Instructions] Instructions pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13ter.1(a) or (b).  [Instructions] Instructions See Supplemental Box for further details.						
See Supplemental Box for further details.						

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

. Statement			
Novelty (N)	Claims	21, 32-33, 37-44	YES
	Claims	1-4, 19-20, 36	NO
Inventive step (IS)	Claims		YES
	Claims	1-4, 19-21, 32-33, 36-44	NO
Industrial applicability (IA)	Claims	1-4, 19-21, 32-33, 36-44	YES
	Claims		NO

#### 2. Citations and explanations:

D1: US 2013/0164393 A1 (JOHNSON & JOHNSON CONSUMER COMPANIES, INC.) 27.06.2013.

D2: Зенков Н.К. и др. Редокс-чувствительная система Keap1/Nrf2/ARE как фармакологическая мишень при сердечно-сосудистой патологии. Сибирский научный медицинский журнал, 2015, Том 35, No 5, c. 5-25 (ZENKOV N.R. et al. Keap1/Nrf2/ARE REDOX-SENSITIVE SYSTEM AS A PHAGMACOLOGICAL TARGET IN CARDIOVASCULAR DISEASES), non-official translation (Siberian Scientific Medical Journal, 2015, Vol. 35, No 5, pp. 5-25).

D3: US 8940342 B1 (PAMELA A JOHNSON) 27.01.2015.

D4: US 2015/0080265 A1 (THE WERE SHOP, LLC) 19.03.2015.

Independent claims 1, 19, 36, 37, 38, 40, 43, 44.

Document D1 ([0009], [0098-0103]) discloses a cosmetic composition for use in the treatment, repair, rejuvenation and beautification of the skin, comprising an effective amount of a the NFκB-inhibitor in combination with at least one additional cosmetic additive and a method of treating a cosmetic condition of the keratinous tissue (the associated oxidative stress, for example, wrinkled skin) of a subject by administering of the composition. The composition can contain other additional cosmetically active agents, for example, antioxidant of resveratrol as a NF-κB signaling inhibitor and a Nrf2 signaling agonist ([0109], [0113]). Prior art discloses that this compound according to the indicated chemical structure has dual activity as a NF-κB signaling inhibitor and a Nrf2 signaling agonist, for example from D2 (table 1, p. 14, column 1, paragraph 2).

Therefore, claims 1, 19 are 36 are not novel.

The invention according to claims 37, 38, 40, 43, 44 differs from D1 in that the composition comprises a compound LD55, also can contain coconut oil and/or jojoba oil, an essential oil and a terpene.

Therefore, claims 37, 38, 40, 43, 44 are novel.

However, it is obvious to the skilled art person that since LD55 is a synthetic analog of resveratrol, it will have dual activity as the NF-kB signaling inhibitor and the Nrf2 signaling agonist.

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#### Supplemental Box

In case the space in any of the preceding boxes is not sufficient. Continuation of V:

The composition can comprise an effective amount of the terpene (a pentacyclic triterpene acid, triterpene (D1, [0049], [0092]).

D3 discloses the composition comprising the coconut oil and/or jojoba oil, the essential oil of of lavender, peppermint, eucalyptus (abstract, claims, table 10).

Therefore, claims 37, 38, 40, 43, 44 do not involve an inventive step.

Dependent claims 2, 3, 4, 20, 21, 32, 33, 39, 41, 42.

Dependent claims 2-4, 20-21, 32-33, 39, 41-42 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step.

D1 discloses different types of additional cosmetic additives ([0102]), additional active agents ([0109]-[0111]), D4 – different types of the terpenes (claims 1, 2, 9, 15).

Therefore, claims 2-4 and 20 are not novel, claims 21, 32-33, 39 and 41-42 do not involve an inventive step.

The inventions of claims 1-4, 19-21, 32-33, 36-44 are industrially applicable.