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Examiner's first report on patent application no. 2008296078
by BioNovo, Inc.

Last proposed amendment no. 2

Dear Madam/Sir,

I am replying to the request for examination. I have based this report on the pamphlet and the statement of proposed amendments under S104 of 30 June 2010. I have examined the application and I believe that there are lawful grounds of objection to the application. These grounds of objection are:

1. There is no Notice of Entitlement on file. You will need to file one because an application without a Notice of Entitlement cannot be accepted.
2. The invention defined in claims 1-12, 15-20, 23-28, 31-46, 59-62 is not novel (and does not involve an inventive step) when compared with the following prior art documents that disclose all the essential features of the invention claimed:

NOTE: The following documents D5-D8 were cited by a third party under Section 27 of the Australian Patent Act of 1990 on 21 January 2011 with a letter written on 10 January 2011. A copy of these documents and translations had been forwarded to the applicant on 22 February 2011.

D5: Kitaab-al-Haawi-fil-Tibb, Vol. XX by Abu Bakr Mohammad.Bin Zakariyya Al-Razi (9th century AD), Dayerah-al-Ma'arif Usmania, Hyderabad, (First Edition) 1967 AD, Pg 525
Relevant to claims: 1-12, 17-20, 25-28, 33-46, 59-62

D6: Kitaab-al-Haawi-fil-Tibb, Vol. VII by Abu Bakr Mohammad.Bin Zakariyya Al-Razi (9th century AD), Dayerah-al-Ma'arif Usmania, Hyderabad, (First Edition) 1958 AD, Pg 38
Relevant to claims: 1-12, 17-20, 25-28, 33-46, 59-62

D7: Qaraabaadeen Najm-al-Ghani by Mohammad Najmul Ghani Khan (20th Century AD), Munshi Nawal Kishore, Lucknow, (Second Edition) 1928 AD, Pg456
Relevant to claims: 1-12, 17-20, 25-28, 33-46, 59-62

D8: Ikseer Azam, Vol. IV by Mohammad Azam Khan (19th century AD), Matba Nizami, Kanpur, 1872 AD, Pg 324

Relevant to claims: 1-12, 15-20, 23-28, 31-46, 59-62

D5 discloses a formulation containing *Rheum palmatum* as a single ingredient used for the treatment of weakness of heart through oral administration.

D6 discloses a formulation containing *Rheum palmatum* as a single ingredient used for the treatment of palpitation through oral administration.

D7 discloses a formulation containing *Rheum palmatum* along with one other ingredient used as cardio-tonic through oral administration.

D8 discloses a formulation containing *Rheum palmatum* along with few other ingredients used for the treatment of cancer through local application.

NOTE: The claims include expressions such as compositions that modulate or methods of modulating the expression of genes under control of an estrogen or TNF response element, which do not limit the scope of the claims.

For example, claims 1 and 62 define a composition “that modulates the expression of a gene under control of an estrogen response element...” This phrase limits the scope of this claim to the extent that the composition must be suitable, but not limited, to such a use. The claims are, therefore, considered to be directed to the compositions *per se*. Therefore, a citation only needs to disclose a composition comprising a compound obtained from *Rheum palmatum* to render claim 1 as not novel. As the citations disclose this (see above), claims 1 and 62 are not novel.

Furthermore, claim 9 defines a method of “modulating the expression of a gene under control of an estrogen response element, comprising administering... a composition comprising one or more compounds obtained from... *Rheum palmatum* ...” Claim 40 defines a method very similar to claim 9 except that the gene is under control of a TNF response element instead of an estrogen response element. Dependent claims 11-16 further define the method to include the treatment or prophylaxis of a variety of conditions or diseases. However, D5, D6, D7 and D8 each disclose methods of treating the same conditions (menopausal symptoms or cancer) with the same composition (comprising extracts of *Rheum palmatum*) as defined in the claims.

Although the citations do not explicitly disclose that the extract modulates the expression of a gene under control of an estrogen (or TNF) response element, the extract would inherently possess the claimed intrinsic mechanism. Therefore the phrase “modulating the expression of a gene under control of an estrogen response element” cannot confer novelty to the claims over the prior art. A similar argument applies to independent claims 17, 25, 33 and 59-62 and their respective dependent claims.

Features added by the remaining dependent claims are considered to be either disclosed by the citations or do not constitute an inventive step because a person skilled in the art who is in possession of the above citations would find it obvious to arrive at the claimed inventions by standard techniques or variations thereof known in the art.

3. The invention defined in claims 1-11, 17-19, 25-27, 33-39 and 59-60, 62 is not novel (and does not involve an inventive step) when compared with the following prior art document that discloses all the essential features of the invention claimed:

D1: US 2005/0204416 A1*

D1 discloses ligands (extracts) from a member of the taxonomic species *Rheum palmatum* L of the *Polygonaceae* family (page 12, [0120]; page 16, [0158]) and compositions thereof which modulate the expression of a gene under control of an estrogen response element (page 3, [0033]). Aqueous and non-aqueous extracts are disclosed (page 12, [0120]).

4. The invention defined in claim 47 is not novel (and does not involve an inventive step) when compared with the following prior art document that discloses all the essential features of the invention claimed:

D3: US 2007/0122492 A1*

D3 discloses a method of obtaining one or more extracts from a member of the taxonomic species *Rheum palmatum* L of the *Polygonaceae* family by contacting plant matter from a member of said plant species with an extraction medium and then separating the extraction medium from the plant matter (page 21, right hand column, line 5; pages 4-5, [0045-47]).

5. The invention defined in claims 1-8, 47 and 62 is not novel (and does not involve an inventive step) when compared with the following prior art document that discloses all the essential features of the invention claimed:

D10: US 2003/0143289 A1**

D10 discloses a pharmaceutical composition named PHY828 which comprises extracts of *Rheum palmatum* (abstract; page 12, [0161]). Methods of obtaining extracts from *Rheum palmatum* comprising contacting plant matter with an extraction medium and then separating the plant matter and extraction medium (page 12, [0156-160]) are also discussed.

Note: Please refer to the Note under Objection 2 which provides a further explanation as to how the composition claims are construed.

6. The invention defined in claims 48-58 does not involve an inventive step when compared to D3 (see objection 4) or D10 (see objection 5). D3 and D10 both disclose a method of obtaining extracts from a member of the taxonomic species *Rheum palmatum* L of the *Polygonaceae* family. The invention defined in claims 48-58 further defines that the method of extraction is performed with standard extraction techniques well known in the art (for example, using chromatography). A person skilled in the art, having read D3 or D10, would find it obvious to use standard techniques to obtain extracts from *Rheum palmatum* L of the *Polygonaceae* family and, therefore, claims 48-58 cannot be considered to involve an inventive step.

7. The invention defined in claims 1-14, 17-22, 25-30, 33-46 and 59-62 is not novel (and does not involve an inventive step) when compared with the following prior art document that discloses all the essential features of the invention claimed:

D14: Life Science Weekly. *Menopause*; Bionovo study confirms potential benefits of compounds to treat hot flashes. Life Science Weekly. Atlanta. September 5, 2006. Page 990***

D14 discloses methods of treating hot flashes and symptoms of menopause with compounds obtained from *Rheum palmatum* known as anthraquinones (abstract). Osteoporosis is a well known symptom of menopause.

Note: Please refer to the Note under Objection 2 which provides a further explanation as to how the composition claims are construed.

NOTE: The following documents are brought to the applicant's attention as they are also relevant citations for the purposes of novelty and inventive step. These documents may be cited in a subsequent report pending the response to objections 2-6.

D11: Lee, J *et al* (2006) Emodin inhibits TNF α -induced MMP-1 expression through suppression of activator protein-1 (AP-1). *Life Sciences* **79**: 2480-2485**

D12: Usui, T *et al* (2002) The phytochemical lindleyin, isolated from Rhei rhizoma, mediates hormonal effects through estrogen receptors *Journal of Endocrinology* **175**: 289-296**

D13: Kuo, YC *et al* (2001) Immune responses in human mesangial cells regulated by emodin from *Polygonum hypoleucum* Ohwi. *Life Sciences* **68**: 1271-1286**

D15: Zhang, CZ *et al* (2005) In vitro estrogenic activities of Chinese medical plants traditionally used for the management of menopausal symptoms. *Journal of Ethnopharmacology* **98**: 295-300^

D16: Kang, SC *et al* (2006) Evaluation of Oriental Medicinal Herbs for Estrogenic and Antiproliferative Activities. *Phytotherapy Research* **20**: 1017-1019^

Documents D11-D13 are relevant to at least claims 1-46 and 59-62. Documents D15-D16 are relevant to claims 1-62.

* cited in ISR/IPRPI

** cited in US Examination Report of 12/205731 dated 15 September 2010

*** cited in US Examination Report of 12/205731 dated 28 March 2011

^ cited in First Examination Report of AU2008296076 (related case to the instant application)

NOTE: There is a current postponement of acceptance in place. If you overcome all other objections before the expiration of that postponement, the Commissioner will only accept the application at that time if you have filed a clear and unambiguous statement requesting the withdrawal of that postponement. Otherwise, a further adverse report will be issued.

You have 21 months from the date of this report to overcome all my objection(s) otherwise your application will lapse.

You will need to pay a monthly fee for any response you file after 12 months from the date of the first report.

You will also need to pay any annual continuation fees that apply. These will normally be first due five years from the filing date. Please note however that earlier commencement dates apply for divisional applications.

Information about fees may be obtained by phoning 1300 651 010.

Yours faithfully,

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This data, for application number 2008296078, is current as of 2012-04-19 22:49 AEST

