# PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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# PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

| | |
|---|---|
| Date of mailing *(day/month/year)* | 03-12-2018 |
| Applicant's or agent's file reference<br>GG237 | **FOR FURTHER ACTION**<br>See paragraph 2 below |

| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
|---|---|---|
| PCT/IB2018/055968 | 08-08-2018 | 08-08-2017 |

International Patent Classification (IPC) or both national classification and IPC
A61K9/00,A61K31/00,A61P35/00,C07D233/86 Version=2018.01

Applicant
DR. REDDY'S LABORATORIES LIMITED

1. This opinion contains indications relating to the following items:

- [x] 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
- [x] Box No. V Reasoned statement under Rule 43*bis*.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.

| Name and mailing address of the ISA/ | Date of completion of this opinion | Authorized officer |
|---|---|---|
| Indian Patent Office<br>Plot No. 32, Sector 14,<br>Dwarka,New Delhi-110075<br>Facsimile No. | 03-12-2018 | Chanchal Kumar Malav<br>Telephone No. +91-1125300200 |

**WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/IB2018/055968

**Box No. I Basis of this opinion**

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into _____ which is the language of a 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 **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a)).

3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:

   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 13*ter*.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*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.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 forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

**WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/IB2018/055968

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

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | | YES |
| | Claims | 1-10 | NO |
| Inventive step (IS) | Claims | | YES |
| | Claims | 1-10 | NO |
| Industrial applicability (IA) | Claims | 1-10 | YES |
| | Claims | | NO |

2. Citations and explanations:

Reference is made to the following documents-

D1: US20140100256A1 (BEND RESEARCH, BEND, OR [US]; ASTELLAS PHARMA INC., TOKYO [JP]; MEDIVATION PROSTATE THERAPEUTICS, INC., SAN FRANCISCO, CA [US]) 10 APRIL 2014 (10-04-2014)

D2: US20160346207A1 (LEK PHARMACEUTICALS D.D., LJUBLJANA [SI]) 01 DECEMBER 2016 (01-12-2016)

D3: US20070004753A1 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA, OAKLAND, CA [US]) 04 JANUARY 2007 (04-01-2007)

The present invention relates to novel oral extrudate pharmaceutical compositions of enzalutamide. The extrudate compositions comprise one or more suitable polymers and are prepared using twin screw extrusion or hot melt extrusion. Methods of preparing such compositions are also provided. The extrudate compositions may be used for the treatment of prostate cancer.

NOVELTY under PCT Article 33(2):

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-10 is not new in the sense of Article 33(2) PCT.

Regarding claims 1-3, 10: D1 discloses pharmaceutical composition comprising a solid dispersion containing enzalutamide and one or more polymers, wherein the polymer is 0.5 to 7 parts by weight, with respect to 1 part by weight of the enzalutamide (see: para

**Supplemental Box**

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

Continuation of Citation and Explanation(Box5)
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[0003], [0014]-[0031], [0071], [0089], [0090]; examples 16-23; claims 1-4 ). Therefore, the subject matter of the claims 1-3, 10 is not novel over D1.

Regarding claim 4: D1 also discloses that polymer is selected from one or more of cellulosic polymer or non-cellulosic polymer or mixtures thereof (see: para [0051]-[0068]). Therefore, the subject matter of the claim 4 is not novel over D1.

Regarding claims 5, 8: D1 also discloses that cellulosic polymer is selected from one or more of hydroxypropyl methyl cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxyethyl methyl cellulose, hydroxyethyl cellulose acetate, hydroxyethyl ethyl cellulose, hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose succinate, hydroxypropyl cellulose acetate succinate, hydroxyethyl methyl cellulose succinate, hydroxyethyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, hydroxyethyl methyl cellulose acetate succinate, hydroxyethyl methyl cellulose acetate phthalate and any mixtures thereof (see: para [0058]-[0067], [0073], [0110], [0111], [0127], [0136]; claim 3). Therefore, the subject matter of the claims 5, 8 is not novel over D1.

Regarding claims 6, 7: D1 also discloses that non-cellulosic polymers is selected from one or more of vinyl polymers and copolymers, polyvinyl alcohol polyvinyl acetate copolymers; polyvinyl pyrrolidone; polyvinylpyrrolidone vinyl acetate, polyethylene polyvinyl alcohol copolymers, carboxylic acid-functionalized vinyl polymers, copolymers of methacrylates and acrylates, graft copolymers of polyethylene glycol, polyvinylcaprolactam, and polyvinylacetate and any mixtures thereof (see: para [0055]-[0057], [0069], [0073]; claim 3). Therefore, the subject matter of the claims 6, 7 is not novel over D1.

Regarding claim 9: D1 also discloses that said composition further comprise one or more pharmaceutically acceptable excipients (see: para [0005], [0106], [0122], [0129], [0134], [0143], [0144], [0159]-[0170]). Therefore, the subject matter of the claim 9 is not novel over D1.

INVENTIVE STEP under PCT Article 33(3):

The subject matter of the claims 1-10 does not meet the requirement of PCT Article 33(3).

Since claims 1-10 are not novel over D1, therefore inventive step cannot be acknowledged for the said claims. However, inventive step can be further analyzed in view of D2 and D3.

D2 (see: page 1, lines 3-6; page 4, line 1- page 10, line 7; page 17, line 20-page 19, line 15; page 21, line 23-page 26, line 13; examples; claims 1-15) discloses a solid pharmaceutical composition useful in the treatment of prostate cancer comprising androgen receptor antagonists, e.g. Enzalutamide or ARN-509, a carrier, a surfactant and at least one further excipient, combined in the form of a solid dispersion or a solid solution of Enzalutamide or ARN-509 with a polymer, wherein in said solid dispersion the weight ratio of Enzalutamide or ARN-509 and the at least one polymer is from about 5:1 to about 1 :40, preferably from about 4:1 to about 1:20, more preferably from about 2:1 to about 1:10; and processes for preparing the same.

D3 (see: page 1, para 1, 8; page 59, para 388-391; claims 1, 16, 20-36) discloses various diarylhydantoins such as (inter alia) enzalutamide, their use in the treatment of cancers such as prostate cancer and pharmaceutical formulations.

Therefore the whole invention is prima facie obvious to a person skilled in the art as described above and lacks the inventive step under article 33(3) of PCT, because every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the teachings of the cited references.

Industrial applicability under PCT Article 33(4):

Claims 1-10 meet the criteria set out in PCT Article 33(4) and thus have industrial applicability because the subject matter claimed can be made or used in the industry.