

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference ONCO-001/03-WO	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2018/027514	International filing date (<i>day/month/year</i>) 13 April 2018 (13-04-2018)	(Earliest) Priority Date (<i>day/month/year</i>) 13 April 2017 (13-04-2017)
Applicant ONCONOVA THERAPEUTICS, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out 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))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6**bis**(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☒ **Unity of invention is lacking** (see Box No III)

4. With regard to the **title**,

- ☐ the text is approved as submitted by the applicant
☒ the text has been established by this Authority to read as follows:

FORMULATION OF (E)-2,4,6-TRIMETHOXYSTYRYL-3-[(CARBOXYMETHYL)AMINO]-4-METHOXYBENZYLSULPHONE WITH ENHANCED STABILITY AND BIOAVAILABILITY

5. With regard to the **abstract**,

- ☒ the text is approved as submitted by the applicant
☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. 1

- ☒ as suggested by the applicant
☐ as selected by this Authority, because the applicant failed to suggest a figure
☐ as selected by this Authority, because this figure better characterizes the invention

b. ☐ none of the figures is to be published with the abstract

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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. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ 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:

see additional sheet

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 report covers 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.

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BOWLES D. W. ET AL: "Phase I Study of Oral Rigosertib (ON 01910.Na), a Dual Inhibitor of the PI3K and Plk1 Pathways, in Adult Patients with Advanced Solid Malignancies", CLINICAL CANCER RESEARCH, vol. 20, no. 6, 3 February 2014 (2014-02-03), pages 1656-1665, XP055483800, US ISSN: 1078-0432, DOI: 10.1158/1078-0432.CCR-13-2506 cited in the application abstract page 1657, column 1, paragraph 2 page 1658, column 2, paragraph 2 -----	1-32
A	OLNES MATTHEW J ET AL: "Directed therapy for patients with myelodysplastic syndromes (MDS) by suppression of cyclin D1 with ON 01910.Na", LEUKEMIA RESEARCH, NEW YORK, NY, US, vol. 36, no. 8, 21 April 2012 (2012-04-21), pages 982-989, XP028494957, ISSN: 0145-2126, DOI: 10.1016/J.LEUKRES.2012.04.002 [retrieved on 2012-04-04] abstract -----	1-32
X	US 2015/313859 A1 (MANIAR MANOJ [US] ET AL) 5 November 2015 (2015-11-05)	33,35,36
Y	claims 1, 4, 16 examples 7, 10-12	33-36
X	----- DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; November 2013 (2013-11), RAZA AZRA ET AL: "Oral Rigosertib (ON 01910.Na) Treatment Produces A Encouraging Rate Of Transfusion Independence In Lower Risk Myelodysplastic Syndromes (MDS) Patients; A Genomic Methylation Profile Is Associated With Responses", XP002788716, Database accession no. PREV201400361728	33,35,36
Y	abstract & BLOOD, vol. 122, no. 21, November 2013 (2013-11), page 2745, 55TH ANNUAL MEETING OF THE AMERICAN-SOCIETY-OF-HEMATOLOGY; NEW ORLEANS, LA, USA; DECEMBER 07 -10, 2013 ISSN: 0006-4971(print) ----- -/--	33-36

INTERNATIONAL SEARCH REPORT

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 2 December 2016 (2016-12-02), NAVADA SHYAMALA C ET AL: "Combination of Oral Rigosertib and Injectable Azacitidine in Patients with Myelodysplastic Syndromes (MDS): Results from a Phase II Study", XP002788717, Database accession no. PREV201700341027	33-36
Y	abstract & BLOOD, vol. 128, no. 22, 2 December 2016 (2016-12-02), 58TH ANNUAL MEETING AND EXPOSITION OF THE AMERICAN-SOCIETY-OF-HEMATOLOGY; SAN DIEGO, CA, USA; DECEMBER 03 -06, 2016 ISSN: 0006-4971(print) -----	33-36
X	DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; December 2015 (2015-12), NAVADA SHYAMALA C ET AL: "A Phase II Study of the Combination of Oral Rigosertib and Azacitidine in Patients with Myelodysplastic Syndromes (MDS)", XP002788718, Database accession no. PREV201600270785	33-36
Y	abstract & BLOOD, vol. 126, no. 23, December 2015 (2015-12), 57TH ANNUAL MEETING OF THE AMERICAN-SOCIETY-OF-HEMATOLOGY; ORLANDO, FL, USA; DECEMBER 05 -08, 2015 ISSN: 0006-4971(print) -----	33-36
Y	KOMROKJI RAMI S. ET AL: "Phase I clinical trial of oral rigosertib in patients with myelodysplastic syndromes", BRITISH JOURNAL OF HAEMATOLOGY, vol. 162, no. 4, 21 June 2013 (2013-06-21) , pages 517-524, XP055483608, GB ISSN: 0007-1048, DOI: 10.1111/bjh.12436 abstract figure 1 -----	33-36

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Information on patent family members

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 8476320	B2	02-07-2013	CA 2675374 A1 24-07-2008
		EP 2124569 A2 02-12-2009	
		IL 199891 A 31-05-2016	
		JP 2010515772 A 13-05-2010	
		KR 20090114398 A 03-11-2009	
		US 2010152096 A1 17-06-2010	
		WO 2008088803 A2 24-07-2008	
US 8063109	B2	22-11-2011	AT 497768 T 15-02-2011
		AU 2005265412 A1 26-01-2006	
		CA 2574491 A1 26-01-2006	
		EP 1773353 A2 18-04-2007	
		HK 1105275 A1 21-10-2011	
		IL 180751 A 30-04-2014	
		JP 4982364 B2 25-07-2012	
		JP 2008506777 A 06-03-2008	
		US 2009036462 A1 05-02-2009	
		WO 2006010152 A2 26-01-2006	
US 2015313859	A1	05-11-2015	EP 2928456 A1 14-10-2015
		JP 6462582 B2 30-01-2019	
		JP 2016501884 A 21-01-2016	
		US 2015313859 A1 05-11-2015	
		WO 2014089483 A1 12-06-2014	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-32

A pharmaceutical composition comprising,

- a) (E)-2,4,6-trimethoxystyryl-3-[(carboxymethyl)amino]-4-methoxybenzylsulphone and pharmaceutically acceptable salts thereof,
- b) basic pre-treated low molecular weight polyethylene glycol;
- c) undiluted pH of about 11.0 to about 14.0; and
- d) less than 5% water or aqueous solution.

A method of treating conditions mediated by abnormal cell proliferation comprising administering an effective amount of the said pharmaceutical composition to a subject in need thereof.

2. claims: 33-36

A method of treating conditions mediated by abnormal cell proliferation comprising administering an effective amount of

(E)-2,4,6-trimethoxystyryl-3-[(carboxymethyl)amino]-4-methoxybenzylsulphone, sodium salt to a patient in need thereof, comprising orally administering a first dose of 840 mg approximately 1-2 hours before breakfast and a second dose of 280 mg about 2 hours after lunch, or administering a first dose of 560 mg approximately 1-2 hours before breakfast and a second dose of 280 - 560 mg about 2 hours after lunch.
