

INFORMATION DISCLOSURE STATEMENT Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	Attorney Docket	REGN-008CIPCON
	First Named Inventor	YANCOPOULOS, GEORGE D.
	Application Number	14/972,560
	Confirmation No.	5391
	Filing Date	December 17, 2015
	Group Art Unit	1647
	Examiner Name	LOCKARD, JON MCCLELLAND
	Title:	<i>“Use of a VEGF Antagonist to Treat Angiogenic Eye Disorders”</i>

Sir:

Applicants submit herewith documents which may be material to the examination of this application and in respect of which there may be a duty to disclose in accordance with 37 C.F.R. § 1.56. This submission is not intended to constitute an admission that any document referred to therein is "prior art" for this invention unless specifically designated as such. A listing of the documents is shown on enclosed Form PTO/SB/08A and copies of the non-patent literature are also enclosed.

The Examiner is requested to make the documents listed on the enclosed PTO/SB/08A of record in this application. Applicants would appreciate the Examiner initialing and returning the initialed copy of form PTO/SB/08A, indicating the document cited therein have been considered and made of record herein.

Statements

☒ **No statement**

☐ **PTA Statement under 37 CFR § 1.704(d)(1):** Each item of information contained in the information disclosure statement filed herewith:

(i) Was first cited in any communication from a patent office in a counterpart foreign or international application or from the Office, and this communication was not received by any individual designated in § 1.56(c) more than thirty days prior to the filing of the information disclosure statement; or

(ii) Is a communication that was issued by a patent office in a counterpart foreign or international application or by the Office, and this communication was not received by any individual designated in § 1.56(c) more than thirty days prior to the filing of the information disclosure statement.

- ☐ **IDS Statement under 37 CFR § 1.97(e)(1):** Each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement; or
- ☐ **IDS Statement under 37 CFR § 1.97(e)(2):** No item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement.
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Fees

- ☐ No fee is believed to be due.
- ☒ The appropriate fee set forth in 37 C.F.R. §1.17(p) accompanies this information disclosure statement.

The Commissioner is hereby authorized to charge any underpayment of fees up to a strict limit of \$3,000.00 beyond that authorized on the credit card, but not more than \$3,000.00 in additional fees due with any communication for the above referenced patent application, including but not limited to any necessary fees for extensions of time, or credit any overpayment of any amount to Deposit Account No. 50-0815, order number REGN-008CIPCON.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: 27 January 2017

By: /Karl Bozicevic, Reg. No. 28,807/
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U.S. PATENT DOCUMENTS					
Examiner Initial*	Cite No.	Patent Number	Issue Date YYYY-MM-DD	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code (if known)			
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U.S. PATENT APPLICATION PUBLICATIONS					
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FOREIGN PATENT DOCUMENTS						
Examiner Initial*	Cite No.	Foreign Document Number	Publication Date YYYY-MM-DD	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T
		Country Code-Number-Kind Code (if known)				
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NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T
	1	Charles, Steve (Guest Lecturer) "VEGF Trap Has Positive DME Data" Tenth Annual Retina Fellows Forum Jan 29 and 30, Chicago, Article Date 03/01/2010	
	2	Dixon et al., "VEGF Trap-Eye for the treatment of neovascular age-related macular degeneration" Expert Opin. Investig. Drugs (2009) 18 (10): 1-8.	
	3	Information from ClinicalTrials.gov archive on the VIEW 2 study (NCT00637377) "VEGF Trap-Eye: Investigation of Efficacy and Safety in Wet AMD (VIEW 2)" version available and updated on 17 March 2008.	
	4	Information from ClinicalTrials.gov archive on the view of NCT00509795 "Vascular Endothelial Growth Factor (VEGF) Trap-Eye: Investigation of Efficacy and Safety in Wet Age-Related Macular Degeneration (AMD)" (12-01-2009)	
	5	Information from ClinicalTrials.gov archive on the view of NCT00789477 "DME and VEGF Trap-Eye: Investigation of Clinical Impact" (11-18-2010)	
	6	Information from ClinicalTrials.gov archive on the view of NCT00509795 "Vascular Endothelial Growth Factor (VEGF) Trap-Eye: Investigation of Efficacy and Safety in Wet Age-Related Macular Degeneration (AMD)" (01-07-2011)	
	7	Mousa and Mousa, "Current Status of Vascular Endothelial Growth Factor Inhibition in Age-Related Macular Degeneration" Biodrugs 2010; 24(3); 183-194.	
	8	Regeneron Pharmaceuticals, Inc. FORM 10-Q, published on 7 November 2007 for the period ending 30 September 2007	
	9	Regeneron, Press release "Regeneron Reports First Quarter 2008 Financial and Operating Results", May 1, 2008.	

Examiner Signature		Date Considered	
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	10	Regeneron Press Release "Bayer and Regeneron Report Positive Top-Line Results of Two Phase 3 Studies with VEGF Trap-Eye in Wet Age-related Macular Degeneration" November 22, 2010		
	11	Regeneron Press Release "Regeneron and Bayer Report Positive Results for VEGF Trap-Eye in Phase 3 Study in Central Retinal Vein Occlusion (CRVO) and in Phase 2 Study in Diabetic Macular Edema (DME)" December 20, 2010		
	12	Simo and Hernandez, "Advances in Medical Treatment of Diabetic Retinopathy" Diabetes Care, Volume 32, Number 8, August 2009		
	13	Slides for the 2008 Retina Society Meeting "VEGF Trap-Eye in Wet AMD CLEAR-IT 2: Summary of One-Year Key Results", September 28, 2008.		
	14	WHO Drug Information, "International Nonproprietary Names for Pharmaceutical Substances (INN)" Vol. 20, No. 2, 2006, pages 115-119.		

Examiner Signature		Date Considered	
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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

NCT00509795 on 2009_12_01: ClinicalTrials.gov Archive

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ClinicalTrials.gov archive

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← History of this study

↑ Current version of this study

View of NCT00509795 on 2009_12_01

ClinicalTrials Identifier: NCT00509795

Updated: 2009_12_01

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5**Descriptive Information**

Brief title Vascular Endothelial Growth Factor(VEGF)Trap-Eye:Investigation of Efficacy and Safety in Wet Age-Related Macular Degeneration (AMD)

Official title A Randomized, Double Masked, Active Controlled Phase III Study of the Efficacy, Safety, and Tolerability of Repeated Doses of Intravitreal VEGF Trap in Subjects With Neovascular Age-Related Macular Degeneration

Brief summary

This study is a phase III, double-masked, randomized, study of the efficacy and safety of VEGF Trap-Eye in patients with neovascular age-related macular degeneration. Approximately 1200 patients will be randomized in the US and Canada.

Detailed description

Phase Phase 3
Study type Interventional
Study design Treatment
Study design Randomized
Study design Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Study design Active Control
Study design Parallel Assignment
Study design Safety/Efficacy Study
Primary outcome Measure: The proportion of subjects who maintain vision at Week 52, where a subject is classified as maintaining vision if the subject has lost fewer than 15 letters on the ETDRS chart compared to baseline (i.e. prevention of moderate vision loss)
Time Frame: Week 52
Safety Issue? Yes
Secondary outcome Measure: Mean change from baseline in BCVA as measured by ETDRS letter score at Week 52
Time Frame: Week 52
Safety Issue? Yes
Secondary outcome Measure: The proportion of subjects who gain at least 15 letters of vision at Week 52
Time Frame: Week 52
Safety Issue? No
Secondary outcome Measure: Mean change from baseline in total NEI VFQ-25 score at Week 52
Time Frame: Week 52
Safety Issue? No

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Secondary outcome	Measure: Mean change from baseline in CNV area at Week 52 Time Frame: Week 52 Safety Issue? Yes	
Enrollment	1200 (Anticipated)	
Condition	Macular Degeneration	
Arm/Group	Arm Label: 1	Experimental
Arm/Group	Arm Label: 2	Experimental
Arm/Group	Arm Label: 3	Experimental
Arm/Group	Arm Label: 4	Active Comparator
Intervention	Drug: VEGF Trap-Eye	Arm Label: 3
	2.0 mg VEGF Trap-Eye administered every 8 weeks (including one additional 2.0 mg dose at week 4) during the first year. Thereafter a dose may be administered as frequently as every 4 weeks, but no less frequently than every 12 weeks.	
Intervention	Drug: VEGF Trap-Eye	Arm Label: 1
	0.5 mg VEGF Trap-Eye administered every 4 weeks during the first year. Thereafter a dose may be administered as frequently as every 4 weeks, but no less frequently than every 12 weeks.	
Intervention	Drug: VEGF Trap-Eye	Arm Label: 2
	2.0 mg VEGF Trap-Eye administered every 4 weeks during the first year. Thereafter a dose may be administered as frequently as every 4 weeks, but no less frequently than every 12 weeks.	
Intervention	Drug: Ranibizumab	Arm Label: 4
	0.5 mg administered every 4 weeks during the first year. Thereafter a dose may be administered as frequently as every 4 weeks, but no less frequently than every 12 weeks.	

Recruitment Information

Status	Active, not recruiting
Start date	2007-08
Last follow-up date	2011-12 (Anticipated)
Primary completion date	2011-12 (Anticipated)

Criteria

Key Inclusion Criteria:

1. Signed Informed Consent.
2. Men and women ≥ 50 years of age.
3. Active primary or recurrent subfoveal CNV lesions secondary to AMD, including juxtafoveal lesions that affect the fovea as evidenced by FA in the study eye.
4. ETDRS best-corrected visual acuity of: 20/40 to 20/320 (letter score of 73 to 25) in the study eye.
5. Willing, committed, and able to return for ALL clinic visits and complete all study-related procedures.
6. Able to read, (or, if unable to read due to visual impairment, be read to verbatim by the person administering the informed consent or a family member. See Appendix

https://clinicaltrials.gov/archive/NCT00509795/2009_12_01

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J.4) understand and willing to sign the informed consent form.

Key Exclusion Criteria:

1. Any prior ocular (in the study eye) or systemic treatment or surgery for neovascular AMD except dietary supplements or vitamins.
2. Any prior or concomitant therapy with another investigational agent to treat neovascular AMD in the study eye, except dietary supplements or vitamins.
3. Any prior treatment with anti-VEGF agents in the study eye.
4. Total lesion size > 12 disc areas (30.5 mm², including blood; scars and neovascularization) as assessed by FA in the study eye.
5. Subretinal hemorrhage that is either 50% or more of the total lesion area, or if the blood is under the fovea and is 1 or more disc areas in size in the study eye. (If the blood is under the fovea, then the fovea must be surrounded 270 degrees by visible CNV.)
6. Scar or fibrosis, making up > 50% of total lesion in the study eye.
7. Scar, fibrosis, or atrophy involving the center of the fovea.
8. Presence of retinal pigment epithelial tears or rips involving the macula in the study eye.
9. History of any vitreous hemorrhage within 4 weeks prior to Visit 1 in the study eye.
10. Presence of other causes of CNV in the study eye.
11. History or clinical evidence of diabetic retinopathy, diabetic macular edema or any other vascular disease affecting the retina, other than AMD, in either eye.
12. Prior vitrectomy in the study eye.
13. History of retinal detachment or treatment or surgery for retinal detachment in the study eye.
14. Any history of macular hole of stage 2 and above in the study eye.
15. Any intraocular or periocular surgery within 3 months of Day 1 on the study eye, except Ild surgery, which may not have taken place within 1 month of day 1, as long as its unlikely to interfere with the injection.

Gender	Both
Minimum age	50 Years
Healthy volunteers	No

Administrative Data

Organization name	Regeneron Pharmaceuticals
Organization study ID	VGFT-OD-0605
Sponsor	Regeneron Pharmaceuticals
Collaborator	Bayer
Health Authority	United States: Food and Drug Administration
Health Authority	Canada: Health Canada

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