NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis

Generic Drug Name

Brolucizumab /RTH258

Trial Indication(s)

Neovascular age-related macular degeneration (nAMD)

Protocol Number

CRTH258A2301E1

Protocol Title

A 24-week, double-masked, multicenter, two-arm extension study to collect safety and efficacy data on brolucizumab 6 mg drug product intended for commercialization in patients with neovascular age-related macular degeneration who have completed the CRTH258A2301 study

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase 3

Study Start/End Dates

Study Start Date: January 2018 (Actual)
Primary Completion Date: September 2018 (Actual)
Study Completion Date: September 2018 (Actual)

Study Design/Methodology

This was a 24-week, double-masked, multicenter, two-arm extension study.
Patients from the United States who had completed the 96-week core study CRTH258A2301 were eligible to participate provided Visit 26/ Week 96 in the core study was ≤ 12 weeks from Baseline visit in the extension study. During the study, subjects received either brolucizumab 6 mg (if they were treated with brolucizumab 3 mg or 6 mg in the core) or aflibercept 2 mg (if they were treated with aflibercept in the core). All subjects were planned to receive 3 intravitreal (IVT) injections during the study. Brolucizumab 6 mg subjects were treated at Baseline, Week 8 and, depending on the disease activity status, at Week 16 (q8w interval) or Week 20 (q12w interval). Aflibercept 2 mg subjects were treated every 8 weeks (q8w interval), at Baseline, Week 8 and Week 16, as per approved label.
This extension study consisted of 7 study visits at 4-week intervals labeled Visit 1/Baseline (exBL) to Visit 7/EOS (exWeek 24). Total study duration was 24 weeks.

Centers

United States(68)

Objectives:

The objective was to collect data on safety and efficacy of the brolucizumab 6 mg drug product intended for commercialization in subjects with nAMD previously treated in CRTH258A2301 study to support comparability to the brolucizumab 6 mg drug product used in Phase III clinical studies.

Test Product (s), Dose(s), and Mode(s) of Administration

The study treatments were brolucizumab 6 mg and aflibercept 2 mg for intravitreal injection. Brolucizumab solution for IVT injection was supplied to the investigators in single use, sterile glass vials. Aflibercept was obtained as commercially available, single use glass vials.

Statistical Methods

Analysis set: The Extension Safety Set included all subjects who entered this extension study and received at least one injection of study treatment in this extension study. The Extension Safety Set was used for the descriptive analyses and listings related to both efficacy and safety for the brolucizumab treatment arm and for the listings for the aflibercept treatment arm.

Efficacy: No formal hypothesis testing was planned for this study.
BCVA was summarized for the study eye. The number and percentage of subjects with a loss in BCVA of 15 letters or more from exBL at each post-exBL visit were presented. Descriptive statistics for change from baseline (exBL and coBL) in BCVA to each post-baseline study visit were presented as well. BCVA assessments after start of alternative anti-VEGF treatment in the study eye were censored and imputed by the last value prior to start of this alternative treatment (LOCF).
For CSFT, descriptive statistics for change from baseline (exBL and coBL) to each post-baseline study visit were presented.
The estimate for the proportion of subjects with a positive q12w treatment status at exWeek 24 was derived from Kaplan Meier time-to-event analyses for the event ‘first q8w-need’. The outcome of the Kaplan-Meier analysis was presented graphically by the estimated probability for maintaining on q12w over time, ie, at each DAA visit.

Safety: The incidence and characteristics of treatment emergent AEs during the extension study were displayed and compared to the corresponding numbers during the last 6 months of the core study (as a reference) on the same population. The number and percentage of subjects presenting at least one AE starting during the last 6 months of the core study and one new AE (for the same Preferred Term) starting during the extension study were summarized as well.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
- Sign written informed consent
- Completed the core study, CRTH258A2301, also known as CRTH258-C002 as defined by assessments at Visit 26/Week 96 within

≤12 weeks of the baseline.

Exclusion Criteria:
- Patient discontinued the treatment or the core study prematurely at any time
- Patient received standard of care treatment for nAMD after completion of the core study
- Pregnant or nursing women and women of child-bearing potential
- Stroke or MI (myocardial infarction) within 3 months of the baseline extension visit

Participant Flow Table

Overall Study

	Brolucizumab - Overall Extension Study	Aflibercept	Total
Arm/Group Description	Subjects treated with brolucizumab 3 mg or brolucizumab 6 mg in the Core study. All subjects received IVT injection at the extension Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at Week 16 or Week 20.	Subjects previously treated with aflibercept 2 mg in the Core study continued to receive aflibercept 2mg IVT injection at the extension Baseline, Week 8 and Week 16 to maintain the masking in the extension trial.	
Started	107	43	150

Completed	106	42	148
Not Completed	1	1	2
Death	1	0	1
Adverse Event	0	1	1

Baseline Characteristics

	Brolucizumab - Overall Extension Study	**Aflibercept**	**Total**
Arm/Group Description	Subjects treated with brolucizumab 3 mg or brolucizumab 6 mg in the Core study. All subjects received IVT injection at the extension Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at Week 16 or Week 20.	Subjects previously treated with aflibercept 2 mg in the Core study continued to receive aflibercept 2mg IVT injection at the extension Baseline, Week 8 and Week 16 to maintain the masking in the extension trial.	

Number of Participants [units: participants]	107	43	150
Age Continuous (units: years) Mean ± Standard Deviation			
	80.6±8.63	77.9±9.20	79.8±8.85
Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)			
Female	69	22	91
Male	38	21	59
Ethnicity (NIH/OMB) (units: participants) Count of Participants (Not Applicable)			
Hispanic or Latino	11	6	17
Not Hispanic or Latino	95	37	132
Unknown or Not Reported	1	0	1

Summary of Efficacy

Primary Outcome Result(s)

Number of Participants with Ocular and Non-Ocular Treatment Emergent Adverse Events

(Time Frame: Up to Week 24)

	Brolucizumab - Overall Extension Study	Brolucizumab Overall Last 6 months from Core study
Arm/Group Description	Subjects treated with brolucizumab	AEs with a start date on or after the

	3 mg or brolucizumab 6 mg in the Core study. All subjects received IVT injection at the extension Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at Week 16 or Week 20.	date of Core study Week 68 visit were counted
Number of Participants Analyzed [units: participants]	107	107
Number of Participants with Ocular and Non-Ocular Treatment Emergent Adverse Events (units: Participants)		
Ocular AEs	20	25
Non-Ocular AEs	51	50

Secondary Outcome Result(s)

Change of Loss in BCVA of 15 letters or more from extension Baseline at each post-baseline visit

(Time Frame: Extension Baseline, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24)

	Brolucizumab 6 mg - 3 mg in Core Study	**Brolucizumab 6 mg - 6 mg in Core Study**	**Brolucizumab - Overall**

			Extension Study
Arm/Group Description	Subjects treated with brolucizumab 3 mg in Core study and given new formulation 6 mg in Extension study. All subjects received IVT injection at the extension Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at Week 16 or Week 20.	Subjects treated with brolucizumab 6 mg in Core study and given new formulation 6 mg in Extension study. All subjects received IVT injection at the extension Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at Week 16 or Week 20.	Subjects treated with brolucizumab 3 mg or brolucizumab 6 mg in the Core study. All subjects received IVT injection at the extension Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at Week 16 or Week 20.
Number of Participants Analyzed [units: participants]	62	45	107
Change of Loss in BCVA of 15 letters or more from extension Baseline at each post-baseline visit (units: Number of Participants)			
exWeek 4 (>=15 letters loss)	2	0	2
exWeek 8 (>=15 letters loss)	4	0	4

exWeek 12 (>=15 letters loss)	4	0	4
exWeek 16 (>=15 letters loss)	6	0	6
exWeek 20 (>=15 letters loss)	4	0	4
exWeek 24 (>=15 letters loss)	3	0	3

Change in BCVA from extension Baseline at each post-baseline visit

(Time Frame: Extension baseline, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24)

	Brolucizumab 6 mg - 3 mg in Core Study	Brolucizumab 6 mg - 6 mg in Core Study	Brolucizumab - Overall Extension Study
Arm/Group Description	Subjects treated with brolucizumab 3 mg in Core study and given new formulation 6 mg in Extension study. All subjects received IVT injection at the extension Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at	Subjects treated with brolucizumab 6 mg in Core study and given new formulation 6 mg in Extension study. All subjects received IVT injection at the extension Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at	Subjects treated with brolucizumab 3 mg or brolucizumab 6 mg in the Core study. All subjects received IVT injection at the extension Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at Week 16 or Week 20.

	Week 16 or Week 20.	Week 16 or Week 20.	
Number of Participants Analyzed [units: participants]	62	45	107
Change in BCVA from extension Baseline at each post-baseline visit (units: Letter read) Mean ± Standard Deviation			
exWeek 4	-1.3 ± 6.26	0.5 ± 3.81	-0.5 ± 5.42
exWeek 8	-1.7 ± 6.90	-0.4 ± 4.29	-1.2 ± 5.96
exWeek 12	-2.7 ± 7.73	-0.3 ± 5.17	-1.7 ± 6.84
exWeek 16	-3.9 ± 8.42	0.8 ± 5.36	-1.9 ± 7.63
exWeek 20	-3.4 ± 7.66	0.5 ± 7.34	-1.8 ± 7.75
exWeek 24	-2.0 ± 8.17	0.3 ± 6.79	-1.0 ± 7.67

Patients with positive q12w treatment status at Week 20

(Time Frame: Week 20)

	Brolucizumab 6 mg - 3 mg in Core Study	**Brolucizumab 6 mg- 6 mg in Core Study**	**Brolucizumab - Overall Extension Study**
Arm/Group Description	Subjects treated with brolucizumab 3 mg in Core study and given new formulation 6 mg in Extension study. All subjects received IVT injection at the extension	Subjects treated with brolucizumab 6 mg in Core study and given new formulation 6 mg in Extension study. All subjects received IVT injection at the extension	Subjects treated with brolucizumab 3 mg or brolucizumab 6 mg in the Core study. All subjects received IVT injection at the extension Baseline, Week 8 and, depending on

	Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at Week 16 or Week 20.	Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at Week 16 or Week 20.	disease activity as assessed by the investigator, at Week 16 or Week 20.
Number of Participants Analyzed [units: participants]	62	45	107
Patients with positive q12w treatment status at Week 20 (units: Percentage of patients)			
	63.3	63.1	63.3

Change in Central Sub-Field Thickness (CSFT) from extension Baseline at each post-baseline visit

(Time Frame: Extension Baseline, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24)

	Brolucizumab 6 mg - 3 mg in Core Study	**Brolucizumab 6 mg- 6 mg in Core Study**	**Brolucizumab - Overall Extension Study**
Arm/Group Description	Subjects treated with brolucizumab 3 mg in Core study and given new formulation 6 mg in Extension study. All subjects	Subjects treated with brolucizumab 6 mg in Core study and given new formulation 6 mg in Extension study. All subjects	Subjects treated with brolucizumab 3 mg or brolucizumab 6 mg in the Core study. All subjects received IVT injection at the extension

	received IVT injection at the extension Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at Week 16 or Week 20.	received IVT injection at the extension Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at Week 16 or Week 20.	Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at Week 16 or Week 20.
Number of Participants Analyzed [units: participants]	62	45	107
Change in Central Sub-Field Thickness (CSFT) from extension Baseline at each post-baseline visit (units: micrometer) Mean ± Standard Deviation			
exWeek 4	-19.2 ± 39.29	-17.5 ± 40.76	-18.5 ± 39.74
exWeek 8	-6.3 ± 25.47	-18.9 ± 31.74	-11.6 ± 28.82
exWeek 12	-17.9 ± 43.07	-28.9 ± 48.80	-22.5 ± 45.66
exWeek 16	-7.8 ± 31.94	-11.7 ± 39.83	-9.4 ± 35.35
exWeek 20	-10.1 ± 59.04	-15.3 ± 46.20	-12.3 ± 53.84
exWeek 24	-19.8 ± 37.67	-24.6 ± 42.10	-21.8 ± 39.47

Percentage of subjects with positive Anti-drug Antibody (ADA) status for Brolucuzumab 6 mg in Extension

(Time Frame: Extension Baseline, Week 8, Week 16, Week 24)

	Brolucizumab - Overall Extension Study
Arm/Group Description	Subjects treated with

	brolucizumab 3 mg or brolucizumab 6 mg in the Core study. All subjects received IVT injection at the extension Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at Week 16 or Week 20.
Number of Participants Analyzed [units: participants]	107
Percentage of subjects with positive Anti-drug Antibody (ADA) status for Brolucuzumab 6 mg in Extension (units: Percentage of participants)	54

Summary of Safety

Safety Results

All-Cause Mortality

	Brolucizumab 6mg Overall Extension study N = 107	Brolucizumab Overall Last 6 months core study N = 107	Aflibercept 2 mg N = 43
Arm/Group Description	Subjects treated with brolucizumab 3 mg or brolucizumab 6 mg in the Core study. All subjects received IVT injection at the extension Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at Week 16 or Week 20.	AEs with a start date on or after the date of Core study Week 68 visit were counted.	Subjects previously treated with aflibercept 2 mg in the Core study continued to receive aflibercept 2mg IVT injection at the extension Baseline, Week 8 and Week 16 to maintain the masking in the extension trial.
Total participants affected	1 (0.93%)	0 (0.00%)	0 (0.00%)

Serious Adverse Events by System Organ Class

Time Frame	From first treatment in the extension study, through study completion, to an average of 24 weeks. Adverse events and serious adverse events were collected for the maximum actual duration of treatment exposure and follow up for a participant per the protocol for approximately 6 months.
Additional Description	Adverse events were recorded for AEs that started during the extension study, and AEs started during the Core study that were ongoing at ext. baseline. Safety assessment of broluizumab 6 mg was based on a within-patient comparison w/the last 6 months of corresponding Core safety data serving as reference. Adverse Events were obtained from subjects and observations by the Investigator as outlined in the study protocol. This analysis set includes all subjects who received at least 1 IVT injection.
Source Vocabulary for Table Default	MedDRA (20.1)
Assessment Type for Table Default	Systematic Assessment

	Brolucizumab 6mg Overall Extension study N = 107	**Brolucizumab Overall Last 6 months core study N = 107**	**Aflibercept 2 mg N = 43**
Arm/Group Description	Subjects treated with brolucizumab 3 mg or brolucizumab 6 mg in the Core study. All subjects received IVT injection at the extension Baseline, Week 8 and, depending on disease activity as assessed by the investigator, at	AEs with a start date on or after the date of Core study Week 68 visit were counted.	Subjects previously treated with aflibercept 2 mg in the Core study continued to receive aflibercept 2mg IVT injection at the extension Baseline, Week 8 and Week 16 to maintain the masking in the extension trial.

	Week 16 or Week 20.		
Total participants affected	7 (6.54%)	7 (6.54%)	10 (23.26%)
Blood and lymphatic system disorders			
Anaemia macrocytic	0 (0.00%)	0 (0.00%)	1 (2.33%)
Lymphadenopathy	0 (0.00%)	0 (0.00%)	1 (2.33%)
Cardiac disorders			
Cardiac failure congestive	1 (0.93%)	0 (0.00%)	0 (0.00%)
Left ventricular failure	0 (0.00%)	0 (0.00%)	1 (2.33%)
Eye disorders			
Retinal artery occlusion - Study eye	1 (0.93%)	0 (0.00%)	0 (0.00%)
Retinal vein occlusion - Study eye	1 (0.93%)	0 (0.00%)	0 (0.00%)
General disorders and administration site conditions			
Multiple organ dysfunction syndrome	1 (0.93%)	0 (0.00%)	0 (0.00%)
Pyrexia	0 (0.00%)	0 (0.00%)	1 (2.33%)
Hepatobiliary disorders			
Bile duct stone	1 (0.93%)	0 (0.00%)	0 (0.00%)
Cholecystitis acute	1 (0.93%)	0 (0.00%)	0 (0.00%)
Cholelithiasis	0 (0.00%)	0 (0.00%)	1 (2.33%)
Infections and infestations			

Influenza	0 (0.00%)	1 (0.93%)	0 (0.00%)
Necrotising fasciitis	0 (0.00%)	0 (0.00%)	1 (2.33%)
Osteomyelitis	0 (0.00%)	0 (0.00%)	1 (2.33%)
Pneumonia	1 (0.93%)	0 (0.00%)	1 (2.33%)
Sepsis	0 (0.00%)	0 (0.00%)	1 (2.33%)
Urinary tract infection	0 (0.00%)	1 (0.93%)	0 (0.00%)
Injury, poisoning and procedural complications			
Accidental overdose	0 (0.00%)	1 (0.93%)	0 (0.00%)
Femur fracture	1 (0.93%)	1 (0.93%)	0 (0.00%)
Patella fracture	0 (0.00%)	0 (0.00%)	1 (2.33%)
Pubis fracture	0 (0.00%)	1 (0.93%)	0 (0.00%)
Metabolism and nutrition disorders			
Malnutrition	0 (0.00%)	0 (0.00%)	1 (2.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer	0 (0.00%)	1 (0.93%)	0 (0.00%)
Prostate cancer metastatic	0 (0.00%)	0 (0.00%)	1 (2.33%)
Nervous system disorders			
Encephalopathy	0 (0.00%)	0 (0.00%)	1 (2.33%)
Haemorrhage intracranial	1 (0.93%)	0 (0.00%)	0 (0.00%)
Syncope	0 (0.00%)	0 (0.00%)	3 (6.98%)

Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease	0 (0.00%)	1 (0.93%)	0 (0.00%)
Pleural effusion	0 (0.00%)	0 (0.00%)	1 (2.33%)
Respiratory failure	1 (0.93%)	0 (0.00%)	0 (0.00%)
Vascular disorders			
Hypertension	1 (0.93%)	0 (0.00%)	0 (0.00%)

Other Adverse Events by System Organ Class

Time Frame	From first treatment in the extension study, through study completion, to an average of 24 weeks. Adverse events and serious adverse events were collected for the maximum actual duration of treatment exposure and follow up for a participant per the protocol for approximately 6 months.
Additional Description	Adverse events were recorded for AEs that started during the extension study, and AEs started during the Core study that were ongoing at ext. baseline. Safety assessment of broluizumab 6 mg was based on a within-patient

	comparison w/the last 6 months of corresponding Core safety data serving as reference. Adverse Events were obtained from subjects and observations by the Investigator as outlined in the study protocol. This analysis set includes all subjects who received at least 1 IVT injection.
Source Vocabulary for Table Default	MedDRA (20.1)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	Brolucizumab 6mg Overall Extension study N = 107	**Brolucizumab Overall Last 6 months core study N = 107**	**Aflibercept 2 mg N = 43**
Arm/Group Description	Subjects treated with brolucizumab 3 mg or brolucizumab 6 mg in the Core study. All subjects received IVT injection at the extension Baseline, Week 8 and, depending on disease activity as assessed by	AEs with a start date on or after the date of Core study Week 68 visit were counted.	Subjects previously treated with aflibercept 2 mg in the Core study continued to receive aflibercept 2mg IVT injection at the extension Baseline, Week 8 and Week 16 to maintain the

	the investigator, at Week 16 or Week 20.		masking in the extension trial.
Total participants affected	12 (11.21%)	14 (13.08%)	13 (30.23%)
Eye disorders			
Cataract - Fellow eye	1 (0.93%)	1 (0.93%)	3 (6.98%)
Neovascular age-related macular degeneration - Fellow eye	2 (1.87%)	2 (1.87%)	3 (6.98%)
Infections and infestations			
Nasopharyngitis	5 (4.67%)	4 (3.74%)	3 (6.98%)
Urinary tract infection	4 (3.74%)	6 (5.61%)	6 (13.95%)
Renal and urinary disorders			
Haematuria	0 (0.00%)	1 (0.93%)	3 (6.98%)

Conclusion:

Safety and efficacy with the intended commercial formulation of brolucizumab 6 mg in nAMD subjects was consistent with that observed in the phase III study CRTH258A2301 (also known as Alcon RTH258-C001).

Date of Clinical Trial Report

06 January 2019

Swiss Authorization date and authorization number

Swissmedic Approval Number: 67245

Swissmedic Approval Date 16.01.2020

Novartis Study Code

CRTH258A2301E1

EudraCT Number

Not applicable.

Planned and Actual Number of Patients

Planned – 75 to 100 subjects

Actual – 150 subjects were enrolled: 107 treated

Batch Numbers & Information on comparators drug dosage, route of administration, batch numbers

Study drug and strength	Batch numbers
Brolucizumab solution for IVT injection, 6 mg/50 µL	2020589
Aflibercept 2 mg	

Publication(s)

Not applicable.

Investigators & Information on Study Centers

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2627	Dr. Lawrence Singerman	Retina Associates of Cleveland Cleveland OH 44122 USA
3250	Dr. Alan Gordon	Associated Retina Consultants Peoria AZ 85381 USA
3943	Dr. Blake Cooper	Retina Associates PA Shawnee Mission KS USA

3947	Dr. David Brown	Vitreoretinal Consultants Houston TX USA
4046	Dr. Pravin Dugel	Retinal Consultants of Arizona Phoenix AZ 85014 USA
4070	Dr. Sunil Gupta	Retina Speciality Institute Pensacola FL USA
4075	Dr. Todd Schneiderman	Retina Center NW Silverdale WA USA
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5447	Dr. Aleksandra Rachitskaya	Cleveland Clinic Cole/Eye Institute Cleveland OH USA
5894	Dr. Joel Pearlman	Retinal Consultants Medical Group Sacramento CA USA
5897	Dr. Adam Berger	Center for Retina and Macular Disease Lakeland FL USA
6154	Dr. H. Logan Brooks	Southern Vitreoretinal Associates Tallahassee FL USA
6221	Dr. Ryan Rich	Retina Consultants of Southern Colorado Colorado Springs CO USA

6222	Dr. Mark Wieland	Northern California Retina Vitreous Associates Medical Group, Inc. Mountain View CA USA
6226	Dr. Ashish Sharma	National Ophthalmic Research Institute Ft. Myers FL USA
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6803	Dr. Mark Michels	Retina-Vitreous Association Incorporated Palm Beach Gardens FL USA
6808	Dr. Steven Rose	Retina Associates of Western New York Rochester NY USA

6855	Dr. David Kenneth Scales	Foresight Studies LLC San Antonio TX USA
6996	Dr. Jeffrey Moore	Maine Eye Center Portland ME 04101 USA
6997	Dr. Eric Guglielmo	Spokane Eye Clinic Spokane WA USA
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7031	Dr. Philip Falcone	Connecticut Retina Consultants Bridgeport CT 06606 USA

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7057	Dr. John Choi	Chesapeake Retina Centers Waldorf MD USA
7066	Dr. David DiLoreto	University of Rochester, Flaum Eye Institute Rochester NY USA
7068	Dr. William Freeman	Regents of the University of California La Jolla CA USA
7069	Dr. Mohammed Hajee	Ocean County Retina Toms River NJ 08755 USA

7070	Dr. G Robert Hampton	Retina Vitreous Surgeons Syracuse NY USA
7071	Dr. Gregory Cohen	Sierra Eye Associates Reno NV USA
7080	Dr. Juan Rubio	Retina Associates of South Texas PA San Antonio TX USA
7082	Dr. Chander Samy	Ocala Research Institute Ocala FL USA
7087	Dr. Allen Thach	Retina Consultants of Nevada Henderson NV USA
7116	Dr. Melvin Chen	Sarasota Retina Institute Research Foundation Sarasota FL USA

7124	Dr. Calvin Mein	Retinal Consultants of San Antonio San Antonio TX USA
7132	Dr. Jay Prensky	Pennsylvania Retina Specialists Camp Hill PA USA
7134	Dr. Michael Rauser	Loma Linda University Eye Institute Loma Linda CA USA
7142	Dr. Sam Mansour	Virginia Retina Center Warrenton VA USA
7146	Dr. Carl Danzig	Rand Eye Institute Deerfield Beach FL USA
7160	Dr. Haroon Chaudhry	Eye Care Associates of Cincinnati Inc DBA Apex Eye Fairfield OH USA

7204	Dr. Michael Elman	Elman Retina Group Baltimore MD USA
7207	Dr. Bryan Schwent	Retina Institute of Virginia Richmond VA USA
7287	Dr. Hani Salehi-Had	Atlantis Eye Care Huntington Beach CA USA
7290	Dr. Michael Cassell	Sabates Eye Center Research Division Leawood KS USA
7301	Dr. Santosh Patel	Retina Specialists Plano TX USA
7336	Dr. Gawain Dyer	San Antonio Eye Center San Antonio TX USA

7342	Dr. James Earl	Retina Specialists of Idaho PLLC Boise ID USA
7344	Dr. Arghavan Almony	Carolina Eye Associates PA Southern Pines NC USA
7353	Dr. John Carlson	Retina Consultants of Southern California Redlands CA USA
7354	Dr. Grant Janzen	Retina Research Institute of Texas Abilene TX USA
7355	Dr. Cecilia Sanchez	Texan Eye Austin TX USA
7358	Dr. Soraya Rofagha	East Bay Retina Consultants Oakland CA USA

7360	Dr. Everton Arrindell	Tennessee Retina PC Nashville TN USA
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7493	Dr. William Wirostko	The Eye Institute: Medical College of Wisconsin Milwaukee WI USA
7515	Dr. Evelyn Fu	Cascade Eye and Skin Centers University Place WA USA

7631	Dr. Ghassan Ghorayeb	West Virginia Eye Institute Morgantown WV US
7693	Dr. Peter Win	Win Retina Arcadia CA USA
7704	Dr. Sumit Bhatia	Gailey Eye Clinic Bloomington IL USA
7733	Dr. Sugat Patel	Midwest Retina Dublin OH USA
7737	Dr. Pamela Weber	Island Retina Shirley NY USA
7765	Dr. Kamalesh Ramaiya	Eye Associates of New Mexico Albuquerque NM 87109 USA

7778	Dr. Stephen Tate	New Vision Eye Center Vero Beach FL USA
enter No.	**Investigator**	**Facility Name** **Address** **Country**
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6808	Dr. Steven Rose	Retina Associates of Western New York Rochester NY USA
6855	Dr. David Kenneth Scales	Foresight Studies LLC San Antonio TX USA
6996	Dr. Jeffrey Moore	Maine Eye Center Portland ME 04101 USA
6997	Dr. Eric Guglielmo	Spokane Eye Clinic Spokane WA USA

6999	Dr. Samantha Xavier	Florida Eye Clinic Altamonte Springs FL USA
7020	Dr. Maria Berrocal	San Juan Health Centre Dr. Berrocal & Associate San Juan PR 00907 USA
7031	Dr. Philip Falcone	Connecticut Retina Consultants Bridgeport CT 06606 USA
7043	Dr. Joseph Khawly	Retina & Vitreous Of Texas Houston TX 77025 USA
7051	Dr. Brian Joondeph	Colorado Retina Associates Golden CO USA

7057	Dr. John Choi	Chesapeake Retina Centers Waldorf MD USA
7066	Dr. David DiLoreto	University of Rochester, Flaum Eye Institute Rochester NY USA
7068	Dr. William Freeman	Regents of the University of California La Jolla CA USA
7069	Dr. Mohammed Hajee	Ocean County Retina Toms River NJ 08755 USA
7070	Dr. G Robert Hampton	Retina Vitreous Surgeons Syracuse NY USA

7071	Dr. Gregory Cohen	Sierra Eye Associates Reno NV USA
7080	Dr. Juan Rubio	Retina Associates of South Texas PA San Antonio TX USA
7082	Dr. Chander Samy	Ocala Research Institute Ocala FL USA
7087	Dr. Allen Thach	Retina Consultants of Nevada Henderson NV USA
7116	Dr. Melvin Chen	Sarasota Retina Institute Research Foundation Sarasota FL USA

7124	Dr. Calvin Mein	Retinal Consultants of San Antonio San Antonio TX USA
7132	Dr. Jay Prensky	Pennsylvania Retina Specialists Camp Hill PA USA
7134	Dr. Michael Rauser	Loma Linda University Eye Institute Loma Linda CA USA
7142	Dr. Sam Mansour	Virginia Retina Center Warrenton VA USA
7146	Dr. Carl Danzig	Rand Eye Institute Deerfield Beach FL USA

7160	Dr. Haroon Chaudhry	Eye Care Associates of Cincinnati Inc DBA Apex Eye Fairfield OH USA
7204	Dr. Michael Elman	Elman Retina Group Baltimore MD USA
7207	Dr. Bryan Schwent	Retina Institute of Virginia Richmond VA USA
7287	Dr. Hani Salehi-Had	Atlantis Eye Care Huntington Beach CA USA
7290	Dr. Michael Cassell	Sabates Eye Center Research Division Leawood KS USA

7301	Dr. Santosh Patel	Retina Specialists Plano TX USA
7336	Dr. Gawain Dyer	San Antonio Eye Center San Antonio TX USA
7342	Dr. James Earl	Retina Specialists of Idaho PLLC Boise ID USA
7344	Dr. Arghavan Almony	Carolina Eye Associates PA Southern Pines NC USA
7353	Dr. John Carlson	Retina Consultants of Southern California Redlands CA USA

7354	Dr. Grant Janzen	Retina Research Institute of Texas Abilene TX USA
7355	Dr. Cecilia Sanchez	Texan Eye Austin TX USA
7358	Dr. Soraya Rofagha	East Bay Retina Consultants Oakland CA USA
7360	Dr. Everton Arrindell	Tennessee Retina PC Nashville TN USA
7376	Dr. Andres Emanuelli	Emanuelli Research & Development Center Arecibo PR 00612 Puerto Rico

7426	Dr. Patrick Williams PI	Texas Retina Associates Fort Worth TX USA
7493	Dr. William Wirostko	The Eye Institute: Medical College of Wisconsin Milwaukee WI USA
7515	Dr. Evelyn Fu	Cascade Eye and Skin Centers University Place WA USA
7631	Dr. Ghassan Ghorayeb	West Virginia Eye Institute Morgantown WV US
7693	Dr. Peter Win	Win Retina Arcadia CA USA

7704	Dr. Sumit Bhatia	Gailey Eye Clinic Bloomington IL USA
7733	Dr. Sugat Patel	Midwest Retina Dublin OH USA
7737	Dr. Pamela Weber	Island Retina Shirley NY USA
7765	Dr. Kamalesh Ramaiya	Eye Associates of New Mexico Albuquerque NM 87109 USA
7778	Dr. Stephen Tate	New Vision Eye Center Vero Beach FL USA