Retina Research Center (RRC) is working with Genentech on three clinical trials for wet age-related macular degeneration (AMD), dry AMD and diabetic macular edema (DME), Avenue, Chroma and Boulevard respectively.

In the Phase III Chroma study, we are assessing the safety and efficacy of repeated intravitreal injections of lampalizumab, a humanized monoclonal antibody fragment, in patients with geographic atrophy. The Phase II study, Mahalo, showed a 20.4% reduction in mean change of geographic atrophy area from baseline to month 18 in the monthly lampalizumab arm. We are optimistic that Chroma will continue to support this positive trend. Recruitment is expected to close this summer and RRC is one of the top 7 enrollers in the world with 15 patients randomized to date.

In the Phase II Avenue study, we are investigating the safety and efficacy of RG7716 compared to Lucentis in treatment naïve wet AMD patients. RG7716 is a bispecific monoclonal antibody that targets vascular endothelial growth factor (VEGF) and angiopoietin-2 (Ang-2). RRC is one of the top 3 enrollers in the country with 10 patients.

The Phase II Boulevard study is also evaluating the safety and efficacy of RG7716, but in treatment naïve DME patients. 150 patients will be randomized in a 1:1:1 ratio to monthly injections of 1.5 mg or 6mg RG7716 versus Lucentis. Enrollment in the Boulevard study recently commenced with only a few patients enrolled to date; RRC enrolled their first patient on June 28, 2016.

Main inclusion criteria include:

- treatment naïve DME with central subfield thickness ≥ 350µm on Heidelberg OCT
- best-corrected visual acuity 20/40-20/320 in the study eye

To refer a potential patient, please contact Ivana Gunderson at 512-279-1251 or igunderson@e-retina.net

Meet the new Diabetic Retinopathy Clinical Research (DRCR) Network Vice-Chair

DRCR is a collaborative network funded by the National Eye Institute (NEI) that facilitates multi-center clinical trials in diabetic retinopathy. The network was formed in 2002 and has over 115 participating sites and 400 physicians in the US. RRC is site number 13 and has been a part of the DRCR network for over a decade enrolling 267 patients in 17 different clinical trials.

In January 2016, Dr. Chirag Jhaveri was designated the new vice chair of the DRCR network. Dr. Jhaveri joined RRC in September 2012 and has participated in over 30 clinical trials as a sub-investigator and 10 as principal investigator at RRC to date. We would like to congratulate him on his position at the DRCR network and we look forward to his continuing contributions to clinical research.
Retina Research Center hosted a cruise on the Jamal Yacht during this year’s annual Association for Research in Vision and Ophthalmology (ARVO) meeting in Seattle, Washington. The cruise took place on Lake Union and Lake Washington on Saturday, April 30, 2016. Our guests included physicians around the country and various study team members from our many research partners including Ora, Novartis, Trial Runners, Allergan, Castle Biosciences, Iconic Therapeutics, Ohr Pharmaceutical, Panoptica, Pfizer, Regeneron, Retina Today, Optos, Acucela and Janssen.

ARVO Poster Presentations by Dr. Berger and Dr. Jhaveri


2. Jhaveri, C: The Effect of Brolucizumab Applied by Microvolume Injection or Infusion in Patients with Neovascular Age-Related Macular Degeneration. Association for Research in Vision and Ophthalmology Annual Meeting, Seattle, WA May 2016. - Dr. Jhaveri
**Enrolling Trials**

### Wet Age-Related Macular Degeneration

**Genentech BP29647 AVENUE** – A Phase II study evaluating the safety, tolerability, pharmacokinetics and efficacy of RO6867461 compared to Lucentis in subjects with wet ARMD

**Daiichi Sankyo Pharma DS7080-A-U101** - A Phase I, dose escalation and expansion study of DS-7080a in subjects with neovascular ARMD

**Tyrogenex, Inc. X-82-OPH-201** - A Phase Ib study of oral X-82 plus PRN Eylea compared to PRN Eylea monotherapy in subjects with neovascular ARMD

**Regeneron R910-3-AMD-1517 ONYX** - A Phase II, randomized, double-masked, active controlled, study of the efficacy, safety and tolerability of repeated doses of intravitreal REGN910-3 in patients with neovascular ARMD

**Santen Inc. 36-001 PAVE** - A Phase I/II, open-label, dose escalating, sequential-cohort study assessing the safety, tolerability, immunogenicity and bioactivity of a single intravitreal injection of DE-122 in refractory wet ARMD patients

### Dry Age-Related Macular Degeneration

**Genentech Chroma** - A Phase III study evaluating the efficacy and safety of Lampalizumab administered intravitreally to patients with geographic atrophy secondary to ARMD

**Novartis CCLG561-2201** - A proof-of-concept study of intravitreal CLG561 as a monotherapy or in combination with LFG316 in subjects with geographic atrophy secondary to ARMD

### Uveitis

**Aciont, Inc. DSPV-201** - A randomized, parallel group, double-masked, active-controlled Phase I/II clinical trial to evaluate the efficacy and safety of dexamethasone sodium phosphate Visulex system for the treatment of non-infectious anterior uveitis

### Diabetic Macular Edema


**DRCR Protocol V** - A study to compare the safety and efficacy of (1) prompt focal/grid photocoagulation + intravitreal Eylea, (2) observation + deferred intravitreal Eylea, and (3) prompt intravitreal Eylea in eyes with central-involved diabetic macular edema and good visual acuity.

**Genentech BP30099 BOULEVARD** – A multi-center, multi-dose, randomized, active comparator-controlled, double-masked 28 week study to investigate the safety, tolerability, pharmacokinetics and efficacy of RO6867461 administered intravitreally ion patients with DME.

### Non-proliferative Diabetic Retinopathy

**DRCR Protocol W** - Intravitreous Anti-VEGF Treatment for Prevention of Vision Threatening Diabetic Retinopathy in Eyes at High Risk

### Upcoming Presentations

Berger, BB. Intravitreal ICON-1 in Patients With Choroidal Neovascularization (CNV) Secondary to Age-related Macular Degeneration (AMD): A Phase 2 Study EMERGE. 49th Annual Retina Society Meeting, September 2016, San Diego, CA.
RESEARCH DINNERS

On April 5, 2016 RRC hosted a recruitment dinner for the Genentech Avenue and Boulevard clinical trials for wet AMD and DME respectively at Estancia Churrascaria in Austin, TX. Mila Malhotra, a medical scientific liaison from Genentech, presented the protocol.

July 19, 2016 RRC will host a recruitment dinner for ophthalmologists for the Regeneron ONYX clinical trial which is evaluating a new therapy for treatment naïve wet AMD. The dinner will take place at Eddie V’s Prime Seafood Restaurant at the Arboretum in Austin, TX. Bethany Beazley, PhD, a medical scientific liaison from Regeneron will present the protocol and Phase I experience with the study drug.

If you are interested in attending this dinner, please e-mail Ivana Gunderson at igunderson@e-retina.net

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Phase I wet AMD Clinical Trials

Santen Inc. DE-122—PAVE study

RRC is working with Santen Inc. to evaluate the safety and efficacy of a single intravitreal injection of DE-122 in refractory wet AMD patients in the PAVE study. DE-122 is an anti-endoglin antibody and is being investigated as monotherapy or adjunctive therapy to anti-VEGF in wet AMD patients.

The PAVE study is a Phase I/II open-label, dose-escalating study designed to enroll a total of 12 patients at 4 sites. The patients will be treated with a single intravitreal injection of DE-122 administered in 4 sequential, dose-escalating cohorts:
- 0.5mg DE-122 (3 patients)
- 1.0mg DE-122 (3 patients)
- 2.0mg DE-122 (3 patients)
- 4.0mg DE-122 (3 patients)

Safety will be assessed after the 1st patient reaches Day 8 in each dosing arm before the next 2 patients are treated. The same process will be followed for each subsequent dosing arm.

To date, two patients have been dosed in the 0.5mg dosing arm and RRC has a patients scheduled to screen in July.

Daiichi Sankyo DS7080-A-U101 study

Daiichi Sankyo is a Japanese company investigating a new drug, DS7080, in wet AMD patients. DS7080 is a agonistic monoclonal antibody against roundabout receptor 4 (ROBO4), which is expressed in endothelial cells and regulates angiogenesis. This Phase I study is being conducted in two parts, a dose escalation and a dose expansion phase. RRC was the highest enrollee in the dose escalation phase with 3 out of 9 patients. All three doses, 1.0mg, 2.0mg and 4.0mg, evaluated in the first phase of the study were well tolerated.

The dose expansion phase opened enrollment on June 13, 2016 and is designed to enroll 27 patients in the following treatment arms:
- 4.0mg DS7080 (9 patients)
- 0.5mg Lucentis (9 patients)
- 4.0mg DS7080 + 0.5mg Lucentis (9 patients)

All treatment arms will receive 3 monthly treatments per their dosing assignment.

RRC enrolled their first patient in the dose expansion phase on June 27, 2016.

Main inclusion criteria
- BCVA 20/32-20/320
- Active CNV with CSFT >315μm on Heidleberg

Phase I wet AMD Clinical Trials

Main inclusion criteria
- BCVA 20/32-20/320
- Active CNV with CSFT >315μm on Heidleberg