On July 25, 2018, Genentech announced positive topline results from their Phase II study, Ladder, evaluating the safety and efficacy of a port delivery system (PDS) in patients with neovascular AMD. The PDS is a small device that is surgically implanted into the eye and filled with a special formulation of ranibizumab to deliver continuous drug to the retina.

The Ladder study enrolled 243 participants across 50 US sites that were randomized to one of three PDS implant arms filled with different concentrations of ranibizumab, 10mg/ml, 40mg/ml or 100mg/ml, compared to monthly intravitreal injections of FDA approved 0.5mg Lucentis. Patients randomized to the PDS arms underwent a minor surgical procedure to implant the PDS into the eye and the PDS was loaded with one of three concentrations of ranibizumab at time of surgery. The patients were then followed monthly and the PDS was refilled if specific refill criteria were met. The PDS refill is an in-office procedure using a proprietary, custom needle. Retina Research Center enrolled 6 patients in the Ladder study.

The primary objective of the Ladder study was time to first refill of the PDS. The majority of the patients in all three PDS arms were able to go six or more months without a refill: 80% in the 100mg/ml, 71.3% in the 40mg/ml and 63.5% in the 10mg/ml arm. Secondary endpoints evaluated best-corrected visual acuity (BCVA) and central subfield thickness on OCT and both were comparable to monthly intravitreal Lucentis injections in the PDS 100mg/ml arm.

This is the first sustained-delivery intraocular implant shown to provide prolonged treatment with a comparable efficacy and safety profile to monthly intravitreal injections. The PDS has the potential to change the way we treat wet AMD and RRC is excited to announce that we will participate in the PDS Phase III program. Enrollment expected to start in early September 2018.

For additional information, please contact Ivana Gunderson at igunderson@e-retina.net
STUDY RESULTS

Genentech Boulevard

Retina Research Center collaborated with Genentech on a Phase II clinical trial, Boulevard, evaluating RG7716, an anti-VEGF/anti-angiopoietin-2 bispecific antibody for treatment of diabetic macular edema. RG7716 is the first bispecific antibody in treatment of retinal disease designed as a single molecule that binds both vascular endothelial growth factor A (VEGF-A) and angiopoietin-2 (Ang2). The molecule also has a modified Fc region for faster clearance.

Study summary:
- 229 participants
- RRC was the 2nd highest enroller with 12 patients
- Randomization: RG7716 1.5mg, RG7716 6.0mg or 0.3mg Lucentis
- Monthly treatment for 20 weeks with a 16 week follow-up
- The study met its primary endpoint with a significant improvement in BCVA in the RG7716 group compared to Lucentis at week 24. Letters gained in all groups:
  - 6mg RG7716: 13.9 letters
  - 1.5mg RG7716: 11.7 letters
  - Lucentis 0.3mg: 10.3 letters
- Secondary endpoints evaluated anatomical changes:
  - Both RG7716 arms achieved greater reduction in central retinal thickness and a 2 step improvement in diabetic retinopathy severity
  - No new safety signals were observed with RG7716

Phase III study starting September 2018 at RRC

Regeneron Panorama

Regeneron’s Phase III study, Panorama, met its 24 week primary endpoint with 58% of the patients in the Eylea group achieving a two step or greater improvement on the Diabetic Retinopathy Severity Scale (DRSS), compared to 6% in the sham arm. This is the first trial designed and proven to show that diabetic retinopathy progression can be reversed in patients with moderate to severe non-proliferative diabetic retinopathy without macular edema. RRC is participating in this ongoing clinical trial and has two patients enrolled.

DRY AGE-RELATED MACULAR DEGENERATION

If you have dry AMD patients with geographic atrophy that are interested in clinical trials, please contact Ivana Gunderson at igunderson@e-retina.net for more information. Enrollment starts soon.

Apellis Pharmaceuticals Derby & Oaks

Apellis Pharmaceuticals is starting a Phase III program evaluating APL-2 in patients with geographic atrophy secondary to AMD in two identical clinical trials, Derby and Oaks. APL-2 is PEGylated cyclic inhibitor of complement C3, administered as an intravitreal injection. Their Phase II study, Filly, met its primary endpoint demonstrating a 29% reduction in the rate of GA growth compared to sham in the monthly arm and 20% reduction in the every other month treatment arm. Retina Research Center enrolled 4 patients in Filly and will participate in the Derby study. Enrollment is expected to start by September. Main criteria include visual acuity of 20/320 or better and presence of GA on fundus autofluorescence.
## Enrolling Trials

Retina Research Center is currently participating in 21 Phase I-IV clinical trials, 10 of which are currently enrolling.

### Wet Age-Related Macular Degeneration

**Santen 36-002 Avante:** A Multi-Center, Randomized, Double Masked and Active Controlled Phase II Study Assessing the Efficacy and Safety of Intravitreal Injections of DE-122 in Combination with Lucentis Compared to Lucentis Monotherapy in Subjects with Wet Age-related Macular Degeneration

**Iconic IT-004:** A Phase 2 Randomized, Open-Label, Multicenter Study Evaluating Administration of Repeated Intravitreal Doses of ICON-1 in Patients with Choroidal Neovascularization Secondary to Age-related Macular Degeneration

### Non-proliferative Diabetic Retinopathy

**Boehringer-Ingelheim Protocol 1386.12 ROBIN** - A Phase IIa study evaluating safety and efficacy of oral BI 1467335 in patients with moderate to severe diabetic retinopathy

### Diabetic Macular Edema

**Novartis Kestrel:** A Phase III evaluating the efficacy of brolucizumab compared to Eylea in patients with diabetic macular edema.

**Kalvista KVD001-201:** A Phase 2 study to assess safety and efficacy of intravitreal plasma kallikrein inhibitor, KVD001, in patients with center-involved DME who have had prior anti-VEGF treatment

**Thrombogenics THR-149-001:** A Phase I, dose-escalation study to evaluate the safety of single intravitreal injection of THR-149 for treatment of DME

**DRCR AC:** A randomized trial comparing intravitreal Eylea versus intravitreal Avastin and deferred Eylea for treatment of center-involved DME

### Retinal Vein Occlusions

**Clearside Biomedical TOPAZ:** A Phase III study to evaluate the safety and efficacy of suprachoroidal CLS-TA in combination with intravitreal anti-VEGF in patients with retinal vein occlusion

### Macular Telangiectasia

**Mactel NHOR:** A natural history observation and registry study of Macular Telangiectasia Type II

**Neurotech NTMT-03-B Renexus:** A Phase 3 Multicenter, Randomized, Sham-Controlled Study to Determine the Safety and Efficacy of Renexus in Macular Telangiectasia Type 2

## Publications

8. Jonna G, Daniels AB. Enhanced Depth Imaging Optical Coherence Tomography of Ultrasonographically Flat Choroidal Nevi Demonstrates 5 Distinct Imaging Patterns. Submitted to *Ophthalmology Retina*
On July 10, 2018 RRC hosted a recruitment dinner for the Clearside TOPAZ study at Estancia Churrascaria in Austin, TX. The TOPAZ study is evaluating the safety and efficacy of suprachoridal CLS-TA in combination with intravitreal anti-VEGF in patients with retinal vein occlusion. If you would like to be included in our future dinner meetings, please email Ivana Gunderson at igunderson@e-retina.net.

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If you or your foundation are interested in making a tax-deductible contribution, please visit our website at www.retinaconsultantsofaustin.com or click HERE.

RESEARCH DINNERS
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Teaching and education are an important part of RRC. Our staff doctors, Dr. Berger, Dr. Jhaveri and Dr. Chexal are directly involved with Dell Medical School, Texas A&M College of Medicine, University of Texas Medical Branch at Galveston and the Health Careers Mentorship Program at the University of Texas at Austin. Our physicians devote their valuable time to train and educate current and future medical students in the latest advances in the field of ophthalmology.

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