

## Stem Cell Research for patients with geographic atrophy secondary to dry age-related macular degeneration



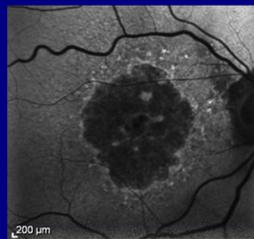
Retina Research Center (RRC) is collaborating with StemCells Inc. on a Phase II clinical trial, Radiant, to evaluate the safety and efficacy of human central nervous system stem cells (HuCNS-SC) for treatment of geographic atrophy secondary to dry age-related macular degeneration (ARMD). The Phase I/II trial was a small open-label study in which 15 patients were enrolled and treated. The results of this study display a strong safety profile of the cells and favorable trends in efficacy measures. The objective of the Radiant study is to demonstrate a reduction in the growth rate of geographic atrophy and therefore, disease progression in the study eye compared to the control eye, the fellow eye.

RRC is the exclusive central Texas site currently enrolling patients into this Phase II cutting-edge clinical trial. The study is planning to enroll 63 participants with bilateral geographic atrophy that will receive a single injection of HuCNS-SC. The HuCNS-SC will be transplanted to the sub-retinal space in an out-patient procedure performed by our vitreoretinal surgeons. The procedure will be performed at a local surgical facility, Oakwood Surgery Center, located in Round Rock, TX. The patients will be followed monthly for 12 months after the procedure to assess safety, anatomic and functional changes. RRC screened their first patient on September 28, 2015.

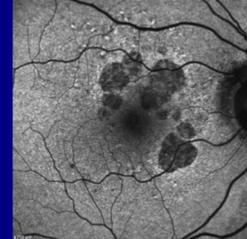
### Basic Inclusion Criteria:

- Male or female age 50-90
- Geography atrophy in both eyes  $\geq 2.5\text{mm}^2$  and  $\leq 17.5\text{mm}^2$
- BCVA 20/320 both eyes

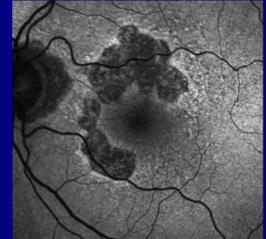
### Examples of eligible patients based on size of geographic atrophy



9.573 mm<sup>2</sup>



3.88 mm<sup>2</sup>



8.93 mm<sup>2</sup>

To refer a potential patient, please contact Ivana Gunderson at 512-279-1251 or [igunderson@e-retina.net](mailto:igunderson@e-retina.net)

### Diabetic Retinopathy Clinical Research (DRCR) Network Summer Meeting Results

#### **Protocol T** - A Comparative Effectiveness Study of Intravitreal Eylea, Avastin and Lucentis for DME

- 2 year results will be presented at American Academy of Ophthalmology in November 2015 in Las Vegas. Dr. Jhaveri is on the writing committee for the year 2 results.
- 1 year results: For patients with 20/40 or better vision, Eylea, Avastin and Lucentis were equally effective. For patients with vision 20/50 or worse, Eylea was more effective at improving vision.

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

- Dr. Jhaveri is on the protocol development committee that wrote this protocol
- Protocol expected to begin enrollment by November 2015

#### **Protocol S** - Prompt Panretinal Photocoagulation (PRP) vs. Intravitreal Lucentis with Deferred PRP for PDR

- Protocol S 1 year results will be published in Journal of the American Medical Association
- Dr. Berger is on the writing committee for the 1 year results

## Evaluating a novel compound, Brolucizumab, in treatment of wet AMD



Retina Research Center (RRC) is working with Alcon Research Ltd. on a Phase III clinical trial, HAWK, to evaluate the safety and efficacy of Brolucizumab compared to Eylea in treatment naïve wet AMD patients. Brolucizumab is a humanized single-chain antibody fragment inhibitor of VEGF. Brolucizumab has smaller molecular size than Eylea or Lucentis; 26 kDa versus 97 kDa and 46 kDa for Eylea and Lucentis respectively. Smaller molecular size allows for a higher drug concentration to be administered, which could potentially lead to a longer treatment effect and therefore reduce the treatment frequency and burden for the patient. RRC evaluated Brolucizumab, formerly known as ESBA1008, in the OWL study. This study evaluated the safety and efficacy of ESBA1008 injected as a microvolume infusion or injection versus Lucentis. RRC was the highest enrolling site and Dr. Berger presented the results of this study at two different venues (see below).

The Phase II study, Osprey, met its primary endpoint, change in best-corrected visual acuity (BCVA) from baseline to week 12, by showing visual acuity gains non-inferior to Eylea. The Phase II results continue to support a good safety profile of Brolucizumab even at the highest dose. RRC is currently enrolling patients in the Phase III, HAWK study, evaluating the safety and efficacy of two different doses of Brolucizumab, 3mg and 6mg, versus Eylea (1:1:1) in treatment naïve wet AMD patients. The HAWK study will enroll 1700 patients over 50 countries. The primary endpoint is change in BCVA from baseline to week 48. RRC is also evaluating the pharmacokinetics of Brolucizumab in an exclusive sub-study, SHRIKE, that is being conducted at 2 sites in the US and in 4 in Japan. RRC is very excited to be a part of the development of this novel compound.



### Results from the Brolucizumab OWL study and MicroPump Study were presented by Dr. Berger at ARVO and Retina Society

1. Efficacy of RTH258 (ESBA1008), an Anti-VEGF Agent, Applied by Microvolume Injection or Infusion I Subjects With Neovascular AMD. Association for Research in Vision and Ophthalmology Annual Meeting, Denver, CO, May 2015.
2. Microvolume Drug Delivery: A Novel Therapeutic Strategy For Patients With Neovascular AMD. Retina Society in Paris, France, October 2015.

## Genentech Avenue

RRC is currently enrolling patients in Avenue, a Phase II study evaluating the safety and efficacy of RO6867461 in patients with treatment naïve wet AMD. RO6867461 is a humanized bispecific monoclonal antibody that selectively binds VEGF and Ang-2.

In the Phase I study, BP28936, single and multiple doses of RO6867461 were administered and well tolerated up to the highest dose; the Phase I study results have not been published yet.

The Avenue study is a 36 week long study expecting to enroll 271 patients that will be randomized to 1 of the 5 treatment arms below. Retina Research Center is planning to host a recruitment dinner for this study in the near future.

### Basic Inclusion Criteria

- Age  $\geq$  50
- BCVA 20/50-20/320 in the study eye
- Treatment naïve subfoveal CNV

### Treatment Arms 3:2:2:2:3

- 0.5mg Lucentis q4weeks
- 1.5mg RO6867461 q4weeks
- 6mg RO6867461 q4weeks
- 6mg RO6867461 q4weeks up to week 12 followed by 6mg RO6867461 q 8 weeks
- 0.5mg Lucentis q4weeks up to week 8 followed by 6mg RO6867461 q4weeks

# Enrolling Trials

## **Wet Age-Related Macular Degeneration**

**Alcon RTH258-C001-** A Phase III study comparing the efficacy and safety of RTH258 versus Aflibercept in subjects with neovascular ARMD

**Iconic Therapeutics IT-002-** A Phase II study evaluating administration of repeated intravitreal doses of hI-con1™ in patients with choroidal neovascularization secondary to ARMD

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

**Panoptica PAN-01-101** - A Phase I study evaluating the safety and tolerability of topical ocular PAN-90806 in patients with neovascular ARMD

**Alcon LMG324-2201-** A Phase I/II study evaluating the safety, tolerability and efficacy of intravitreal LMG324 in subjects with neovascular ARMD

**Alcon RTH258-E003** - A Phase II evaluating the safety and pharmacokinetic study evaluating 3 intravitreal injections of RTH258 in subjects with neovascular 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 IIb study of oral X-82 plus PRN Eylea compared to PRN Eylea monotherapy in subjects with neovascular ARMD

## **Dry Age-Related Macular Degeneration**

**StemCells Inc. RADIANT** - A Phase II, proof-of-concept study of the safety and efficacy of human CNS stem cell subretinal transplantation in subjects with geographic atrophy secondary to ARMD

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

**University of Virginia TOGA (Treatment with Oracea for Geographic Atrophy)** - A Phase III study evaluating the efficacy of ORACEA®, a tetracycline derivative compared to placebo geographic atrophy in patients with dry ARMD.

**Apellis Pharmaceuticals Inc. FILLY** - A Phase II study evaluating safety, tolerability and evidence of activity of intravitreal APL-2 therapy in subjects 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

## **Central Retina Vein Occlusion**

**SCORE 2**—A study comparing intravitreal Avastin q4weeks with intravitreal Eylea q4weeks in eyes with macular edema secondary to central retinal vein occlusion.

## **Uveitis**

**Aciont, Inc. DSPV-201** - A randomized, parallel group, double-masked, active-controlled Phase 1/2 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 U** - A short-term evaluation of combination corticosteroid + Anti-VEGF treatment for persistent diabetic macular edema following Anti-VEGF therapy in pseudophakic eyes.

**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.

**Astellas VIDI Protocol 8232-CL-3001** - A Phase II study the efficacy and safety of oral ASP8232 alone or in combination with Lucentis on patients with Diabetic Macular Edema

**Allegro Ophthalmics, LLC Protocol DME 202B** - A Phase II study evaluating safety and exploratory efficacy of Luminite (ALG-1001) compared to Avastin and focal laser in treatment of Diabetic Macular Edema

## **Non-proliferative Diabetic Retinopathy**

**DRCR Protocol AA** - A study evaluating peripheral diabetic retinopathy lesions on ultrawide-field fundus images and risk of diabetic retinopathy worsening over time.

## Retina Research Center Staff Update

RRC would like to welcome our two new clinical research coordinators, Kimberly Hosein, BS and Tina Seidu, BA, MHS



Kimberly joined Retina Research Center as a clinical research coordinator in April 2015. She earned her Bachelor of Science degree from the University of Texas at Austin in 2012. Kim worked as ophthalmic technician and Dr. Jhaveri's assistant at Retina Consultants of Austin from August 2013 until she transitioned to her coordinator role at RRC. Kim is currently coordinating trials for various retinal diseases including macular degeneration, diabetic macular edema, vein occlusion and uveitis.

Tina earned her Bachelor of Arts degree in Public Health Studies with departmental honors from Johns Hopkins University in May 2014. She then completed her Master of Health Science degree in Biochemistry and Molecular Biology, with a Certificate in Population and Health at Johns Hopkins Bloomberg School of Public Health in May 2015. Tina endeavors to go to medical school with hopes of having a lifelong career of merging science and medicine in research, providing holistic care, and aiding in the upliftment of women and children. Tina is the lead coordinator on our DRCR network trials and BCVA examiner on all other enrolling studies.



### Institute for Retina Research

If you or your foundation are interested in making a tax-deductible contribution, please visit our website at [www.e-retina.net](http://www.e-retina.net) or click [HERE](#).

**Brian Berger, MD** has been selected as one of the instructors of the November 17, 2015 AAO course in Las Vegas:

*Course # 693: Update on Treatments for Diabetic Retinopathy Clinically Relevant Results From the Diabetic Retinopathy Clinical Research.*

### RESEARCH DINNERS

On May 28, 2015 RRC sponsored a recruitment dinner for the Genentech Chroma clinical trial for dry AMD at Ruth's Chris Steakhouse in San Antonio, TX. Saradha Chexal, MD presented the protocol and RRC has enrolled 10 patients in this study.

October 27, 2015 RRC will host a recruitment dinner for the Tyrogenex APEX clinical trial evaluating an oral agent, X-82 in conjunction with Eylea vs. Eylea alone in patients with wet AMD. The dinner will take place at Fleming's Steakhouse & Wine Bar at the Domain in Austin, TX. Dr. O'Shaughnessy from Tyrogenex will present the Phase I data and the study design for the currently enrolling Phase II Apex study. If you are interested in attending this dinner, please e-mail Ivana Gunderson at [igunderson@e-retina.net](mailto:igunderson@e-retina.net)

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