

# ***REGENERON***

## **Investor Day** **VEGF Trap–Eye**

**July 15, 2010**

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**Clinical Sciences, Ophthalmology**

## Safe Harbor Statement

Except for historical information, the matters contained in this presentation may constitute forward-looking statements that involve risks and uncertainties, including uncertainties related to product development and clinical trials, unforeseen safety issues resulting from the administration of products in patients, uncertainties related to the need for regulatory and other government approvals, risks related to third party patents and proprietary technology, the need for additional capital, uncertainty of market acceptance of Regeneron's product candidates, the receipt of future payments, the continuation of business partnerships, and additional risks detailed from time to time in Regeneron's filings with the Securities and Exchange Commission (SEC). Please refer to Regeneron's recent Forms 10-K, 10-Q, and 8-K for additional information on the uncertainties and risk factors related to our business.

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# Wet Age-Related Macular Degeneration (AMD)

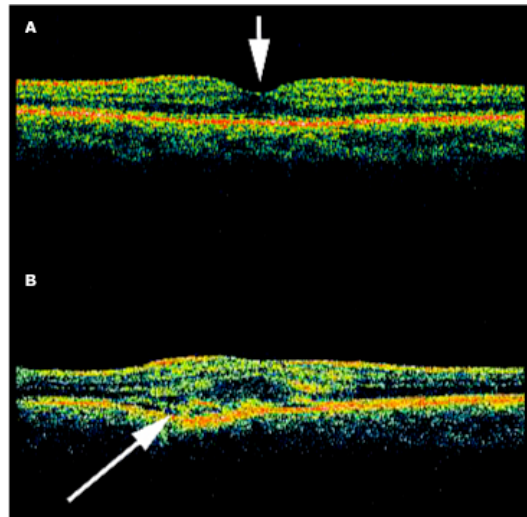
## *The Leading Cause of Blindness in the U.S. and EU*



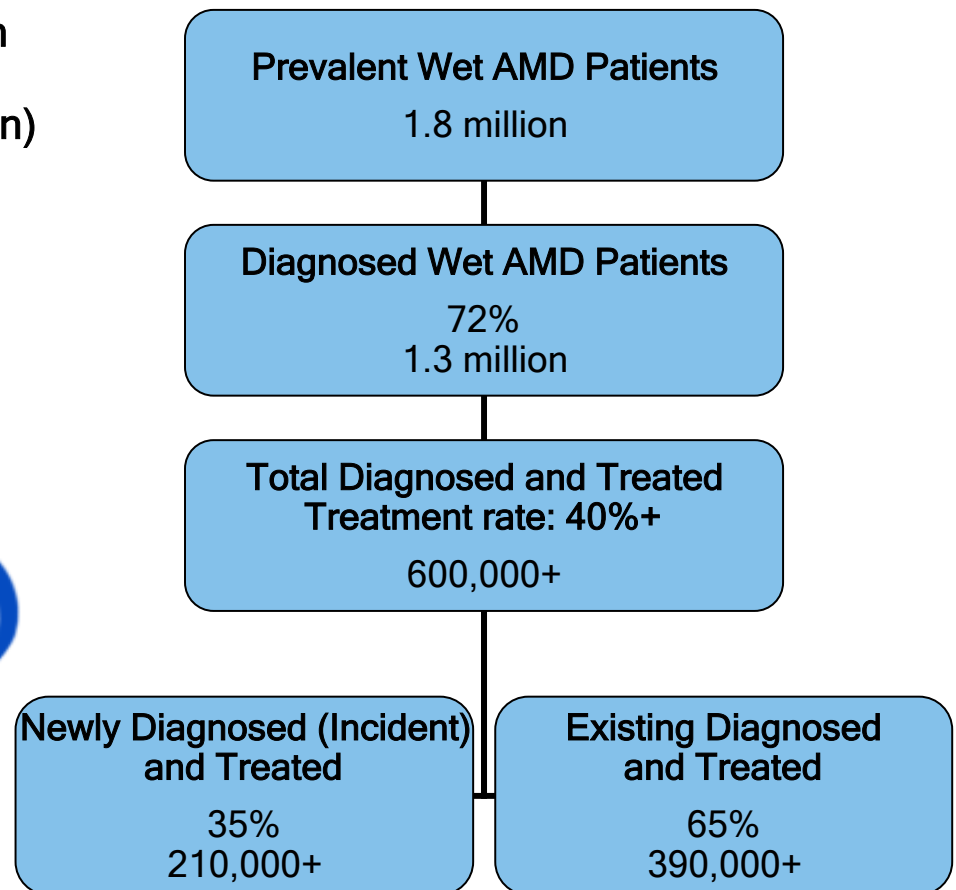
Abnormal blood vessel formation  
(choroidal neovascularization)

↓  
Increased  
retinal thickness

↓  
Decreased  
visual acuity

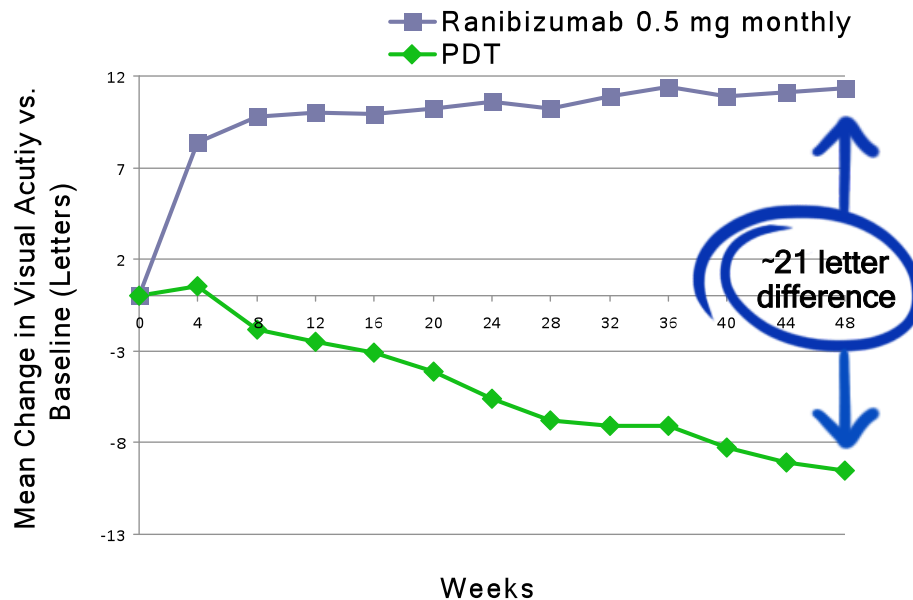


### U.S. Epidemiology

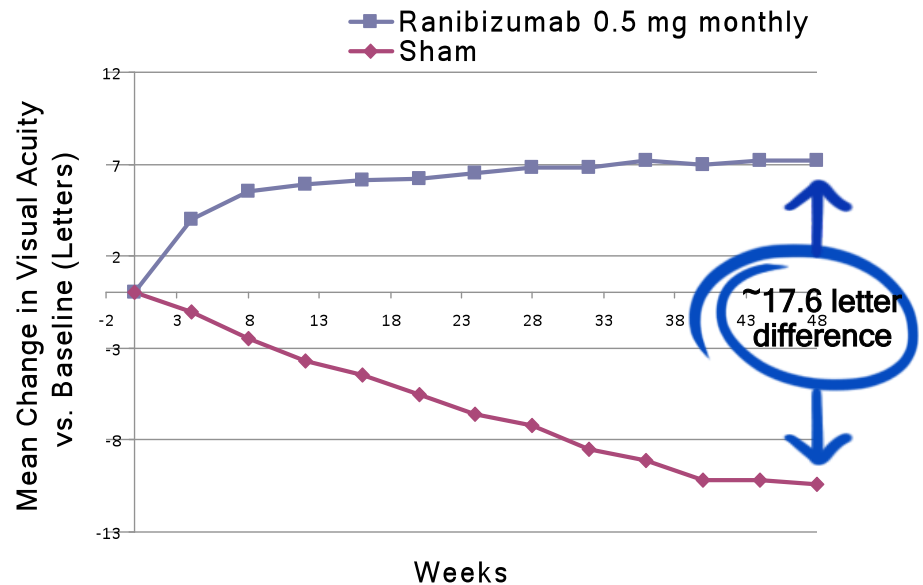


# Anti-VEGF Therapy Revolutionized Wet AMD Treatment *Not Only Slows Progression, but Can Reverse Vision Loss*

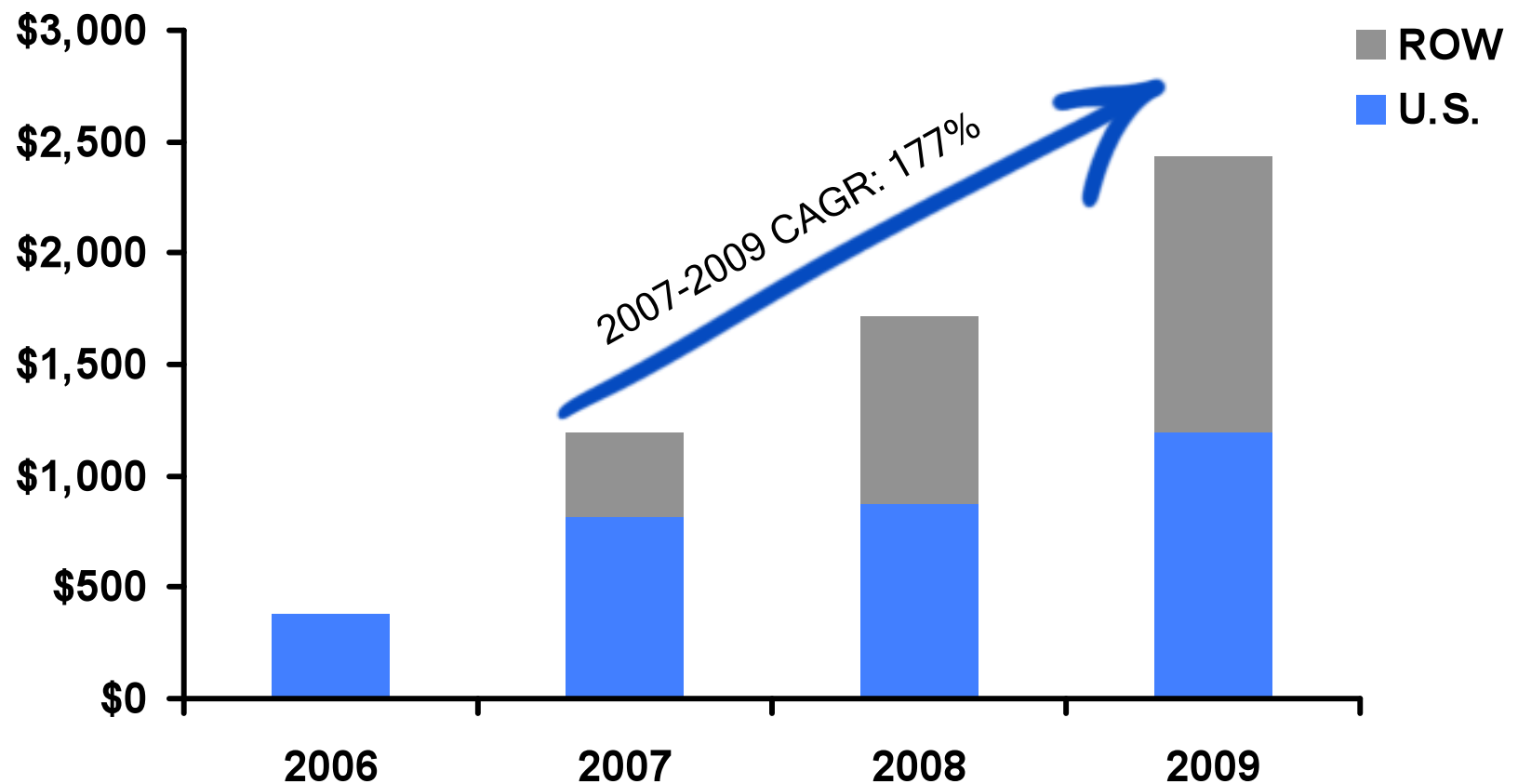
ANCHOR Study of Ranibizumab  
in Classic/Predominantly Classic Wet AMD



MARINA Study of Ranibizumab  
in Occult/Minimally Classic Wet AMD

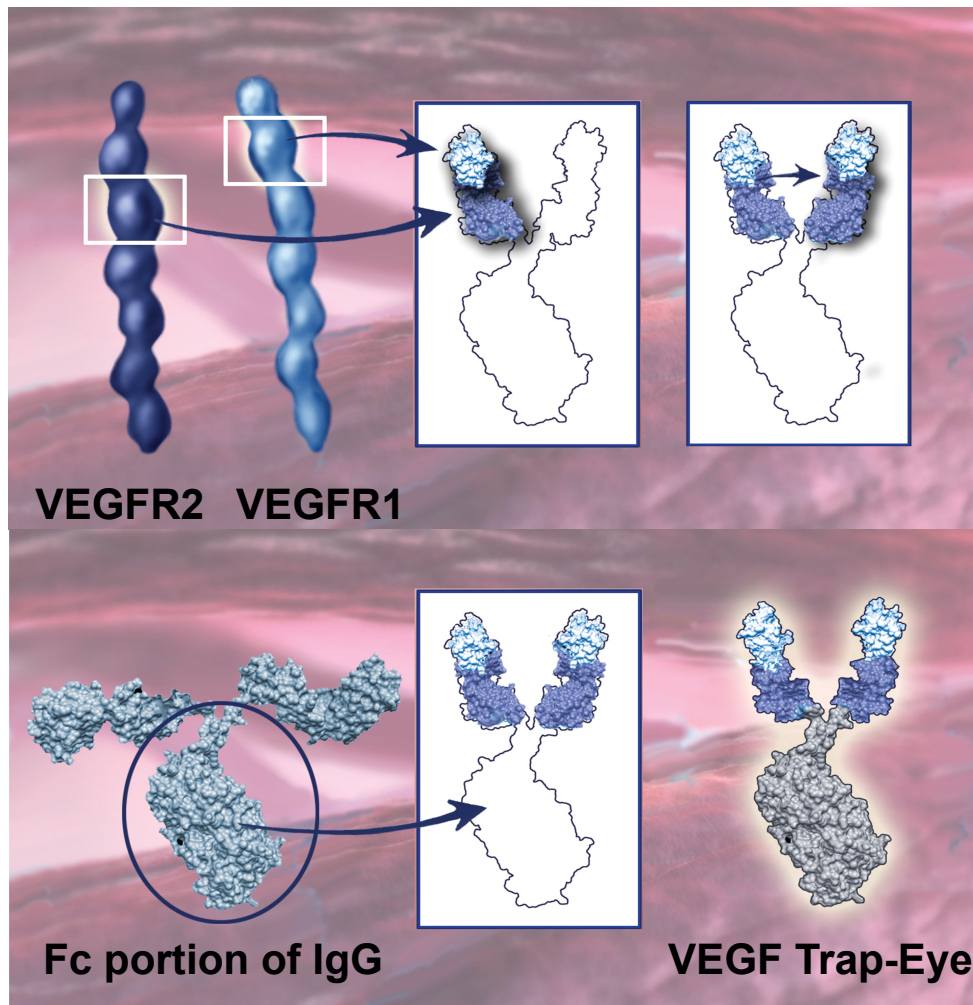


## Ranibizumab Annual Global Sales Likely to Exceed \$2.5B Despite 60% Patient Share for Bevacizumab in U.S.



# VEGF Trap-Eye

## *Regeneron's Novel Anti-VEGF Compound For Eye Disease*



IgG = immunoglobulin G

- ▶ Fusion protein of key domains from human VEGF receptors 1 and 2 with human IgG Fc
- ▶ Blocks all VEGF-A isoforms and placental growth factor (PlGF)
- ▶ High affinity – binds VEGF-A and PlGF more tightly than native receptors
- ▶ Contains all human amino acid sequences
- ▶ Penetrates all layers of the retina
- ▶ VEGF Trap-Eye is specially purified and formulated for intravitreal injection

# VEGF Trap-Eye Phase 3 Program in Wet AMD Fully Enrolled *Head-to-Head Against Lucentis® (ranibizumab)*



Two identical  
(N.A. and. ex-N.A.  
multicenter,  
active-controlled,  
double-masked  
trial  
N=1200/trial  
1:1:1:1  
randomization

Randomize



VEGF Trap-Eye  
0.5mg q4 wks



VEGF Trap-Eye  
2mg q4 wks



VEGF Trap-Eye  
2mg q8 wks  
(following 3 monthly doses)



Ranibizumab  
0.5mg q4 wks



Primary Endpoint:  
Non-inferiority vs.  
ranibizumab for the  
proportion of patients  
maintaining vision  
at 52 weeks

# VEGF Trap-Eye in Wet AMD

*Potential for Differentiation Relative to Ranibizumab 0.5 mg Monthly*

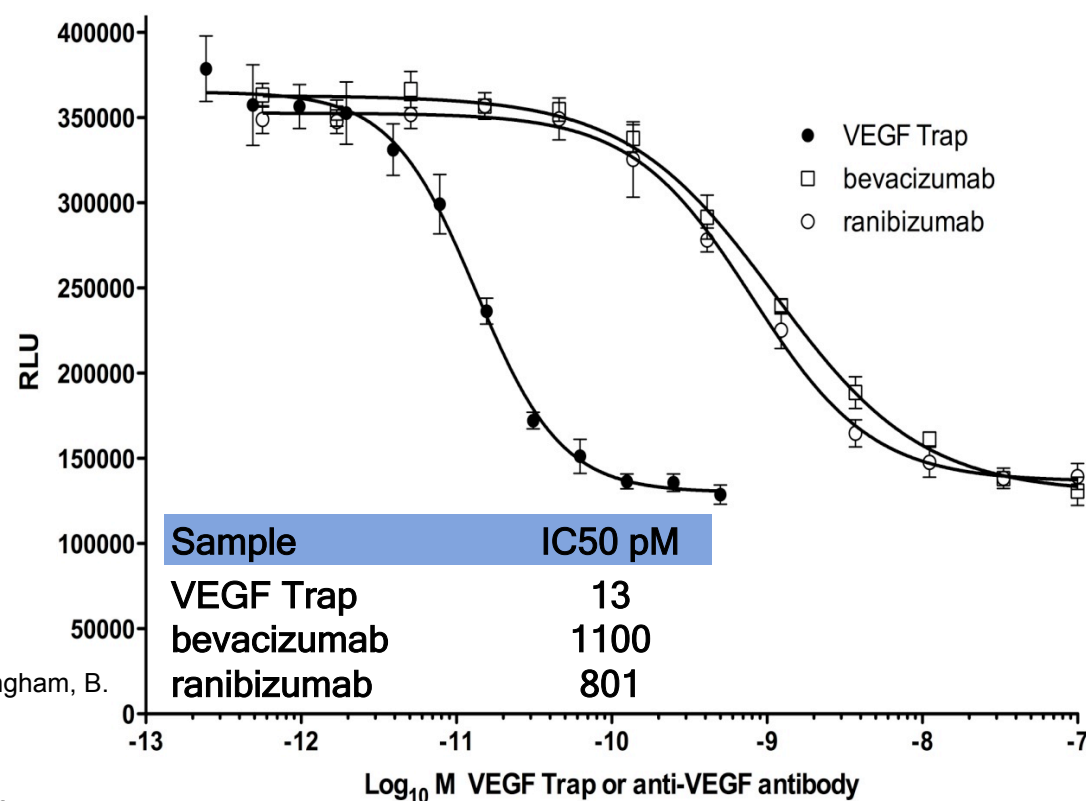
	$K_D$ (pM) <sup>*</sup>
<b>Bevacizumab<sup>a</sup></b>	<b>2900</b>
<b>Ranibizumab<sup>b</sup></b>	<b>140</b>
<b>VEGF Trap</b>	<b>0.5</b>

**300x greater binding affinity**

<sup>\*</sup>Affinity values reported in literature

<sup>a</sup>Muller, Y. A., Chen, Y., Christinger, H. W., Li, B., Cunningham, B. C., Lowman, H. B. & de Vos, A. M. (1998a). VEGF and the Fab fragment of a humanized neutralizing antibody: crystal structure of the complex at 2.4 Å resolution and mutational analysis of the interface. Structure, 6, 1153-1167.

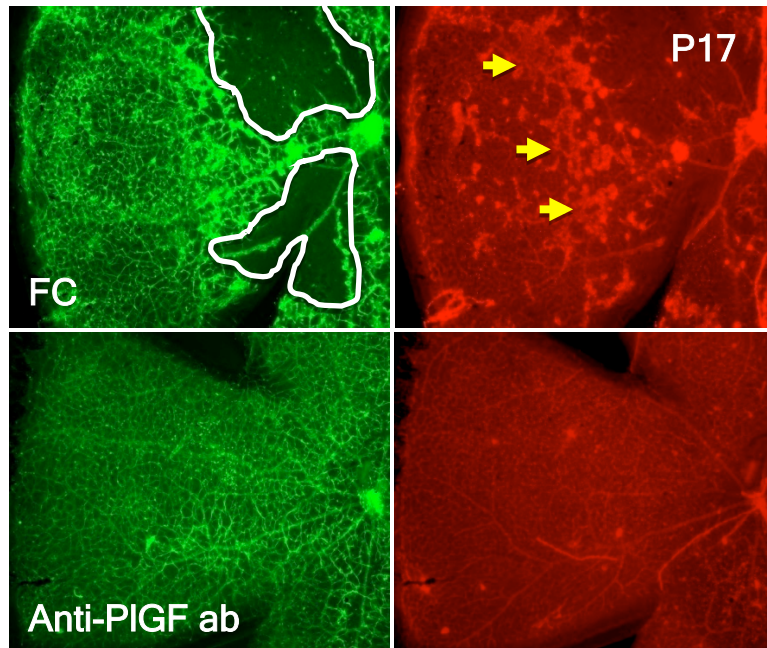
<sup>b</sup>Yvonne Chen, Christian Wiesmann, Germaine Fuh, Bing Li, Hans W. Christinger, Patrick McKay, Abraham M. de Vos, Henry B. Lowman (1999). Selection and analysis of an optimized anti-VEGF antibody: crystal structure of an affinity-matured fab in complex with antigen. Journal of Molecular Biology, Volume 293, Issue 4, 5 November 1999, Pages 865-881



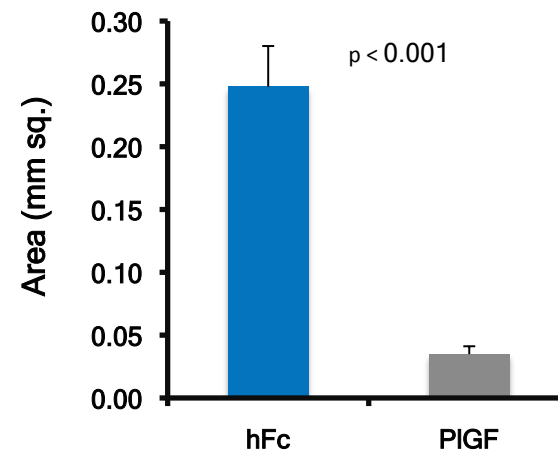
**Blocks at 60-80x lower concentration  
in a cell-based assay**

# VEGF Trap-Eye in Wet AMD

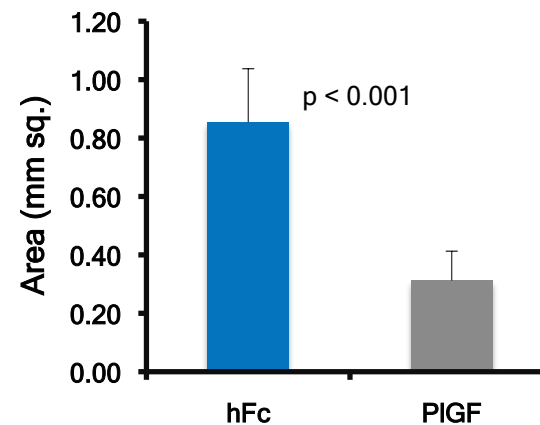
*Potential for Differentiation Relative to Ranibizumab 0.5 mg Monthly*



Abnormal vascular area



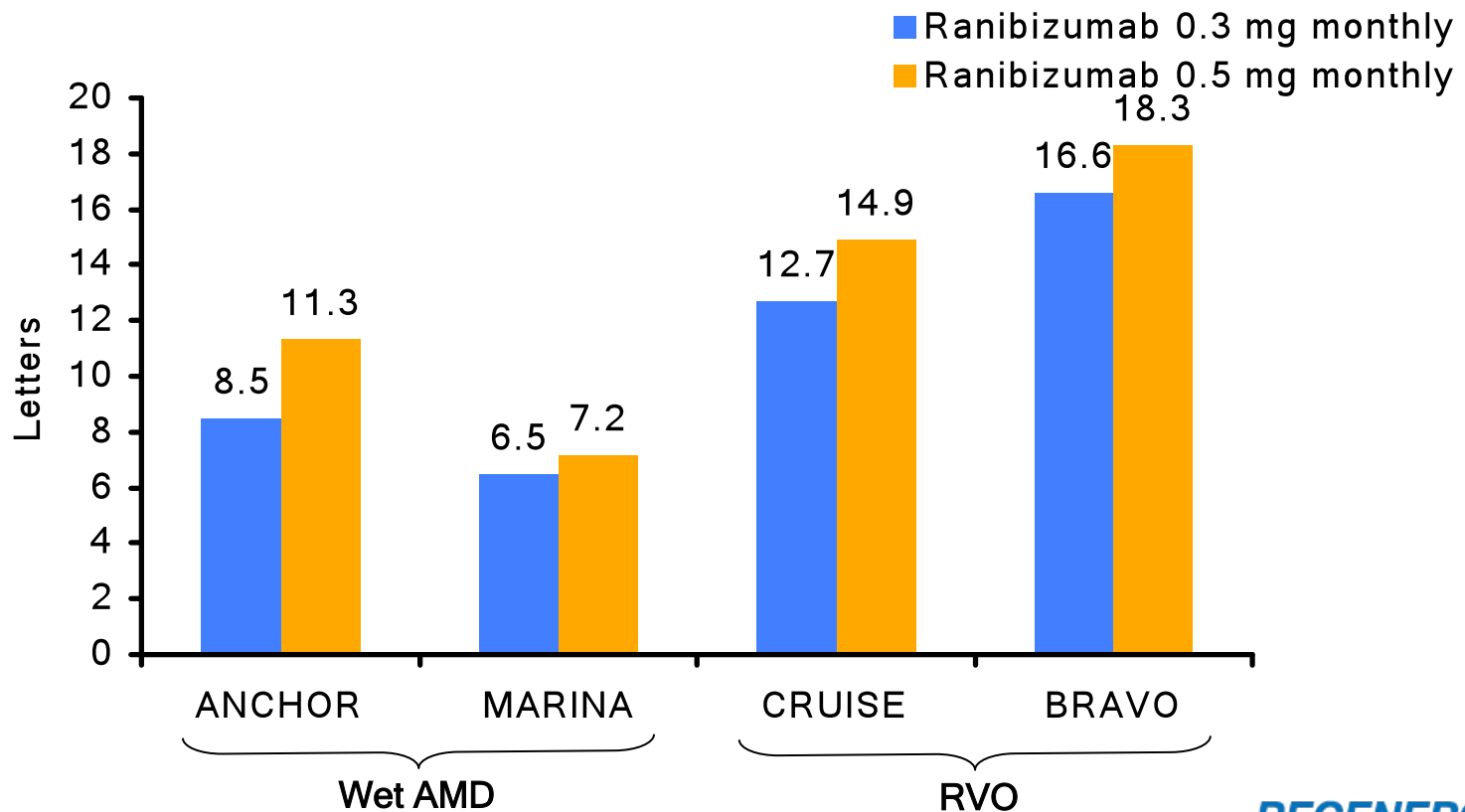
Avascular area



# VEGF Trap-Eye in Wet AMD and RVO

*Potential for Differentiation Relative to Ranibizumab 0.5 mg Monthly*

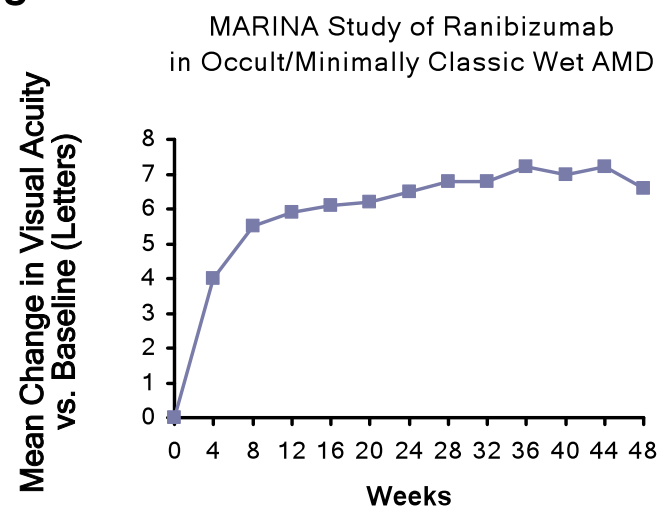
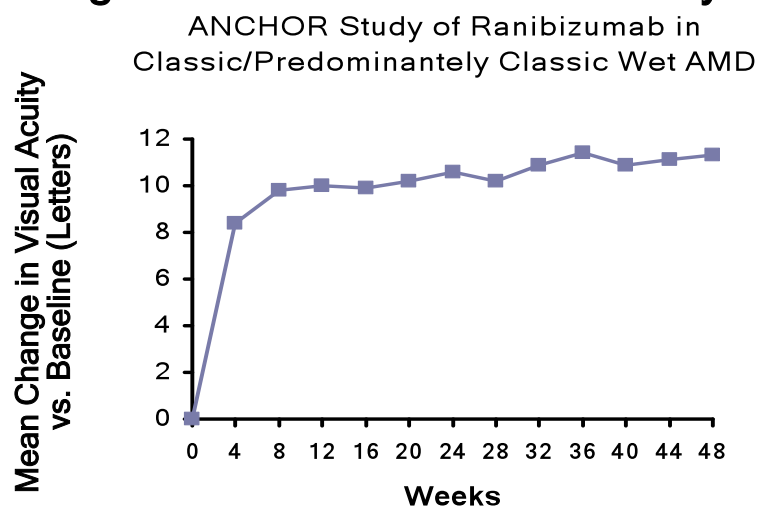
Mean Change in Visual Acuity from Baseline to 12 Months



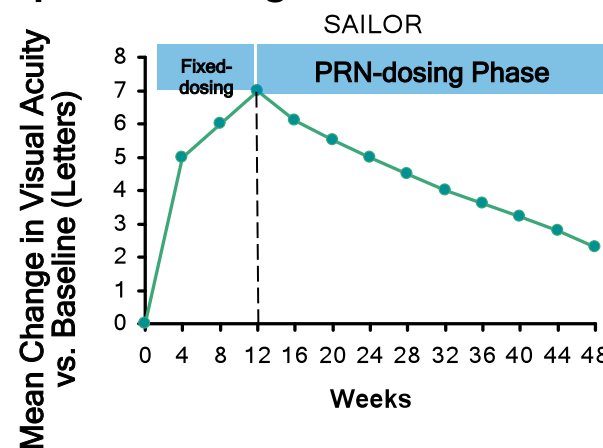
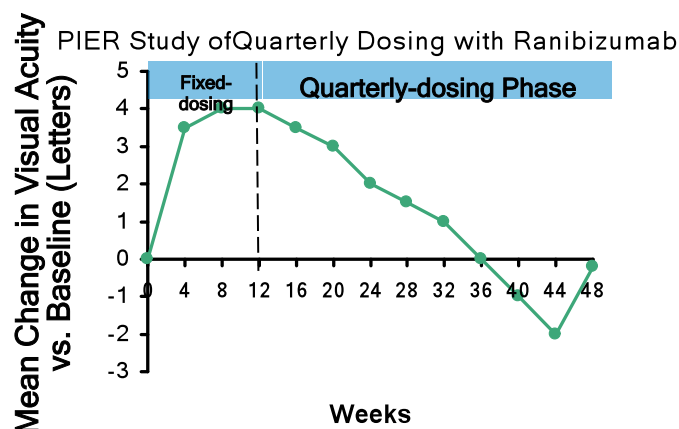
# VEGF Trap-Eye in Wet AMD

*Ranibizumab Generally Requires Monthly Dosing Intervals to Maintain Efficacy*

## ► Vision gains maintained with monthly dosing



## ► Vision gains appear to diminish with less frequent dosing



# VEGF Trap-Eye in RVO

*Lucentis® Generally Requires Monthly Dosing Intervals to Maintain Efficacy*

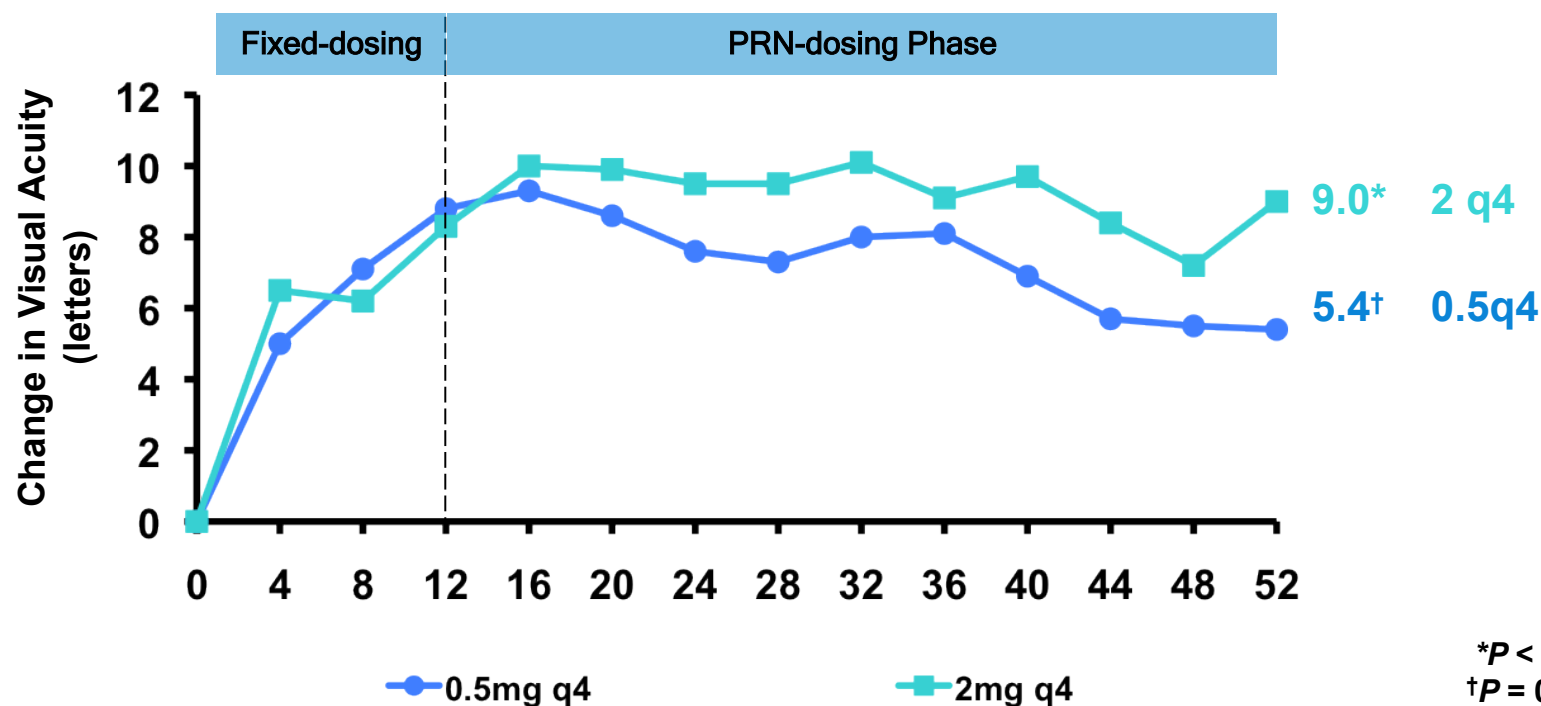


**In the RVO clinical studies, patients received monthly injections of Lucentis for six months. In spite of being guided by optical coherence tomography and visual acuity re-treatment criteria, patients who were then not treated at Month 6 experienced on average, a loss of visual acuity at Month 7, whereas patients who were treated at Month 6 did not. Patients should be treated monthly.**



*— Full U.S. Prescribing Information for Lucentis®  
(ranibizumab)*

## CLEAR-IT 2: Phase 2 Data in AMD Encouraging Vision Gains Are Maintained in PRN Dosing Phase

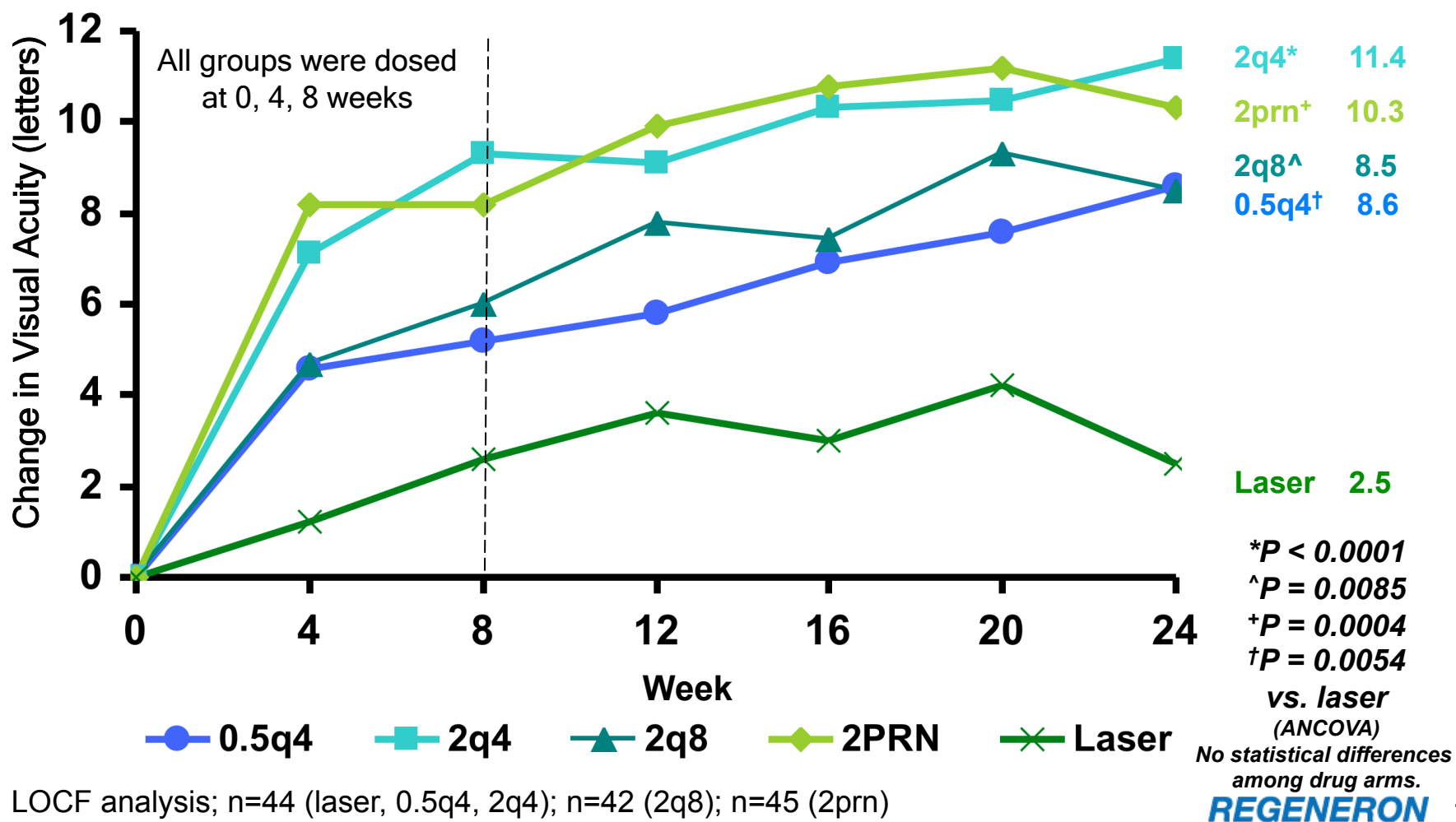


LOCF analysis; paired t-test; 0.5mg q4: n=32; 2mg q4: n=31

At 52 weeks, visual acuity was most improved for 2mg q4 week group demonstrating a statistically significant gain of 9.0 letters from baseline ( $P < 0.0001$ ). This group only required, on average, an additional 1.6 doses over 40 weeks in the PRN dosing phase.

# DA VINCI: Phase 2 Data in DME Also Encouraging

## *Vision Continued to Improve Post Loading Dose in q8 Dosing Arm*



# VEGF Trap-Eye Development Program

- ▶ Phase 3 program in wet Age-related Macular Degeneration, VIEW 1 and VIEW2
  - ▶ Year 1 primary endpoint results for both studies expected in 4Q10

The logo for VIEW 1, featuring the word "view" in blue lowercase letters with a stylized eye graphic, followed by the number "1" in blue.The logo for VIEW 2, featuring the word "view" in red lowercase letters with a stylized eye graphic, followed by the number "2" in red.

- ▶ Phase 3 program in Central Retinal Vein Occlusion (CRVO) initiated 3Q09
  - ▶ Two identical studies (n=330)
  - ▶ 2 arms: 2 mg VEGF Trap-Eye vs. sham control injection
  - ▶ Primary endpoint: Visual acuity change vs. baseline after 6 months of treatment
  - ▶ Data expected in 1H11

The logo for GALILEO, featuring the word "GALILEO" in blue uppercase letters, followed by a stylized orange and blue circular graphic.The logo for COPERNICUS, featuring a stylized orange and blue graphic above the word "COPERNICUS" in blue uppercase letters.

- ▶ Phase 2 program in Diabetic Macular Edema (DME) primary results presented in 1Q10
  - ▶ Full year data expected in 2H10

## VEGF Trap-Eye: Conclusions

- ▶ Anti-VEGF therapy in eye disease is a multi-billion dollar market globally
- ▶ Phase 3 program in wet AMD to report in 4Q10
  - ▶ Head-to-head with Lucentis® (ranibizumab)
  - ▶ Could differentiate by greater efficacy and/or less frequent dosing frequency
- ▶ Phase 3 program results in CRVO expected in 1H11
- ▶ One-year data from Phase 2 program in DME expected in 2H10