Forward-looking statements

This presentation includes “forward-looking statements,” within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements express a belief, expectation or intention and are generally accompanied by words that convey projected future events or outcomes such as “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “design,” “intend,” “expect,” “could,” “plan,” “potential,” “predict,” “seek,” “should,” “would” or by variations of such words or by similar expressions. The forward-looking statements include statements relating to, among other things, REGENXBIO's future operations, clinical trials, costs and cash flow. REGENXBIO has based these forward-looking statements on its current expectations and assumptions and analyses made by REGENXBIO in light of its experience and its perception of historical trends, current conditions and expected future developments, as well as other factors REGENXBIO believes are appropriate under the circumstances. However, whether actual results and developments will conform with REGENXBIO’s expectations and predictions is subject to a number of risks and uncertainties, including the timing of enrollment, commencement and completion and the success of clinical trials conducted by REGENXBIO, its licensees and its partners, the timing of commencement and completion and the success of preclinical studies conducted by REGENXBIO and its development partners, the timely development and launch of new products, the ability to obtain and maintain regulatory approval of product candidates, the ability to obtain and maintain intellectual property protection for product candidates and technology, trends and challenges in the business and markets in which REGENXBIO operates, the size and growth of potential markets for product candidates and the ability to serve those markets, the rate and degree of acceptance of product candidates, and other factors, many of which are beyond the control of REGENXBIO. Refer to the “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” sections of REGENXBIO’s Annual Report on Form 10-K for the year ended December 31, 2017 and comparable “risk factors” sections of REGENXBIO’s Quarterly Reports on Form 10-Q and other filings, which have been filed with the U.S. Securities and Exchange Commission (SEC) and are available on the SEC’s website at www.sec.gov. All of the forward-looking statements made in this presentation are expressly qualified by the cautionary statements contained or referred to herein. The actual results or developments anticipated may not be realized or, even if substantially realized, they may not have the expected consequences to or effects on REGENXBIO or its businesses or operations. Such statements are not guarantees of future performance and actual results or developments may differ materially from those projected in the forward-looking statements. Readers are cautioned not to rely too heavily on the forward-looking statements contained in this presentation. These forward-looking statements speak only as of the date of this presentation. REGENXBIO does not undertake any obligation, and specifically declines any obligation, to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.
REGENXBIO: seeking to improve lives through the curative potential of gene therapy

4 clinical stage programs
with next data readout for RGX–314
expected in late 2019

13 clinical stage product candidates
being developed by third-party licensees;
over 20 partnered programs in total

Proprietary NAV® Technology Platform
includes exclusive *worldwide rights to over 100 AAV vectors*,
including AAV7, AAV8, AAV9 and AAVrh10
<table>
<thead>
<tr>
<th>Indication</th>
<th>Development Stage</th>
<th>Anticipated Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Retinal Disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RGX–314 wet AMD</td>
<td>Research</td>
<td>Phase I/Ila data and initiation of Phase IIb trial in late 2019</td>
</tr>
<tr>
<td>RGX–314</td>
<td>Preclinical</td>
<td>IND submission in 2H 2019</td>
</tr>
<tr>
<td>Undisclosed indication</td>
<td>Phase I/II</td>
<td></td>
</tr>
<tr>
<td><strong>Neurodegenerative Disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RGX–121 MPS II</td>
<td>Research</td>
<td>Interim data update in 2H 2019</td>
</tr>
<tr>
<td>RGX–111 MPS I</td>
<td>Preclinical</td>
<td>Begin enrollment in Phase I trial in mid-2019</td>
</tr>
<tr>
<td>RGX–181 CLN2 disease</td>
<td>Phase I/II</td>
<td>IND submission in 2H 2019</td>
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<tr>
<td><strong>Metabolic Disease</strong></td>
<td></td>
<td></td>
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<tr>
<td>RGX–501 HoFH</td>
<td>Research</td>
<td>Interim data update in 2H 2019</td>
</tr>
</tbody>
</table>

- ▲ Orphan Drug Designation
- ★ Rare Pediatric Disease Designation
- ■ Fast Track Designation

*REGENXBIO’s lead programs
Internally developed product candidates*
REGENXBIO’s **NAV Technology Platform** has been widely adopted

*Over 20 partnered product candidates being developed by NAV Technology Licensees*

<table>
<thead>
<tr>
<th>Research</th>
<th>Preclinical</th>
<th>Phase I / II</th>
<th>Phase III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication</td>
<td>Licensee</td>
<td>Indication</td>
<td>Licensee</td>
</tr>
<tr>
<td><strong>Liver / hematologic</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Citrullinemia Type I</td>
<td>Ultragenyx</td>
<td>Hemophilia A</td>
<td>Shire</td>
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<tr>
<td>PKU</td>
<td>Ultragenyx</td>
<td>Hemophilia A</td>
<td></td>
</tr>
<tr>
<td>Wilson Disease</td>
<td>Ultragenyx</td>
<td>OTC Deficiency</td>
<td>Ultragenyx</td>
</tr>
<tr>
<td>PKU</td>
<td>Ultragenyx</td>
<td>GSD Ia</td>
<td>Ultragenyx</td>
</tr>
<tr>
<td><strong>Retina</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Achromatopsia</td>
<td>Biogen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Choroideremia</td>
<td>Biogen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parkinson’s w/ GBA</td>
<td>Prevail</td>
<td>Rett Syndrome</td>
<td>Novartis</td>
</tr>
<tr>
<td>Undisclosed</td>
<td>Voyager</td>
<td>ALS SOD1</td>
<td>Novartis</td>
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<tr>
<td>CDKL5 Deficiency</td>
<td>Ultragenyx</td>
<td>ALS SOD1</td>
<td>Voyager</td>
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<tr>
<td>CLN1</td>
<td>Abeona</td>
<td>MPS IIIA</td>
<td>Esteve</td>
</tr>
<tr>
<td>CLN3</td>
<td>Abeona</td>
<td>MPS IIIB</td>
<td>Abeona</td>
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<td><strong>Central nervous system</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Friedreich’s Ataxia</td>
<td>Voyager</td>
<td>Danon Disease</td>
<td>Rocket</td>
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<tr>
<td>Pompe Disease</td>
<td>Ultragenyx</td>
<td></td>
<td>Audientes</td>
</tr>
</tbody>
</table>
Key features of REGENXBIO’s NAV Technology Platform

- Higher gene expression
- Lower immune response
- Improved manufacturability
- Longer-term gene expression
- Broad and novel tissue selectivity

**References**

- Nature Biotechnology: Intravascular AAV9 Preferentially Targets Neonatal Neurons and Adult Astrocytes
REGENXBIO | cGMP Manufacturing

Strength in AAV production and deep experience in biologics scale up and commercialization

- Natural host for AAV
- Robust process utilizing mammalian cell lines with known regulatory history
- Core in-house capability in adapting adherent cell lines to suspension cell culture-based systems
  - Suspension cell culture process developed and transferred to CMO

- Focus on process, quality and analytics
  - Deep in-house knowledge of AAV characterization and production
  - Focused efforts on integrated upstream and downstream process optimization and scale-up
  - Significant expertise and investment in quality systems and downstream analytics

- Large-scale cGMP capacity at CMOs
  - Agreements with multiple leading biologics CMOs for production of materials under cGMP, including secured large-scale (up to 2,000L) capacity and commercial production at FUJIFILM
  - REGENXBIO platform processes transferred to all CMO partners with robust performance and yields
  - FUJIFILM relationship supports clinical development and potential future commercial needs
  - Leveraging flexibility and scale at CMOs to ensure supply while managing capital investment

- Clinical manufacturing status
  - Completed production of investigational product for four lead product candidates in an amount which is expected to supply on-going clinical trials; GMP campaign in progress for RGX–181
  - In-house GMP testing established to accelerate release of clinical supplies
  - Capability to progress from candidate selection to clinical material in 12 months
# The REGENXBIO team

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
<th>Prior Affiliations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ken Mills</td>
<td>President, CEO &amp; Co-Founder; Director</td>
<td></td>
</tr>
<tr>
<td>Olivier Danos, Ph.D.</td>
<td>SVP and Chief Scientific Officer</td>
<td>Biogen</td>
</tr>
<tr>
<td>Vit Vasista</td>
<td>SVP and Chief Financial Officer</td>
<td>PRTM</td>
</tr>
<tr>
<td>Curran Simpson</td>
<td>SVP, Product Development and Chief Technology Officer</td>
<td></td>
</tr>
<tr>
<td>Ram Palanki, Pharm.D.</td>
<td>SVP, Commercial Strategy and Operations</td>
<td>Santen, Genentech</td>
</tr>
<tr>
<td>Patrick Christmas, J.D.</td>
<td>SVP and General Counsel</td>
<td>Lumara Health, Wellstat Therapeutics</td>
</tr>
<tr>
<td>Laura Coruzzi, Ph.D., J.D.</td>
<td>SVP, Intellectual Property</td>
<td></td>
</tr>
<tr>
<td>Shiva Fritsch</td>
<td>SVP, Human Resources</td>
<td>NOVA VAX, Human Genome Sciences</td>
</tr>
</tbody>
</table>
**THE DISEASE**

- Blurring of central vision and progressive vision loss due to formation of leaky blood vessels in the eye
- VEGF inhibitors are standard of care to treat fluid and associated vision loss
- Frequency / uncomfortable administration of current anti-VEGF therapies affects compliance and ultimately efficacy
- >2 million patients estimated in U.S., Europe and Japan

---

**RGX–314 for treatment of wet age-related macular degeneration (wet AMD)**

**RGX–314 PRODUCT CANDIDATE**

- **Vector:** AAV8
- **Gene:** anti-VEGF fab

**Mechanism of action**

Reducing leaky blood vessel formation by giving ocular cells the ability to produce an anti-VEGF fab

**Route of administration**

Subretinal
**RGX-314 clinical trial summary through six months**

<table>
<thead>
<tr>
<th>Cohort 1</th>
<th>3x10⁸ GC/eye (N=6)</th>
<th>Aqueous RGX-314 protein one month post–treatment</th>
<th>Mean # of anti–VEGF injections through six months</th>
<th>Mean change in CRT through six months (range)</th>
<th>Mean change in BCVA through six months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2.4 ng/ml</td>
<td>4.7 inj*</td>
<td>-14 µm** (-181µm to +92 µm)</td>
<td>-2 letters** (-8 to +10 letters)</td>
</tr>
</tbody>
</table>

| Cohort 2 | 1x10¹⁰ GC/eye (N=6) | 12.8 ng/ml                                    | 3.8 inj                                        | +26 µm (-7µm to +62 µm)                      | +7 letters (-4 to +15 letters)         |

| Cohort 3 | 6x10¹⁰ GC/eye (N=6) | 160.2 ng/ml                                   | 1.3 inj                                        | -14 µm (-27µm to +7 µm)                      | +8 letters (0 to +21 letters)          |

* One subject in Cohort 1 discontinued from the study at four months with four injections and was imputed as requiring six injections through six months

** N=5; one subject in Cohort 1 discontinued from the study at four months
Cohort 3: Three subjects with no additional anti–VEGF injections through nine months

<table>
<thead>
<tr>
<th>Previous therapy</th>
<th>Study subjects received on average &gt;35 injections since wet AMD diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-RGX–314 anti–VEGF injections</td>
<td>0 injections through nine months post-RGX–314</td>
</tr>
<tr>
<td>BCVA</td>
<td>Mean change in BCVA of +13 ETDRS letters from baseline through nine months</td>
</tr>
<tr>
<td>SD–OCT</td>
<td>Maintained with a mean change in CRT of -37 µm from baseline through nine months</td>
</tr>
</tbody>
</table>
Featured Retina Specialist Guest Speakers

John Pollack, M.D.
- Partner at Illinois Retina Associates
- Assistant Professor of Ophthalmology at Rush University Medical Center
- President of the American Society of Retina Specialists (ASRS)

Pravin U. Dugel, M.D.
- Managing Partner at Retinal Consultants of Arizona, Phoenix
- Clinical Professor at Roski Eye Institute and University of Southern California Keck School of Medicine
- Subspecialty Day Board Chairman Emeritus for the American Academy of Ophthalmology (AAO) Board of Directors and Executive Committee of ASRS
- Board of Trustees of EURETINA

Allen C. Ho, M.D.
- Professor of Ophthalmology at Sidney Kimmel Medical College at Thomas Jefferson University
- Director of Retina Research at Wills Eye Hospital
- Executive Committee of the Retina Society
- Investigator in the RGX-314 Phase I/IIa clinical trial

Jeffrey Heier, M.D.
- Co-President, Medical Director and Retina Service Director of Retina Research Ophthalmic Consultants of Boston
- Principal Investigator of the RGX-314 Phase I/IIa clinical trial
Agenda

**Olivier Danos, PhD**  
SVP and Chief Scientific Officer

- Optimizing the gene therapy construct for wet AMD

**John Pollack, MD**

- Overview of retinal diseases, standard of care and unmet need in wet AMD

**Pravin U. Dugel, MD**

- Changing retinal landscape and implications for future therapies

**Allen C. Ho, MD**

- Facts about vitrectomies and subretinal procedures

**Jeff Heier, MD**

- RGX-314 Phase I/IIa clinical data

**Ram Palanki**  
SVP, Commercial Strategy & Operations

- RGX-314 market opportunity

**Q&A**

Moderator: Ram Palanki
RGX-314 Analyst and Investor Day
Optimizing the gene therapy construct
February 21, 2019
Olivier Danos, Ph.D.
SVP and Chief Scientific Officer
RGX–314 for treatment of wet age-related macular degeneration (wet AMD)

**RGX–314 PRODUCT CANDIDATE**

- **Vector**: AAV8
- **Gene**: anti-VEGF fab

**Route of administration**: Subretinal

**Mechanism of action:**
Reducing leaky blood vessel formation by giving ocular cells the ability to produce an anti-VEGF fab

---

**Improved AAV vector technology**

- AAV8
- AAV2

**More efficient gene delivery to the RPE**

- Current standard of care includes FDA-approved mAbs and mAb fragments that inhibit VEGF
- RGX–314 gene encodes an anti-VEGF mAb fragment (fab)

**Leveraging current standard of care in transgene**

**RGX–314**: AAV8 encoding anti-VEGF fab

**Potential for long-term therapeutic anti-VEGF expression**

1. Vandenberghe et al. 2011 Science Translational Medicine
NAV Vectors: higher gene expression than early generation AAV vectors

NAV Vector AAV8: 10x–100x greater gene expression

NAV Vector AAV8: More efficient gene delivery to sites of most retinal dystrophies

1 Vanderberghe et al. 2011 Science Translational Medicine
AAV8 anti-VEGF fab (RGX-314)

RGX-314 (AAV2/8.CB7.CI.amd42.rBG) is a non-replicating, recombinant adeno-associated virus (AAV), serotype 8 (AAV8) vector containing an amd42 expression cassette encoding for a soluble anti-VEGF Fab protein.

AAV8 Capsid:
An icosahedron formed by three viral proteins, VP1, VP2 and VP3.
Subretinal injection of RGX-314 suppresses choroidal neovascularization in mice

Rho/VEGF neovascularization in mice in response to RGX-314

Dose response: area of neovascularization

Long-term anti-VEGF protein expression is measured in non-human primates

4 week protein expression\(^1\)

<table>
<thead>
<tr>
<th></th>
<th>1E10</th>
<th>1E11</th>
<th>1E12</th>
</tr>
</thead>
<tbody>
<tr>
<td>anti-VEGF Fab (ng/mL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RGX-314 GC/Eye</td>
<td><img src="image1.png" alt="Graph" /></td>
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</table>

Protein expression up to 300 days\(^2\)

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>100</th>
<th>200</th>
<th>300</th>
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</thead>
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<tr>
<td>anti-VEGF Fab (ng/mL)</td>
<td><img src="image2.png" alt="Graph" /></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) NHP Study #8 & #12
\(^2\) RGX-314 1E11, group 6
Data on file at REGENXBIO
RGX-314 anti-VEGF fab distributes throughout the retina

- Cynomolgus monkeys administered $1 \times 10^{11}$ GC/eye of AAV8 vector subretinally

- Concentrations of anti-VEGF Fab were determined in:
  - ACF = anterior chamber fluid
  - VIT = vitreous
  - Retina:
    - SUP = superior retinal section
    - FOV = fovea
    - ODI = middle section w optic disk
    - INF = inferior retinal section

Transgene product distributes beyond peripheral injection site

Source: NHP Study #14
Data on file at REGENXBIO
RGX–314 transgene product binding and affinity for VEGF

- Compared binding of in vitro synthesized RGX–314 transgene product with synthesized ranibizumab on human tissue samples
  - No difference in tissue binding profile vs. ranibizumab
- Determined binding affinity of RGX–314 transgene product for human VEGF¹
  - RGX–314 transgene product affinity as high or higher than published range for ranibizumab
  - Measured by Biacore (surface plasmon resonance)

<table>
<thead>
<tr>
<th>Ligand</th>
<th>Analyte</th>
<th>ka (1/Ms)</th>
<th>kd (1/s)</th>
<th>R_{max}</th>
<th>K_D (M)</th>
<th>Concentration (nM)</th>
<th>χ²</th>
</tr>
</thead>
<tbody>
<tr>
<td>VEGF (97 RU)</td>
<td>RGX-314 transgene product</td>
<td>2.42 x 10^5</td>
<td>8.06 x 10^{-5}</td>
<td>21.8</td>
<td>3.33 x 10^{-10}</td>
<td>0 to 100</td>
<td>0.0653</td>
</tr>
</tbody>
</table>

Abbreviations: ka = association rate constant; kd = dissociation rate constant; K_D equilibrium binding affinity constant; R_{max} = maximum binding capacity (in RU) of ligand captured/immobilized on the surface; RU = response unit.

RGX–314 transgene product binding and affinity for VEGF consistent with ranibizumab data

RGX–314 has potential advantages over earlier generation candidates for wet AMD gene therapy

<table>
<thead>
<tr>
<th>Sponsor</th>
<th>Vector</th>
<th>ROA</th>
<th>Transgene</th>
<th>Dose (GC/eye)</th>
<th>Max. expression (ng/ml)</th>
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</thead>
<tbody>
<tr>
<td>genzyme ¹</td>
<td>AAV2</td>
<td>Intravitreal</td>
<td>sFLT01</td>
<td>2.4e10</td>
<td>528</td>
</tr>
<tr>
<td>AVANCHE ²</td>
<td>AAV2</td>
<td>Subretinal</td>
<td>sFlt</td>
<td>8.0e11</td>
<td>0.217</td>
</tr>
<tr>
<td>REGENXBIO</td>
<td>AAV8</td>
<td>Subretinal</td>
<td>anti-VEGF fab</td>
<td>1.0e11</td>
<td>4,992</td>
</tr>
</tbody>
</table>

¹ MacLachlan et al. 2011 Molecular Therapy
² Lai et al. 2012 Gene Therapy
³ Maximum expression in the anterior chamber of non-human primate eyes
Overview of retinal diseases, standard of care and unmet need in wet AMD

John Pollack, MD
FINANCIAL DISCLOSURES

Allegro - Consultant

Covalent Medical – Stock

Dutch Ophthalmic Research Company – Consultant

Genentech – Grant Support, Consultant

Notal Vision - BOD, Stock, Consultant

Novartis - Consultant

REGENXBIO - Consultant

Vestrum Health - Stock
## MAJOR RETINAL DISEASES OVERVIEW

<table>
<thead>
<tr>
<th>Disease Overview</th>
<th>Treatments</th>
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<tbody>
<tr>
<td><strong>Wet AMD</strong></td>
<td>• PDT &amp; chronic anti-VEGF therapy</td>
</tr>
<tr>
<td>Avg age of onset</td>
<td>Prevalence*</td>
</tr>
<tr>
<td>70 yrs</td>
<td>1.9</td>
</tr>
<tr>
<td><strong>Diabetic Macular Edema</strong></td>
<td>• Anti-VEGF, steroids, laser &amp; surgeries</td>
</tr>
<tr>
<td>Avg age of onset</td>
<td>Prevalence*</td>
</tr>
<tr>
<td>60 yrs</td>
<td>1.9</td>
</tr>
<tr>
<td><strong>Retinal Vein Occlusion</strong></td>
<td>• Anti-VEGF, steroids &amp; laser</td>
</tr>
<tr>
<td>Avg age of onset</td>
<td>Prevalence*</td>
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<tr>
<td>55 yrs</td>
<td>2.5</td>
</tr>
<tr>
<td><strong>Diabetic Retinopathy w/o DME</strong></td>
<td>• PRP, anti-VEGF &amp; surgeries</td>
</tr>
<tr>
<td>Avg age of onset</td>
<td>Prevalence*</td>
</tr>
<tr>
<td>45-50 yrs</td>
<td>5.1</td>
</tr>
</tbody>
</table>

### Disease Overview
- **Wet AMD**: A leading cause of blindness in the elderly
- **Diabetic Macular Edema**: Most frequent cause of blindness in middle aged adults
- **Retinal Vein Occlusion**: Second most common cause of vision loss due to vascular disease
- **Diabetic Retinopathy w/o DME**: Common cause of vision loss among diabetics; Classified as non-proliferative (NPDR) and proliferative (PDR)

### Treatments
- **PDT & chronic anti-VEGF therapy**
- **Anti-VEGF, steroids, laser & surgeries**
- **Anti-VEGF, steroids & laser**
- **PRP, anti-VEGF & surgeries**

### Notes
- wAMD = wet AMD; DME = Diabetic Macular Edema; BRVO = Branch Retinal Vein Occlusion; CRVO = Central Retinal Vein Occlusion; NPDR = Non-Proliferative Diabetic Retinopathy; PDR = Proliferative Diabetic Retinopathy
- Prevalence*: Numbers may be rounded; Source: epidemiology data based on multiple literature sources, diagnosis rates based on Datamonitor Report, DRG Market Forecast Assumptions; other sources: Regeneron USA: 230k anti-VEGF treated patients, Roche USA: 200k patients under ophtha care [https://www.gene.com/stories/retinal-diseases-fact-sheet](https://www.gene.com/stories/retinal-diseases-fact-sheet) and DRG Market Forecast Assumptions
- *US, EUS, Japan
# ANTI-VEGF TREATMENT EFFICACY IN PHASE III TRIALS

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Drug Name</th>
<th>Dose Frequency</th>
<th>Mean age (years) Baseline</th>
<th>Mean ETDRS letters Baseline</th>
<th>Mean Gain in ETDRS letters at 24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 ANCHOR</td>
<td>Ranibizumab</td>
<td>0.5mg every 4 wks</td>
<td>76</td>
<td>47.1</td>
<td>+10.7</td>
</tr>
<tr>
<td>2 MARINA</td>
<td>Ranibizumab</td>
<td>0.5mg every 4 wks</td>
<td>77</td>
<td>53.7</td>
<td>+6.6</td>
</tr>
<tr>
<td>3 CATT</td>
<td>Ranibizumab</td>
<td>0.5mg every 4 wks</td>
<td>79</td>
<td>60.1</td>
<td>+8.8</td>
</tr>
<tr>
<td>3 CATT</td>
<td>Bevacizumab</td>
<td>1.25mg every 4 wks</td>
<td>80</td>
<td>60.2</td>
<td>+7.8</td>
</tr>
<tr>
<td>4 VIEW 1 &amp; 2</td>
<td>Afiblercept</td>
<td>2mg every 8 wks</td>
<td>76</td>
<td>55.7</td>
<td>+7.6</td>
</tr>
<tr>
<td>4 VIEW 1 &amp; 2</td>
<td>Ranibizumab</td>
<td>0.5mg every 4 wks</td>
<td>76</td>
<td>54.0</td>
<td>+7.9</td>
</tr>
<tr>
<td>5 HARBOR</td>
<td>Ranibizumab</td>
<td>0.5mg every 4 wks</td>
<td>79</td>
<td>54.2</td>
<td>+9.4</td>
</tr>
<tr>
<td>5 HARBOR</td>
<td>Ranibizumab</td>
<td>0.5mg PRN</td>
<td>79</td>
<td>54.5</td>
<td>+7.9</td>
</tr>
</tbody>
</table>

Mean: 8.3

5 Ho AC et al., HARBOR Study 2-Year Results. Ophthalmology 2014.
THE MAJORITY OF WET AMD PATIENTS DO NOT RECEIVE RECOMMENDED TREATMENT REGIMEN

What percentage of your wet-AMD patients do you continue treating with q4w anti-VEGF injections?

- <= 10%: 43.2% Intl, 47.2% US
- 11%-20%: 24.0% Intl, 33.2% US
- 21%-30%: 17.1% Intl, 12.5% US
- > 30%: 15.7% Intl, 7.1% US

MULTIPLE TREATMENT REGIMENS ARE USED IN THE "REAL WORLD"

In general, how do you treat wet-AMD patients with active CNV?

A. Treat until dry on OCT, then PRN
- 33.9%

B. Treated until dry on OCT, then extend (treat and extend)
- 42.1%

C. Treat until dry on OCT, then follow up every 3-4 months
- 2.2%
- 0.8%

D. Inject monthly regardless of fluid or exam
- 19.2%
- 1.5%

A + B
- 19.2%
- 18.9%

Other
- 1.9%
- 1.4%
REAL WORLD OUTCOMES HAVE SIGNIFICANT ROOM FOR IMPROVEMENT

Number of anti-VEGF injections correlates with vision improvement

Five-Year Outcomes with Anti-Vascular Endothelial Growth Factor Treatment of Neovascular Age-Related Macular Degeneration

The Comparison of Age-Related Macular Degeneration Treatments Trials

Patients who switched from monthly to prn (year 2) lost -2 to -3 letters

Post-protocol, real-world outcomes show patients lost an additional -11 letters

Figure 2. Graphs showing the mean visual acuity and 95% confidence interval for 647 patients in the Comparison of Age-Related Macular Degeneration Treatments Trials Follow-up Study: (A) overall and by drug assigned in the clinical trial and (B) overall and by dosing regimen assigned in the clinical trial. PRN = pro re nata.
In **2020**, the prevalent number of cases of bilateral blindness (VA ≤20/200) due to retinal diseases (wAMD, DME & PDR) is **estimated to be 246,422**

By **2050**, the number of individuals with bilateral blindness is projected to **increase more than two-fold** and the overall cost burden is estimated to **triple to $64 billion**

### CAREGIVING COSTS ARE THE LARGEST CONTRIBUTOR

<table>
<thead>
<tr>
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<th>2020</th>
<th>2030</th>
<th>2040</th>
<th>2050</th>
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<tbody>
<tr>
<td><strong>Number of cases</strong></td>
<td>246,423</td>
<td>346,273</td>
<td>461,722</td>
<td>515,745</td>
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<tr>
<td><strong>Direct cost, $ billions</strong></td>
<td>1.22</td>
<td>1.84</td>
<td>2.71</td>
<td>3.48</td>
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<tr>
<td><strong>Indirect (caregiver) cost, $ billions</strong></td>
<td>13.46</td>
<td>23.18</td>
<td>36.54</td>
<td>47.41</td>
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<tr>
<td><strong>QALYs lost</strong></td>
<td>61,757</td>
<td>86,748</td>
<td>115,621</td>
<td>129,133</td>
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<tr>
<td><strong>Years of life lost</strong></td>
<td>9,741</td>
<td>14,468</td>
<td>20,434</td>
<td>23,170</td>
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<tr>
<td><strong>Intangible cost, $ billions</strong></td>
<td>6.18</td>
<td>8.68</td>
<td>11.56</td>
<td>$12.91</td>
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<tr>
<td><strong>Total cost, $ billions</strong></td>
<td><strong>20.85</strong></td>
<td><strong>33.70</strong></td>
<td><strong>50.81</strong></td>
<td><strong>63.81</strong></td>
</tr>
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</table>

Source: DME, diabetic macular edema; PDR, proliferative diabetic retinopathy; RVO, retinal vein occlusion; wAMD, wet age-related macular degeneration. Moshfeghi et al, Angiogenesis 2019.
**SUMMARY**

1. **Frequent intravitreal anti-VEGF treatment has been shown to reduce the risk of blindness in RCTs***
   Real world evidence shows patients lose vision over time due to a treatment burden of current anti-VEGF injections

2. **The societal cost of blindness is significant**
   Treatment strategies that mitigate the social and economic impact of blindness are urgently needed

3. **Sustained treatment strategies that close the gap between RCTs and real world outcomes are needed**
   Single interventions that can provide long-lasting treatment outcomes would be ideal

---

*Randomized Controlled Trials*
Changing retinal landscape and implications for future therapies

Pravin U. Dugel, MD
FINANCIAL DISCLOSURES

- Bausch + Lomb Pharma
- ORA
- Omeros
- Alcon Surgical (RACII)
- Santen Inc
- Clearside Biomedical
- Shire Human Genetics
- Genentech
- Allergan
- Avalanche
- Opthea
- Alcon Surgical
- Ophthotech
- TrueVision
- Graybug Vision
- Alcon Pharmaceutical (C)
- Lux BioScience
- Orbis International
- CDR-Life Inc
- NeoVista
- Digisight
- Lutronic
- Irenix
- MacuSight
- Roche
- Alimera Sciences
- ByeOnics
- Novartis (C)
- Acucela
- Neurotech
- PanOptica
- ArcticDX
- TopCon
- Optovue
- Chengdu Kanghong Biotechnology
- AMO
- Stealth Biotherapeutics
- Aerpio
- SciFluor Life Sciences
- Thrombogenics
- Pentavision
- DOSE Medical
- Annidis
The majority of retina specialists are trained to do surgeries...

Are you a medical retina specialist, a surgical retina specialist, or both?

**United States**
- Surgical retina only, 1.8%
- Medial retina only, 10.2%
- Other, 0.0%
- Medical and surgical retina, 88.0%

**International**
- Surgical retina only, 3.5%
- Medial retina only, 7.7%
- Other, 1.0%
- Medical and surgical retina, 87.8%
... BUT THIS IS THE CURRENT STATUS OF RETINAL PRACTICE
PRINCIPLES OF ACTIVITY BASED COSTING (ABC)

1. Identify main activities
   - Profit/loss centers

2. Assign time and resource values to each activity

3. Determine total $ and per unit costs for each activity

ABC’s for two distinct practice types calculated:

Large Single Specialty Retina Practice
- (Retinal Consultants of Arizona)

#1 Ranked University Practice in Ophthalmology
- (Bascom Palmer Eye Institute, Miami)

Seven service centers analyzed:
1. Non-laser surgery (SB, PPV, PR)
2. Laser surgery (Thermal, PDT)
3. Office visits
4. OCT
5. Non-OCT diagnostic (FA, ICG, ULS, VF)
6. Injections
7. Drugs

THE RISE OF INTRAVITREAL INJECTIONS INCREASED REVENUE AND OPERATING COSTS

Change in collections by service

-16% -11% 25% 414% 472% 377% 42%

% Change

Intravitreal injections to treat wet AMD led to increases in revenues from injections, drugs and monitoring

Increase in Operating Costs

59% 20% 28% -8% 8% 28% 36% 64%

% Change

Surgical revenues decreased over the same period

Operating costs, related to drugs, increased more than revenues

Despite a large increase in revenues, the practice has seen a 14% decline in profit margin.

Efficiency – Profit Margin Across Services (Profit divided by revenue)

PERCENT CHANGE IN RETINA PHYSICIAN REIMBURSEMENT

Percent Change in Reimbursement (2005-2017) (Ophthalmic Surgery)

Percent Change in Reimbursement (2005-2017) (Office-based procedures and diagnostics)

FUTURE TRENDS INFLUENCING CONSOLIDATION OF OPHTHALMIC CARE

• Increased reimbursement for surgery and ASCs
• Explosion of baby boomer senior population
• Relative shortage of physicians
• Increasing population with diabetes
• New surgical treatments for AMD, dystrophies, damaged retinal tissue
  • Gene therapy
  • Implantable devices and prosthesis
  • Stem cell therapy
• Reimbursement pressures and escalating malpractice premiums
• Large capital need for investment into back office functions
OPHTHALMIC CARE CONSOLIDATION DRIVERS

- Demographic induced demand growth
- Insular specialty ripe for consolidation
- Provider supply/demand imbalance
- Payer risk
- Increasing complexity of the business
- Existence of multiple profit streams
- "Cash pay" component
- Availability of growth capital
<table>
<thead>
<tr>
<th>Original Transaction Date</th>
<th>PE Firm(s)</th>
<th>MSO (if known)</th>
<th>Affiliated Practices**</th>
<th>States Located</th>
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<tbody>
<tr>
<td>1/18/2011</td>
<td>CanMedrol Partners</td>
<td>Sold Clear Vision to Undisclosed Strategic Acquirer 03/18</td>
<td>Korth Eye Associates Eye Health Vision Centers</td>
<td>Southcoast Eye Care Manchester Eye Associates RI, MA</td>
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<td>2014</td>
<td>Axeler Private Equity, Charlottesville, VA; others</td>
<td>Vision Group Holdings</td>
<td>The LASK Vision Institute TLC Laser Eye Centers California Vision Institute Qualitech LASIK</td>
<td>Global Laser Vision Atlantic Eye Wilshire Vision LASH &amp; Eye Care Services Panoramic New Vision Institute</td>
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<tr>
<td>5/12/2014</td>
<td>Vision HealthCare Partners</td>
<td>EyeCare Services Partners</td>
<td>Kollins Eye Group Duvalin Eye Institute Delaware Eye Care Center Inland Eye Specialists Ozone Eye Specialists (Denver)</td>
<td>Lasko Eye Group Leesburg Eye Group Eye Centers of Philadelphia Yancey Eye Center Florida Vision Institute Smith-Perry Eye Institute National Retina Institute Shields Eye Medical Group</td>
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<tr>
<td>12/15/2016</td>
<td>Canet Group</td>
<td>EVP EyeCare</td>
<td>ICON Eyecare Kamel Evangelical Eye Center</td>
<td>Swagel-Kolowich Eye Center (Added 07/2017)</td>
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<tr>
<td>5/21/2017</td>
<td>Canewsi Partners (Direct Investment)**</td>
<td>Acuity Eye Group</td>
<td>Acuity Eye Group Restoration Institute Glendale Medical Group Premiere Eye Centers Eye Associates of San Diego Ophthalmic Eye Center</td>
<td>West Coast Eye Care Tricity, South Carolina</td>
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<td>8/21/2017</td>
<td>Stone Capital</td>
<td>EyeSouth Partners</td>
<td>Georgia Eye Partners Georgia Retina</td>
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<td>8/28/2017</td>
<td>Wind Capital Partners</td>
<td>UnityVision Partners</td>
<td>Minnesota Eye Consultants</td>
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</tbody>
</table>

**Original Transaction Date** | **PE Firm(s)** | **MSO (if known)** | **Affiliated Practices** | **States Located**

<table>
<thead>
<tr>
<th>Original Transaction Date</th>
<th>PE Firm(s)</th>
<th>MSO (if known)</th>
<th>Affiliated Practices**</th>
<th>States Located</th>
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<tbody>
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<td>2/27/2017</td>
<td>FlexPoint Ford</td>
<td>SouthEast Eye Specialists</td>
<td>Eye Surgery Center of Chattanooga, LLC Pediatric Eye Specialists Barnes-Dulaney Perkins Eye Center Southwestern Eye Center</td>
<td></td>
</tr>
<tr>
<td>4/17/17</td>
<td>HIG Capital</td>
<td>American Vision Partners</td>
<td></td>
<td></td>
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<tr>
<td>7/8/2017</td>
<td>New Mainstream Capital</td>
<td>OMNI Ophthalmic Management Consultants (OMIC)</td>
<td>OMNI Eye Services Phillips Eye Center (Added January of 2016)</td>
<td>Keeler Eye Center (Added April of 2016)</td>
</tr>
<tr>
<td>7/26/17</td>
<td>Centre Partners</td>
<td>Chesapeake Eye Care Company; Former One Vision Eye Partners in Jan 2016</td>
<td>Whitaker Laser Eye Chesapeake Eye Care and Laser Center</td>
<td>Arlington Eye Center (Added Later) Maryland Vision Institute (Added March 2018)</td>
</tr>
<tr>
<td>11/17/17</td>
<td>Blue Sea Capital</td>
<td>SpectraVision Partners</td>
<td>Ophthalmic Consultants of Long Island New Vision Cataract Center (Added Later)</td>
<td>Ophthalmic Consultants of Connecticut (Added Later)</td>
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<tr>
<td>2/20/18</td>
<td>Gauge Capital</td>
<td>Comprehensive EyeCare Partners (&quot;CompEye&quot; originally formed in 2015)</td>
<td>New Eyes of Southern Nevada Shepherd Eye Center</td>
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<tr>
<td>3/21/18</td>
<td>LRL Partners</td>
<td>EyeHealth America</td>
<td>Carson Eye</td>
<td>The Eye Associates</td>
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<td>5/24/2018</td>
<td>Revesta Capital Partners</td>
<td>CEI Vision Partners (CEVIP)</td>
<td>Cincinnati Eye Institute</td>
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<tr>
<td>9/18</td>
<td>Undisclosed Investor</td>
<td>Seemingly Unannounced</td>
<td>Boston Eye Group The Eye &amp; LASH Institute</td>
<td>Eye Care Specialists</td>
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<tr>
<td>9/18</td>
<td>Zephyr Partners</td>
<td>ReFocus Eye Health</td>
<td>Newly formed; no acquisitions announced</td>
<td></td>
</tr>
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CONSOLIDATED OPHTHALMOLOGY PRACTICES

Source: BSM Consulting.
Note: Map may not include all ophthalmology practices. Location markers indicate presence in a given city, but may not represent number of physical locations in that city.
GENE THERAPY HAS THE POTENTIAL TO PROVIDE FOUNDATIONAL ANTI-VEGF THERAPY THAT MAY SUSTAIN VISON GAINS AND PREVENT BLINDNESS WITH A SINGLE TREATMENT

**Anti-VEGF Exposure (Illustrative)**

**Visual Acuity**

IMPLICATIONS FOR LONG-LASTING THERAPIES IN CONSOLIDATED PRACTICES

1. Highly profitable procedures that offer long term solutions to patients will be prioritized due to costly at-risk contracts
   Potential to offer significant value proposition to all patients responsive to anti-VEGF therapy

2. Centrally managed patient referrals to facilitate immediate access to treatments with durable outcomes
   Faster switch to durable surgical solutions for patients responsive to IVT anti-VEGF

3. Consolidation will solve individual physician reimbursement pressures
   Ensure risk-free access to value-based treatments
GENE THERAPY IS A POTENTIAL SOLUTION TO THE CURRENT BURDEN OF CARE...
Facts about vitrectomies and subretinal delivery

Allen C. Ho, MD
FINANCIAL DISCLOSURES

Aerpio (C)
AGTC (G)
Alcon (C, G)
Allergan (C, G)
Apellis (G)
Asclepix (C)
Beaver EndoOptiks (C)
BioTime (C)
Covalent (O)
DigiSight (C, O)

Eloxx (C)
Genentech (C, G)
Iconic (G)
Iridex (C, G)
Janssen (C, G)
NEI/NIH (G)
Notal (C)
ONL (C, O)
Ophthotech (C, G)
Optovue (C)

Orbit Biomedical (C)
PanOptica (C, G)
PRN (C, O)
ProQR (C, G)
Regeneron (C, G, O)
RegenxBio (C, G)
Sanofi (C, G)
Second Sight (C, G)
OVER 500,000 VITRECTOMIES PERFORMED ANNUALLY ON MEDICARE PATIENTS ALONE

<table>
<thead>
<tr>
<th>Rank</th>
<th>ICD-10 Diagnosis Code/Description</th>
<th>Est. No. of vitrectomies</th>
<th>Est. No. of unique vitrectomy patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H353x Degeneration of macula and posterior pole (macular pucker)</td>
<td>259,340</td>
<td>210,125</td>
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<tr>
<td>2</td>
<td>H431x Vitreous hemorrhage</td>
<td>73,141</td>
<td>58,637</td>
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<tr>
<td>3</td>
<td>H433x Other vitreous opacities</td>
<td>35,207</td>
<td>28,637</td>
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<tr>
<td>4</td>
<td>E113x Type 2 diabetes mellitus with ophthalmic complications</td>
<td>21,942</td>
<td>17,479</td>
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<td>5</td>
<td>H590x Disorders of the eye following cataract surgery</td>
<td>17,108</td>
<td>14,380</td>
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<tr>
<td>6</td>
<td>H438x Other disorders of vitreous body</td>
<td>14,876</td>
<td>12,893</td>
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<tr>
<td>7</td>
<td>H330x Retinal detachment with retinal break</td>
<td>12,521</td>
<td>10,041</td>
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<td>8</td>
<td>H440x Purulent endophthalmitis</td>
<td>11,653</td>
<td>9,050</td>
</tr>
<tr>
<td>9</td>
<td>H271x Dislocation of lens</td>
<td>9,793</td>
<td>8,058</td>
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<tr>
<td>10</td>
<td>T852x Mechanical complication of intraocular lens</td>
<td>9,793</td>
<td>8,182</td>
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<tr>
<td></td>
<td>ALL OTHER DIAGNOSES COMBINED</td>
<td>48,967</td>
<td>39,918</td>
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<tr>
<td></td>
<td>ALL DIAGNOSES</td>
<td>514,342</td>
<td>417,399*</td>
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Source: CMS database, 2017
*2017 Standard Analytic Fails, adjusted for Medicare Advantage enrollment (Medicare Enrollment Dashboard) and payer mix (Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality).
*Not corrected for double counting of patients with multiple diagnoses.
ERM PEELING IS A DELICATE SURGICAL PROCEDURE PERFORMED BY ALL RETINAL SURGEONS

Preoperative (20/50)

Postoperative at 6 months (20/25)

Vitrectomy and delicate membrane peeling from the surface of the macula and fovea

*Courtesy of Allen Ho, MD at Wills Eye Hospital; ERM = epiretinal membrane
WET AGE RELATED MACULAR DEGENERATION

wet AMD

Subretinal approach

Subretinal, Intravitreal, Choroidal

Fundus photography

Source: Moorfields Eye Hospital & University College London
© American Academy of Ophthalmology 2019
Courtesy of Allen Ho, MD at Wills Eye Hospital
Stable transgene expression in rod photoreceptors after recombinant adenovirus-mediated gene transfer to monkey retina


ABSTRACT: Intravitreal administration of adenovirus (AAV) is contraindicated for delivery of viral vectors to the retina because of subretinal injection, difficulty in locating the retina, and lack of transduction efficacy in the subretinal space. Here we demonstrate the feasibility of injecting AAV into the vitreous to transduce rod photoreceptors. Our results indicate that AAV is a suitable vector for delivering gene therapy to the retina. This finding is consistent with the results of other investigators who have demonstrated that AAV can be used for gene delivery to the retina via the intravitreal route.

METHODS: AAV vectors were injected into the vitreous of adult monkeys. The vectors were delivered either by direct injection or by injection through a microinjection needle. The vectors were delivered to the subretinal space using a 3D-printed guide designed to deliver the vector to the retina. The vectors were evaluated for their ability to transduce rod photoreceptors.

One drawback of the injectable vector is the limited duration of gene expression. The duration of gene expression is determined by the number of transduced cells and the time course of the transduction. The duration of gene expression is typically limited to a few weeks. The duration of gene expression can be extended by using a viral vector that expresses a longer-lasting transcript. The viral vector must be designed to express a transcript that is stable in the retina. The viral vector must also be designed to express a transcript that is stable in the retina.

This presentation demonstrates the feasibility of delivering transgenes to the retina via the intravitreal route. The findings are consistent with the results of other investigators who have demonstrated that AAV can be used for gene delivery to the retina via the intravitreal route.
MULTIPLE TRIALS HAVE DEMONSTRATED THE SAFETY OF SUBRETINAL DELIVERY
SUBRETINAL DELIVERY IS PREFERRED FOR GENE THERAPY

• Broader retinal coverage and higher protein expression
  • Broader transduction than intravitreal – IV only transduces cells in fovea due to ILM, which acts as a barrier\(^1\)
  • 100 to 1,000x more efficient than intravitreal injection

• Reduced sensitivity to neutralizing antibodies – seropositive patients can be treated with subretinal delivery
  • Pre-existing AAV neutralizing antibodies (NAbs) may limit intravitreal gene therapy\(^2,3\)
  • Intravitreal Nab prevalence: 30-50% for AAV8 and up to 70% for AAV2\(^4\)

• Procedure safety has been demonstrated in previous wet AMD trials\(^5,6\)

• Bilateral administration is unaffected by prior treatment\(^7\)

\(^1\) Yin L, et al. Intravitreal Injection of AAV2 Transduces Macaque Inner Retina. IOVS April 2011.
\(^5\) Constable I, et al. Phase 2a Randomized Clinical Trial: Safety and Post Hoc Analysis of Subretinal rAAV.sFLT-1 for Wet Age-Related Macular Degeneration. EBioMedicine November 2016.
RGX-314 TRANSVITREAL SUBETINAL DELIVERY
MicroDose Injection Kit  Surgeon foot pedal control

Source: Moorfields Eye Hospital & University College London, MedOne Surgical, Inc.
RGX-314 STANDARDIZED AUTOMATED SUBRETINAL DELIVERY PROCEDURE

Step 1 – Vitrectomy

Step 2 – Subretinal Injection

MedOne MicroDose Syringe

Performed Under Local Anaesthesia in the OR
Same Day Surgery - Patients go home, similar to cataract surgery
Automated Delivery

- Vitrectomy is performed
- Subretinal bleb is placed away from the macula in a healthy area of retina
- Air-fluid exchange is performed

*Courtesy of Allen Ho, MD at Wills Eye Hospital*
RETINAL SPECIALISTS BELIEVE A DURABLE BENEFIT OF 6-12 MONTHS JUSTIFIES A SURGICAL PROCEDURE IN WET AMD

Durability needed for an anti-VEGF therapy to justify a 30 minute surgical procedure

- 3 mo: US 2.6% Intl 3.8%
- 6 mo: US 7.3% Intl 6.9%
- 9 mo: US 6.9% Intl 7.3%
- 12 mo: US 21.4% Intl 27.9%
- 18+ mo: US 18.8% Intl 25.0%
- Other: US 1.5% Intl 0.3%

US vs Intl Durability needed for an anti-VEGF therapy to justify a 30 minute surgical procedure.
Almost all retina specialists are trained surgeons (~2100 retina specialists in US\textsuperscript{1})

- Over 500,000 vitrectomies performed annually in Medicare patients alone

Retina specialists perform delicate surgical procedures routinely

- Subretinal gene therapy injection is standardized and performed peripheral to the macula and fovea

Majority of retina specialists report they would perform a 30 minute surgical procedure to treat wet AMD\textsuperscript{2}

- A durable benefit of 6-12 months justifies a surgical procedure in wet AMD

\textsuperscript{1} Registered with American Academy of Ophthalmology; \textsuperscript{2} ASRS 2018 Preferences and Trends Survey
RGX-314 phase I/IIa clinical data

Jeffrey Heier, MD
# FINANCIAL DISCLOSURES

## Board of Directors

### Ocular Therapeutix

## Scientific Advisory Board

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<thead>
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<th>Adverum</th>
<th>B&amp;L</th>
<th>Hemera</th>
<th>Regeneron</th>
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<td>AsclepIX</td>
<td>Heidelberg</td>
<td>Quark</td>
<td></td>
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</tbody>
</table>
INABILITY TO COMPLY WITH FREQUENT ANTI-VEGF INJECTIONS LEADS TO SIGNIFICANT LOSS OF VISION

AURA: Retrospective, Observational Trial

- Conducted in 8 countries
- 2227 patients

What did we learn?

- > 7.9 injections in year 1 needed to gain > 15 letters
- > 8.3 injections in year 2 needed to maintain visual acuity in year 2
**RGX-314 PHASE I/IIA TRIAL: DESIGN**

**BASELINE ASSESSMENT**
- anti-VEGF injection
- SD-OCT assessment
- RGX-314 administration

**TREATMENT EVALUATION**
- **anti-VEGF PRN Rescue Injection Criteria**

**FOLLOW UP**
- Safety endpoint
- Secondary endpoints

**Previously Treated Subjects Requiring Frequent Injections**

<table>
<thead>
<tr>
<th>Dose 1</th>
<th>Dose 2</th>
<th>Dose 3</th>
<th>Dose 4</th>
<th>Dose 5</th>
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<tr>
<td>n = 6</td>
<td>n = 6</td>
<td>n = 6</td>
<td>n = 12</td>
<td>n = 12</td>
</tr>
<tr>
<td>3x10^9 GC/eye</td>
<td>1x10^10 GC/eye</td>
<td>6x10^10 GC/eye</td>
<td>1.6x10^11 GC/eye</td>
<td>2.5x10^11 GC/eye</td>
</tr>
</tbody>
</table>

**Dosing Completed in 24 Subjects**

1 Dose escalation safety review to occur four weeks after final subject in each cohort has been dosed

Data cut Dec 3rd, 2018

SD-OCT = spectral domain optical coherence tomography
RGX-314 PHASE I/IIA: ELIGIBILITY CRITERIA

Key inclusion criteria

• Male or female ≥ 50 to 89 years of age

• Wet AMD subjects requiring ≥4 anti–VEGF injections in the 8 months prior to trial entry

• Documented response to anti–VEGF at trial entry (assessed by SD–OCT at week 1)

• Vision of 20/63 to 20/400 for the initial subject, then 20/40 to 20/400 for the rest of each cohort

• Pseudophakic (status post cataract surgery)
Anti-VEGF May Be Given **Beginning 4 Weeks** Post-treatment with RGX-314 and **Every 4 Weeks Thereafter PRN**

**Per the Investigator’s Discretion**
If One or More of the Following Criteria Apply:

- CNV-related increased, new, or persistent fluid
- Vision loss of ≥5 letters associated w/ accumulation of fluid
- New ocular hemorrhage
### RGX-314: PHASE I/IIA TRIAL DEMOGRAPHICS & BASELINE FOR COHORTS 1-3

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cohort 1 (n=6)</th>
<th>Cohort 2 (n=6)</th>
<th>Cohort 3 (n=6)</th>
<th>Total (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Age (Years)</td>
<td>78.2</td>
<td>78.0</td>
<td>80.0</td>
<td>78.7</td>
</tr>
<tr>
<td>Female (Number, %)</td>
<td>4 (66.7%)</td>
<td>3 (50.0%)</td>
<td>2 (33.3%)</td>
<td>9 (50.0%)</td>
</tr>
<tr>
<td>Caucasian, No. (%)</td>
<td>6 (100.0%)</td>
<td>6 (100.0%)</td>
<td>6 (100.0%)</td>
<td>18 (100.0%)</td>
</tr>
<tr>
<td><strong>Baseline Characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Months Since First anti-VEGF Injection</td>
<td>53.5</td>
<td>59.3</td>
<td>71.6</td>
<td>61.5</td>
</tr>
<tr>
<td># Injections Since Diagnosis (Mean)</td>
<td>40.7</td>
<td>32.5</td>
<td>34.2</td>
<td>35.8</td>
</tr>
</tbody>
</table>
RGX-314: PHASE I/IIA TRIAL PROTEIN LEVELS AT ONE MONTH FOR COHORTS 1-3

RGX-314 Protein (as measured from aqueous samples by ECL-based assay)

Mean RGX-314 Protein (ng/mL) (log scale)

- **Cohort 1**: 2.4 ng/ml
  - 3x10^9 GC/eye
  - n=6

- **Cohort 2**: 12.8 ng/ml
  - 1x10^{10} GC/eye
  - n=6

- **Cohort 3**: 160.2 ng/ml
  - 6x10^{10} GC/eye
  - n=6
RGX-314: PHASE I/IIA TRIAL MEAN CHANGE IN BCVA, CRT AND AVERAGE INJECTIONS OVER SIX MONTHS, BY COHORT

Best Corrected Visual Acuity (BCVA)

Cohort 1

-2 letters

Cohort 2

+7 letters

Cohort 3

+8 letters

Central Retinal Thickness (CRT) on SD-OCT

Cohort 1

-14 µm

Average Injections: 4.7

Cohort 2

+26 µm

Average Injections: 3.8

Cohort 3

-14 µm

Average Injections: 1.3
## RGX-314: PHASE I/IIA TRIAL SUMMARY OF INTERIM RESULTS THROUGH SIX MONTHS

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Dose Level</th>
<th>Mean Aqueous RGX-314 Protein One Month Post-treatment</th>
<th>Mean # of Anti-VEGF Injections through Six Months</th>
<th>Mean Change in CRT through Six Months (Range)</th>
<th>Mean Change in BCVA through Six Months (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cohort 1</strong></td>
<td>3x10⁹ GC/eye (n=6)</td>
<td>2.4 ng/ml</td>
<td>4.7 inj*</td>
<td>-14 µm** (-181 to +92 µm)</td>
<td>-2 letters** (-8 to +10 letters)</td>
</tr>
<tr>
<td><strong>Cohort 2</strong></td>
<td>1x10¹⁰ GC/eye (n=6)</td>
<td>12.8 ng/ml</td>
<td>3.8 inj</td>
<td>+26 µm (-7 to +62 µm)</td>
<td>+7 letters (-4 to +15 letters)</td>
</tr>
<tr>
<td><strong>Cohort 3</strong></td>
<td>6x10¹⁰ GC/eye (n=6)</td>
<td>160.2 ng/ml</td>
<td>1.3 inj</td>
<td>-14 µm (-27 to +7 µm)</td>
<td>+8 letters (0 to +21 letters)</td>
</tr>
</tbody>
</table>

* One subject in Cohort 1 discontinued from the study at four months with four injections and was imputed as requiring six injections through six months
** n=5; one subject in Cohort 1 discontinued from the study at four months
**RGX-314: SUSTAINED PROTEIN LEVELS AT SIX MONTHS**

All Subjects (N=6) in Cohort 3 (6x10^{10} GC/eye)

- **Month 1**: Mean RGX-314 Protein (ng/mL) = 160.2 ng/ml
- **Month 6**: Mean RGX-314 Protein (ng/mL) = 217.8 ng/ml

*One subject received an anti-VEGF rescue injection 1 month prior to sample.*
RGX-314: SUSTAINED PROTEIN LEVELS AT SIX MONTHS

Subjects with No Rescue Injections (n=3) in Cohort 3 ($6 \times 10^{10}$ GC/eye)
**RGX-314 PHASE I/IIA TRIAL: COHORT 3 SUBJECTS WITH NO RESCUE INJECTIONS THROUGH NINE MONTHS (N=3)**

<table>
<thead>
<tr>
<th>Previous Therapy</th>
<th>Study subjects received on average &gt;35 injections since wet AMD diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Post-RGX-314 Anti-VEGF Injections</strong></td>
<td>0 injections through nine months post-RGX-314</td>
</tr>
<tr>
<td><strong>BCVA</strong></td>
<td>Mean gain in BCVA of +13 ETDRS letters from baseline through nine months</td>
</tr>
<tr>
<td><strong>SD-OCT</strong></td>
<td>Maintained with a mean change in CRT of -37 µm from baseline through nine months</td>
</tr>
</tbody>
</table>
RGX-314 PHASE I/IIA TRIAL: MEAN CHANGE IN BCVA, CRT OVER NINE MONTHS IN COHORT 3 SUBJECTS WITH NO RESCUE INJECTIONS

**Best Corrected Visual Acuity (BCVA)**

![Graph showing BCVA over time with 3 subjects (n=3) and no rescue injections. The graph displays a gradual increase in letters read from D1 to M9 with a +13 letters change.]

**Central Retinal Thickness (CRT) on SD-OCT**

![Graph showing CRT over time with 3 subjects (n=3) and no rescue injections. The graph displays a decrease in CRT from D1 to M9 with a -37 µm change.]

**Cohort 3 with No Rescue Injections (n=3)**
RGX-314 PHASE I/IIA TRIAL: SAFETY FOR COHORTS 1–4*

- RGX-314 was **well-tolerated** (n=24)

- **No drug-related AEs or drug-related SAEs**

- Most AEs were assessed as mild (Grade 1 – 83%)

- **No observed clinically-determined immune responses**, drug-related ocular inflammation, or any post-surgical inflammation beyond what is expected following routine vitrectomy

- **Six SAEs that were not drug-related were reported in four subjects**
  - One subject with a peripheral retinal detachment which was repaired and resolved without sequelae
  - One subject with a hospitalization related to a pre-existing condition that resulted in death
  - One subject with an event assessed mild in severity with no relationship to RGX-314
  - One subject with a diagnosis of cancer recurrence

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* Data cut Dec 3rd, 2018
**RGX-314: PHASE I/IIA TRIAL INTERIM RESULTS**

RGX-314 was **well-tolerated** at all doses (n=24)

Cohort 3: **sustained RGX-314 protein at six months with stability in vision and anatomy** despite **few to no injections**

Cohort 3: **50% of subjects** continue to remain free of injections at **nine months**; **improved vision (+13 letters) and stable CRT (-37 µm)**

Dose dependent protein expression observed from Cohort 1 to Cohort 3

Recently reported Cohort 4: **detectable protein** at one month with a mean higher than Cohort 3

**One-time gene therapy** for wAMD offers the potential to **sustain clinical outcomes** while alleviating treatment burden

* Data cut Dec 3rd, 2018
Robert Avery, MD (Santa Barbara, CA)
David Brown, MD (Houston, TX)
Peter Campochiaro, MD (Baltimore, MD)
Jorge Calzada, MD (Memphis, TN)
Jeff Heier, MD (Boston, MA)
Allen Ho, MD (Philadelphia, PA)
Dante Pieramici, MD (Santa Barbara, CA)
Charles Wykoff, MD PhD (Houston, TX)
Szilard Kiss, MD (New York, NY)
Albert Maguire, MD (Philadelphia, PA)
Sherri Van Everen, PharmD (REGENXBIO)
Darin Curtiss, PharmD (REGENXBIO)
RGX-314 Analyst and Investor Day
Market Opportunity

February 21, 2019
Ram Palanki
SVP, Commercial Strategy and Operations
Topics

What is the current unmet need in wet AMD?

Where does RGX-314 fit in the clinical management of wet AMD?

Will a surgical solution for wet AMD be widely adopted?

What is the potential value of a one-time gene therapy for the treatment of wet AMD?

What is the overall market opportunity for RGX-314 in wet AMD and other retinal conditions?
Topics

What is the current unmet need in wet AMD?

Where does RGX-314 fit in the clinical management of wet AMD?

Will a surgical solution for wet AMD be adopted widely?

What is the potential value of a one-time gene therapy for the treatment of wet AMD?

What is the overall market opportunity for RGX-314 in wet AMD and other retinal conditions?
Real world data suggests patients on average lose visual acuity over time on current treatment regimens

Visual Acuity

Clinical Trial data*

Real-world data**

BCVA Loss
-11 letters

Source: *HARBOR and CATT data; **CATT data
Retina specialists confirm reduced treatment burden and long-acting treatment solutions as the greatest unmet needs

What are the greatest unmet needs regarding wet-AMD treatment?

- **Improved efficacy**: 37.1% (Intl), 31.9% (US)
- **Reduced treatment burden**: 66.1% (Intl), 73.2% (US)
- **Improved safety**: 13.6% (Intl), 6.3% (US)
- **Long-acting/sustained delivery**: 70.6% (Intl), 56.3% (US)
- **New treatment mechanisms of...**: 37.1% (Intl), 37.0% (US)
Topics

What is the current unmet need in wet AMD?

Where does RGX-314 fit in the clinical management of wet AMD?

Will a surgical solution for wet AMD be adopted widely?

What is the potential value of a one-time gene therapy for the treatment of wet AMD?

What is the overall market opportunity for RGX-314 in wet AMD and other retinal conditions?
Single administration of RGX-314 can potentially establish foundational anti-VEGF therapy

**RGX-314 positioning:** Potential one-time anti-VEGF therapy could be sustained over time

*Illustrative*

**Continuous anti-VEGF expression**

*RGX-314 Foundational anti-VEGF Therapy*
Single treatment with RGX-314 has the potential to close the gap between randomized clinical trials and real world outcomes

Visual Acuity

![Graph showing the potential anti-VEGF gene therapy curve](image)

Source: *HARBOR and CATT data; **CATT data

Potential anti-VEGF gene therapy curve hypothesized
Topics

What is the current unmet need in wet AMD?

Where does RGX-314 fit in the clinical management of wet AMD?

**Will a surgical solution for wet AMD be widely adopted?**

What is the potential value of a one-time gene therapy for the treatment of wet AMD?

What is the overall market opportunity for RGX-314 in wet AMD and other retinal conditions?
The majority of retina specialists are surgeons

Are you a medical retina specialist, a surgical retina specialist, or both?

### United States
- Medical and surgical retina: 88.0%
- Medical retina only: 10.2%
- Surgical retina only: 1.8%
- Other: 0.0%

### International
- Medical and surgical retina: 87.8%
- Medical retina only: 7.7%
- Surgical retina only: 3.5%
- Other: 1.0%

n = 1031
Topics

What is the current unmet need in wet AMD?

Where does RGX-314 fit in the clinical management of wet AMD?

Will a surgical solution for wet AMD be adopted widely?

What is the potential value of a one-time gene therapy for the treatment of wet AMD?

What is the overall market opportunity for RGX-314 in wet AMD and other retinal conditions?
**RGX-314 can potentially mitigate the social and economic impact of blindness**

One in five cases of blindness in the US attributable to retinal disease characterized by angiogenic processes\(^1\) that can be prevented with anti-VEGF treatment\(^2\)–\(^7\).

---

**Annual cost per patient*, $**

<table>
<thead>
<tr>
<th>Excess cost per blind patient</th>
<th>Direct Costs</th>
<th>Indirect Costs</th>
<th>Intangible Costs</th>
</tr>
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<tbody>
<tr>
<td>$0</td>
<td>$84,622</td>
<td>$25,062</td>
<td>$54,614</td>
</tr>
<tr>
<td>$10,000</td>
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<td>$4,943</td>
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<tr>
<td>$100,000</td>
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</tbody>
</table>

**Aggregated annual costs*, $MM**

<table>
<thead>
<tr>
<th>Cost in millions</th>
<th>Direct Costs</th>
<th>Indirect Costs</th>
<th>Intangible Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>$1,218</td>
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<td>$1,218</td>
</tr>
<tr>
<td>$13,458</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$20,853 MM</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Topics

What is the current unmet need in wet AMD?

Where does RGX-314 fit in the clinical management of wet AMD?

Will a surgical solution for wet AMD be adopted widely?

What is the potential value of a one-time gene therapy for the treatment of wet AMD?

What is the overall market opportunity for RGX-314 in wet AMD and other retinal conditions?
Anti-VEGF is the largest global ophthalmic pharmaceutical market

Anti-VEGF market projected growth by indication (2018-2023)

- Almost all wet AMD patients are on chronic anti-VEGF Tx
- 50% of patients with DME are on chronic anti-VEGF Tx
- 50% of patients with RVO are on chronic anti-VEGF Tx
- Majority of patients with DR (NPDR and PDR) without DME require chronic anti-VEGF Tx

Number of patient eyes treated with IVT anti-VEGF injections annually (in ‘000s)

<table>
<thead>
<tr>
<th></th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
<th>2022</th>
<th>2023</th>
</tr>
</thead>
<tbody>
<tr>
<td>wAMD</td>
<td>1,306</td>
<td>1,312</td>
<td>1,319</td>
<td>1,325</td>
<td>1,331</td>
<td>1,338</td>
</tr>
<tr>
<td>w/o DME</td>
<td>173</td>
<td>209</td>
<td>245</td>
<td>281</td>
<td>283</td>
<td>284</td>
</tr>
<tr>
<td>NPDR**</td>
<td>237</td>
<td>285</td>
<td>334</td>
<td>383</td>
<td>384</td>
<td>386</td>
</tr>
<tr>
<td>PDR**</td>
<td>497</td>
<td>500</td>
<td>502</td>
<td>505</td>
<td>508</td>
<td>511</td>
</tr>
<tr>
<td>w/o DME</td>
<td>604</td>
<td>606</td>
<td>609</td>
<td>612</td>
<td>615</td>
<td>617</td>
</tr>
<tr>
<td>DME</td>
<td>284</td>
<td>285</td>
<td>334</td>
<td>383</td>
<td>384</td>
<td>386</td>
</tr>
<tr>
<td>RVO</td>
<td>1,306</td>
<td>1,312</td>
<td>1,319</td>
<td>1,325</td>
<td>1,331</td>
<td>1,338</td>
</tr>
</tbody>
</table>

Assumptions: Population growth of ~1% US and ~0% EU5 and Japan

Source: epidemiology data based on literature, diagnosis rates based on Datamonitor Report, DRG Market Forecast Assumptions and REGENXBIO primary market research

*US, EU5, Japan
**NPDR and PDR data only include US population; assuming increase from 50% to 80% aVEGF patient share among treated patients over 3 years

wAMD = wet AMD; DME = Diabetic Macular Edema; RVO = Retinal Vein Occlusion; NPDR = Non-Proliferative Diabetic Retinopathy; PDR = Proliferative Diabetic Retinopathy

*https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5278808/
Thank you
Q & A

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- Board of Trustees of EURETINA

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- Executive Committee of the Retina Society
- Investigator in the RGX-314 Phase I/IIa clinical trial

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- Principal Investigator of the RGX-314 Phase I/IIa clinical trial