Six Month Results of the Phase I Study to Evaluate Safety & Tolerability of RGX-314 Gene Therapy in nAMD Subjects

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RGX-314: Optimized NAV® Gene Therapy for Wet AMD

RGX-314 is Designed to Deliver a Gene Encoding for an anti-VEGF fab Protein
RGX-314: Utilizing AAV8 for Higher Protein Expression in NHPs

AAV2

AAV8

More Efficient Gene Delivery to the RPE

1Vandenberghe et al. 2011 Science Translational Medicine
RGX-314 Phase I Trial: Design

Previously Treated Subjects Requiring Frequent Injections

Dose 1
n = 6
3x10^9 GC/eye

Dose 2
n = 6
1x10^{10} GC/eye

Dose 3
n = 6
6x10^{10} GC/eye

Dose 4
n = 6
1.6x10^{11} GC/eye

Dosing Completed in Four Cohorts

1 Dose escalation safety review to occur four weeks after final subject in each cohort has been dosed
RGX-314: Standardized Automated Subretinal Delivery Procedure

**Step 1 – Vitrectomy**
- Standard **small gauge** vitrectomy to perform a core vitrectomy
- Automated delivery with a **MedOne subretinal cannula** attached to the vitrectomy machine

**Step 2 – Subretinal Injection**
- **Inject 250μl** to create subretinal bleb in a healthy area of retina
- Target superior to the superotemporal arcade vessel or outside the arcades
- Can create another **bleb** area if needed
- Keep margin of the bleb at least 2DA away from the fovea

**Performed Under Local Anaesthesia in the OR**

- **Air fluid exchange** and then **Sub-conj steroids** at the end of procedure
- No positioning mandated and patient is discharged home with follow-up the next day
RGX-314 Phase I Trial: Outcome Measures and Eligibility Criteria

Objectives

Primary

- To determine the safety and tolerability of RGX-314 in patients with nAMD though 6 months

Secondary

- Expression of RGX-314 protein in the eye
- Effect of RGX-314 on best corrected visual acuity (BCVA) and central retinal thickness (CRT)
- Additional anti-VEGF injections post-RGX-314 (“Rescue”)

Rescue: New or Persistent Fluid/ Loss in Vision

- Per the Investigator's discretion

Key Inclusion Criteria

- Documented nAMD with response to anti-VEGF at trial entry
- Vision of 20/63 to 20/400 for the initial patient, then 20/40 to 20/400 for the rest of each cohort
- Pseudophakic (status post cataract surgery)

Subjects: 24 Patients dosed

- 7 study sites across the United States
Anti-VEGF may be given beginning 4 weeks post-treatment and PRN every 4 weeks thereafter per investigator’s discretion if one or more of the criteria apply:

- CNV-related increased, new, or persistent fluid
- Vision loss of ≥5 letters associated with accumulation of fluid
- New ocular hemorrhage
### RGX-314 Phase I Trial: Baseline Demographics 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 Trial: Safety for Cohorts 1-3*

- RGX-314 was **well-tolerated** (n=18)
- 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
- Five SAEs that were not drug-related were reported in three 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

* Data cut July 27th, 2018
RGX-314 Phase I Trial: Protein Levels at One Month for Cohorts 1-3

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 Trial: Mean Change in BCVA, CRT and Average Injections Over Six Months, by Cohort

Best Corrected Visual Acuity (BCVA)

Central Retinal Thickness (CRT) on SD-OCT

Average Injections: 4.7  Average Injections: 3.8  Average Injections: 1.3

Cohort 1  Cohort 2  Cohort 3
# RGX-314 Phase I Trial: Summary of Interim Results Through Six Months

<table>
<thead>
<tr>
<th>Cohort 1</th>
<th>3x10⁹ GC/eye (N=6)</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></td>
<td></td>
<td>2.4 ng/ml</td>
<td>4.7 inj*</td>
<td>-14 µm**</td>
<td>-2 letters**</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(-181 to +92 µm)</td>
<td>(-8 to +10 letters)</td>
</tr>
</tbody>
</table>

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

| Cohort 3 | 6x10¹⁰ GC/eye (N=6) | 160.2 ng/ml                                            | 1.3 inj                                       | -14 µm                                      | +8 letters                                  |
|          |                    |                                                      |                                               | (-27 to +7 µm)                              | (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
RGX-314 Phase I Trial: Sustained Protein Levels at Six Months

All Subjects (N=6) in Cohort 3

*One subject received an anti-VEGF rescue injection 1 month prior to sample.
RGX-314 Phase I Trial: Sustained Protein Levels at Six Months

Subjects with No Rescue Injections (n=3) in Cohort 3

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

Month 1

236.2 ng/ml

Month 6

274.9 ng/ml
RGX-314 Phase I Trial: Mean Change in BCVA, CRT Over Six Months in Cohort 3 Subjects with No Rescue Injections

**Best Corrected Visual Acuity (BCVA)**

Cohort 3 with No Rescue Injections (n=3)

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

Cohort 3 with No Rescue Injections (n=3)
RGX-314: Phase I Trial Interim Results at Six Months Conclusions

- RGX-314 was well-tolerated at all doses
- Dose-dependent RGX-314 protein expression
- Cohort 3: sustained RGX-314 protein at six months with stability in vision and anatomy despite few to no injections
- Cohort 4: a higher dose recently completed dosing
- Gene therapy for nAMD offers the potential to optimize outcomes while alleviating treatment burden
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- Darin Curtis, PharmD (REGENXBIO)
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