A Novel Integrin-Regulating Portfolio for Front and Back of the Eye Diseases

October 10, 2019
Allegro: Corporate Highlights

Privately owned biopharmaceutical company focused on the development of a novel integrin-regulating portfolio for ocular diseases

Strong leadership with over 125 years of combined experience in drug development in ophthalmology

Risuteganib, our lead integrin-regulating compound in retina:
- First to show a reversal of vision loss in dry AMD: Primary endpoint met with statistical significance
- End of Phase 2 meeting with FDA took place late September 2019 with a clear path forward

Expanded our integrin-regulating portfolio with the development of a new drug candidate ALG-1007 for topical use in dry eye disease (DED)
- Ex-US proof-of-concept study will be presented at AAO
- Larger ex-US Phase 2 trial is ongoing
### Allegro’s Novel Integrin-regulating Portfolio Looks Promising in Front and Back of the Eye Diseases

<table>
<thead>
<tr>
<th>Product Candidate</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Milestones</th>
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</thead>
<tbody>
<tr>
<td><strong>Risuteganib</strong></td>
<td>Intermediate Dry AMD</td>
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<td>Positive US Ph 2 results</td>
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<td>(IVT)</td>
<td>Diabetic Macular Edema</td>
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<td>End of Ph 2 meeting with FDA Sept 2019</td>
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<td></td>
<td>Retinitis Pigmentosa</td>
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<td>Ph 3 planned in US</td>
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<td>Evaluating human proof-of-concept</td>
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<td><strong>ALG-1007</strong></td>
<td>Dry Eye Disease</td>
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<td>Successfully completed first human POC study</td>
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<td>(Topical)</td>
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<td>Ex-US Ph 2 read out early 2020</td>
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Risuteganib Regulates Key Integrins to Improve Disease Outcomes

Risuteganib

Key integrin functions

- Mitochondrial Dysfunction
- Inflammation
- Angiogenesis

- Mitochondrial Stabilization (Dry AMD, DME)
- Leakage (DME) Corneal dryness (DED)
- Neovascularization (DME)

Visual acuity gains in Dry AMD and DME come from the mitochondrial stabilization effects of the drug
Objective:
To evaluate the safety and efficacy of 1.0mg of Risuteganib (RSG) intravitreal injection in patients with intermediate non-exudative macular degeneration

Primary Endpoint:
Percentage of population with ≥ 8 letters BCVA gain for 1.0mg RSG (baseline – week 28) vs Sham (baseline - week 12)
### Study Design

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<thead>
<tr>
<th></th>
<th>BSL</th>
<th>Week</th>
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<tr>
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<tr>
<td>Risuteganib 1.0 mg (n=25)</td>
<td>![Inject]</td>
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<tr>
<td>Sham/Crossover (n=14)</td>
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**Multicenter, double masked, sham controlled study at the following sites –**
- Maturi (Midwest Eye Institute); Kunimoto (Retinal Consultants of Arizona); Boyer (Retina-Vitreous Associate Medical Group); Gonzalez (Texas-Valley Retina Institute); Xavier (Miami-Florida Eye Clinic); Singer (Medical Center Ophthalmology Associates)
- Duke Reading Center
## Study Design: Primary Endpoint

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<tr>
<td>Risuteganib 1.0 mg (n=25)</td>
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<td>16</td>
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<tr>
<td>Sham/Crossover (n=14)</td>
<td>Sham Injection</td>
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**Primary Endpoint:** ≥8 letter BCVA gain

**RSG at Week 28 compared to Sham at Week 12**
Positive US Phase 2 Results in Dry AMD
48% of Patients Gained ≥ 8 Letters of BCVA from Baseline

- First to show a reversal of vision loss in dry AMD in a US Phase 2 study
- Primary Endpoint: proportion of subjects with a ≥ 8 letters BCVA gain vs sham injection
- Secondary Endpoints: microperimetry, color vision, and OCT analysis
- No drug related SAEs

Percentage of Subjects with ≥8 Letters Improvement in BCVA

\[ \text{Sham (n=14)} \quad \text{Luminar 2 IVT (n=25)} \]

\[ p^* = 0.013 \]
US Phase 2a Secondary Endpoints

Percentage of Subjects with ≥10 and ≥15 Letters Improvement in BCVA

- Sham (n=14): 1/14 (7.1%) for ≥10 and 0.0% for ≥15
- Luminate 2 IVT (n=25): 8/25 (32.0%) for ≥10 and 5/25 (20.0%) for ≥15

p* = 0.118 for ≥10 letters improvement
p* = 0.139 for ≥15 letters improvement

*2-sided Fisher’s Exact Test
Allegro Is Gearing Up To Initiate Larger Phase 2b/3 in the US

- Successful End of Phase 2 meeting with the FDA Sept 2019
- Clear path forward for a larger Phase 2b/3 in the US
- **Allegro has identified strong baseline OCT anatomic predictors of vision response**
  - Masked OCT analysis done by 2 separate reading centers
- Study design currently under discussion with Allegro’s scientific advisory board with input from retina community
- Larger US Phase 2b/3 trial planned for 1H 2020
Front of the Eye Programs
A **topical** small synthetic peptide that regulates inflammatory integrin functions

**Targets include** αMβ2, the integrin subunit involved in inflammatory pathways and more specifically the complement 3 pathways

By downregulating αMβ2, ALG-1007 **interferes with T-cell adhesion and migration**

This results in **downregulation** of ocular surface inflammation and **improvement** in the signs and symptoms of dry eye disease (DED)
Ex-US Phase 1 Human POC study in Dry Eye Disease: Study Overview

Objective:
To evaluate the safety and dose ranging efficacy of ALG-1007 topical eye drop in patients with moderate dry eye disease (DED)

Exploratory Endpoints:
The improvement in the signs and symptoms of DED at study day 90
ALG-1007: Promising Results in Human POC Clinical Trial

Robust statistically significant efficacy with 0.6% in multiple signs and symptoms

Dose response curve observed - indicating the effect is due to the active ingredient

No AEs even at the highest dose

No reported blurring of vision or eye irritation

NASAL CONJ STAIN - MEAN CFB

- Score
- Weeks
- n=40

p value = analysis of variance between 0.125% and 0.6%, week 12 CFB
Error bars = Standard Error of the Mean

p < 0.001
In Summary

Allegro is focused on a novel integrin-regulating portfolio for ocular diseases.

Lead compound **risuteganib** is being studied in dry AMD and DME.

**Risuteganib met primary endpoint** in intermediate dry AMD US clinical trial.

**Risuteganib is the first to show a reversal of vision loss** in dry AMD.

Allegro has a clear path forward and is gearing up for a **larger US Phase 2b/3 trial** in dry AMD in **1H 2020**.

**ALG-1007** for topical use in dry eye disease demonstrated an **improvement in both signs and symptoms of DED**.

Allegro has initiated a second larger exploratory ex-US DED study looking at higher doses in a vehicle-controlled study.