The Helmsley Charitable Trust

- **Goal:** The Helmsley Charitable Trust aspires to improve lives by supporting exceptional non-profits and other organizations in the U.S. and around the world in health, place-based initiatives, and education and human services.

- **Goal of Type 1 Diabetes (T1D) Program:** Improve the lives of patients with T1D.

- **T1D Program Funding to Date:** ~$180 million to 100+ initiatives.

- **Main Driver of the Technology and Research Portfolios:** Identify and support projects that have a clear impact on T1D patients and a well-defined commercialization pathway.

- **Prime Example:** Allegro, unique business model and a passionate, experienced team.
Allegro Ophthalmics, LLC

- Dedicated to improving vision for patients with **vascular eye diseases** that cause **blindness**

- **Innovative approach** to drug development
  - **Speed**: less than 4 years, from drug discovery to Phase II IND clearance
  - **Efficiency**: less than $20MM, taking Allegro through Phase III for first indication over the next 2 years
Innovative Approach

1. Experienced management with world class support
2. Unmet patient need
3. Clearly defined clinical and regulatory endpoints
4. Novel approach to disease with unique patient benefits
5. Strong IP protection
6. Quick acceleration from drug discovery to human safety & efficacy
7. Efficient leverage of capital to reach key milestones
#1: Experienced Management with World Class Support

**Management Team:** 100+ years combined experience in ophthalmic drug discovery, development & manufacturing

**Board of Directors:** executives experienced in building & growing drug companies; engaged in Allegro’s business strategy & execution

**Scientific Advisory Board:** world class team of seven KOLs guiding Allegro’s R&D strategy & execution
#2: Unmet Patient Need

- **Wet Age-Related Macular Degeneration**
  - *1.5MM patients* in US today; projected 3MM by 2020
  - Current treatment options benefiting approx 40% of patients
  - Annual sales for current treatment options: approx $5B

- **Diabetic Macular Edema**
  - *4.0MM patients* in US today and growing
  - Current treatment options benefiting approx 45% of patients

- **Vitreomacular Traction & Macular Holes**
  - More than *250,000 patients* in US affected with VMT
  - Current pharmaceutical treatment option benefiting only 26% of patients (or surgery for worst cases)
#3: Clearly Defined Clinical & Regulatory Endpoints

- **Wet AMD and DME**
  - Improvement in best corrected visual acuity
  - Reduction in central macular thickness, measured by OCT imaging

- **VMT**
  - Release of vitreomacular traction
  - Closure of macular holes (secondary)
First in class molecule for ophthalmology with unique MoA
  - Targeting integrin vs. VEGF
  - Small molecule vs. large antibody

Differentiated from current treatment options
  - Longer lasting clinical benefit: quarterly vs. monthly injections
  - Additional vision improvement over current treatment options
  - Vision improvement for the ~60% not responding to current treatment options
#5: Strong IP Protection

- Composition of matter patents pending
  - US and internationally
  - Patent first filing dates: 2009 & 2010

- PCT written opinion issued
  - Novel
  - Inventive
  - Industrial applicability
If it is not going to be safe and effective, let’s find out ASAP!

- **2009**: Molecule discovered
  - First in vitro testing

- **2010**: Phase I DME Study
  - (15 patients)
  - SAB and BoD formed

- **2011**: PK Study
  - Genotoxicity studies
  - cGMP manufactured product

- **2012**: Animal safety studies (x5)
  - First provisional patent application

- **2013**: In vivo mouse model efficacy studies
  - (x4)
  - Phase Ib/Ila Wet AMD Study (22 patients)

- **2014+**: Phase II VMT Study
  - (60 patients)
  - Phase II DME Combo Study (28 patients)
  - IND clearance

- **2014+**: Phase II/III VMT & Wet AMD Studies
Animal Efficacy (HCT Funded Research)

- ALG-1001 uniquely modulates the three destructive aspects of retinal angiogenesis
  - Regresses existing blood vessels (CNV/Wet AMD Model)
  - Inhibits development of new blood vessels (ROP/Diabetic Retinopathy Model)
  - Reduces vascular leakage (hVEGF Model)

Source: Peter Campochiaro, MD (Johns Hopkins University).
Phase I Human DME Study

- End-stage patients, many not responding to anti-VEGF
- Average BCVA improvement: 11 letters (or ~2 lines) 2 months off-treatment
- 8 patients improved 3-5 lines on eye chart
- Improvements held 3+ months off-treatment
- Corresponding improvement of BCVA and CMT
- No patients lost vision
Phase Ib/IIa Human Wet AMD Study

- Peak average BCVA improvement with 3.2mg: 5.2 letters 60 days off-treatment
- Corresponding improvement of BCVA and CMT
- Improvements held 4+ months off-treatment
- Several patients still holding 6+ months off-treatment
In Progress & Planned

- **Objective**: Request FDA approval for VMT by 2016 and Wet AMD by 2018

- **IND clearance from FDA in September 2013**
  - Phase II VMT Study
  - Phase II Wet AMD Study

- **Two clinical studies in progress**
  - Phase II DME Combo Study (ALG-1001 + anti-VEGF)
  - Phase II VMT Study

- **Additional planned studies for 2014**
  - Phase III VMT Study
  - Phase II Wet AMD Study
#7: Efficiently Leverage Capital

**Speed**
Less than 4 years: from drug discovery to Phase II IND clearance

**Efficiency**
Less than $20MM: taking Allegro through Phase III for first indication over the next 2 years
Molecule discovered
First in vitro testing

Phase I DME Study (15 patients)
SAB and BoD formed

PK Study
cGMP manufactured product
Genotoxicity studies

Animal safety studies (x5)
First provisional patent application

In vivo mouse model
efficacy studies (x4)
Phase Ib/IIa Wet AMD Study (22 patients)

Phase II VMT Study (60 patients)
Phase II DME Combo Study (28 patients)
IND clearance

Phase II/III US Clinical Studies

Step 1: Founders’ Seed Funding
Step 2: Grant from HCT
Step 3: Series A Financing
Step 4: License to Senju

2009 2010 2011 2012 2013 2014
The Role of Entrepreneurial Philanthropy

- **$620,000 grant** from The Helmsley Charitable Trust to Johns Hopkins University
- Grant to **achieve specific milestones** to progress ALG-1001 toward commercialization
- Complemented by **private investment**
- Enabling (and validated by) **licensing deal** that further progresses ALG-1001
- **Additional opportunity for entrepreneurial philanthropy:** Phase II Wet AMD Study ($12MM over 2 years)
Marching Forward to Commercialization

• Motivated and inspired by:
  – Unmet patient need
  – Opportunity to treat multiple retinal diseases
  – Results to date showing significant improvement for patients

• Appreciation for HCT’s vision and commitment

• Continued focus: efficiency and speed to bring ALG-1001 to patients across multiple conditions