Gaining Momentum in Gene Therapy

OIS@ASRS

July 25, 2019
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Adverum is a Clinical-stage Gene Therapy Company with Industry-leading Expertise

**ADVM-022, single-injection gene therapy candidate targeting wet AMD:**
- First intravitreally-delivered gene therapy for wet AMD utilizing proprietary AAV.7m8 vector
- OPTIC Phase 1 trial evaluating ADVM-022 in patients with wet AMD
- OPTIC 24-week primary and secondary endpoint data from first cohort (n=6) to be presented at Retina Society 9/2019

**Industry-leading AAV platform and capabilities:**
- Next-generation vectors
- Robust patent portfolio
- Scalable manufacturing process

**~$189.5M in cash* to fund operations into 2021**

**Leadership team with extensive industry expertise**

*Cash, cash equivalents, and short-term investments as of March 31, 2019 (unaudited).
# Advancing Gene Therapies for Ocular and Rare Diseases

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<thead>
<tr>
<th>Gene Therapy Candidate</th>
<th>Research</th>
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<th>Phase 1</th>
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<tr>
<td><strong>Programs – Worldwide Rights</strong></td>
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<tr>
<td>ADVM-022</td>
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<td>OPTIC Trial for Wet Age-related Macular Degeneration (AMD)</td>
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<td>Additional VEGF-driven Retinal Diseases</td>
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<td>Hereditary Angioedema (HAE)</td>
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<td>Alpha-1 Antitrypsin (A1AT) Deficiency</td>
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<td><strong>Partnered Programs</strong></td>
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<td>Up to 5 Undisclosed Targets</td>
<td>Inherited Retinal Disease</td>
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<td>X-linked Retinoschisis +3 Undisclosed Targets</td>
<td>Ophthalmic Disease</td>
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ADVM-022: Gene Therapy Designed to Provide Long-term Anti-VEGF Treatment with a Single Intravitreal Injection

- **Single intravitreal** injection of ADVM-022 to provide sustained delivery of standard-of-care anti-VEGF protein
- **Robust protein levels** measured in non-human primate (NHP) vitreous humor up to **30 months** post injection
- **Long-term efficacy demonstrated** in NHPs comparable to an anti-VEGF standard-of-care therapy
- **Long-term safety demonstrated**: Normal retinal structure and function is **maintained out to 30 months** in NHPs post injection
- Proprietary AAV.7m8 vector and promoter sequences
- Broad patent protection
- FDA Fast Track Designation for wet AMD
Single Injection of ADVM-022 in NHPs Shows Efficacy 13 Months Post Injection Comparable to Standard-of-Care

ADVM-022 Long-term Efficacy (AAV.7m8-aflibercept)

- 40% Grade IV CNV Lesions for Vehicle (n=8 eyes)
- 5% Grade IV CNV Lesions for Aflibercept (n=8 eyes)
- 6% Grade IV CNV Lesions for ADVM-022 (n=8 eyes)

13 months post-injection (2x10^{12} vg/eye)
Administered at time of lesion

*p < 0.0001 vs. vehicle


NHP = Non-human primates
Single IVT ADVM-022: Long-Term Sustained Aflibercept Expression Levels Comparable to Aflibercept-injected Eyes

ADVM-022 Sustained Expression in Vitreous up to 21 Months

ADVM-022 Sustained Expression in Vitreous and Aqueous Humor 30 Months Post Injection

› ADVM-022 induces robust and persistent aflibercept expression in the vitreous over the 21-month study in lasered and non-lasered eyes

› At 30 months post-injection of ADVM-022, pharmacologically-relevant levels of aflibercept were induced in the vitreous and aqueous humor

* Time after IVT bolus of aflibercept protein (1.2 mg/eye) when similar aflibercept levels were observed in NHPs. (Grishanin et al, ESGCT 2018)

Source: Oral presentation, American Society of Gene and Cell Therapy (ASGCT) 22nd Annual Meeting, May 2019

NHP = Non-human primates
ADVM-022 Induced Aflibercept Levels in NHPs within Therapeutic Window for Standard-of-care Aflibercept Treatment

Levels of vector-derived aflibercept measured in the vitreous humor 56 days post ADVM-022 injection match levels of aflibercept recombinant protein 3-4 weeks post-bolus of protein injection.

Measured levels are within the duration of action for aflibercept.

Source: Poster presentation, American Society of Gene and Cell Therapy (ASGCT) 21st Annual Meeting, May 2018
NHP = Non-human primates
Long-term Expression of Aflibercept in Retina from ADVM-022 Does Not Affect Retinal Morphology

OCT sections of retinas from NHP IVT injected with ADVM-022 (2 x 10^{12} vg/eye) at baseline and 30 months post-dose

Source: Oral presentation, American Society of Gene and Cell Therapy (ASGCT) 22nd Annual Meeting, May 2019
Normal ERG Responses upon Sustained Expression of Aflibercept in NHP Eyes Dosed with ADVM-022

No significant difference between vehicle and ADVM-022 groups observed

Treated eyes 30 months post-dose is within normal mfERG response limits

Source: Oral presentation, American Society of Gene and Cell Therapy (ASGCT) 22nd Annual Meeting, May 2019
NHP = Non-human primates
ERG = Electroretinography
ADVM-022 OPTIC Phase 1 Trial for Wet AMD
Initiated 4Q18, Currently Enrolling Cohort 2

Baseline assessment

Treatment evaluation

Follow-up

**Screening**
- Aflibercept Injection
- SD-OCT Assessment

**Anti-VEGF rescue therapy administered if retreatment criteria met**

**Primary endpoint (Safety) 24 weeks**
- Change in BCVA at 24 weeks
- Change in CRT at 24 weeks
- Anti-VEGF rescue injections through 104 weeks

**Secondary endpoints (Efficacy)**

- Change in BCVA at 24 weeks

- Change in CRT at 24 weeks
- Anti-VEGF rescue injections through 104 weeks

- Additional cohort, if needed

**Cohort 1:** 6x10^{11} vg n=6

**Cohort 2:** 2x10^{11} vg n=6

✓ DMC Safe to Proceed

Assess tolerability and efficacy

**Day 1**
- ADVM-022 Injection
- Prophylactic oral corticosteroid taper (13 days total)

**Weeks**
- 4
- 8
- 12
- 16
- 20
- 24
- 104

OCT = Optical Coherence Tomography
Upcoming Corporate Milestones

<table>
<thead>
<tr>
<th>ADVM-022 for Wet AMD</th>
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<tr>
<td>✓ Dosed first patient in OPTIC phase 1 cohort 2 at $2 \times 10^{11}$ vg/eye</td>
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<td>OPTIC phase 1 data from first cohort to be presented at The Retina Society 52\textsuperscript{nd} Annual Meeting</td>
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<td>Occupy new facility with expanded in-house process development capabilities to 1000L</td>
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|$189.5M in cash^*$ to fund operating expenses and capital expenditures into 2021

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Nasdaq: ADVM