



Gaining Momentum in Gene Therapy

Corporate Presentation

August 2017

Forward-looking Statements

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Gene Therapy Leader With Strong Capabilities and Expertise to Develop Novel Medicines for Patients



Industry-leading process development and vector development capabilities



Three programs moving towards the clinic for serious rare and ocular diseases:
A1AT deficiency, HAE, and wet AMD



\$197M in cash* to fund lead programs through 2019



Leadership team with **extensive clinical development expertise**

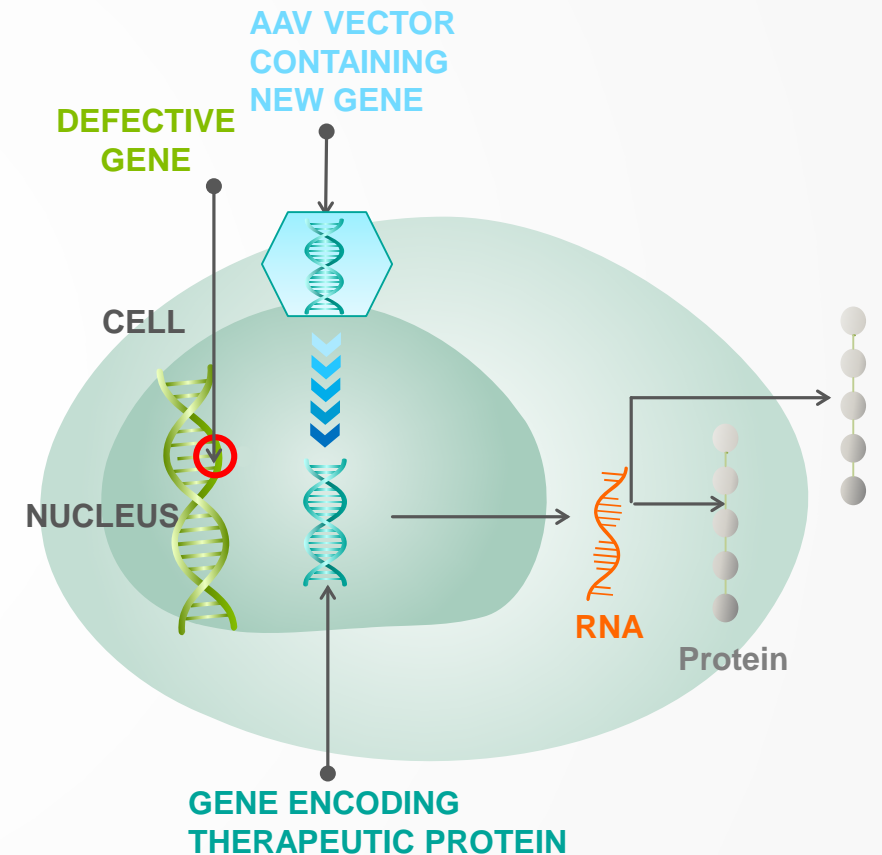
Adverum's Approach: AAV Gene Therapy Platform

Efficacy

- › Highly efficient transfer of DNA to patient
- › Long-lasting potential

Safety

- › Non-integrating vector genome
- › Therapeutic proteins expressed from within, rather than introducing an exogenous protein
- › No known associations with disease
- › Safely used in more than 100 gene therapy clinical trials to date¹





Adverum's In-house Manufacturing Expertise Derisks Process to Support Clinical and Commercial Product Supply



- › Process development capabilities to deliver scalable process to GMP contract manufacturer
 - Baculovirus/Sf9 production system applicable to multiple AAV serotypes
 - State-of-the-art bioindustry technology for purification
 - Process is readily transferred to CMO
- › Assay development capabilities and GMP quality control to optimize product release for human use

Advancing Gene Therapies for Serious Rare & Ocular Diseases

Product Candidate	Stage of Development		
	Research	Preclinical	Phase 1/2
Lead Programs – Worldwide Rights			
ADVM-043 (Rare Disease)	Alpha-1 Antitrypsin (A1AT) Deficiency		
ADVM-053 (Rare Disease)	Hereditary Angioedema (HAE)		
ADVM-022 (Ocular Disease)	Wet Age-related Macular Degeneration (wAMD)		
Partnered Programs			
Up to 5 Undisclosed Targets	Inherited Retinal Disease		 Collaboration
X-linked Retinoschisis and 3 Undisclosed Targets	Ophthalmic Disease		 Collaboration

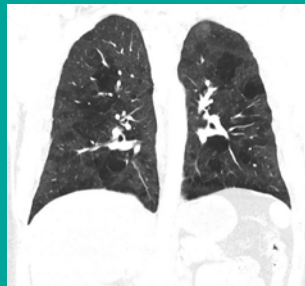
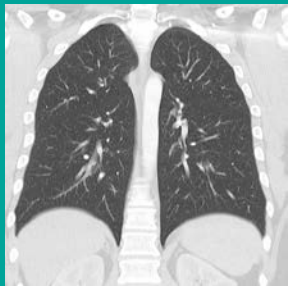
Adverum's Lead Gene Therapy Programs



Alpha-1 Antitrypsin (A1AT) Deficiency

Healthy

Affected



Hereditary Angioedema (HAE)



Wet Age-related Macular Degeneration (wAMD)

A1AT Deficiency is an Orphan Disease and Compliance With Current Treatment is Challenging



- › 100,000 U.S. patients¹
- › Genetic mutation results in very low levels of A1AT
 - A1AT deficiency is associated with premature emphysema
- › Challenging compliance
 - Need for weekly IV infusions² (\$100K annually)
 - Worsening lung function from underdosing

¹ Healthcare Provider's Guide. The Alpha-1 Foundation. Version 2.0 (2015).

² Glassia, Prolastin-C, Aralast NP, Zemaira.

Potential to Treat A1AT Deficiency With ADVIM-043

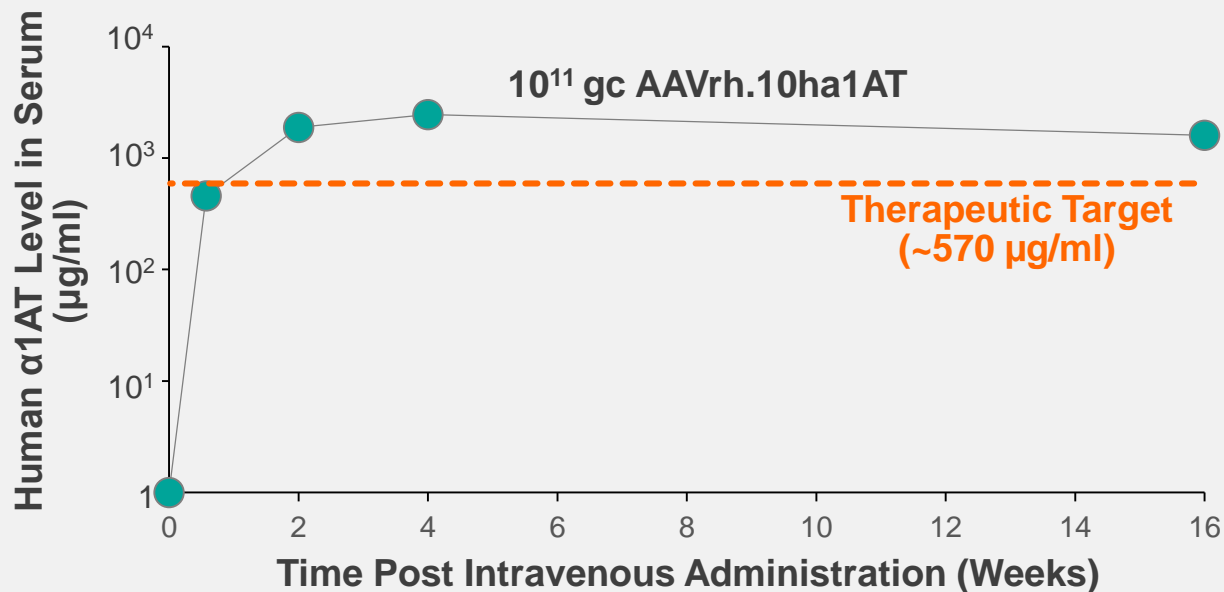


- › **Single administration of ADVIM-043** demonstrated robust A1AT expression in preclinical proof-of-concept study
 - A1AT protein expression above therapeutic levels in mice following either intravenous or intrapleural administration
- › Evidence of stable long-term expression of hA1AT mRNA out to 1 year following intrapleural administration in non-human primates¹
- › ADVIM-043 has the potential to induce stable, long-term A1AT expression at therapeutic levels

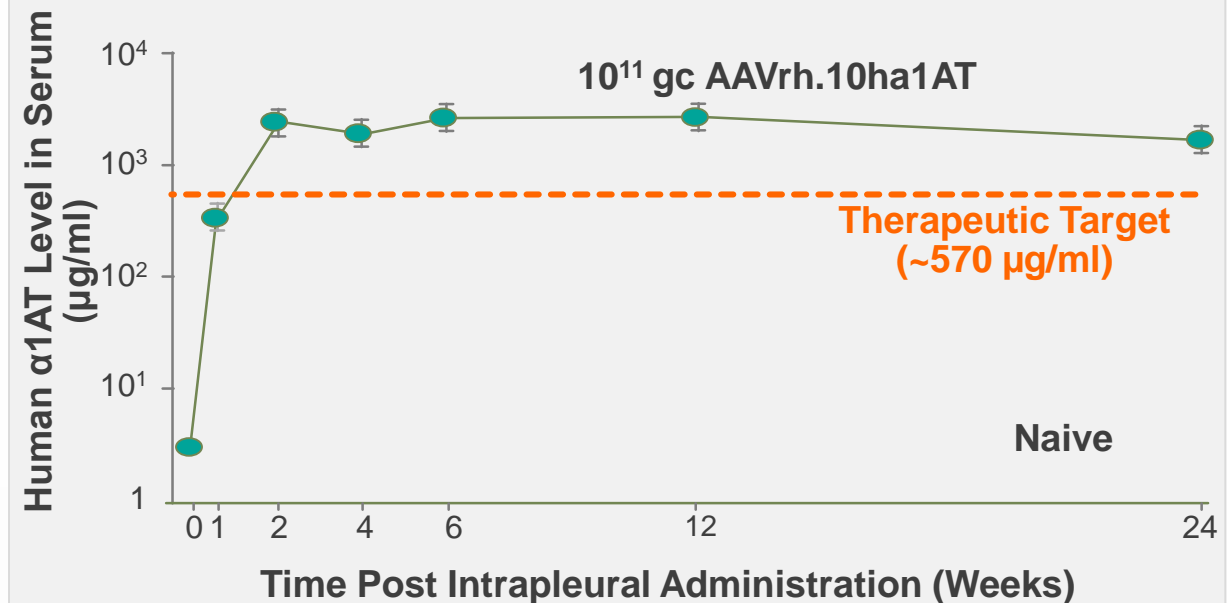
Proof-of-concept Study: Single Administration of ADVM-043 Induces Stable, Long-term Expression of hA1AT

Human A1AT Expression in Serum After ADVM-043 Administration

Intravenous (IV) Delivery¹



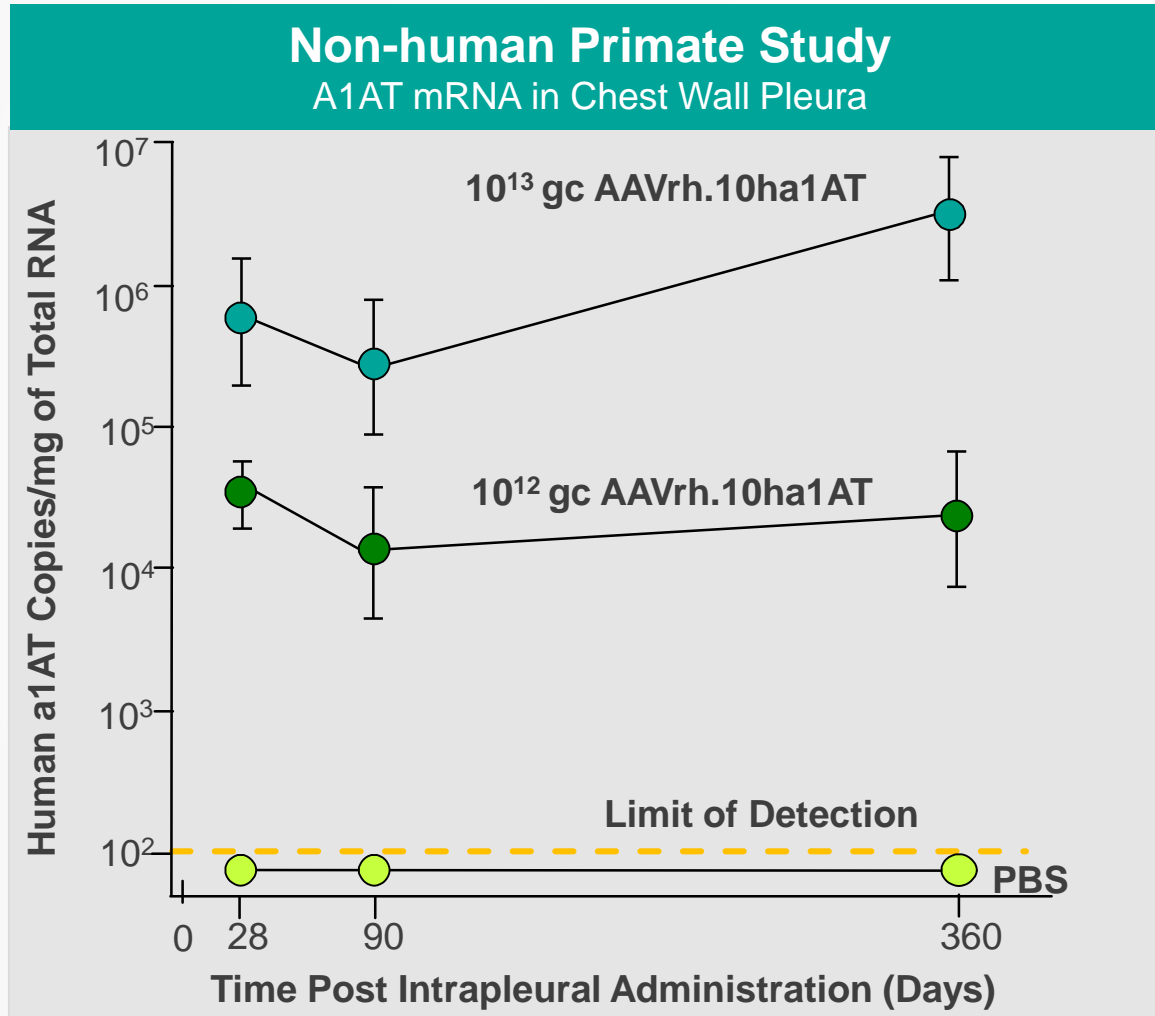
Intraleural (IP) Delivery²



¹ Company data on file

² High Levels of Persistent Expression of A1-Antitrypsin Mediated by the Nonhuman Primate Serotype rh.10 Adeno-associated Virus Despite Preexisting Immunity to Common Human Adeno-associated Viruses, Mol Ther Vol. 13, No. 1 (January 2006), De et al.

Proof-of-concept: Single Intrapleural Injection of ADVM-043 Induces High, Stable Human A1AT mRNA Expression Out to 12 Months



➤ Stable expression of human A1AT mRNA >1 year after single intrapleural delivery¹

Advancing ADVIM-043 for A1AT Deficiency Into the Clinic



Next steps

- › Upgrading manufacturing process to robust, commercial-grade baculovirus-based process
- › Met with FDA regarding open IND in July 2017
- › Planning to begin enrolling patients in a Phase 1/2 trial in 4Q17

Adverum's Lead Gene Therapy Programs



**Alpha-1 Antitrypsin
(A1AT) Deficiency**



**Hereditary
Angioedema (HAE)**



**Wet Age-related
Macular Degeneration
(wAMD)**

HAE is an Orphan Disease That is Challenging to Manage



- › 8,000 U.S. patients¹
- › Genetic mutation results in low levels of C1-esterase inhibitor (C1EI)
 - Low C1EI levels lead to sudden swelling/edema of respiratory airways, GI tract, and extremities
- › Challenging management strategy
 - Prophylaxis requires 2-3x/week IV infusions of C1EI²
 - Breakthrough attacks still occur

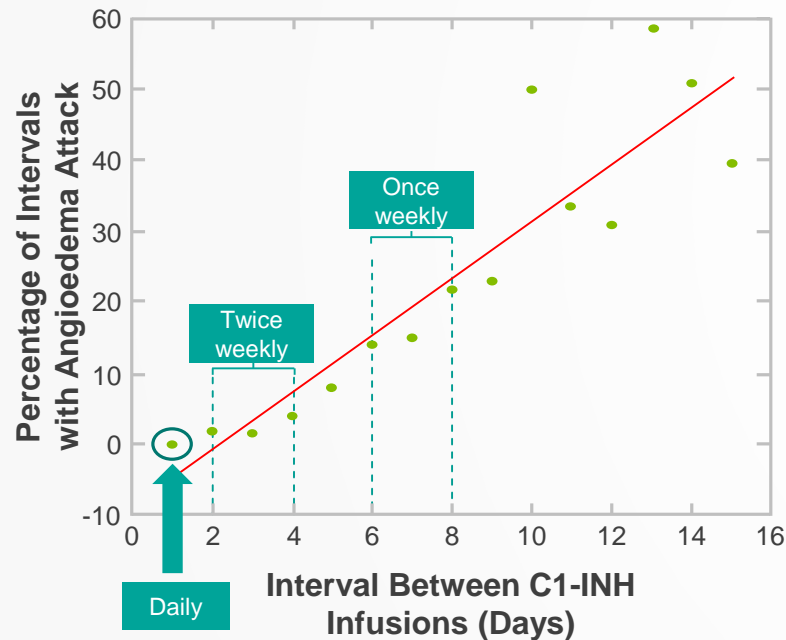
Potential to Prevent HAE Attacks with ADVM-053



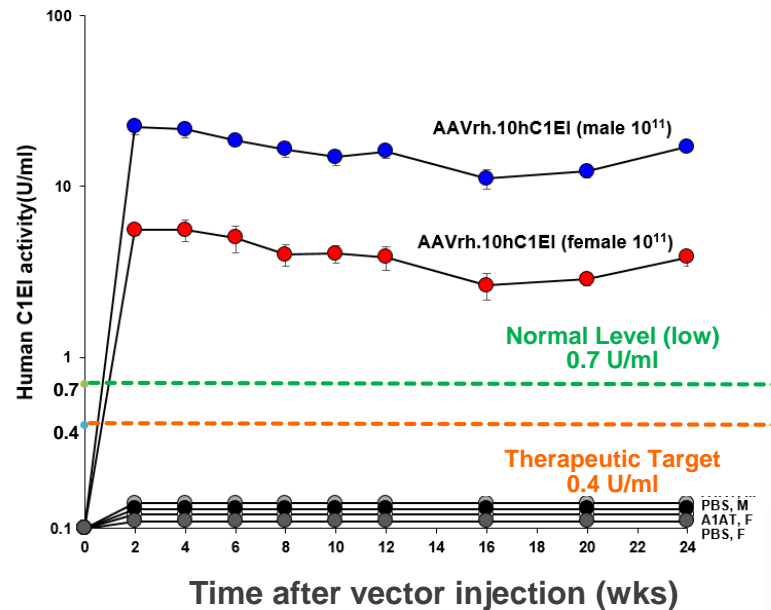
- › **Single intravenous administration of ADVM-053** showed robust C1EI expression in preclinical studies
 - C1EI protein expression above therapeutic levels
 - Decreased vascular permeability, the hallmark of the disease
- › ADVM-053 has the potential to prevent HAE attacks

Proof-of-concept Study: Single IV Injection of ADVM-053 Induces Protein Expression Above Therapeutic Level

Attack rate drops to near zero with daily C1-INH infusion¹
(not clinically practical)



ADVM-053 induces expression above therapeutic level in mice



ADVM-053 showed decrease in vascular permeability to wild type levels

Efficacy in C1EI Deficient Mouse Model



Wild Type²

S63
C1EI Deficient

S63
ADVM-053

24 Weeks Post Injection

Presence of pathology will result in dye leaking into tissues (vasodilation)

¹ Safety and Efficacy of Prophylactic nanofiltered C1-inhibitor in Hereditary Angioedema, Amer J Med 2012;125, 938.e1-938.e7, Zuraw BL and Kalfus I

² Wild type picture is two weeks post injection

Advancing ADVIM-053 for HAE



Next steps

- › Held pre-IND meeting with FDA in 1Q17
- › Transferring robust process to contract manufacturing organization to produce clinical materials
- › Planning to file IND

Adverum's Lead Gene Therapy Programs



**Alpha-1 Antitrypsin
(A1AT) Deficiency**



**Hereditary
Angioedema (HAE)**



**Wet Age-related
Macular Degeneration
(wAMD)**

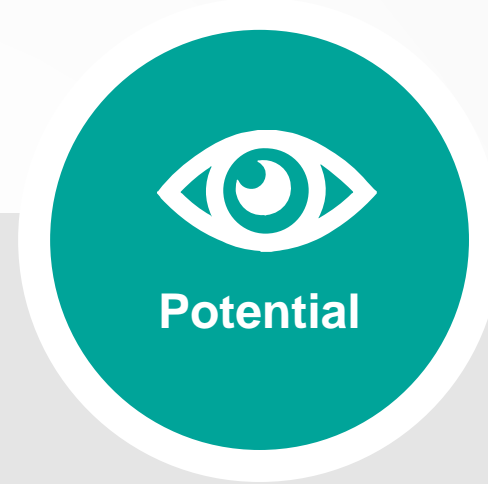
wAMD is a Large Market with Challenging Compliance Issues



Intermediate AMD - 20/20-20/30 Vision



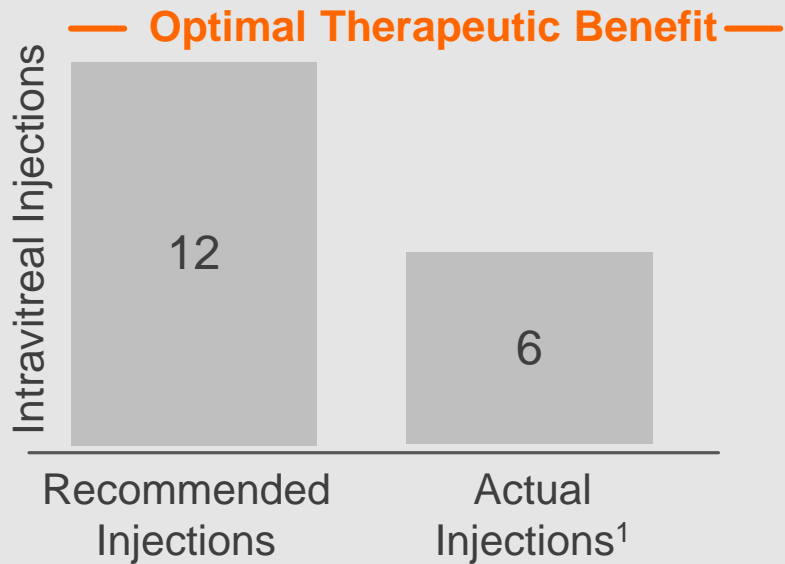
Wet AMD at Diagnosis - 20/80 Vision



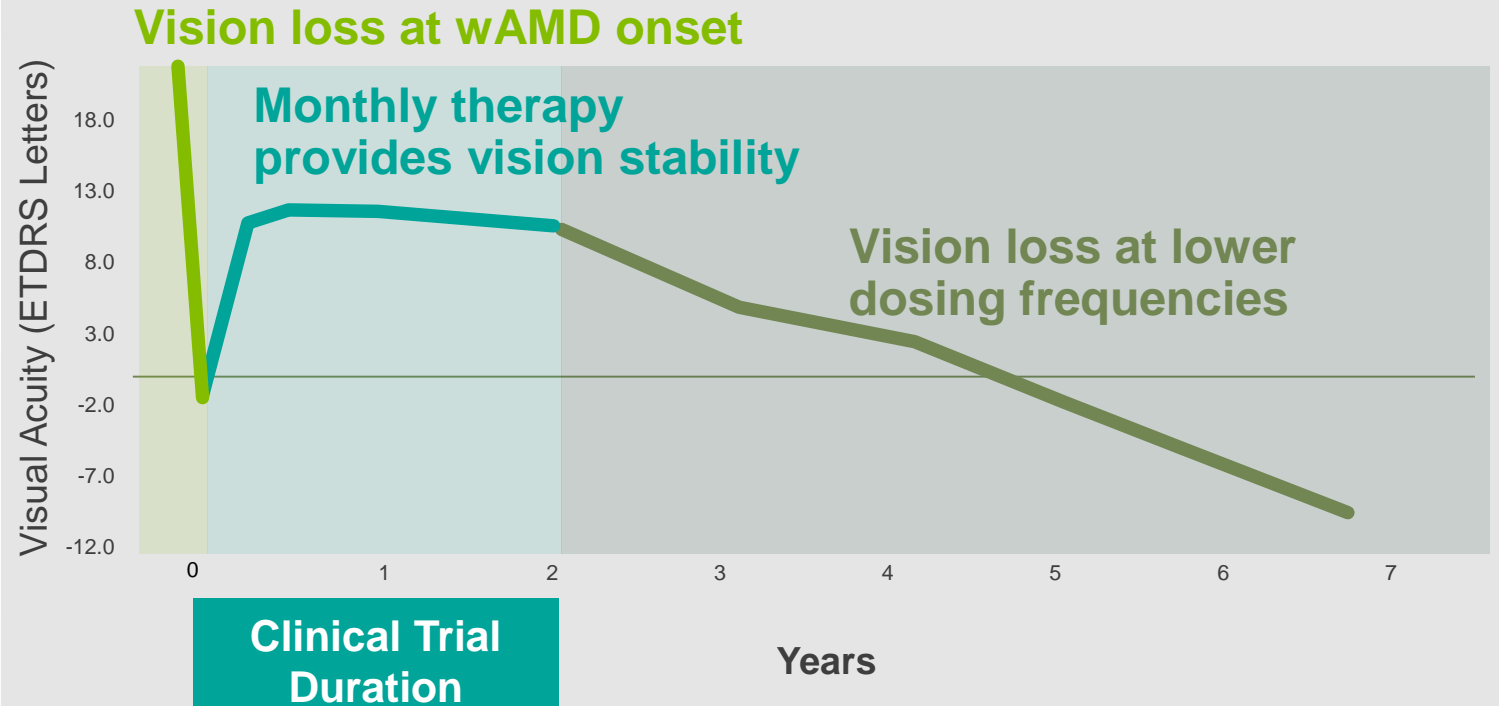
- › Vision loss from abnormal blood vessel proliferation and leakage due to VEGF activity
- › 1.2M U.S. patients¹, 3M globally
- › \$8B global sales for anti-VEGF proteins
- › Challenging compliance
 - Need for monthly/every other month intravitreal injections
 - Vision loss from underdosing

Significant Opportunity to Improve wAMD Therapy

Compliance with Monthly Injections is Difficult



Poor Compliance Leads to Vision Loss²



¹ Clinical utilization of anti-VEGF agents and disease monitoring in neovascular age-related macular degeneration, Am J Ophthalmol. 2014;157(4):825-833, Holekamp NM, et al.

² Multiple studies (MARINA/ANCHOR & HORIZON/SEVEN-UP, SECURE, CATT) indicate that vision benefits are lost at less than recommended dosing frequencies

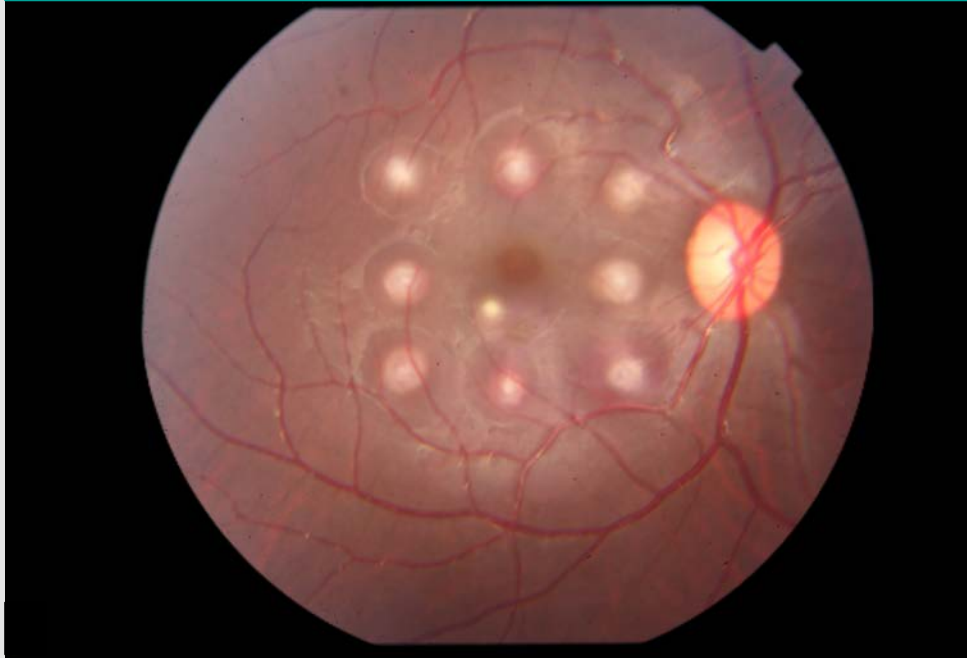
Potential to Treat wAMD With a Intravitreal Injection



- › **Intravitreally-delivered** gene therapy, ADVIM-022, showed durable anti-VEGF expression in pre-clinical proof-of-concept studies
 - **Injection avoids subretinal surgery**
- › **ADVIM-022** (AAV.7m8-aflibercept) advancing
 - Robust protein levels seen in vitreous and retinal tissue at 20 weeks post injection

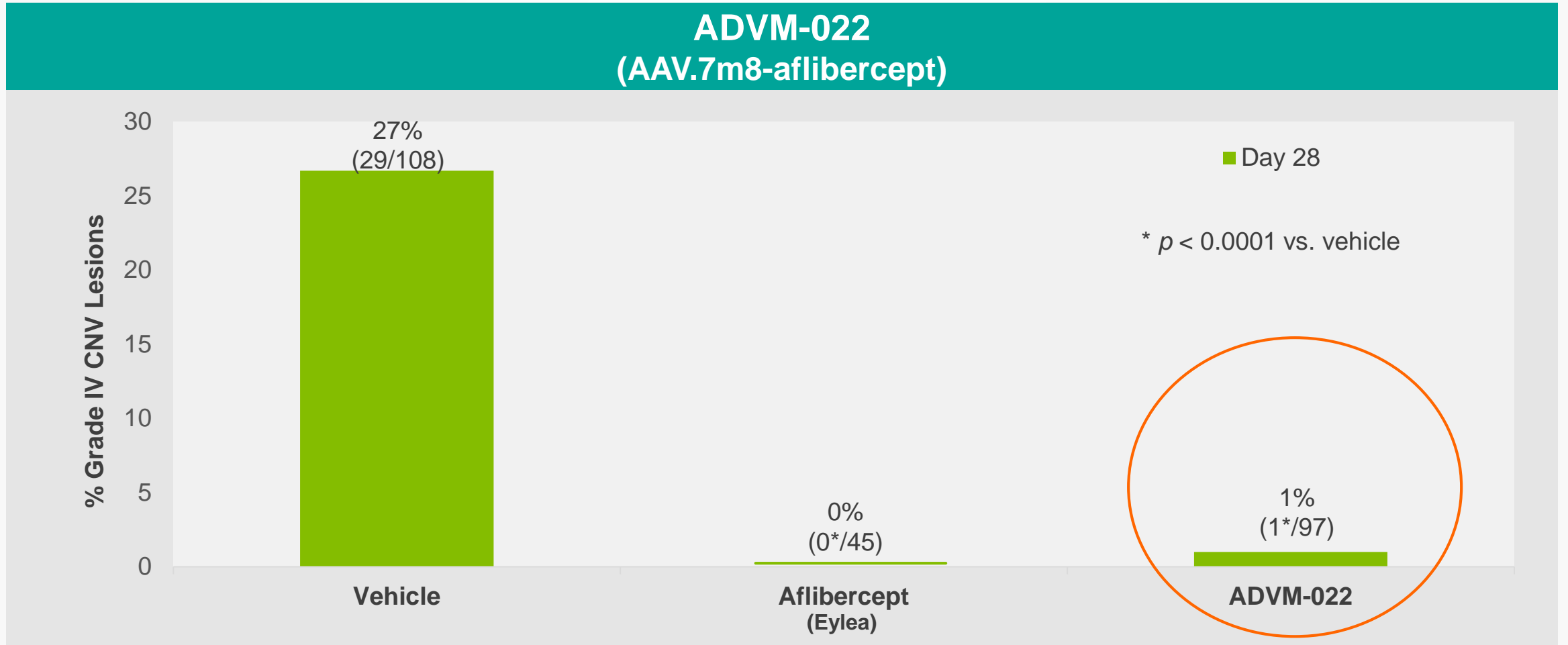
Industry-standard Model Used to Test New wAMD Therapies

Retinal Image after Laser Treatment



- › Choroidal neovascularization (CNV) is induced experimentally by laser
- › Nine lesions per eye are graded for severity (grades I-IV)
- › Efficacy is assessed by reduction of the number of most severe, clinically relevant (grade IV) lesions

Single Injection ADVM-022: 28-Day Efficacy Comparable to Positive Control



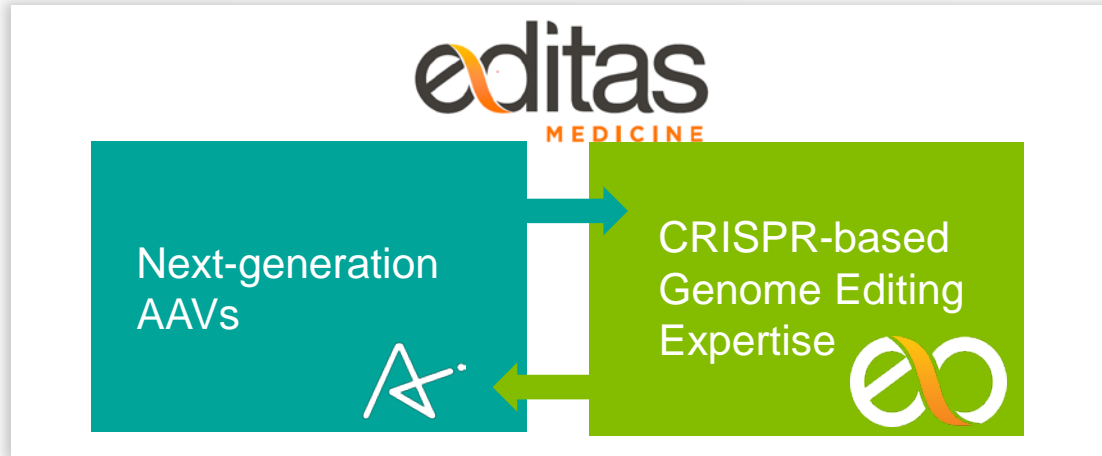
Advancing Intravitreally-delivered ADVM-022



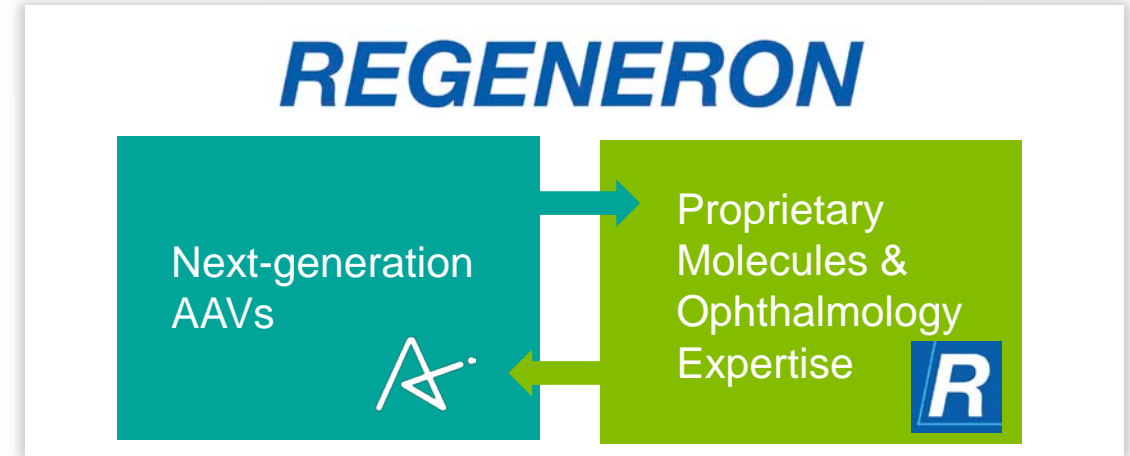
Next steps

- › Evaluating durability of anti-VEGF protein expression beyond 20 weeks
- › Held pre-IND meeting with FDA in 1Q17
- › Planning to file IND

Adverum's Leadership in Ophthalmic Vector Development, Product Delivery Has Led to Collaborations



- › Up to 5 ophthalmic indications
- › CRISPR technology delivery
- › \$1M upfront* to evaluate next-generation AAV vectors
- › \$1M option exercise fee for each indication
- › Up to a mid-teen, million-dollar amount in development and commercialization milestones for each product
- › Tiered royalties from mid-single digits to low-teens on net sales of each product



- › Up to 8 ocular therapeutic targets (4 already identified)
 - AVA-311 for juvenile X-Linked Retinoschisis (XLRS) as first collaboration program
- › Adverum has option to share up to 35% on profits and development costs for two targets
- › \$8M initial payment, up to \$640M in payments upon achievement of milestones, low to mid-single digit royalties on WW net sales
- › Initial 3-year collaboration term recently extended by additional 3 years to May 2020






Industry-leading Capabilities in Novel Vector Development



Adverum's Research Initiatives

- › Research to discover next-generation vectors
 - Directed evolution and rational design of AAV capsids
 - Potential for better transduction efficiency, antibody neutralization profiles
- › Discovery of improved ubiquitous and cell-specific promoters, expression cassettes
 - Potential for optimal transgene expression upon transduction in target tissue
 - Opportunity to decrease off-target effects
- › Production of sufficient high-throughput libraries for screening in large animal studies
- › Development of novel expression cassettes

Leadership Team: Significant Clinical Development Experience

Name	Background	Experience
<p>Amber Salzman, Ph.D. President and CEO</p>	<p>25+ years experience in pharma and biotech management with 15+ years leading gene therapy and rare disease initiatives</p>	
<p>Leone Patterson Chief Financial Officer</p>	<p>20+ years experience in management and financial operations</p>	
<p>Athena Countouriotis, M.D. SVP, Chief Medical Officer</p>	<p>10+ years experience leading drug development programs with several successful approvals, orphan oncology experience</p>	
<p>Mehdi Gasmi, Ph.D. Chief Science and Technology Officer</p>	<p>20+ years experience developing gene therapy vectors for the treatment of common and rare diseases</p>	
<p>Jennifer Cheng, Ph.D., J.D. VP and General Counsel</p>	<p>15+ years experience in biotechnology companies, including legal and intellectual property counsel and research</p>	

Adverum: Clinical-stage Company in 2017



Industry-leading AAV Platform



Pipeline of three lead gene therapy programs with worldwide rights and freedom to operate



Cash resources* to fund lead programs through 2019



Team with extensive gene therapy expertise

* \$197M in cash, cash equivalents, and marketable securities as of June 30, 2017
43.3M shares outstanding as of July 31, 2017

The logo for Adverum Biotechnologies features the word "ADVERUM" in a large, teal, sans-serif font. The letter "A" is stylized with a small yellow dot above it. Below "ADVERUM", the word "BIOTECHNOLOGIES" is written in a smaller, green, all-caps, sans-serif font. The background is white with decorative, curved lines in shades of teal and green on the left and right sides.

ADVERUM
BIOTECHNOLOGIES

Nasdaq: ADVM