



Gaining Momentum in Gene Therapy

Corporate Presentation

May 2017

Forward-looking Statements

Statements contained in this document regarding matters that are not historical facts are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements include, but are not limited to, statements regarding Adverum Biotechnologies, Inc.’s (“Adverum”) plans, potential opportunities, expectations, projections, goals, objectives, milestones, strategies, product pipeline, the sufficiency of its resources to fund the advancement of any development program or the completion of any clinical trials, and the safety, efficacy, and projected development timeline and commercial potential of products under development, all of which are based on certain assumptions made by us on current conditions, expected future developments and other factors we believe are appropriate in the circumstances. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, risks and uncertainties inherent in the product development and the regulatory approval process, delays in clinical trials and other matters that could affect the availability or commercial potential of product candidates, the risk of a delay in the enrollment of patients in Adverum’s clinical studies or in the manufacturing of products to be used in such clinical studies, reliance on third parties, the ability to project future cash utilization and reserves needed for contingent future liabilities and business operations, the availability of sufficient resources for its operations and to conduct or continue planned development programs and planned clinical trials and the ability to successfully develop any of its product candidates. Risks and uncertainties facing Adverum are described more fully in Adverum’s periodic reports filed with the SEC. All forward-looking statements contained in this press release speak only as of the date on which they were made. Adverum undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

This document contains estimates, projections and other information concerning Adverum’s industry, business and the markets for certain drugs, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources believed to be reliable, but the accuracy or completeness of such information is not guaranteed by, and should not be construed as representations made by Adverum.

Strong Capabilities and Expertise to Develop Novel Gene Therapies for Patients



Industry-leading process development and vector development capabilities



Advancing pipeline of three lead gene therapy programs for **wet AMD, A1AT deficiency, and HAE**



\$210M in cash* to fund lead programs through 2019



Leadership team with **extensive clinical development expertise**

Merged to Become a Gene Therapy Leader

Avalanche Biotechnologies (Public company)

Industry-leading capabilities
in AAV technology

Annapurna (Private company)

Diverse gene therapy pipeline
in rare diseases

ADVERUM
BIOTECHNOLOGIES
NASDAQ: ADVM

Combined Resources

- Experienced leadership
- Robust patent portfolio
- Proprietary vectors
- Strong cash position

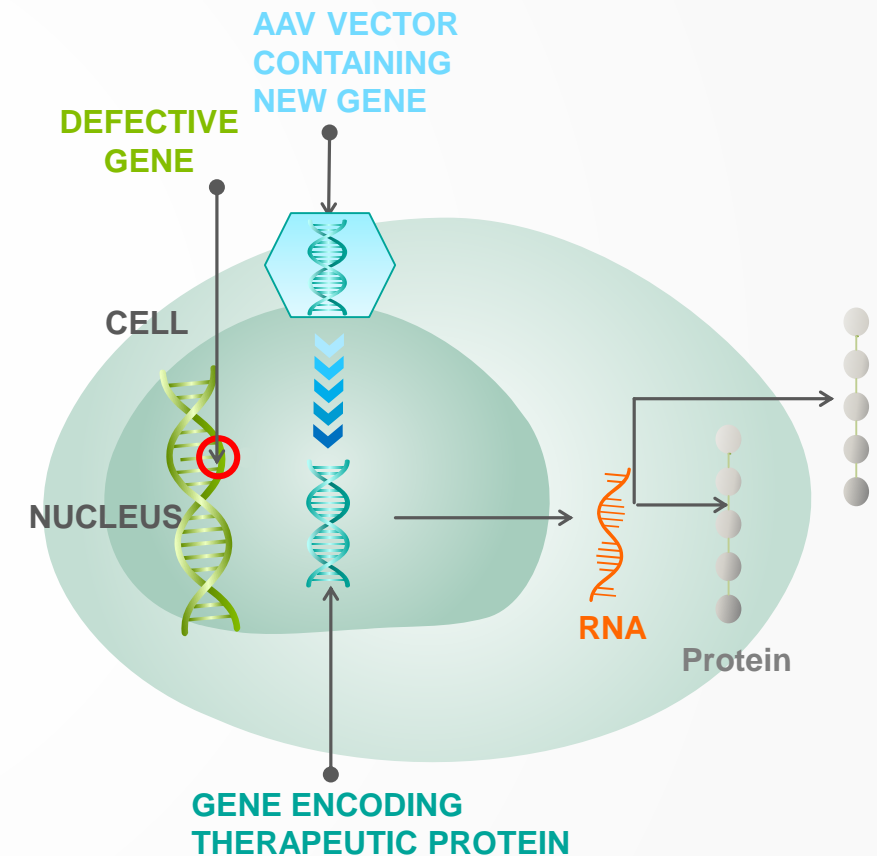
Adverum's Approach: AAV Gene Therapy Platform

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 Ocular and Rare Diseases

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

Adverum's Lead Gene Therapy Programs



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

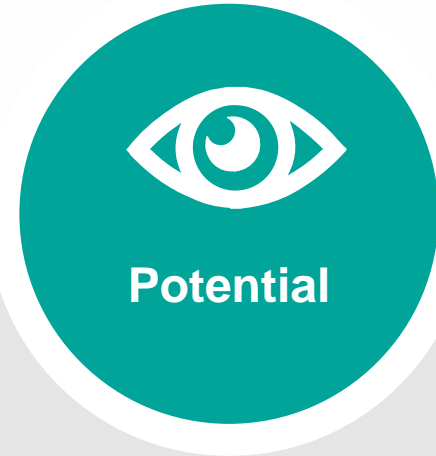


**Alpha-1 Antitrypsin
(A1AT) Deficiency**



**Hereditary Angioedema
(HAE)**

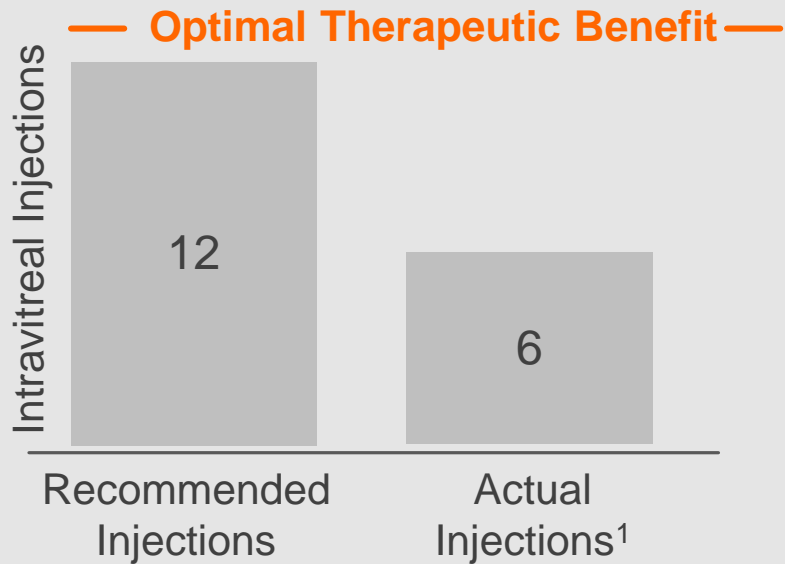
wAMD is a Large Market with Challenging Compliance Issues



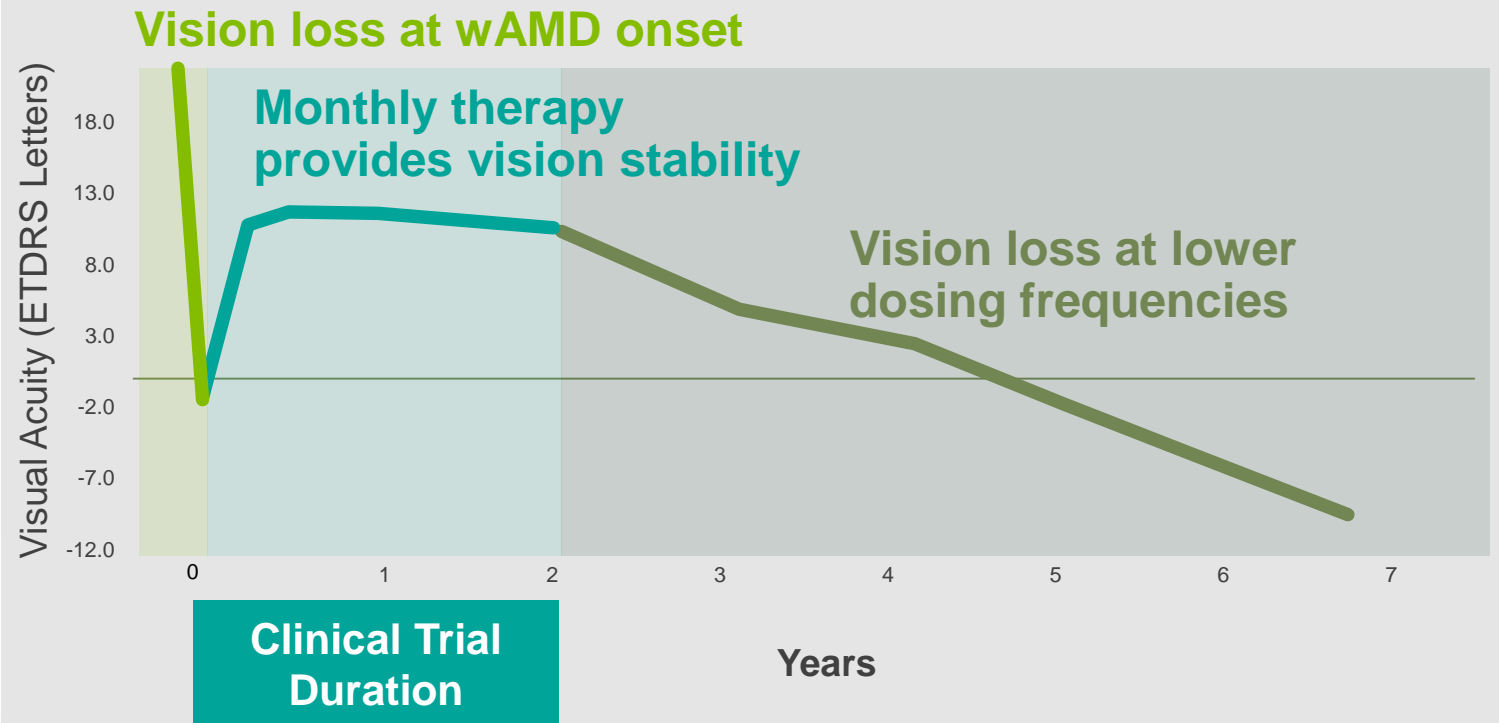
- › Vision loss from abnormal blood vessel proliferation and leakage due to VEGF activity
- › 1.2M U.S. patients¹, 3M globally
- › \$8B global sales for anti-VEGF proteins
- › Challenging compliance
 - Need for monthly/every other month intravitreal injections
 - Vision loss from underdosing

Significant Opportunity to Improve wAMD Therapy

Compliance with Monthly Injections is Difficult



Poor Compliance Leads to Vision Loss²



¹ Holekamp NM, et al. Am J Ophthalmol. 2014;157(4):825-833.

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

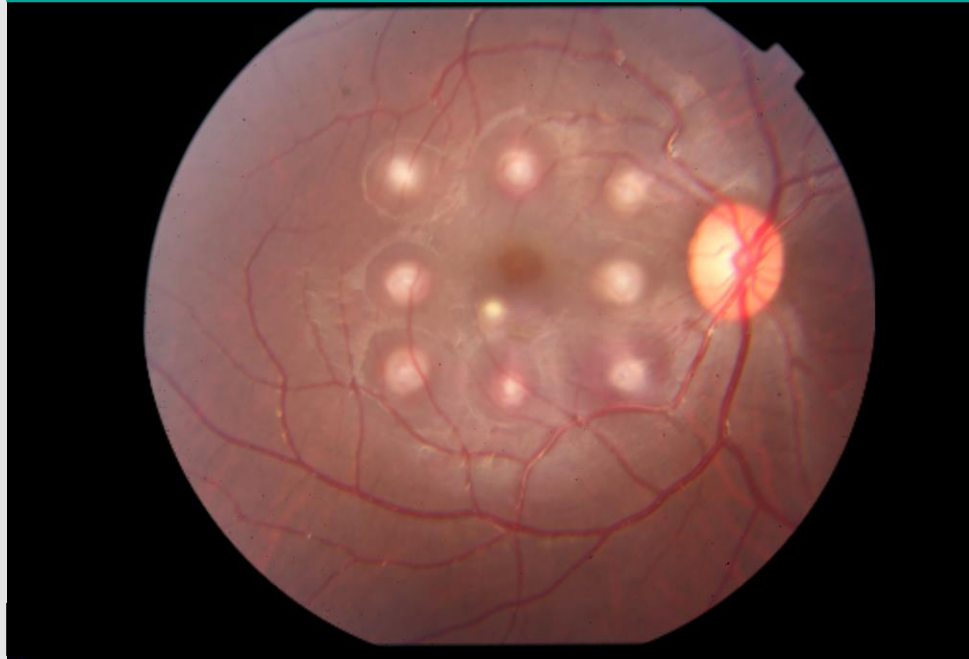
Potential to Treat wAMD with a Intravitreal Injection



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

Industry-standard Model Used to Test New wAMD Therapies

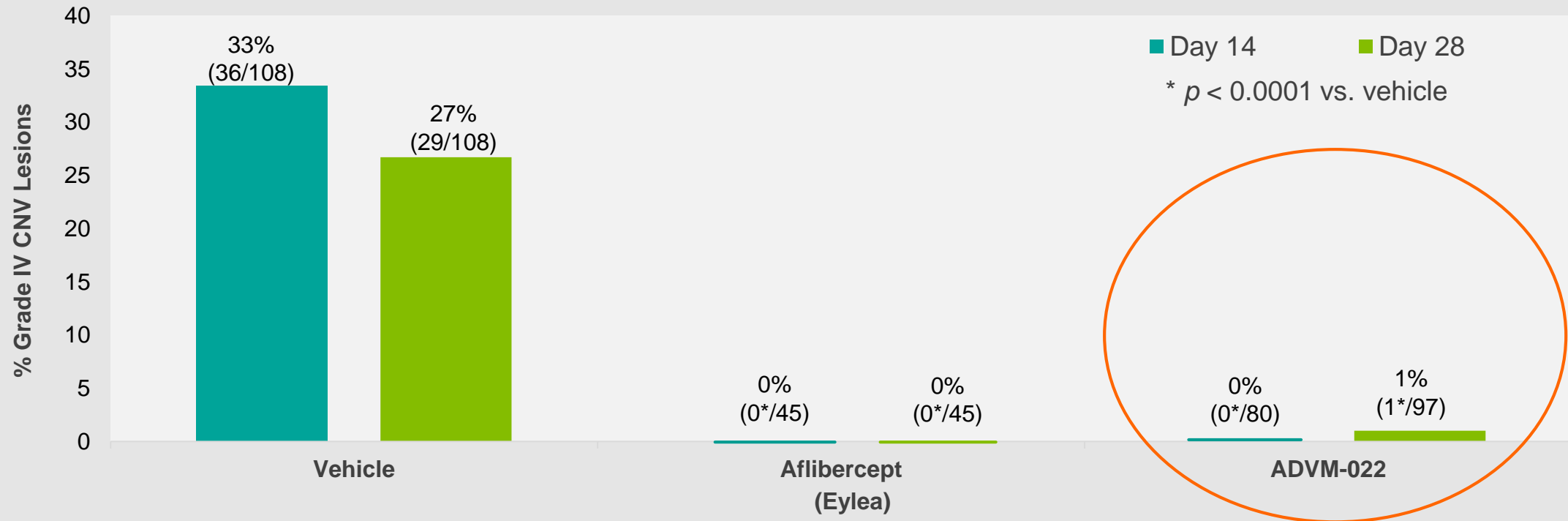
Retinal Image after Laser Treatment



- › 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: Efficacy Comparable to Positive Control

ADVM-022 (AAV.7m8-aflibercept)



Advancing Intravitreally-delivered ADVM-022



Next steps

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

Adverum's Lead Gene Therapy Programs



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



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



**Hereditary Angioedema
(HAE)**

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.

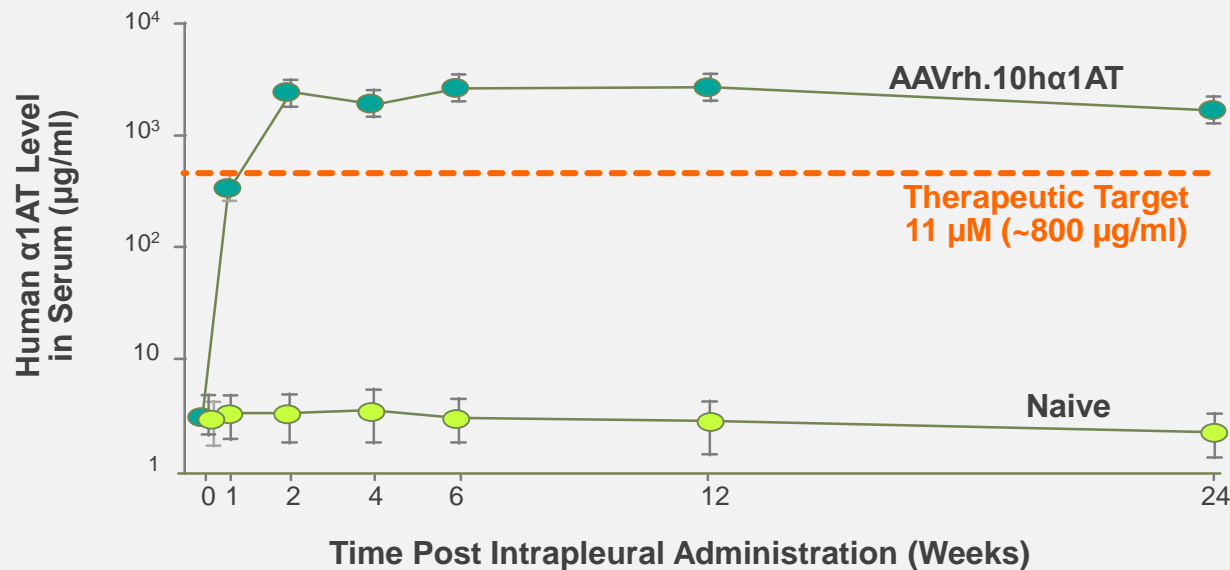
Potential to Treat A1AT Deficiency with ADVUM-043



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

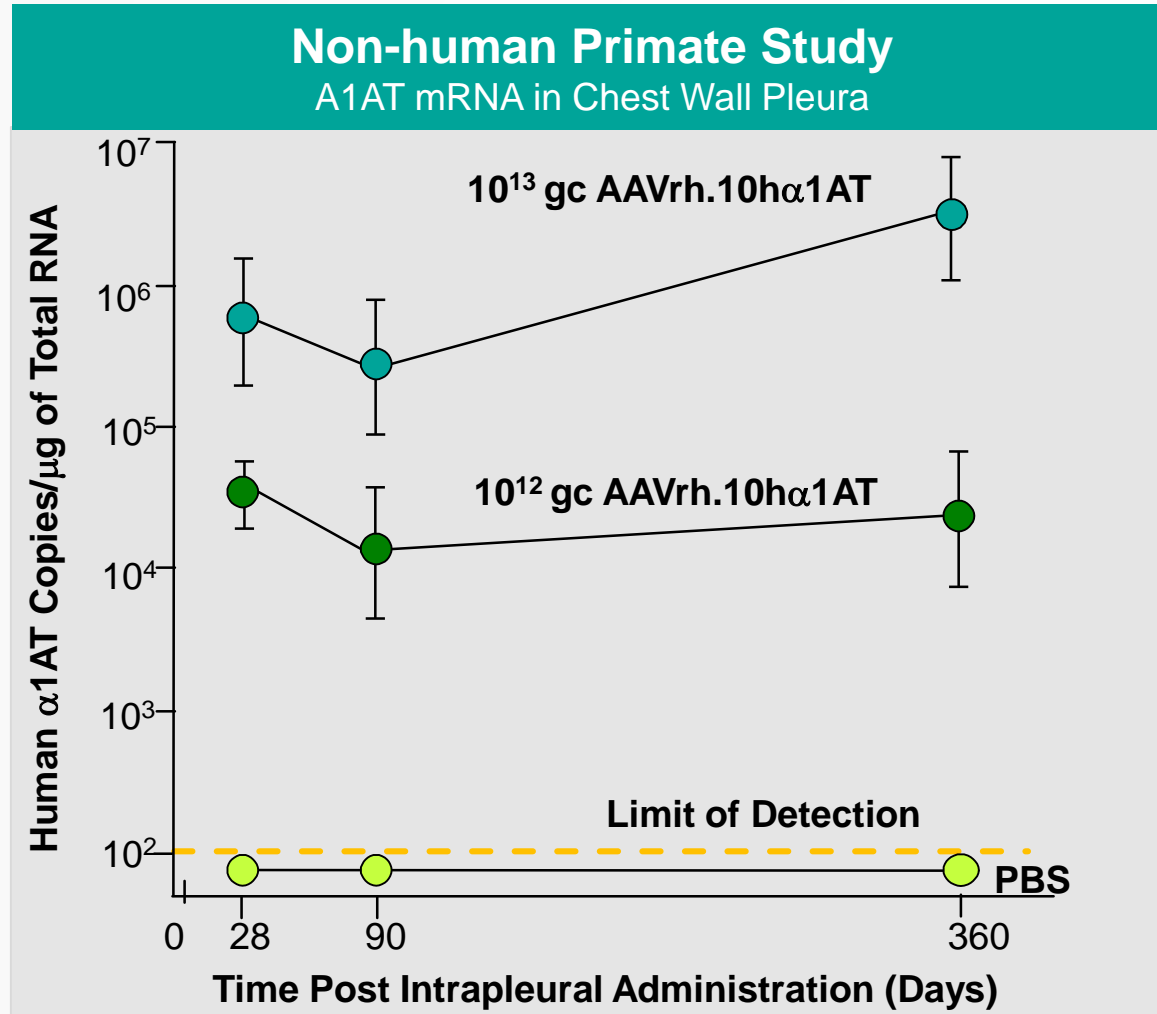
Proof-of-concept Study: Single Administration of ADVM-043 Induces Stable, Long-term Expression of hA1AT

Mice Study Human A1AT Expression in Serum



- Protein levels 2.5x therapeutic threshold generated by $\sim 5 \times 10^{12}$ vg/kg in treated mice¹
- mRNA expressed in lung following either intrapleural or intravenous administration in mice

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



➤ 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
- › Engaging with the FDA regarding open IND in 1H17
- › Planning to initiate patient enrollment in a Phase 1/2 trial in 4Q17

Adverum's Lead Gene Therapy Programs



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



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



**Hereditary Angioedema
(HAE)**

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

¹ Decision Resources Group; Wu, Jing; Anderson, Sarah. November 2015.

² Prophylactic use: Cinryze / Acute treatment: Firazyr, Berinet, Ruconest, Kalbitor.

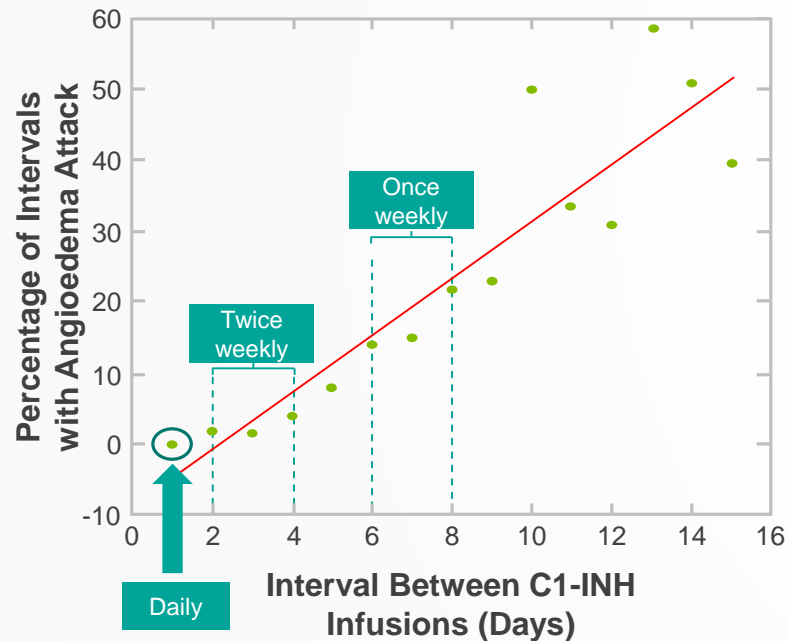
Potential to Prevent HAE Attacks with ADVIM-053



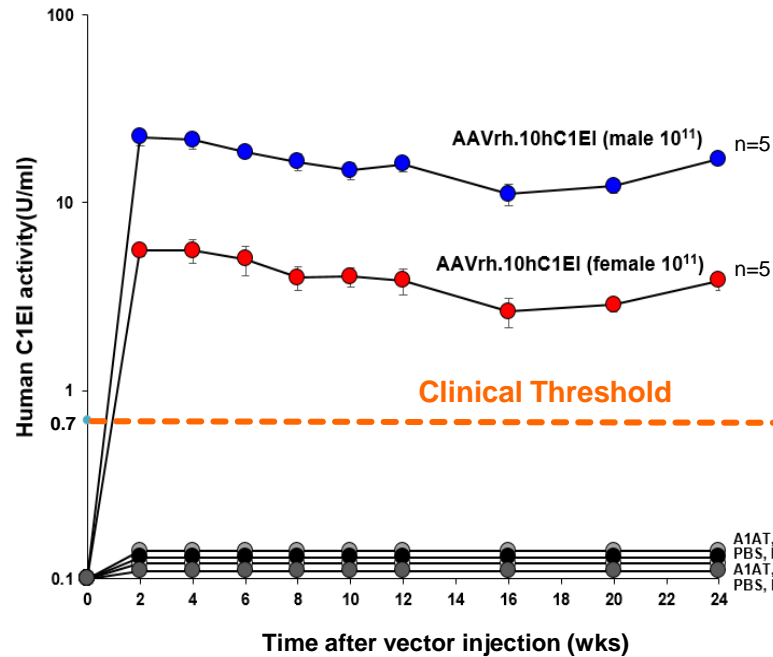
- › **Single intravenous administration of ADVIM-053** showed robust C1EI expression in preclinical studies
 - C1EI protein expression above therapeutic levels
 - Decreased vascular permeability, the hallmark of the disease
- › ADVIM-053 has the potential to prevent HAE attacks

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 Zuraw BL and Kalfus I Amer J Med 2012;125, 938.e1-938.e7.

² Wild type picture is two weeks post injection

Advancing ADVIM-053 for HAE into IND-enabling Studies



Next steps

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

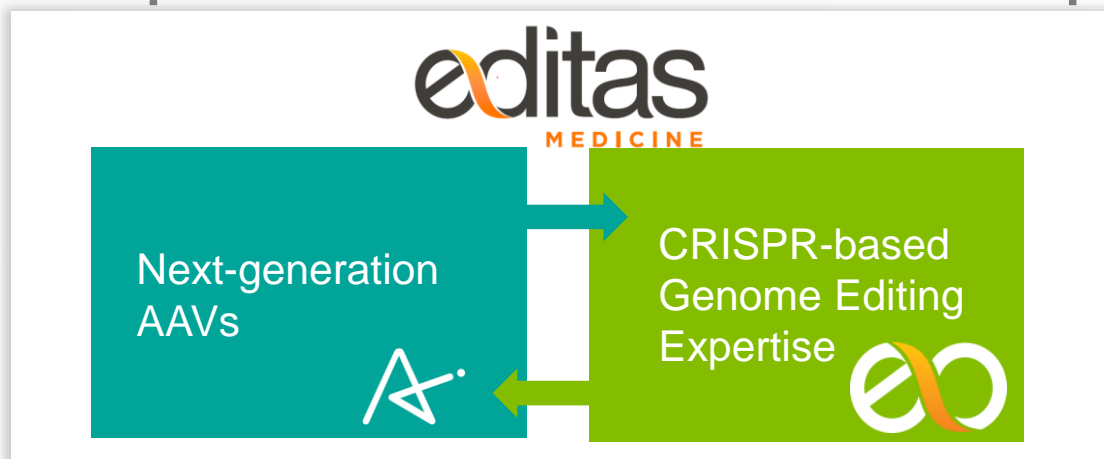
Industry-leading Capabilities in Novel Vector Development



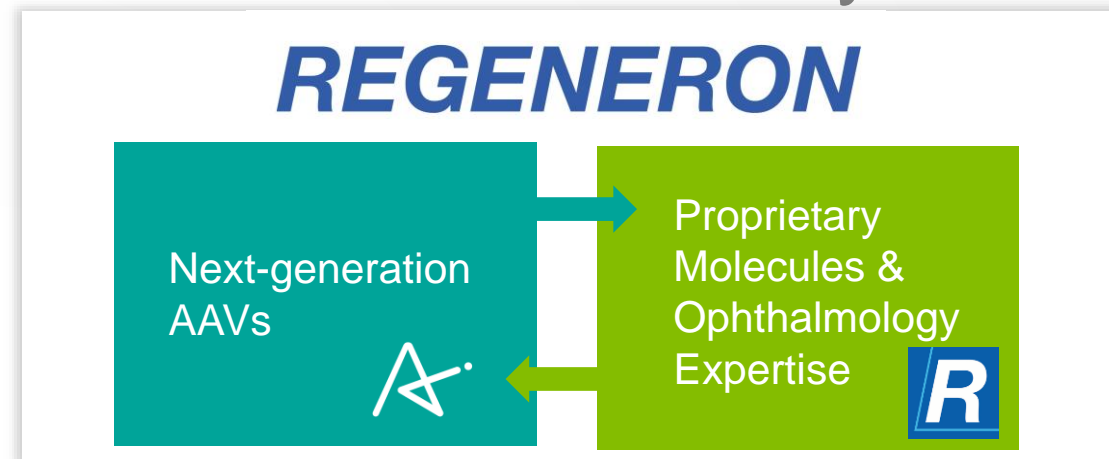
Adverum's Research Initiatives

- › 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

Validating Collaborations Leverage Adverum's Leadership in Ophthalmic Vector Development and Product Delivery








- › 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

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>Mehdi Gasmi, Ph.D. Chief Science and Technology Officer</p>	<p>20+ years experience in developing gene therapy vectors for the treatment of frequent and rare diseases</p>	
<p>Leone Patterson Chief Financial Officer</p>	<p>20+ years experience in management and financial operations</p>	
<p>Jennifer Cheng, Ph.D., J.D. Vice President and General Counsel</p>	<p>15+ years experience in biotechnology companies, including legal and intellectual property counsel and research</p>	
<p>Samuel Barone, M.D. Senior Vice President, Clinical Development</p>	<p>Ophthalmologist and vitreoretinal surgeon, 4 years with the Office of Tissues and Advanced Therapies at FDA</p>	

Adverum: Clinical-stage Company in 2017



Industry-leading AAV Platform



Pipeline of three lead gene therapy programs



Cash resources* to fund lead programs through 2019



Team with extensive gene therapy expertise

* \$210M in cash, cash equivalents, and marketable securities as of March 31, 2017
42.9M shares outstanding as of April 30, 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