Abeona Therapeutics

Working together to find a cure.

NASDAQ: ABEO
www.abeonatherapeutics.com
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Abeona Therapeutics

Clinical-stage Company: Delivering Therapies for Children with Rare Genetic Diseases

- **Pronunciation:** ay-bee-oh-nuh
- **Origin:** Roman Goddess thought to be the protector of children as they start out on their journey
- **Focus:** Abeona Therapeutics delivers gene therapy and plasma-based products for severe and life-threatening rare diseases

Janette and Inaki, MPS IIIA
Company Overview

Clinical-stage gene therapy company focused on rare diseases

- Sanfilippo Syndrome
  - ABO-102 (MPS IIIA): IND FDA allowance received for Phase 1/2 clinical study
    - First Patient Dosed – May 2016
  - ABO-101 (MPS IIIB): IND FDA allowance received for Phase 1/2 clinical study
  - Orphan Drug and Pediatric Rare Disease Designations from FDA
  - Nationwide Children’s Hospital Natural History Study

- Juvenile Batten
  - AAV-based gene therapy for juvenile Batten disease (CLN3)
  - World class research from Dr. Tammy L. Kielian at University of Nebraska Medical Center
  - IND enabling studies to commence in 2H 2016

- Fanconi Anemia
  - Proprietary CRISPR-Cas9 ex vivo and in vivo approaches for Fanconi anemia
  - World class research from Dr. Jakub Tolar and team at the University of Minnesota
  - IND enabling studies to commence in 2016

- Inherited COPD & Other Ultra-Orphan Proteins
  - Proprietary SDF process expands yields significantly relative to Cohn process
  - Finalize clinical program and initiate trial 2016
# Rare Disease Pipeline

<table>
<thead>
<tr>
<th>Gene Therapy</th>
<th>Research</th>
<th>Preclinical</th>
<th>Phase I/II</th>
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<tbody>
<tr>
<td>ABO-102 (scAAV-SGSH)</td>
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<tr>
<td>Sanfilippo syndrome Type A</td>
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<td>ABO-101 (AAV-NAGLU)</td>
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<td>Sanfilippo syndrome Type B</td>
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<td>ABO-201 (scAAV-CLN3)</td>
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<td>Juvenile Batten disease (JNCL)</td>
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<td>ABO-301 (AAV-FANCC)</td>
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<td>Fanconi anemia (FA)</td>
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<td>CRISPR-Cas9-AAV</td>
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<td>Rare blood diseases TBA</td>
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<tr>
<th>Plasma Protein Therapy</th>
<th>Research</th>
<th>Preclinical</th>
<th>Phase I/II</th>
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<tr>
<td>SDF Alpha™ (alpha-1 protease inhibitor)</td>
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<tr>
<td>Inherited COPD</td>
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<tr>
<td>SDF IVIG™ (intravenous immunoglobulin)</td>
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<tr>
<td>Autoimmune, infectious, and idiopathic diseases</td>
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</table>

**Current** → **Planned**
GENE THERAPY
Lysosomal Storage Diseases

*Inherited mutations that cause deficits in a cell recycling center*

- Enzymes in lysosomes break down sugars – cell recycling center
- Genetic defects can cause enzymes to not function properly
- Buildup in the lysosome of unbroken down sugars (GAGs)
- Class of lysosomal storage disorders (LSDs)
Routes of Administration for AAV Gene Therapies

- **Intravenous: Injection into a blood vessel**
  - Whole body delivery for treatment of multiple organs systems, including brain
  - Strong patient adoption, low safety risk
  - Abeona’s approach utilizes AAV9 for treating lysosomal storage diseases

- **Intracerebral: Direct injection into the brain**
  - Requires holes drilled into skull
  - Minimal peripheral organ delivery

- **Intrathecal: Direct injection into the spinal cord**
  - Spinal injections
  - Minimal peripheral organ delivery
AAV 1, 2, 5, 8, 9, 10 injected into CNS: Serotype makes a difference

Brain-directed injection of AAV vectors encoding green fluorescent protein gene (AAV/GFP). Approximately $2.0 \times 10^{10}$ vg of AAV/GFP vectors (serotypes 1, 2, 5, 8, 9, and 10) were injected into the right striatum over a period of 5 min. Expression of GFP was analyzed using fluorescent microscopy at 2 weeks.

Single Stranded vs. Self-Complementary AAV

After $7.0 \times 10^{12}$ vg of AAV9/GFP vectors were injected via tail veins of adult (7-week-old) mice; GFP images 5 weeks post administration

Systemic scAAV9 Administration Transduces the Spinal Cord

- **Self-Complementary AAV9**
- **13-months post intravenous injection of scAAV9-CLN3**
- **Demonstrates robust and uniform expression in spinal cord**
AAV9 Vectors Cross the Blood-Brain Barrier

Single, intravenous AAV9 injection used by Abeona

- Only vector to cross the Blood Brain Barrier
- Expressed in multiple nervous system cell types
- Supra-physiological enzyme expression in brain for over a year observed in animals
- Self-complementary AAV (scAAV) persists as a stable episome in non-dividing cells with transgene expression for years
- scAAV vectors are 10-100-fold more efficient than traditional single-stranded (ss) AAV vectors
- Robust, uniform expression in all areas of brain and peripheral tissues

GREEN = cells that received vector
scAAV-GFP expression in whole brain of juvenile Batten disease mouse after intravenous injection at 5 months post-injection

Global Foundation Supporters

Spain

Spain

USA

Switzerland

USA

USA

Canada

USA

Mexico

Australia
Sanfilippo Syndrome (MPS IIIB & MPS IIIA)
Sanfilippo syndrome (MPS III)

Rare Lysosomal storage disease affecting children

- **Sanfilippo syndrome (mucopolysaccharidosis (MPS) type III)**
  - Divided into four types (A to D) based on specific enzyme defect
    - IIIA - N-sulfoglucosamine sulfohydrolase (SGSH)
    - IIIB - α-N-acetylglucosaminidase (NAGLU)
  - Results in the abnormal accumulation of glycosaminoglycans (GAGs) (sugars)
  - GAGs accumulate in the brain (CNS) and body (somatic) tissues
  - Deterioration is severe, progressive and universally lethal with death by end of teens–early 20’s

- **No treatment currently available**
  - Incidence is estimated to be 1 in 70,000 births
  - Types A and B more common in North America and Europe

Abeona received FDA Allowance of IND for Phase 1/2 Clinical Study for Patients with Sanfilippo syndrome A (MPS IIIA) and B (MPS IIIB)

http://www.sophieandtom.co.uk/sophie-and-tom/
Differentiated Whole Body Approach

Abeona’s Treatment by Intravenous AAV Injection crosses blood brain barrier

- Increased enzyme activity
- Normalized GAG content
- Neuromuscular correction
- Cognitive improvements
- 100% improved survival

- 4 – 6 week old MPS III animals
- 4 – 6 month old MPS III animals
- Non-human primates (safety)
### ABO-101 Enzyme Expression in MPS IIIB Mouse Brain

<table>
<thead>
<tr>
<th>Vector Dose (vg/kg)</th>
<th>AOI</th>
<th>NAGLU Activity (% of wt levels)</th>
<th>16-27 mo pi</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1mo pi</td>
<td>3mo pi</td>
</tr>
<tr>
<td>1x10^{13}</td>
<td>4-6wk</td>
<td>60-560%</td>
<td>80-440%</td>
</tr>
<tr>
<td>1x10^{13}</td>
<td>4-6mo</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>2x10^{13}</td>
<td>4-6wk</td>
<td>40-440%</td>
<td>50-674%</td>
</tr>
<tr>
<td>2x10^{13}</td>
<td>4-6mo</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

*NAGLU expression at or above heterozygote (and often above wild-type)*
Clearance of Lysosomal GAGs after single ABO-101 treatment

Normalizing GAGS for whole body improvement

- IV Delivery of ABO-101 induced clearance of lysosomal GAG storage in the CNS and somatic tissues

- **Lower** bars are better

- Demonstrates that treated IIIB mice have reduced GAG content, similar to unaffected animals, in multiple tissues compared to untreated IIIB mice (with exception of kidney)

Source: Fu et al (2011) Correction of Neurological Disease of Mucopolysaccharidosis IIIB in adult mice by rAAV9 Trans-Blood-Brain Barrier Gene Delivery, Mol. Ther 19
ABO-101 Normalizes Cognitive and Motor Function

*Demonstrates normalization of cognitive and motor function after IV injection into 4-6 week old MPS IIIB mice*

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**Morris Water Maze**

**Rotarod**

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5.0 - 5.5 months old (4 months post-injection)

Source: Fu et al (2011) Correction of Neurological Disease of Mucopolysaccharidosis IIIB in adult mice by rAAv9 Trans-Blood-Brain Barrier Gene Delivery, Mol. Ther 19
ABO-101 Normalizes Survival in MPS IIIB

*Single iv infusion of ABO-101 at 4–6 weeks of age normalized the survival in MPS IIIB mice*

Source: Fu et al (2011) Correction of Neurological Disease of Mucopolysaccharidosis IIIB in adult mice by rAAV9 Trans-Blood-Brain Barrier Gene Delivery, Mol. Ther 19
ABO-101 Demonstrates sustained activity in Non-human Primates

- NAGLU (MPS IIIB Enzyme) in CNS and preclinical tissue 6 months postadministration
- Brain and somatic NAGLU activity is significantly increased over normal enzyme levels 6 months post-injection despite modest decreases in peripheral serum NAGLU levels

Natural History Study

25-patient with Sanfilippo

- Enrollment complete: 25 subjects, 15 MPS IIIA and 10 MPS IIIB
- Study visits – assessments at 0, 6, and 12 months:
  - Neurocognitive (Leiter) and parental rating assessments (ABAS II)
  - Timed functional motor tests
  - Standard laboratory assessments
  - Serum/leukocyte NAGLU or SGSH activity
  - Quality of life (PedsQL)
  - Urine GAG levels
- Study visits – assessments at Baseline and 12-month assessments
  - Brain MRI (including DTI and 1H spectroscopy)
  - CSF for standard chemistries/cell counts and NAGLU or SGSH activity
- All subjects through >1 year follow up
  - Multiple patient cross-over into clinical trials

Source: Bain et al (2015) Design and Enrollment in a Natural History Study of Mucopolysaccharidosis Types IIIA and IIIB, ACMG

Mullen Scales: ALL subjects at or below a 3 year old developmental age at baseline visit, declining with age
Two Ongoing Phase 1/2 Clinical Trials: Overview

- Phase 1/2 open-label, dose-escalation clinical trials
  - ABO-102 (scAAV-SGSH) for MPS IIIA clinicaltrials.gov - NCT02716246
  - ABO-101 (AAV-NAGLU) for MPS IIIB: clinicaltrials.gov - TBD

- Each trial:
  - Low Dose: n = 3 patients
  - High Dose: n = 3-6 patients

- Three sites: United States, Spain and Australia

- Multiple global Phase 1/2 studies with n=~25 patients
Juvenile Batten Disease (JBD)
Juvenile Batten Disease
(Juvenile Neuronal Ceroid Lipofuscinosis)

*Estimated incidence of 1:100,000 births*

- Autosomal recessive (inherited) mutation in the CLN3 gene
- Lysosomal storage diseases accumulation of the autoflorescent ceroid lipopigments and proteins
- Initially presents as blindness, progressing to behavioral issues, sleep disturbances, seizures, cognitive loss, motor abnormalities, and premature death (late teens-early 20s)
- Neurodegeneration occurs primarily in thalamus, cortex, and hippocampus, although inclusions are observed throughout the CNS

Source: Moving towards therapies for Juvenile batten disease, Experimental Neurology, 2008
Fanconi anemia (FA)
ABO-301 for Fanconi anemia

Rare (1: 160,000) pediatric, autosomal recessive (inherited) disease

- Characterized by multiple physical abnormalities, organ defects, bone marrow failure, and a higher than normal risk of cancer—with 20 to 30 year average lifespan
  - The major function of bone marrow is to produce new blood cells. In FA, a DNA mutation renders the FANCC gene nonfunctional
  - Loss of FANCC causes patient skeletal abnormalities and leads to bone marrow failure
  - Higher rates of hematological diseases, such as acute myeloid leukemia (AML) or tumors of the head, neck, skin, gastrointestinal system, or genital tract

- ABO-301 (AAV LK19 FANCC) using CRISPR/Cas9 in vivo (delivery vector with hematopoietic tropism) demonstrates in vivo efficacy in multiple models, with no off target effects

- Next steps: Complete IND enabling pre-clinical studies; and establish safety and preliminary efficacy in human subjects

PLASMA THERAPY
Alpha-1 Antitrypsin (AAT) Deficiency

- AAT deficiency is a protein folding disease; leads to inherited COPD
- Protein folding: an unfolded polypeptide chain folds into a specific native and functional structure
- Misfolding and retention in the ER (endoplasmic reticulum) leads to aggregation in cells of synthesis

AAT Augmentation Treatment

- AAT deficiency predisposes those affected to COPD and liver disease
- AAT treatment improves morbidity ($FEV_1$/breathing capacity) and mortality (survival)
- First approved in 1988 as weekly i.v. infusion at 60 mg/kg
  - Four currently approved products: (Glassia® (Kamada), Aralast-NP™ (Baxter Healthcare), Prolastin-C® (Grifols), Zemaira® (CSL Behring))
- ~10K US patients are currently on AAT augmentation therapy
  - Estimated 80-100K require augmentation in US
  - ~$1 B market, CAGR 20%
  - Reimbursed at ~$100K/year, with average of 22 years on treatment
  - Up to 3% of all people diagnosed with COPD may have undetected AATD

Cumulative Mortality
AAT augmentation

Sources: AJRCCM 1998; 158:49; Worldwide racial and ethnic distribution of alpha(1)-antitrypsin deficiency. Chest 2002;122:1818
## Benefits of SDF Process

<table>
<thead>
<tr>
<th>SDF Delivers...</th>
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<tr>
<td><strong>Kinder, Gentler</strong></td>
<td>▪ 2-stage sodium citrate precipitation + diafiltration</td>
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<td></td>
<td>▪ Compared with Cohn method:</td>
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<td></td>
<td>▪ No ethanol or harmful pH changes</td>
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<td></td>
<td>▪ Less denaturing of select proteins</td>
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<td></td>
<td>▪ 3 v. 6 day fractionation process</td>
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<tr>
<td><strong>Yield improvements</strong></td>
<td>▪ Up to 10-fold alpha-1 yield increase</td>
</tr>
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<td></td>
<td>▪ Potential for multiple orphan proteins (IVIG, C1 esterase)</td>
</tr>
<tr>
<td><strong>Margin improvements</strong></td>
<td>▪ Increase in margins to ~80% v industry standard ~30%</td>
</tr>
<tr>
<td></td>
<td>▪ with Cohn method</td>
</tr>
<tr>
<td><strong>Broad Intellectual Property</strong></td>
<td>▪ Three issued US and worldwide patents; additional IP pending</td>
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</table>
PTB-101 (SDF Alpha™) Registration Program

- Seeking FDA concurrence for registration studies to determine safety and bio-equivalency comparison of PTB-101 SDF Alpha™ versus approved API in individuals with AATD

- Endpoints with weekly 60 mg/kg dosing:
  - To demonstrate that the pharmacokinetics of antigenic and/or functional PTB-101 is not inferior to approved active comparator
  - To measure the efficacy of PTB-101 maintains antigenic and/or functional plasma levels of at least 11μM (57 mg/dL)
  - To compare alpha-1 protease inhibitor (API) trough levels (antigenic and functional) over weeks 7-12 (6 infusions)

- Study population of n=50 subjects; five week wash-out period prior to dosing

- Seeking additional regulatory guidance on potential long term follow up with enhanced dosing and schedules, as well as clinical and/or biomarker surrogate endpoints
Management, Directors & SABs
Management & Board

Management

- Tim Miller, Ph.D - President and Chief Executive Officer & Director
- Jeffrey B. Davis - Chief Operating Officer & Director
- Harrison G. Wehner - Chief Financial Officer
- David P. Nowotnik, Ph.D - Senior Vice President, Research & Development

Board of Directors

- Steven H. Rouhandeh - Executive Chairman
- Mark J. Ahn, Ph.D - Vice Chairman, Director
- Mark J. Alvino - Director
- Stephen B. Howell, MD - Director
- Todd Wider, MD - Director
Rare Disease
Scientific Advisory Board (SAB)

Gene Therapy
- Pol Boudes, MD
  - Cymabay Therapeutics
- Brian Kaspar, PhD
  - Nationwide Children’s Hospital & Ohio State University
- Maria Escolar, MD, MS
  - University of Pittsburgh Center for Neurodegenerative Disorders

Plasma Products
- Eugene J. Zurlo, BS (Pharmacy), MS
- Charles H. Heldebrant, PhD
- Robert A. Sandhaus, MD, PhD, FCCP
  - National Jewish Health
- Charlie B. Strange, MD, FCCP
  - Medical University of South Carolina
# Financial Summary

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<th>Capitalization</th>
<th>Issued and Outstanding Shares</th>
<th>WAEP (Weighted Average Exercise Price)</th>
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<td>Common shares (ABEO)</td>
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<td>Warrants (ABEOW, fully traded)</td>
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<td><strong>DEBT</strong></td>
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1. Does not include 653,727 “old” warrants and options outstanding with WAEP of approximately $28.77
Milestones

✓ **1Q16:** FDA Allowances for phase 1/2 clinical study for both ABO-102 for MPS IIIA & ABO-101 for MPS IIIB

✓ **2Q16:** Dosed First Patient in Phase 1/2 clinical studies for MPS IIIA

✓ **2Q16:** FDA Allowance for phase 1/2 clinical study for ABO-101 (AAV-NAGLU) for MPS IIIB

➢ **2016:** Initiate PTB-101 (SDF Alpha™) preclinical and clinical studies

➢ **2016:** Finalize clinical program for ABO-201 (scAAV CLN3) gene therapy for Juvenile Neuronal Ceroid Lipofuscinosis (JNCL)

➢ **2016:** Dose First Patient in Phase 1/2 clinical study for MPS IIIB

➢ **2016:** CTA Allowance in Spain for both MPS IIIA and MPS IIIB

➢ **2016:** CTN Allowance in Australia for both MPS IIIA and MPS IIIB
Investment Summary

Abeona Therapeutics is clinical-stage gene therapy company focused on rare diseases

- Validated and scalable technology for gene therapy and plasma-based products
- Ongoing rare disease Clinical trials:
  - ABO-102 (scAAV-SGHG) - AAV gene therapies for Sanfilippo syndrome (MPS IIIA)
  - ABO-101 (AAV-NAGLU) - AAV gene therapies for Sanfilippo syndrome (MPS IIIB)
- Rare disease pipeline:
  - ABO-201 (scAAV-CLN3) – AAV gene therapy for juvenile Batten disease (JBD)
  - ABO-301 (AAV-FANCC) for Fanconi anemia (FA) disorder using a novel CRISPR/Cas9-based gene editing approach to gene therapy program for rare blood diseases
  - SDF Alpha™ (alpha-1 protease inhibitor) for inherited COPD using proprietary SDF™ (Salt Diafiltration) ethanol-free process

Broad intellectual property (IP), and regulatory exclusivity (Orphan, Rare Pediatric Disease designation)
Investor Contacts

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Email: alucca@abeonatherapeutics.com
Working together to find a cure.