Bringing life changing treatments to people with genetic diseases regardless of prevalence or commercial interest

Novel Anc80 AAV Platform, and Late-Preclinical Stage Gene Therapy to Treat Inherited Retinal Disorder, LCA6/RPGRIP1

reImagining drug development for rare disease

Non-Confidential Presentation
January 2022
About Odylia

Independent nonprofit organization founded in 2017

Mission
Utilize a unique, nonprofit business model to accelerate the development of gene therapies for people with rare disease, changing the way treatments are brought from the lab to the clinic

Vision
Bring life changing treatments to people with genetic disease regardless of prevalence or commercial interest
About Odylia Therapeutics, Inc.

Odylia Therapeutics

- Nonprofit rare disease biotech
- Founded through a collaboration between Mass Eye & Ear and Usher 2020 Foundation
- Funding from biopharma partnerships and philanthropy
- Headquarters in Atlanta, Georgia
Odylia Leadership Team

Luk Vandenbergh, PhD, Co-Founder
- Assistant Professor, Harvard Medical School, and Director, Grousbeck Gene Therapy Center, Massachusetts Eye and Ear.
- Has discovered and developed many new technologies in the gene therapy field and started numerous companies (e.g. Akouos) to bring treatments to patients.

Scott Dorfman, Co-Founder & Chief Executive Officer
- Fulcrum Equity Partners, Operations Partner
- Usher 2020 Foundation, co-Founder
- Nacuity Pharmaceuticals, Board

Ashley Winslow, PhD, President & Chief Scientific Officer
- PhD in Medical Genetics, University of Cambridge
- Postdoc at Massachusetts General Hospital and Harvard Medical School
- Pfizer R&D, Precision Medicine and Human Genetics and Computational Biomedicine
- Orphan Disease Center at the University of Pennsylvania
Board Members & Advisors

Board of Directors

Luk Vandenberghe, Ph.D.
Assistant Professor, Harvard Medical School
Director, Grousbeck Gene Therapy Center, Massachusetts Eye and Ear

Scott Dorfman, B.B.A.
CEO, Odylia Therapeutics

Emil Kakkis, M.D., Ph.D.
President, CEO, and Founder
Ultragenyx Pharmaceutical Inc

Mat Pletcher, PhD
Senior Vice President, Head of Research
Audentes Therapeutics; Board Member, The RDH12 Fund for Sight

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Massachusetts Eye and Ear

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University of Pennsylvania

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Chief Scientific Officer

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National Eye Institute, NIH

Alberto Auricchio, Ph.D.
Associate Professor of Medical Genetics
"Federico II" University Napoli
Principal Investigator, TIGEM
The Future with Odylia

Odylia navigates common obstacles for rare disease and mitigates risk

We do this through:

■ a blend of science and business
■ a patient-centric model, ensuring outcomes are focused on getting treatments to people, hand-in-hand with the patient community
■ strategic research plans to lower costs, save time, and minimize risks
■ creative collaboration with patient groups, academics labs, and drug manufacturers to advance treatments in timely, economical, and effective ways

Odylia remains nimble in order to create opportunities for treatments
### Rare Disease Portfolio

#### Gene Therapy Pipeline (disclosed)

<table>
<thead>
<tr>
<th>Phase</th>
<th>Exploratory</th>
<th>Early Preclinical</th>
<th>Late-stage Preclinical</th>
<th>Phase 1/2</th>
<th>Phase 3</th>
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<tbody>
<tr>
<td>AAV-RPGRIP1</td>
<td>Seeking Partners</td>
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<td>Orphan Drug Designation- granted Rare Pediatric Disease- granted</td>
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<tr>
<td>LCA6</td>
<td></td>
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<td></td>
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<tr>
<td>AAV-USH1C</td>
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<tr>
<td>Vision loss, Usher Syndrome</td>
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</tr>
</tbody>
</table>

#### Brydge Solutions- 2021 Patient Group Partnerships

- SATB2 Gene Foundation
- RDH12 Fund for Sight
- Usher 2020 Foundation
- CLOVES Foundation
- Open Treatments
Gene Therapy Programs for Inherited Retinal Disorders
Gene Therapies for Inherited Retinal Disorders (IRDs)

- At least 5 million people worldwide suffer from inherited and incurable retinal disorders
- Genetically heterogeneous Mendelian disorders with 270+ disease-causing genes identified to date
- Leber Congenital Amaurosis (LCA) accounts for about 4-6% of all IRDs. LCA causes severe vision loss early in life
Gene Therapies for Inherited Retinal Disorders (IRDs)

Of 45+ clinical-stage programs for IRDs and AMD, some listed here

<table>
<thead>
<tr>
<th>Company</th>
<th>Molecule</th>
<th>Disorder</th>
<th>Dev. Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spark/Roche</td>
<td>Luxturna, voretigene AAV-RPE65</td>
<td>LCA2/RPE65</td>
<td>Mkt</td>
</tr>
<tr>
<td>Gensight Biologics</td>
<td>GS010, AAV2 7m8</td>
<td>Leber Hereditary Optic Neuropathy</td>
<td>3</td>
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<tr>
<td>Nightstar/Biogen</td>
<td>BIIB111</td>
<td>Chorioideremia (REP1), NSR-REP1</td>
<td>3</td>
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<tr>
<td>RegenxBio</td>
<td>RGX-314</td>
<td>Wet AMD</td>
<td>2/3</td>
</tr>
<tr>
<td>Gyroscope</td>
<td>GT005, Complement Factor 1</td>
<td>AMD (dry)</td>
<td>2</td>
</tr>
<tr>
<td>Nightstar/Biogen</td>
<td>BIIB-111</td>
<td>X-linked RP (RPGR)</td>
<td>2/3</td>
</tr>
<tr>
<td>Tubingen Hospital</td>
<td>rAAV2.REP1</td>
<td>Choroideremia (REP1)</td>
<td>2</td>
</tr>
<tr>
<td>MeiraGTx/Janssen</td>
<td>ACHM, AAV-CNGA3</td>
<td>Achromatopsia (ACHM)</td>
<td>1/2</td>
</tr>
<tr>
<td>MeiraGTx</td>
<td>AAV-RPE65</td>
<td>RP-Associated Retinal Dystrophy</td>
<td>1/2</td>
</tr>
<tr>
<td>Atsena</td>
<td>GUCY2D</td>
<td>LCA1, GUCY2D</td>
<td>1/2</td>
</tr>
<tr>
<td>MiraGTx/Janssen</td>
<td>MGT009. XLRP</td>
<td>LCA and RP (RPE65)</td>
<td>1/2</td>
</tr>
<tr>
<td>Editas Medicine</td>
<td>Edit-101</td>
<td>LCA10, CRISPR/Cas9 gene editing of CEP290</td>
<td>2</td>
</tr>
</tbody>
</table>

LCAs are in pink font

Odylia’s RPGRIP1 program, a unique opportunity to invest early in a low-risk, late-stage preclinical program
Commercial Projection of RPGRIP1 Gene Therapy for LCA6

Using Luxturna as benchmark RPGRIP1 is an Attractive Commercial Opportunity

1. Luxturna for LCA2 (RPE65) received FDA approved in 2017 and was launched 2018
2. LCA2 has prevalence of 1,000 - 2,000 in US, 6,000 WW (Spark IPO S-1)
3. Studies estimate that RPGRIP1 or LCA6, has a prevalence range of 600-1200 in the US, and 10,000-20,000 WW (Hanany, 2020) or 5-12% of all LCAs
4. Price of Luxturna treatment – About $410,000 per eye or $820,000 per individual (*WAC, USA); Price would approx be same WW. One injection for lifetime correction. Good durability of effect
5. When this RPGRIP1 product is approved, more knowledge of benefits will be available, and the new pricing/payer/usage uptake models should be favorable
6. Health economics to prevent permanent vision loss in youth for life has clear payer return
7. 10% to 40% US market penetration is expected in years 1 through 5
Gene Therapy Competitive Landscape for Leber Congenital Amaurosis (LCA)

- LCA most severe and common form of blindness in children with incidence of 10,000+ in US
- Evidence suggests LCA6 is underdiagnosed
- No known competition for LCA6 gene therapy

<table>
<thead>
<tr>
<th>LCA</th>
<th>Mutations</th>
<th>Companies</th>
<th>Therapeutic Name</th>
<th>% of LCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCA6</td>
<td>RPGRIP1</td>
<td>Odylia</td>
<td>RPGRIP1-Anc80 AAV</td>
<td>5-12%</td>
</tr>
<tr>
<td>LCA1</td>
<td>GUCY2D</td>
<td>Atsena/Janssen</td>
<td>Dual AAV GT</td>
<td>10-20%</td>
</tr>
<tr>
<td>LCA10</td>
<td>CEP290</td>
<td>Editas/Allergan</td>
<td>AGN-15187 (EDIT-101)</td>
<td>15-20%</td>
</tr>
<tr>
<td>LCA10</td>
<td>CEP290</td>
<td>3 RNAi programs</td>
<td>-</td>
<td>15-20%</td>
</tr>
<tr>
<td>LCA2</td>
<td>RPE65</td>
<td>Spark/Roche</td>
<td>AAV2-hRPE65v2</td>
<td>3-16%</td>
</tr>
</tbody>
</table>
Novel Anc80 Capsid
Anc80 Capsid profile and tissue tropism

Anc80 Tropism: retina, CNS, liver, muscle, cochlea

- Anc80 AAV capsid:
  - Anc80 is an ancestral AAV serotype developed by Luk Vandenberghe’s lab using ancestral sequence reconstruction; the predicted ancestor of AAV serotypes 1, 2, 8, and 9 and shows broad tissue tropism
  - Superior expression & kinetics (NHP, pig, murine testing) with onset of expression as early as day 3 post injection
  - Preliminary data sets from collaborators show more favorable immune profile compared to commonly used AAVs
  - 14-year patent life remaining (WO15054653)

- Tropism - multiple tissues:
  - Central Nervous system tropism in mouse: Hudry et al., 2018
  - Eye: Zinn, 2015; Carvalho, 2017; Carvalho, 2018
  - Liver: Zinn, 2015
  - Muscle: Zinn, 2015
  - Kidney: Ikeda, 2018
  - Inner Ear: Landegger, 2015; Pan 2017; Suzuki, 2017; Tao, 2018
Anc80 AAV Vector

- Mass Eye & Ear developed Anc80 AAV technology
- Odylia licensed worldwide exclusively for rare retinal diseases
- Option to expand into additional genetic diseases and organ systems
- Sensorimotor (hearing) exclusively licensed to Akous
- PCT (WO/2015/054653) United States
- A highly favorable license. Sub-licensor to Odylia pays no license fee or royalties to ME&E
- Vector deeply characterized by Akous, that has advanced anc80 based products into clinicals
Anc80 shows high levels of expression in multiple retinal layers

Anc80 shows increased expression across different retinal layers.

Expression is higher than other capsids tested: AAV2, AAV8, AAV9, AAV5

Ultimately higher expression of the transgene can mean lower doses in patients.

Carvalho, 2018
Anc80 expression in the NHP retina compared to AAV9 and AAV5:
- Anc80 expression started earlier in NHP, similar to mice
- Expression seen beyond the bleb in Anc80 and AAV9 but not in AAV5
- High expression with Anc80 in ONL and RPE
RPGRIP1 Gene Therapy
RPGRIP1 localizes to the cilia in photoreceptors and is necessary for normal function.
## RPGRIP1 Gene Therapy

### Clinical Overview:
Biallelic RPGRIP1 mutations can result in diagnoses of **LCA6, CORD13, or juvenile Retinitis Pigmentosa**.

<table>
<thead>
<tr>
<th>Clinical Symptom</th>
<th>RPGRIP1-mediated LCA6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>reported in clinical publications specific to RPGRIP1 mutations</td>
<td>Reduced ERG</td>
</tr>
<tr>
<td></td>
<td>Nystagmus</td>
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<tr>
<td></td>
<td>Macular Degeneration/blurred vision</td>
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<tr>
<td></td>
<td>Reduced visual acuity</td>
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<tr>
<td></td>
<td>Fundus pigmentary deposits (bone spicule, granularity)</td>
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<tr>
<td></td>
<td>Photophobia</td>
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<tr>
<td></td>
<td>Night blindness</td>
</tr>
<tr>
<td></td>
<td>Hyperopia</td>
</tr>
<tr>
<td></td>
<td>Vascular attenuation</td>
</tr>
<tr>
<td></td>
<td>Reduced visual acuity (limited to light perception)</td>
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<tr>
<td></td>
<td>Eye poking in infants</td>
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<tr>
<td></td>
<td>Drusen-like deposits</td>
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<tr>
<td></td>
<td>Peripheral vision loss</td>
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<tr>
<td></td>
<td>Disc pallor</td>
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<tr>
<td></td>
<td>Chorioretinal atrophy</td>
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<tr>
<td></td>
<td>Keratoconus/keratoglobus</td>
</tr>
<tr>
<td><strong>Age at onset</strong></td>
<td>Usually in early infancy but before 1 year of age</td>
</tr>
<tr>
<td></td>
<td>Can be variable</td>
</tr>
<tr>
<td><strong>Age at major decline points</strong></td>
<td>Visual loss onset within first year of life</td>
</tr>
<tr>
<td></td>
<td>Potential treatment windows exist in pediatric and young adult populations</td>
</tr>
</tbody>
</table>

*Of Note*: While RPGRIP1 mutations are predominately diagnosed as LCA6, there are reports of both retinitis pigmentosa (RP) and cone-rod dystrophy (CORD13) clinical diagnoses.
RPGRIP1 Clinical Advisory Group

Robert K. Koenekoop MD, MSc, PhD, FRCS(C), FARVO
Professor of Paediatric Surgery, Human Genetics and Adult Ophthalmology at McGill University
Director of the Laboratory for Retinal Genetics and Therapeutics
Chief Paediatric Ophthalmology
Montreal Children's Hospital

Jiong Yan, MD
Associate Professor of Ophthalmology
Director, Vitreo-Retina Surgery Fellowship
Emory University School of Medicine

Thaddeus (Ted) Dryja, MD
Professor of Ophthalmology, Harvard Medical School
Physician and Surgeon, Massachusetts Eye and Ear Infirmary
Massachusetts Eye and Ear Infirmary

Tiansen Li, PhD
Senior Investigator, Retinal Cell Biology and Degeneration Section
National Eye Institute

Eric A. Pierce, MD, PhD
Director, Inherited Retinal Disorders Service, Massachusetts Eye and Ear
William F. Charls Professor of Ophthalmology, Harvard Medical School
Massachusetts Eye and Ear
RPGRIP1 Gene Therapy: Pre-clinical data

RPGRIP1 Expression in LCA6 mouse model

- RPGRIP1 protein localizes to the appropriate part of the photoreceptor subcellular structure
- There is a clear dose-dependent increase in expression of RPGRIP1

Effectiveness of RPGRIP1 gene therapy in a mouse model of LCA6

- Protection against retinal degeneration and preservation of outer nuclear layer and inner nuclear layer thickness
- Improved ERG (functional outcome)

Feasibility in non-human primates

- Well-tolerated, no clinical findings related to the gene therapy
- Dose-dependent increase in gene therapy delivery and RPGRIP1 expression
RPGRIP1 Program Milestones

Completed

Mouse expression study
Mouse efficacy study
NHP feasibility study
NHP GLP tox study

Initiated/Underway

Manufacturing - partner dependent; GMP plasmid produced and available
Clinical Development
Pre-IND meeting
IND submission
FIH

Orphan Drug & Rare Pediatric Disease Designation granted (Nov 2021)
Types of Partnership We Are Seeking

• Programmatic funding: donations, venture philanthropy, grants
• License and commercialization options for single program or portfolio options
• Co-development opportunities
• Additional Anc80 programs on a gene-by-gene basis
• Odylia R&D team can handle, share, or hand-off preclinical through Phase I/II trial work for these or other programs
• Co-discovery for other rare diseases. Not restricted to retinal diseases or gene therapy or Anc80
Odylia Contact Information:

Ashley Winslow, PhD, President & Chief Scientific Officer
Email: awinslow@odylia.org

Confidential deck available upon request