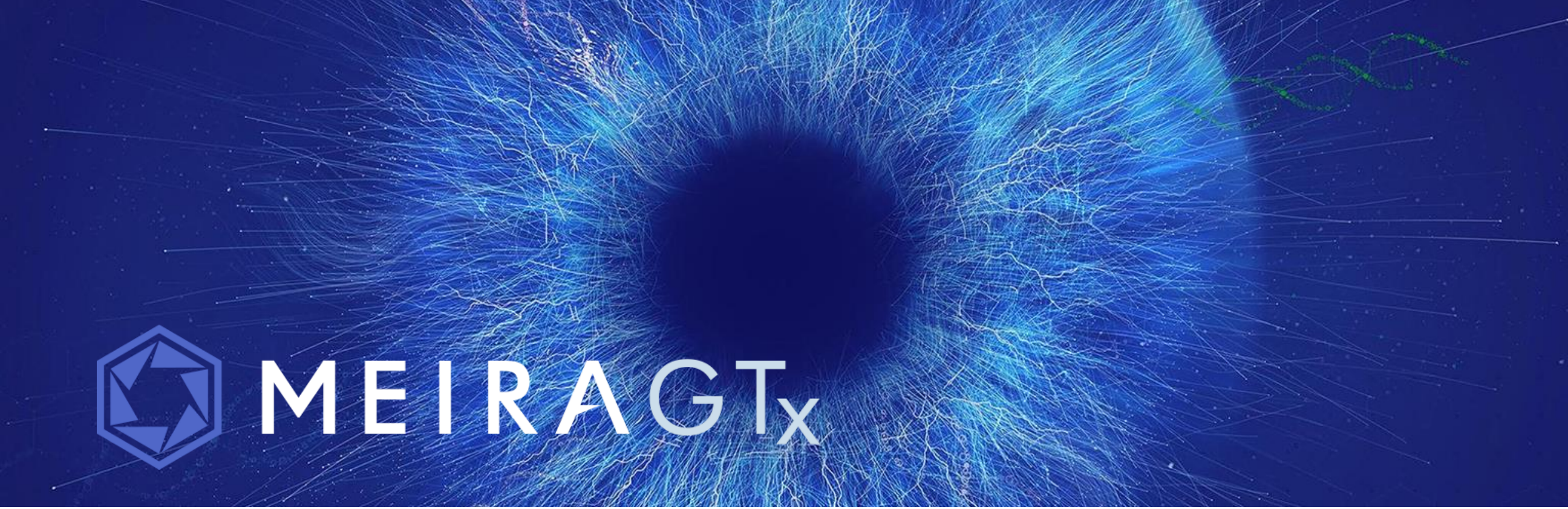


Corporate Presentation
August 2021

Forward Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding our product development and anticipated milestones regarding our pre-clinical and clinical data and reporting of such data and the timing of results of data, including in light of the COVID-19 pandemic, as well as statements that include the words “expect,” “intend,” “plan,” “believe,” “project,” “forecast,” “estimate,” “may,” “should,” “anticipate” and similar statements of a future or forward-looking nature. These forward-looking statements are based on management’s current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, our incurrence of significant losses; any inability to achieve or maintain profitability, raise additional capital, identify additional and develop existing product candidates, successfully execute strategic priorities, bring product candidates to market, expansion of our manufacturing facilities and processes, successfully enroll patients in and complete clinical trials, accurately predict growth assumptions, recognize benefits of any orphan drug designations, retain key personnel or attract qualified employees, or incur expected levels of operating expenses; the impact of the COVID-19 pandemic on the status, enrollment, timing and results of our clinical trials and on our business, results of operations and financial condition; failure of early data to predict eventual outcomes; failure to obtain FDA or other regulatory approval for product candidates within expected time frames or at all; the novel nature and impact of negative public opinion of gene therapy; failure to comply with ongoing regulatory obligations; contamination or shortage of raw materials or other manufacturing issues; changes in healthcare laws; risks associated with our international operations; significant competition in the pharmaceutical and biotechnology industries; dependence on third parties; risks related to intellectual property; changes in tax policy or treatment; our ability to utilize our loss and tax credit carryforwards; litigation risks; and the other important factors discussed under the caption “Risk Factors” in our most recent quarterly report on Form 10-Q or annual report on Form 10-K or subsequent 8-K reports, as filed with the Securities and Exchange Commission. These and other important factors could cause actual results to differ materially from those indicated by the forward-looking statements made in this presentation. Any such forward-looking statements represent management’s estimates as of the date of this presentation. While we may elect to update such forward-looking statements at some point in the future, unless required by law, we disclaim any obligation to do so, even if subsequent events cause our views to change. Thus, one should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation. Unless otherwise stated or the context otherwise requires, the information herein is as of August 1, 2021.

Advancing the Next Generation of Gene Therapies

Developing a new pharmaceutical modality designed for the cost-effective treatment of a broad range of serious disorders

Diverse Pipeline

6 ONGOING CLINICAL PROGRAMS:

- Inherited retinal diseases
- Salivary gland hypofunction
- Parkinson's disease

DEEP PIPELINE OF PRE-CLINICAL PROGRAMS

- Wet AMD / DME
- Glaucoma, Uveitis
- Multiple additional IRDs
- Sjogren's, Dry Eye
- ALS

Core Viral Vector Engineering Capabilities

VIRAL VECTOR DESIGN PLATFORM:

- Synthetic promoter design and screening platforms
- Novel capsids
- Cassette optimization: transgene engineering, sequence optimization, ITR and plasmid backbone optimization, immunogenicity
- Organoids / iPSC preclinical platforms

In-house GMP Manufacturing & Process Development

FULL END TO END MANUFACTURING INFRASTRUCTURE:

- cGMP facilities: Scalable and Flexible
- Capacity for clinical through commercial supply for all programs
- QA and QC to support first in man through commercialization
- Fill and Finish
- Process Development facility; proprietary Process Development platform
- Non GMP vector core for pre-clinical supply
- GMP plasmid production facility

Inducible Gene Regulation Platform

PROPRIETARY GENE REGULATION PLATFORM:

- Riboswitch technology allows control of gene expression with a high dynamic range
- Gene expression is turned on/off with proprietary small molecules

POTENTIAL TO REGULATE ANY GENE: Antibodies, hormones, cytokines, within BBB

A Deep Pipeline of Transformative Gene Therapies

Six clinical studies across multiple therapeutic areas

Product	Indication	Preclinical	Phase 1/2	Phase 3
Ocular				
Inherited Retinal Diseases				
AAV-RPGR* (janssen)	X-linked RP		*PRIME, Fast Track, Orphan Drug*	lumeos XLRP study
AAV-RPE65	RPE65-Associated Retinal Dystrophy		*RPDD, Orphan Drug*	
AAV-CNGB3* (janssen)	Achromatopsia		*RPDD, PRIME, Fast Track, Orphan Drug*	
AAV-CNGA3* (janssen)	Achromatopsia		*RPDD, Fast Track, Orphan Drug*	
AAV-AIPL1	LCA4	Compassionate use under MHRA Specials License		
A007, A008	Undisclosed IRD Targets			
Degenerative Ocular Diseases (non-inherited)				
A006	Wet AMD (anti-VEGFR2)			
Neurodegenerative Disease				
AAV-GAD	Parkinson's Disease			
AAV-UPF1	ALS			
Undisclosed Targets				
Salivary Gland				
AAV-AQP1	Xerostomia		*Orphan Drug*	
	Sjögren's Syndrome			

**Co-development program with Janssen Pharmaceuticals*

Diverse Targets Across Multiple Therapeutic Areas

OCULAR

Clinical Development
- IRD franchise: XLRP, ACHM, RPE65, LCA4

Research / Pre-Clinical
- Wet AMD, DME
- Glaucoma, Uveitis

Gene Regulation
- Eye Drops

NEURODEGENERATIVE

Clinical Development
- Parkinson's disease

Research / Pre-Clinical
- Amyotrophic Lateral Sclerosis (ALS)
- Undisclosed indication

Gene Regulation
- CNS expression with BBB-penetrant small molecules

SALIVARY GLAND

Clinical Development
- Radiation-induced Xerostomia (Grade 2/3)

Research / Pre-Clinical
- Sjogren's Syndrome
- Dry eye, Dry mouth

Gene Regulation
- Peptide and hormone salivary gland delivery

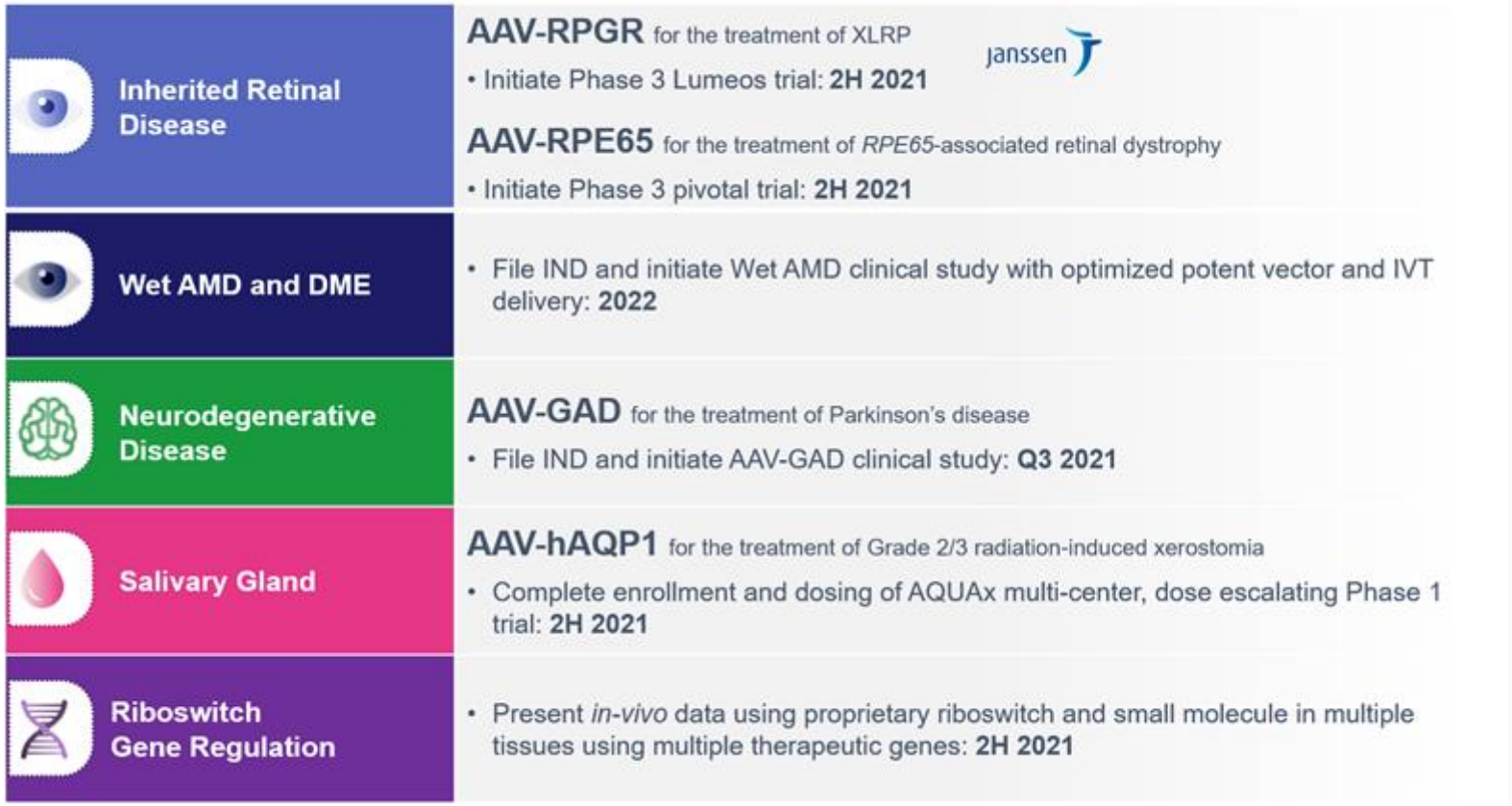
RIBOSWITCH GENE REGULATION

- **Proprietary riboswitch technology allows control of gene expression using a small molecule**
- Applications beyond gene replacement – e.g., delivery of therapeutic proteins
- Improved dosing and cost effectiveness of biologic drugs through spatial and temporal control

Clinical studies ongoing across ocular, neurodegenerative and salivary gland indications

In-house vector development & optimization technology create opportunities to treat many indications

Anticipated Upcoming Milestones and Objectives



- **Expect to advance 3-5 additional programs into the clinic by YE 2022**
- **Potential to have up to 11 clinical stage programs by y/e 2022**
- **Supported by internal manufacturing, QC and QA infrastructure**
- **Capacity for the development of all programs from first in man through commercialization**

A Unique, Diverse and Inclusive Culture

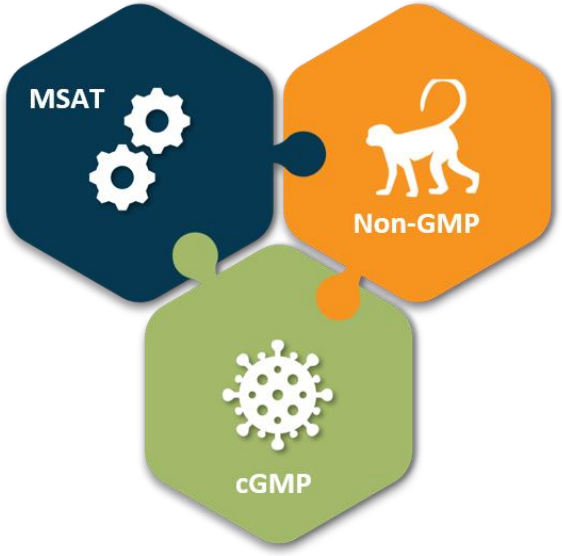
MEIRAGTx

- 250+ full-time employees
- 46% female, 54% male
- 4 locations: US, UK, Netherlands, Ireland
- 29 different nationalities represented

Industry-Leading cGMP Manufacturing of AAV

Fully Integrated Manufacturing Ecosystem

120+ FTEs dedicated to best-in-class AAV manufacturing



cGMP Manufacturing

- Two independent viral vector production facilities
- Flexible and scalable manufacturing process; fit for commercialization; global regulatory CMC input
- Single use philosophy, closed system unit operations
- Highly flexible and scalable for clinical and commercial needs
- In-house QC hub (end 2021)
- London facility GMP certified 2018 and 2020 – facility and quality management systems supports first in man clinical through commercialization
- In-house GMP plasmid production
- In-house fill and finish

MSAT Facility: Process Development

- Dedicated MSAT facility adjacent to London cGMP facility; process development and optimization
- Rapid vector-specific process optimization for new products: 2-5 months
- QC and potency assay development, validation and qualification for BLA supporting GMP runs
- Optimized plasmid backbones for producibility driving yield and increasing production capacity
- Vectors optimized for potency (promoters, capsids, gene sequence) may reduce dose, increase efficacy and decrease cost of goods

Non-GMP Vector Core

- Produce consistent vector batches for pre-clinical studies
- Synergize with MSAT to prepare for vector process optimization pre-tech-transfer to GMP

Flexible and Scalable GMP Manufacturing for Clinical & Commercial Production

London Facility

- **cGMP 29,000 sq ft**
- 2 cell suites; 3 viral vector suites
- Each with independent air handling
- Single use philosophy / fully enclosed technologies
- Designed for minimal downtime and maximum flexibility
- Designed to meet MHRA, EMA and FDA regulatory requirements
- Support laboratories: Quality Control
- Adjacent MSAT (Manufacturing Science and Technology) area/pilot plant for process development and optimization
- MSAT to GMP tech transfer

Ireland Facility

- **cGMP 150,000 sq ft**
- Up to 12x viral vector suites with 2x 500L bioreactor per suite (each suite with capacity for multiple 2000L or larger bioreactors)
- Flexible high capacity GMP manufacturing hub for clinical through commercial supply
- Fully scalable automated fill and finish
- Full QC laboratories for global release
- cGMP plasmid manufacturing facility
- Extensive warehouse and Clinical supply storage
- Covered by QA to support clinical through commercial supply

Britannia Walk Facility – London, UK





11

Shannon Facility – Ireland, EU

Shannon Facility – Ireland, EU

Comprehensive Preclinical Development Capabilities

Preclinical Development Centers (London – New York – Amsterdam)

- Team built with a mix of academic excellence and industrial experience around: AAV engineering, vector engineering and protein engineering

In-vivo Platform

- Using a range of relevant animal models (rodents, lagomorphs and non-human primates) for establishing efficacy and toxicology
- IND-enabling data set generation (POC and toxicology) for monogenic and acquired disorders

Organoid and iPSC Platform

- 3D cellular models for relevant human in-vitro platforms – increased relevance and architecture for complex/laminated tissues (CNS)
- Potency assay development across multiple programs

In-House non-GMP vector core (Amsterdam)

- Produce consistent vector batches for pre-clinical studies
- Synergize with MSAT to prepare for vector process optimization pre-tech-transfer to GMP

Vectorology Toolkit

- Promoters, Capsids, gene sequence, optimizing for increased expression and decreased immunogenicity, protein engineering, ITRs, gene regulation
- ITRs – packaging efficiency (and impact on vector genome transduction and expression)
- Plasmid backbone design – cap/rep organization, stuffer sequences, non-plasmid transfection agent – minicircles, doggybone, linear DNA

Extensive Vector Engineering Toolkit

Gene Sequence Optimization

- Promoter-enhancer-intron-exon configuration
- cDNA engineering/Protein Engineering – vector stability, transgene size, mini genes, increase protein activity and potency
- Codon optimization for translational efficiency or inclusion of sequences for immune evasion
- Kozac optimization, Poly A optimization

Promoters

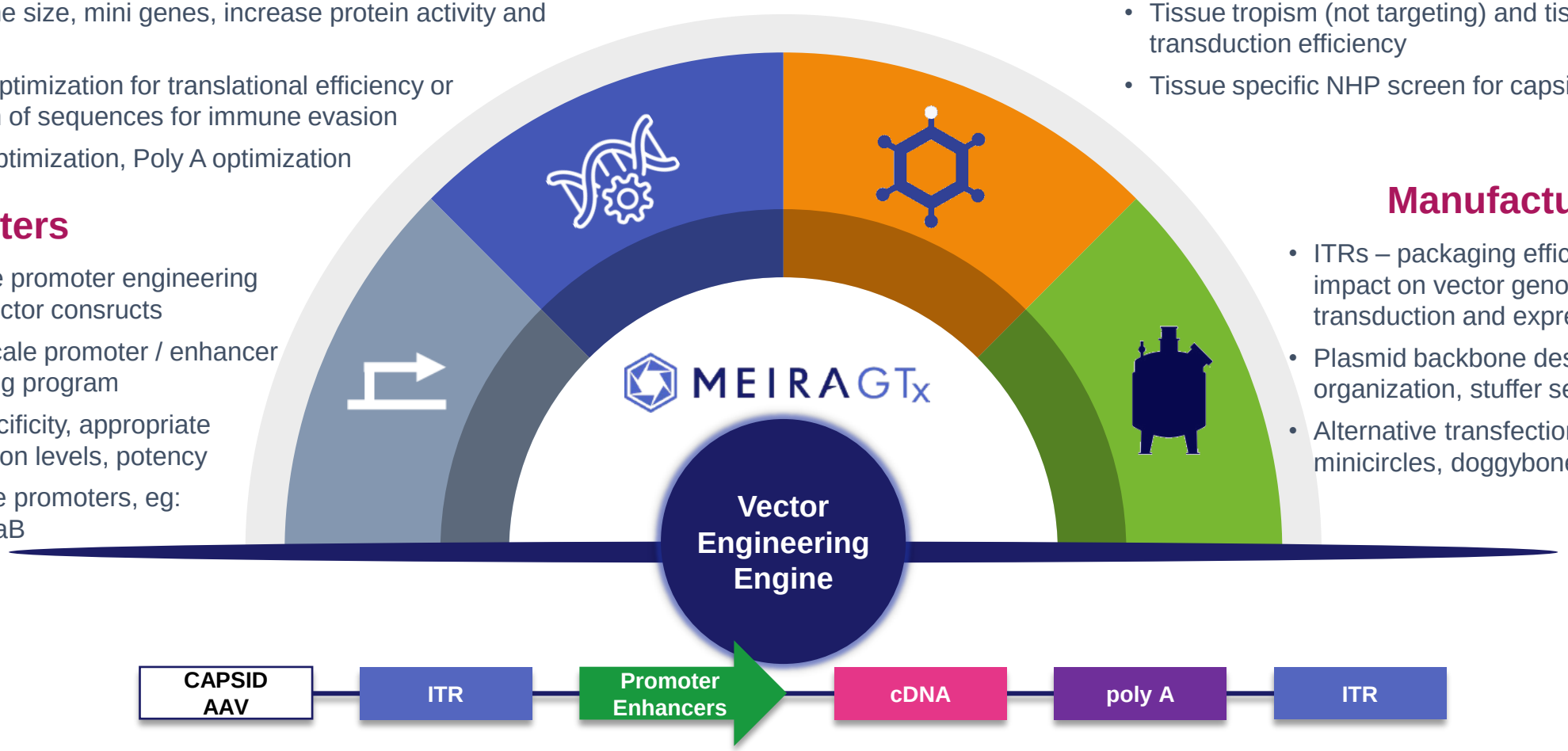
- Bespoke promoter engineering for all vector consructs
- Large scale promoter / enhancer screening program
- Cell specificity, appropriate expression levels, potency
- Inducible promoters, eg: NFkappaB

Capsid Optimization

- Capsid selection for efficacy for each indication and cell type
- Tissue tropism (not targeting) and tissue specific transduction efficiency
- Tissue specific NHP screen for capsid tropism

Manufacturability

- ITRs – packaging efficiency (and impact on vector genome transduction and expression)
- Plasmid backbone design – cap/rep organization, stuffer sequences
- Alternative transfection DNA – minicircles, doggybone, linear DNA



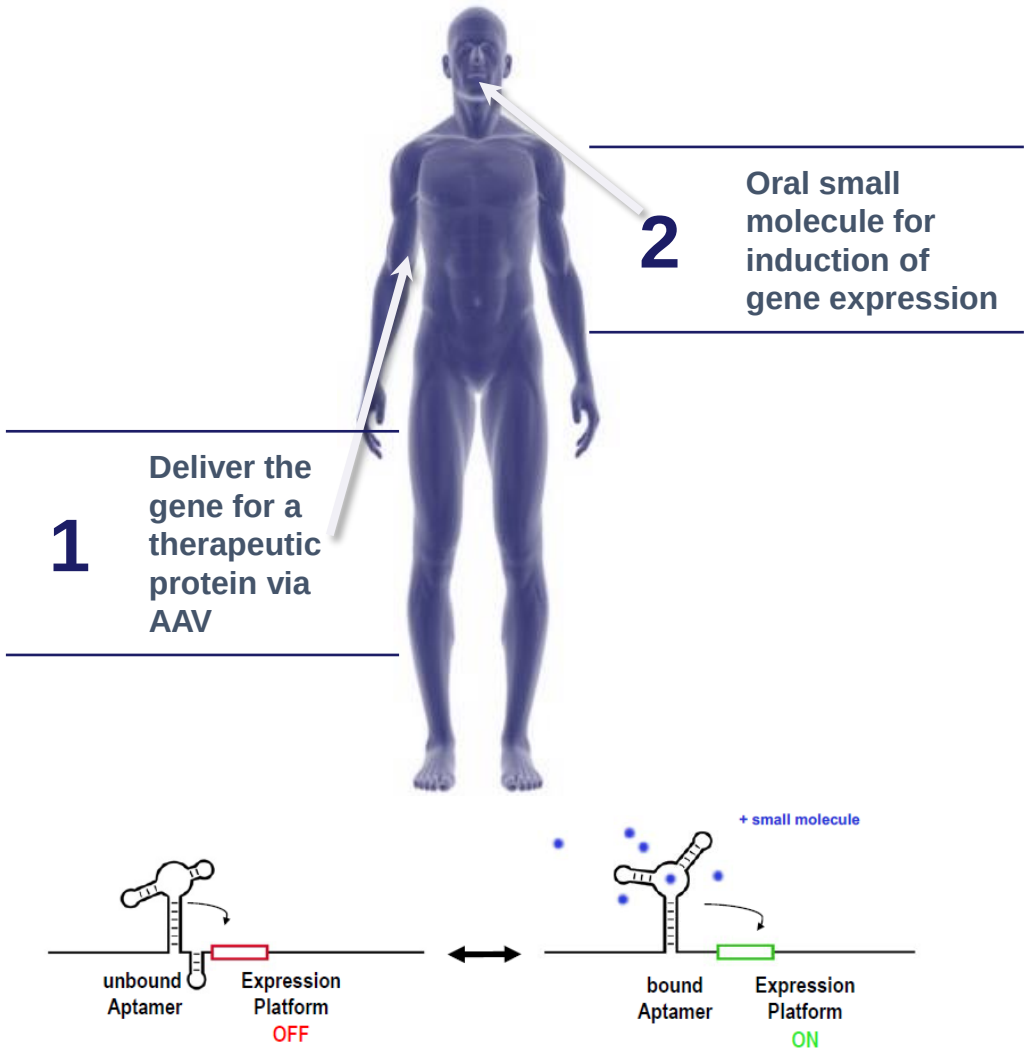
MEIRAGTx

Gene Regulation

Transforming Gene Therapy with a First of its Kind Gene Regulation Platform

Small molecule responsive switch enables control of gene expression at high dynamic ranges

- Modular switch based on **rationally designed synthetic riboswitches** - allows activation of gene expression by small molecule inducer
- Riboswitch – uses RNA shape – does not regulate via the promoter
- Promoter control intact – allowing promoter driven specificity and potency with high expression levels and dynamic range
- Unprecedented dynamic range of more than 5,000-fold achieved
- The switch is modular - multiple regulation cassettes have been designed
- Cassette can be optimized for expression level and dynamic range depending on the therapeutic need
  - Switch can be designed for a specific dosing need
  - Switch can be driven by different aptamer/small molecule pairs
  - Each gene may be driven by its own small molecule
  - Small molecule can be selected for appropriate PK and distribution for a specific gene and specific indication
- Demonstrated regulation of multiple transgenes, including antibodies, hormones, peptides, enzymes and cytokines
- Demonstrated *in-vivo* gene regulation with several transgenes, with high reproducibility



Regulatable Gene Therapy Opens the Way to a New Class of Vectorized Biologics

Controlled Expression of Vectorized Biologics

- Activate production of biologic (e.g. antibodies, enzymes, hormones) within the patient body in response to a small molecule inducer.
- New potential targets for gene therapy, and biologics

Temporospatial Control in Difficult to Access Regions

- Activation in sites difficult to access for biologics – e.g. Blood-Brain-Barrier crossing

Better Per-Patient Dosing

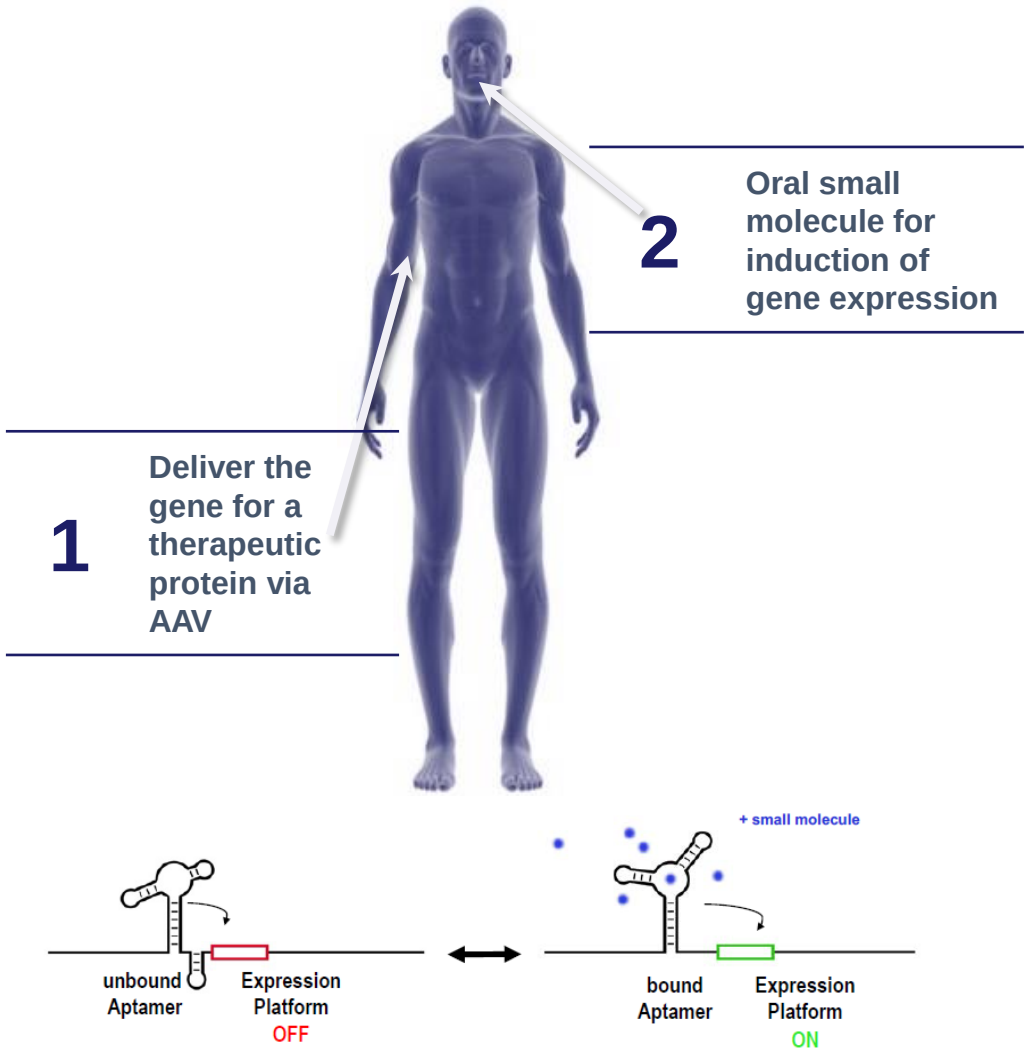
- Potential to achieve effective dosing of hard to deliver biologic drugs
  - Short acting peptides to be dosed effectively for enhanced efficacy
  - Long lived proteins – optimal dosing driven by the PK of the small molecule - enhanced efficacy

Potential for Improved safety

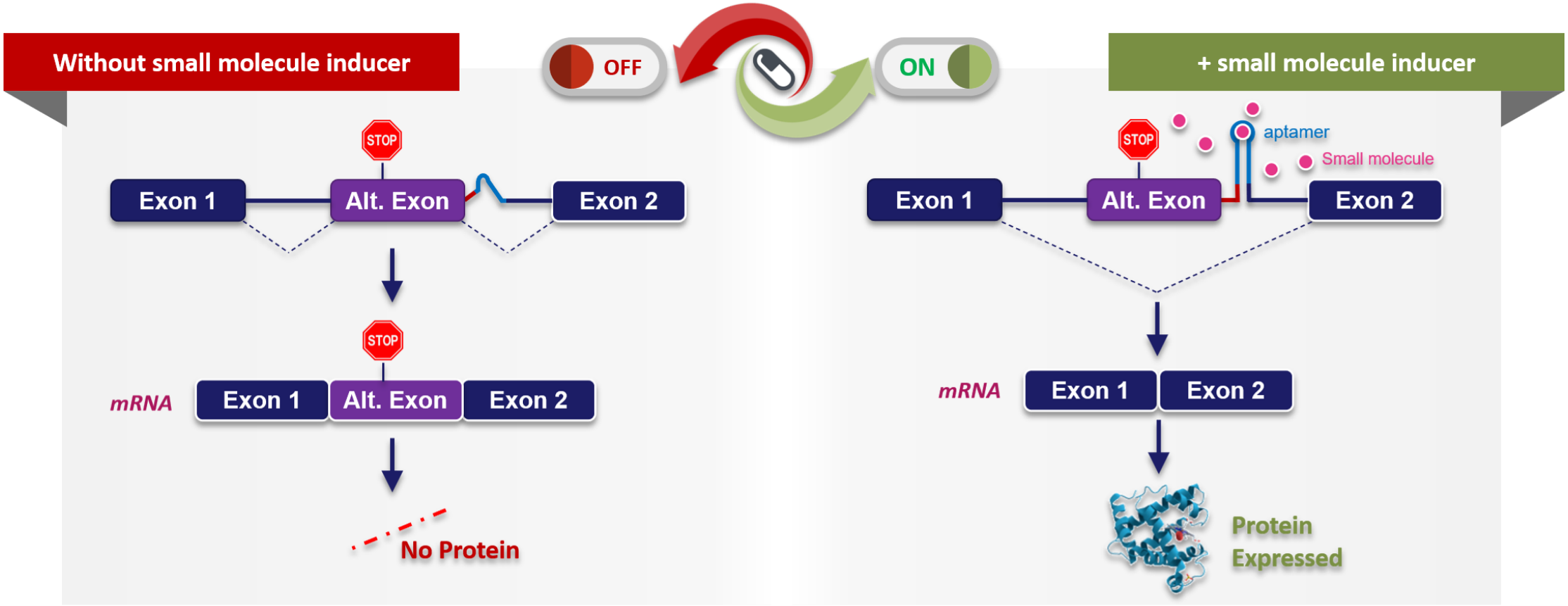
- Tight regulation of gene expression with a default “off” state.
- Transient activation of gene expression occurs solely following administration of a small molecule with well defined PK profile.

New Pricing Model

- Gene therapy is no longer a 1-time treatment but dosed with a small molecule over time



Inducible Gene Expression Platform Based on Novel Synthetic Riboswitches



In the absence of small molecule inducer:

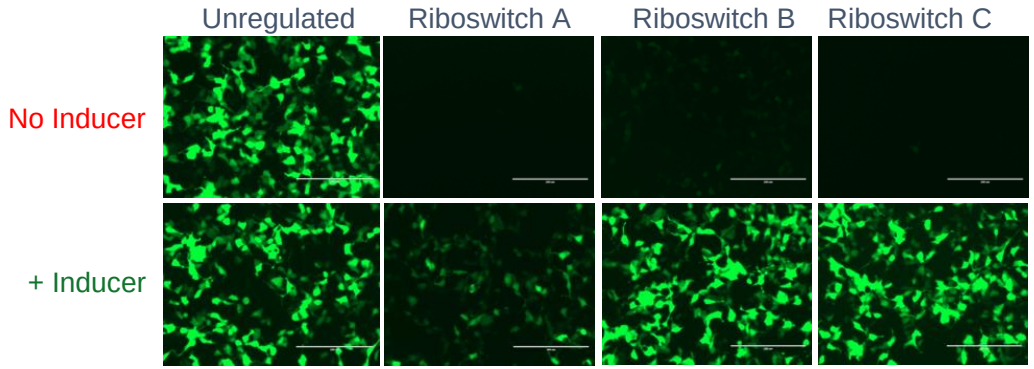
1) Alternative 5'ss is accessible
2) Stop codon-containing alternative exon is included
3) No protein is produced

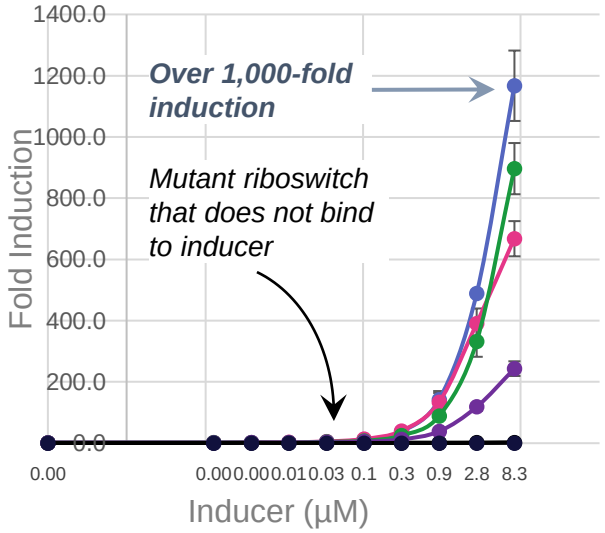
In the presence of small molecule inducer:

1) Alternative 5'ss is sequestered
2) Stop codon-containing alternative exon is excluded
3) Protein is expressed

Inducible Gene Expression Driven by Novel Synthetic Riboswitches

Development of Potent and Specific Regulatory Cassettes





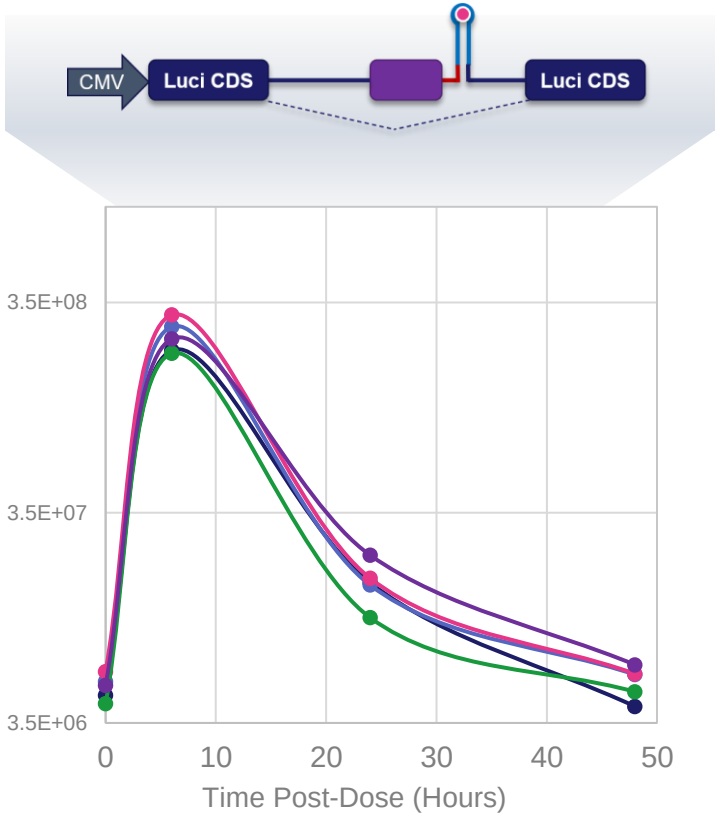
Top Panel:

- HEK 293 cells transfected with riboswitch-controlled EGFP construct
- Three different switches with different dynamic ranges and total expression levels

Bottom Panel:

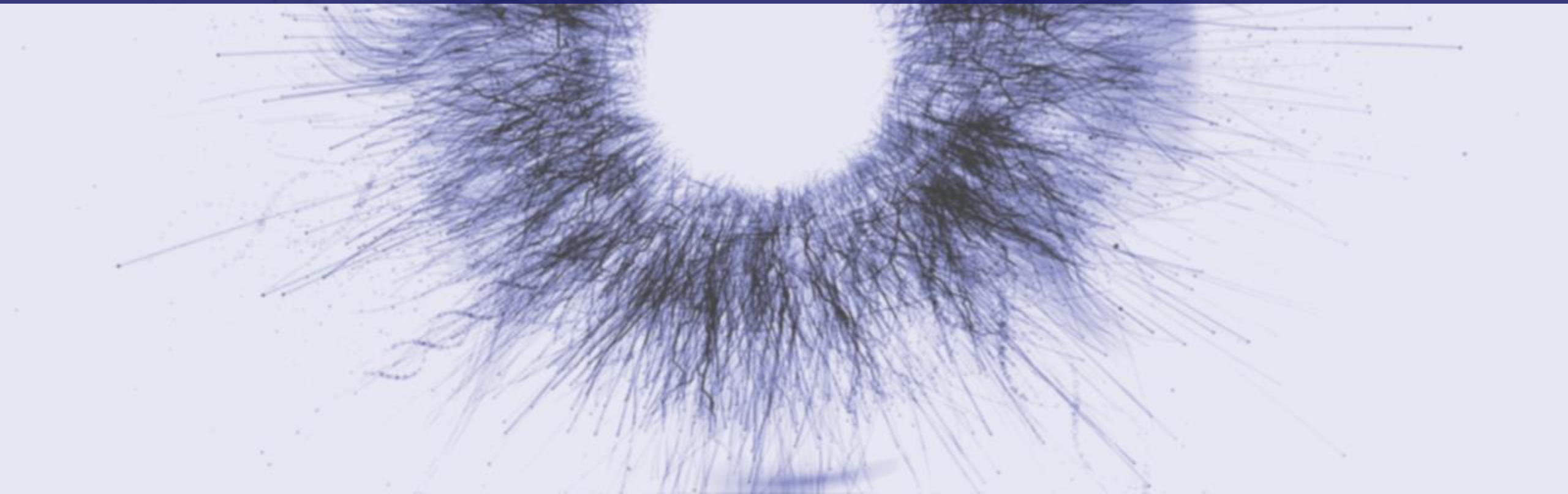
- **Evolution of novel aptamers:** Improvement in dynamic range as riboswitch sequences are mutated, increasing potency and specificity of small molecule binding

Regulated Luciferase Expression in Mouse Liver in Response to Orally Delivered Inducer (30 mg/kg PO)



- Mice (n=5) transduced via tail vein delivery to the liver, with AAV8 encoding for riboswitch-regulated luciferase
- Reproducible robust induction of gene expression in liver *in-vivo* (measured by luciferase activity) is observed in response to a single oral dose of the inducer

Ocular Pipeline



Ophthalmology Toolkit: Applied to Large Indications in the Eye

Vectorlogy toolkit:

- **Increase Potency**
  - promoter engineering - enhanced potency and activity – strong cell specific and ubiquitous promoters from MeiraGTx promoter discovery platform
  - Regulatory elements, enhancers, introns, polyA and ITR
  - Kozak and Codon optimization
- **Intravitreal delivery: Capsid selection**
  - Two proprietary intravitreal capsids in NHP head-to-head testing
  - Ongoing NHP directed evolution screen for capsids for different parts of the eye
- **Reduced immunogenicity**
  - Design elements to reduce innate immune response
  - Codon Optimization
  - Manufacturing: potential alternative to plasmid DNA - linear DNA, mini-circles
  - Multiple study experience to optimize steroid regimen
- **Retinal organoid technology**
- **Suprachoroidal Delivery:** In development

Large ophthalmology indications in development:

- Wet AMD – two novel potent mechanisms
- Dry AMD – transformative rod-to-cone technology
- Glaucoma
- Uveitis

Strategic Collaboration with Janssen in the IRD Space

MEIRAGTx / Janssen Pharmaceutical Companies of Johnson & Johnson

Clinical Development

- Janssen and MeiraGTx collaborate to advance AAV-RPGR, AAV-CNGB3, AAV-CNGA3 through clinical development
- Janssen responsible for 100% of costs

Janssen Commercial Infrastructure

- Janssen has worldwide exclusive commercial rights to AAV-RPGR, AAV-CNGB3, AAV-CNGA3 and specific future IRD programs
- IRD portfolio benefits from worldwide reach of Janssen commercial infrastructure
- MeiraGTx receives 20% untiered royalty
- MeriaGTx is commercial manufacturer for IRD products

Pre-Clinical IRD Research

- Collaboration leverages MeiraGTx vector design and optimization technology to develop potential gene therapy treatments for multiple IRDs
- Janssen to receive exclusive rights to develop & commercialize programs from IRD research collaboration
- Janssen pays majority of research costs, opt in at IND, and pays 100% development thereafter, milestones and high teens untiered royalty

Manufacturing and Process Development

- Janssen accesses MeiraGTx advanced manufacturing capabilities with clinical and commercial supply agreements
- Joint development of AAV manufacturing technologies to expedite and optimize development
- MeiraGTx commercial manufacturing for potential Janssen IRD programs

MeiraGTx retains global rights to all non-inherited ocular programs

e.g., Wet AMD, Dry AMD, Glaucoma, Uveitis

Inherited Retinal Disease (IRD) Strategy

Portfolio Approach to IRDs

- In the US, 200,000–300,000 people affected by an IRD, which projects a worldwide prevalence estimate of 4.5–6.8 million people that may be caused by one of 270 or more different genes[1]
- Synergies in clinical, regulatory, assay development, manufacturing, and commercialization

Optimized Vector for each Indication

Each with the best selected capsid, cell specific promoter expressing at appropriate level for the molecular profile of the disease

Natural History studies

- Large prospectively designed natural history study for each clinical indication with 2-5 years of data on each patient
- Rapid enrollment; Well validated endpoints for each disease
- Well characterized patients appropriate for treatment and potential signals of activity

Strong Relationships with Ophthalmology Partners and Centers of Excellence:

- **UCL Institute of Ophthalmology**
  One of the world's leading research institutes pioneering ophthalmology gene therapy
- **Moorfields Eye Hospital**
  Provides access to the world's largest catchment of patients with inherited retinal diseases, well characterized patients, prospective Natural History studies
- US footprint through links with **University of Michigan Kellogg Eye Center, Massachusetts Eye and Ear (MEEI)**, **Casey Eye Institute** and other leading centers globally
- Partnership with **Foundation Fighting Blindness (FFB)**
- Global expertise in imaging and validated endpoints in each of our target diseases

UCL INSTITUTE OF OPHTHALMOLOGY · KELLOGG EYE CENTER MICHIGAN MEDICINE · CASEY EYE Institute OHSU · Moorfields Eye Hospital NHS Foundation Trust · Massachusetts Eye and Ear sense life. experience life. · FOUNDATION FIGHTING BLINDNESS

[1]Mansfield BC, Yerxa BR,Branham KH. Implementation of a registry and open access genetic testing program for inherited retinal diseases within a non-profit foundation. Am J Med Genet Part C. 2020;e31825.

AAV-RPGR: Gene Therapy for XLRP

Disease Overview

Retinitis Pigmentosa (RP)

- Group of IRDs which represents the most common genetic cause of blindness
- X-linked RP is the most severe form of RP and accounts for 10-15% of RP patients

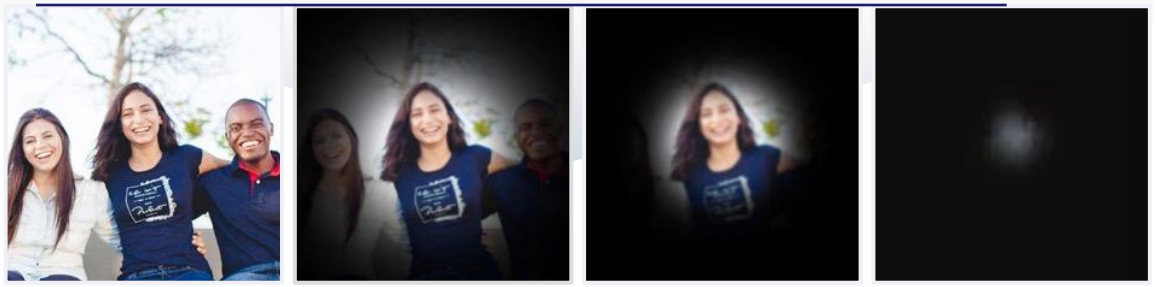
Disease progression

- Loss of night vision
- Progressing into tunnel vision
- Blindness in 4th decade

Prevalence

- ~1/40,000
- Total patients in US, EU5, Japan: ~20,000

Patient Experience:



Product: AAV-RPGR | Stage: Clinical

Developed to deliver stable gene sequence to rod and cone photoreceptors, driving expression of functional RPGR protein, resulting in rescue of photoreceptor function and consequently improving vision

Optimized RPGR ORF15 transgene

Selective deletion in highly repetitive purine-rich region of RPGR ORF15 stabilizes the transgene resulting in expression of functional protein with correct photoreceptor localization

AAV5 capsid

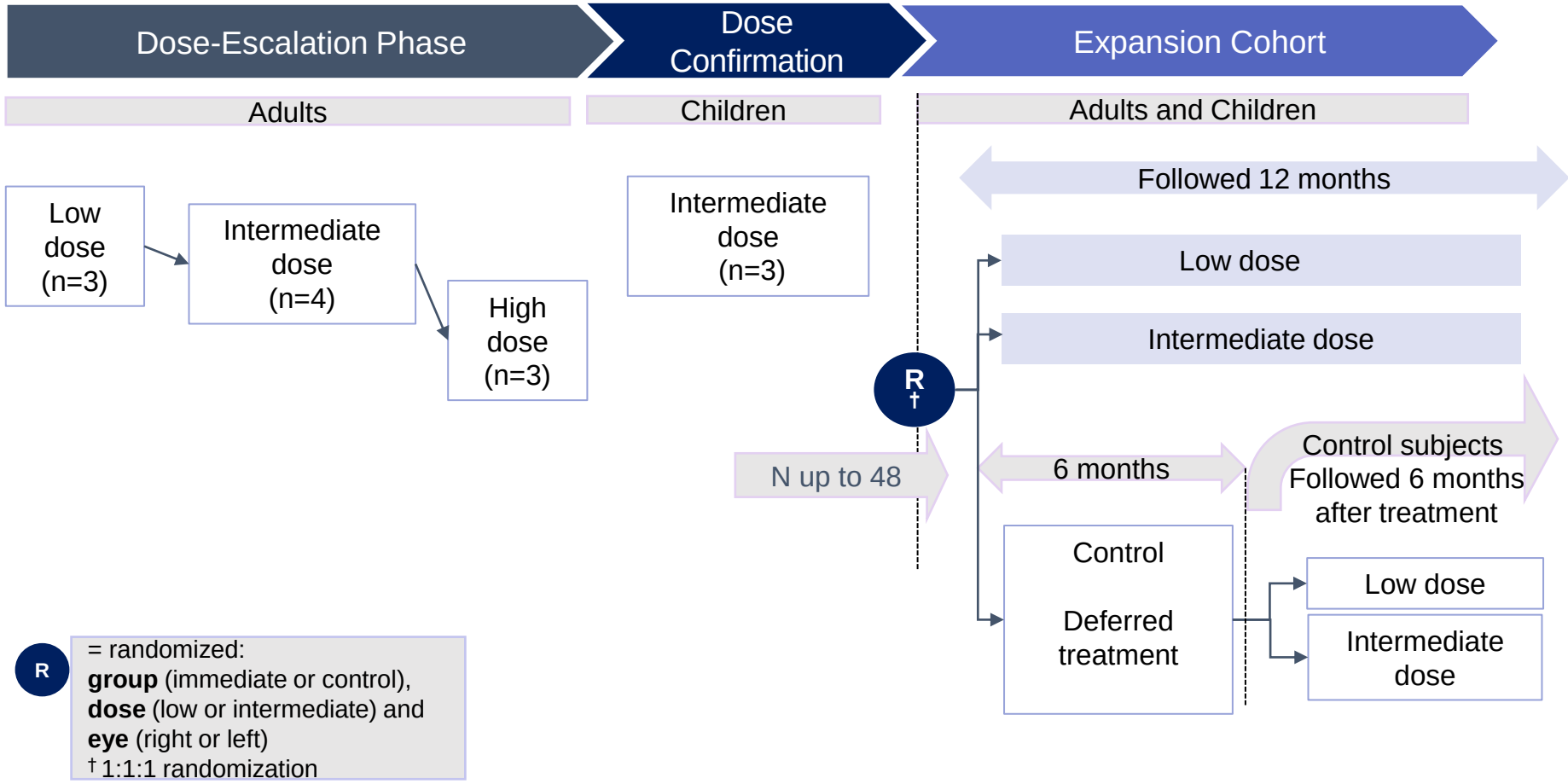
Efficiently delivers vector genome to both rods and cones

Human rhodopsin kinase promoter (hRKp)

Photoreceptor-specific promoter restricts expression of transgene to photoreceptor cells

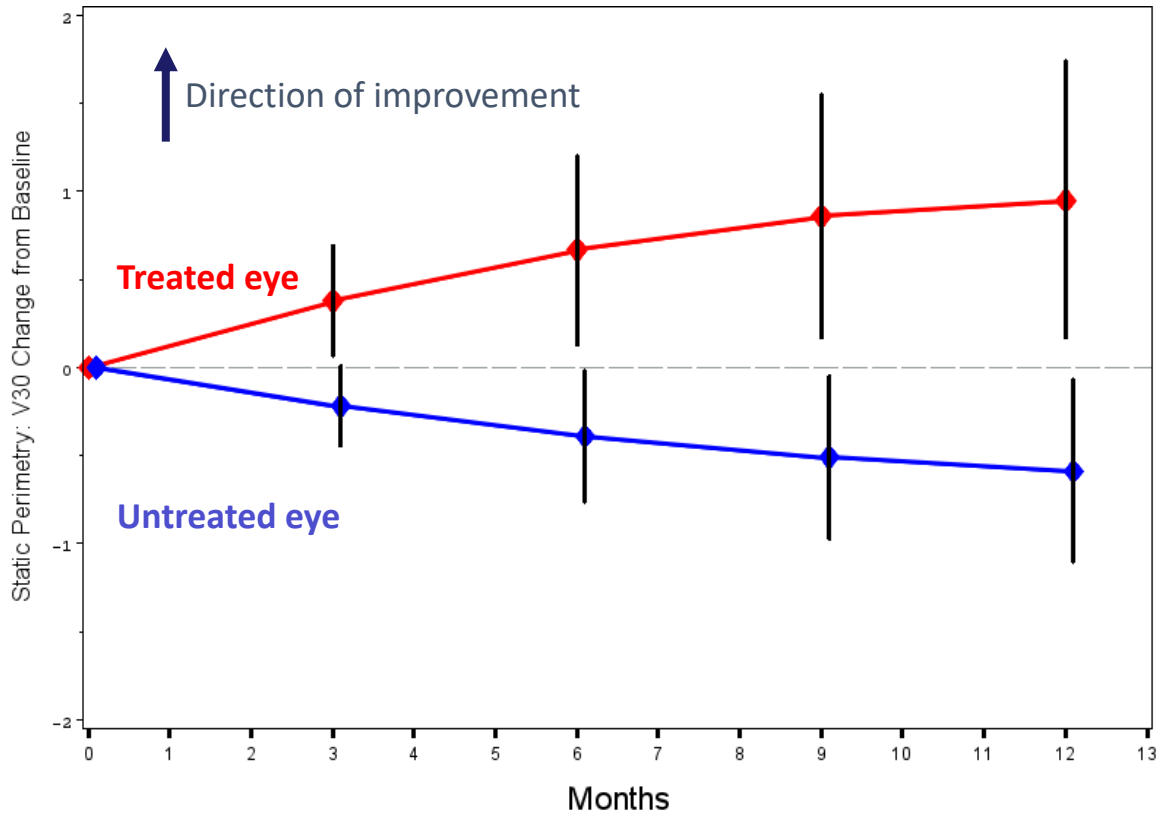
AAV-RPGR Phase 1/2 Trial: Dose Escalation and Randomized Expansion

Multicenter open-label Phase 1/2 trial of an AAV5-RPGR gene therapy (NCT03252847) conducted at 5 sites across the United States and United Kingdom



Statistically Significant Improvement in Retinal Sensitivity in Low and Intermediate Dose Cohorts (n=6)

Change in Retinal Sensitivity Over Time (V30 change from Baseline)



Change in Retinal Sensitivity @ 12 months (treated – untreated eye)

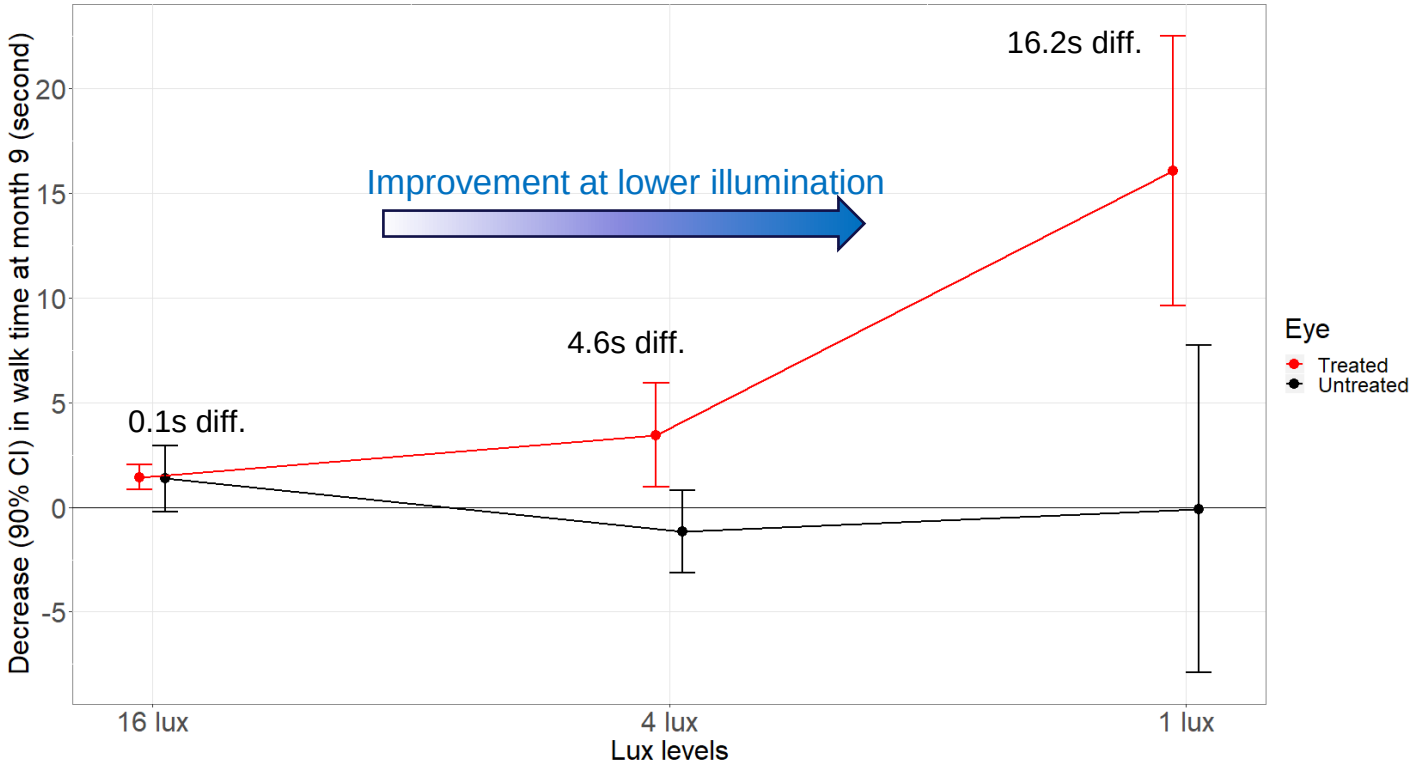
Mean Retinal Sensitivity (dB)	Treated-Untreated Eye Difference @ 12 months (90% CI adjusted for baseline)
Low	0.76 (–0.14, 1.66)
Intermediate	1.05 (0.81, 1.29)*
High	–1.05 (–1.77, 0.06)

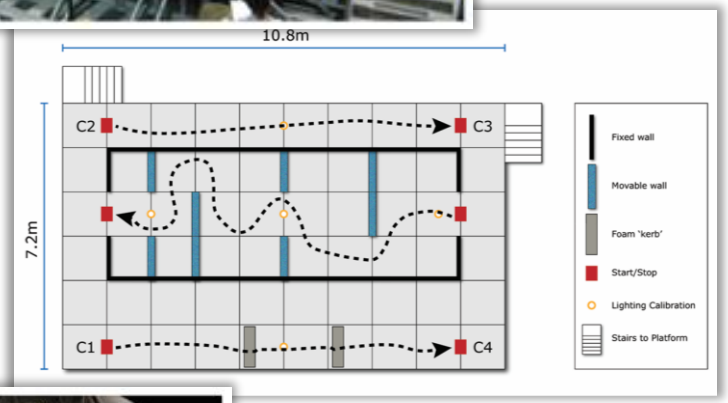
Central 30° Hill-of Vision (V30, dB-sr/y)	Treated-Untreated Eye Difference @ 12 months (90% CI adjusted for baseline)
Low	1.10 (0.10, 2.10)*
Intermediate	1.26 (0.65, 1.86)*
High	–0.89 (–1.70, –0.01)

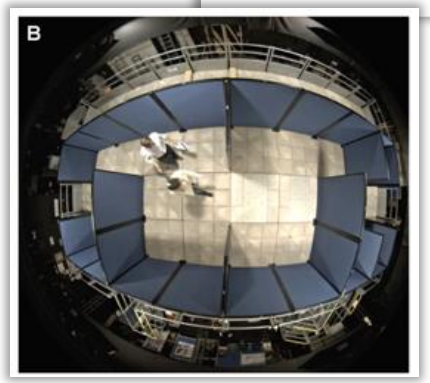
Response was treated-untreated eye adjusted for baseline (double-delta).
*Statistically significant effects at a one-sided 5% level.
Excludes one subject with panuveitis in the low dose.

Significant improvement in retinal sensitivity sustained 12 months after treatment

Significant Improvement in Vision-Guided Mobility Compared to Baseline (Low and Intermediate Dose, n=6)







VMA endpoint	Low Dose (n=2)*	Intermediate Dose (n=4)
Number of subjects improving at 1, 4 or 16 lux (treated – untreated < 0 sec)	**2/2**	**3/4**

*Excludes one subject with panuveitis in the low dose.
Maze assessments were not conducted in the high dose cohort at the 9 month timepoint.

*Maze assessment shown at 9-month time point; maze assessment not conducted at 12 months.

To view the maze assessment please click **here**

Summary: 12-Month Dose Escalation Data from Ongoing Phase 1/2 Study of AAV-RPGR in Patients with XLRP

Significant vision improvement sustained 12 months after treatment

- Meaningful improvement from baseline in retinal sensitivity across multiple metrics and modalities in low and intermediate dose cohorts
- Meaningful improvement from baseline in vision-guided mobility in low and intermediate dose cohorts (mobility testing undertaken at 9-month timepoint)
- Statistically significant improvements from baseline compared to untreated eyes in low and intermediate dose cohorts

AAV-RPGR was generally well tolerated, with a favorable safety profile

- Most AEs were ocular, anticipated due to the surgical procedure, transient and resolved without intervention

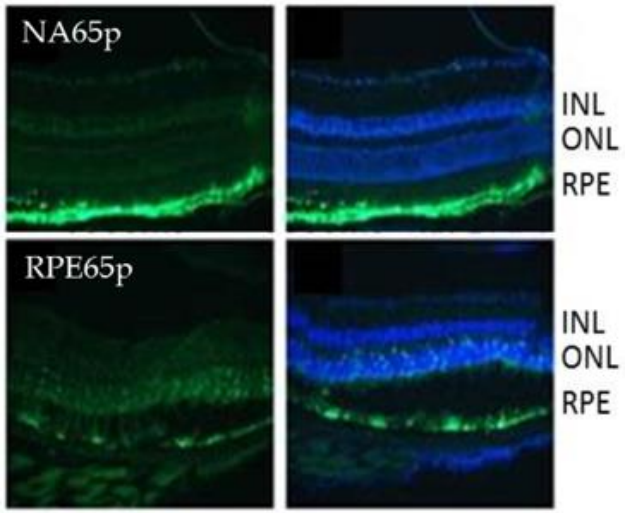
Data support advancing AAV-RPGR into Phase 3 clinical trial

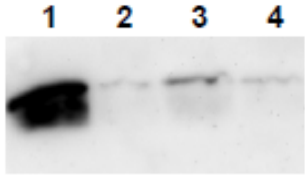
lumeos XLRP study

AAV-RPE65: Optimized Viral Vector for the Treatment of LCA2

Optimization Details

- **AAV5 capsid selected over AAV2 capsid** → 4x transfection efficiency of human RPE cells
- **RPE cell-specific promoter optimization** → 20x protein expression in the RPE cells
- **Optimized transgene sequence** → 7x protein expression in human cells through codon-optimization and an optimized Kozak sequence
- **SV40 intron sequences** regulatory sequences to improve RNA processing → 2.5x increased mRNA stability



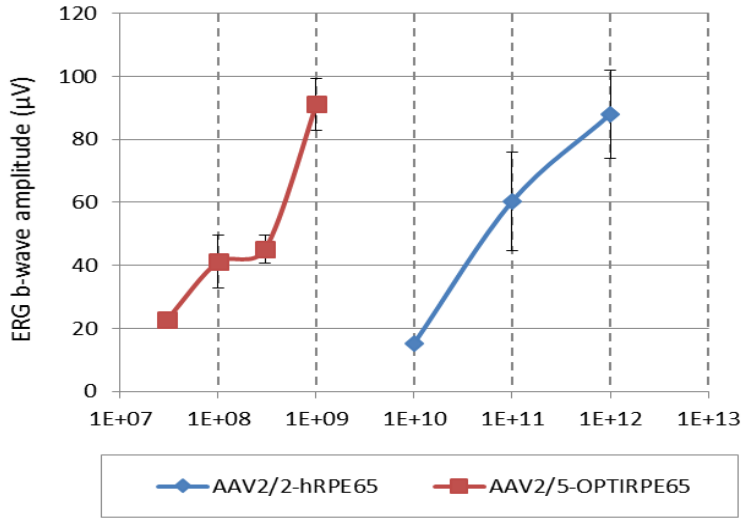


1: AAV. RPE65OPT.GFP
2: AAV. RPE65OPT.GFP (1:20 dilution)
3: AAV.BGL65p.GFP (alt promoter fragment)
4: AAV.hRPE65.GFP

Head-to-Head Comparison

- Head-to-head comparison in-vivo of AAV2/5-OPTIRPE65 and AAV2/2-hRPE65, the first generation used in the clinical trial

- After subretinal injection into RPE65-deficient mice, AAV2/5-OPTIRPE65 can restore retinal function at **300-1000 fold** lower doses than first generation clinical vector AAV2/2-hRPE65



Summary of Topline Data from Phase 1/2 Trial of AAV-RPE65

AAV-RPE65 STUDY	**15 patients treated** • 9 young adults (16-24) across three dose escalation cohorts • 6 children (5-12) in a pediatric expansion cohort
PRIMARY ENDPOINT: SAFETY	**AAV-RPE65 was generally well-tolerated after six months of follow up** • AAV-RPE65 safety profile consistent with other approved and investigational ocular gene therapies • Subretinal injection targeting the central retina, including the fovea, was demonstrated to be well tolerated
SECONDARY ENDPOINTS	**Mobility testing*** • Statistically significant improvement in the time taken to navigate a visually-guided mobility maze was demonstrated across the full spectrum of light levels tested **Retinal Sensitivity**** • Statistically significant improvement in retinal sensitivity at six months compared to baseline (Octopus 900 full-field static perimetry) **Visual Acuity**** • Statistically significant improvement in the ETDRS letter score from baseline to six months **Contrast Sensitivity**** • Statistically significant improvement in contrast sensitivity from baseline to six months (Pelli-Robson assessment)

*Statistical significance demonstrated across entire study (cohort 1, cohort 2, cohort 3, pediatric expansion cohort)
**Statistical significance demonstrated in subset of adults and children treated at $1x10^{11}$ (cohort 1, pediatric expansion cohort)

Data support initiation of pivotal trial (2H 2021)

AAV-CNGB3 & AAV-CNGA3 for the Treatment of Achromatopsia

Disease Overview

Achromatopsia (ACHM)

Retinal defect:

- Complete absence of cone photoreceptor function from birth

Disease characterization:

- Very poor visual acuity from birth (typically 20/200)
- Photophobia (disabling aversion to light)

Prevalence and genes

- Overall ACHM prevalence is around 1/30,000 in US
- Total patients in US, EU5 and Japan:~24,000
- CNGB3 (~50% of cases), CNGA3 (~40% of cases)

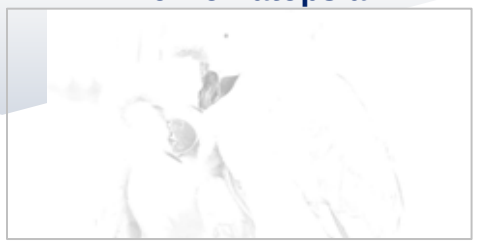
Natural history study ongoing:

- >90 patients well characterized

Patient Experience:

Healthy

Achromatopsia



Product: AAV-CNGB3/CNGA3 | Stage: Clinical

Ongoing Clinical Trials:

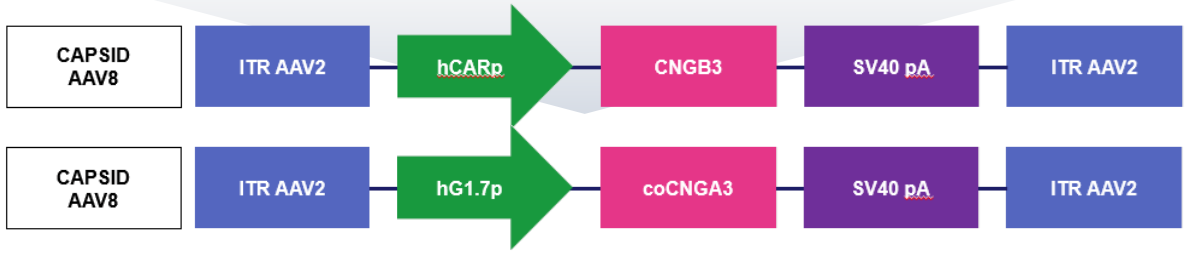
Phase 1/2 trial of AAV-CNGB3

- Dosing completed, follow up ongoing
- 23 patients treated (11 adults, 12 children)

Phase 1/2 trial of AAV-CNGA3

- Dose completed Q1/2021
- 11 patients treated (2 adults, 9 children)

Update on further clinical studies for AAV-CNGA3 and AAV-CNGB3 in 2H 2021



Salivary Gland Pipeline

Radiation-Induced Xerostomia (RIX): Large Patient Population with High Unmet Medical Need

Target Indication: Treatment of Xerostomia persisting >2 years after radiation therapy for head and neck cancer

- 85% of radiation-treated patients experience reduced saliva production, of whom 40% have persistent Grade 2/3 RIX[1] 2 or more years following treatment
- >170,000 existing patients in the US alone who are cancer free 2 or more years post-radiation treatment with Grade 2/3 RIX (orphan drug designation)[2]
- 58,000 new cases of head and neck cancer **per year** in the US
- 650,000 new cases of head and neck cancer worldwide[3]
- **Serious, debilitating complications as a result of reduced saliva:**
  - Dryness of mouth and lips make it difficult to eat, chew, swallow
  - Sore throat and changes in vocal quality
  - Burning present in 40% of patients with dry mouth[1]
  - Unable to wear/tolerate dentures
  - Increased risk of dental cavities and tooth loss
  - Increased risk of fungal infection
  - Taste changes – loss of taste or food tastes metallic/salty
- **Current treatment options for this serious condition are limited**

[1]Jensen S.B., *et al.* (2010). A systematic review of salivary gland hypofunction and xerostomia induced by cancer therapies: prevalence, severity and impact on quality of life. *Support Care Cancer*. 18(8):1039-1060.

[2]Cox J.D., *et al*. (1995). Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment for Cancer (EORTC). *Int. J. Radiation Oncology Biol. Phys.* 31(5):1341-1346.

[3] Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018; 68:394.

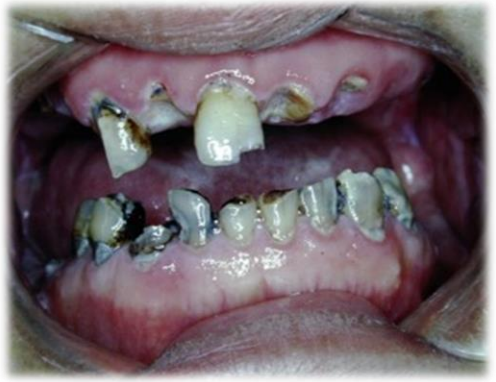
Radiation-Induced Xerostomia

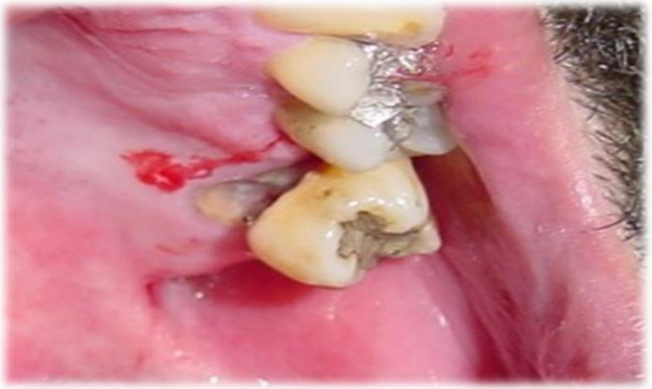
Xerostomia (Dry Mouth)

- One of the most common complications of treatment for head and neck cancer
- Progressive, irreversible, significantly impairs quality of life of potentially cured cancer patients
- Changes in quantity and quality of saliva occur, impacting lubrication, cleansing, antimicrobial effect, digestion and taste
- Often leads to severe and lasting oral issues

Clinical Signs and Symptoms

- Dryness of mouth and lips make it difficult to eat, chew, swallow
- Sore throat and changes in vocal quality
- Burning present in 40% of patients with dry mouth[1]
- Unable to wear/tolerate dentures
- Increased risk of dental cavities and tooth loss
- Increased risk of fungal infection
- Taste changes - decreased or food tastes metallic/salty





[1]Rouleau, Tanya S. et al, A retrospective, cohort study of the prevalence and risk factors of oral burning in patients with dry mouth Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:720-725

Limitations in Current Management of Xerostomia

Current Treatment Options

- **Over the counter mechanical and gustatory stimulants**
  - Not all patients tolerate frequent gum chewing
  - May exacerbate temporomandibular disorder symptoms
- **Parasympathomimetics**
  - Cevimeline and Pilocarpine
  - Not well tolerated
    - Side effects - flushing, upset stomach, sweating
    - Ineffective in addressing lower salivary function
- **Saliva substitutes**
  - Carboxymethyl cellulose and mucin
  - Short term benefit

Current options do not modify this condition or adequately address symptoms of reduced salivary output

AAV-hAQP1 for Radiation-Induced Xerostomia (RIX)

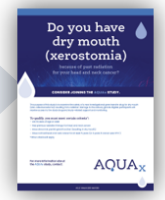
Strategy for Repair

- Water-impermeable duct cells generate an osmotic gradient (lumen > interstitium)
- Introduction of non polarized human aquaporin 1 gene (hAQP1) into remaining salivary gland cells via viral vector, making cells permeable to water
- Allows water to flow into the salivary duct and out to moisten the mouth

Salivary gland as target for gene therapy

- Non-invasive: allows local administration and avoids systemic exposure
- Isolated and encapsulated
- Small volume of vector
- Additional Indications: Sjogren's Syndrome (dry mouth and dry eye), Dry Eye

AAV-AQP1 is currently being evaluated in two Phase 1 studies:



Multi-center Phase 1 Trial AQUAx (NCT04043104)

- Dose escalation ongoing
- 5 Centers (4 US + 1 Canada)

NIH National Institutes of Health

Phase 1 trial at NIH (NCT02446249)

- Dose escalation ongoing

NIH Study: Phase 1 Dose Escalation of AAV-hAQP1

Study Design

Open label, dose escalation study of a single administration of AAV2hAQP1 to one parotid gland in subjects with IR-induced parotid salivary hypofunction

Target Enrollment: up to 27 subjects

- Five dose cohorts with minimum of 3 subjects per cohort
- Up to 12 subjects at Maximum Tolerated Dose (MTD)
- Last subject targeted to be treated by June 2022
- All subjects to be followed for 3 years post treatment

Dose Cohort	Dose (in VP/Gland)
1	1×10^{10}
2	3×10^{10}
3	1×10^{11}
4	3×10^{11}
5	6×10^{11}

NIH
National Institutes of Health

Study Endpoints:

Primary

- Safety of a single dose of AAV2hAQP1 administered to one parotid gland in adults with IR-induced parotid gland hypofunction

Secondary

- Effectiveness of AAV2hAQP1 to increase parotid gland salivary flow
- Subjective improvement as measured by questionnaires

Study Status:

- Completed treatment of first 3 cohorts (N = 9 subjects)
- Two patients treated in Cohort 4 (2020)
- All subjects have tolerated the vector well with no dose limiting toxicity, drug-related SAEs or concerning pattern of AEs observed
- COVID-19-associated hold on new enrollment has been lifted
- Tele-visits continue for active subjects

AQUAx: Phase 1 Study Design

Study Design

- Open label, multi-center, dose escalation study of a single administration of AAV-hAQP1 to one parotid gland in patients with radiation-induced parotid salivary hypofunction and xerostomia

Target Enrollment: Up to 30 subjects

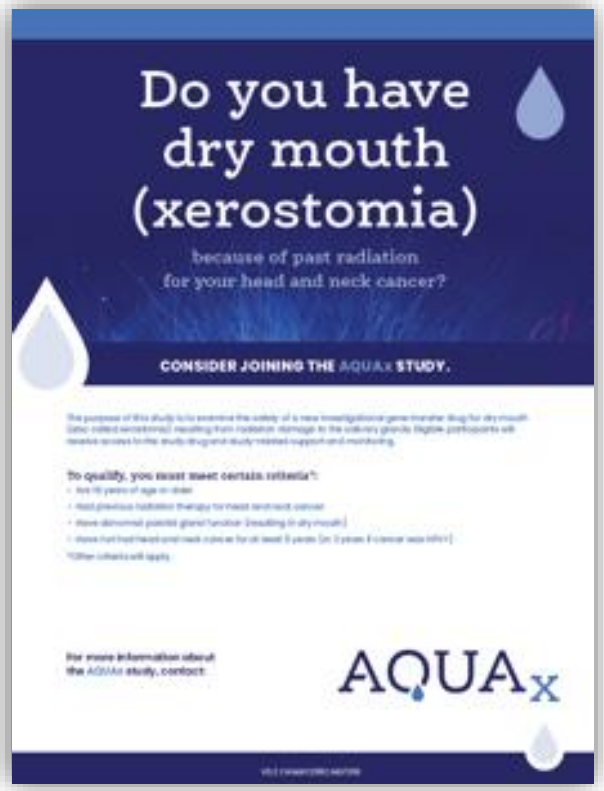
- Four dose cohorts with minimum of 3 subjects per cohort
- May treat up to 9 subjects in dose expansion cohorts
- 5 centers (4 in US, 1 in Canada)
- All subjects to be followed for 1-year post-treatment

Primary Endpoint

- Safety

Secondary Endpoints

- Patient reported measures of xerostomia symptoms
- Unstimulated and stimulated salivary volume



Phase 1 AQUAx Study

Study Status

- 2 centers currently open for enrollment
- All 5 centers to be open during 1H 2021
- Cohort 2 recruitment ongoing

AQUAx 1st patient cohort (n=3)

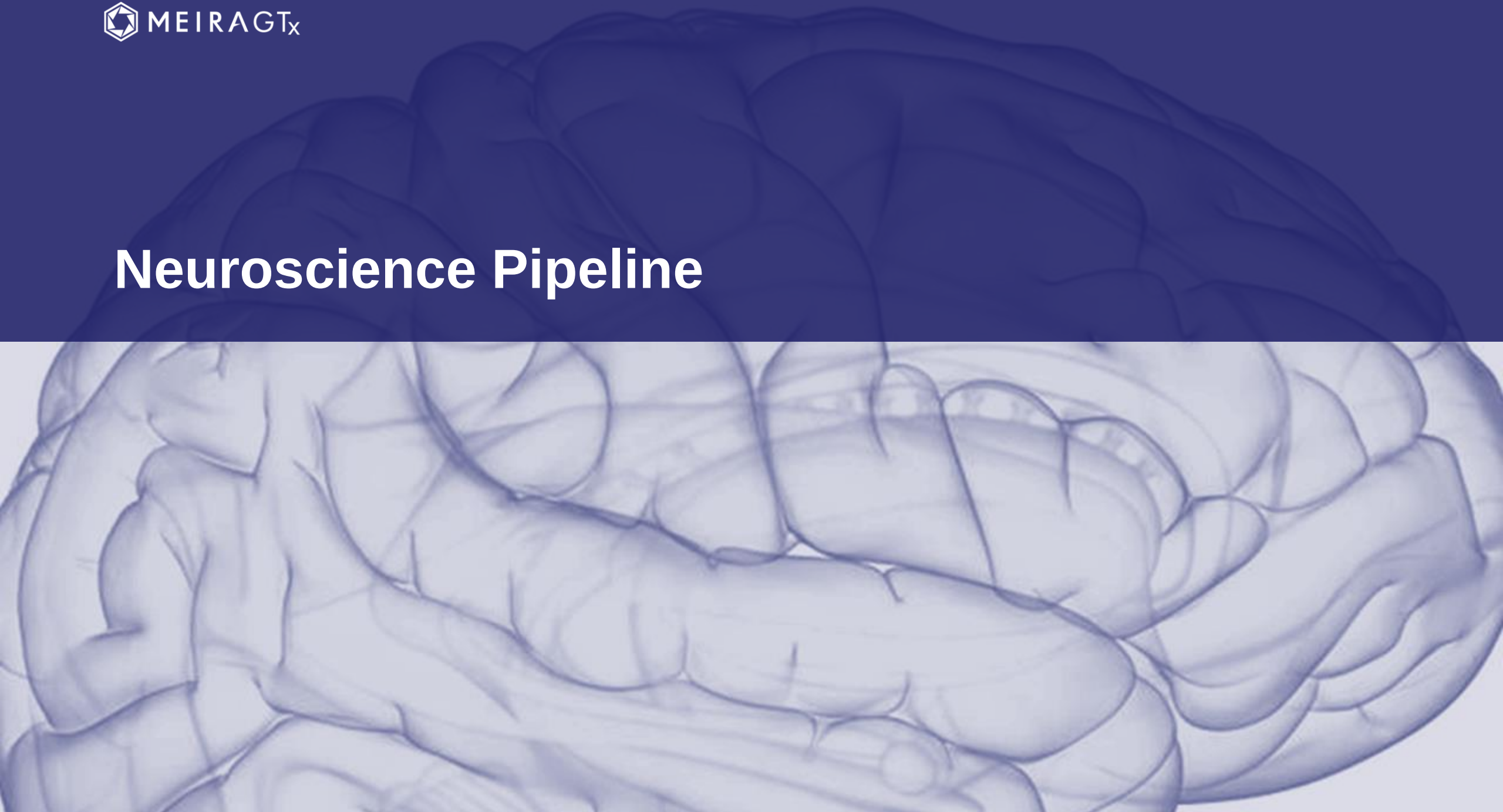
Administration of AAV-hAQP1:

- Non-invasive procedure
- Easy to perform
- Well tolerated by patients

Interim Data from AQUAx Cohort 1 (n=3)

- **Treatment was well tolerated**
- **No serious adverse events or DLTs**
- **Improvements in patient reported quality of life measures**
  - Less pain
  - Less burning
  - Better sleep
  - Fewer throat symptoms
- **Increase in salivary output**
- Of the three patients treated in Cohort 1, one patient reached the 12-month assessment and two passed the six-month assessment
- **The patient who reached 12-months saw complete resolution of symptoms**

Neuroscience Pipeline



AAV-GAD Rationale: Addressing Major Unmet Needs

Dopamine replacement therapy (L-dopa agonists) over time associated with high complication rates

- Symptomatic relief for around 5 years with reduced benefit over time
- Increased doses required over time with high rates of non-adherence and increased side effects
- Motor fluctuations, dyskinesias, cognitive/affective side effects
- 300,000 PD patients in the U.S. no longer responding adequately to oral medications

Subthalamic Nucleus (STN) Deep Brain Stimulation (DBS) Effective but Limited

- Device implants limit patient uptake and have considerable hardware-related complications
- Ongoing management requires proximity to expert centers

AAV-GAD is a Unique, Disease-Modifying Therapy With Potential To Address Many Unmet Needs in Parkinson's Disease

---

- Local AAV-GAD delivery into the STN reverses basal ganglia dysregulation and creates new polysynaptic connections to modify brain circuitry and normalize motor function
- No residual hardware or post-surgical maintenance increases patient and caregiver acceptance
- Most advanced gene or cell therapy for PD supported by the only positive randomized, blinded trial
- Proximity of STN to substantia nigra makes AAV-GAD the only biological therapy currently in development capable of combining reversal of circuit dysfunction and dopaminergic neuroprotection in a single treatment

AAV-GAD: Gene Therapy for Parkinson's Disease

Disease Overview

Parkinson's Disease (PD)

- Parkinson's disease is a severe and progressive neurodegenerative disorder associated with a range of motor and non-motor symptoms.
- PD affects more than seven million people worldwide. patients suffer from a range of non-motor symptoms

Current therapy is associated with high rates of complications over time

- Symptomatic relief for around 5 years with reduced benefit over time
- Increased doses required over time with high rates of non-adherence and increased side effects
- Motor fluctuations, dyskinesias, cognitive/affective side effects

High unmet medical need

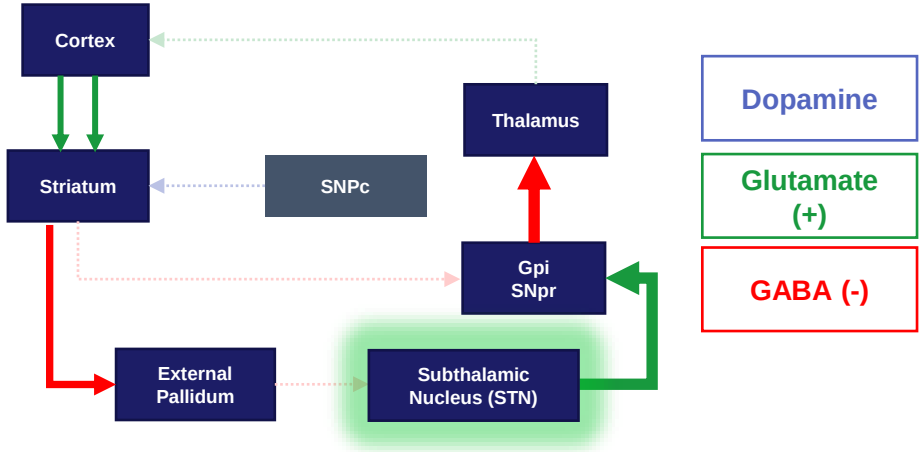
- 300,000 PD patients in the U.S. no longer responding adequately to oral medications

Product: AAV-GAD | Stage: Clinical

- **AAV-GAD is an investigational gene therapy designed to deliver the glutamic acid decarboxylase (GAD) gene to the subthalamic nucleus in order to increase production of GABA, the primary inhibitory neurotransmitter in the human brain.**
- **Non-dopaminergic strategy**
  - AAV-GAD potentially applicable to large patient population not adequately treated with currently available therapies
- **AAV-GAD previously completed a Phase 2 study and is the ONLY gene or cell therapy to meet primary clinical efficacy endpoint in a randomized, blinded PD trial**
  - Imaging biomarker developed which correlates with clinical outcome
  - Routine and brief surgical procedure, minimal OR time, virtually no special training, and without general anesthesia

Rationale for STN as Target for Localized AAV-GAD Treatment in Parkinson's Disease

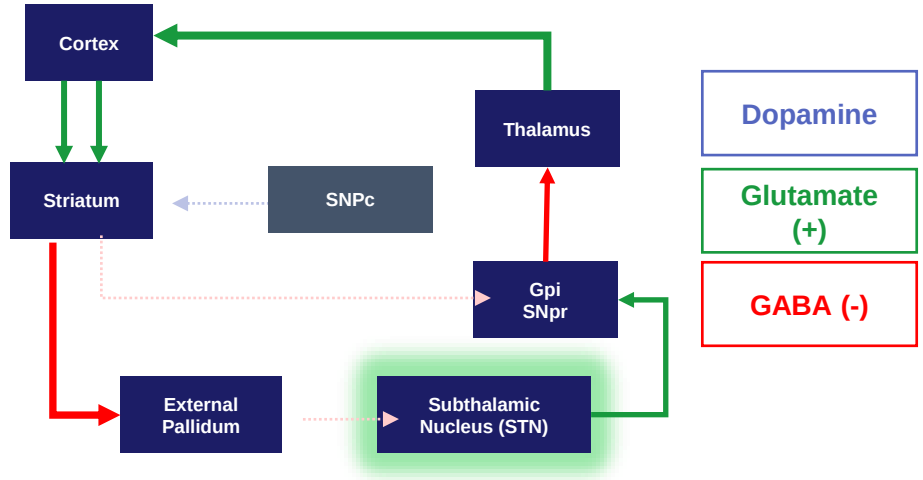
Dysregulation of basal ganglia in PD leads to STN overactivity due to reduced GABA



STN is a key structure downstream of dopamine circuitry which is overactive in PD

- Deep Brain Stimulation (DBS) specifically targets STN to modulate basal ganglion circuitry output
- Direct STN infusion of muscimol, a GABA agonist, reduces motor symptoms in human PD

AAV-GAD gene therapy to STN rebalances basal ganglia circuitry to normalize outflow



AAV-GAD restores glutamate/GABA imbalance in the basal ganglia

- **Normalizes STN neuronal firing**
- **Releases brake on the thalamus and improves motor function**

AAV-GAD Gene Therapy Approach – Local Delivery to STN

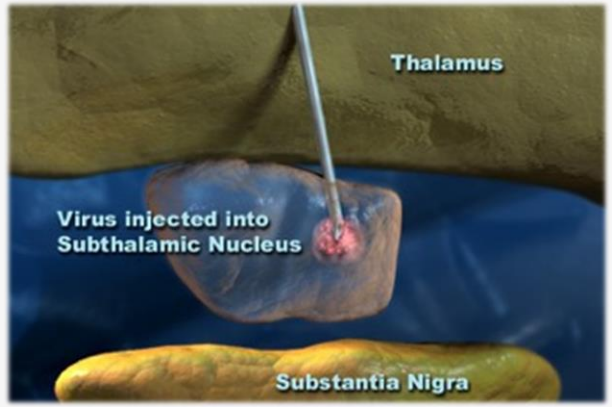
Product

Glutamic acid decarboxylase (*GAD*) is the rate-limiting enzyme in the synthesis of GABA

- *GAD* catalyzes the conversion of glutamate to GABA
- Key enzyme found in all inhibitory neurons and regulates excitability

Preclinical Data

- STN AAV-GAD improves motor function and normalizes motor circuits in rodent and primate PD models[1,2]
- Extensive preclinical rodent and primate efficacy, safety and toxicology package supports translation into human subjects



1. Luo J. Subthalamic GAD Gene Therapy in a Parkinson's Disease Rat Model. Science. 2002; 298:425-429.
2. Emborg ME. Subthalamic glutamic acid decarboxylase gene therapy: changes in motor function and cortical metabolism. J Cereb Blood Flow Metab. 2007; 27:501-509

Phase 1 Study of AAV-GAD STN Gene Therapy

- **Study design**: dose escalation study of unilateral STN AAV-GAD delivery in 12 patients (3 cohorts of 4 subjects each)
- **Safety findings**:
  - Unilateral STN AAV-GAD was safe and well tolerated
  - No evidence of induction immune response or effect on outcome of pre-immunity in two patients
- **Efficacy findings:**
  - Significant improvement in both “off” and “on” UPDRS largely limited to hemibody opposite treated hemisphere
  - Effects seen starting at 3 months (trend at 1 month) and stable to one year
  - No decline in neuropsych scores or other non-motor parameters
  - Functional imaging demonstrated significant improvement in abnormal circuitry function specific only to treated hemispheres

Safety & efficacy findings together supported entry into Phase 2

Phase 2 Study of AAV-GAD STN Gene Therapy

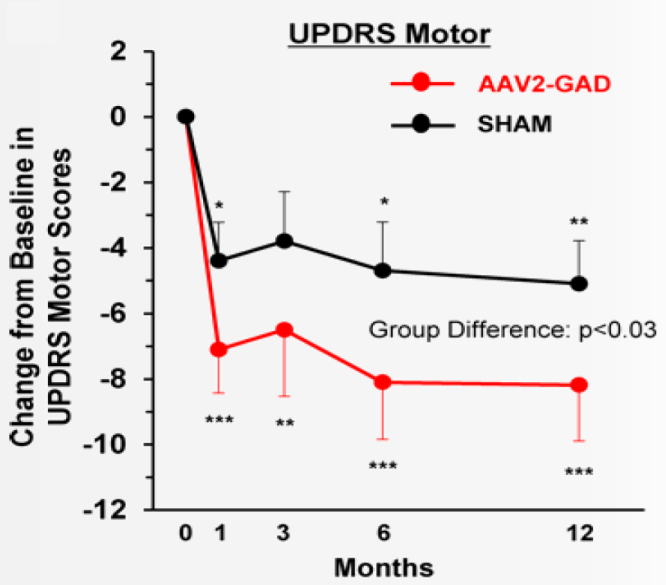
- **Study Design**: Randomized (n=45,1:1) double-blind study of bilateral STN AAV-GAD vs. Sham surgery
- **Efficacy findings**:
  - Met primary endpoint: Per protocol group showed significantly greater improvement in off-medication UPDRS part 3 for AAV-GAD subjects compared with sham
  - Positive secondary endpoints for AAV-GAD included greater responder rate at 6 and 12 months
- **Safety findings**:
  - No adverse effects related to AAV-GAD across all time points
  - Worsening PD as an adverse event in 35% of sham vs. 0% GAD further supports efficacy
- **Functional imaging with same findings as phase 1 and new biomarker specific to AAV-GAD treated subjects, which significantly correlated with clinical outcome**

AAV-GAD is the only gene or cell therapy to meet a primary clinical efficacy endpoint in a randomized, blinded multi-center PD trial

Niethammer M. Long-term follow-up of a randomized AAV2-GAD gene therapy trial for Parkinson's disease. JCI Insight. 2017; 2(7):e90133

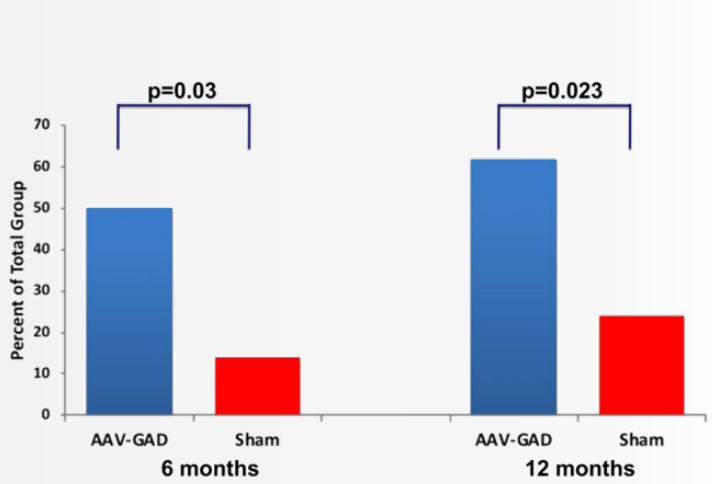
Results from Sham-Controlled Phase 2 Study: Meaningful Improvements in Clinical Outcomes Following Treatment with AAV-GAD

Primary Outcome Measure: Change in UPDRS Part 3 (Motor Score)



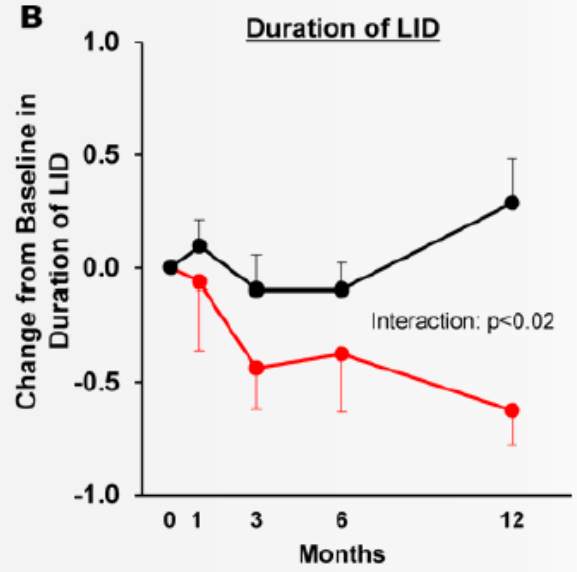
- Greater improvements in motor scores observed in the AAV-GAD treatment group across all follow-up time points
- **Met primary outcome measure: UPDRS 3 improvement vs. sham at 6 months**

UPDRS Part 3 Clinically Meaningful Responder Rate



- Clinically meaningful response, with >9 point reduction in UPDRS Part 3 “off” scores
- Well above moderate clinically important difference (4.5-6.7 points) and close to large clinically important difference (10.7-10.8 points)

Reduction in dyskinesia duration



- Increase in overall ON time w/o dyskinesias and reduction in dyskinesia duration

Niethammer M. Long-term follow-up of a randomized AAV2-GAD gene therapy trial for Parkinson’s disease. JCI Insight. 2017; 2(7):e90133

Development of an Objective FDG-PET Biomarker: GADRP

FDG-PET can be utilized to evaluate brain physiology in multiple ways

- **Measure changes in specific brain regions of interest**
- **Determine interactions between brain regions during disease progression**
- **Determine interactions between brain regions as a biomarker of response to therapy**

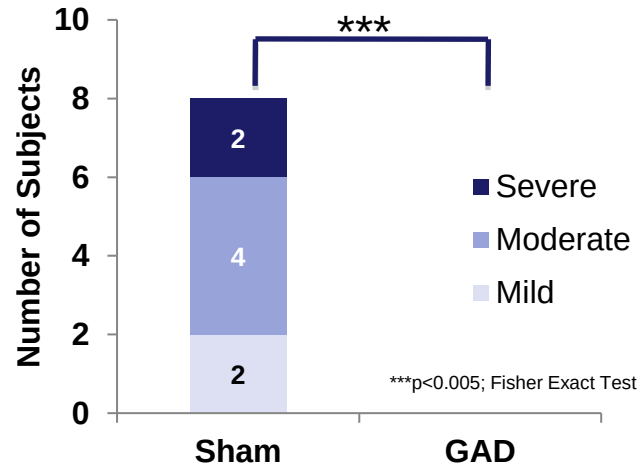
Functional Imaging – GAD Related Pattern (GADRP)

- Subjects that respond to AAV-GAD have a unique FDG-PET imaging pattern (GAD related pattern, GADRP)
- GADRP reflects corrective changes is polysynaptic brain circuitry in response to AAV-GAD treatment
- Statistically significant correlation between UPDRS motor ratings and GADRP expression ($p < 0.009$)
- GADRP expression correlates with UPDRS response only in AAV-GAD treated subjects and does not develop in Sham responders
- The GADRP is a unique imaging biomarker that objectively distinguishes AAV-GAD treatment-driven responses from placebo responses in Sham subjects
- AAV-GAD is the first gene or cell therapy for PD to have an objective imaging biomarker of treatment effect that is significant relative to sham surgery patients and correlates with clinical improvement

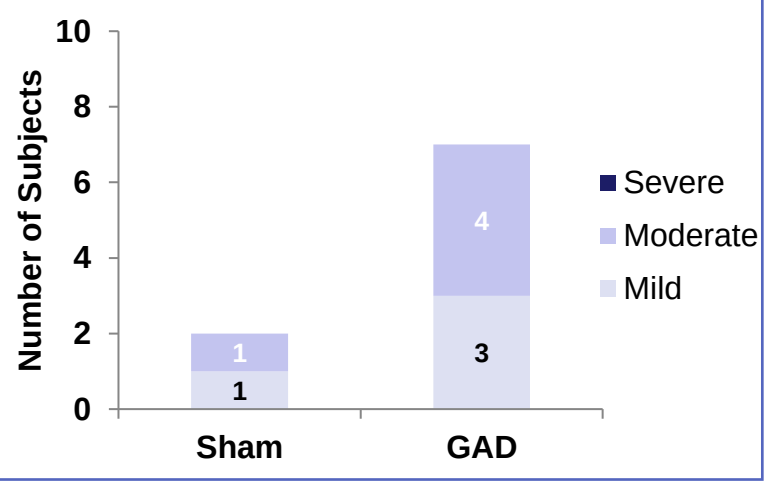
Niethammer M. Gene therapy reduces Parkinson's disease symptoms by reorganizing functional brain connectivity. Sci. Trans. Med. 2018; 10(469). pii: eaau0713

Adverse Events Over 12 Months (20% or Greater Frequency)

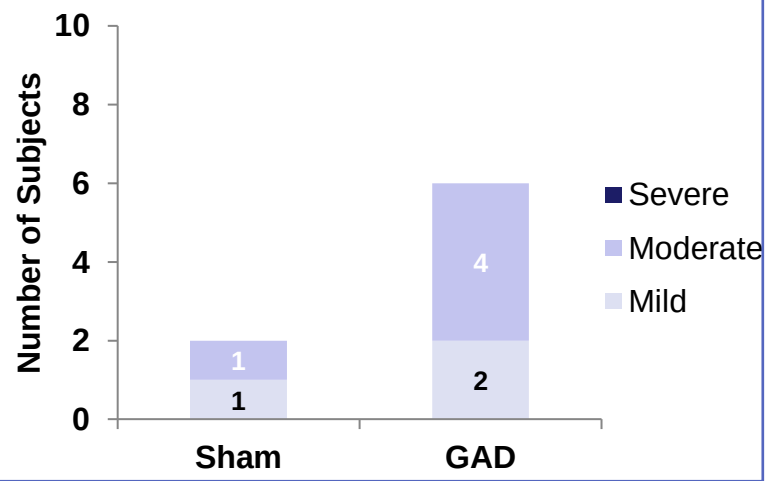
Worsening of Parkinson's Disease



Headache



Nausea



Serious Adverse Events*
(Number of Subjects)

	Sham	GAD
Intestinal obstruction		1
Accidental drug overdose		1
Prostatitis		1
Delusion, Hallucination Parkinson's Disease worse	1	

*All SAEs occurred 4-12 months post-surgery and all resolved

Summary of Key AAV-GAD Features

- **AAV-GAD is the only gene or cell therapy:**
  - To meet primary clinical efficacy endpoint in a randomized, blinded multi-center PD trial
  - With an imaging biomarker supporting efficacy which correlates with clinical outcome
  - With a routine and brief surgical procedure that requires minimal OR time, virtually no special training, no general anesthesia
- **Improvement in off-medication clinical ratings, ON time without dyskinesia and complications of medical therapy without declines in neuropsychological function or speech**
- **Consistency in clinical outcomes and imaging from phase 1 to phase 2**
- **AAV-GAD could be accessible to more patients than current standard of care**
  - Absence of retained hardware
  - No need for specialized post-op care
- **Non-dopaminergic strategy**
  - AAV-GAD potentially applicable to large patient population not adequately treated with currently available therapies

AAV-UPF1: A Novel Gene Therapy Approach for Amyotrophic Lateral Sclerosis (ALS)

Disease Overview

Amyotrophic Lateral Sclerosis (ALS)

- ALS is a neurodegenerative disease affecting motor neurons resulting in progressive paralysis and death usually within 5 years of diagnosis.
- 90% of ALS is sporadic (sALS), whereas only 10% of ALS cases are inherited, familial ALS (fALS).
- In the vast majority (>95%) of ALS patients, both fALS and sALS, cytoplasmic mis-localization and aggregation of the proteins TDP43 or FUS can be detected.

Rationale for targeting UPF1

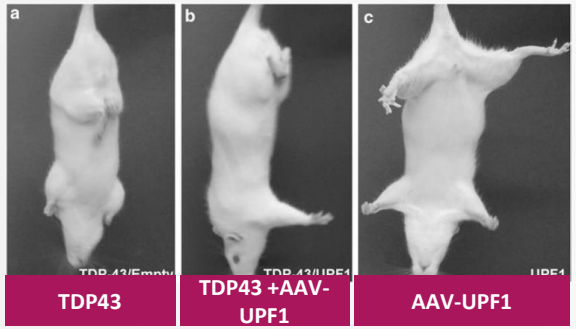
- UPF1 was identified in a yeast Gain of Function screen that looked for genes that rescue TDP43 and FUS toxic phenotype.
- UPF1 is a key regulator of the Nonsense Mediated Decay (NMD) pathway, which plays a major role in RNA metabolism and is dysregulated in ALS.
- A role of UPF1 in ALS was validated in multiple preclinical models

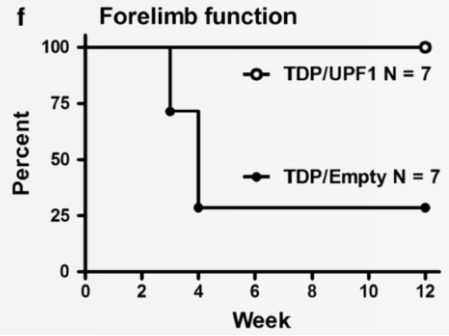
Product: AAV-UPF1 | Stage: Preclinical

- **MeiraGTx is preclinically developing AAV-UPF1, an investigational gene therapy designed to target the underlying cellular defect driving the disease.**
- **Potential to address both familial and sporadic forms of the disease, may be genotype agnostic, and may have an effect in both ALS and FTD.**
- **AAV-UPF1 is able to ameliorate ALS disease phenotype in a variety of preclinical models caused by different genotypes:**
  - Administration of AAV-UPF1 reduces motor neuron death and gliosis driven by the toxic effects of several different genetic causes of ALS including, TDP43, FUS and C9orf72
  - Improvements in ALS-like symptoms related to limb strength and mobility in rodent models

Preclinical Data Demonstrates the Therapeutic Potential of AAV-UPF1 in a Variety of ALS Models

AAV-UPF1 Protects Rats from Forelimb Impairments Induced by TDP43





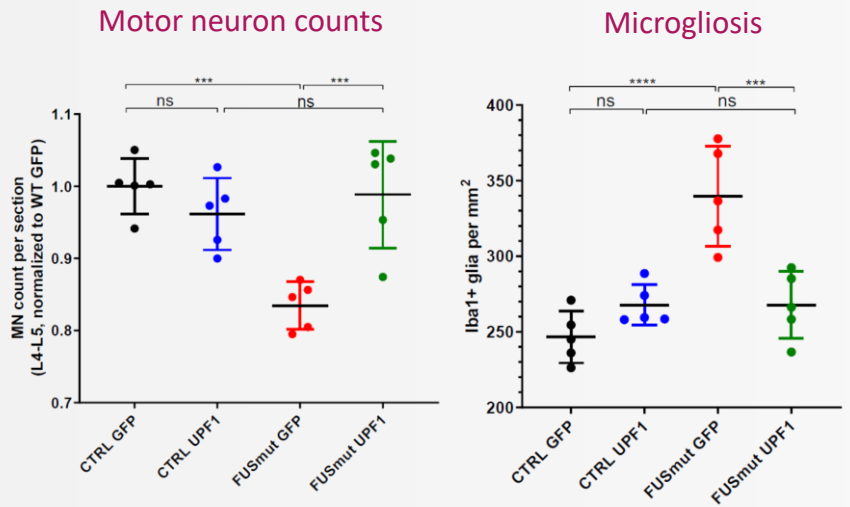
Top:

- TDP43 rats exhibit clasping of both hindlimbs and forelimbs in the escape reflex test.
- Co-injection of AAV-hUPF1 and AAV-TDP43 shows normal forelimb extension

Bottom:

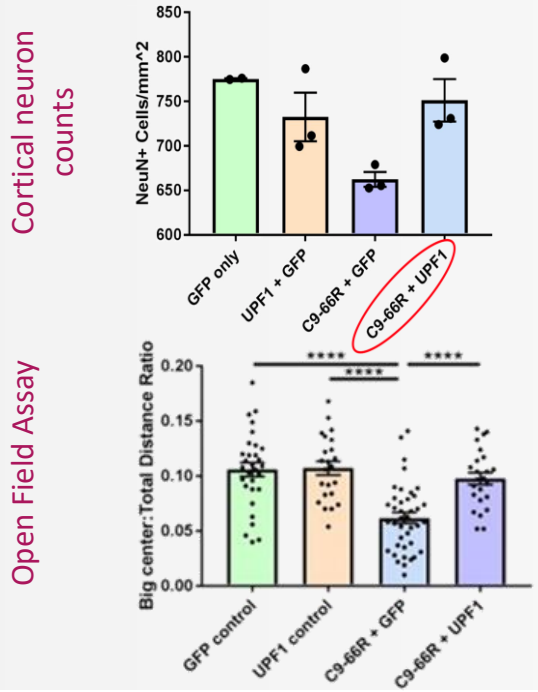
- AAV-UPF1 restores forelimb function as assessed by the escape reflex test

AAV-UPF1 Rescues Motor Neuron Degeneration in a Conditional FUS Mouse Model



- AAV-hUPF1 prevents motor neuron loss (left) and microgliosis (right) in a FUS conditional mouse model

AAV-UPF1 Rescues Neuronal Loss & Motor Deficits in C9orf72 Mouse Model



Top:

- AAV-UPF1 rescues cortical neuron loss in a mouse C9orf72 model

Bottom:

- Motor deficits improved with UPF1 expression by AAV-UPF1

Jackson et al. (2015): Preservation of forelimb function by UPF1 gene therapy in a rat model of TDP-43-induced motor paralysis

Advancing the Next Generation of Gene Therapies

Diverse Pipeline

6 ONGOING CLINICAL PROGRAMS:

- Inherited retinal diseases
- Salivary gland hypofunction
- Parkinson's disease

DEEP PIPELINE OF PRE-CLINICAL PROGRAMS

- Wet AMD / DME
- Glaucoma, Uveitis
- Multiple additional IRDs
- Sjogren's, Dry Eye
- ALS

Core Viral Vector Engineering Capabilities

VIRAL VECTOR DESIGN PLATFORM:

- Synthetic promoter design and screening platforms
- Novel capsids
- Cassette optimization: transgene engineering, sequence optimization, ITR and plasmid backbone optimization, immunogenicity
- Organoids / iPSC preclinical platforms

In-house GMP Manufacturing & Process Development

FULL END TO END MANUFACTURING INFRASTRUCTURE:

- cGMP facilities: Scalable and Flexible
- Capacity for clinical through commercial supply for all programs
- QA and QC to support first in man through commercialization
- Fill and Finish
- Process Development facility; proprietary Process Development platform
- Non GMP vector core for pre-clinical supply
- GMP plasmid production facility

Inducible Gene Regulation Platform

PROPRIETARY GENE REGULATION PLATFORM:

- Riboswitch technology allows control of gene expression with a high dynamic range
- Gene expression is turned on/off with proprietary small molecules

POTENTIAL TO REGULATE ANY GENE: Antibodies, hormones, cytokines, within BBB

MEIRAGTx

MEIRAGTx