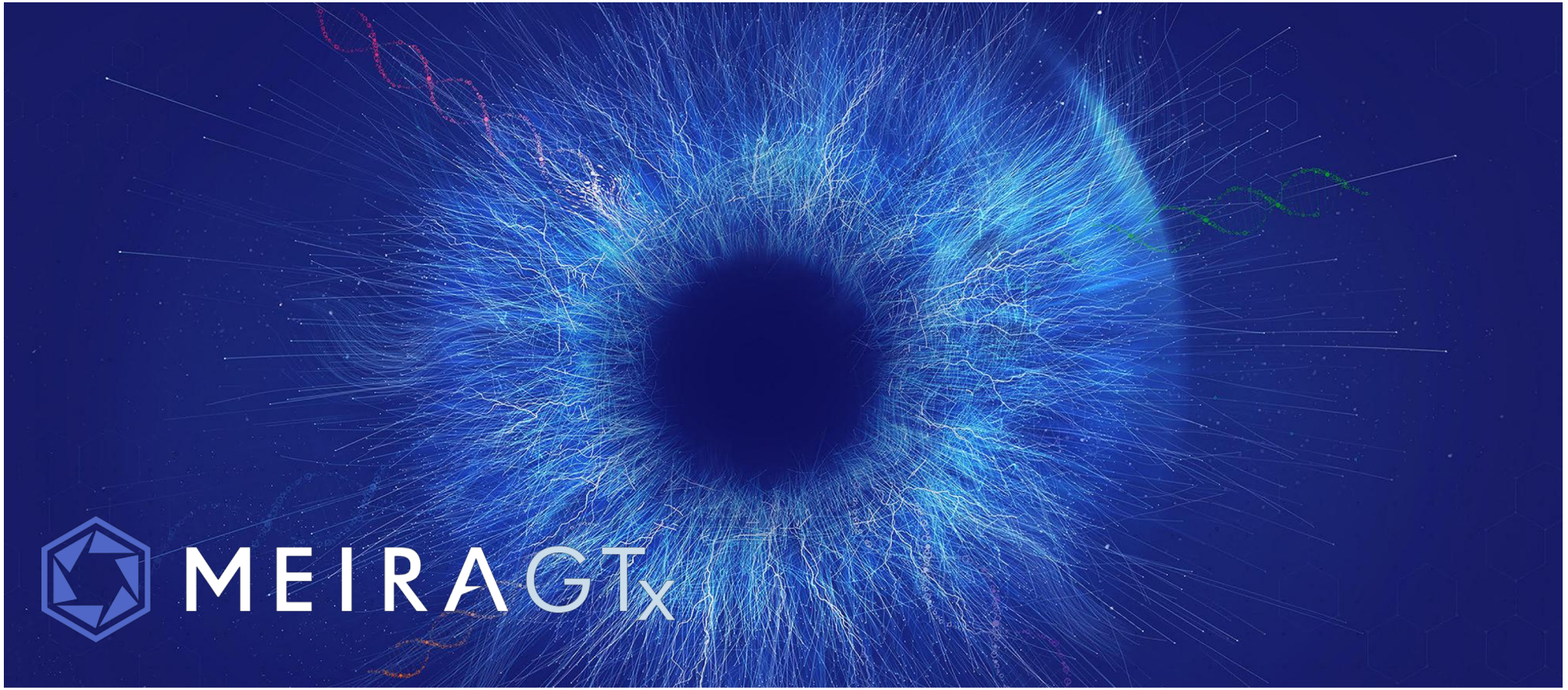


Cowen 40th Annual Health Care Conference

March 2, 2020

Forward Looking Statements

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 expectations relating to meetings with global regulatory authorities and the FDA, product pipeline, anticipated product benefits, goals and strategic priorities, product candidate development and status and expectations relating to clinical trials, growth expectations or targets and pre-clinical and clinical data expectations in respect of collaborations, 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, acquire additional capital, identify additional and develop existing product candidates, successfully execute strategic priorities, bring product candidates to market, build-out the manufacturing facility 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; 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; 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; 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 March 2, 2020.

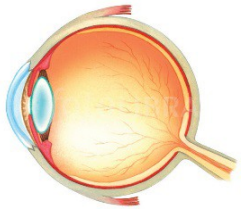
A Vertically Integrated, Clinical Stage Gene Therapy Company

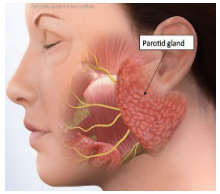
Developing a new pharmaceutical modality designed for the cost effective treatment of a broad range of serious disorders

Diversified Pipeline of Gene Therapy Candidates

6 ongoing clinical programs:

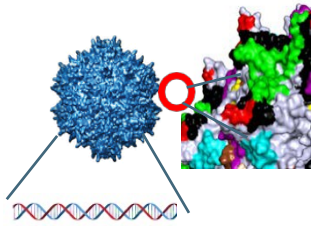
- Inherited retinal diseases
- Salivary gland
- Parkinson's Disease

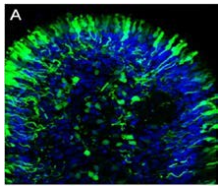




Platform of Core Viral Vector Engineering Capabilities

Viral vector design, promoters, capsid, transgene optimization, **process development** expertise



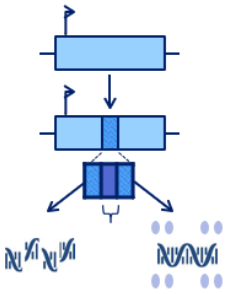


Manufacturing Capacity & Know-How

Flexible and **scalable cGMP manufacturing facility** with capacity for commercial supply for our programs

Next Generation Gene Therapy Riboswitch-Based Gene Regulation

Proprietary technology that may allow for innovative gene therapy treatments whose **expression can be turned on and off** with an easily administered small molecule



cGMP Certified Manufacturing Facility: Flexible and Scalable

Central London facility

- cGMP certified 29,000 sq. ft multi-product, multi-viral vector manufacturing facility
- Designed to meet MHRA, EMA and FDA regulatory requirements
- Single use philosophy / fully enclosed technologies
- 2 cell suites; 3 viral vector suites
- Independent air handling
- Designed for minimal downtime and maximum flexibility
- Adherent / non-adherent cell lines – HEK293
- Support laboratories: Quality Control
- Adjacent MSAT (Manufacturing Science and Technology) area/pilot plant

Expanding manufacturing footprint

- Construction on 2nd cGMP viral vector manufacturing facility & cGMP plasmid production facility expected to begin in 2020

Plan

MEIRAGTx

Gene Therapy Pipeline

Ocular, Neurodegenerative, Salivary Gland Programs

Multiple Therapeutic Targets

OCULAR

Clinical Development
- IRD franchise: XLRP, achromatopsia, *RPE65*-associated retinal dystrophy, LCA4

Research
- Wet AMD, Dry AMD

Gene Regulation
- VEGFR2 Ab – eye drops

NEURODEGENERATIVE

Clinical Development
- Parkinson's disease

Research
- Amyotrophic Lateral Sclerosis (ALS)

Gene Regulation
- CNS expression with BBB penetrant small molecules

SALIVARY GLAND

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

Research
- Sjogren's Syndrome

Gene Regulation
- Peptide and hormone salivary gland delivery

Human proof of concept demonstrated across ocular, neurodegenerative and salivary gland pipelines

Vector development & optimization technology create opportunities to treat broader indications beyond rare, inherited genetic disorders

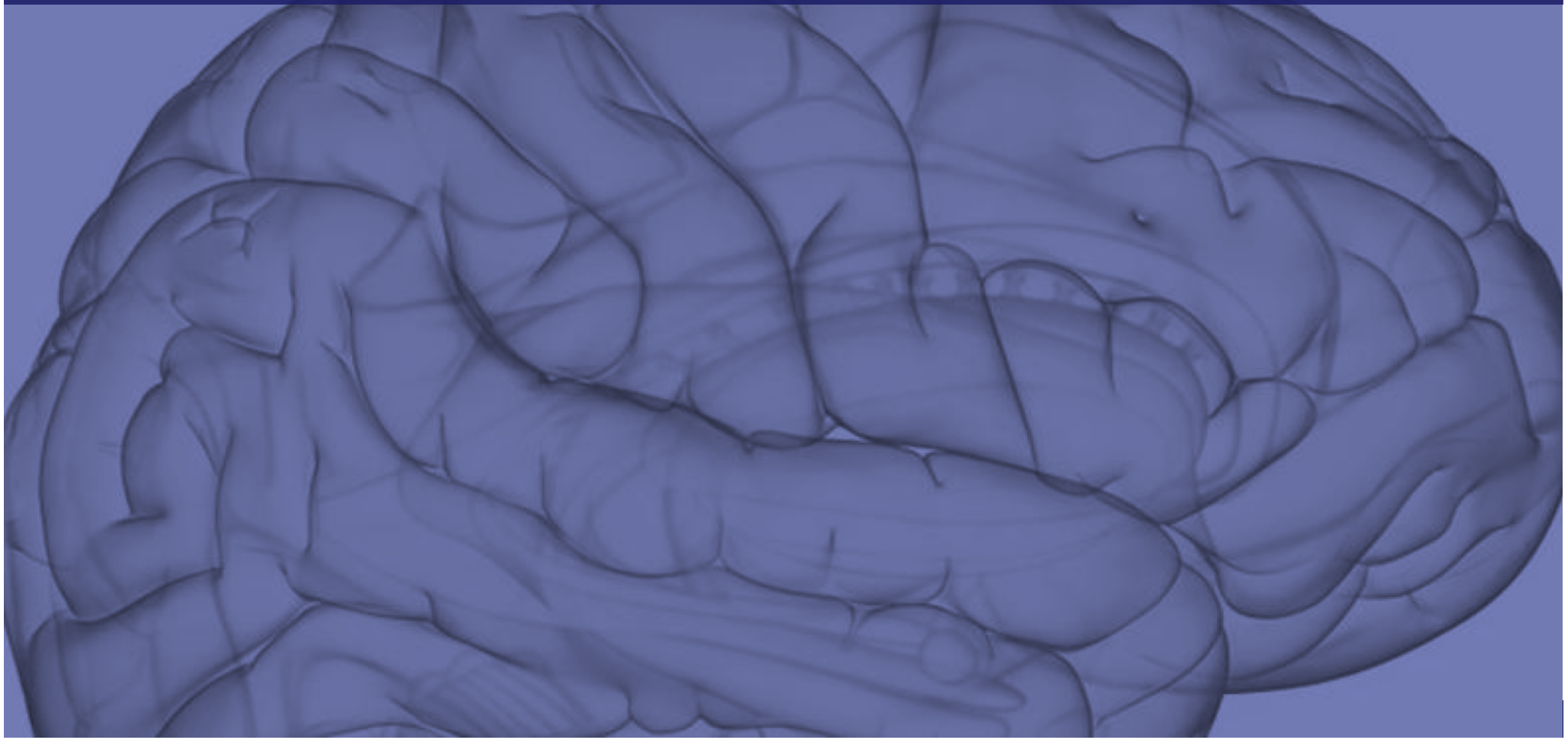
Broad Clinical Pipeline

Product	Indication	Preclinical	Phase 1/2	Details
Ocular				
AAV-RPE65	RPE65-Deficiency	RPDD, Orphan Drug		
AAV-CNGB3*	Achromatopsia (CNGB3)	RPDD, PRIME, Fast Track, Orphan Drug		janssen
AAV-RPGR*	X-linked RP (RPGR)	PRIME, Fast Track, Orphan Drug		janssen
AAV-CNGA3*	Achromatopsia (CNGA3)	RPDD, Orphan Drug		janssen
AAV-AIPL1	LCA4 (AIPL1)	Orphan U.S. & EU		Compassionate use under MHRA Specials License
A006	Wet AMD (anti-VEGFR2)			
Neurodegenerative Disease				
AAV-GAD	Parkinson's Disease (GAD)			
Salivary Gland				
AAV-AQP1	Xerostomia (hAQP1)	Orphan Drug		Phase 1 study at NIH ongoing; multi-site Phase 1/2 trial ongoing
AAV-AQP1	Sjögren's Syndrome (hAQP1)			

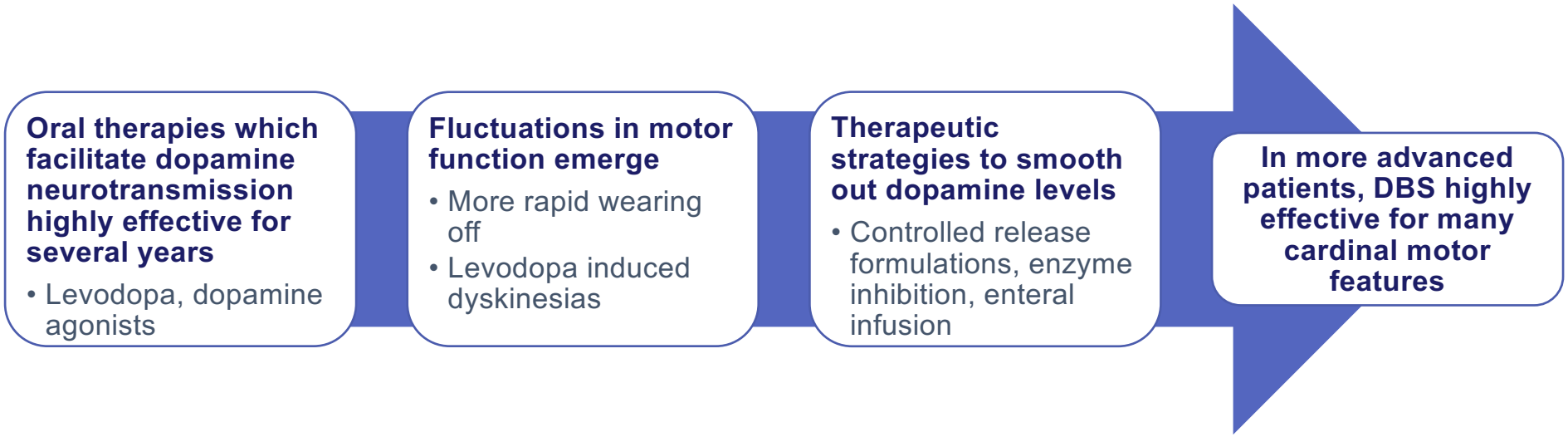
*Co-development program with Janssen Pharmaceuticals pursuant to a collaboration agreement.

MEIRAGTx

AAV-GAD for Parkinson's Disease



Rationale to Go Beyond a Dopamine Strategy When Levodopa and Equivalents Fail



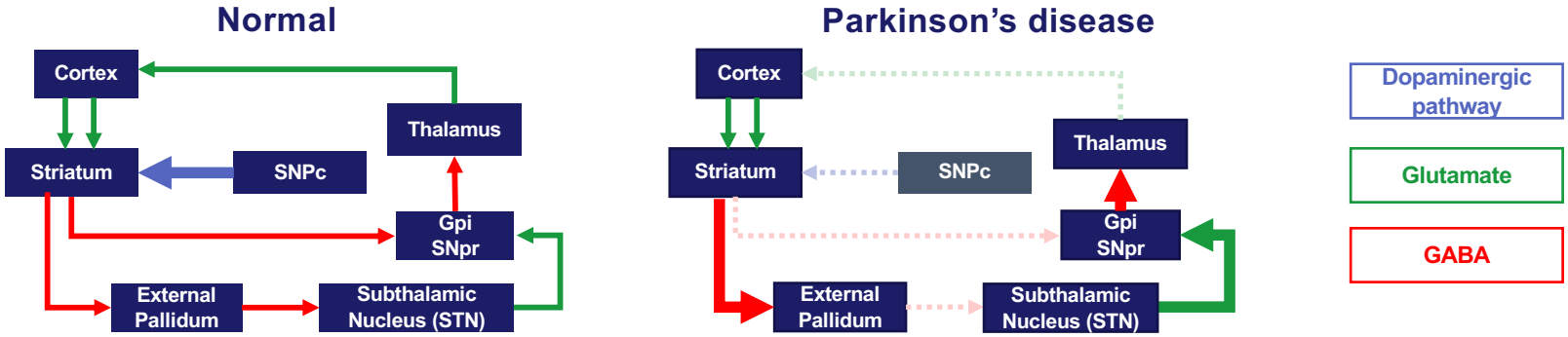
Physiological dopamine release in the putamen is synaptic and regulated

- Dopamine neurons show tonic and burst firing
- Dopamine from cell transplants or dopamine synthetic enzyme gene transfer leads to non-physiological release
- Biological strategies to directly deliver dopamine into the putamen/caudate have been unsuccessful in past blinded controlled studies
  - Severe, disabling and difficult to treat dyskinesias have resulted from such approaches
- Pharmacological treatment with levodopa and DA agonists leads to changes in receptor function which make a dopamine strategy as the disease advances challenging

AAV-GAD for Parkinson's Disease

Persistent activation of STN in Parkinson's disease

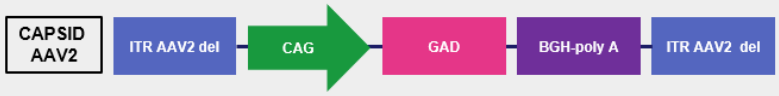
- Dysregulation of basal ganglia signaling in PD with substantia nigra pars compacta (SNPc) degeneration
- Reduced GABA inhibitory input results in persistent activation of the STN
- The STN acts through the major basal ganglia output nuclei to put a brake on the thalamus
- AAV-GAD to the STN relieves this brake, enabling restoration of thalamic and cortical activity to improve motor function



AAV-GAD gene therapy to rebalance excitation and inhibition in key nuclei

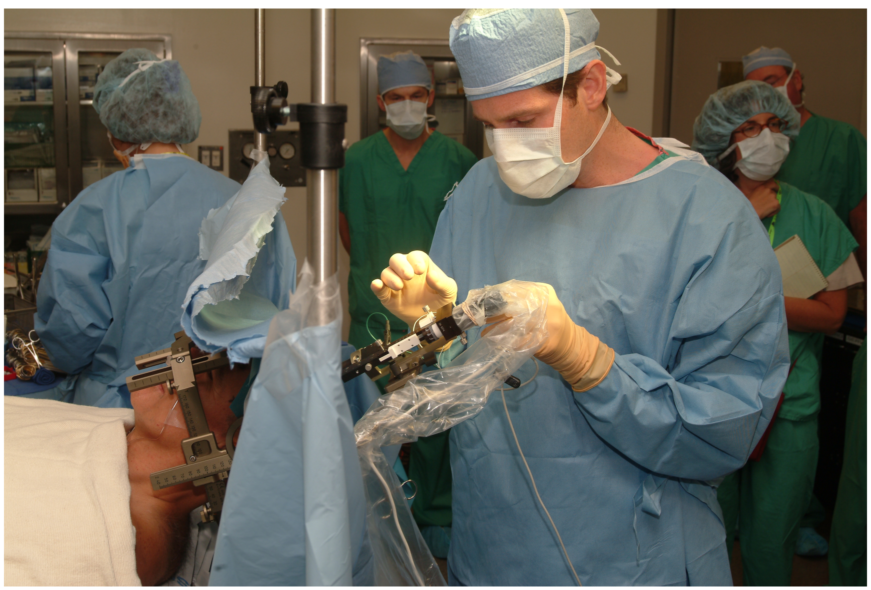
Glutamic Acid Decarboxylase converts glutamate (excitatory neurotransmitter) into GABA (inhibitory neurotransmitter)

- Delivered directly into the STN, bypassing circuitry disrupted by dopamine loss
- AAV-GAD converts some STN neurons to inhibitory phenotype
  - Reduce STN activity
  - Normalize neuronal firing
  - Normalize basal ganglia outflow to the motor cortex



Phase 1 Study of AAV-GAD STN Gene Therapy

- ✓ 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
- ✓ 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



Articles

Safety and tolerability of gene therapy with an adeno-associated virus (AAV) borne *GAD* gene for Parkinson’s disease: an open label, phase I trial

Michael G Kaplitt, Andrew Feigin, Chengke Tang, Helen L Fitzsimons, Paul Mattis, Patricia A Lawlor, Ross J Bland, Deborah Young, Kristin Strybing, David Eidelberg, Matthew J During

Summary

Background Dopaminergic neuronal loss in Parkinson’s disease leads to changes in the circuitry of the basal ganglia, such as decreased inhibitory GABAergic input to the subthalamic nucleus. We aimed to measure the safety, tolerability, and potential efficacy of transfer of glutamic acid decarboxylase (*GAD*) gene with adeno-associated virus (AAV) into the subthalamic nucleus of patients with Parkinson’s disease.

Methods We did an open label, safety and tolerability trial of unilateral subthalamic viral vector (AAV-GAD) injection in 11 men and 1 woman with Parkinson’s disease (mean age 58·2, SD=5·7 years). Four patients received low-dose, four medium-dose, and four high-dose AAV-GAD at New York Presbyterian Hospital. Inclusion criteria consisted of Hoehn and Yahr stage 3 or greater, motor fluctuations with substantial off time, and age 70 years or less. Patients were assessed clinically both off and on medication at baseline and after 1, 3, 6, and 12 months at North Shore Hospital. Efficacy measures included the Unified Parkinson’s Disease Rating Scale (UPDRS), scales of activities of daily living (ADL), neuropsychological testing, and PET imaging with ^{18}F-fluorodeoxyglucose. The trial is registered with the ClinicalTrials.gov registry, number NCT00195143.

Findings All patients who enrolled had surgery, and there were no dropouts or patients lost to follow-up. There were no adverse events related to gene therapy. Significant improvements in motor UPDRS scores (p=0·0015), predominantly on the side of the body that was contralateral to surgery, were seen 3 months after gene therapy and persisted up to 12 months. PET scans revealed a substantial reduction in thalamic metabolism that was restricted to the treated hemisphere, and a correlation between clinical motor scores and brain metabolism in the supplementary motor area.

Interpretation AAV-GAD gene therapy of the subthalamic nucleus is safe and well tolerated by patients with advanced Parkinson’s disease, suggesting that in-vivo gene therapy in the adult brain might be safe for various neurodegenerative diseases.

Lancet 2007; 369: 2097–105

See Comment page 2056

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Correspondence to: Matthew J During, The Ohio State University School of Medicine, 912 BRT, 460 West 12th Avenue, Columbus, OH 43210, USA During.1@osu.edu

Introduction

Gene therapy has yielded encouraging preclinical results for various disorders; however, safety and technical concerns have restricted successful translation into clinical therapy. In 1999, the death of a patient with ornithine transcarbamylase deficiency in a gene therapy trial with adenovirus led to a temporary suspension of gene therapy trials,[1] but technological advances and regulatory changes have renewed interest in the approach. Nonetheless, challenges remain. A recent study in patients with haemophilia B showed no clear toxic effects caused by the adeno-associated virus (AAV) vector, but after an initial promising improvement seen in patients deficient in the factor IX protein, anti-AAV immunity developed, which might have caused nearly complete loss of the therapeutic gene from transduced liver cells.[2] The lack of similar findings in animals further emphasises the importance of testing in human beings; however, safety concerns call for careful design of appropriate dose-ranging clinical trials.

The brain is an attractive organ for gene therapy, because production of biologically active molecules within the brain might circumvent poor penetration of compounds that are delivered systemically due to a tight vascular blood–brain barrier. Local gene expression might also focus therapy in specific brain regions, thereby avoiding exposure of other areas to agents that might cause undesirable effects. Several attempts have been made to use gene therapy for malignant tumours, including those in the brain, but the main aim of these studies was to destroy target cancer cells.[3] A trial aimed at correcting the genetic defect in the rare and lethal paediatric neurogenetic Canavan disease was also undertaken.[4] Furthermore, a phase I study of intracerebral transplantation of genetically-modified cells in patients with Alzheimer’s disease (“ex-vivo” gene therapy) was reported.[5] However, the use of modified viruses (vectors) to introduce genetic material into endogenous neurons directly (so-called “in-vivo” gene therapy) has not been previously attempted for any adult neurodegenerative disorder.

Parkinson’s disease is associated with degeneration of many brainstem, limbic, and midbrain neurons, but its hallmark is the loss of dopaminergic neurons of the substantia nigra, which leads to alterations in the activity of brain networks that control movement.[6,7] The consequence is dysregulation of interacting inhibitory and

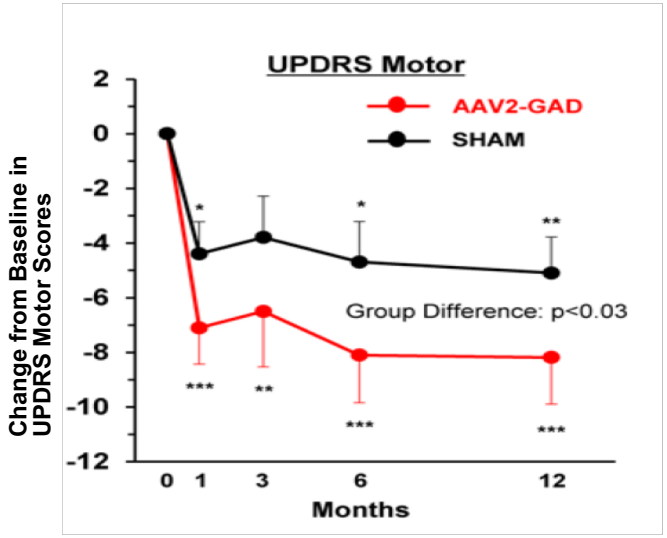
www.thelancet.com Vol 369 June 23, 2007 2097

Kaplitt MG. Safety and tolerability of gene therapy with an adeno-associated virus (AAV) borne GAD gene for Parkinson's disease: an open label, phase I trial. Lancet. 2007;369:2097-2105

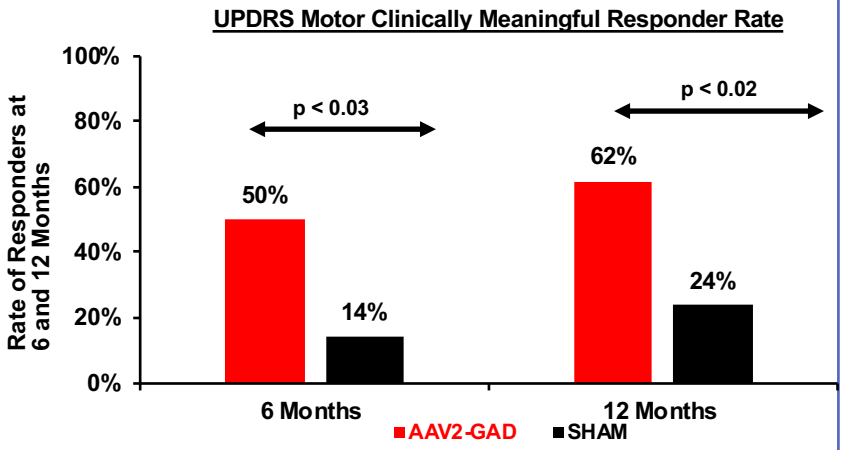
Randomized, Double Blind, Sham-Controlled Phase 2 Trial of AAV-GAD

45 patients randomized 1:1 to bilateral AAV-GAD or sham surgery

Met primary endpoint: 6 month change in UPDRS part 3 (motor score) (p<0.03)[1]



Responders with clinically meaningful ≥ 9 pt UPDRS motor score improvement[1]



- **At 6 months, 8.1 point improvement for AAV-GAD vs. 4.7 point improvement for sham**
  - Greater improvements observed in the AAV-GAD treatment group over all follow-up time points

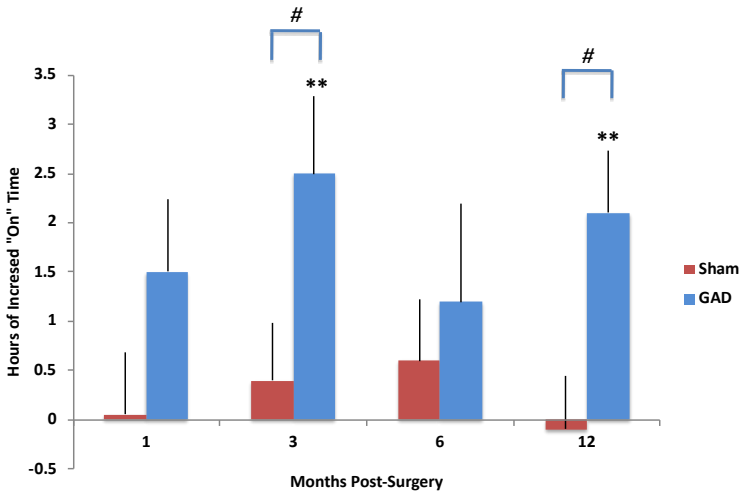
Group effect: p < 0.03; 2 × 5 RMANOVA; *p < 0.05, **P < 0.01, ***p <0.001, post-hoc Bonferroni tests relative to baseline

- **6 months: 50% responder rate for AAV-GAD vs. 14% responder rate for sham**
- **12 months: 62% responder rate for AAV-GAD vs. 24% responder rate for sham**
- **≥9 point reduction in UPDRS Part 3 "off" scores**
  - Approximately 25% improvement 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)[2]

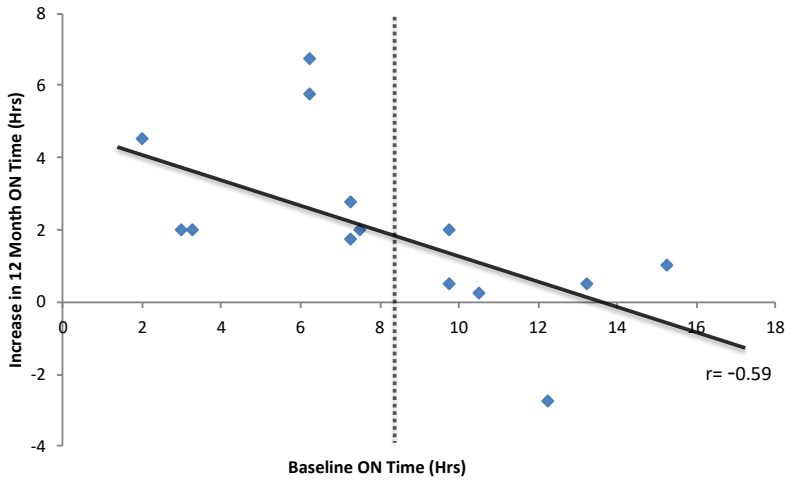
1. Niethammer M. Long-term follow-up of a randomized AAV2-GAD gene therapy trial for Parkinson's disease. JCI Insight. 2017; 2(7):e90133
2. Shulman LM. The clinically important difference on the unified Parkinson's disease rating scale. Arch Neurol. 2010; 67(1):64-70

Increased ON Time Without Dyskinesia

A. Increased ON time w/o dyskinesias following AAV-GAD

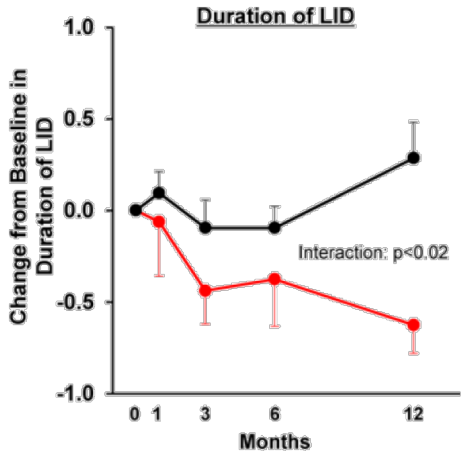


B. Correlation between lower baseline ON time (worse) & increased ON time w/o dyskinesias 12 mo after AAV-GAD



Overall change in ON time GAD vs. sham p=0.044 (ANOVA)

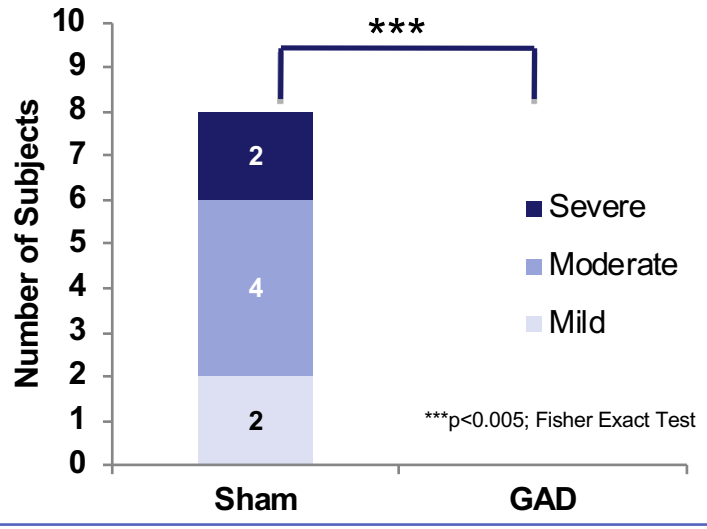
C. Reduction in dyskinesia duration following AAV-GAD



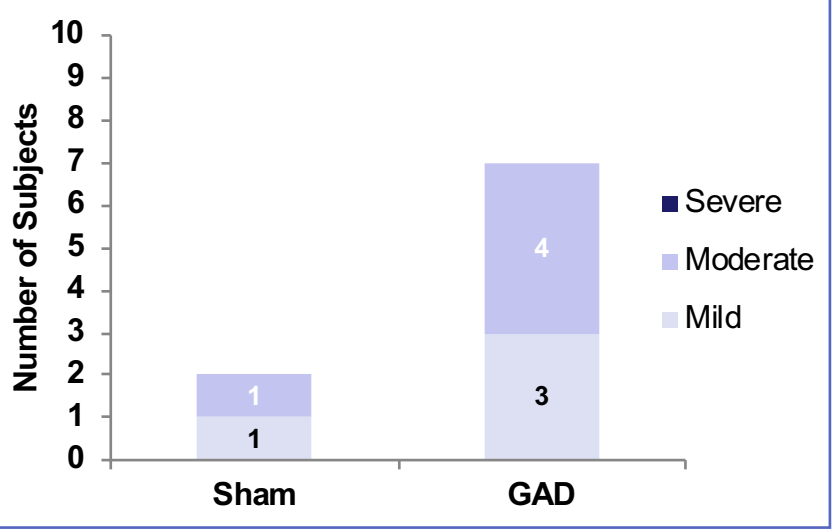
Niethammer M. Long-term follow-up of a randomized AAV2-GAD gene therapy trial for Parkinson's disease. JCI Insight. 2017; 2(7):e90133

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

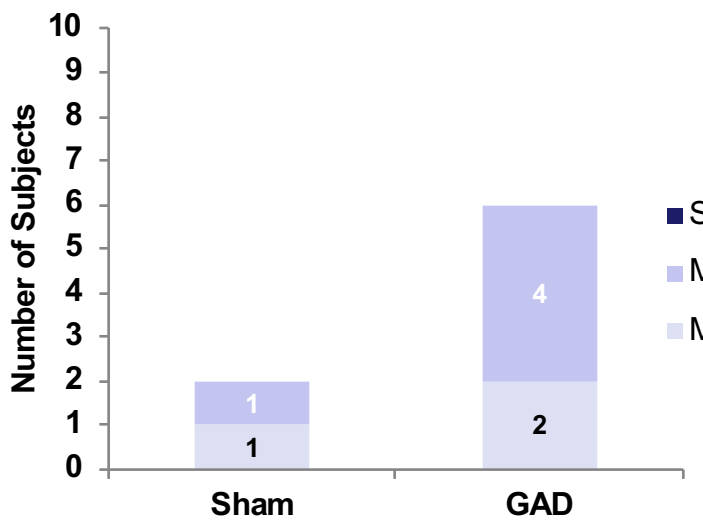
Worsening of Parkinson's Disease



Headache



Nausea



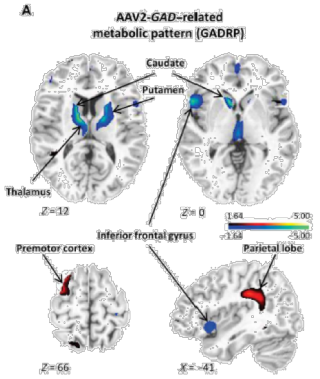
Serious Adverse Events*
(Number of Subjects)

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

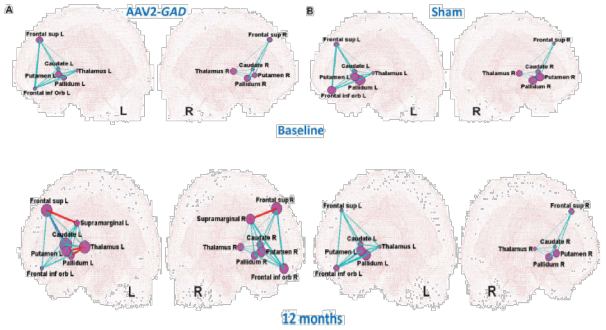
*All SAEs occurred 4-12 months post-surgery and all resolved

Functional Imaging – GAD Related Pattern (GADRP)

- **AAV-GAD recipients developed unique treatment-dependent polysynaptic brain circuit (GAD related pattern, GADRP)**
- **Statistically significant correlation between improvement in UPDRS motor ratings and GADRP expression (p< 0.009)**
- **This treatment-induced brain circuit is a novel endpoint to isolate true treatment-driven responses from placebo responses**
- **AAV-GAD is the first gene or cell therapy for PD to have an objective imaging biomarker of treatment effect that was significant relative to sham surgery patients and correlated with clinical improvement**



- Decreased metabolic activity in striatum and thalamus
- Increased metabolic activity in premotor cortex



- New polysynaptic pathways connecting STN to motor cortex

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

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


Articles

AAV2-GAD gene therapy for advanced Parkinson's disease: a double-blind, sham-surgery controlled, randomised trial

JCI insight

CLINICAL MEDICINE

Long-term follow-up of a randomized AAV2-*GAD* gene therapy trial for Parkinson's disease

MEIRAGTx

Salivary Gland

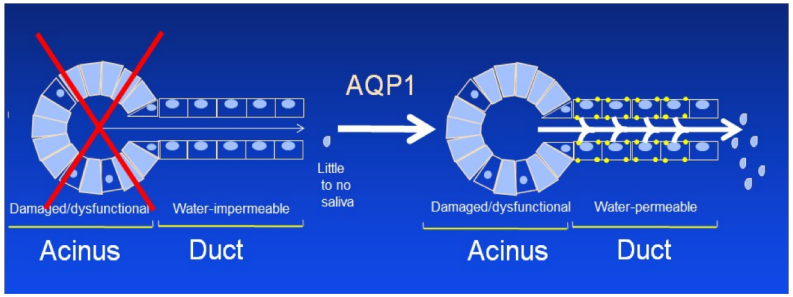
AAV-AQP1 for Radiation-Induced Xerostomia (RIX)

Significant unmet medical need: xerostomia persisting >2 years after radiation therapy for oral cancer

- 170,000 existing patients in the U.S.
- 50,000 new cases of head and neck cancer/yr treated in US
- 85% of radiation-treated patients experience reduced saliva production, of whom 40% have persistent Grade 2/3 RIX
- Serious, debilitating complications: dental caries, enamel erosion, oral infections, sleep disturbances, difficulty talking, chewing, swallowing, weight loss and malnutrition

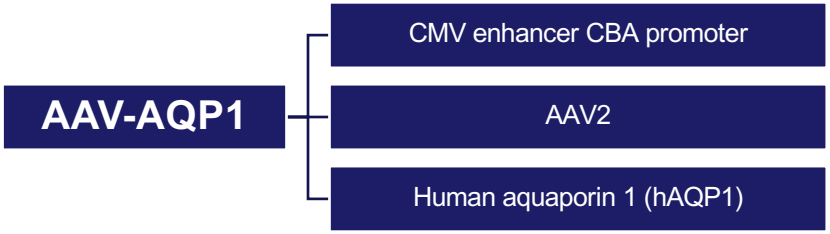
Strategy for the repair

- Water-impermeable duct cells generate an osmotic gradient (lumen > interstitium)
- Introduction of human aquaporin 1 gene (hAQP1) into duct cells via viral vector, making duct 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



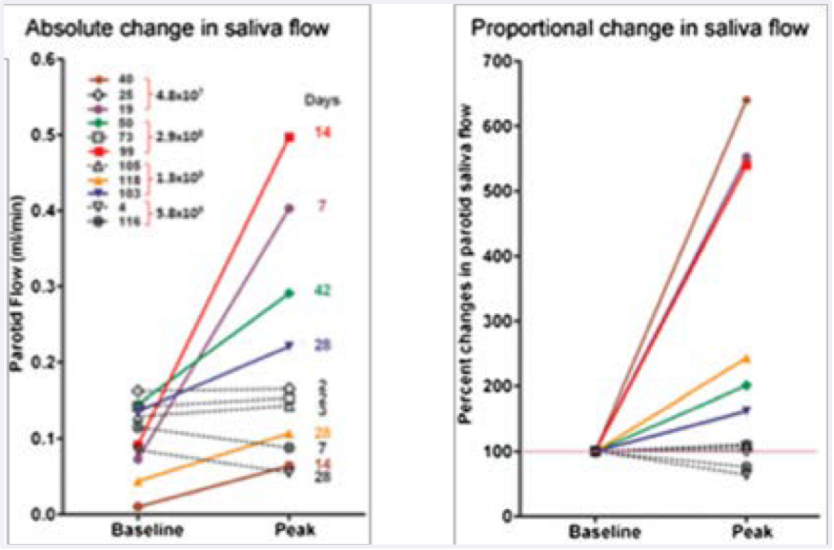
Human Proof-of-Concept Established: Phase 1 trial of AdhAQP1

Adenoviral-mediated aquaporin-1 cDNA transfer for radiation-induced salivary hypofunction

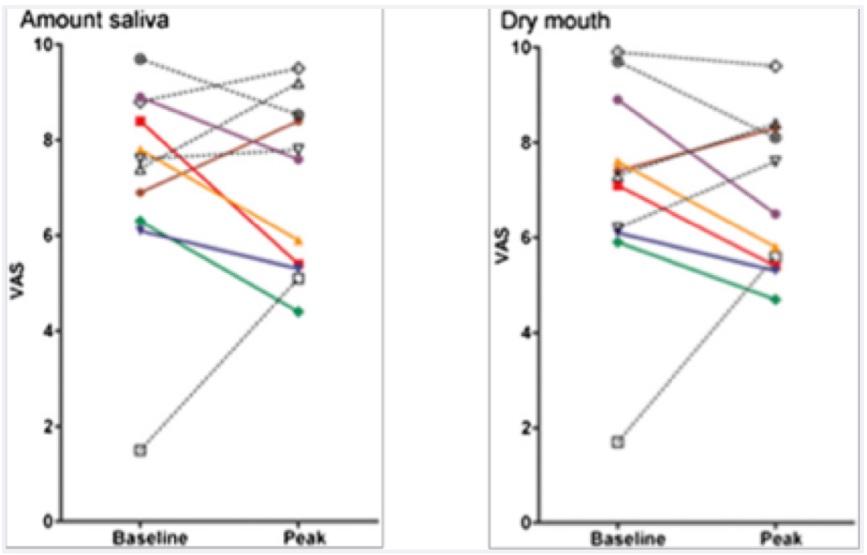
- AdhAQP1 treatment was well tolerated: no SAEs
- Responses seen in 2 of 3 patients in each of the first 3 cohorts
- 60% to 540% increase in parotid flow in responding patients
- 5 of 6 patients also reported subjective improvement in symptoms

NIH
National Institute of Dental and Craniofacial Research

Change in parotid salivary flow rate

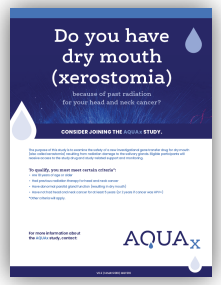


Visual analogue scale (VAS)



Baum BJ et al. *PNAS,* 2012.

Ongoing Clinical Trials of AAV-AQP1 for the Treatment of Radiation-Induced Xerostomia



Multi-center Phase 1/2 Trial – AQUAx (NCT04043104)

- Dose escalation ongoing

National Institutes of Health

Phase 1 trial at NIH (NCT02446249)

- Dose escalation ongoing

Clinical trial overview			
Grade 2/3 Xerostomia	History of radiation therapy for head and neck cancer	Disease-free of head and neck cancer for at least 5 years (at least 2 years if HPV+)	Aged 18+

- **Design:** 3+3 dose escalation
- **Administration:** AAV-AQP1 is slowly injected into a single parotid salivary gland
- **Study period:** Patients will complete assessments at the clinical trial site over the course of one year
- **Primary endpoint:** safety
- **Secondary endpoint:** parotid gland salivary output

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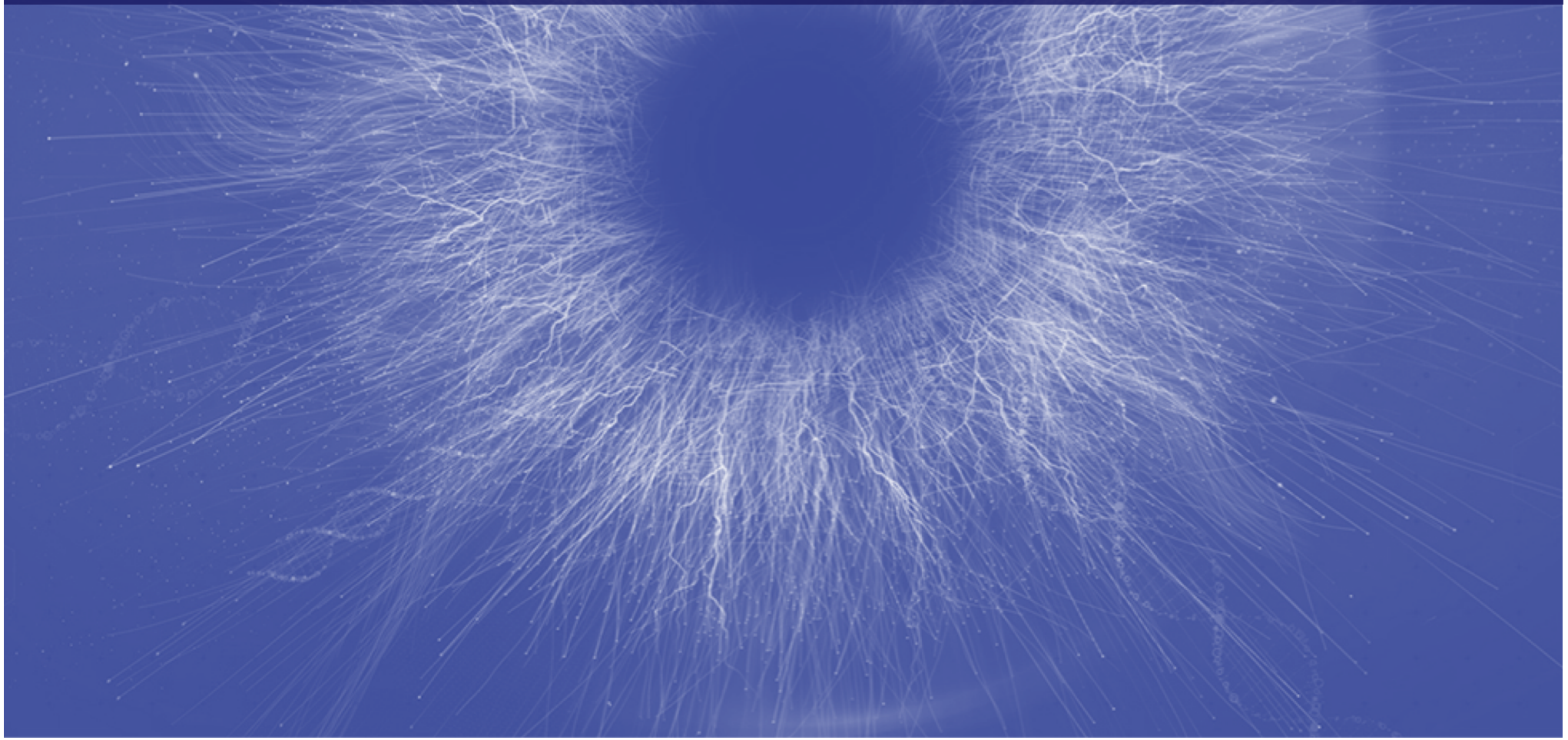
Ocular Franchise

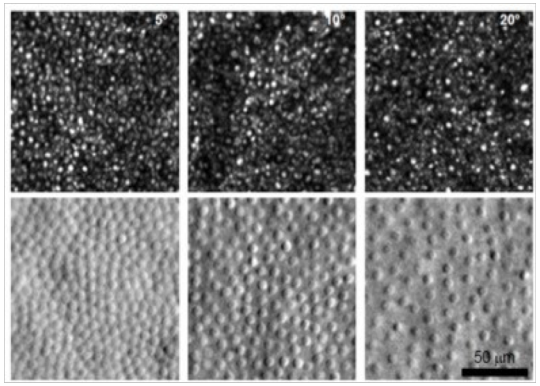


MeiraGTx Ocular Programs

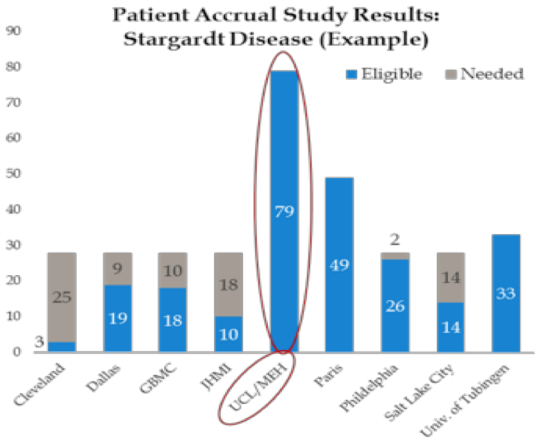
Ophthalmology Partners and Centers of Excellence

- **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
- Partnership with **Foundation Fighting Blindness (FFB)**
- Global expertise in imaging and validated endpoints in each of our target diseases

Our Partners Possess World Leading Imaging, Endpoint Development and Validation

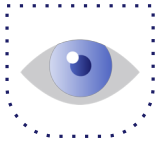


Patient Access



Inherited Retinal Disease Worldwide Strategic Collaboration

Clinical development



Janssen and MeiraGTx collaborating to advance AAV-CNGB3, AAV-CNGA3, AAV-RPGR through clinical development

Janssen commercial infrastructure

- Janssen has worldwide exclusive commercial rights to AAV-CNGB3, AAV-CNGA3, AAV-RPGR and future IRD programs
- IRD portfolio to benefit from worldwide reach of Janssen commercial infrastructure

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

Manufacturing and process development

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

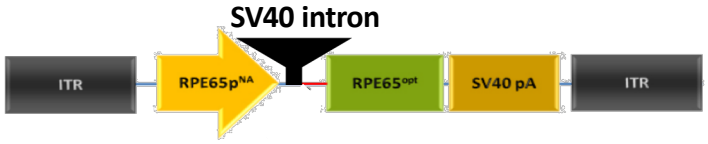
AAV-RPE65 for the Treatment of *RPE65*-Associated Retinal Dystrophy

RPE65-Associated Retinal Dystrophy

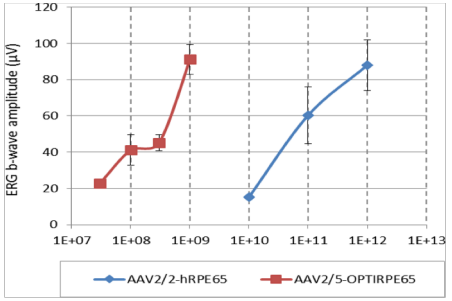
- **Rod-cone dystrophy**
  - Ultra-rare, severe IRD caused by mutations in the *RPE65* gene
  - RPE65 expressed in retinal pigment epithelium (RPE), supporting cells of photoreceptors
  - RPE65 required for recycling of the visual pigments allowing photoreceptors to sense light
- **Disease progression**
  - Complete lack of rod function and night blindness from birth
  - Reduced cone function early in life
  - In addition to diminished photoreceptor function, both rods and cones degenerate progressively
  - Complete retinal degeneration and blindness in early adulthood
- **Natural history study ongoing**
  - >30 patients well characterized

AAV-RPE65: optimized and highly potent cell-specific vector

- **Increased efficiency of transduction, transcription and translation**
  - RPE strong cell-specific promoter
  - Optimized transgene sequence
  - AAV5 capsid selected over AAV2 capsid



Georgiadis et al 2016 *Gene Therapy*



In RPE65-deficient mice, AAV2/5-OPTIRPE65 restores retinal function at 300-1,000-fold lower doses than unoptimized AAV2/2-RPE65 vector

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)

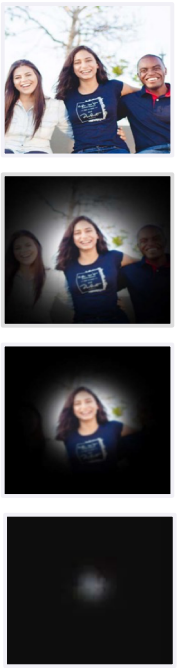
*Statistical significance demonstrated across entire study (cohort 1, cohort 2, cohort 3, pediatric expansion cohort)
**Statistical significance demonstrated in subset of adults and children treated at $1x10^{11}$ (cohort 1, pediatric expansion cohort)

AAV-RPGR for the Treatment of X-Linked Retinitis Pigmentosa due to RPGR-Deficiency

X-Linked Retinitis Pigmentosa (XLRP)

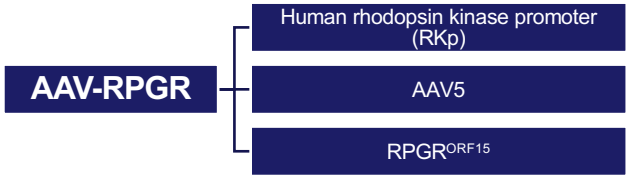
- **Retinitis Pigmentosa (RP)**
  - Group of IRDs which represents the most common genetic cause of blindness
  - X-linked RP is the most severe form of RP and accounts for 10-15% of RP
- **Disease progression**
  - Loss of night vision → progression to tunnel vision → blindness in 4th decade
- **Prevalence**
  - ~1/40,000
  - Total patients in US, EU5, Japan: ~20,000
- **Natural history study ongoing**
  - >100 patients well characterized

Patient Experience



Phase 1/2 trial of AAV-RPGR

- **Dose escalation complete**
  - 10 young adults (aged 18-30)
  - 3 children in pediatric expansion cohort
- **Randomized, controlled extension study ongoing**
  - Evaluating 2 doses of AAV-RPGR + deferred treatment arm



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

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

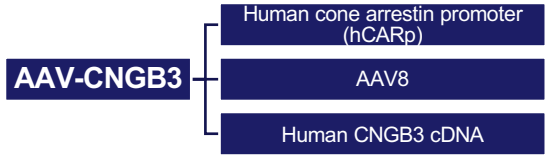
Patient Experience

Normal

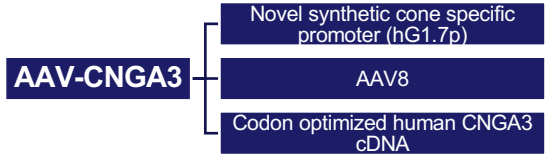
Achromatopsia

Ongoing clinical trials

- **Phase 1/2 trial of AAV-CNGB3**
  - 23 patients treated (11 adults, 12 children)
  - Dosing complete, follow up ongoing



- **Phase 1/2 trial of AAV-CNGA3**
  - Dose escalation began in pediatric patients
  - Enrolling children aged 3-15



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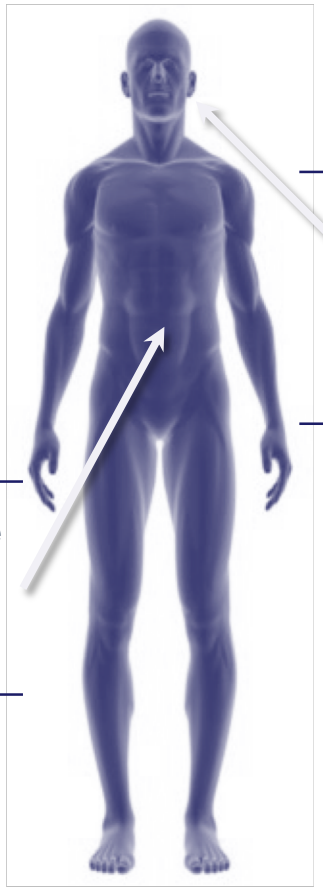
Gene Regulation

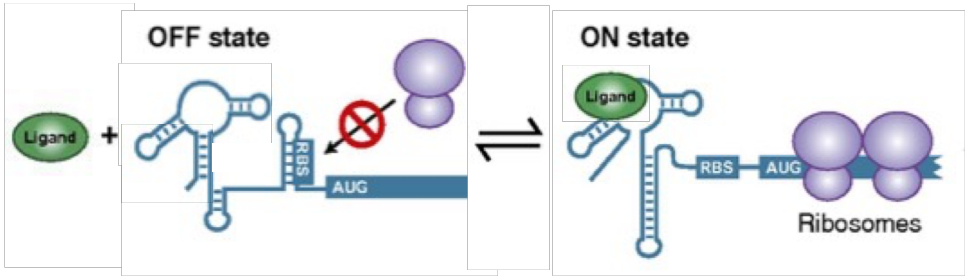
Next Generation Gene Therapy: Gene Regulation Platform

- **Modular switch cassette based on RNA shape**
- Regulate a chosen transgene in vivo using a different **small molecule** for each transgene
- **Platform can regulate multiple genes:** antibodies, hormones, cytokines
- **Demonstrated regulation in vivo in the liver of AAV delivered genome**



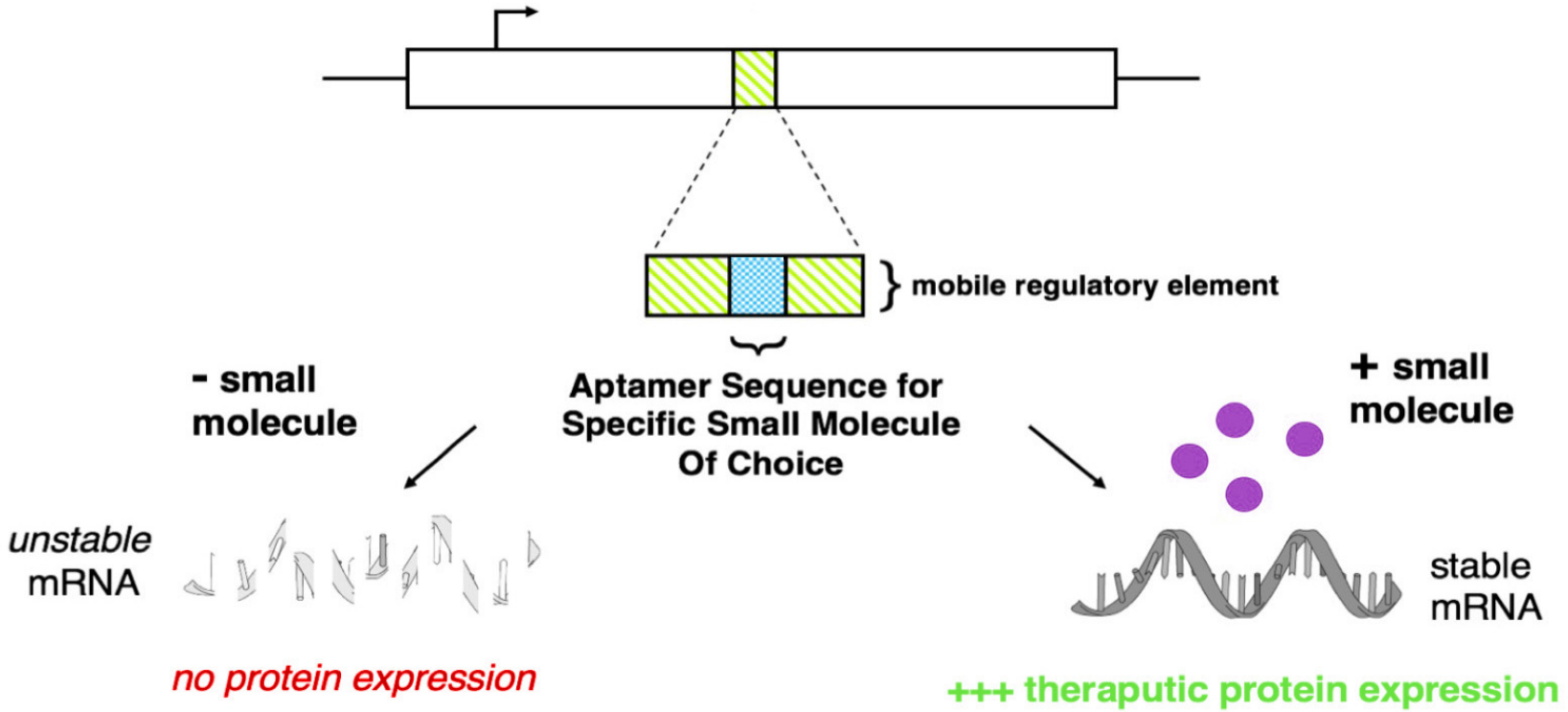
1 **Insert the gene for a therapeutic protein**

2 **Oral small molecule for ongoing control of gene expression**

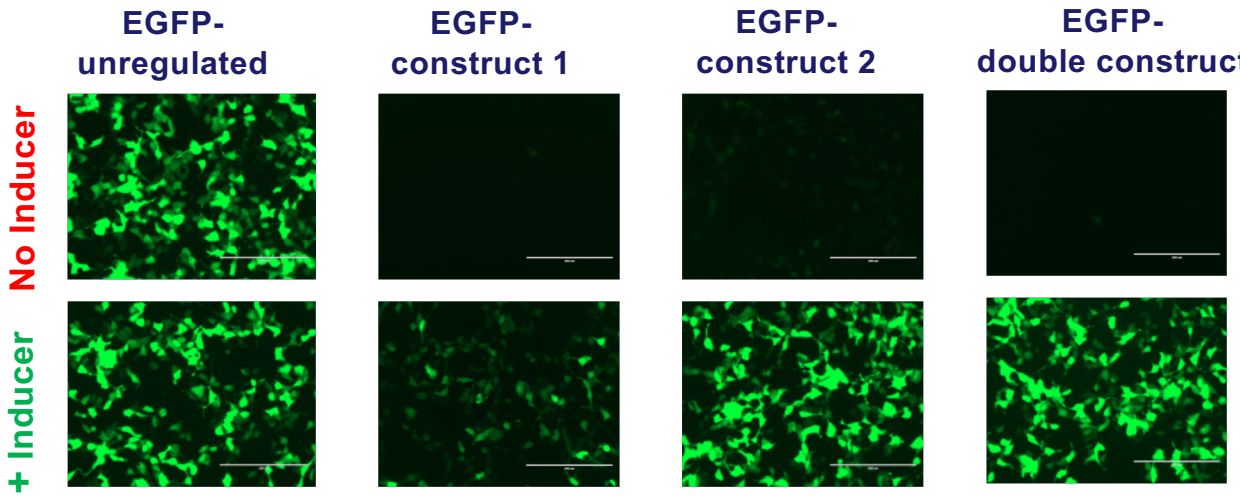


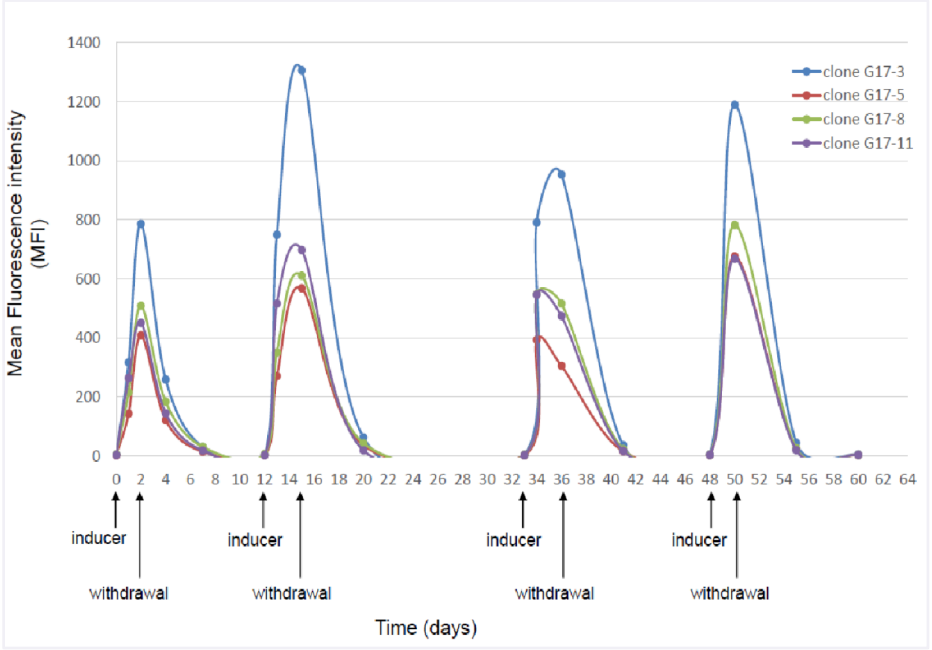
Regulation of Transgenes using Proprietary Riboswitch Technology

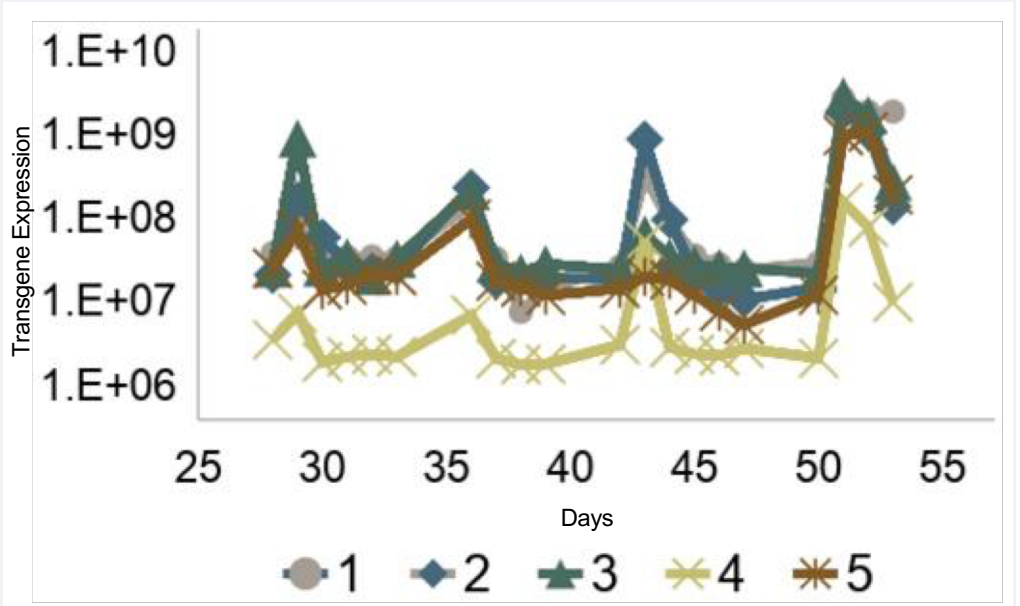
Regulation driven by specific small molecule / RNA binding driving functional changes in RNA configuration, splicing and translation



Regulation of Transgene Expression







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