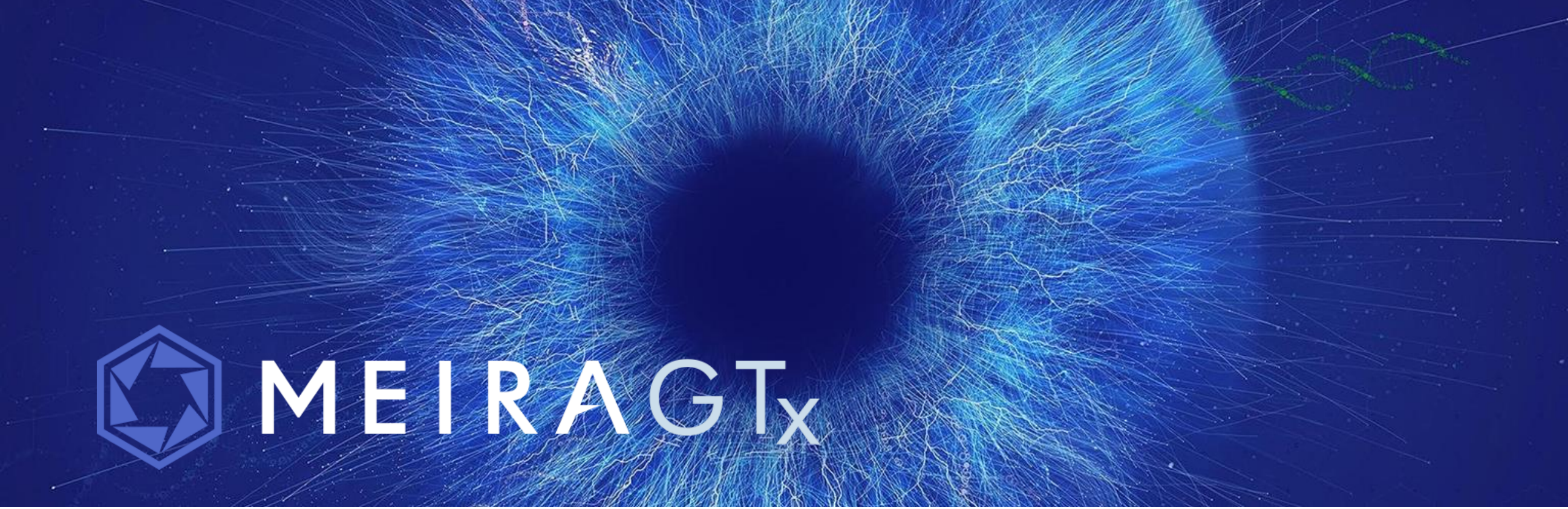


Corporate Presentation

May 2022

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 May 12, 2022.

MEIRAGTx

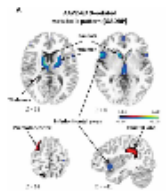
A Vertically Integrated, Clinical Stage Gene Therapy Company

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:

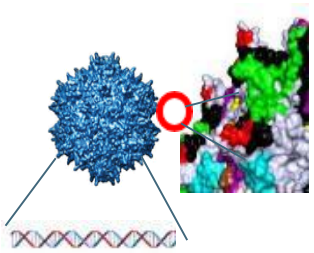
- Inherited retinal diseases
- Salivary gland
- Parkinson's disease

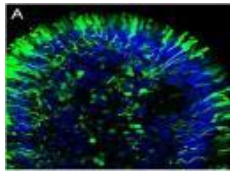


Platform of Core Viral Vector Engineering Capabilities

Viral vector design platform:

- Promoter, capsid, transgene optimization, ITRs, immunogenicity



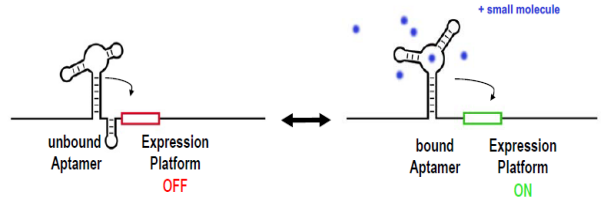


cGMP Manufacturing Capacity & Commercial Ready Scalable Process

- **Flexible** and **scalable cGMP** manufacturing facility with quality and capacity for commercial supply
- **Internal Plasmid production** for GMP and Analytics for QC release and stability
- **Process Development Platform**

Next Generation Gene Therapy Riboswitch-Based Gene Regulation Platform

- **Proprietary technology** allows precise control of gene therapy expression level via dose response to orally delivered small molecules
- Transformative platform with unprecedented dynamic range
- Potentially **applicable to any gene, any vector** with novel synthetic small molecules



Multiple Therapeutic Targets

OCULAR

Clinical Development
- IRD franchise: Phase 3 pivotal study dosing and enrolling
- XLRP, CNGB3, CNGA3, RPE65, LCA4

Preclinical and Research
- 4 IRD programs undisclosed
- Wet AMD, Dry AMD
- Glaucoma

Gene Regulation
- Small molecules delivered as topical eye drops
- Uveitis, Glaucoma, AMD

NEURODEGENERATIVE

Clinical Development
- Parkinson's disease

Preclinical and Research
- Amyotrophic Lateral Sclerosis (ALS)

Gene Regulation
- CNS expression with BBB penetrant small molecules

SALIVARY GLAND

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

Preclinical and Research
- Sjogren's Syndrome
- Dry eye

Gene Regulation
- Peptide and hormone regulated delivery from salivary gland

Clinical programs de-risked: Human proof of concept demonstrated across ocular, neurodegenerative and salivary gland pipelines, small doses, locally delivered, immune protected sites

All target tissues are good candidates for sites of regulated gene therapies for second and third generation programs

A Deep Pipeline of Transformative Gene Therapies

Six clinical studies across multiple therapeutic areas

Product	Indication	Discovery / Preclinical	Phase 1/2	Phase 3
Ocular				
Inherited Retinal Diseases				
Botaretigene sparoparvovec*[1] (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			
Salivary Gland				
AAV-AQP1	Xerostomia		***Orphan Drug***	
	Sjögren's Syndrome			
Riboswitch Inducible Expression Programs				
Diabetes/Metabolic Disorders	Undisclosed Targets			
Ophthalmology	Undisclosed Targets			
Oncology	Undisclosed Targets			

* Co-development program with Janssen Pharmaceuticals [1] Formerly referred to as AAV-RPGR

Anticipated Upcoming Milestones and Objectives

Inherited Retinal Disease	Botaretigene sparoparvovec* | XLRP (janssen)	Phase 1/2 Randomized Expansion Cohort Data to be presented	1H 2022
	Botaretigene sparoparvovec* | XLRP (janssen)	Phase 3 Enrollment	2022
	AAV-CNGB3 and AAV-CNGA3 I Achromatopsia (janssen)	Initiate additional studies in CNGB3 and CNGA3 with Janssen	2022
	Undisclosed IRDs (janssen)	IND for an additional IRD target with Janssen	2022
Degenerative Ocular Disease (non-inherited)	Regulation of ophthalmology viral vector expression for large eye indications	Formulation of multiple small molecules for regulation in the eye	2022
Neurodegenerative Disease	AAV-GAD | Parkinson's disease	File IND and initiate AAV-GAD clinical study	1H 2022
Salivary Gland	AAV-hAQP1 | Grade 2/3 RIX	Phase 1 dose escalation data	YE 2022
	AAV-hAQP1 | Grade 2/3 RIX	Initiate randomized, multi-dose Phase 2 trial of AAV-hAQP1 in RIX (radiation-induced xerostomia)	YE 2022
	AAV-hAQP1 | Sjögren's study	IND enabling studies completed	2022
Riboswitch Gene Regulation	Oral Small Molecule | multiple indications with riboswitch cassette	File IND Phase 1 safety	2022
	Small Molecule + Peptide / Hormone | undisclosed metabolic disease(s)	IND enabling	2023
	Small Molecule + Antibody | undisclosed	IND enabling	2023

* Formerly referred to as AAV-RPGR

A Unique, Diverse and Inclusive Culture

MEIRAGTx

- 290+ full-time employees
- 55% female, 45% male
- 4 locations: US, UK, Netherlands, Ireland
- 31 different nationalities represented

Industry-Leading cGMP Manufacturing of AAV

A Fully Integrated Manufacturing Ecosystem

185+ FTEs Dedicated to Best-in-Class AAV Manufacturing

cGMP Manufacturing

- Two independent cGMP viral vector production facilities
- Flexible and scalable manufacturing process; fit for commercialization; global regulatory CMC input
- Single use philosophy, closed system unit operations
- In-house QC hub
- London facility GMP certified in 2018 and 2020 – facility and quality management systems support first in man clinical through commercialization
- In-house GMP plasmid production
- In-house Fill & Finish

MSAT Process Development Facility

- Dedicated Process Development facilities in London and Ireland; flexible and scalable platform production process
- 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, improving yield and increasing production capacity
- Vectors optimized for potency (promoters, capsids, gene sequence) to reduce dose, increase efficacy and decrease cost of goods

Non-GMP Vector Core

- Dedicated non-GMP production facility for pre-clinical supply in Amsterdam
- Produce consistent vector batches for preclinical studies in scale-down models pre-GMP
- Synergizes with MSAT to prepare for vector process optimization before tech-transfer to GMP

Flexible & Scalable GMP Manufacturing for Clinical and Commercial Production

Shannon Facilities

cGMP, 150,000 sq ft

- Up to 12 viral vector suites with 2x 500L bioreactor per suite (each suite with capacity up to 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

185+ FTEs Dedicated to Best-in-Class AAV Manufacturing

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

Shannon GMP Manufacturing Facility – Ireland, EU

Britannia Walk GMP Manufacturing Facility – London, UK

Comprehensive Preclinical Development Capabilities

Preclinical Development Centers (London – New York – Amsterdam)

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

In-Vivo Platform

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

Organoid and iPSC Platform

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

In-House Non-GMP Vector Core (Amsterdam)

- Production of consistent vector batches for pre-clinical studies
- Synergizes with MSAT to prepare for vector process optimization before 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 DNA (minicircles, doggybone, linear DNA)

Extensive Vector Engineering Toolkit

Gene Sequence Optimization

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

Gene Regulation Switch Technology

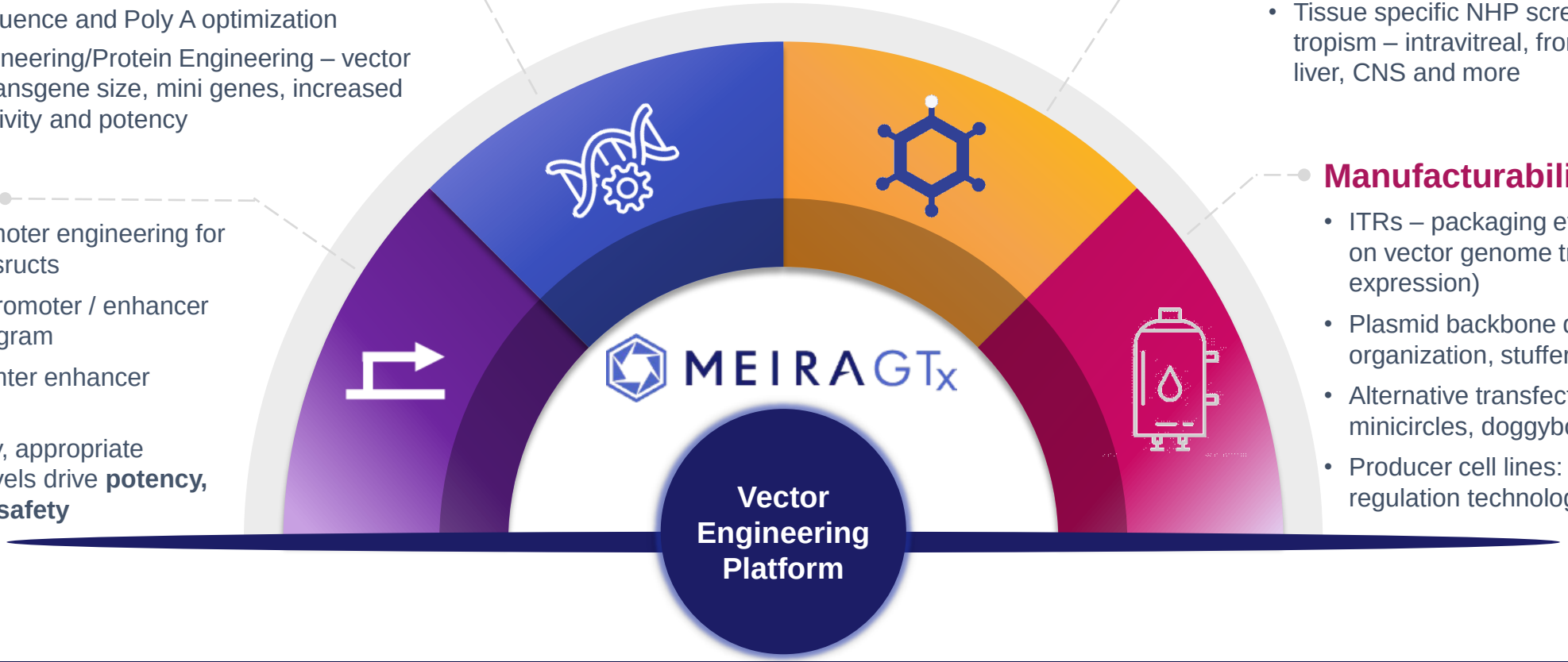
- Broad gene regulation platform to overlay onto cell specific promoter control dose dependent regulation by novel small molecules at unprecedented dynamic range and dosing

Capsid Selection

- Capsid selection for each indication and cell type
- Tissue specific NHP screens for capsid tropism – intravitreal, front of the eye, liver, CNS and more

Promoters

- Bespoke promoter engineering for all vector consructs
- Large scale promoter / enhancer screening program
- AI driven promter enhancer discovery
- Cell specificity, appropriate expression levels drive **potency, efficacy and safety**



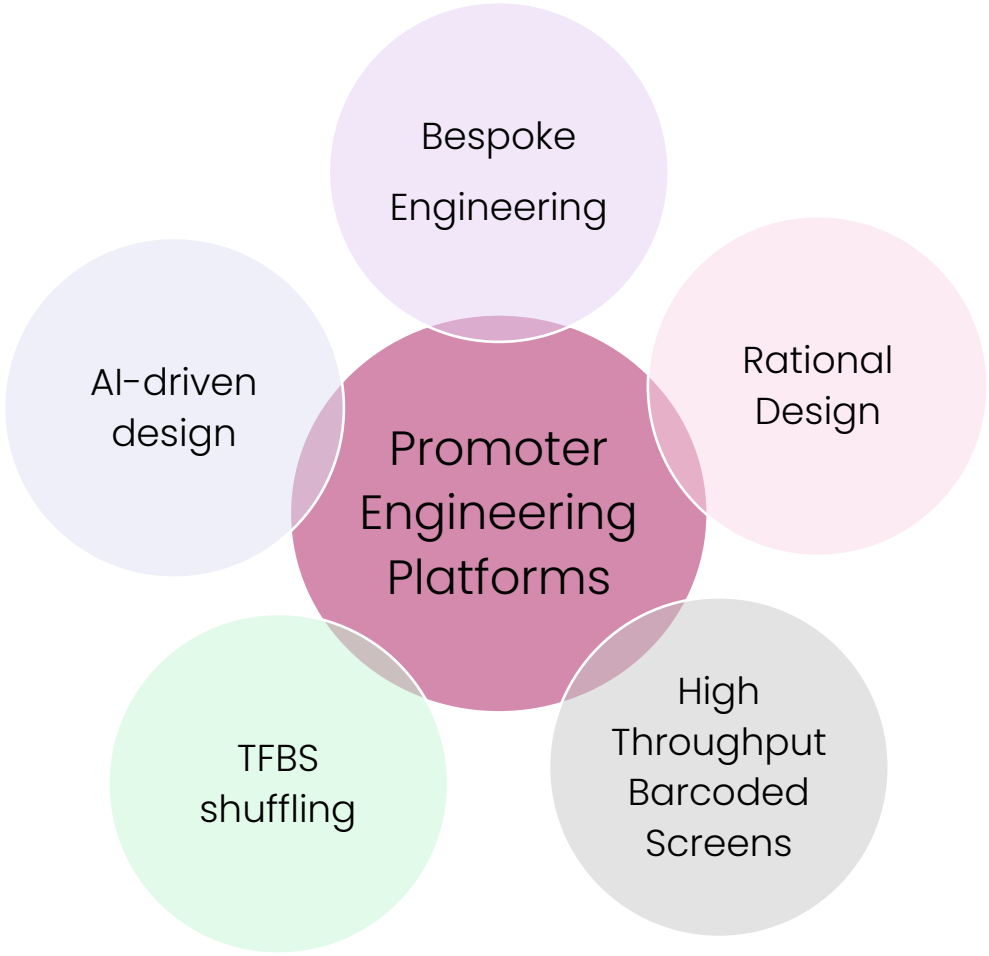
Manufacturability

- 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
- Producer cell lines: incorporating gene regulation technology

Gene Regulation Platform

Multiple Promoter Engineering Platforms Creating Libraries of Strong, Small Tissue Selective Promoters-Enhancer Combinations

Multiple engineering and screening strategies for design and selection of strong constitutive, tissue specific promoter/enhancer elements – driving potency and safety



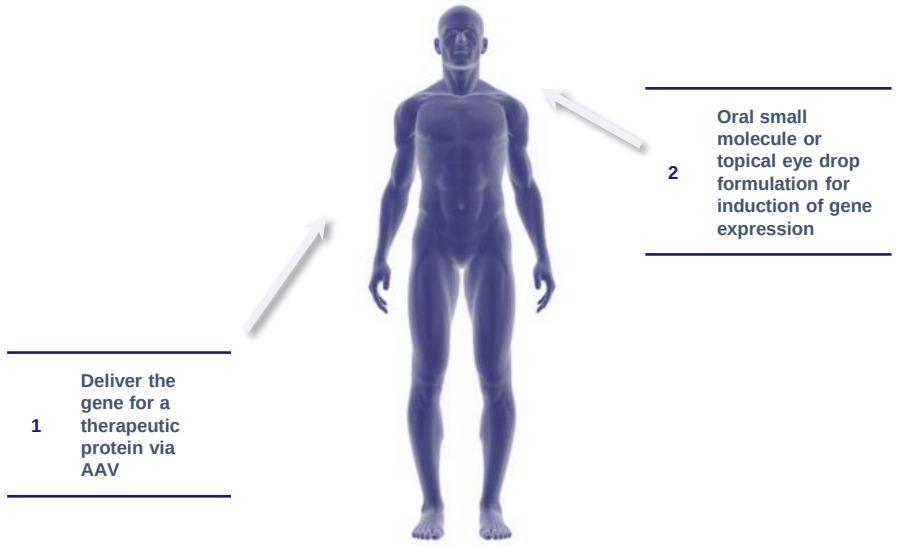
Libraries of synthetic novel promoters with smaller size, greater strength and cell selectivity compared to CAG, CMV and cell specific promoters; ongoing optimization of library to increase the promoter toolkit

- Multiple cell specific promoters for all the different cell types in the eye for different levels of expression: e.g., the strongest known human pan-cone promoter
- 40 constitutive promoters up to 10-fold stronger than CAG and/or CMV
- 10+ neuronal promoters up to 12x stronger than CAG in both human and mouse neuronal cell lines
- 13 liver-specific promoters up to 4-fold stronger than CAG and stronger than promoters currently used clinically (AAT, LP1, TBG). All smaller than CAG
- 9 muscle-specific promoters that are stronger than tMCK (which is currently used in clinical trials)
- A synthetic muscle-specific promoter is durable and >17-fold stronger than tMCK in the mouse muscle *in vivo*
- A 751 bp ubiquitous promoter is stronger in muscle than CAG
- *In silico* screening and evolution of promoters via machine learning methods further enhances potency and cell specificity of promoters identified by other methods

Oral Small Molecules Precisely and Specifically Control Gene Therapy Activity

For the first time, a Gene Regulation System that precisely and specifically controls the activity of genetic medicines using orally dosed pills

- It is not just an ‘on’ / ‘off’ switch but a system for dose response of gene therapies to oral drugs
- Gene regulation at **unprecedented high dynamic range of >5000**
- Any gene, any vector; cell therapy, gene editing can be controlled with this system
- With vectorology and gene regulation toolkit we can rapidly build new regulated genetic therapies
- Multiple Regulation Cassettes optimized for each gene
- Libraries of small molecules specifically designed to match synthetic aptamers, with different drug properties
- Potential for a different small molecule to precisely regulate each specific gene
- Drug characteristics (PK, metabolism, distribution) tailored to that gene and that indication



Unique technology transforms the field of genetic medicine and delivery of biologics

Unique Gene Regulation System Transforms Genetic Medicine

Vectorized Biologics

We can not only vectorize and optimize viral vectors for expressing Antibodies and other therapeutic proteins – but we can precisely control their expression: rare disease gene replacement consistency of dosing or systemic Vectorized Antibodies
Improved **Safety** and **Consistency** of dosing between patients

Passive and Active Vaccines with built-in capacity for Oral Small Molecule Boosters

Active Vaccine: regulated vaccine mRNA can be boosted multiple times any time after first IM delivery as needed with an oral pill
Passive Vaccine: neutralizing antibodies activated systemically and durably as needed with an oral pill e.g., COVID-19, universal flu

CNS expression of biologics – across the BBB

Potential to address one of the biggest challenges in medicine: getting large molecules across the blood-brain-barrier
Gene Therapy delivered 1x within the BBB and activated using a small molecule that crosses the BBB

Short-lived Therapeutic Hormones and Peptides

Precise activation of naturally short-lived peptides and hormones using an oral pill; and allows for combinations of multiple natural peptides regulated together.

Ocular expression of therapeutic proteins

Tight control of expression of therapeutic proteins in the eye with eye drop formulation of small-molecule inducer; improved safety and new targets

Gene Editing

Tight regulation of nucleases targeting DNA or RNA e.g., Cas9 and CasRx

Cell Therapy

Controlled expression of CAR, ‘Kill switches’; both ’on’ and ‘off’ switches

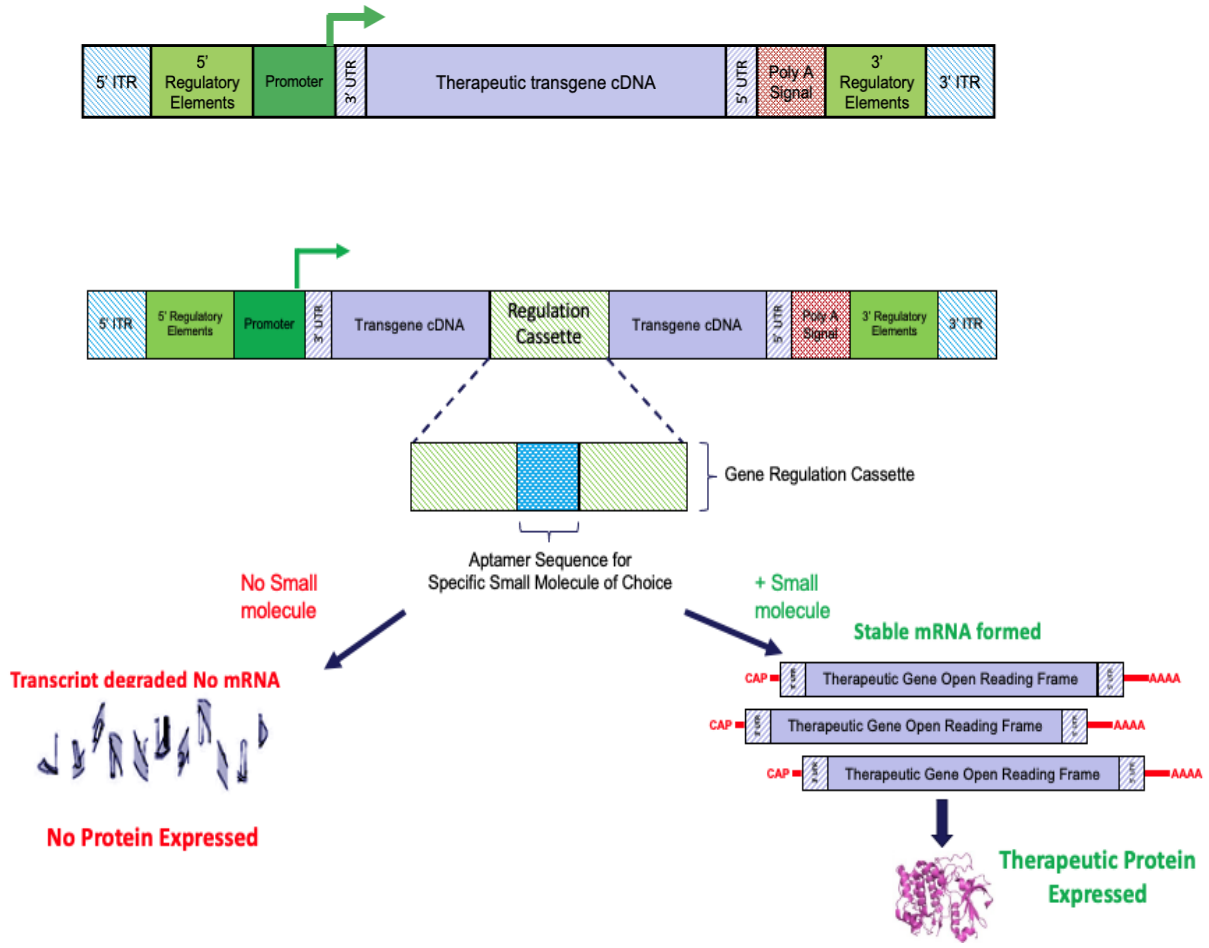
Pricing of Gene Therapies

Pay for the pill which delivers the active therapeutic protein, not just the 1x delivery of the gene therapy

MeiraGTx Riboswitch Driven Gene Regulation Cassette

We created a Gene Regulation Cassette controlled by a Riboswitch

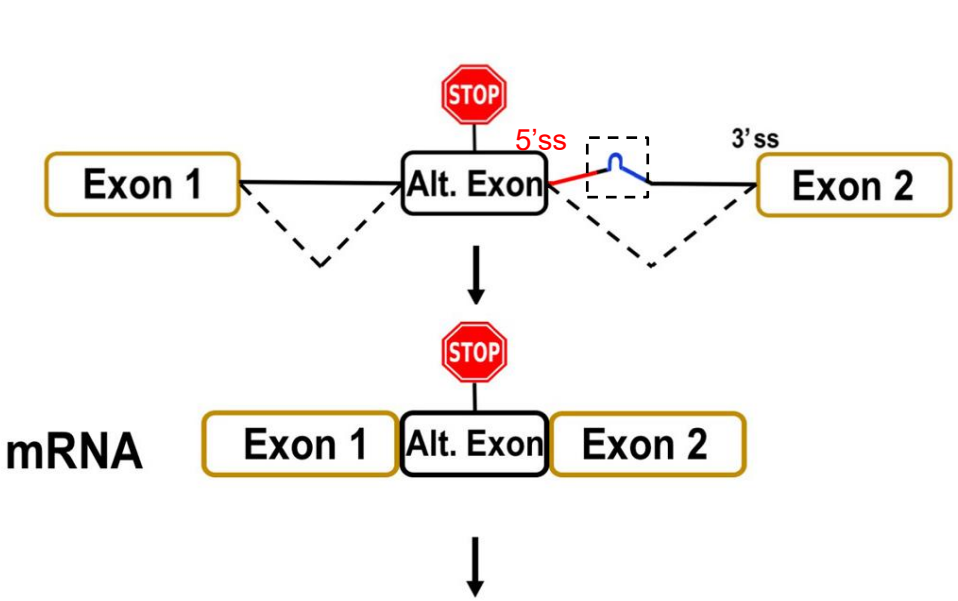
- Promoters and transcriptional regulatory elements are critical in determining the potency, efficacy and safety of gene therapies
- We have developed a gene control system that retains all of that promoter driven control and overlays a temporal control driven by an oral small molecule
- Dynamic range is unprecedented >5000 fold, high expression when on, low expression when off
- This system uses RNA Shape to turn gene on and off
- Gene Expression is controlled via Small Molecule RNA interaction
- Gene Regulation Cassette is incorporated into the cDNA sequence of the gene therapy vector genome
- When the DNA containing the cassette is transcribed to RNA the transcript takes on a configuration that results in complete RNA degradation
- When a specific small molecule binds to a small aptamer region within the cassette – the RNA shape configuration changes and the entire cassette is cut out and a mRNA is formed
- The mRNA produced in this way is identical to that produced by the gene therapy cDNA without the cassette - as if the cassette was never there –a perfect copy of the gene therapy mRNA



Gene Regulation Cassette driven by Splicing-based Mammalian Synthetic Riboswitch

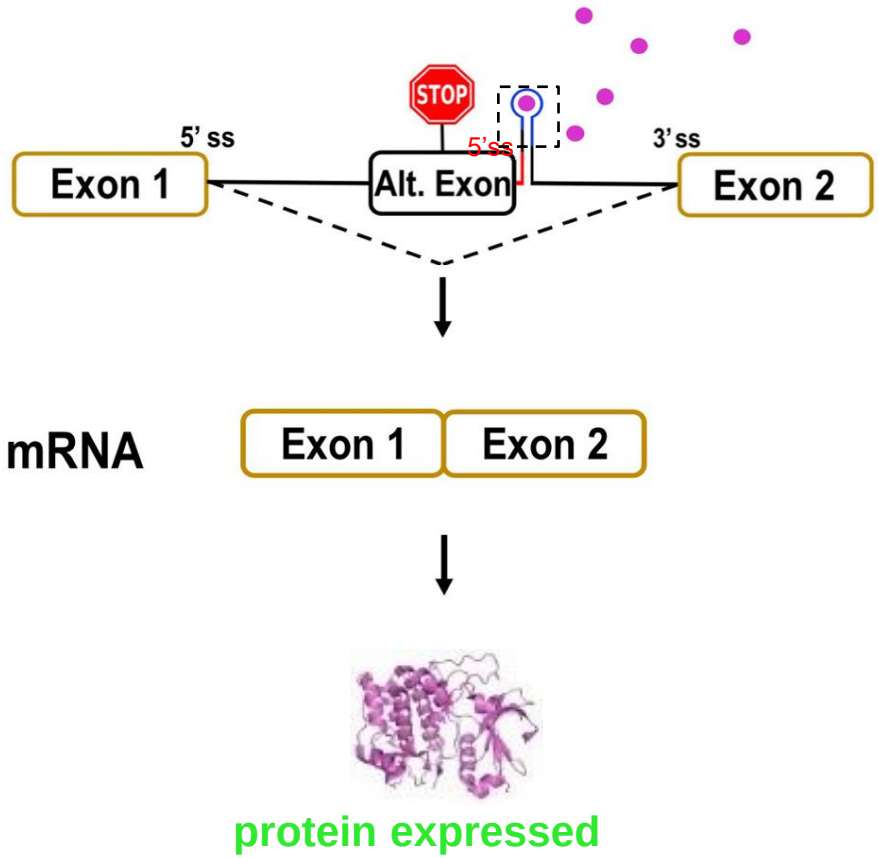
Riboswitch-mediated Modulation of alternative splicing

No Small molecule (OFF state)



no protein

+ Small molecule (ON state)



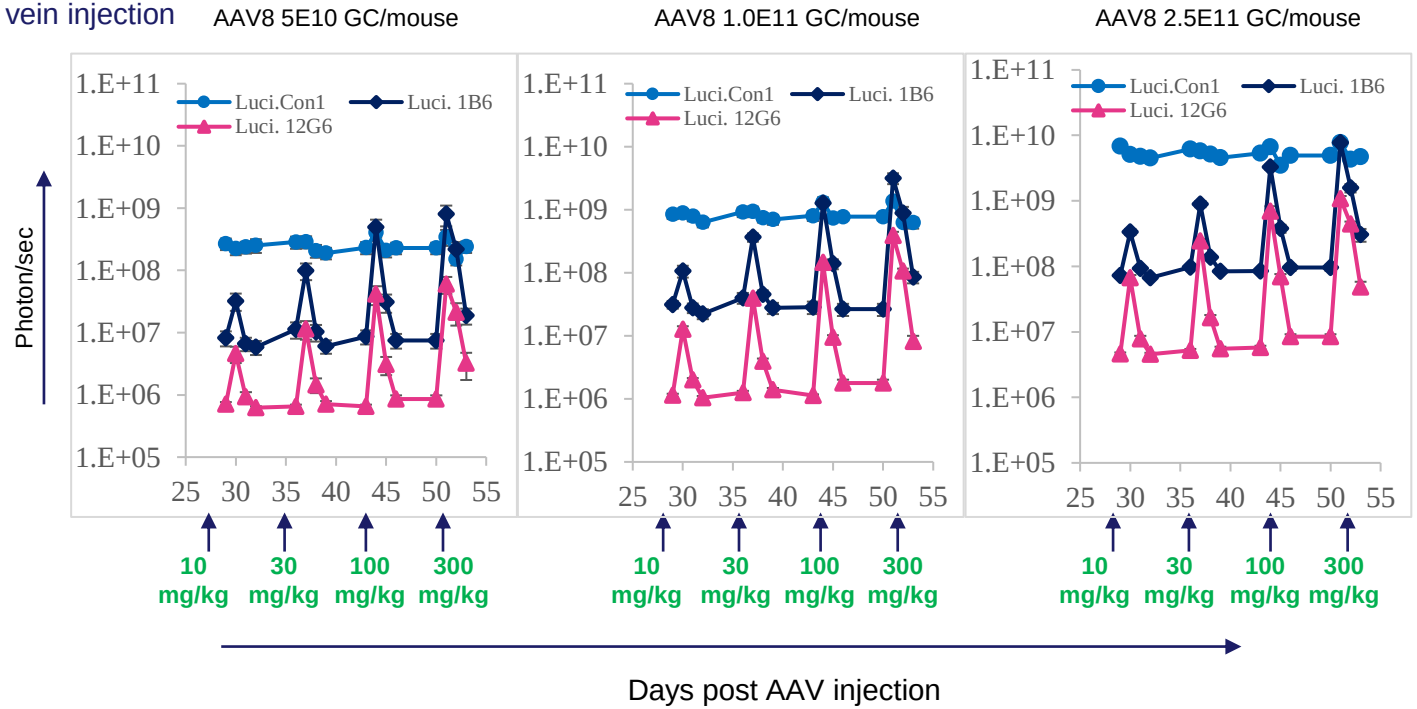
protein expressed

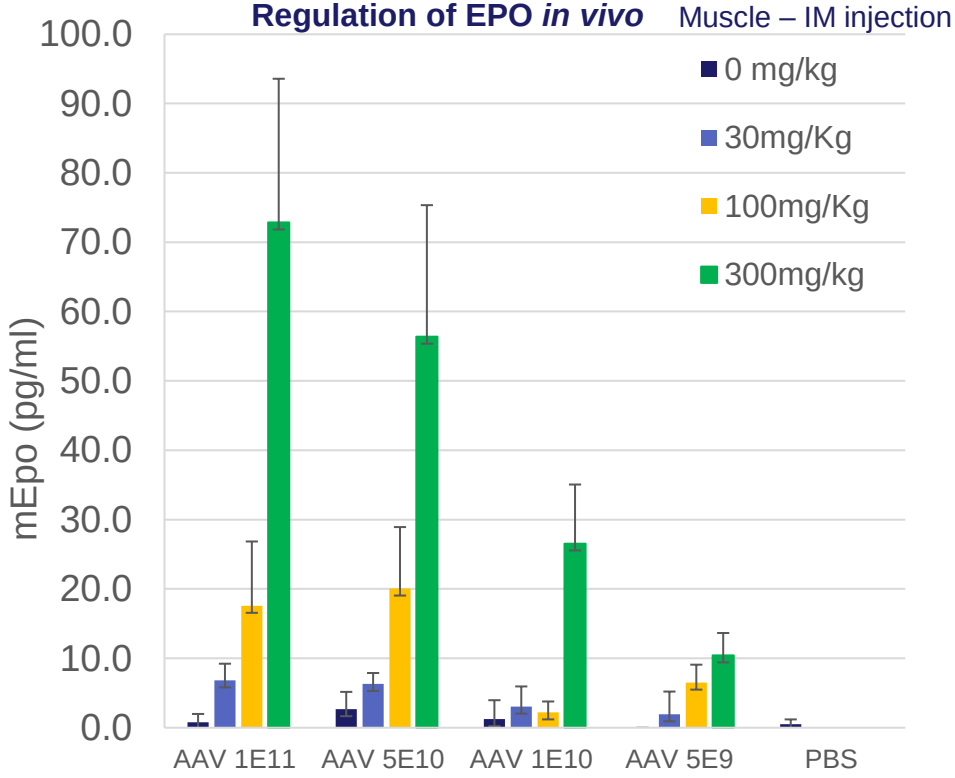
Novel Riboswitch Regulates Transgene Expression *in vivo* in Precise Dose Response to Orally Delivered Inducer

Precise control of transgene expression with single doses of orally delivered small molecule inducer

- Differential response to viral vector dose
- Dose response to small molecule inducer dose
- Dose response (and dynamic range difference) with different aptamer sequences

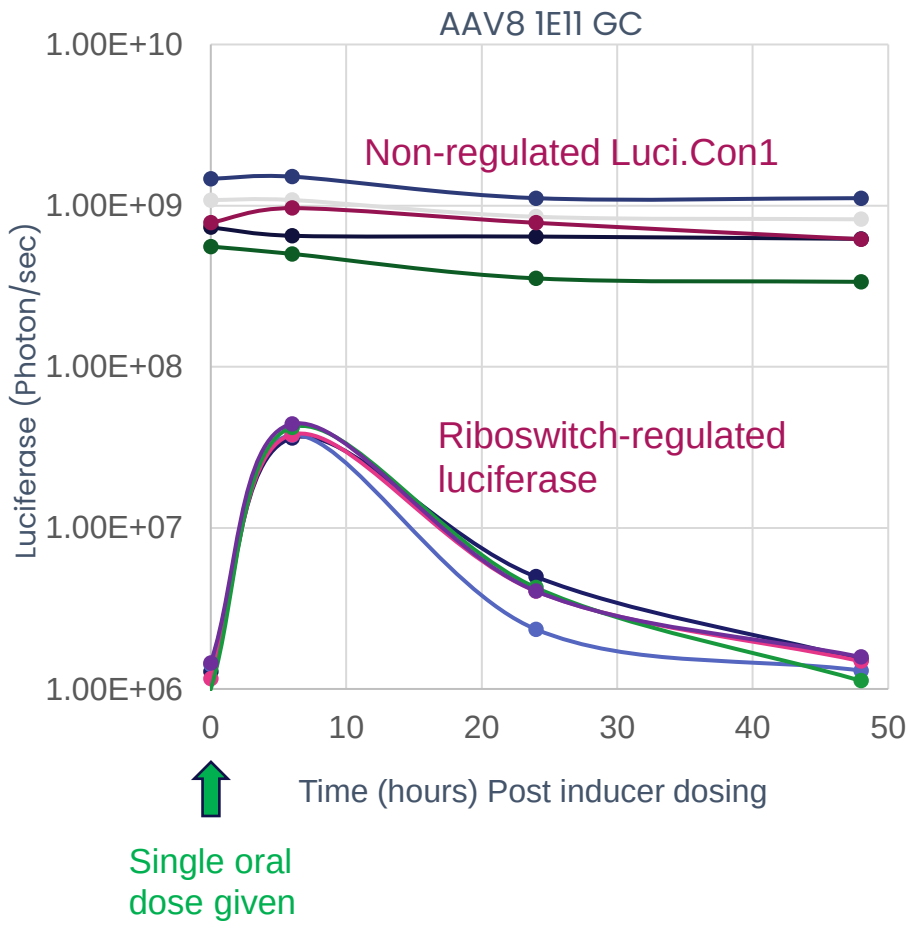
Liver
Tail vein injection

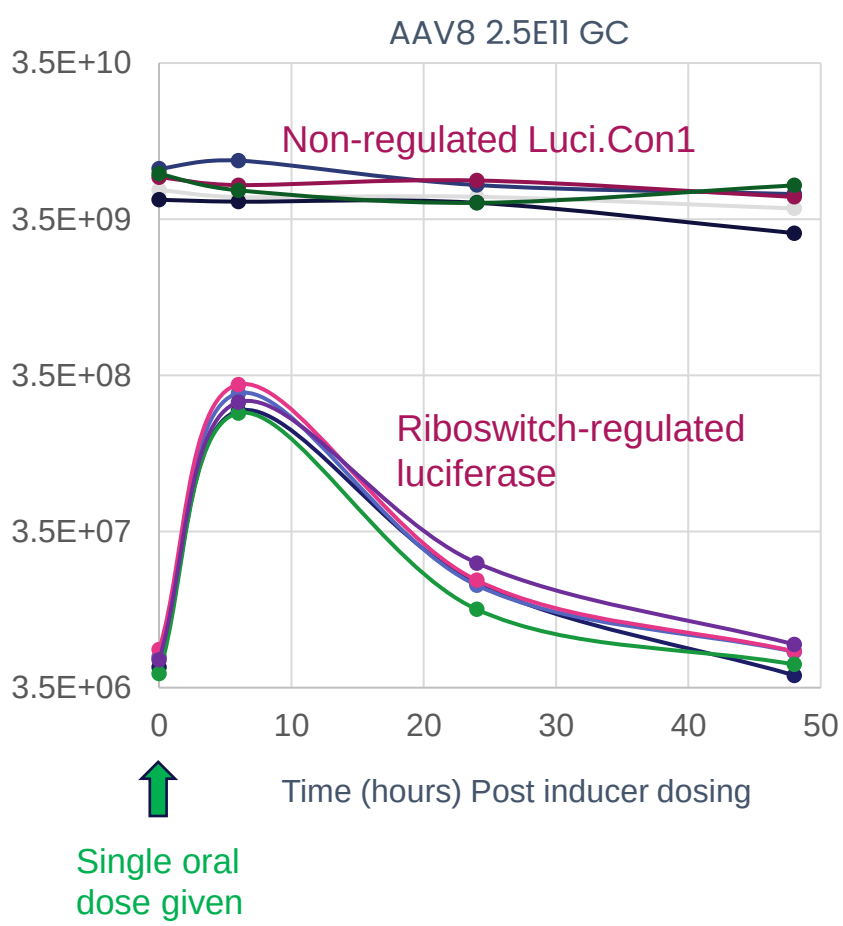




Precise Regulation of Transgene Expression in the Liver in Response to Orally Delivered Inducer

Transgene induction following a single inducer dosing 30 mg/kg PO

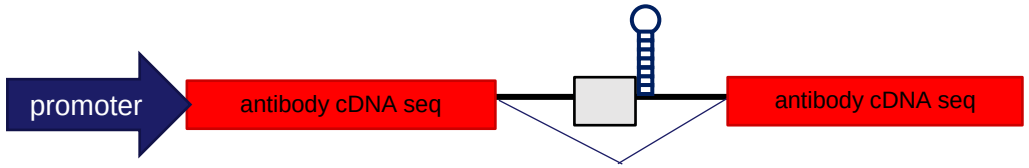


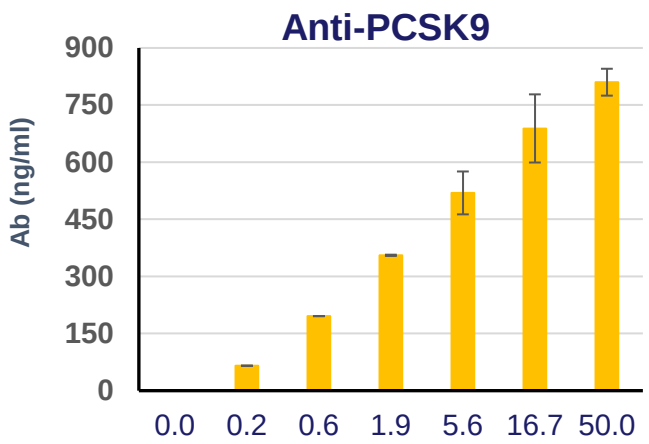


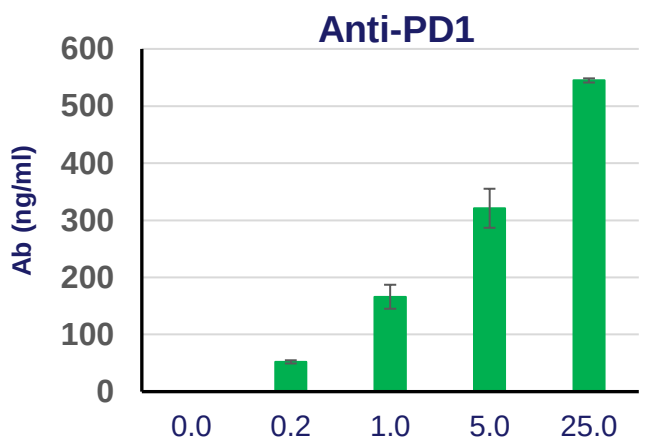
Therapeutic Genes Vectorized, Optimized and Regulated by Riboswitch Technology

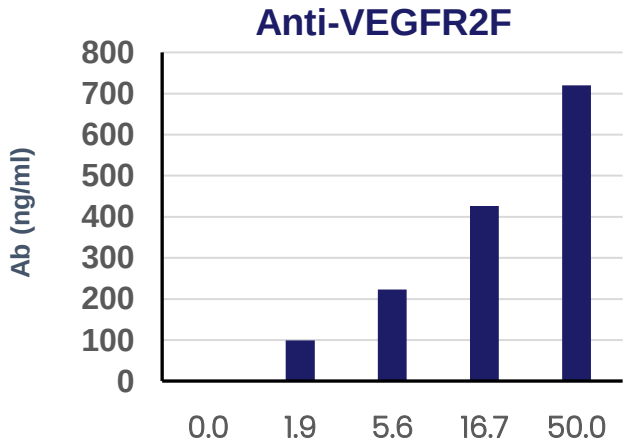
Therapeutic Antibodies:	Therapeutic Hormones/Cytokines/Peptides:	Therapeutic Nucleases (Targeting RNAs):
• Anti-PCSK9 • Anti-VEGFR2 (ophthalmology) • Anti-Amyloid • Anti-IL-17 • Anti-PD1 • Anti-HER2	• Epo • hGH • PTH • Insulin • GLP-1R agonists • Gut peptide combinations: GLP1- GIP; GLP1 GIP PYY Glucagon etc.	• Cas9 • CasRx

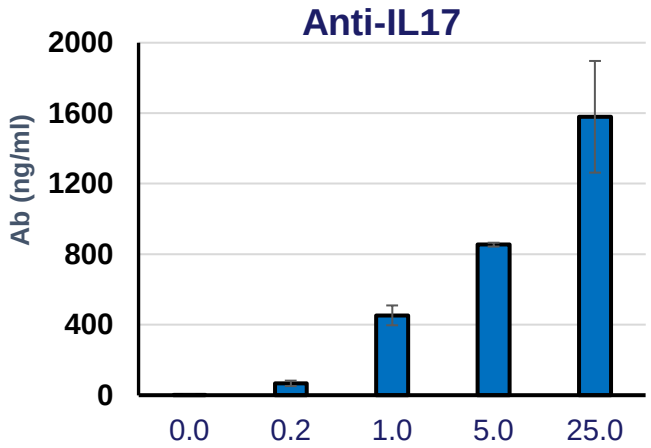
Riboswitch Tightly Regulates Expression of Therapeutic Antibodies

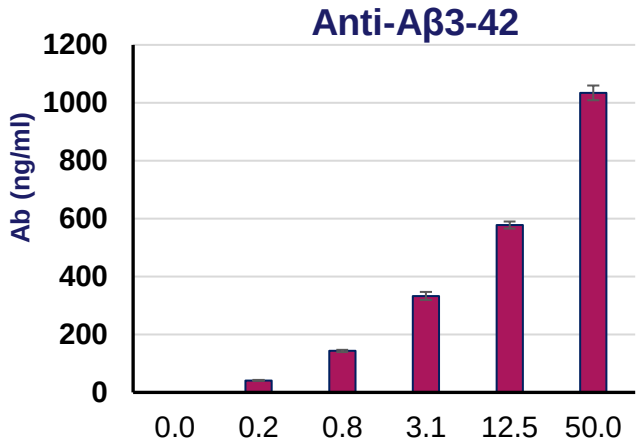


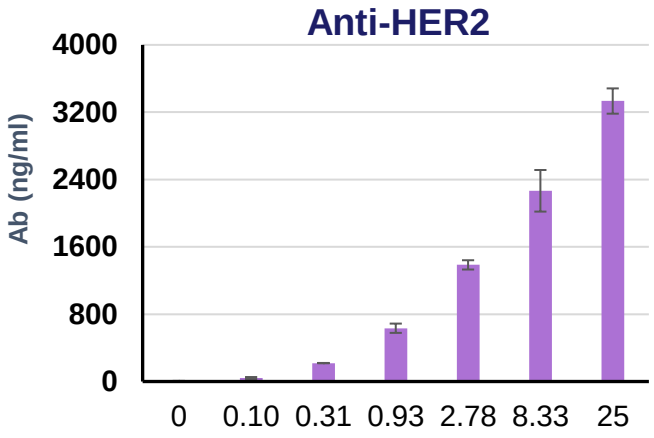








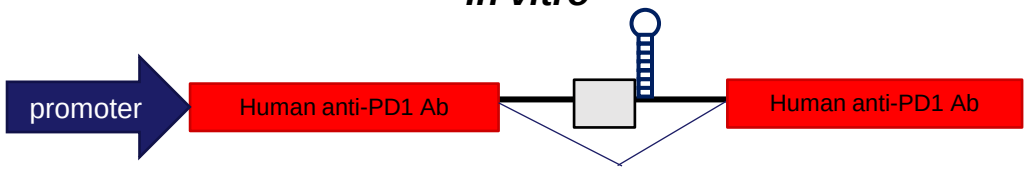


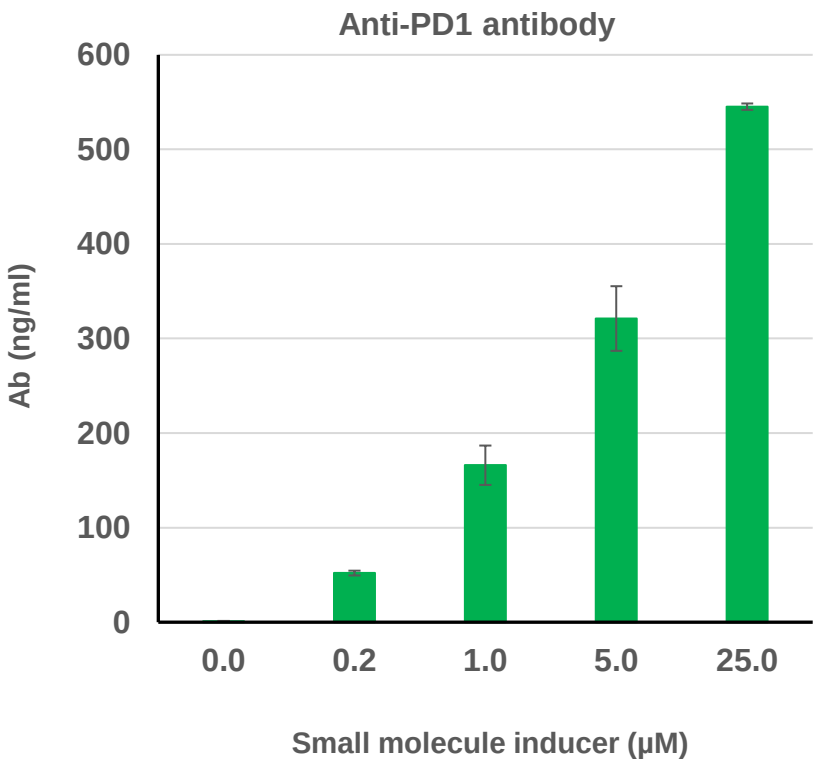


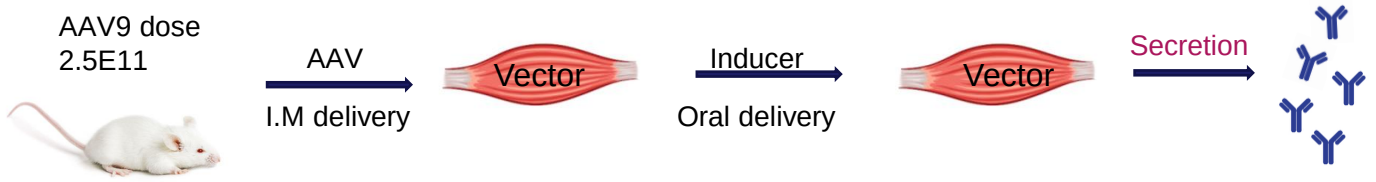
Small molecule inducer (µM)

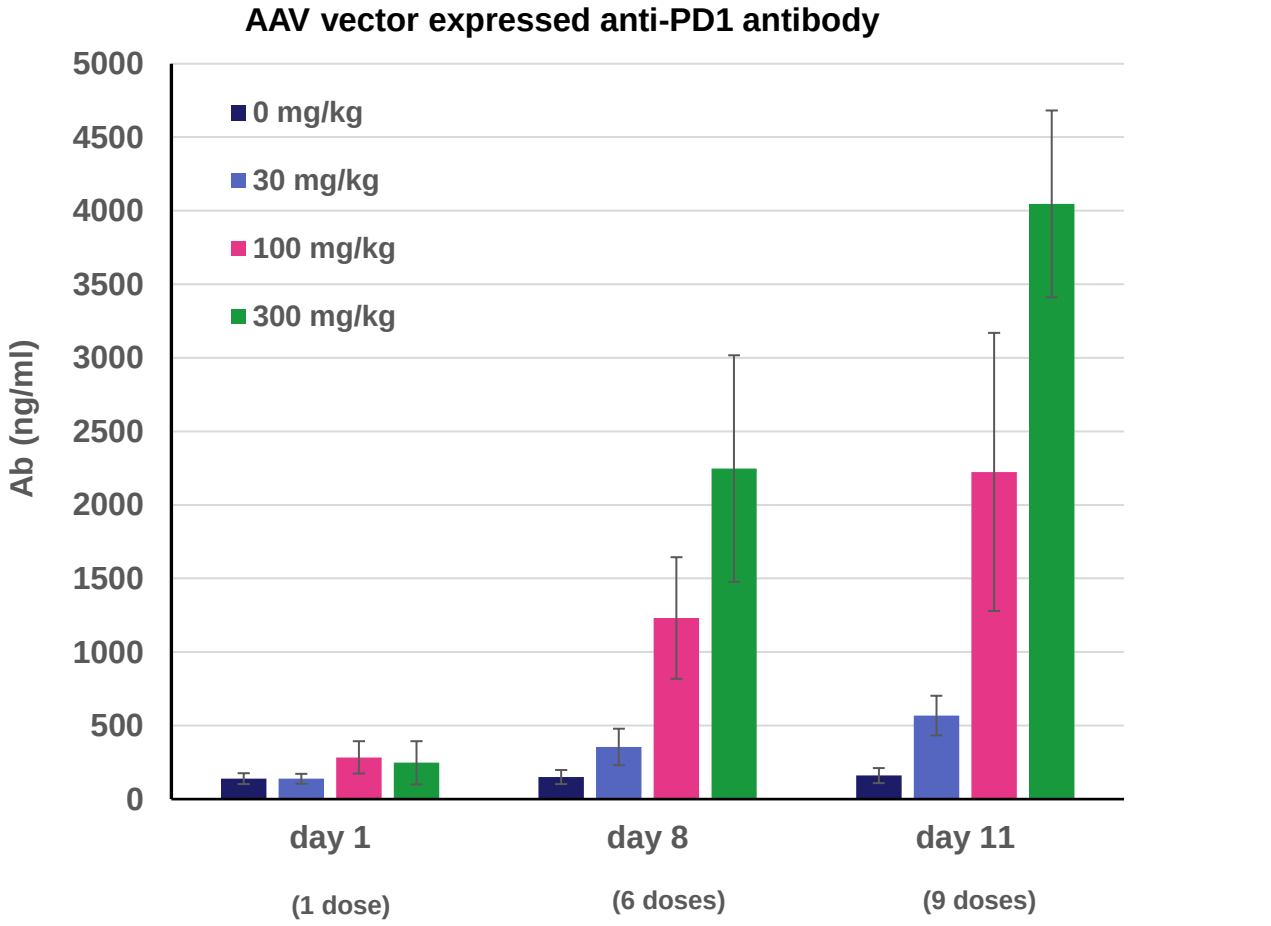
Riboswitch Regulated Anti-PD1 Antibody Expression in Mice in Response to Orally Administered Inducer

In vitro





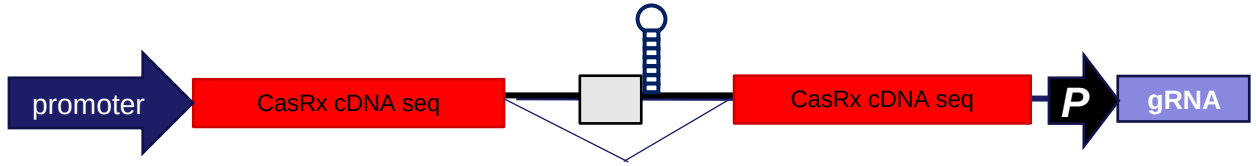




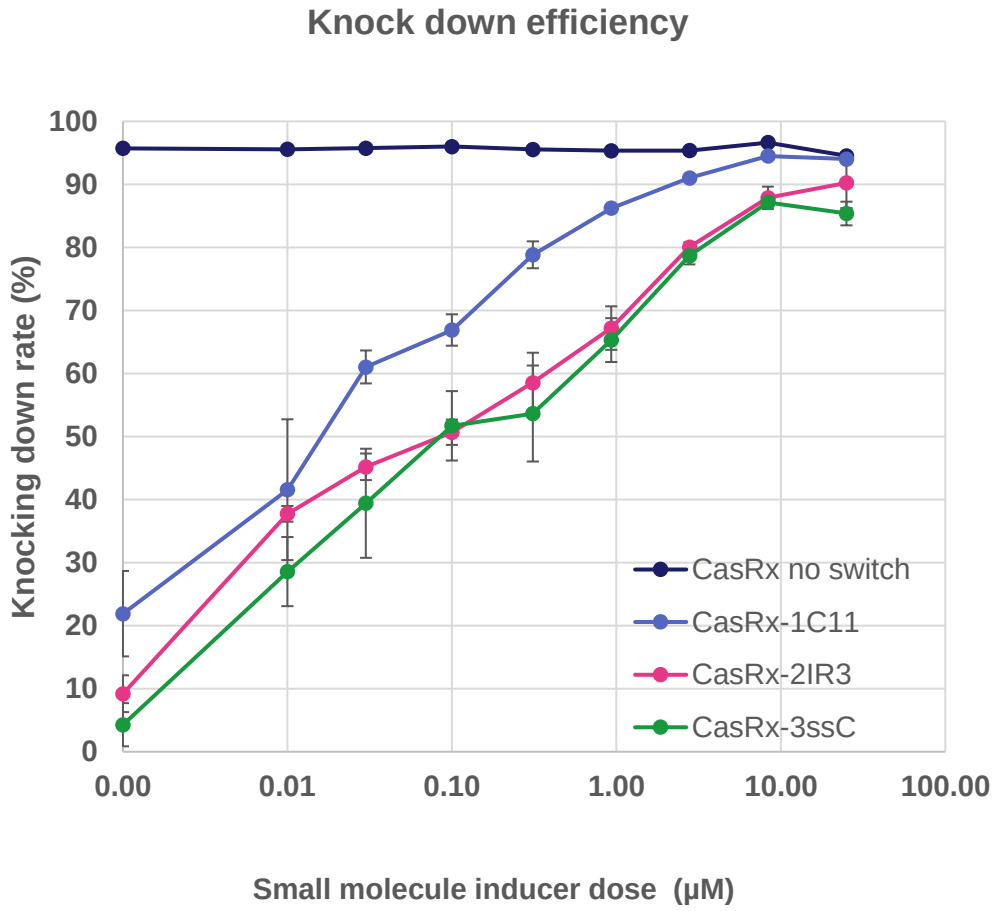
Therapeutic Genes Vectorized, Optimized and Regulated by Riboswitch Technology

Therapeutic Antibodies:	Therapeutic Hormones/Cytokines/Peptides:	Therapeutic Nucleases (Targeting RNAs):
• Anti-PCSK9 • Anti-VEGFR2 (ophthalmology) • Anti-Amyloid • Anti-IL-17 • Anti-PD1 • Anti-HER2	• Epo • hGH • PTH • Insulin • GLP-1R agonists • Gut peptide combinations: GLP1- GIP; GLP1 GIP PYY Glucagon etc.	• Cas9 • CasRx

Riboswitch Regulated CRISPR-CasRx Activity



gRNA targeting metabolic gene RNA



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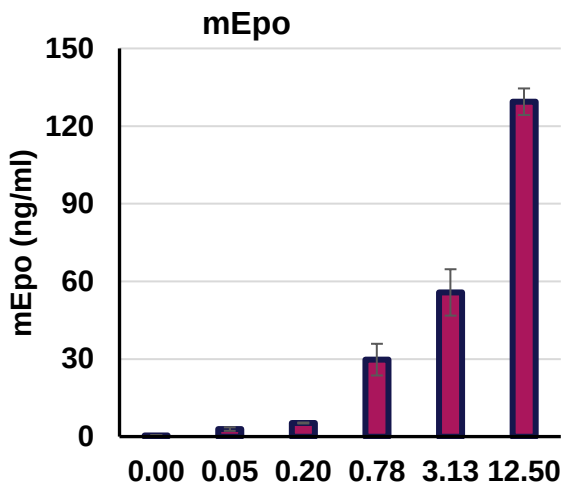
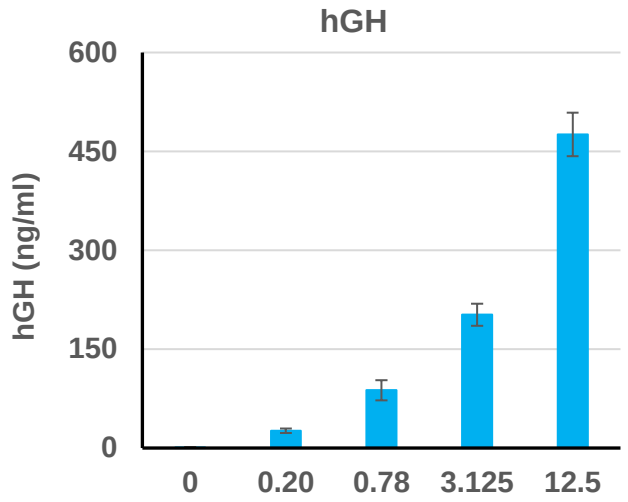
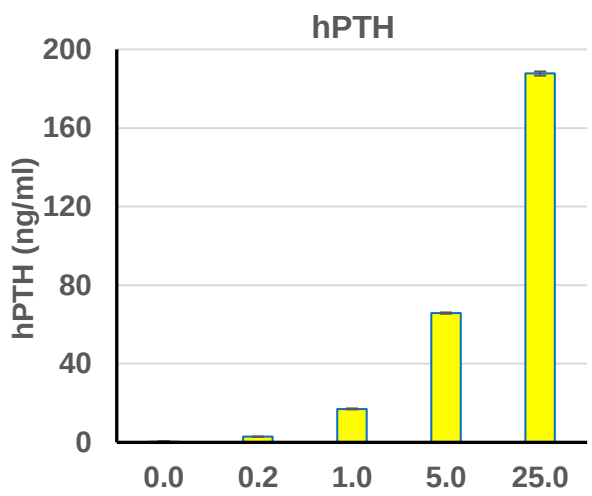
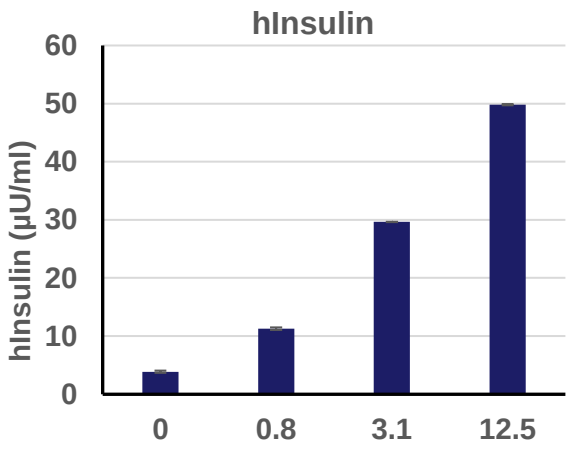
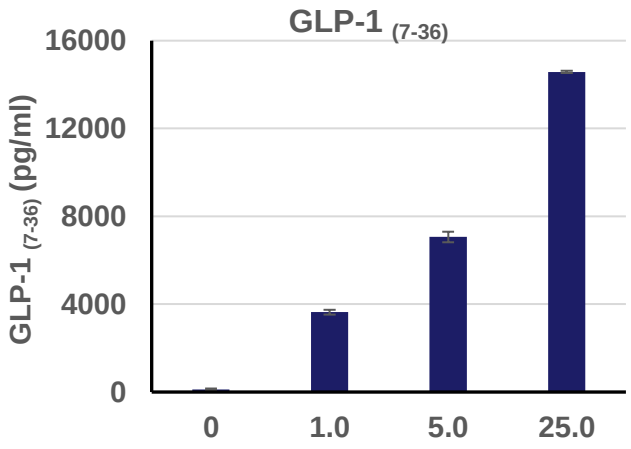
Tight Dose Response Control of Expression of Peptides and Hormones

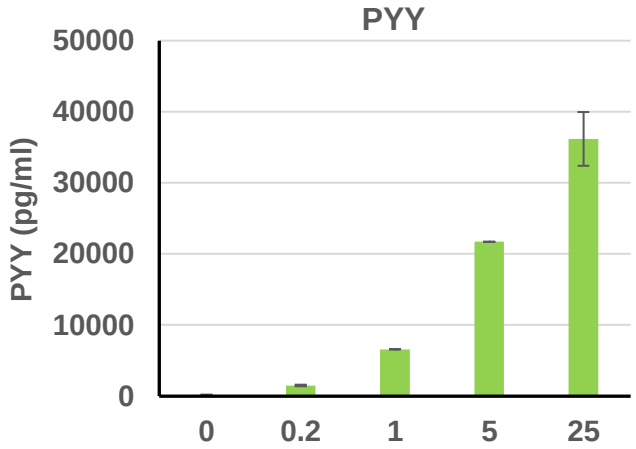








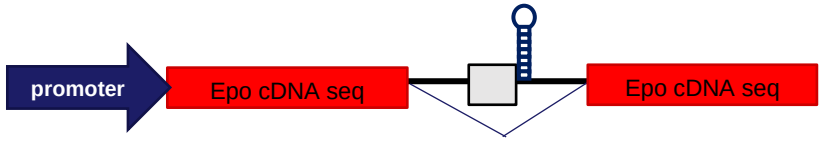


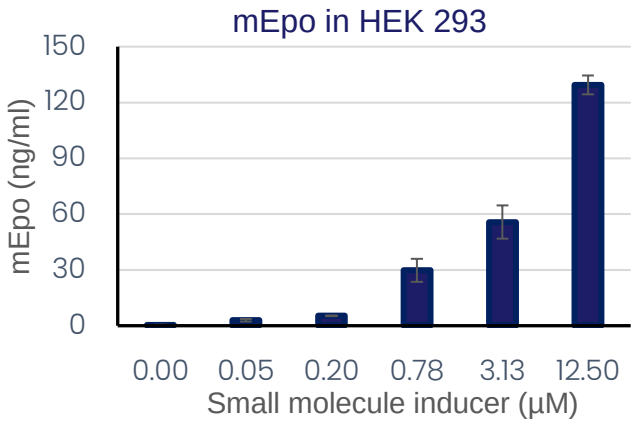


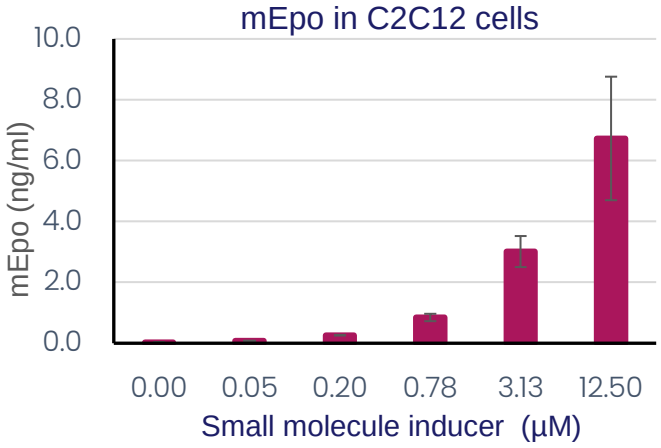
Small molecule inducer (µM)

Tight Dose Response Regulation of Expression of Erythropoietin (Epo) in Mammalian Cells and *in vivo*

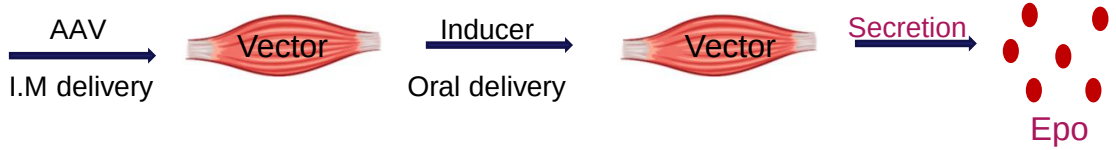
In vitro

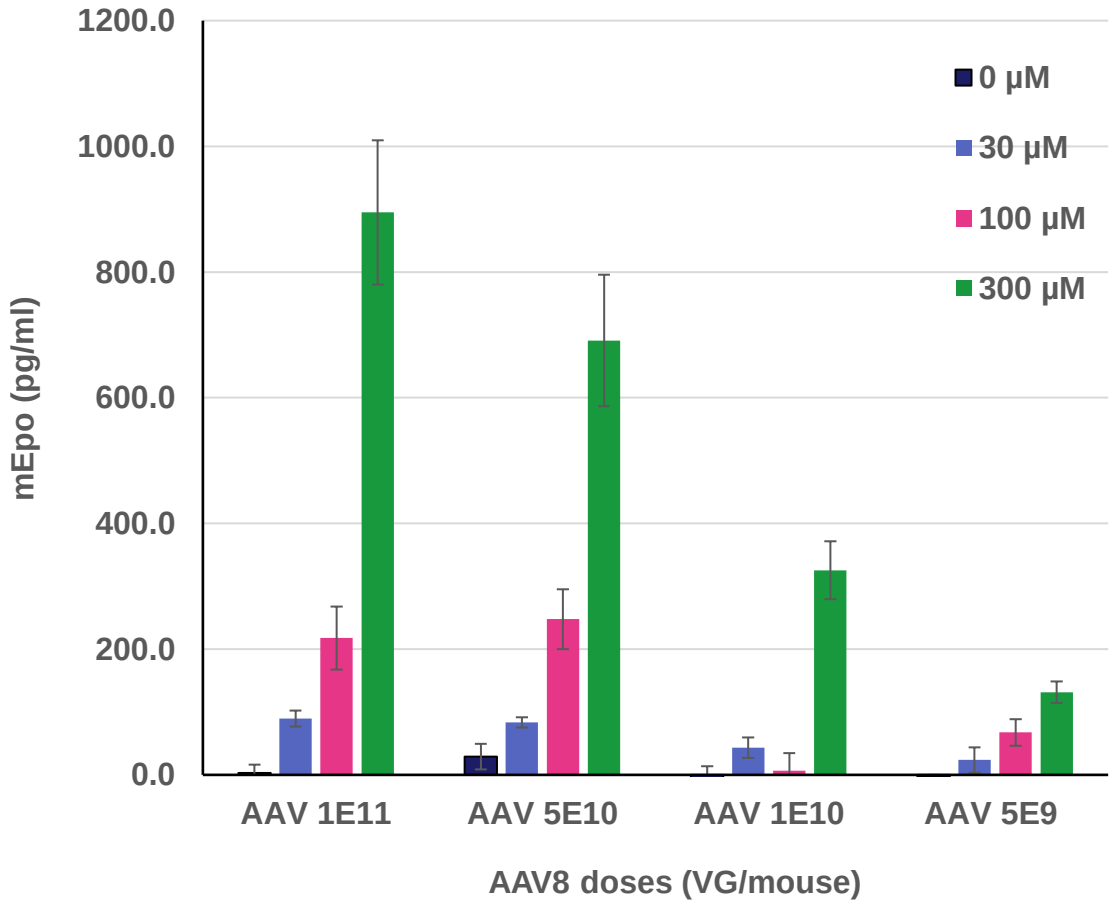






In vivo



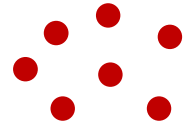


Riboswitch Controlled Secretion of Erythropoietin Restores Hematocrit in Chronic Kidney Disease (CKD) Associated Anemia in a Dose Response to Oral Small Molecule

I.M. delivery →

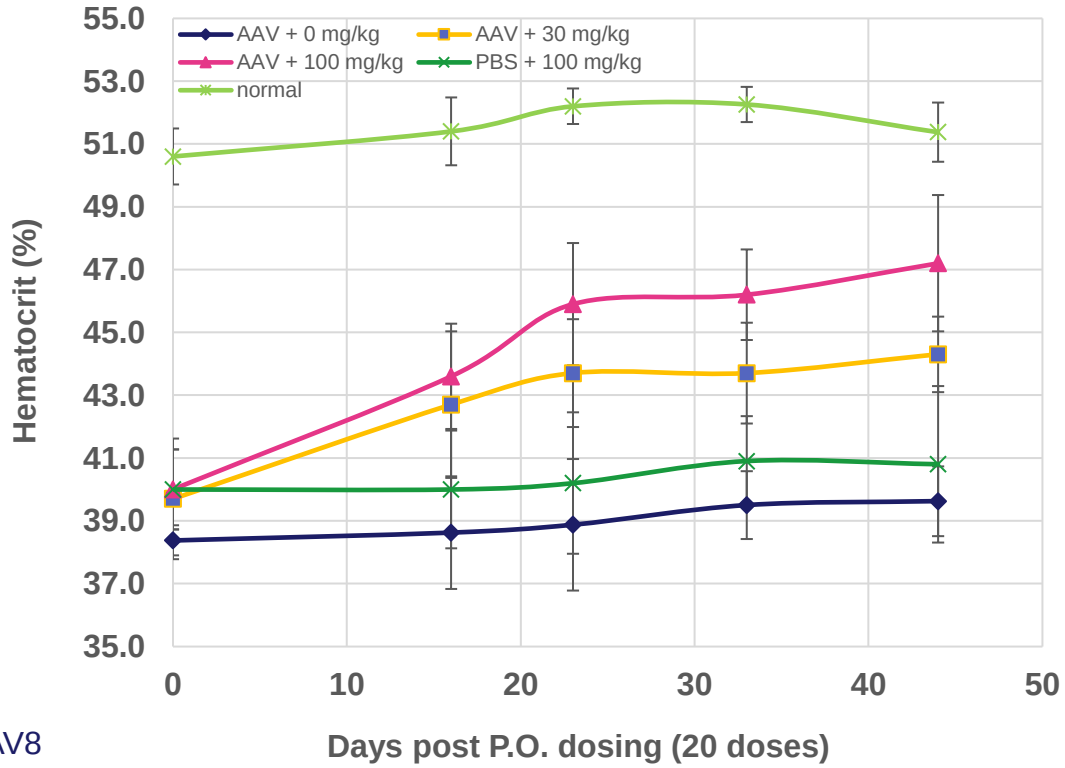
Inducer
Oral delivery →

Secretion →



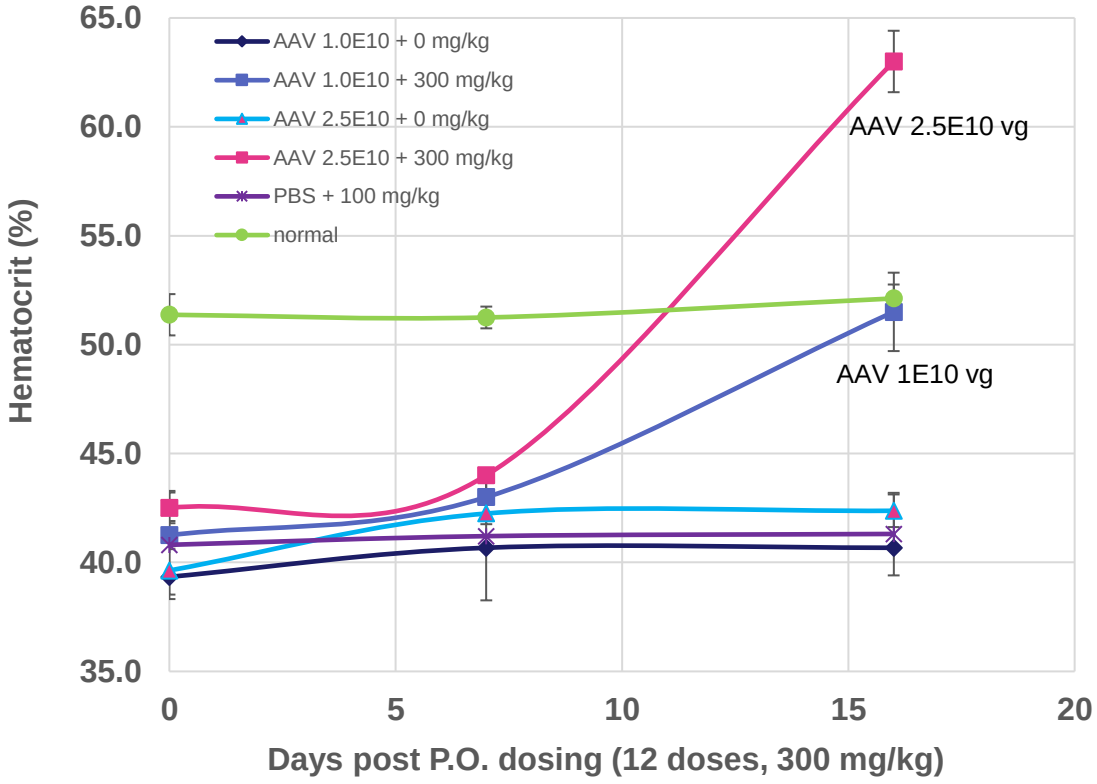
Epo

Low dose inducer

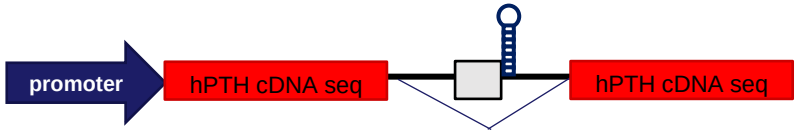


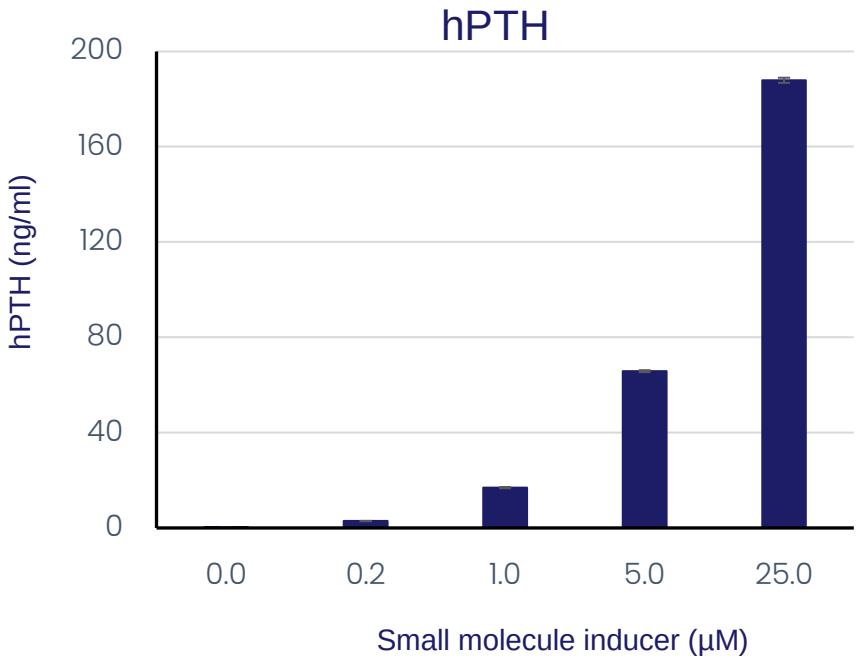
AAV8
2.5e10

High dose inducer

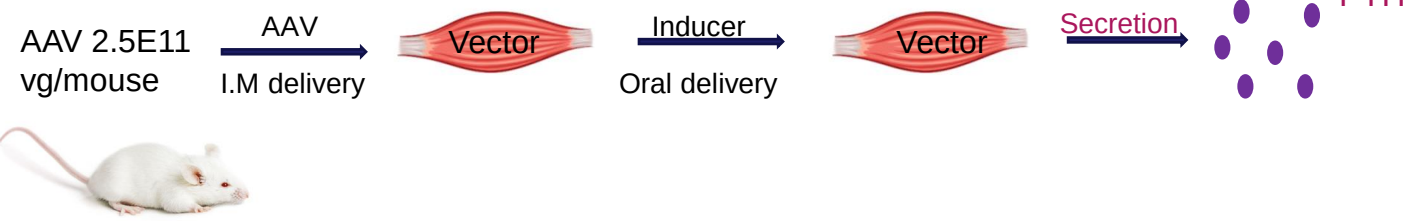


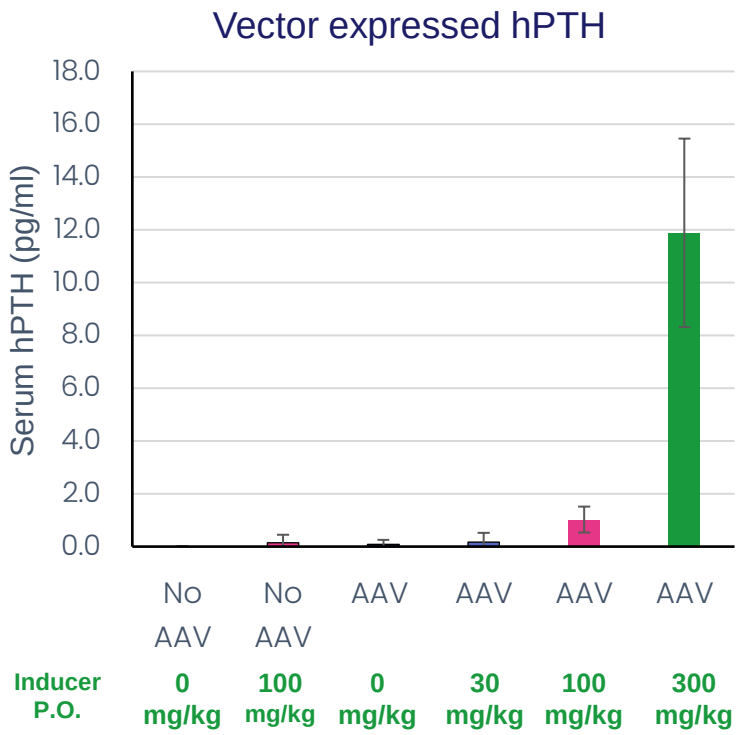
Controlled Secretion of Parathyroid Hormone (PTH) Increased Serum Calcium

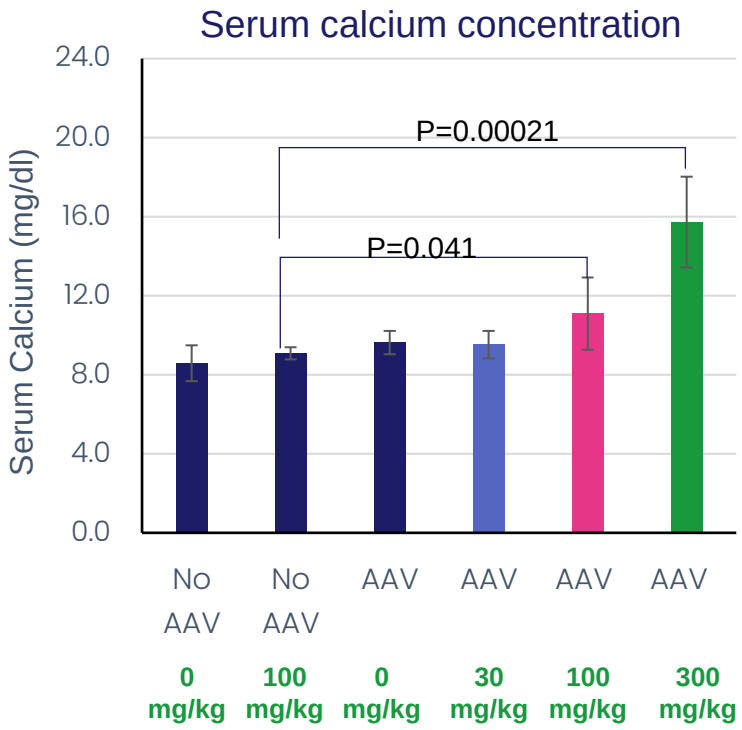




Oral daily dosing of inducer

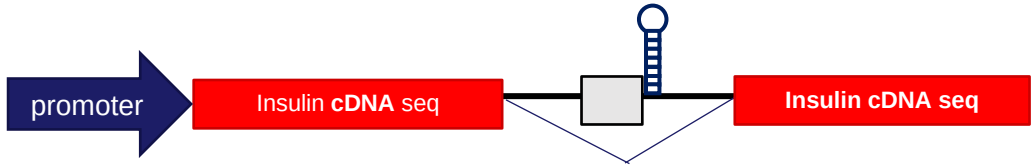


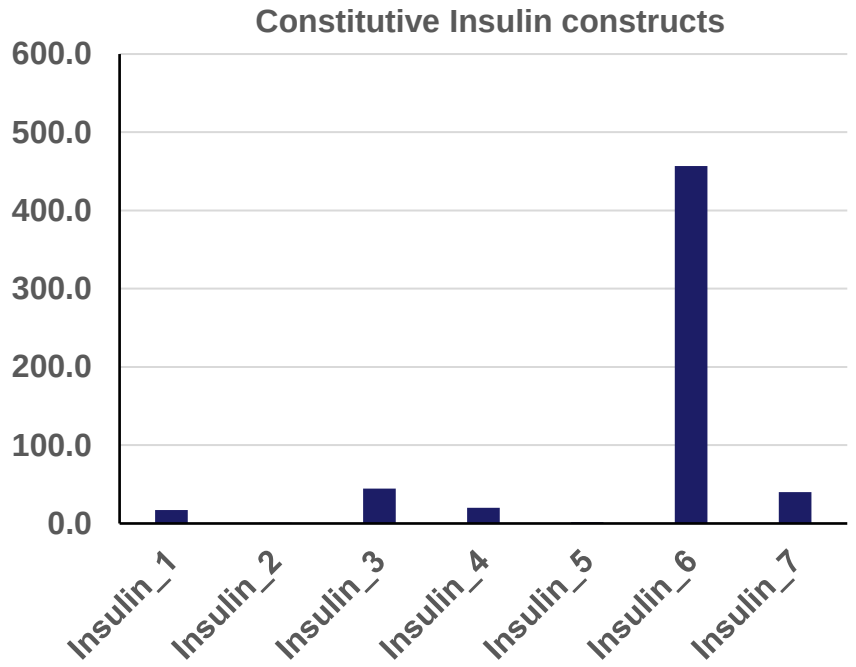


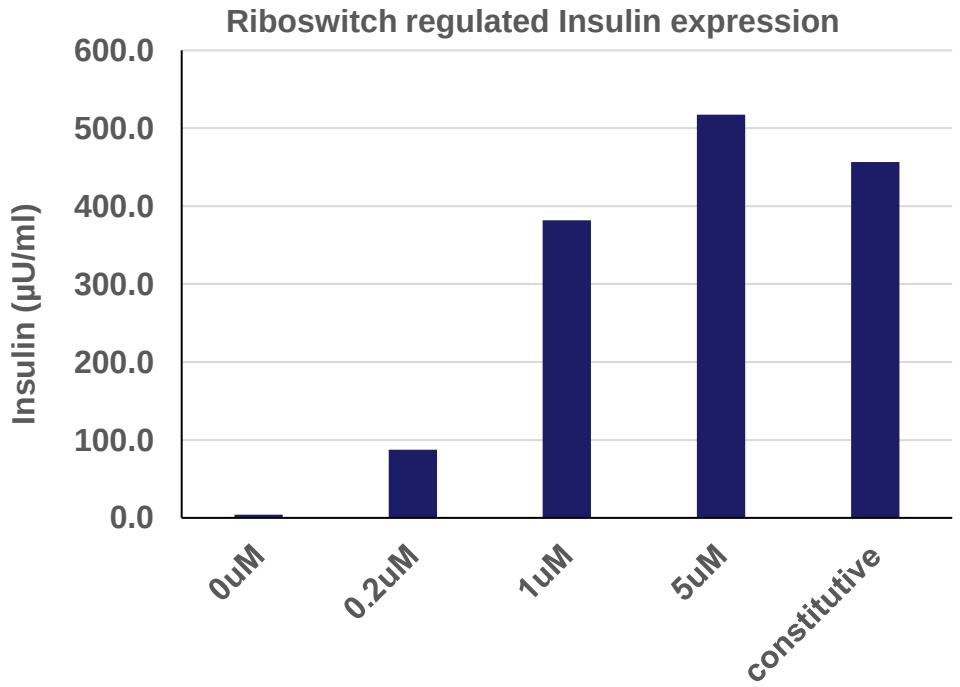


Post 3 oral doses

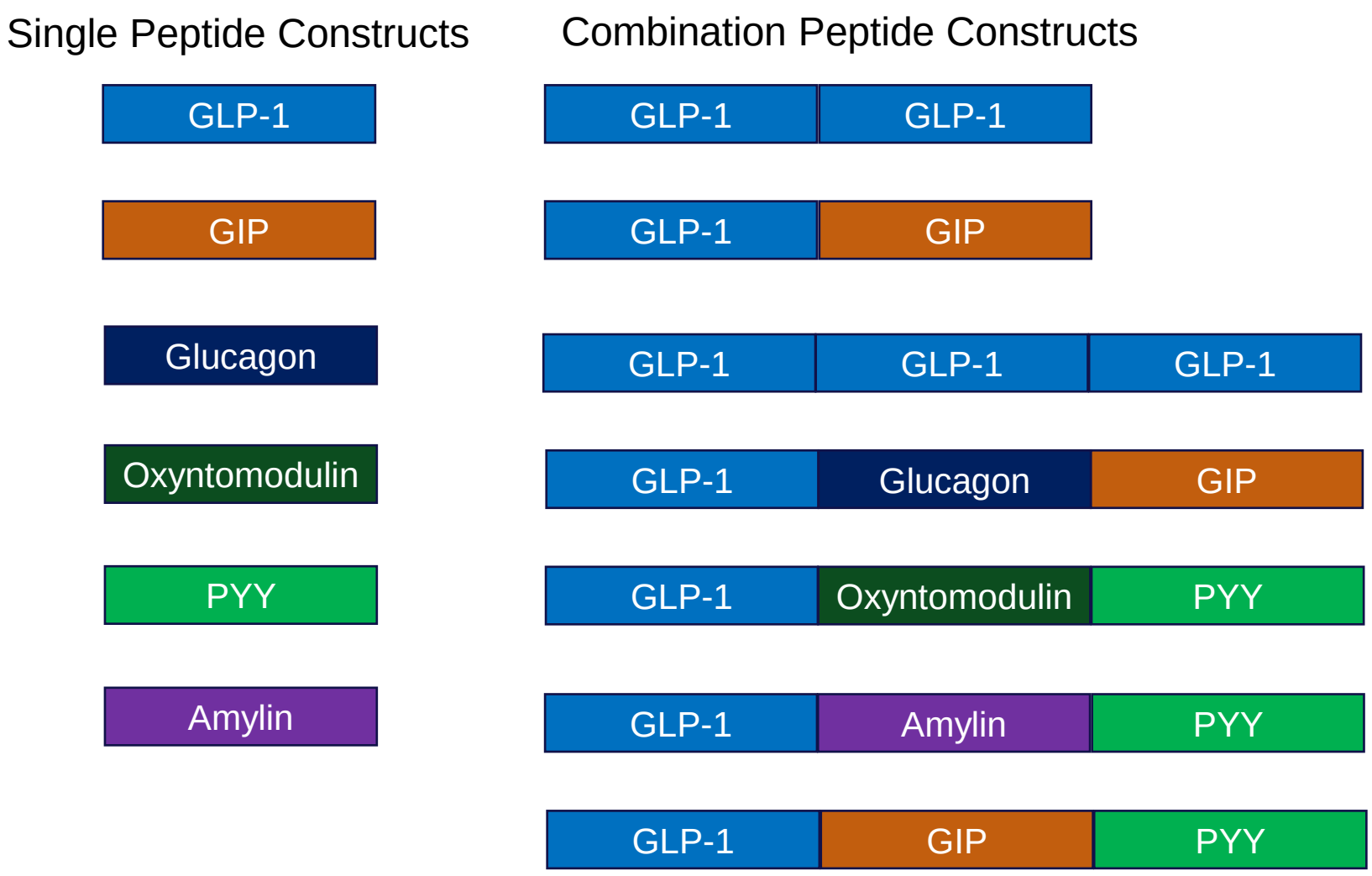
Tight Regulation of High Expressing Insulin Vector



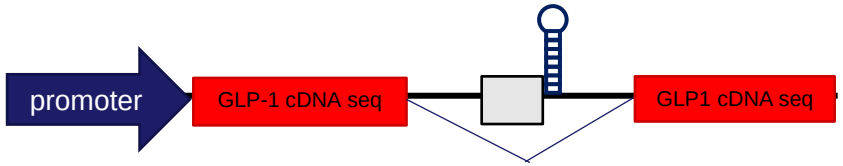


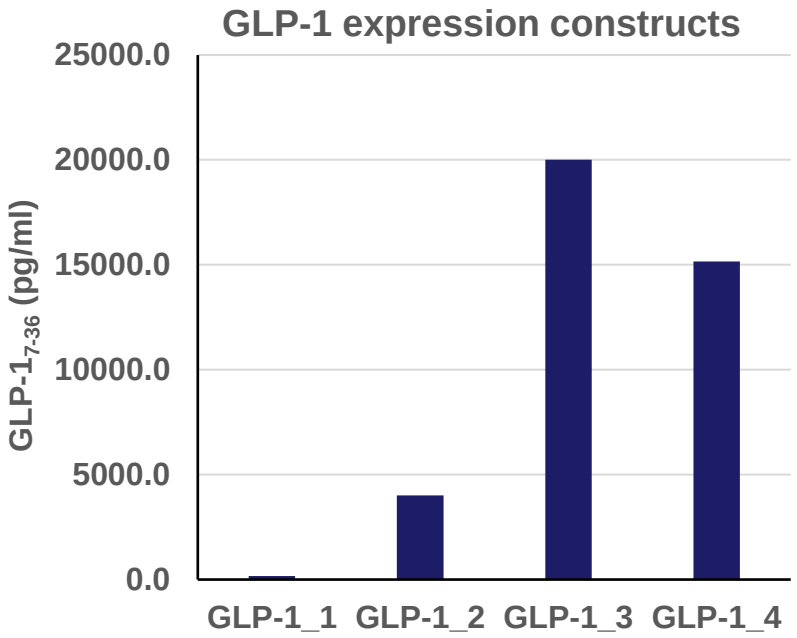


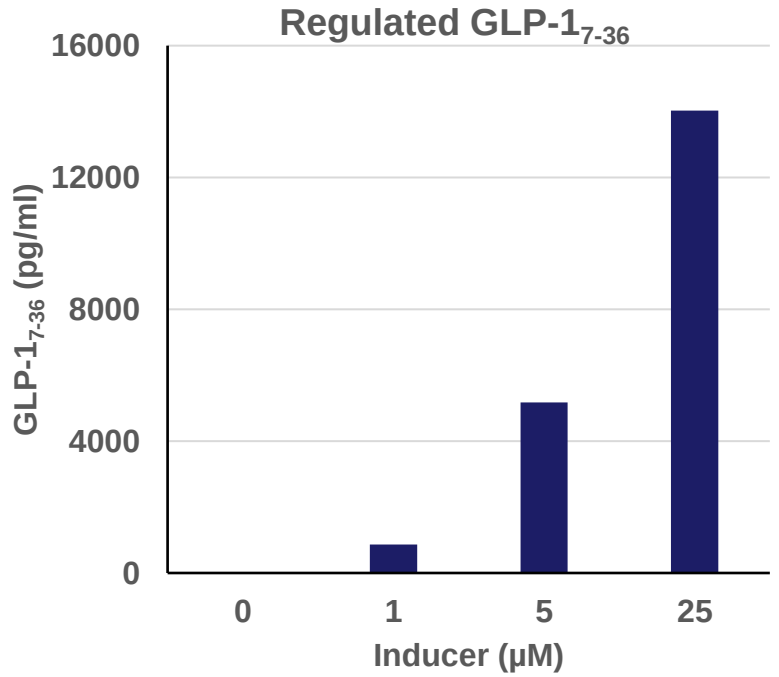
Expressing Gut Peptides



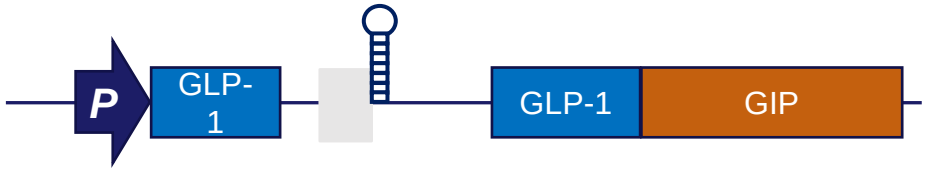
Gut Peptide GLP-1 is Tightly Regulated in Mammalian Cells

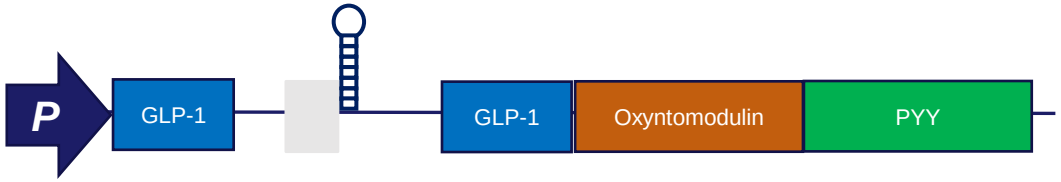


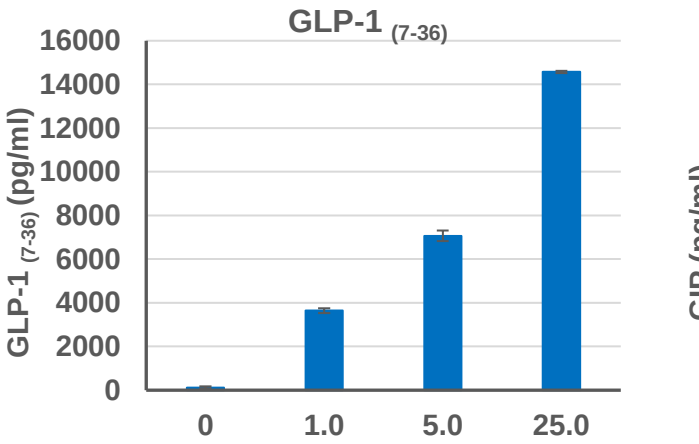


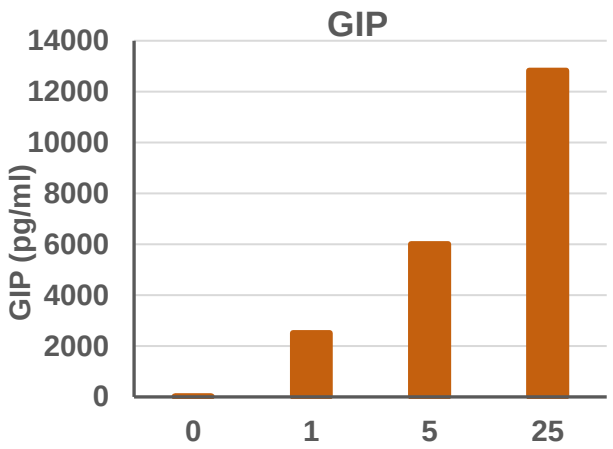


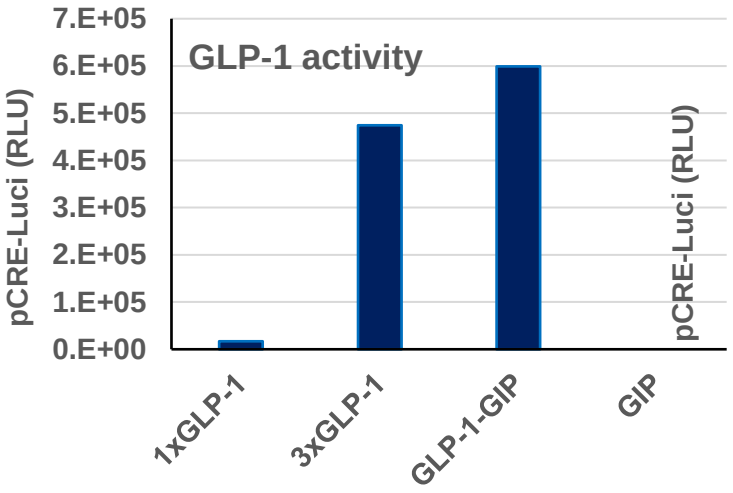
Gene Regulation Cassette Controls the Expression of Combinations of Gut Peptides, GLP-1 plus GIP and PYY

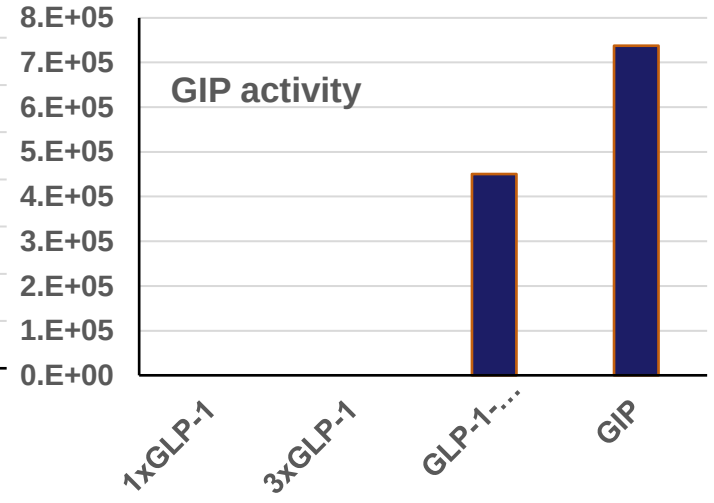


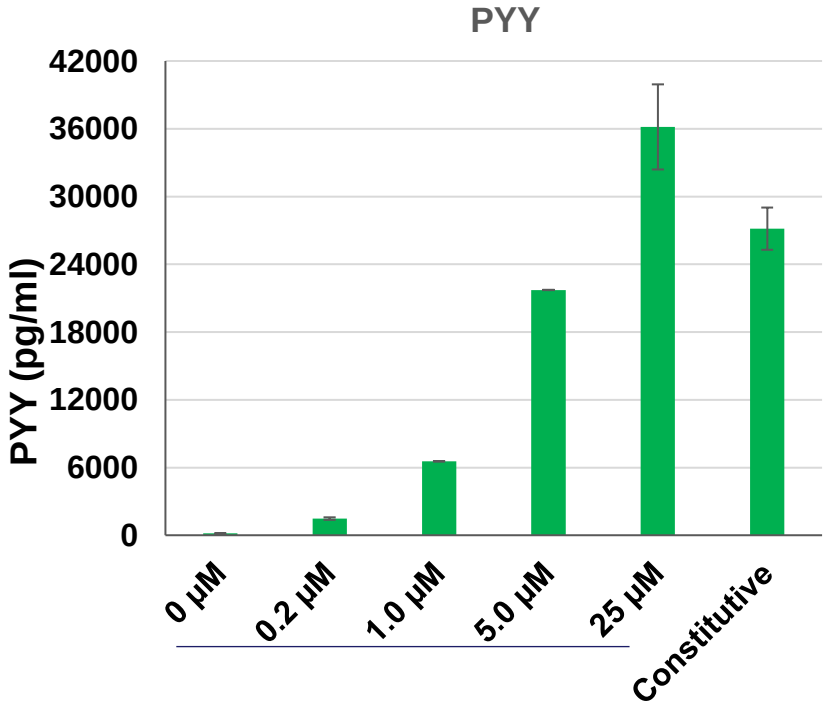




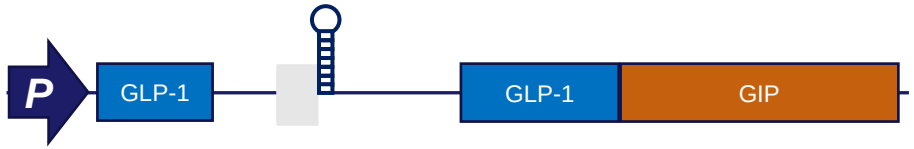








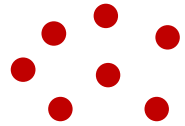
Combination of Gut Peptides, GLP-1 and GIP, Regulated by Orally Delivered Small Molecule Improves Glucose Tolerance in Rodents



I.M. delivery

Inducer
Oral delivery

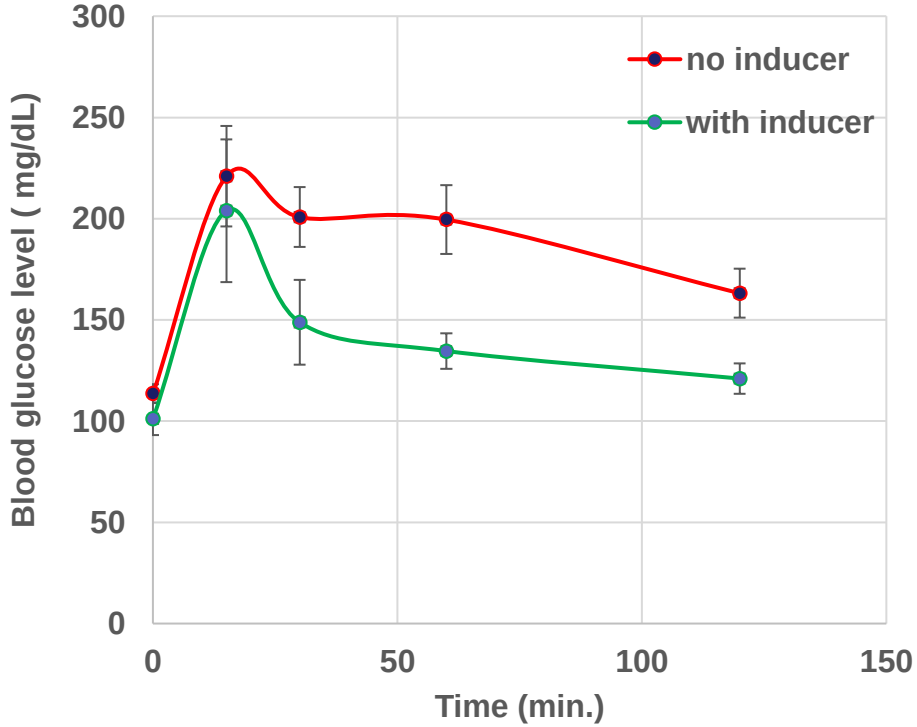
Secretion



GLP-1 and GIP

2.5E11 vg/mouse AAV8

Glucose tolerance



Target Tissues for Production of Regulated Gene Therapy: Eye and Salivary Gland

The Eye

Gene Regulation with small molecule

- Regulate gene therapies using small molecule formulated as a **topical eye drop**
- Ophthalmological formulation of current strong specific inducer small molecules into eye drops during 2022

Large Ocular Indications:

- **Wet AMD** : regulated VEGFR2
- **Dry AMD** : regulated anti-complement
- **Uveitis** : regulated cytokine inhibitors
- **Glaucoma:** regulated inhibitors of water flow (AQP1) and fibrosis

Large Ocular Vectorology Toolkit

- Retinal organoid technology – vectorology and phenotype rescue
- Promoter engineering - enhanced potency and activity – Meira library of strong cell specific as well as ubiquitous promoters
- Regulatory elements, enhancers, introns, polyA, and codon optimization
- Capsid engineering: Ongoing NHP directed evolution screen for capsids for all parts of the eye – including cells towards the front of the eye that can secrete therapeutic proteins into the vitreous
- Delivery: Intravitreal and Suprachoroidal Delivery – Multiple proprietary technologies under development

Reduced Inflammation

- Delivery technology, capsid and site of transduction
- Construct design to block innate immune response
- Well tested effective prophylactic regimens

Salivary Gland

Salivary Gland as a Secretory Organ for Genetic Medicines

- Parotid is one of the largest secretory organs in the body
- Specific signal peptides drive secretion **into the serum** rather than saliva
- Epo, PTH and hGH have all been shown to be secreted from salivary glands when the transgene is delivered into the parotid in rodent and mini-pigs
- Expression levels are therapeutic and durable

We have Vectorolgy and Clinical Experience of Salivary Gland Gene Therapy

- Easy administration – retro-ductal instillation via Stensen's Duct
- Small dose locally delivered
- AAV2 local delivery gives minimal serum exposure
- Durable expression expected as salivary gland cells – both acinar but also duct cells are differentiated and not rapidly turning over

Targets for Salivary Gland Regulation:

- **Gut Peptide Combinations: Metabolic Disease and Obesity** – alternative to Bariatric Surgery
- **Genetic Endocrine Deficiency Disorders**
- **hPTH:** Hypoparathyroidism, congenital, autoimmune, acquired
  - Unmet need because of short half life of natural PTH 1-34; hypercalciuria, impaired renal function and renal failure
  - Osteoporosis
- **hGH:** Growth factor deficiency
- **hEpo:** kidney disease
- **Insulin:** Diabetes - basal and post prandial insulin

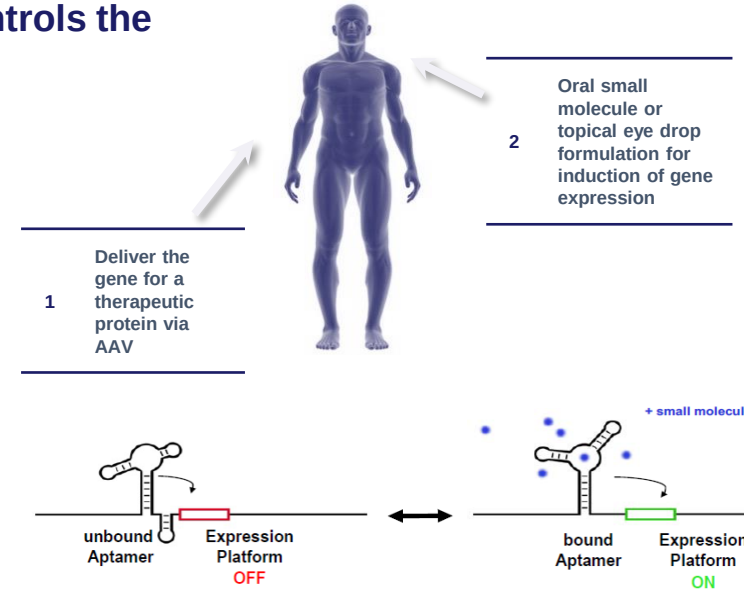
Current Small Molecules with Good Salivary Gland Exposure:

- Regulates gene therapies in rodent parotid
- Small Molecule IND 2022
- IND enabling studies of Vector Constructs together with small molecules 2022

Unique Technologies Transform the Fields of Genetic Medicine and Biologic Drugs

For the first time, a Synthetic Gene Regulation System precisely and specifically controls the activity of genetic medicines using orally dosed pills

- Gene Regulation Cassette driven by novel mammalian Riboswitches
- Gene regulation at unprecedented high dynamic range
- Precise, tight control of genetic medicines by novel small molecules
- Any gene, any vector; cell therapy, gene editing can be controlled with this system
- Currently >15 targets have been built that are vectorized at Meira, optimized and tightly regulated,
- With vectorology and gene regulation toolkit we can rapidly build new regulated genetic therapies
- Libraries of small molecules specifically designed to match synthetic aptamers, with different drug properties
- Both regulated viral vectors and small molecules are currently in IND enabling studies
- We have particular expertise in expression of gene therapies in the eye, salivary gland and muscle, all good sites for local delivery of regulated gene therapies
- This platform technology provides boundless opportunity and transforms genetic medicine
- New paradigm for delivery and pricing of gene therapies as well as biologic drugs



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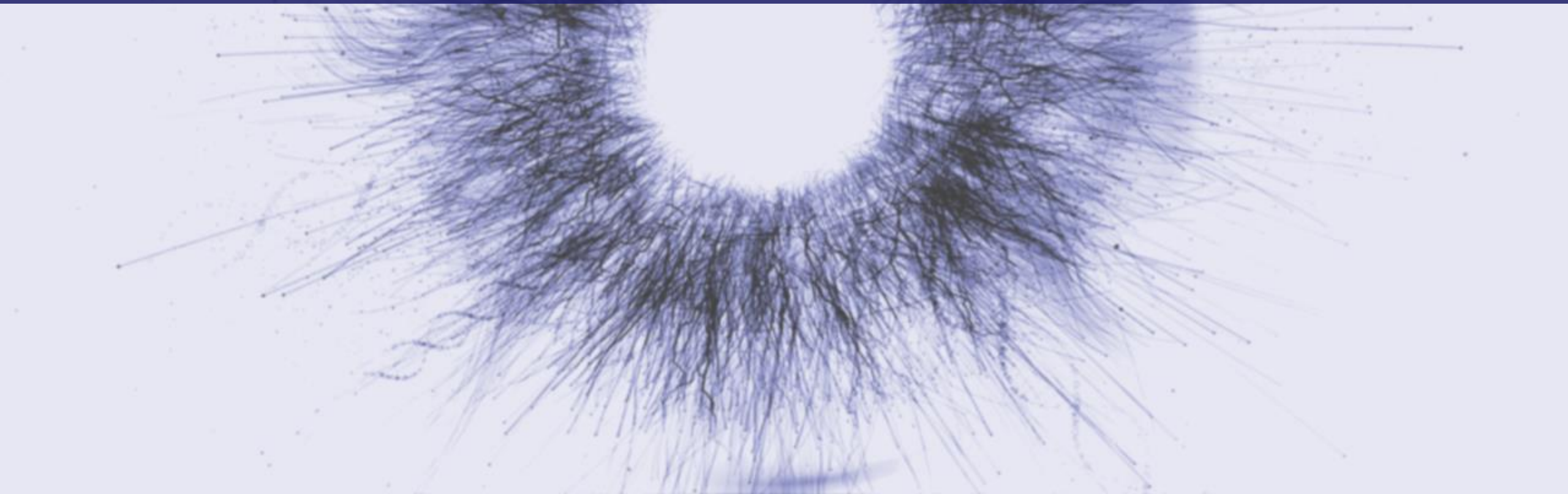
Ocular Pipeline



Industry-Leading Toolkit for Ophthalmology Gene Therapy

Ophthalmology Toolkit:

- Retinal organoid technology
- Increased 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
  - 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
- Suprachoroidal Delivery**:** 3 devices 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

MEIRAGTx

Janssen
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Clinical Development

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

Janssen Commercial Infrastructure

- Janssen has worldwide exclusive commercial rights to botaretigene sparoparvovec*, 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 the commercial manufacturer for IRD products

Pre-Clinical IRD Research

- Collaboration leverages MeiraGTx vector engineering technologies to develop gene therapy treatments for multiple IRDs
- Janssen can opt-in to receive exclusive rights to develop & commercialize programs from research collaboration
- Janssen pays majority of research costs, and pays 100% development costs after opt-in. MGTx receives milestones and high teens untiered royalty

Manufacturing and Process Development

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

MeiraGTx retains global rights to all non-inherited ocular programs
e.g., Wet AMD, Dry AMD, Glaucoma, Uveitis

* Formerly referred to as AAV-RPGR

AAV-RPGR: Gene Therapy for Treatment of X-Linked Retinitis Pigmentosa: Pivotal Phase 3 Study Lumeos ongoing

Disease Overview

Retinitis Pigmentosa (RP)

- A 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

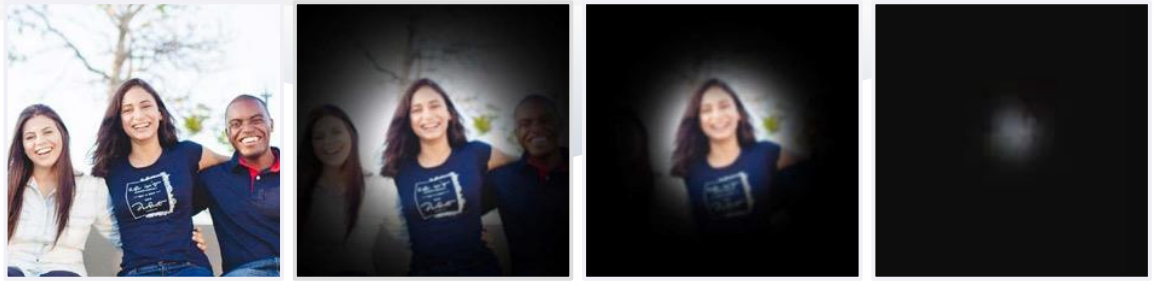
Disease progression

- 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: Botaretigene sparoparvovec | Stage: Clinical

Developed to deliver stable transgene sequence to rod and cone photoreceptors, driving expression of a 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

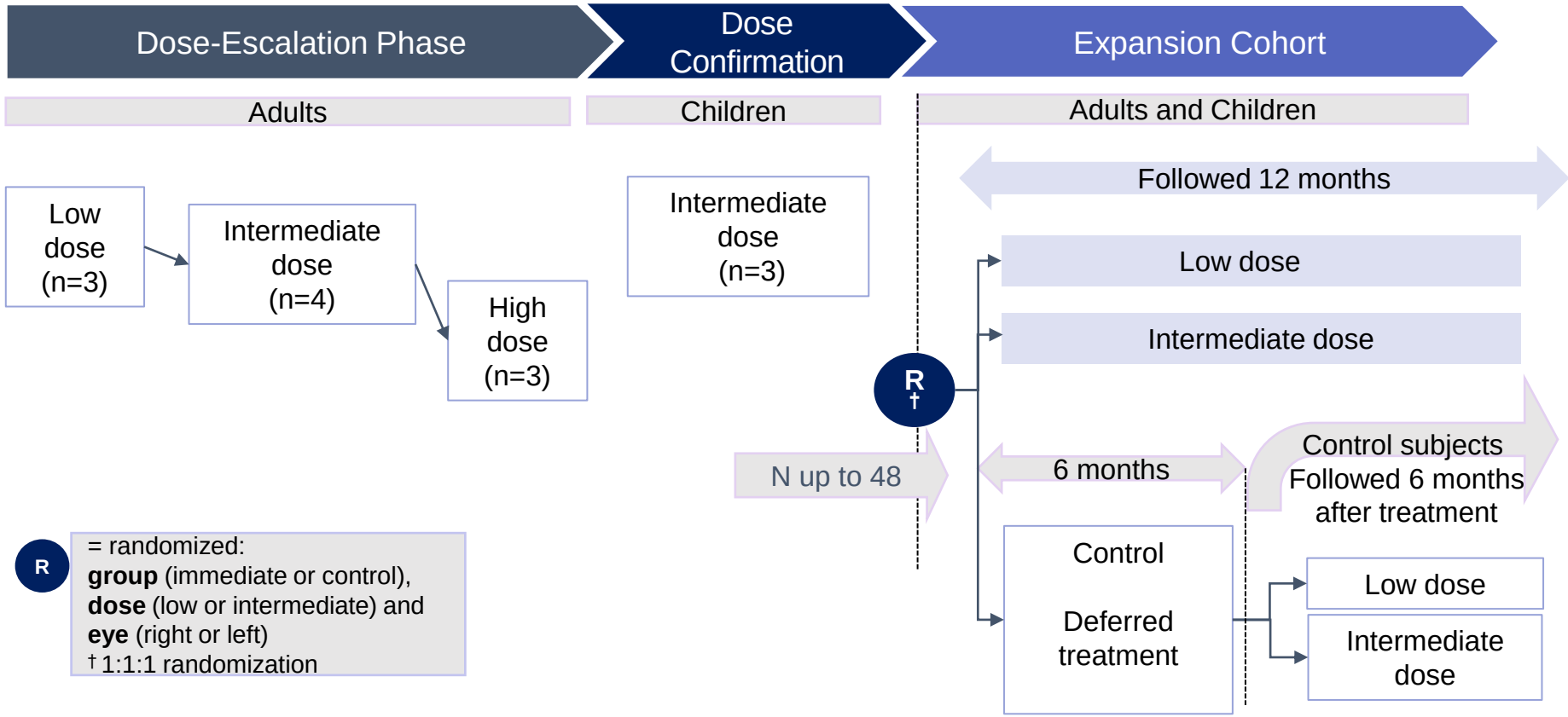
Efficiently delivers vector genome to both rods and cones

Human rhodopsin kinase promoter (hRKp)

Photoreceptor-specific promoter restricts expression of transgene to photoreceptor cells

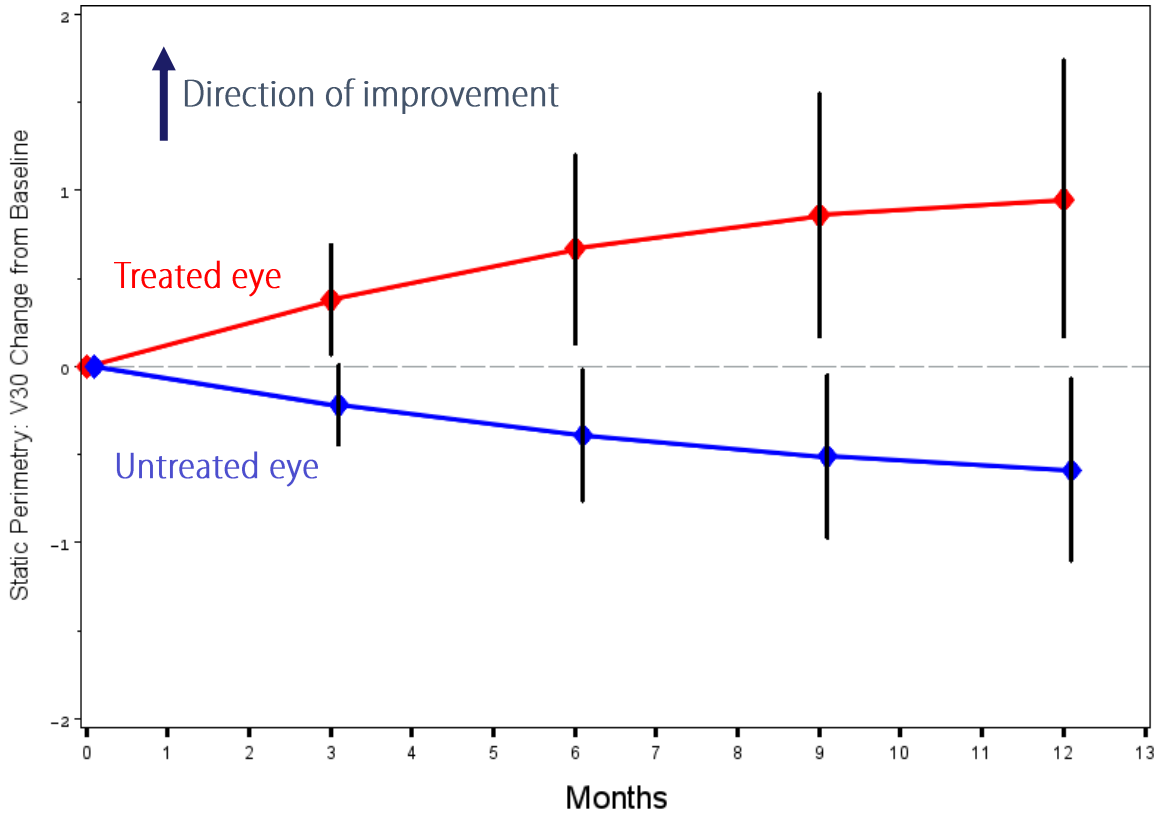
AAV-RPGR Phase 1/2 Trial: Dose Escalation and Randomized Expansion

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)

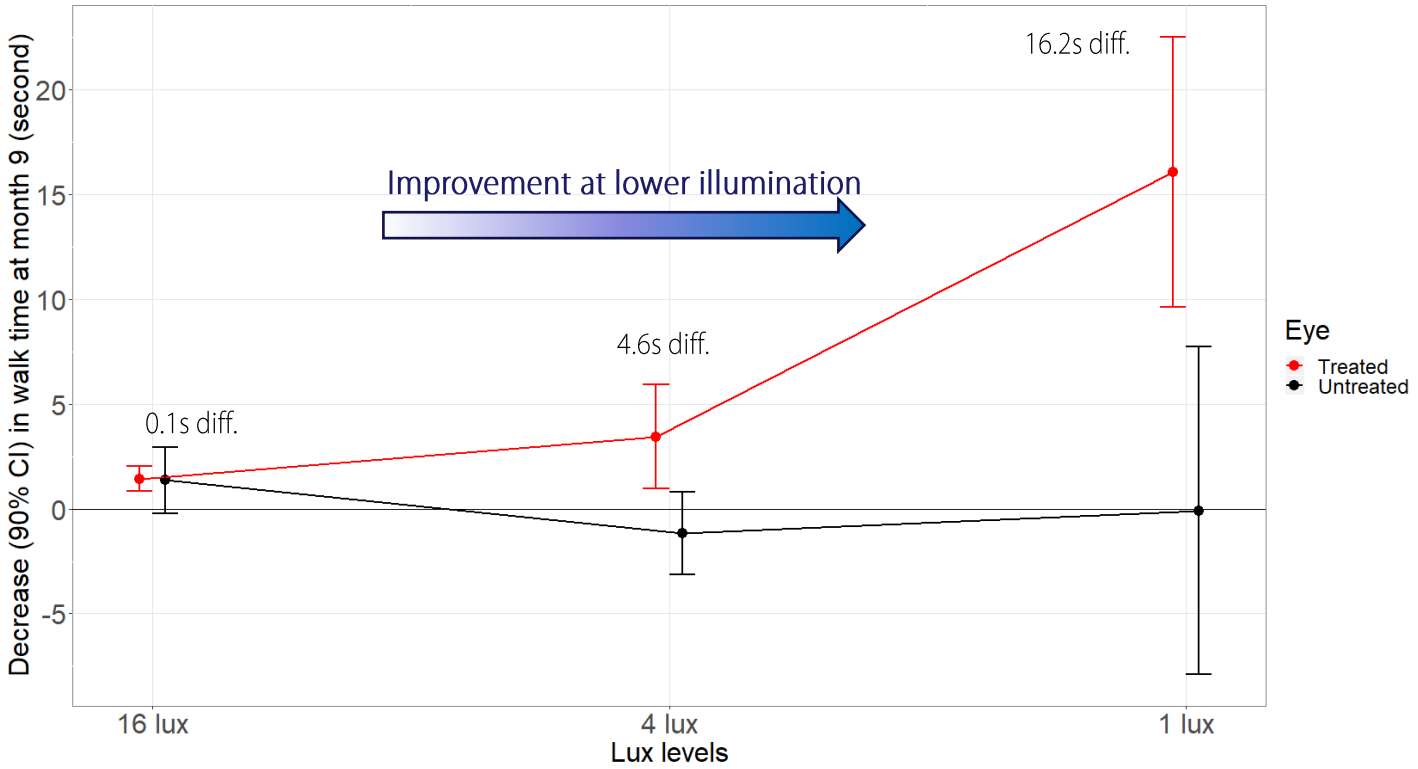
Mean Retinal Sensitivity (dB)	Treated-Untreated Eye Difference @ 12 months (90% CI adjusted for baseline)
Low	0.76 (–0.14, 1.66)
Intermediate	1.05 (0.81, 1.29)*
High	–1.05 (–1.77, 0.06)

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

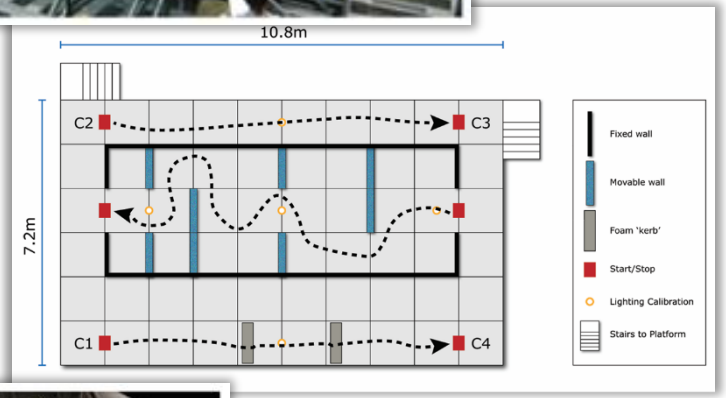
Significant Improvement in Vision-Guided Mobility Compared to Baseline (Low and Intermediate Dose, n=6)

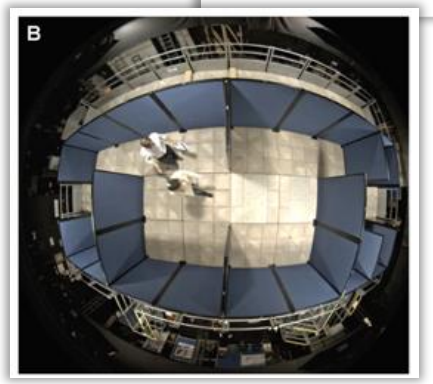


VMA endpoint	Low Dose (n=2)*	Intermediate Dose (n=4)
Number of subjects improving at 1, 4 or 16 lux (treated – untreated < 0 sec)	**2/2**	**3/4**

*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

Phase 3 Lumeos study ongoing and enrolling

lumeos XLRP study

MEIRAGTx

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]
- 54,000 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[4]
  - 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.

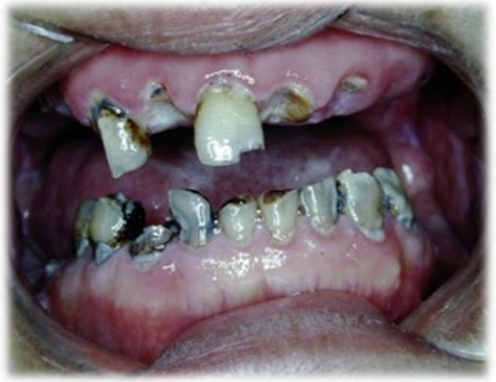
[3] Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018; 68:394.

[4]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

Radiation-Induced Xerostomia

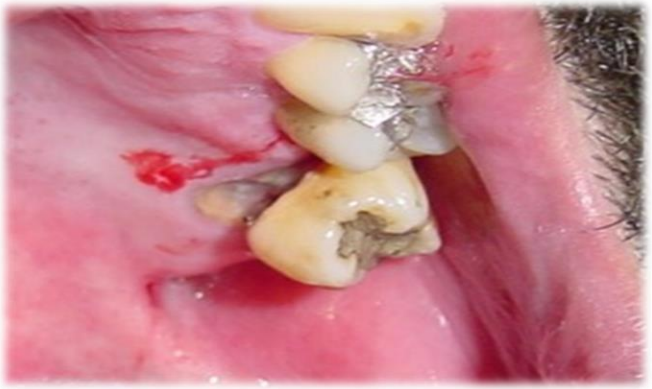
Xerostomia (Dry Mouth)

- 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)

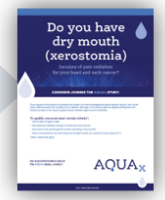
Strategy for Repair

- 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}

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
- Treatment was well tolerated in all subjects without DLTs, drug-related SAEs or concerning pattern of AEs
- COVID-19-associated hold on new patient enrollment has been lifted
- Tele-visits continue for active subjects

MGT016 AQUAx Phase 1 Study Design

Study Design

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

- Four unilateral treated escalating dose cohorts with a minimum of 3 subjects per cohort
- Four bilateral treated escalating dose cohorts have been added to the protocol to further assess potential efficacy
- May treat additional subjects in dose expansion cohorts
- 6 centers (5 in US, 1 in Canada)
- All subjects to be followed for 1-year post-treatment
- Long-term follow-up study will follow patients for a total of 5 years per FDA guidelines

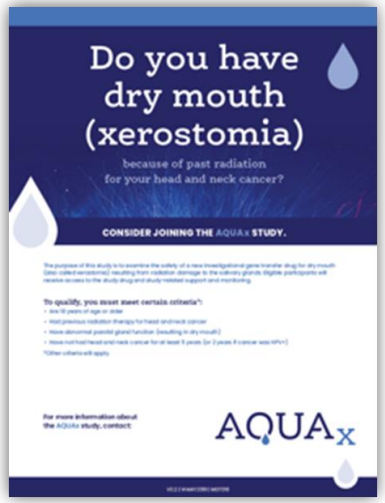
Cohort	Dose
1	1×10^{11} vg/gland (single gland)
2	3×10^{11} vg/gland (single gland)
3	1×10^{12} vg/gland (single gland)
4	3×10^{12} vg/gland (single gland)
1b	3×10^{10} vg/gland (both glands)
2b	1×10^{11} vg/gland (both glands)
3b	3×10^{11} vg/gland (both glands)
4b	1×10^{12} vg/gland (both glands)

Primary Endpoint

- Safety

Secondary Endpoint

- Patient reported measures of xerostomia symptoms



MGT016 AQUAx Phase 1 Study

Study Status

- All centers open for enrollment
- All four unilateral dose cohorts treated (n=12)
- One bilateral dose cohort treated (n=3)
- Completion of enrollment of bilateral cohorts in the coming months

7 participants (3 each from Cohorts 1 & 2 and 1 from Cohort 3) have data available through Day 90 following treatment:

- Treatment well tolerated
- No dose limiting toxicity
- No serious adverse events
- Improvements observed in validated patient reported assessments of xerostomia symptoms

Assessment: McMaster Global Rate of Change

- 6 of the 7 participants to date reaching 90-day assessments reported their symptoms of dry mouth as better following treatment
- All 6 of these participants rated changes in xerostomia scores that were important or very important (a score of 2 or more)
- 3 participants rated the change in xerostomia symptoms with the highest level improvement scores of 6 or 7
- Improvement in xerostomia symptoms can be seen persisting through 1 year in two patients who reached Day 360
- Participant 1-1 has just reached the 24-month assessment and the score of 7 was maintained
- Only one participant, 2-1, reported no improvement and this participant had no saliva production at baseline
- No participant reported any worsening of xerostomia symptoms

		Dry Mouth Symptoms? Better (+), Worse (X), or Same (=)			How Much Better / Worse?		
Cohort	Participant	Day 90	Day 180	Day 360	Day 90	Day 180	Day 360
1	1-1	+	+	+	5	6	7
	1-2	+	+	+	3	3	6
	1-3	+	+	=	3	3	
2	2-1	=	=				
	2-2	+	+		2	4	
	2-3	+			6		
3	3-1	+			4		

Xerostomia Questionnaire (XQ)

- A Patient Reported Outcome measure consisting of 8 symptom-specific questions wherein the patient rates each symptom from 0 (not present) to 10 (worst possible)
- The responses are summed (0-80), providing an overall measure of disease burden
- This is refined from the Xerostomia Inventory which consists of 11 questions and for which a 6-point change in disease burden is defined as a clinically meaningful improvement
- In the AQUAx study, 6 of 7 participants reaching the 90-day assessment reported decreases in disease burden of 10 points or more on the XQ at 90 days – indicating a clinically meaningful alleviation in disease burden
- More dramatic reductions of 19, 25, 26, and 41 points were reported by 4 of 7 participants at 90 days
- In the subjects that reached additional timepoints, scores improved or stabilized at later timepoints
- One participant reported complete resolution of symptoms at 12 months following treatment with no symptoms of xerostomia, a complete response

Summary: AQUAx Preliminary Data

Dosing in the unilateral dose escalation and first cohort of bilateral dosing phase completed

Safety

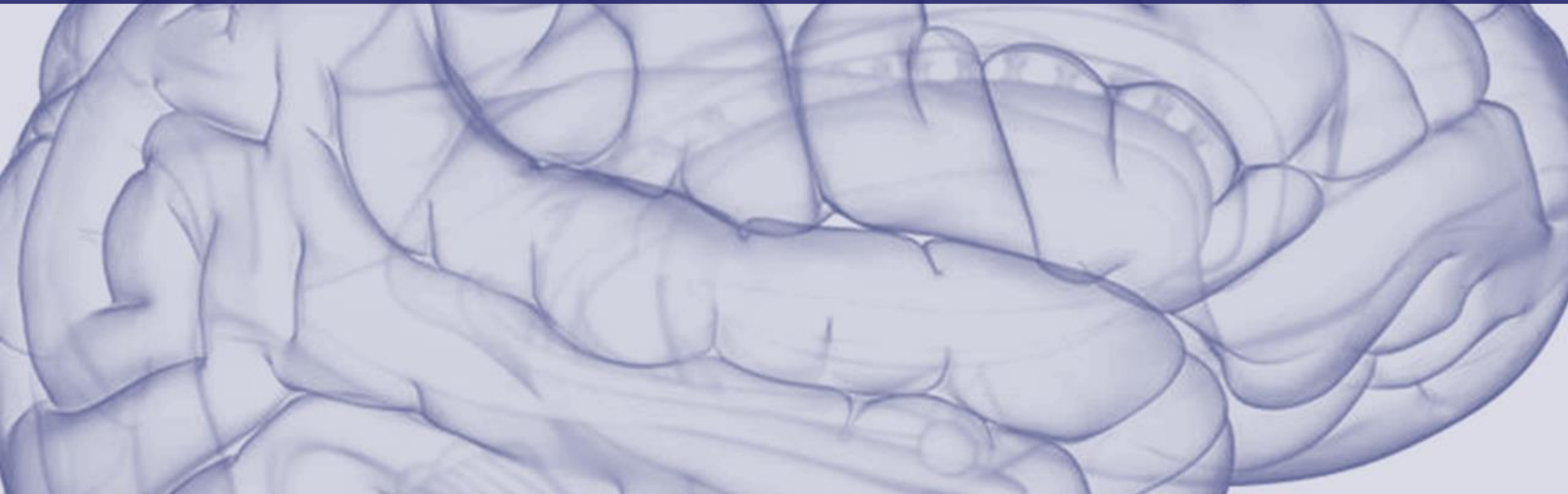
- AAV-hAQP1 treatment appears safe and well tolerated at each dose tested
- No DLT or SAEs

Efficacy

- Improvements in xerostomia symptoms and disease burden reported in two different PRO tools validated for xerostomia
  - McMaster – which has been the basis of approval of other drugs for xerostomia
  - Xerostomia questionnaire – a higher bar than the McMaster
- AAV-hAQP1 treatment response rate and effect size encouraging
- 6 of the 7 participants through 90 days following treatment achieved clinically meaningful improvement in symptoms
- One participant with the maximum response evaluable at 12 months has now reached 24 months and the same level of response/xerostomia symptom improvement is maintained

Phase 2 double-blind randomized two dose study expected to initiate by y/e 2022

Neuroscience Pipeline



AAV-GAD for Treatment of 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.

Current therapy is associated with high rates of complications over time:

- Symptomatic relief lasts ~5 years with reduced benefit over time
- Increased doses required over time, with high rates of non-adherence and increased side effects
- Side effects include motor fluctuations, dyskinesias, cognitive/affective

High unmet medical need :

- PD affects more than seven million people worldwide
- 300,000 PD patients in the U.S. no longer responding adequately to oral medications

Product: AAV-GAD | Stage: Clinical

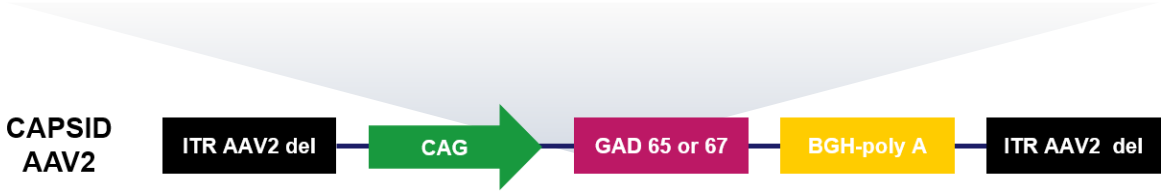
AAV-GAD is an investigational gene therapy designed to deliver the glutamic acid decarboxylase (GAD) gene locally to the subthalamic nucleus to increase production of GABA, the primary inhibitory neurotransmitter in the brain.

Non-dopaminergic strategy:

- GAD is the rate-limiting enzyme in the conversion of glutamate to GABA
- AAV-GAD potentially applicable to a 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



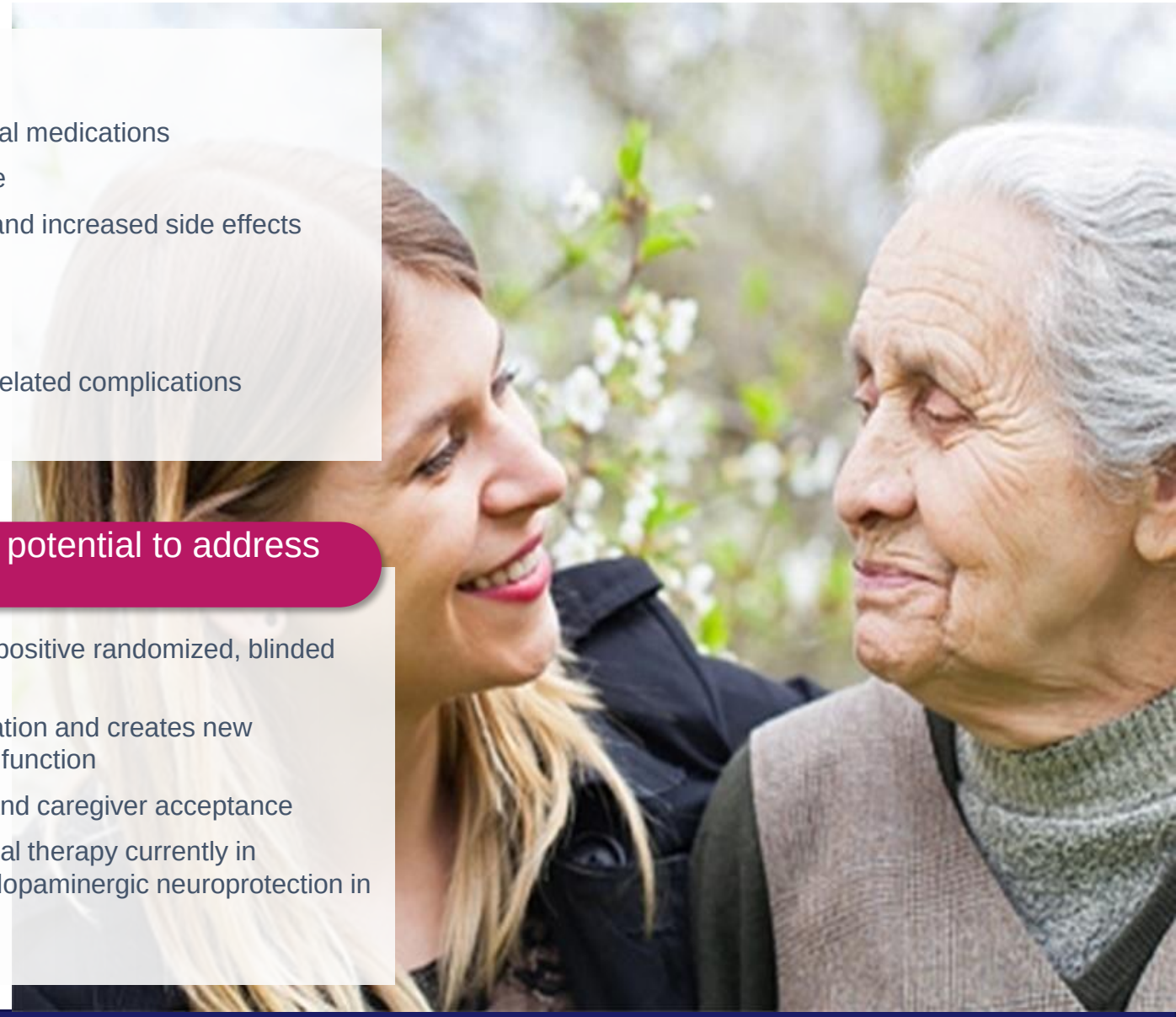
AAV-GAD Has The Potential to Address Major Unmet Needs

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

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

STN Deep Brain Stimulation (DBS) is effective, but limited in penetration

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

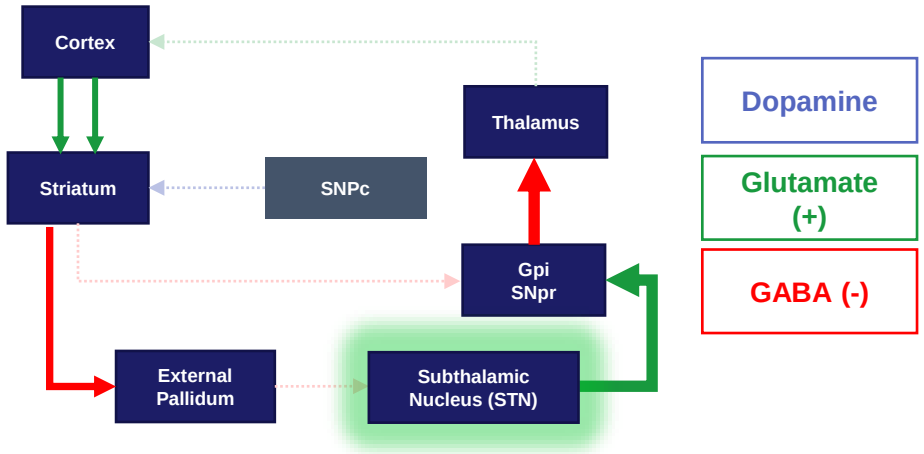


AAV-GAD is a unique, disease-modifying therapy with potential to address key unmet needs in Parkinson's disease

- The most advanced gene or cell therapy for PD supported by the only positive randomized, blinded trial
- 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
- 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

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

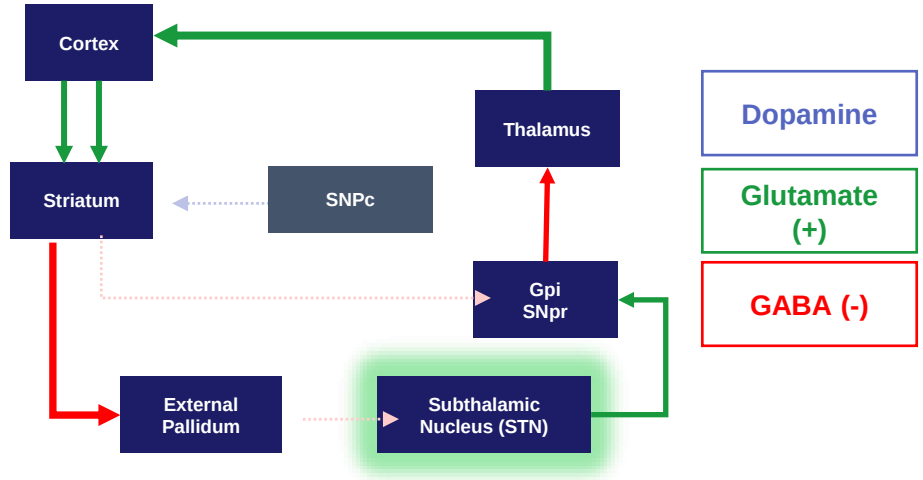
Dysregulation of basal ganglia in PD leads to STN overactivity due to reduced GABA



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

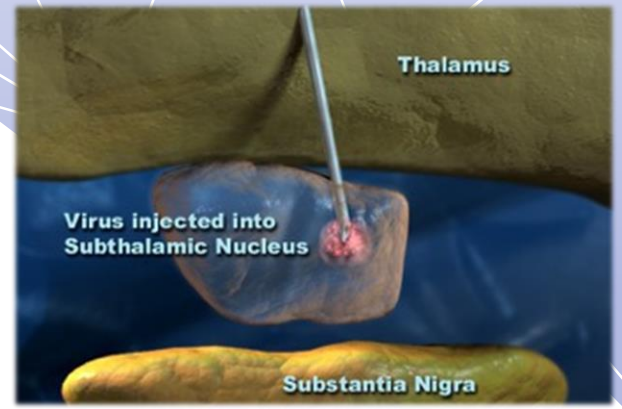
Product

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 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

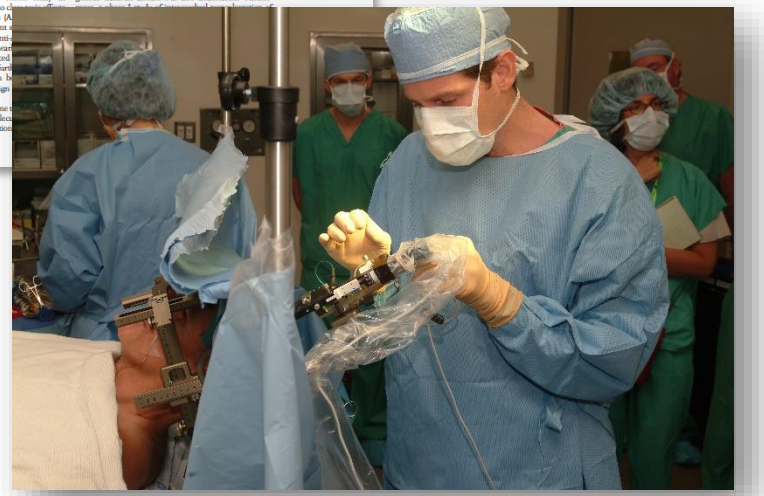
Efficacy findings:

- 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

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

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



Safety & efficacy findings supported initiation of Phase 2 studies

Phase 2 Study of AAV-GAD Gene Therapy

Study Design:

Randomized (n=45,1:1) double-blind study of bilateral STN AAV-GAD vs. Sham surgery control

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
- Functional imaging with same findings as phase 1 and new biomarker specific to AAV-GAD treated subjects, which significantly correlated with clinical outcome

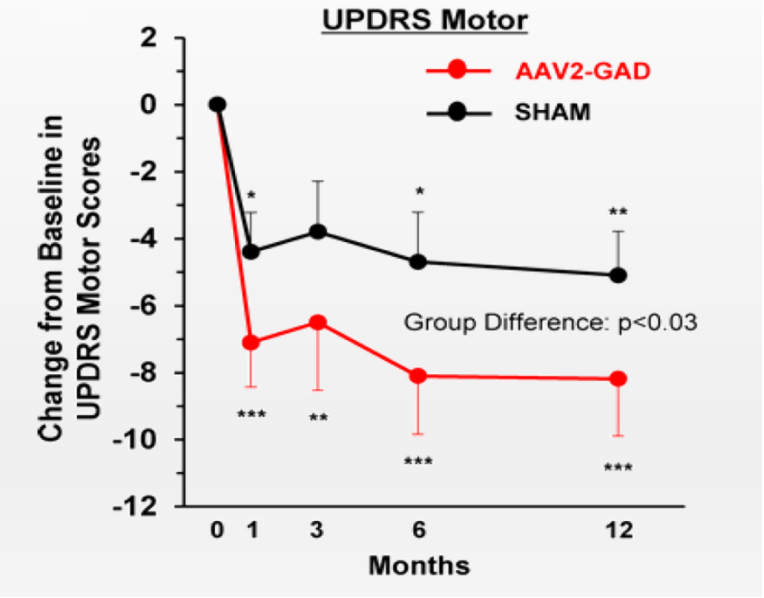
Safety findings:

- No adverse events related to AAV-GAD across all time points
- Worsening PD as an adverse event in 35% of sham vs. 0% GAD, further supports efficacy

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

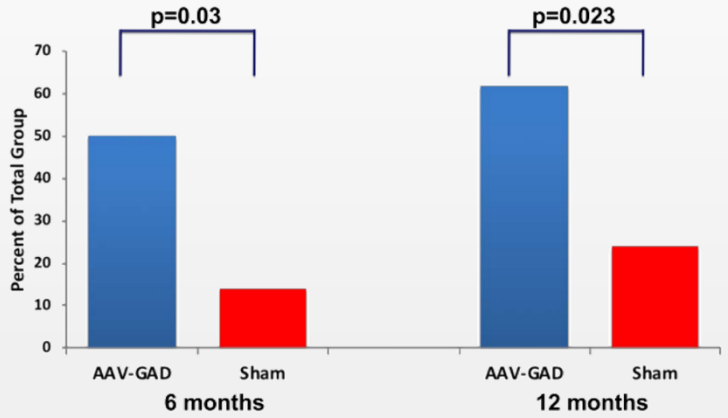
Results from Sham-Controlled Phase 2 Study: Meaningful Improvements Compared to Sham in Clinical Outcomes After Treatment with AAV-GAD

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



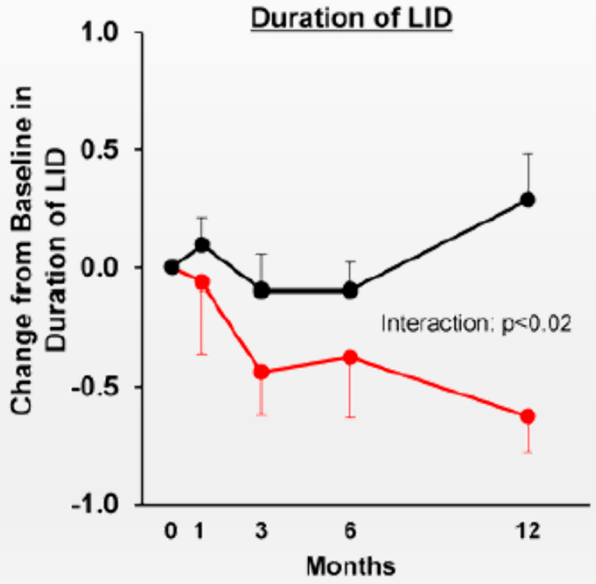
- Greater improvements in motor scores observed in the AAV-GAD treatment group across all follow-up time points
- Met primary outcome measure: UPDRS 3 improvement vs. sham at 6 months

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



- Significant reduction in the duration of levodopa-induced dyskinesias (LID) in AAV-GAD treated group

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

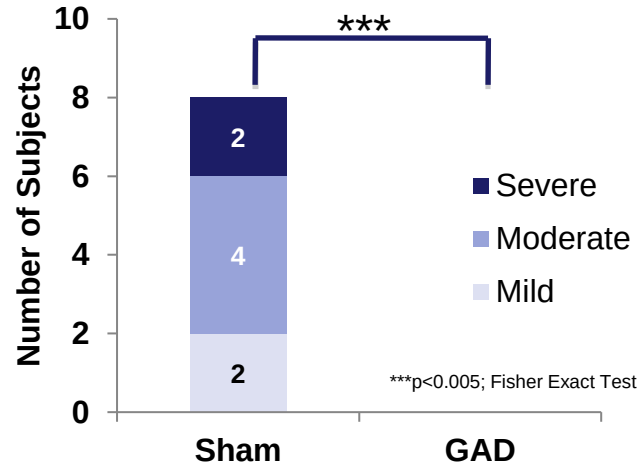
Functional Imaging – GAD Related Pattern (GADRP)

- 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

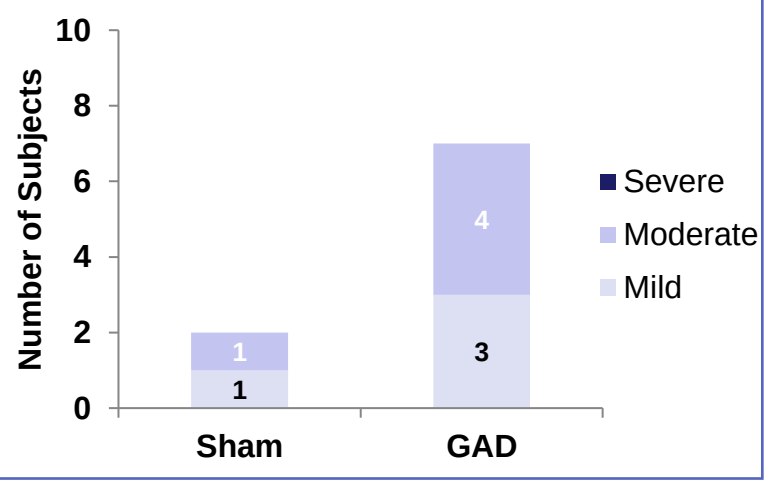
Niethammer M. Gene therapy reduces Parkinson's disease symptoms by reorganizing functional brain connectivity. Sci. Trans. Med. 2018; 10(469). pii: eaau0713

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

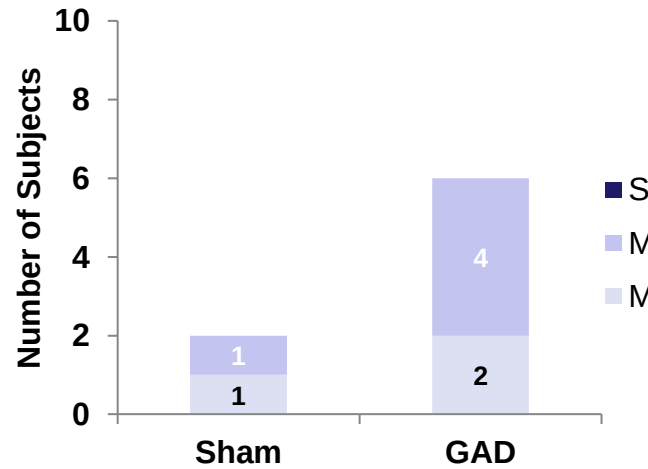
Worsening of Parkinson's Disease



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 compared to Sham
- 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:

- Non-dopaminergic strategy Potentially applicable to large patient population not adequately treated with currently available therapies
- Absence of retained hardware
- No need for specialized post-op care

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.

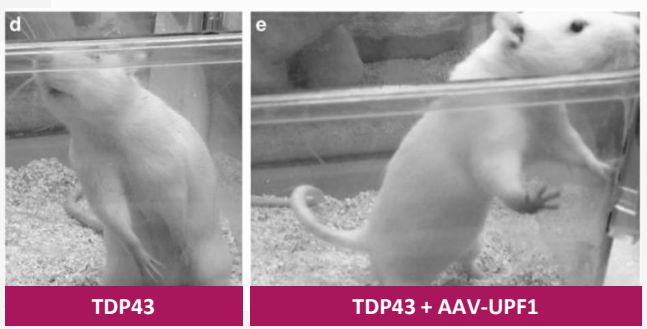
- Potential to address **both familial and sporadic forms** of the disease, may be genotype agnostic, and may have an effect in both ALS and FTD.

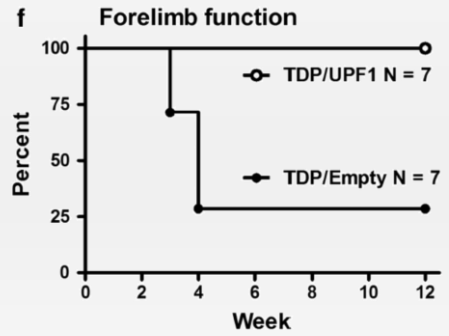
AAV-UPF1 was demonstrated to ameliorate ALS disease phenotype in a variety of preclinical models caused by different genotypes:

- 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





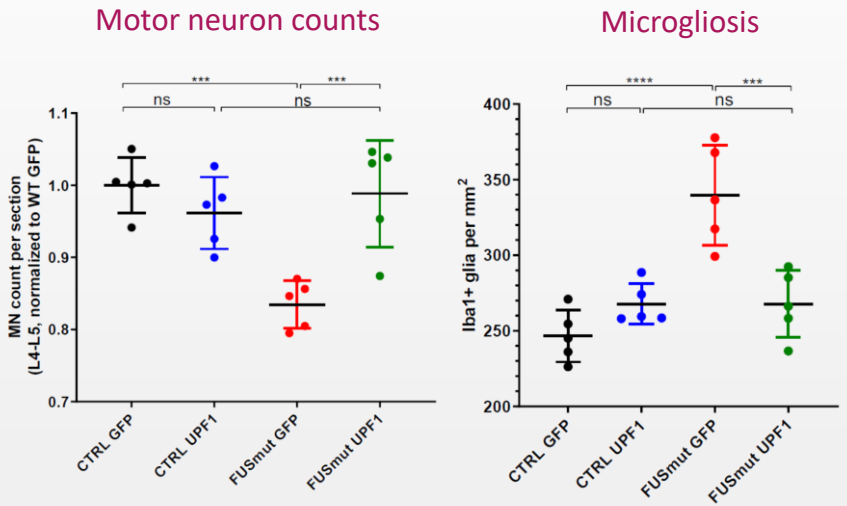
Top:

- Co-injection of AAV-TDP-43 and empty AAV vector shows abnormal rearing with both forelimbs lowered
- Co-injection of AAV-hUPF1 and AAV-TDP-43 shows normal rearing posture with both forelimbs extended

Bottom:

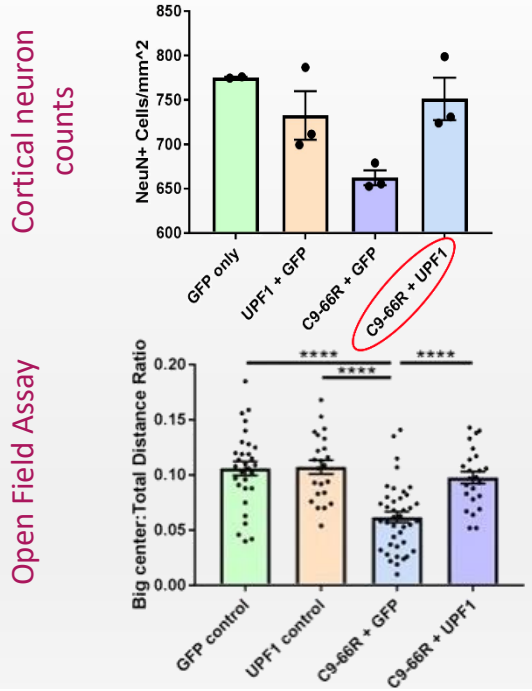
- AAV-UPF1 restores forelimb function as assessed by the escape reflex test

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

Broad and Diverse Pipeline

6 Ongoing Clinical Programs:

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

Deep Pipeline of Preclinical Programs:

- Multiple IRDs
- Wet AMD / DME
- Glaucoma, Uveitis
- Sjogren's, Dry Eye
- ALS
- Wilson disease
- Metabolic disease/diabetes/obesity

In-House Vector Engineering

Broad Viral Vector Engineering Platform:

- Novel capsids
- Vector optimization:
  - transgene engineering
  - sequence optimization
  - ITR
  - plasmid backbone optimization
- Organoids and iPSC preclinical platforms

Promoter Discovery Platform:

In-house synthetic promoter design and screening platforms

In-House GMP Manufacturing

Complete End-to-end Manufacturing Infrastructure:

- cGMP manufacturing facilities – flexible & scalable production
- Designed and built with global regulatory input
- Non-GMP vector core with scale down production for preclinical development
- Capacity to supply clinical and commercial products for all programs
- Proprietary Process Development platform
- Rapid process optimization for new products within 2-5 months
- In-house plasmid production
- In-house QC and fill & finish
- Global QA organization supporting preclinical through commercialization

Inducible Gene Regulation Platform

Proprietary Gene Regulation Platform:

- Riboswitch technology allows tight control of gene expression with unprecedented dynamic range and dose response
- Gene expression is controlled with proprietary, de-novo designed small molecules

Potential to Regulate Any Gene of Interest:

The expression of any gene can be tightly controlled in the context of any vector.

Transgenes regulated to-date include: antibodies, hormones, peptides, cytokines, DNA- & RNA-targeting nucleases

MEIRAGTx

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

MEIRAGTx