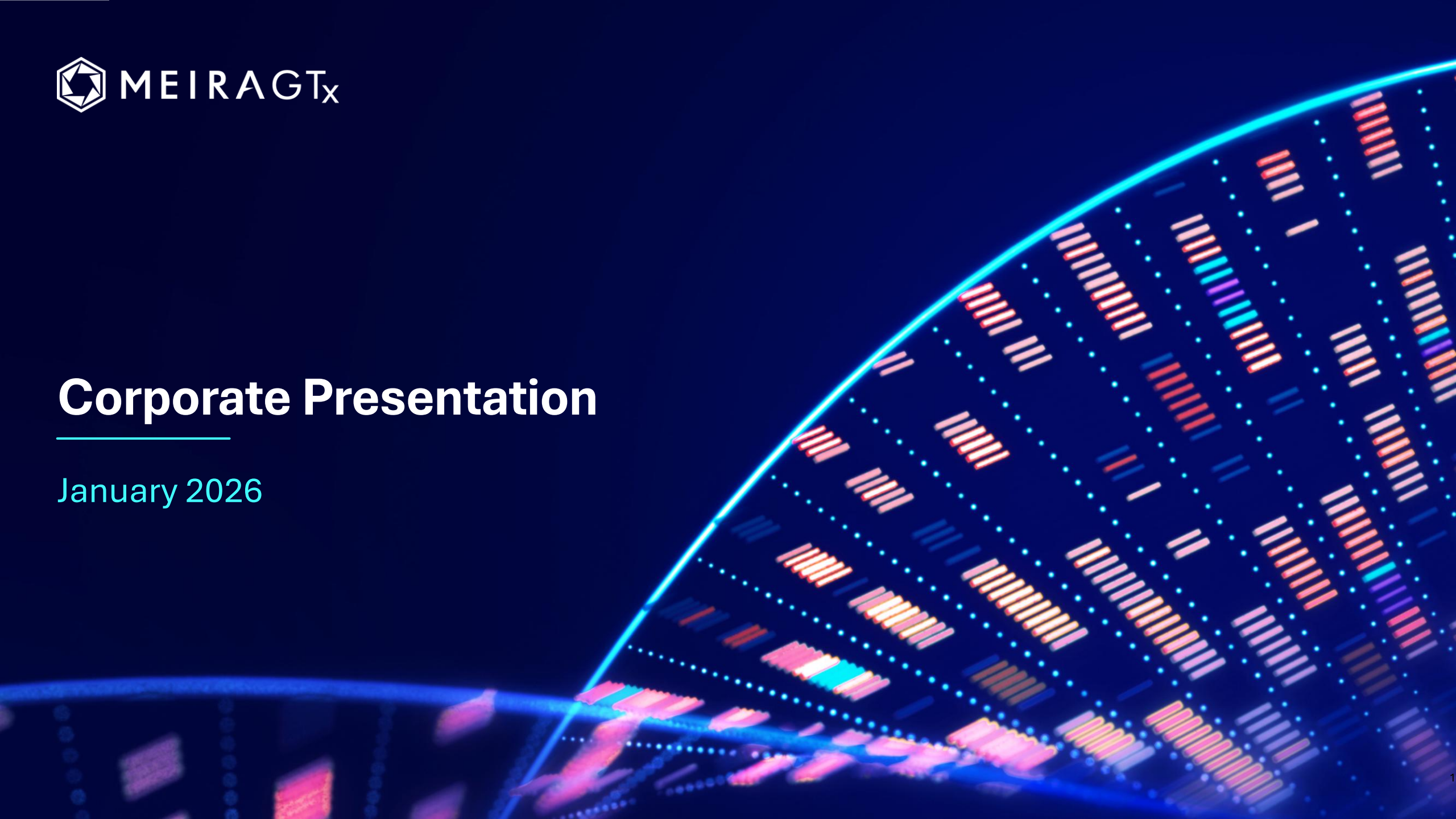
MEIRAGTx

Corporate Presentation

January 2026



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, our ability to manufacture product candidates, potential milestone payments and the achievement of such milestones, and our pre-clinical and clinical data, reporting of such data and the timing of results of data, 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, repay our debt obligations, identify additional and develop existing product candidates, successfully execute strategic transactions or 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 or rare pediatric disease designations, retain key personnel or attract qualified employees, or incur expected levels of operating expenses; the impact of pandemics, epidemics or outbreaks of infectious diseases 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 January 11, 2026.

Company Overview

MEIRAGTx

MeiraGTx: late-stage clinical pipeline and comprehensive end-to-end capabilities & technologies in genetic medicine

Diverse Program Pipeline

Broad pipeline across neuro, salivary gland, and ophthalmology

4 pivotal and BLA ready programs:

- Radiation-induced xerostomia
- Parkinson's disease
- AIPL1 retinal dystrophy (Eli Lilly)
- X-linked retinitis pigmentosa[1]

Diverse preclinical pipeline:

- ALS, Neuropathic pain
- Obesity: incretin combinations, leptin, BDNF, PTH, Epo, hGH
- Ophthalmology: pipeline Stargardt's, wet and Dry AMD
- Specials license: BBS10, pain

End-to-End GMP Manufacturing

In-house manufacturing and industry-leading process

- 2 cGMP viral vector manufacturing facilities
- cGMP plasmid production
- QC facility for release and stability
- In-house Fill & Finish, warehouse and supply chain
- Dedicated MSAT facility
- Commercial ready Platform Process and QC

Commercial licenses for both viral vector production as well as QC

Next-Generation Vector Optimization

Improved potency & safety, lower dose and lower COGS

- >250k promoter library
- AI enhanced promoter optimization
- Proprietary intravitreal capsids
- Capsid development: muscle, CNS
- Human organoids

Improve potency up to 3 to 4 logs, reducing dose 3-4 logs, reducing Cost of Goods and improving safety

Transformative *in vivo* production Technology

Proprietary Riboswitch platform for precise control of therapeutic proteins

***in vivo* production of physiological, efficacious levels of any therapeutic protein via bespoke small molecule oral dosing**

- **Gene agnostic**: multiple antibodies, peptides, hormones, nucleases, cell therapy validated in animal models
- **Delivery agnostic:** AAV, Lentivirus and CRISPR all demonstrated equivalent tight control
- **Leptin**: first into the clinic, 2026

[1] Remaining interests in program sold to Johnson & Johnson Innovative Medicine in December 2023; MeiraGTx to receive up to an aggregate of $350.0 million upon achievement of milestones and will manufacture and supply commercial product for Johnson & Johnson Innovative Medicine

Broad Pipeline of Transformative Genetic Medicines

Advanced clinical programs across multiple therapeutic areas

Product	Indication	Preclinical	Phase 1	Phase 2	Phase 3 / Registrational
Salivary Gland					
AAV-AQP1	**Radiation-induced xerostomia**				*RMAT, Orphan Drug*
	Sjögren's disease				*IND ready*
	PSMA radioligand xerostomia prophylaxis and treatment				
Neurodegenerative Disease					
AAV-GAD[1]	**Parkinson's disease**				*RMAT* — *Phase 3 ready*
AAV-UPF1, AAV-CNTFR	**ALS**				
Ophthalmology					
Botaretigene sparoparvovec[2]	**X-linked RP (RPGR)** Johnson&Johnson Innovative Medicine				*PRIME, Fast Track, Orphan Drug*
AAV-AIPL1	**LCA4 congenital blindness** Lilly				*RPDD, Orphan Drug, MHRA Specials License*
AAV-ABCA4	**Stargardt's disease**				
AAV-VEGFR2	**Wet AMD**				
Undisclosed	**Dry AMD/GA**				
BBS10	**Bardet-Biedl syndrome**				*RPDD, Orphan Drug* — *Developed under MHRA Specials License*
Riboswitch Regulated Therapies					
RiboLeptin	**Lipodystrophies**				
Undisclosed	**Intractable neuropathic pain**				
GLP-1, GIP, incretin combinations	**Obesity/MASH/Metabolic Disease**				
Ribo-CAR-T	**Oncology, autoimmune disease**				
Genetic Obesity					
AAV-BDNF[1]	**MC4R/BDNF genetic obesity**				

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[1] Joint venture with Hologen AI (see press release here)

[2] Remaining interests in program sold to Johnson & Johnson Innovative Medicine in December 2023; MeiraGTx to receive up to an aggregate of $350.0 million upon achievement of milestones and will manufacture and supply commercial product for Johnson & Johnson Innovative Medicine

Four pivotal stage programs in prevalent and rare indications

Radiation-Induced Xerostomia

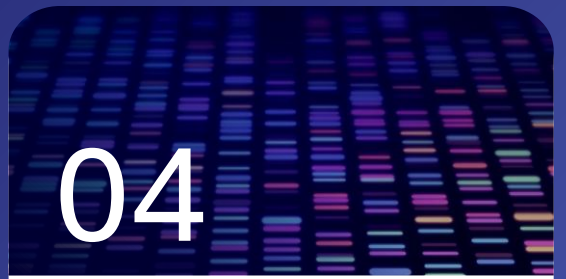
- Pivotal Phase 2
- **Potential BLA filing early 2027**
- Large patient population with no effective therapies available
- ‘Pipeline in a product’

Parkinson’s Disease

- Phase 3 ready
- **Potential BLA filing in 2028**
- Large patient population inadequately controlled by dopamine therapy

AIPL1-Associated Congenital Blindness

- Developed under ‘specials’ license
- **Near term BLA and MAA filings– FDA and MHRA**
- **Potential approvals 2026**
- Transformative effect - 11/11 blind to seeing children under 4 years



X-Linked Retinitis Pigmentosa (RPGR)

- Completed Phase 3
- **BLA and MAA ready – Clinical and PPQ**
- Acquired by Johnson & Johnson Innovative Medicine; MeiraGTx manufactures commercial product

Unique end-to-end, in-house GMP manufacturing infrastructure and production platform process, scalable and flexible, fit for clinical & commercial supply

End-to-end internal manufacturing infrastructure, capabilities and production process

Best in class, fully end-to end internal capabilities: Two flexible & scalable cGMP vector production facilities, London, UK and Shannon, Ireland; cGMP plasmid production facility; cGMP QC facility for release and stability; fill and finish; dedicated MSAT process development facility

Commercial licenses in Ireland and UK for viral vector production and QC

Proprietary Commercial Ready Manufacturing Process at IND: Saves 2-3 years in AAV clinical development timeline from IND to commercial and allows faster move to pivotal with expedited time to market

Global regulatory relationships and extensive experience from pre-IND through BLA/commercial

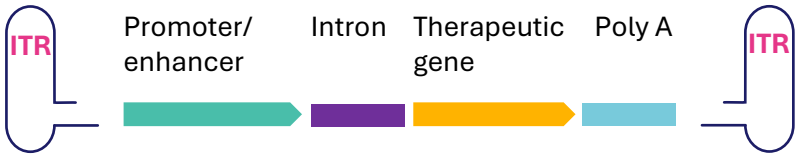
Commercial grade manufacturing with scalable and flexible capacity, clinical and commercial supply

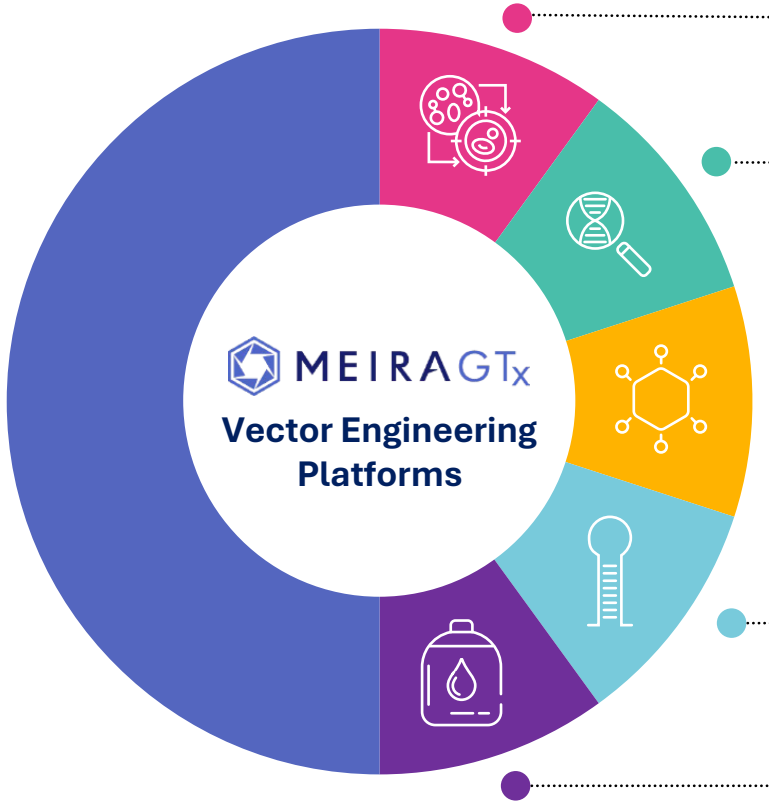
Comprehensive vector engineering technologies

Potency & safety optimization and precise control of gene expression

In-house vector engineering platforms

Extensive in-house vectorology capabilities addressing each element of the vector genome sequence





Promoter engineering & discovery

>250k promoter library
Combine rational design, massive high throughput screening, and AI to optimize proprietary promoters

Gene sequence optimization

Intron/exon configuration, poly A, translation efficiency, mRNA stability, reduced immunogenicity

Capsid design

Proprietary capsids with high transduction efficiency, including novel intravitreal capsids targeting back or front of the eye – screened directly in NHPs; muscle and CNS capsids

Riboswitch gene regulation

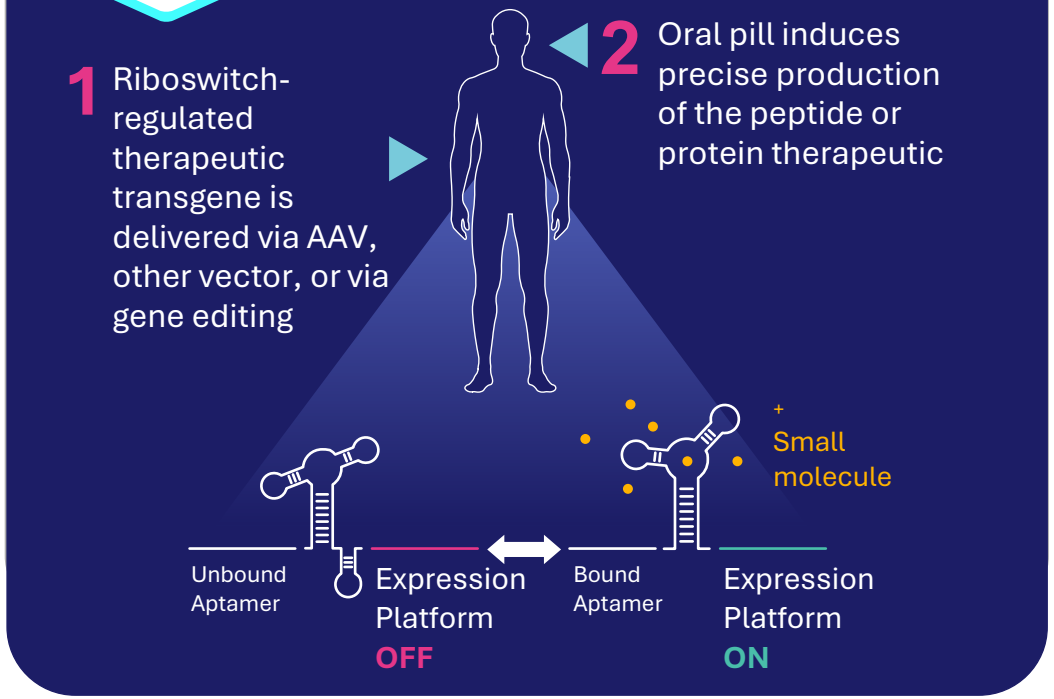
Precise dose responsive control of *in vivo* therapeutic protein production with bespoke oral small molecule inducer

Manufacturability

Optimal plasmid design and vector genome sequence optimization for industry-leading high yield and full/empty ratio

Riboswitch platform: precise *in vivo* production of therapeutic proteins using oral small molecule inducers

Riboswitch technology enables unprecedented precise *in vivo* delivery of biologic therapeutics with orally administered inducers



Riboswitch technology can be applied across many therapeutic areas and modalities, providing titratable control of gene expression with an oral pill

- Vectorized biologics
- Cell Therapy
- Gene Editing
- Short-lived hormones & peptides
- Control CNS & PNS Therapies
- Control Ocular Therapies

A broad range of therapeutic proteins encoded by Riboswitch-containing transgenes show tight control via oral small molecule dosing, *in vivo*

Therapeutic Antibodies

- Anti-PCSK9
- Anti-VEGFR2 (eye)
- Anti-Amyloid
- Anti-IL-17
- Anti-PD1
- Anti-HER2
- Anti-IL4Ra
- Anti-Myostatin

Cell Therapy

RiboCAR:

- Anti-CD19
- Anti-PSMA
- Anti-mesothelin
- Anti-HER2
- Cytokines

- ProTcell (progenitor T cell) derived riboCAR-T

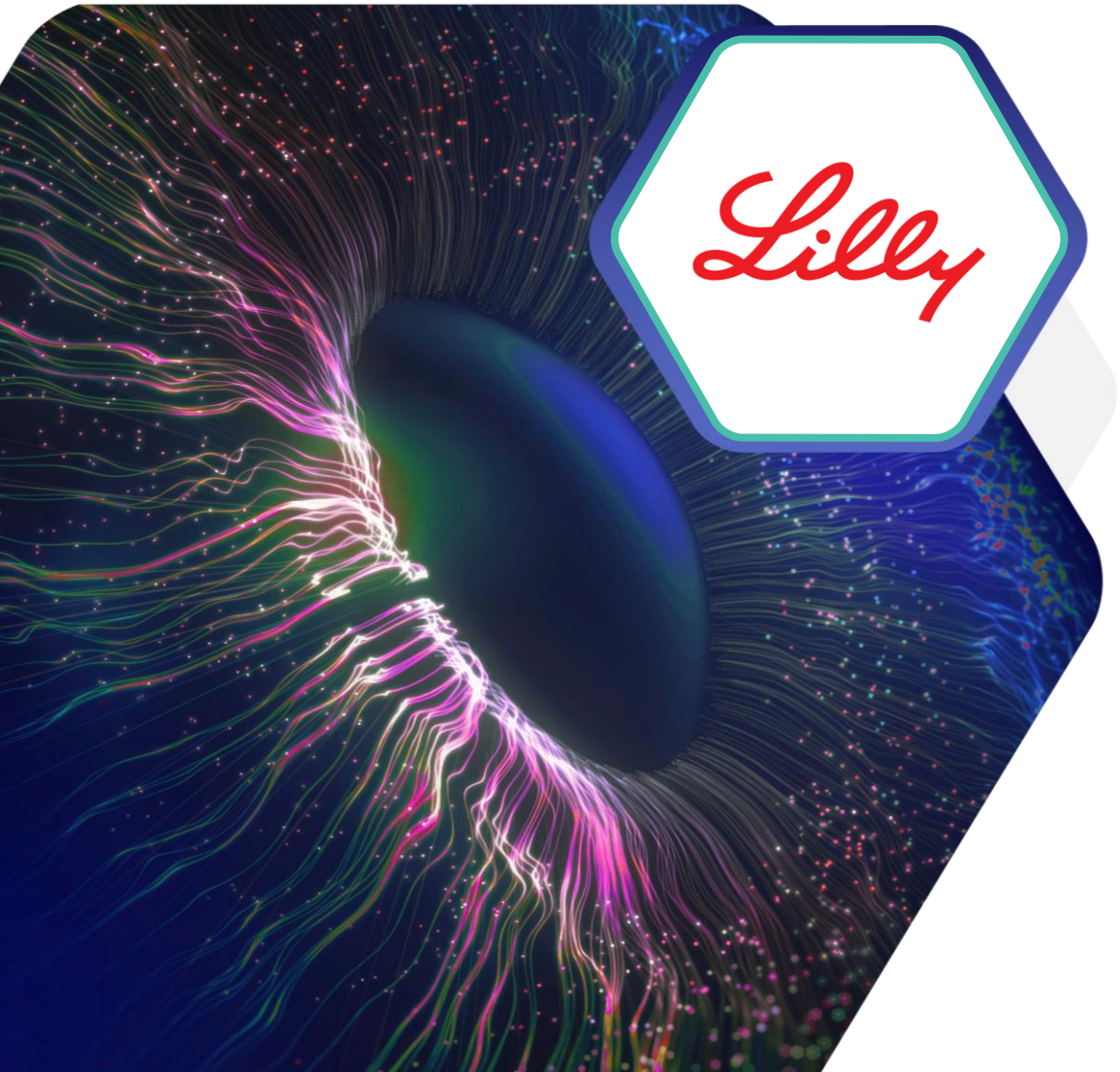
Therapeutic Hormones/Cytokines / Peptides

- Epo
- hGH
- PTH
- Insulin
- GLP-1R agonists
- Gut peptide combinations: GLP1- GIP; GLP1, GIP, PYY, Glucagon, Amylin, Oxyntomodulin
- Myokines
- Adipokines e.g: leptin

Gene/RNA Editing Nucleases

- Cas9
- CasRx

Strategic collaboration with Eli Lilly in ophthalmology (November 2025)



MeiraGTx enters into a broad strategic collaboration with Eli Lilly to develop and commercialize genetic medicines in ophthalmology – Link to press release

- **MeiraGTx received $75 million in upfront cash, as well as up to $135 million in near-term milestone payments related to AAV-AIPL1**
- **MeiraGTx is also eligible to receive additional milestone payments and tiered royalties on licensed products**
- Under the terms of the agreement, Lilly obtained:
  - Worldwide exclusive rights to MeiraGTx's AAV-AIPL1 product for LCA4, a rare form of congenital blindness, as well as two other preclinical product candidates for inherited retinal dystrophies
  - Exclusive license to certain MeiraGTx proprietary intravitreal capsids as well as certain proprietary promoters for use with up to five ocular disease targets
  - A Right of First Negotiation (ROFN) to MeiraGTx's proprietary Riboswitch Technology in the field of gene editing in the eye

Strong industry partnerships

Johnson&Johnson Innovative Medicine

MeiraGTx entered into a $415 million asset purchase agreement with Johnson & Johnson Innovative Medicine for the remaining interests in bota-vec for the treatment of XLRP

- **MeiraGTx will receive a total of up to $415 million:**
  - $130 million in upfront and near-term milestone payments
  - Additional $285 million upon first commercial sales of bota-vec in U.S. & EU and manufacturing technology transfer
- MeiraGTx will manufacture and supply commercial product for Johnson & Johnson Innovative Medicine at MeiraGTx's cGMP facilities

Link to press release

sanofi

In October 2023, MeiraGTx received a $30 million strategic investment from Sanofi through sale of 4 million ordinary shares at $7.50 per share

Sanofi received a Right of First Negotiation (ROFN) for MeiraGTx's phase 2 xerostomia program, as well as for the use of MeiraGTx's Riboswitch gene regulation technology in certain targets:

- Immunology and Inflammation (I&I), including IL-4 and IL-13
- GLP-1 and other gut peptides for metabolic disease and obesity
- Central Nervous System (CNS)

In August 2024, Sanofi made an additional $30 million equity investment in MeiraGTx as part of a $50 million offering of ordinary shares

Link to press release

HOLOGEN AI

MeiraGTx entered into a strategic collaboration with Hologen AI to expedite Phase 3 development of AAV-GAD and industrialize MeiraGTx's proprietary manufacturing process

- **MeiraGTx to receive $200 million in upfront cash consideration**
- MeiraGTx and Hologen will form a JV with an additional $230 million committed capital from Hologen to fund 100% of AAV-GAD program through to commercialization, as well as other potential pipeline products
- Hologen will also fund a portion of MeiraGTx's manufacturing operations and will own a minority stake in MeiraGTx's manufacturing subsidiary

Link to press release

AAV-AQP1 for treatment of xerostomia - pivotal Phase 2 enrolling

Large patient population with no effective treatment options

Radiation-Induced Xerostomia (RIX)

Pivotal Phase 2 study currently enrolling
Granted RMAT and Orphan Drug designations

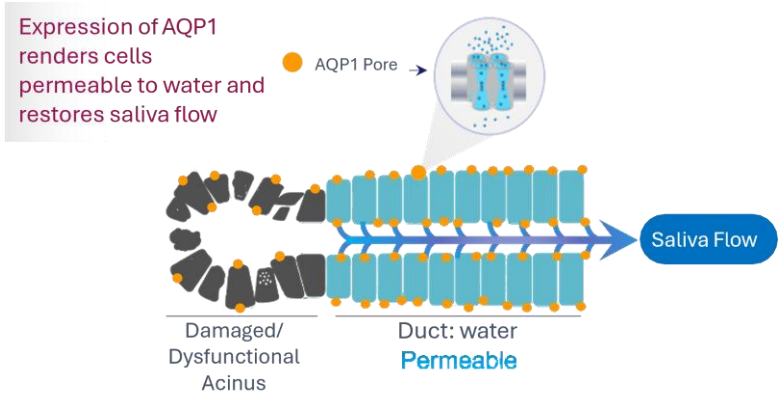
- **RIX is one of the most frequent complications of radiation treatment for head & neck cancer**
- **~200K patients in the US alone**
- **Large patient population with severe unmet need**

AAV-AQP1 Treatment:

- **Small dose delivered directly to salivary gland**
- **In-office procedure**
- **No general anesthesia**
- **One-time therapy**
- **Low cost of goods**

MECHANISM OF ACTION

- Saliva-producing cells are vulnerable to Ionizing radiation used to treat head & neck cancer and PSMA radioligands
- Expression of the water channel Aquaporin 1 (AQP1) in the salivary gland duct allows water to flow into the salivary duct and out to the oral cavity to moisten the mouth



TRANSFORMATIVE CLINICAL IMPROVEMENTS

- Compelling Phase 1 data presented June 2023 with 24 patients - with magnitude of improvements unprecedented in this condition (see here)
- **Improvements across all efficacy endpoints considered 'unprecedented' and 'transformative' by KOLs**
- **Granted RMAT designation; written alignment with FDA on path to BLA**
- **Pivotal Phase 2 enrolling**

PIPELINE IN A PRODUCT

- ☑ **Radiation-induced xerostomia**
- ☑ **Sjögren's disease**
- ☑ **Radioligand therapies (xerostomia is a dose limiting AE for PSMA radioligands)**
- ☑ **Prevention of radiation-induced or PSMA radioligand xerostomia**

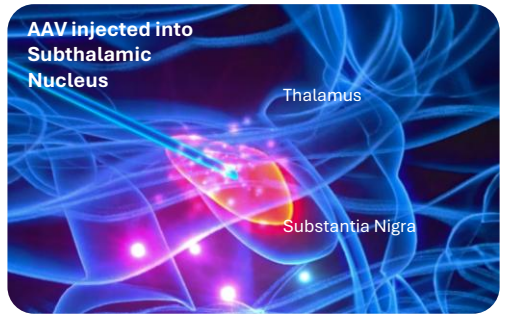
AAV-GAD for treatment of Parkinson's disease - Phase 3 ready

Meaningful clinical improvements with evidence of disease modification

The only CNS gene therapy program with two randomized, double-blind, sham surgery-controlled trials which met the prespecified primary endpoint

MECHANISM OF ACTION

- AAV-GAD delivers a functional copy of the Glutamic Acid Decarboxylase (GAD) gene locally to the sub-thalamic nucleus (STN)
- GAD converts glutamate (excitatory neurotransmitter) to GABA (inhibitory neurotransmitter) to alleviate PD-associated hyperexcitation of the STN



LARGE PATIENT POPULATION IN NEED OF EFFECTIVE TREATMENT

- ☑ **Small dose, local delivery – favorable safety & low COGS**
- ☑ **One-time treatment; brief surgical procedure with no general anesthesia**
- ☑ **No in-dwelling hardware**
- ☑ **Internally manufactured by MeiraGTx using commercial-ready process**

MEANINGFUL EFFICACY VS. SHAM SURGERY CONTROL

- 58 patients in 3 independent multicenter clinical studies were treated with AAV-GAD
- Generally safe and well tolerated in all doses tested, with no treatment-related SAEs
- **Phase 2 study met primary endpoint of UPDRS 3 motor score improvement vs. sham at 6 months; Improvements persisted at 12 months**
- **Evidence of disease modification – in collaboration with Hologen AI**
- Improvements in multiple secondary outcome measures

STATUS: PHASE 3 READY

- **Granted RMAT designation, May 2025**
- **October 2024: positive data reported from AAV-GAD sham-controlled bridging study, using higher dose and material manufactured in-house by MeiraGTx:**
  - **Significant improvement of 18 points over baseline in UPDRS Part 3 in the high dose group at 26 weeks**
  - Significant improvement in quality of life measures (PDQ-39), in both the high and low dose groups at 26 weeks

AAV-AIPL1 for treatment of LCA4 congenital blindness

Restoring vision in children who are born legally blind

AIPL1 Retinal Dystrophy (LCA4)[1]

- **Children with AIPL1-associated retinal dystrophy are blind from birth and by age 4, retinal degeneration is complete and irreversible**
- **Near Term Path to Marketing Authorization under Exceptional Circumstances**

[1] Partnered with Eli Lilly

MECHANISM OF ACTION

- AAV8-AIPL1 delivers the wild-type human AIPL1 gene under control of a photoreceptor-specific rhodopsin kinase promoter, hRK
- AAV-AIPL1 is administered subretinally as a one-time treatment

TRANSFORMATIVE CLINICAL IMPROVEMENTS

- 11 children have been successfully treated in the UK under an MHRA Specials License – 4 unilaterally & 7 bilaterally
- There were no safety concerns in either of the patient groups
- **Efficacy has been demonstrated in all 11 patients: 100% of treated children who were legally blind from birth regained visual acuity, with benefits seen from 1 month following treatment**
- In the unilateral treatment group, durable efficacy has been shown **up to 4 years** (the longest follow up point)

NEAR-TERM PATH TO MARKETING AUTHORIZATION

The company presented data produced under the Specials License to the MHRA and FDA:

- MeiraGTx has been advised by MHRA to file for 'Marketing Authorization Under Exceptional Circumstances'. No further clinical data was requested
- In addition, a CMC package appropriate for such a rare condition was agreed
- Similar feedback received from FDA on path for expedited US approval
- AAV-AIPL1 for LCA4 received rare pediatric disease designation (RPDD) from FDA - approval may result in a Priority Review Voucher (PRV)

Late-stage clinical programs

AAV-AQP1 for treatment of grade 2/3 xerostomia: Pivotal Study enrolling

AAV-AIPL1 for treatment of LCA4: near-term path to regulatory approvals

AAV-GAD for treatment of Parkinson's Disease (Phase 3 ready)

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AAV-AQP1: a pipeline in a product for treatment of xerostomia

Pivotal Study enrolling in radiation induced xerostomia

Granted RMAT and Orphan Drug designations

Alignment with FDA on pivotal clinical trial design and CMC for BLA filing

Pipeline in a product: multiple prevalent indications with high unmet need

01

Radiation-induced xerostomia

- Pivotal Phase 2 Enrolling
- >170,000 patients with grade 2/3 xerostomia in US alone
- Large ex-US incidence and prevalence
- >80% inadequately controlled by current SOC

02

Xerostomia associated with Radioligand Therapy

- Xerostomia is the most common AE of PSMA radioligand therapy, and a dose-limiting toxicity
- AAV-AQP1 has the potential to treat xerostomia in this rapidly growing market as a treatment, but more importantly pretreatment prophylaxis

03

Sjögren's-related xerostomia

- Prevalent autoimmune condition disrupting tear- and saliva-producing glands
- No effective treatments for Sjögren's-related xerostomia
- >550,000 Sjögren's patients with grade 2/3 xerostomia in the US alone

04

Prevention of radiation-induced xerostomia

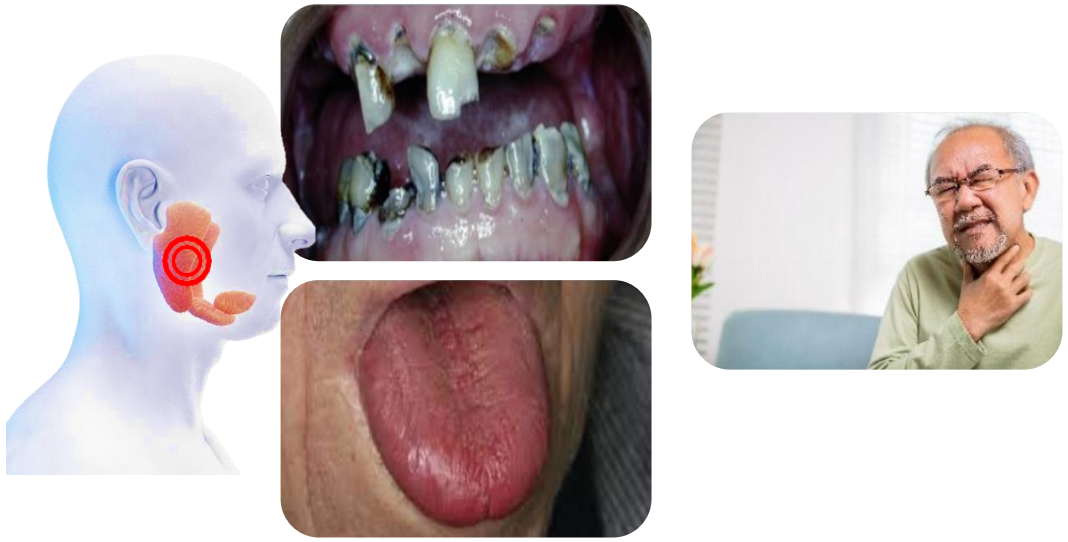
- Preclinical data suggest that treatment with AAV-AQP1 prior to radiation reduces risk of RIX; importantly this would include PSMA Radioligand therapy
- Each year, >50,000 patients receive radiation for head & neck cancer in the US and >25,000 receive PSMA radioligand therapy

Radiation-induced xerostomia (RIX): a severely debilitating condition with no effective treatment options for grade 2/3 patients with persistent RIX

> **Radiation treatment frequently causes irreversible damage to the salivary glands, leading to this severe life-long condition**

Severe impact on daily life:

- **Daily Function:** Inability to eat solid foods, difficulty speaking, choking, constant sleep disruption due to oral dryness.
- **Oral Health:** Rapid dental decay, frequent oral infections, chronic oral and throat pain, inability to wear dentures.
- **Treatment Gap:** Current palliative options (sprays, lozenges) provide only transient and partial relief and do not restore gland function.



Large patient population with significant unmet need: US

Patient Need in Radiation-Induced Xerostomia (RIX)

Large patient population with high unmet need:

- **>170,000** long term grade 2/3 RIX patients in the US [1,2,3]
- (>2 years post radiation - called 'late xerostomia')
- **~ 54,000** new cases of head and neck cancer / year in US
- **>15,000** new persistent grade 2/3 RIX patients / year in the US [1,2,3]
- Patients are in the healthcare system in remission
- Patients seeing physicians at least annually

There are no effective treatment options for grade 2/3:

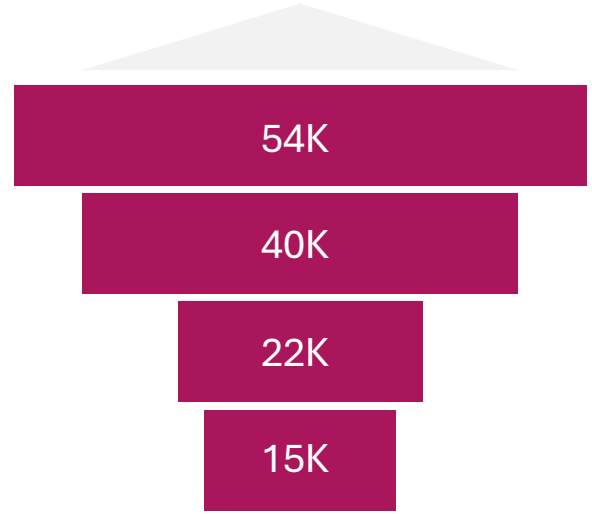
- **~83%** of grade 2 & 3 patients do not respond or do not tolerate currently available treatments

Prevalence (US)

170K
Grade 2/3 persistent late RIX patients in the US

Incidence (US)

15K
New cases of persistent late grade 2/3 RIX annually



AAV-AQP1 has the potential to provide meaningful benefit for moderate to severe RIX patients and to be the first disease-modifying therapy for RIX

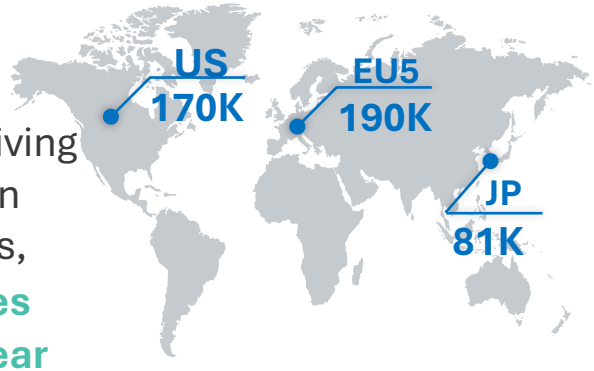
1. SEER, Cancer.net. 2 Marta GN et al (2014). Intensity-modulated radiation therapy for head and neck cancer: systematic review and meta-analysis. Radiother Oncol. 110(1):9-15. 3. Jensen S.B., et al. (2010). A systematic review of salivary gland hypofunction and xerostomia induced by cancer therapies: prevalence, severity and impact on quality of life. Support Care Cancer. 18(8)1039-1060.

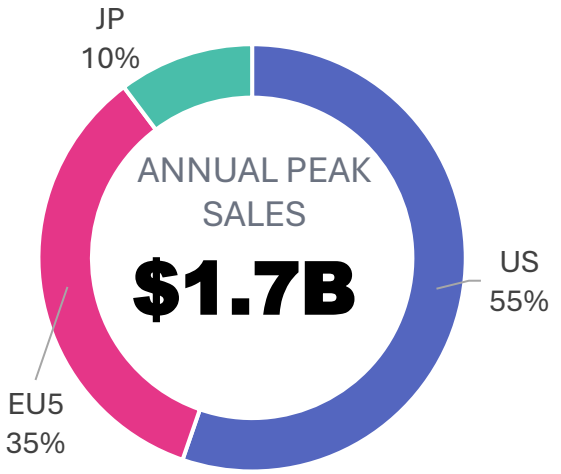
Significant commercial opportunity for a first-in-class treatment of a large patient population without effective therapeutic options in the 7 major markets

SIGNIFICANT PATIENT POPULATION

450K

Patients currently living with grade 2/3 RIX in the 7 major markets, with **58K new cases diagnosed each year**





Annual peak sales (RIX only) of **$1.7B globally** using conservative price assumption of $100K/patient in the US

Multiple opportunities for **higher peak sales from** label expansion: PSMA tx, Sjogren's

VERY LOW COGS

Low vector dose, efficient manufacturing process, and in-house manufacturing capabilities result in extremely low COGS, providing flexibility to support a broad range of sustainable price points

NO COMPETITION

There are currently no other industry-sponsored xerostomia treatments in clinical development

HIGH UNMET MEDICAL NEED

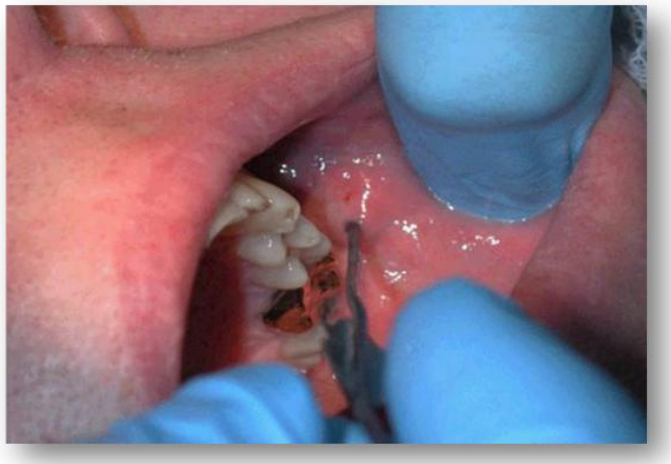
83%

of treated grade 2 & 3 RIX patients are inadequately controlled or cannot tolerate current SoC therapy (pilocarpine, cevimeline), which is **transient and ineffective**

AAV-AQP1: a one-time, outpatient treatment with disease-modifying potential

Therapeutic Approach

- AAV-AQP1 introduces the human aquaporin 1 gene (hAQP1) directly to salivary gland cells, rendering them permeable to water and increasing saliva output
- AQP1 forms a water conducting channel that increases the permeability of the salivary gland epithelium, permitting water to flow into the intra-ductal space
- **AAV-AQP1 is a one-time treatment with the potential to restore salivary function in patients with intractable RIX**



AAV-AQP1 is delivered locally to the parotid gland in a minimally invasive, brief, one-time outpatient procedure

Outpatient setting

Simple, minimally invasive procedure, with no need for anesthesia. ENTs and many dentists/oral surgeons are already trained in this procedure

Small, locally delivered dose

Avoiding potential safety risks associated with high dose / systemic exposure of AAV
No safety concerns in current clinical studies

One-time treatment

1x

Well tolerated by patients, a one-time treatment with durable efficacy

Disease-modifying therapy

Results in durable change in gland physiology and function – allowing water to flow through otherwise damaged impermeable glands

AQUAx: Phase 1 clinical study design

- Open-label, multi-center, dose-escalation study (4 sites, US/Canada)
- One-time administration of AAV-AQP1 to one (unilateral) or both (bilateral) parotid glands
- Four dose-escalating cohorts with 3 participants per cohort (n=12 for unilaterally treated and n=12 for bilaterally treated)
- All participants are followed for 1-year post-treatment and then invited to enroll in a long-term follow-up study for a total of 5 years

Primary endpoint

- Safety

Secondary endpoint

- Patient reported measures of xerostomia symptoms
- Xerostomia Questionnaire (XQ)
- MD Anderson Symptom Inventory – Head and Neck
- Global Rate of Change Questionnaire (GRCQ)
- Unstimulated whole saliva flow rate

Cohort	Dose
Unilateral treatment	
1	1×10^{11} vg/gland
2	3×10^{11} vg/gland
3	1×10^{12} vg/gland
4	3×10^{12} vg/gland
Bilateral treatment	
1b	3×10^{10} vg/gland
2b	1×10^{11} vg/gland
3b	3×10^{11} vg/gland
4b	1×10^{12} vg/gland

AQUAx: Safety

AAV2-hAQP1 was generally safe and well-tolerated at all doses tested

- No treatment-related serious adverse events
- No dose-limiting toxicities
- No participant discontinued from the study
- 6 mild, treatment-related, treatment-emergent adverse events (TEAEs)
  - All resolved without sequelae

Treatment-Related Treatment-Emergent Adverse Events in AQUAx study:

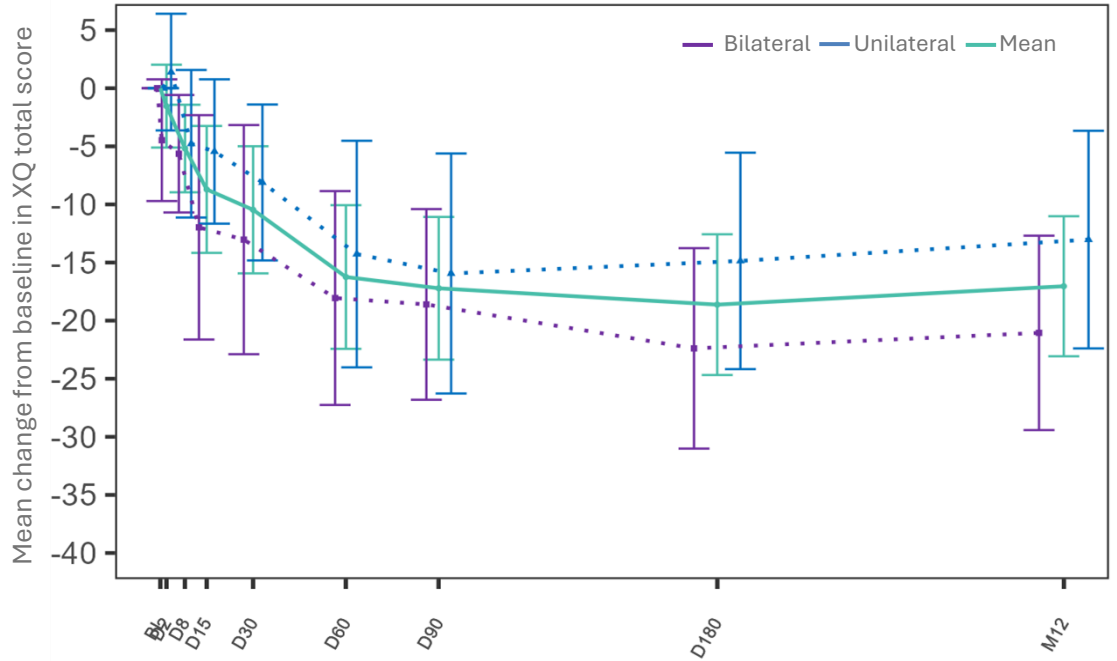
System Organ Class Preferred Term	All Participant N=24 N (%)
Participants with ≥1 treatment-related TEAE	6 (25.0)
Gastrointestinal disorders	2 (8.3)
Oral disorder	1 (4.2)
Salivary gland pain	1 (4.2)
General disorder and administration site conditions	2 (8.3)
Chills	1 (4.2)
Fatigue	1 (4.2)
Injection site pain	1 (4.2)
Eye disorders	1 (4.2)
Eye disorder	1 (4.2)
Investigations	1 (4.2)
Amylase increased	1 (4.2)
Nervous system disorders	1 (4.2)
Dysgeusia	1 (4.2)

AQUAx: Xerostomia Questionnaire (XQ)

- 8 symptom-specific questions which the participant answers using a scale from 0 (not present) to 10 (worst possible)
- Responses to individual questions are summed to provide the Total Score (0-80), an overall measure of disease burden
- An improvement (decrease) of **≥8 is considered clinically meaningful**[1,2], whereas an improvement of **≥10 points is considered transformative**

- **Average XQ score improved by 17 points (39.5%) at Month 12 (i.e., transformative improvement)**
- **Bilaterally treated participants reported greater improvement than those treated unilaterally (21 points vs. 13-points at Month 12)**
- **67% of participants reported an improvement of ≥8 points in the XQ total score at Month 12, with 75% of bilateral patients reporting transformative (>10 point) improvement at Month12**
- **Responses were durable up to 3 years (latest visit)**

Average change in XQ score



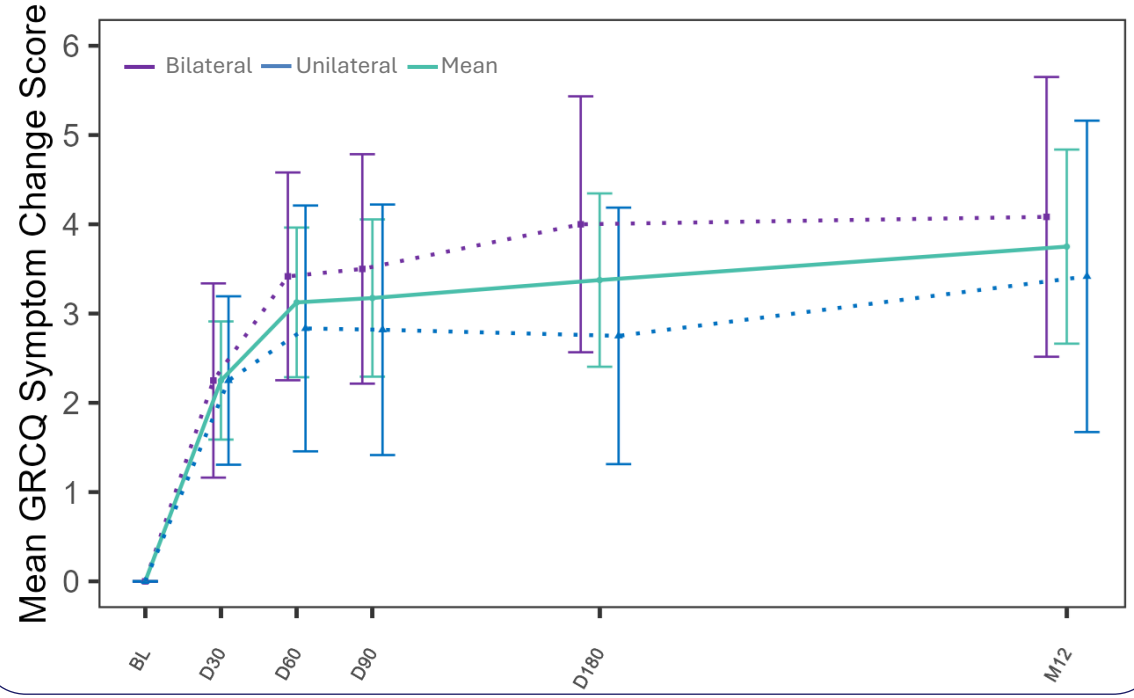
1. Eisbruch A et al. Xerostomia and its predictors following parotid-sparing irradiation of head-and-neck cancer. Int J Radiat Oncol Biol Phys. 2001 Jul 1;50(3):695-704. 2. Jabbari S et al. Matched Case–Control Study of Quality of Life and Xerostomia after Intensity-Modulated Radiotherapy or Standard Radiotherapy for Head-and-Neck Cancer: Initial Report. Int. J. Radiat. Oncol. Biol. Phys. 2005;63:725–731.

AQUAx: McMaster global rate of change questionnaire (GRCQ)

- A 2-point change in GRCQ is considered 'significant' by KOLs
- **A 3-point or greater change is considered a substantial improvement over standard of care and 'transformative' by KOLs**
- **The unilaterally-treated cohort achieved overall improvement of >3 points at 12 months**
- **The bilaterally-treated cohort achieved an overall improvement of 4 points by 6 months, which was maintained at 12 months**
- Overall improvements were maintained and increased over time in both unilateral and bilateral cohorts

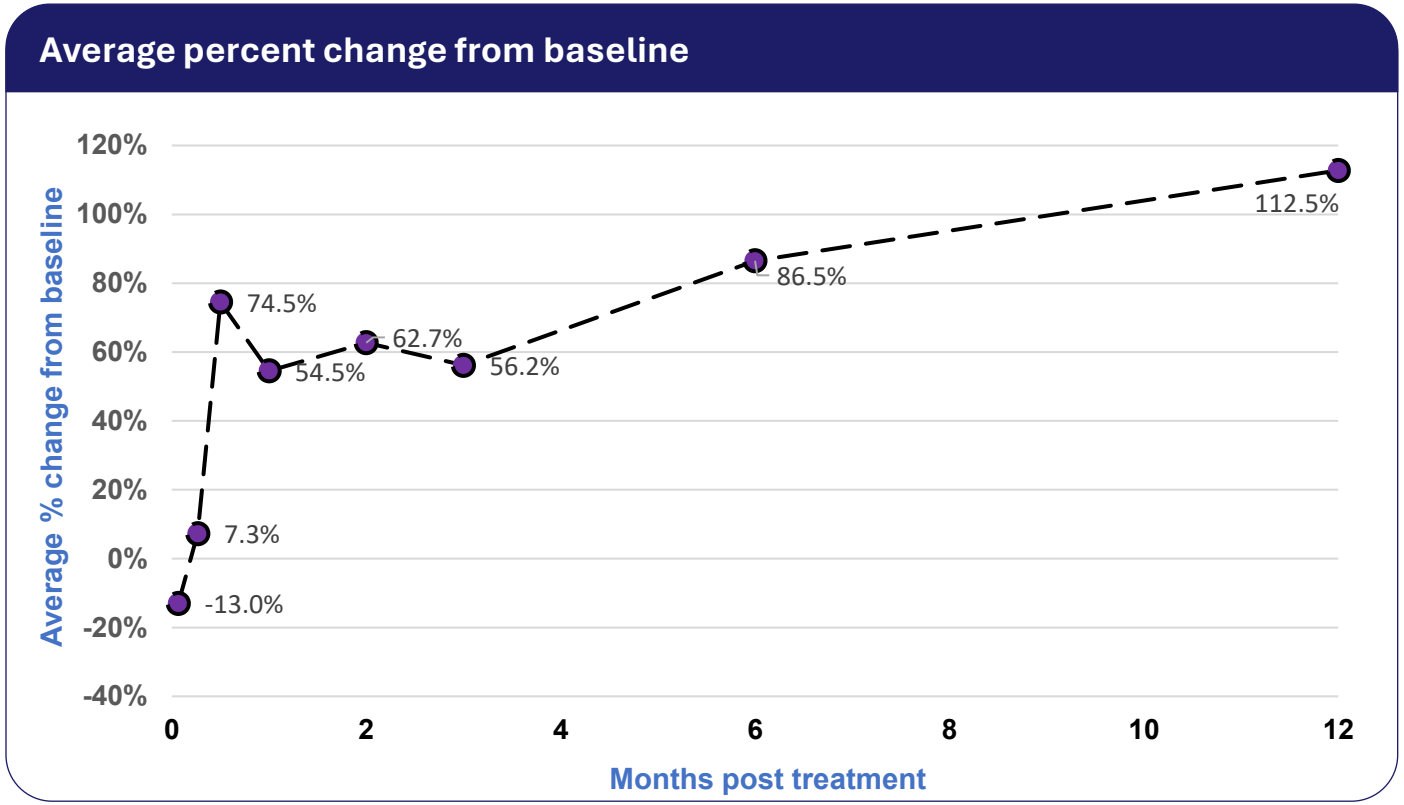
- **At Month 12, the average GRCQ Score was 3.8 (i.e., 'transformative' change), with bilaterally-treated participants reporting larger improvements than those treated unilaterally**
- **19/24 (79%) of participants reported "important" improvements in xerostomia symptoms at Month 12**

Average change in GRCQ score



AQUAx: Unstimulated whole saliva flow rate average percent change from baseline

At Month 12, the Unstimulated Whole Saliva Flow Rate increased from baseline by 112.5%

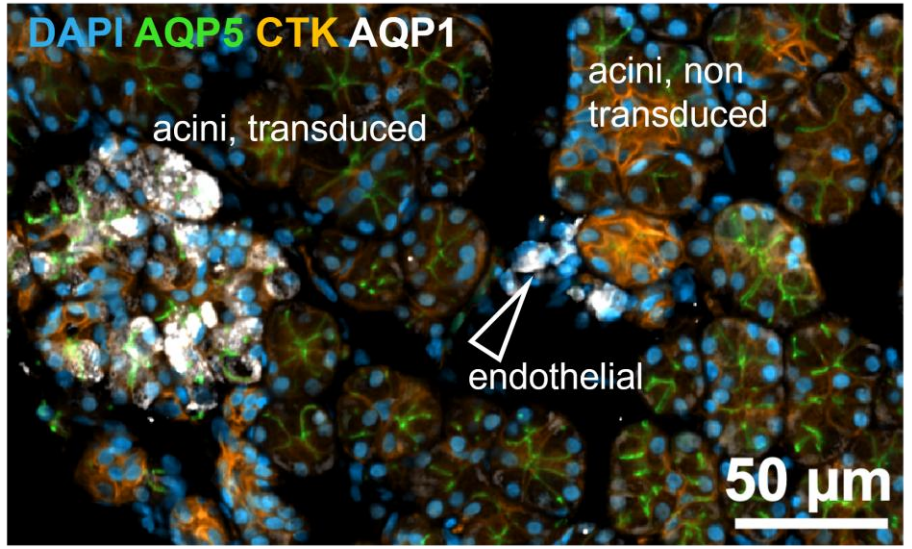


Biopsies indicate that AAV2-hAQP1 persists in the salivary gland

- Core needle biopsy were obtained in 7 participants who enrolled in a NIH Phase 1 study of AAV2-hAQP1 (MGT001).
- **6/7 biopsies showed AAV2-hAQP1 genomes 12-30 months post-treatment (depending on time point biopsy was taken)**
- There was a trend of increasing copy number of transduced vector genomes with increasing viral vector dose

Participant	Cohort	Dose per gland	Visit of Biopsy	Copy #/ng DNA	Copy #/Cell
AAV001	1	1E10	18 Months	160	0.96
AAV005	1	1E10	24 Months	122	0.73
AAV002	2	3E10	18 Months	236	1.4
AAV019	3	1E11	24 Months	5393	32
AAV020	4	3E11	30 Months	ND	ND
AAV021	4	3E11	12 Months	87390	524
AAV031	5	6E11	12 Months	7313	43

- The image on the right shows a core needle biopsy from a participant in the NIH Phase 1 study
- **AQP1 protein expression was observed in parotid gland cells at 24 months post-treatment**
- Acinar cells in this section express AQP1 (shown in white) whereas they normally express only AQP5 – here shown in green
- Levels of AQP1 protein in transduced acinar cells appear similar to the endogenous levels seen in non-parotid endothelial cells



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AQUAx: Summary of clinical data

Patient Reported Outcomes (PRO)

> **Three different instruments showed clinically meaningful and statistically significant improvements by Day 30 that were maintained through Month 12**

> **Across three PROs, bilaterally-treated participants reported greater improvement than those treated unilaterally**

- **Xerostomia Questionnaire (XQ):** A change of 10 points or more is considered a transformative improvement by KOLs. At Month 12, the average total XQ score improved by **17 points** from baseline, with **75%** of bilaterally-treated patients reporting transformative improvements
- **Global Rating of Change Questionnaire (GRCQ):** A change of 3 points or more is considered transformative. At Month 12, the average improvement in GRCQ score was **3.8**, with **79%** of participants reporting 'important' improvements in xerostomia symptoms
- **M. D. Anderson Symptom Inventory (MDASI):** At Month 12, the MDASI-HN-DM score improved by **2.7 points (42.2%)** from baseline

Unstimulated Saliva Flow Rate

Increased by **112.5%** over baseline at Month 12. An objective measure of therapeutic response.

Favorable Safety Profile

No treatment-related serious adverse events or dose-limiting toxicities were reported. All participants completed the study

AAV-AQP1: Program highlights

AAV-AQP1 has the potential to become the standard of care for long-term, grade 2/3 radiation-induced xerostomia patients based on its disease-modifying mechanism and meaningful improvements in both objective and subjective outcome measures

- One-time, minimally-invasive, local delivery of a single, small dose delivered through an outpatient cannulation procedure that ENTs and dentists trained in oral medicine are familiar with
- AAV-AQP1 treatment for grade 2/3 xerostomia is a large commercial opportunity given the high unmet need and large prevalent/incident patient population
- Expected to provide durable long-term benefit in this large population of severely affected patients with no other effective current treatment options
- AAV-AQP1 uses a small dose with low associated COGS - providing flexibility to support a range of sustainable price points for patients and payors
- Granted Orphan Drug and RMAT designations by FDA.
  RMAT provides benefits of both Fast Track and Breakthrough Therapy designations, including frequent FDA communication and guidance
- Written alignment with FDA on clinical design and requirements of BLA supportive Phase 2 study and CMC requirements for approval
- Pivotal Phase 2 study ongoing

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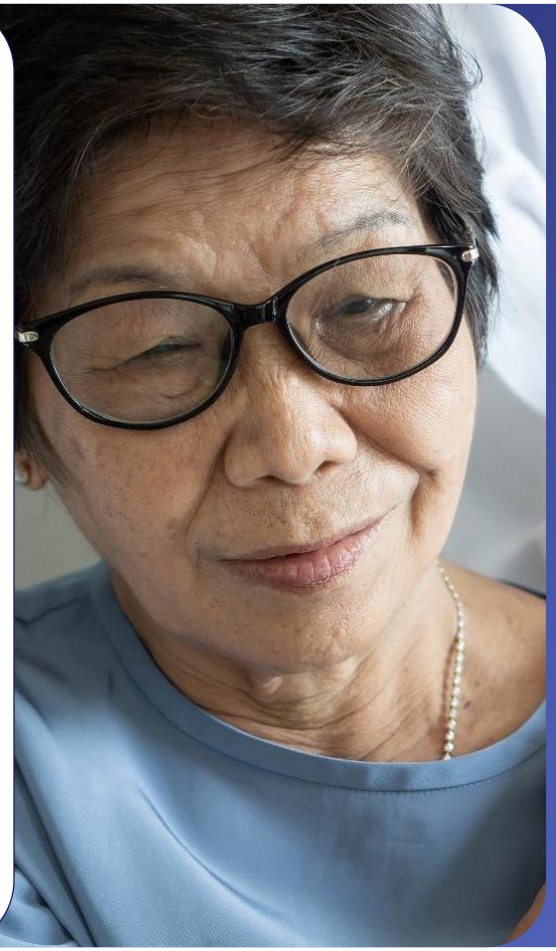
AAV-GAD: a first-in-class genetic medicine for treatment of Parkinson's disease

Phase 3 ready | evidence of disease modification | RMAT designation

Parkinson’s Disease

AAV-GAD overview

- Parkinson’s disease (PD) is the second most common neurodegenerative disease
- Approximately one million patients in the U.S. currently living with Parkinson's disease
- Individuals with PD initially respond to dopamine replacement therapy; however, over time, most patients become inadequately controlled by therapy or suffer from treatment-related complications
- **AAV-GAD is designed to locally deliver GABA, a neurotransmitter that can help restore normal brain circuitry in any form of Parkinson’s disease**
- **AAV-GAD has been tested in 58 patients across three clinical studies and is the only cell or gene therapy in PD to meet the prespecified primary endpoint in two randomized, double-blind, sham surgery-controlled trials**
- Granted RMAT designation by FDA – providing benefits of both Fast Track and Breakthrough Therapy designations



10M

Parkinson’s patients worldwide

$52B

Estimated economic burden of PD in the US

AAV-GAD: a first-in-class therapy for Parkinson's Disease

Therapeutic Approach

AAV-GAD delivers the Glutamic Acid Decarboxylase (GAD) gene locally into the sub-thalamic nucleus (STN)

GAD converts glutamate (excitatory neurotransmitter) to GABA (inhibitory neurotransmitter) to alleviate PD-associated hyperexcitation of circuitry controlling movement

- **Localized delivery of AAV-GAD directly into the STN**
  avoids safety risks associated with high dose/broad exposure of AAV in CNS. No safety signals in any studies
- **Standard and brief surgical procedure (same target site as DBS)**
  no need for general anesthesia, well-known surgical route for administration
- **One-time therapy**
  Post infusion no further intervention and no frequent follow-ups for tuning stimulation required

The Glutamic Acid Decarboxylase (GAD) gene is delivered locally to the STN.

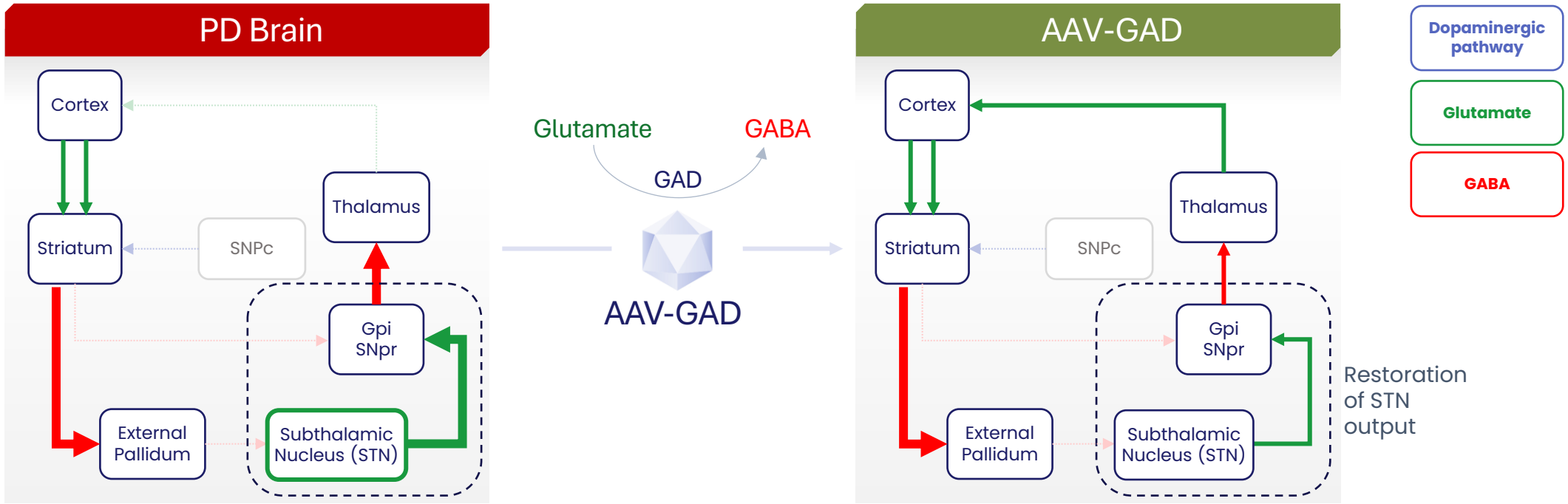
Conversion of glutamate to GABA via GAD normalizes GABA levels in the STN and at STN targets alleviating PD-related motor symptoms

Status: Phase 3 Ready

- **Positive clinical data from three clinical studies:**
  - Phase 1: unilateral, dose escalation study
  - Phase 2: bilateral, sham-controlled study
  - Sham-controlled bridging study using GMP material manufactured using commercial ready process in-house at MeiraGTx
- **Phase 3 ready – commercial ready drug product released early 2026**

Mechanism of action

AAV-GAD circumvents need for dopamine input to suppress STN hyperactivation, resulting in improved motor function



- In PD, loss of dopaminergic neurons in the substantia nigra (SNPc) results in decreased GABA input to the STN
- As a result of decreased GABA input, the STN is hyperactivated
- This results in uncontrolled activation of the basal ganglia output nuclei (GPi, SNpr), which then act to continually repress the activity of the thalamus – leading to the motor symptoms of PD

- **AAV-GAD, delivered directly to the STN, results in conversion of glutamate (excitatory neurotransmitter) to GABA (inhibitory neurotransmitter) locally in the STN**
- **Increased GABA and reduced glutamate output of the STN, releases the GPi and SNpr inhibition of the thalamus, leading to restored cortical activity and improved motor function**
- **Self-limiting autoregulation:** STN neurons express $GABA_A$ receptors, which inhibit further release of GABA upon increase in extracellular GABA levels

Results from a Phase 1, dose escalation study of AAV-GAD

Study design

Single-arm, open-label, dose escalation study of **unilateral** subthalamic administration of AAV-GAD in patients with PD (n=12)

Safety

- AAV-GAD was generally safe and well tolerated, with no adverse events related to the therapy
- No abnormalities were noted on postsurgical MRIs up to 1 year
- No evidence of adverse events in the perioperative period and for at least 1 year after treatment (most patients followed up for >2 years)
- No evidence of vector-related immunity

Efficacy findings

- Significant improvements in motor UPDRS scores, predominantly on the side of the body contralateral to surgery, were seen as early as 3 months after therapy and persisted to 12 months (latest follow-up)
- PET scans revealed a substantial improvement in thalamic metabolism that was restricted to the treated hemisphere
- Correlation found between clinical motor scores and brain metabolism in the supplementary motor area

Kaplitt MG et al. 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

Results from a Phase 2, randomized, double-blind, sham-controlled, multi-center study of AAV-GAD

Study design

- Randomized (n=45, 1:1) double-blind study of bilateral STN AAV-GAD against sham control in patients with advanced Parkinson's Disease
- Primary endpoint: change in off-medication UPDRS Part 3 score at 6 months between treated and sham

Safety

- AAV-GAD was generally safe and well tolerated with no SAEs related to the therapy
- Other adverse events were mild or moderate, likely related to surgery and resolved
- Worsening of PD was reported in 35% of sham patients vs. 0% of AAV-GAD, further supporting efficacy
- No difference in neuropsychological, speech and depression ratings

AAV-GAD is the only interventional gene or cell therapy study in PD to meet the primary clinical endpoint in a sham-controlled study

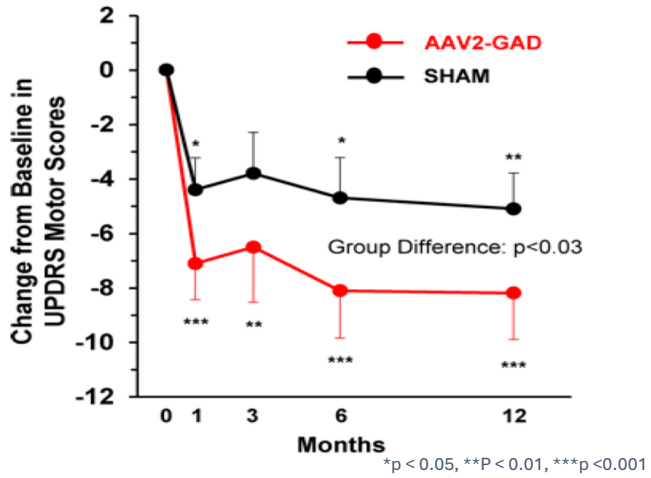
Efficacy findings (summary):

- **Study met primary endpoint: UPDRS 3 motor score improvements were significantly greater in the AAV-GAD treated group vs. sham at 6 months; Improvements persisted at 12 months**
- Significantly greater responder rate in AAV-GAD treated group (50%) compared with sham (14.3%)
- Improvements in secondary outcome measures, including ON time across 12 months (no change in sham at any time point)
- Significant reduction in medication complications at 6 and 12 months (UPDRS 4) in AAV-GAD group (vs. no change in sham at any point)
- FDG-PET imaging showed significant changes in brain motor networks of AAV-GAD subjects not observed in the sham group

LeWitt PA. AAV2-GAD gene therapy for advanced Parkinson's Disease: a double-blind, sham-surgery controlled, randomized trial. Lancet Neurology. 2011; 10(4):309-19.
Niethammer M. Long-term follow-up of a randomized AAV2-GAD gene therapy trial for Parkinson's disease. JCI Insight. 2017; 2(7):e90133.

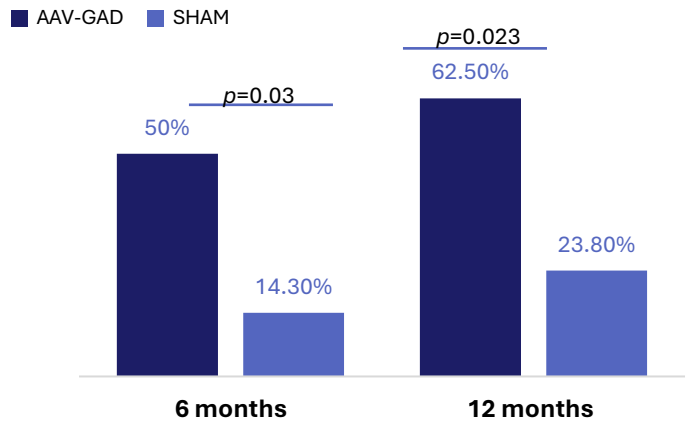
Results from the Phase 2 study: significant improvements following AAV-GAD treatment compared to sham surgery control

Significant improvements in UPDRS 3 motor scores



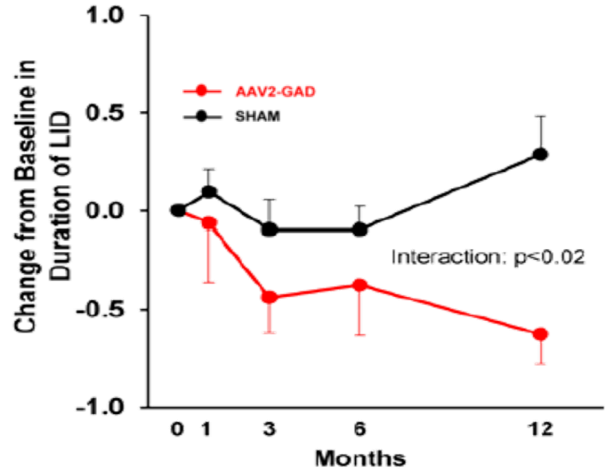
- **Met primary outcome measure: improvement in UPDRS 3 motor scores vs. sham at 6 months**
- Improvements in the AAV-GAD group were observed at all time points

Significantly greater responder rate ≥9 points UPDRS



- A 9.0 point improvement in UPDRS motor score corresponds with a 25% improvement from average baseline score
- **Significantly greater responder rate was observed in the AAV-GAD group (50%, 8/16) vs. sham group (14%, 3/21) at 6 months and 12 months (10/16 vs. 5/21 patients)**
- 7/8 subjects in the AAV-GAD group who were classified as responders at 6 months, remained responders at 12 months (vs. only 1 of 3 subjects in the sham group)

Reduction in duration of levodopa-induced dyskinesia



- **Significant improvement in drug-induced dyskinesia at 12 months relative to baseline in the AAV-GAD group (vs. no change in the sham group)**

LeWitt PA. AAV2-GAD gene therapy for advanced Parkinson's Disease: a double-blind, sham-surgery controlled, randomized trial. Lancet Neurology. 2011; 10(4):309-19.
Niethammer M. Long-term follow-up of a randomized AAV2-GAD gene therapy trial for Parkinson's disease. JCI Insight. 2017; 2(7):e90133

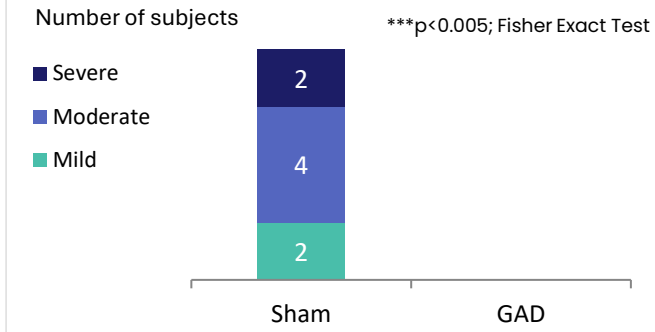
AAV-GAD treatment is safe & well tolerated

Worsening of Parkinson's observed in sham group but not in AAV-GAD treated group

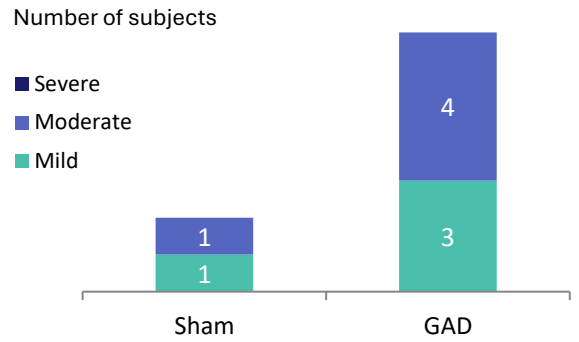
Adverse events over 12 months (20% or greater frequency)

- **Worsening of Parkinson's Disease occurred in 8 sham subjects but was not reported for any AAV-GAD subject, further supporting efficacy outcomes in the AAV-GAD group**

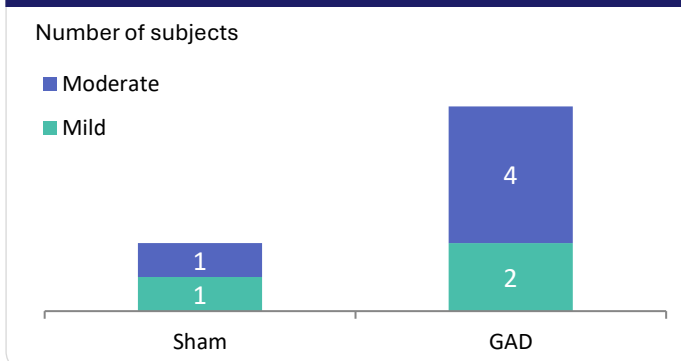
Worsening of Parkinson's Disease



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	

AAV-GAD therapy shows evidence of disease modification

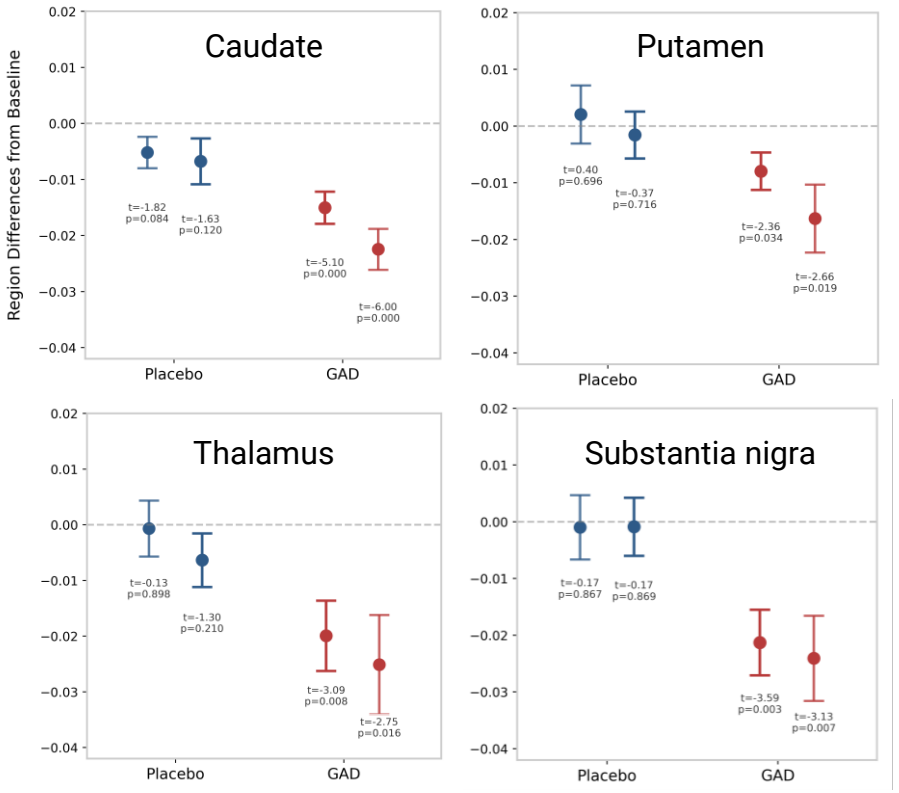
Disease modification in preclinical models[1]

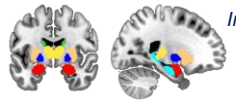
- Preclinical studies in animal models of PD have shown that treatment with AAV-GAD directly into the STN not only normalizes the function of the STN but also leads to consequent reduction in the pathological hyperexcitation of the downstream basal ganglia and the substantia nigra
- **These experiments also demonstrated a significant neuroprotective effect in the substantia nigra, increasing the survival of dopaminergic neurons i.e., physiologically slowing the progression of the disease**

Evidence of disease modification from clinical studies

- Comparison of blinded FDG-PET data from sham and treated patients in the double-blind sham controlled AAV-GAD clinical studies has shown significant reduction in the activity of critical basal ganglia regions known to be hyperexcited in PD
- **This demonstrates a disease-modifying effect on the pathological circuitry of the brain that underpins the clinical manifestations of PD**
- **In addition, FDG-PET analysis has shown reduction in pathological hyperexcitability within the substantia nigra**, confirming the observations in animal studies, exerting a neuroprotective effect with the potential to reduce the rate of dopaminergic loss
- **No other treatment in PD has shown such potentially disease modifying effect**

FDG-PET data from AAV-GAD clinical trials shows disease-modifying effects in the basal ganglia circuitry, including the substantia nigra – the site of dopamine-producing neurons affected in PD





In collaboration with

HOLOGEN AI

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1- Luo J, Kaplitt MG, Fitzsimons HL, et al. Subthalamic GAD gene therapy in a Parkinson's disease rat model. Science. 2002;298(5592):425-429.

Positive topline data summary from AAV-GAD sham surgery-controlled Bridging Study

A 6-month, three-arm, randomized, double-blind, sham-controlled study using material manufactured in-house at MeiraGTx

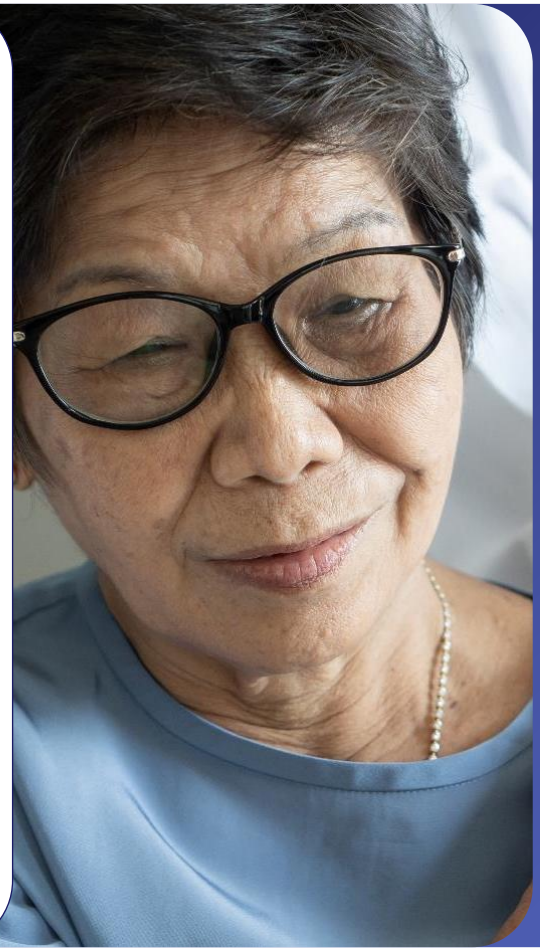
- 14 subjects were randomized to one of three groups receiving bilateral STN AAV-GAD infusions: low dose group (3.5×10^{10} vg per STN, n=5), high dose group (10.5×10^{10} vg per STN, n=5) and sham control (n=4)
- AAV-GAD Drug Product was manufactured at MeiraGTx using its commercial platform process at its wholly-owned facilities

Summary of results:

- **AAV-GAD was generally safe and well tolerated with no serious adverse events related to AAV-GAD treatment**
- **Significant, clinically meaningful improvements demonstrated in AAV-GAD treated subjects for key efficacy endpoints**
- **At Week 26, a statistically significant 18-point average improvement from baseline in UPDRS part 3 "off" medication score was demonstrated in the high dose group (p=0.03), with no significant change in the sham or low dose groups**
- **Significant improvement from baseline in the disease-specific, patient-reported quality of life PDQ-39 score was demonstrated in both the high and low dose groups with no change in the sham group at Week 26**
- For more information on the AAV-GAD bridging study, please see press release here

Summary: AAV-GAD for treatment of Parkinson's disease

- **AAV-GAD is the only CNS gene therapy program tested in three human trials – meeting a prespecified efficacy primary endpoint**
  - A total of 58 patients in 3 independent multicenter clinical studies received AAV-GAD treatment
  - AAV-GAD was safe and well tolerated in all doses tested, with no treatment-related SAEs
- **The only CNS gene therapy program with two randomized, double-blind, sham surgery-controlled trials which met prespecified primary endpoint**
- **Evidence of disease modification – from blinded FDG-PET imaging from the sham controlled clinical studies supported by data frompreclinical models**
- **Granted RMAT designation in 2025**
- **Program status: Phase 3 ready**



- ☑ Large market with high unmet need in patients no longer responding to dopamine therapy
- ☑ One-time treatment; standard surgical procedure, short OR time, no need for general anesthesia
- ☑ One time local delivery of AAV – safety and low COGS
- ☑ Internally manufactured by MeiraGTx using commercial-ready, high yield process

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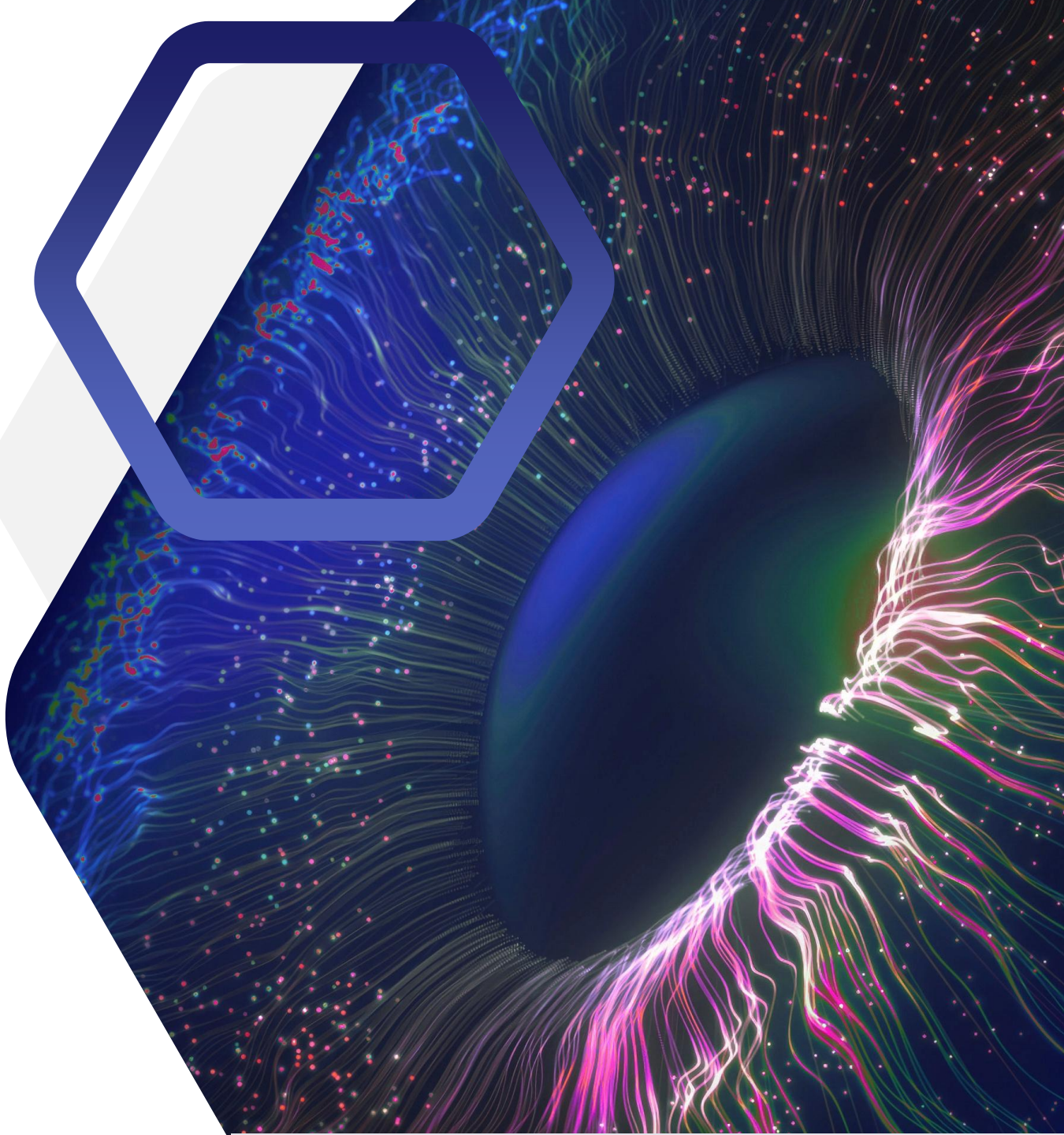
AAV-AIPL1 for treatment of AIPL1-associated retinal dystrophy[1]

Restoring vision in children who are born legally blind

Near term Path to Marketing Authorization under exceptional circumstances | RPDD, Orphan Drug Designation in US & EU



[1] Partnered with Eli Lilly

AIPL1 video

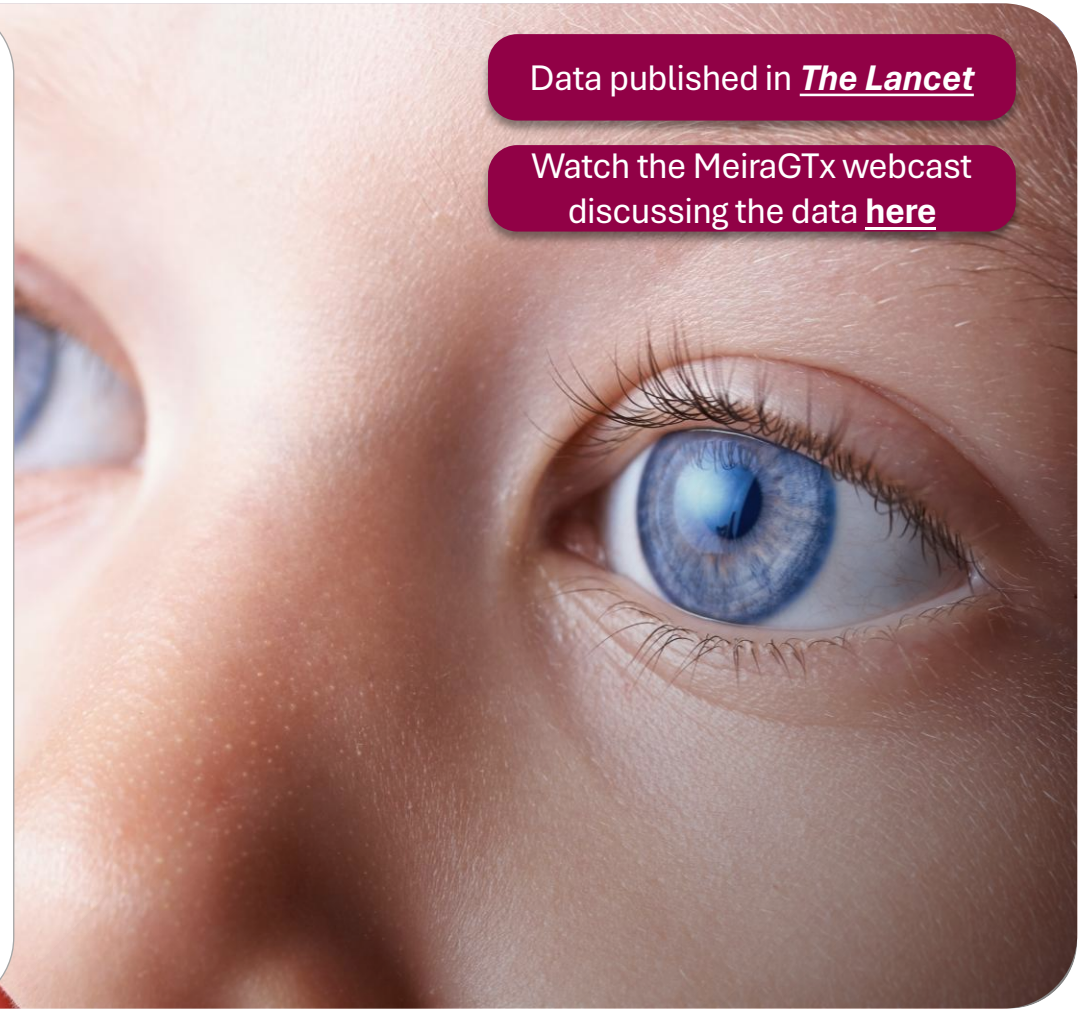
Click to play video

AAV-AIPL1 for treatment of LCA4 retinal dystrophy[1]

Near term path to marketing authorization in UK and US

A novel treatment for AIPL1 congenital blindness

- Children with AIPL1-associated retinal dystrophy (LCA4) are blind from birth. By age 4, retinal degeneration is complete and irreversible
- There are currently no approved treatments for AIPL1-LCA4
- **Clinical data from 11 children demonstrated transformative efficacy[2]: 100% of treated children, who were legally blind from birth, now have visual acuity with benefits seen as early as one month following treatment**
- The visual improvements in all 11 children have also resulted in life-changing benefits in all areas of development, including communication, behavior, schooling, mood, psychological benefits and social integration
- AAV-AIPL1 treatment was generally safe and well tolerated with no treatment-related SAEs
- **These improvements are unrivalled in treatment benefit compared to any other ocular therapy, including any approved or published ocular gene therapy**
- **Near-term path to marketing approval in UK and US**



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[1] Partnered with Eli Lilly

2- Michaelides, M., Laich, Y., Wong, S. C., Georgiadis, I., Moosajee, M., Lanza, R., Ali, R. R., & Saper, V. (2025). Gene therapy in children with AIPL1-associated severe retinal dystrophy: an open-label, first-in-human interventional study. The Lancet, 405(10479), 648–657.

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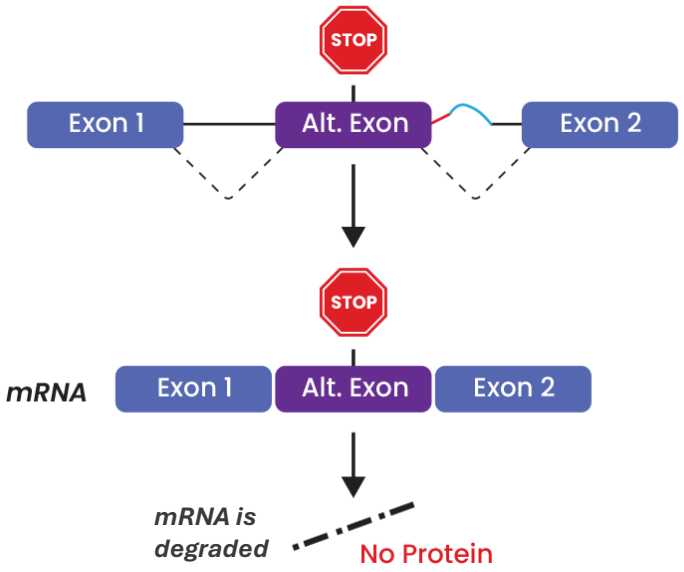
Riboswitch Gene Regulation Platform

In vivo production of vectorized therapeutic proteins and peptides with oral inducers

Riboswitch platform: precise *in vivo* production of therapeutic proteins via oral small molecule inducers

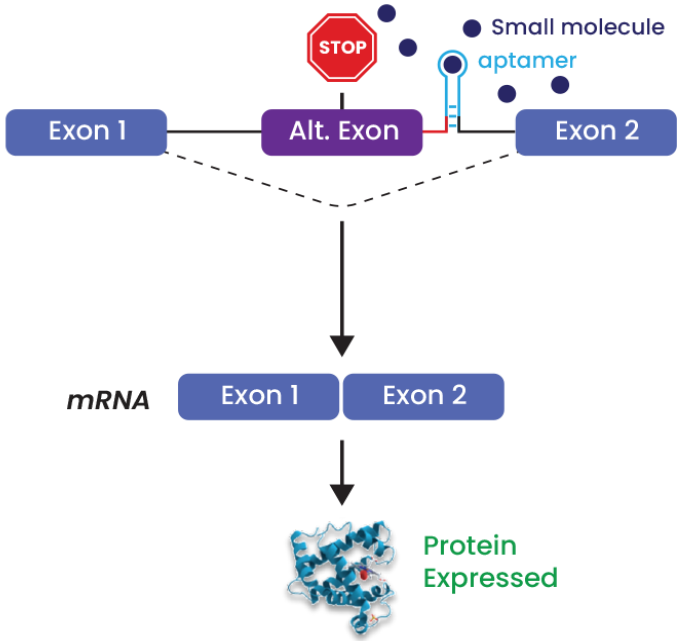
mRNA formation is controlled by alternative splicing cassette via binding of a small molecule inducer to the Riboswitch cassette

No small molecule (OFF state)



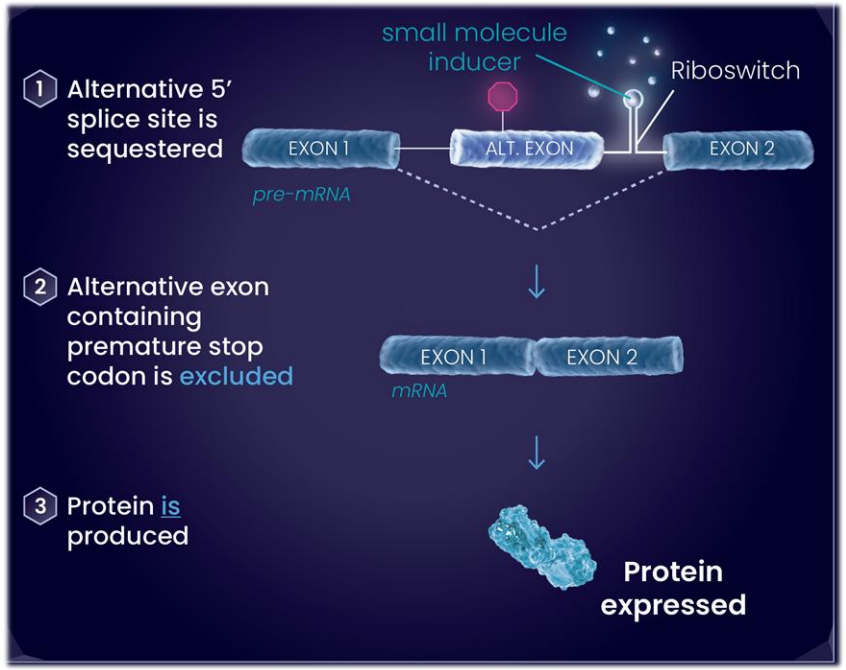
In the absence of the small molecule inducer ("OFF state"), the incorporation of an alternative exon with a premature stop codon drives degradation of the mRNA transcript via the ubiquitous process of nonsense-mediated decay (NMD)

With small molecule (ON state)



Binding of the small molecule inducer to the Riboswitch aptamer drives stabilization of a hairpin structure which incorporates the 5' splice site of the second intron, triggering splicing out of the alternative exon and production of a stable, protein-encoding transcript

Riboswitch provides significant advantages over other inducible systems



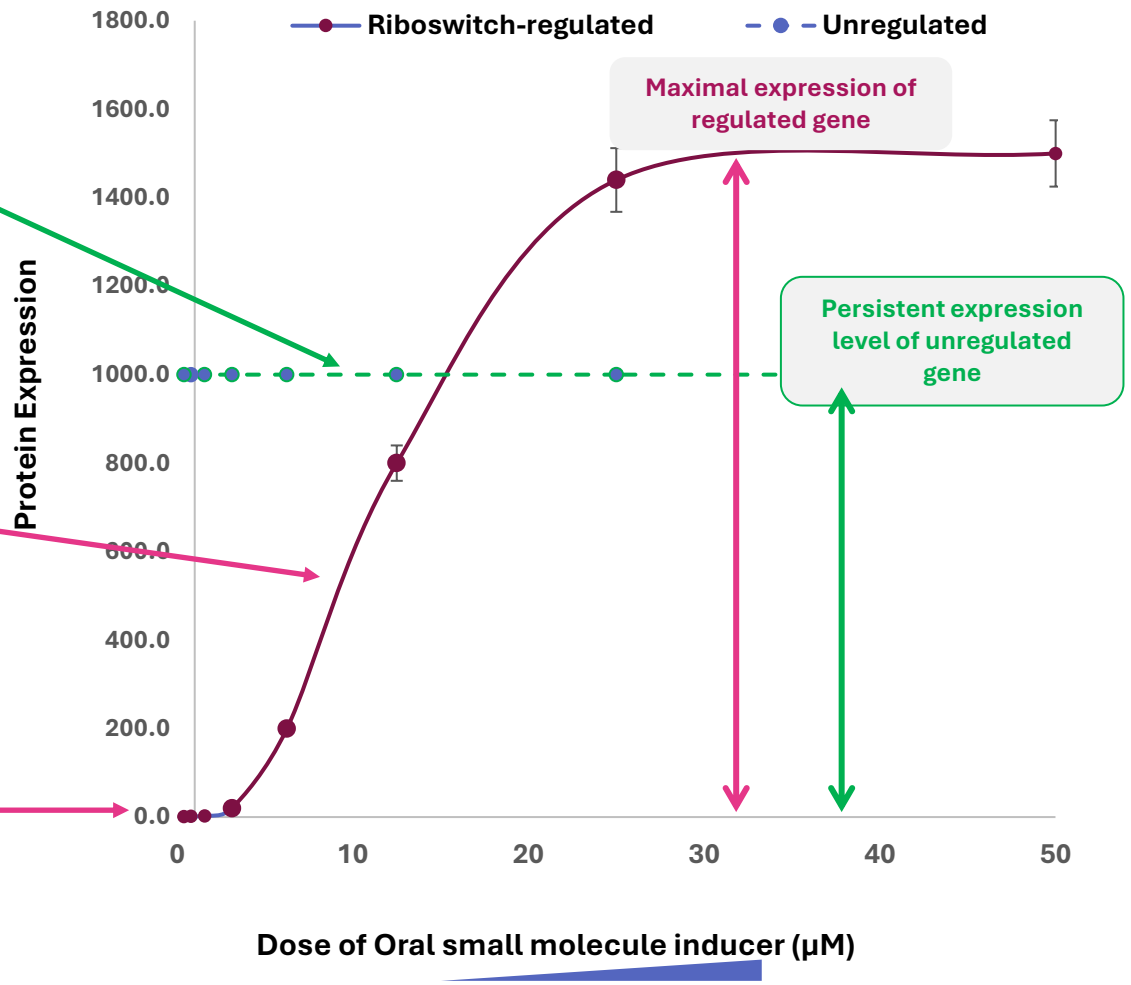
- The native form of any biologic therapeutic can be encoded by the DNA template and produced *in vivo*, controlled by bespoke oral small molecules
- Extremely precise dosing of biologic therapeutics with the production of the therapeutic protein dependent on the oral small molecule inducer pharmacodynamics (PD)
- Dosing of native form of therapeutic results in same properties and function as the endogenous protein or peptide: i.e.: crosses the BBB and acts on CNS receptors
- Pulsatile delivery of naturally short-lived peptides results in more physiological function with improved efficacy and reduced side effects - in contrast to infrequent high doses of synthetic long-lasting peptides.
- Durability of biologic therapeutic production and maintenance of efficacy, PD and dynamic range demonstrated for greater than a year in murine models
- DNA template be delivered via any vector (viral or non- viral), *ex vivo* or *in vivo*

Riboswitch splicing cassette drives precise control of therapeutic protein production with unprecedented dynamic range and precision

Expression level of the gene construct without the Riboswitch cassette is independent of small molecule dosing

Expression of Riboswitch containing transgene in precise dose response to the oral small molecule inducer dose

Basal expression of regulated construct without small molecule inducer



Riboswitch regulated gene expression:

- Precise dose response to oral small molecule dose
- Basal level with no small molecule undetectable
- Maximum expression higher than the identical gene construct lacking the Riboswitch cassette – splicing event drive mRNA efficiency and stability improving protein production

A broad range of therapeutic proteins encoded by Riboswitch-containing transgenes show tight control via oral small molecule dosing, *in vivo*

Therapeutic Antibodies

- Anti-PCSK9
- Anti-VEGFR2 (eye)
- Anti-Amyloid
- Anti-IL-17
- Anti-PD1
- Anti-HER2
- Anti-IL4Ra
- Anti-Myostatin

Cell Therapy

Ribo-CAR:

- Anti-CD19
- Anti-PSMA
- Anti-mesothelin
- Anti-HER2

Therapeutic Hormones/Cytokines /Peptides

- Epo
- hGH
- PTH
- Insulin
- GLP-1R agonists
- Gut peptide combinations: GLP1- GIP; GLP1, GIP, PYY, Glucagon, Amylin, Oxyntomodulin
- Myokines
- Adipokines e.g: leptin

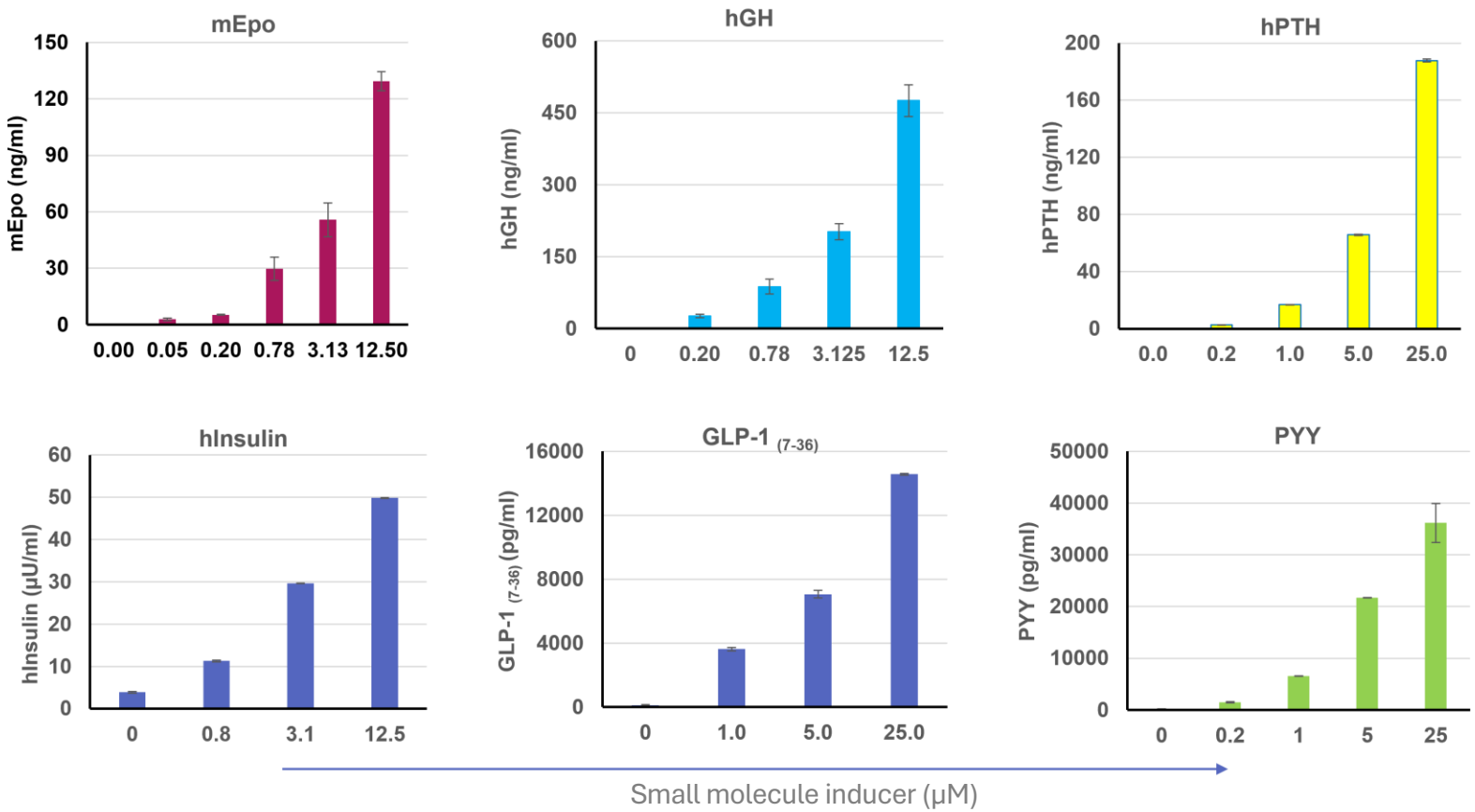
Gene/RNA Editing Nucleases

- Cas9
- CasRx

Precise regulation of multiple therapeutic hormones and peptides with riboswitch, *in vitro*

The riboswitch platform can be applied to any transgene and delivered by any vector - achieving *in vivo* production of the therapeutic protein or peptide in a precise dose response to a bespoke orally administered small molecule inducer.

- Graphs to the right show examples of regulation of human hormones in response to dosing with a small molecule riboswitch inducer, *in vitro*
- Many of these targets have been validated in relevant animal models, showing precise control of therapeutic protein serum levels and therapeutic effect driven by the dose of the oral small molecule inducer



Riboswitch regulation of metabolic peptides, alone or in combination

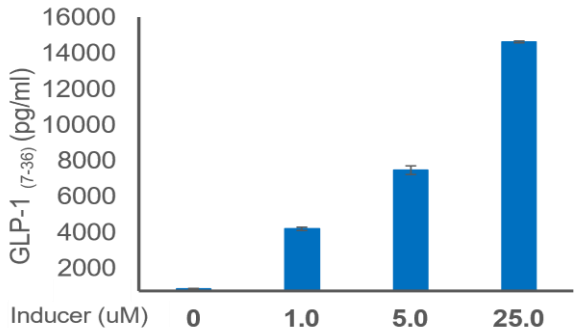
In vivo production of natural gut peptides

- Delivery of high effective levels of active peptides can be challenging. MeiraGTx has achieved high expression of natural gut peptides, alone or in combination produced by the oral dosing of a small molecule activator
- The Riboswitch platform provides tight and controlled expression of unmodified, wild-type peptides
- Delivery of multiple combinations of peptides can be achieved using a single vector

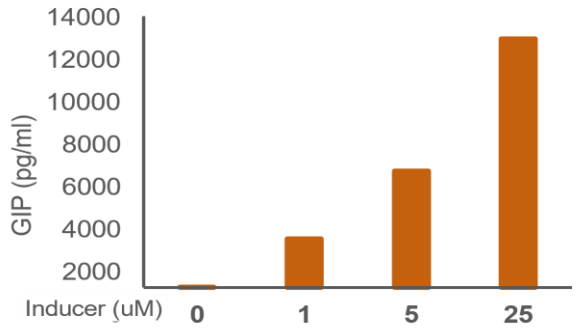
These can be constructed and tested rapidly head-to-head to provide fast *in vivo* proof of concept of efficacy and benefit on **muscle mass, metabolism, and feeding as well as behavior and CNS impact**

Riboswitch regulation cassette controls the expression of combinations of gut peptides GLP-1, GIP and PYY, *in vitro*

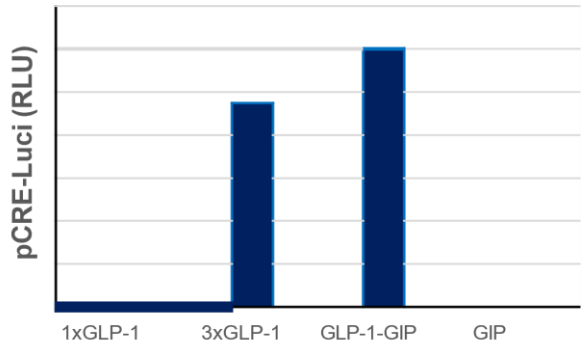
GLP-1 expression



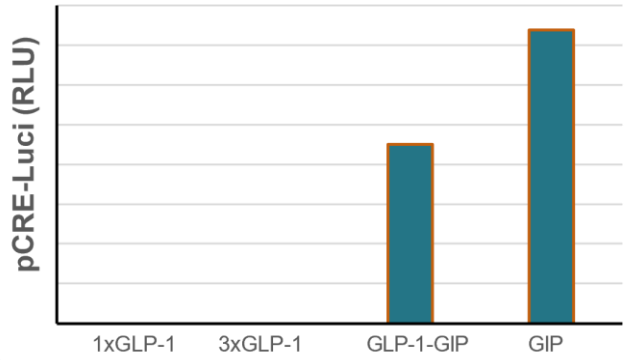
GIP expression



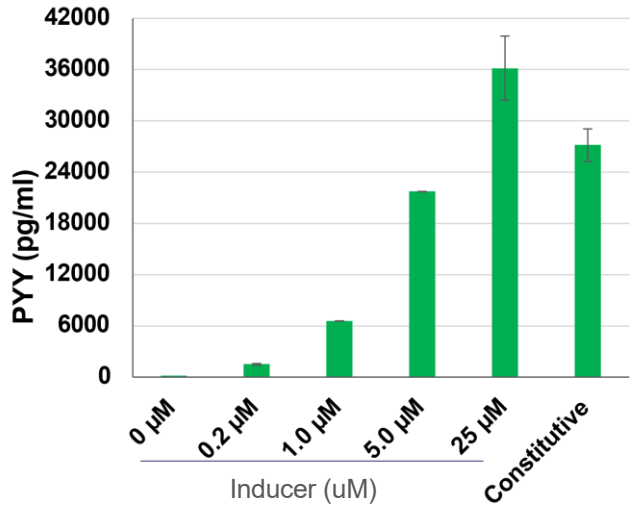
GLP-1 activity specifically on GLP-1 receptor



GIP activity specifically on GIP receptor



PYY expression

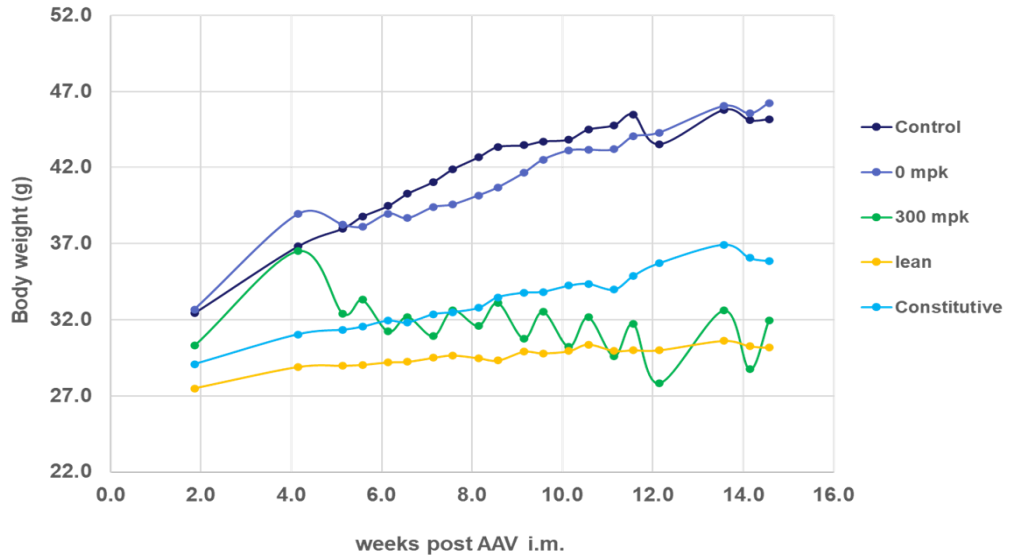


MEIRAGTx

In vivo delivery of GLP1-GIP via daily oral inducer dosing significantly improves weight loss and glucose control compared to constitutively expressed GLP1-GIP

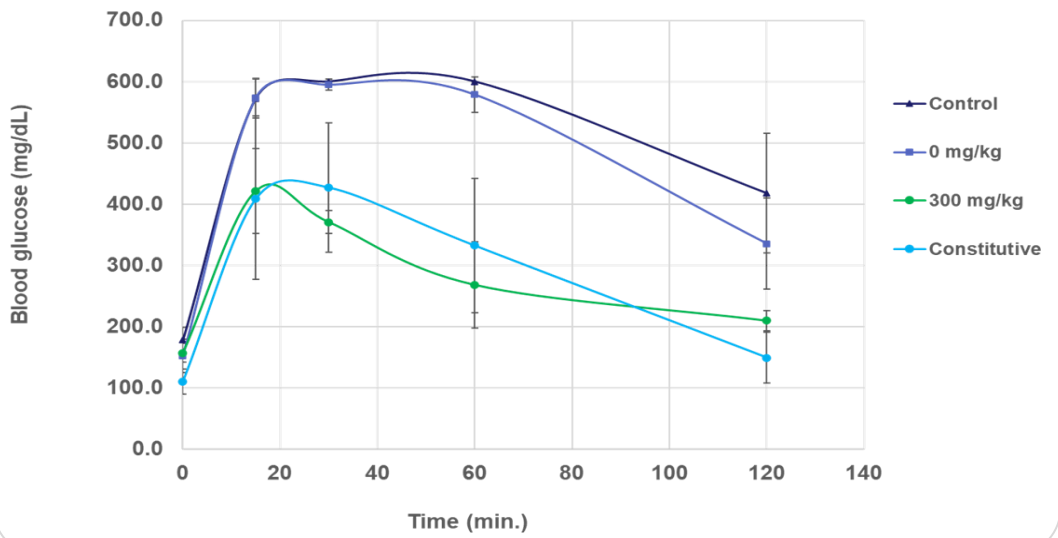
GLP1-GIP: comparison of constitutive expression of the dual peptides compared to daily *in vivo* delivery induced by oral small molecule

Weight loss in DIO mice



- Untreated DIO mice gain weight persistently over the 15 weeks of the experiment (dark blue line). Expression of GLP1-GIP from the constitutive vector (light blue line) results in weight reduction
- **Daily oral dosing of the small molecule (green line) results in rapid and persistent weight loss, with mice reaching lean weight (black line) 8-10 weeks after small molecule dosing has begun**
- **The "zig zag" line reflects the fact that the animals were only dosed on weekdays and not on weekends, indicating that in the absence of the small molecule, GLP1-GIP production diminishes; the native form of the peptide is expressed in a pulsatile fashion resulting in improved efficacy over time**

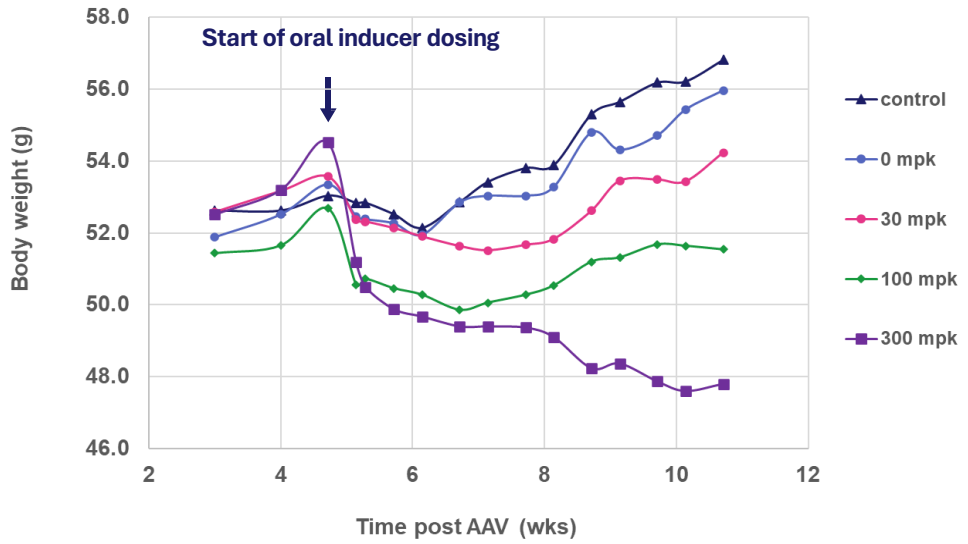
Glucose Control in DIO mice



- Control untreated DIO animals (green line) show poor glucose control following a glucose challenge
- No improvement in glucose control is observed in animals with the regulated GLP1-GIP construct in the absence of oral dosing of the small molecule (light blue line 0 mg/kg)
- Glucose control is clearly improved when GLP1-GIP is constitutively present (dark blue line)
- **Rapid glucose control is seen in animals receiving GLP1-GIP via daily dosing of the small molecule (pink line)**

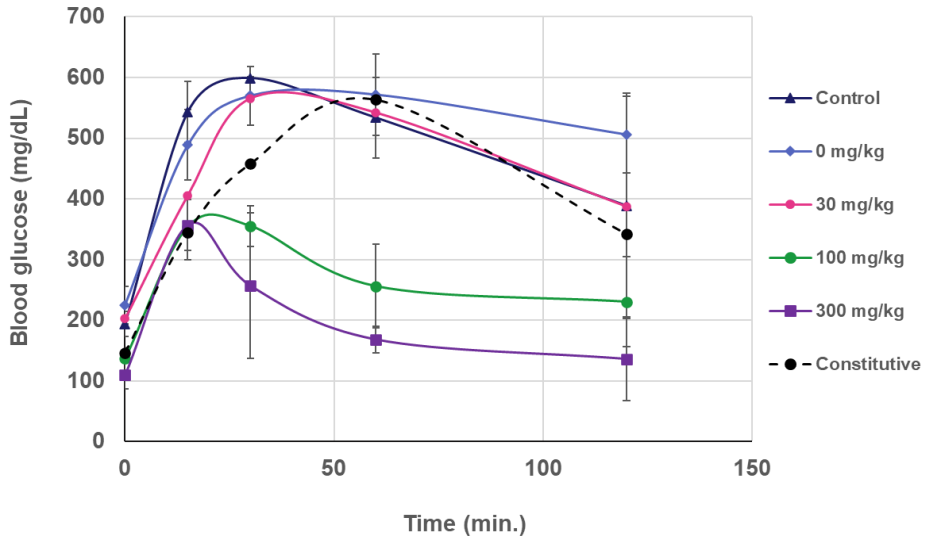
In vivo delivery of GLP1-GIP-Glucagon via daily oral inducer dosing significantly improves weight loss & glucose control vs. constitutive GLP1-GIP-Glucagon

Weight loss in DIO mice



- Untreated DIO mice show persistent weight gain over 10 weeks (black line - control)
- The regulated construct in the absence of the small molecule (blue line, 0 mg/k) shows no significant difference in weight gain from the DIO mice
- A 30 mg/kg and 100 mg/kg dose of the small molecule delivered orally daily (including weekends) resulted in weight loss in a dose dependent manner (pink and green lines)
- **When the oral small molecule dose was further increased (purple line) - persistent and significant weight loss was observed**
- In this experiment, animals received an oral dose of the small molecule every day, including weekends

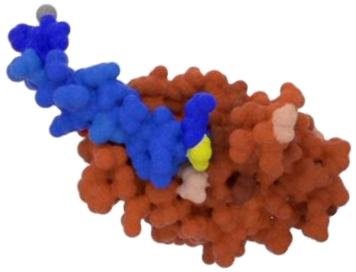
Glucose Control in DIO mice



- Untreated DIO animals show poor glucose control post glucose challenge (black line - control)
- The regulated construct in the absence of the small molecule (blue line, 0 mg/k) shows no difference from untreated DIO mice in glucose control
- **A dose response is seen with respect to glucose control - with the higher dose providing the most rapid glucose control (purple line)**
- **In contrast, animals with persistent GGG activity showed complete failure in glucose control (dotted line)**

In vivo production of peptide therapeutics addresses several challenges in current pharmacological treatment of metabolic disorders

Short lived agonists in responsive homeostatic systems which function to rapidly react to environmental changes (e.g. food intake) work better when the receptors are not persistently activated



GLP-1 and receptor complex

Efficacy

- Native/natural short acting peptides can be delivered and precisely controlled with oral small molecule inducers
- These may be more efficacious than synthetic injected peptides due to receptor binding dynamics and ability to cross the BBB. Ie: native peptide target the right receptors in the right places
- More efficacious combinations can be designed and tested in weeks without synthetic peptide chemistry, addressing key shortcomings such as muscle loss and fat re-gain
- *in vivo* delivery of short acting agonist peptides results in significantly improved efficacy compared to the same constitutively active peptides
- Improved weight loss and post prandial glucose control

Safety & Tolerability

- Lower levels of short acting native peptides produced endogenously in response to bespoke oral small molecules may have better efficacy, safety and tolerability than persistently active synthetic injectable peptides or small molecule receptor activators

Patient Access, Manufacturing & COGS

- Patient's cells produce the therapeutic peptides, circumventing costly peptide manufacturing and need for injection

Riboswitch-regulated leptin therapy (riboLeptin) - Summary

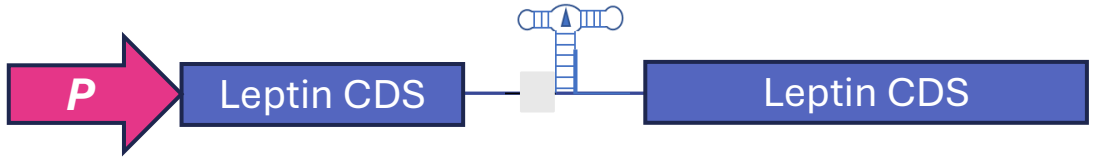
- **Leptin** is a key hormone regulating energy balance and metabolic homeostasis. In healthy individuals, when fat reserves are high, leptin levels rise – signaling satiety and promoting energy expenditure. Conversely, when fat stores are low, leptin levels decrease, triggering hunger and encouraging the body to conserve fat
- **Lipodystrophy:** deficiency or loss of Leptin causes lipodystrophy - a group of potentially life-threatening disorders that affect how the body stores and uses fat. Patients present with a broad range of symptoms, including organ abnormalities (e.g. hepatic steatosis, nephropathy and pancreatitis) and metabolic abnormalities (diabetes, insulin resistance and hypertriglyceridemia)

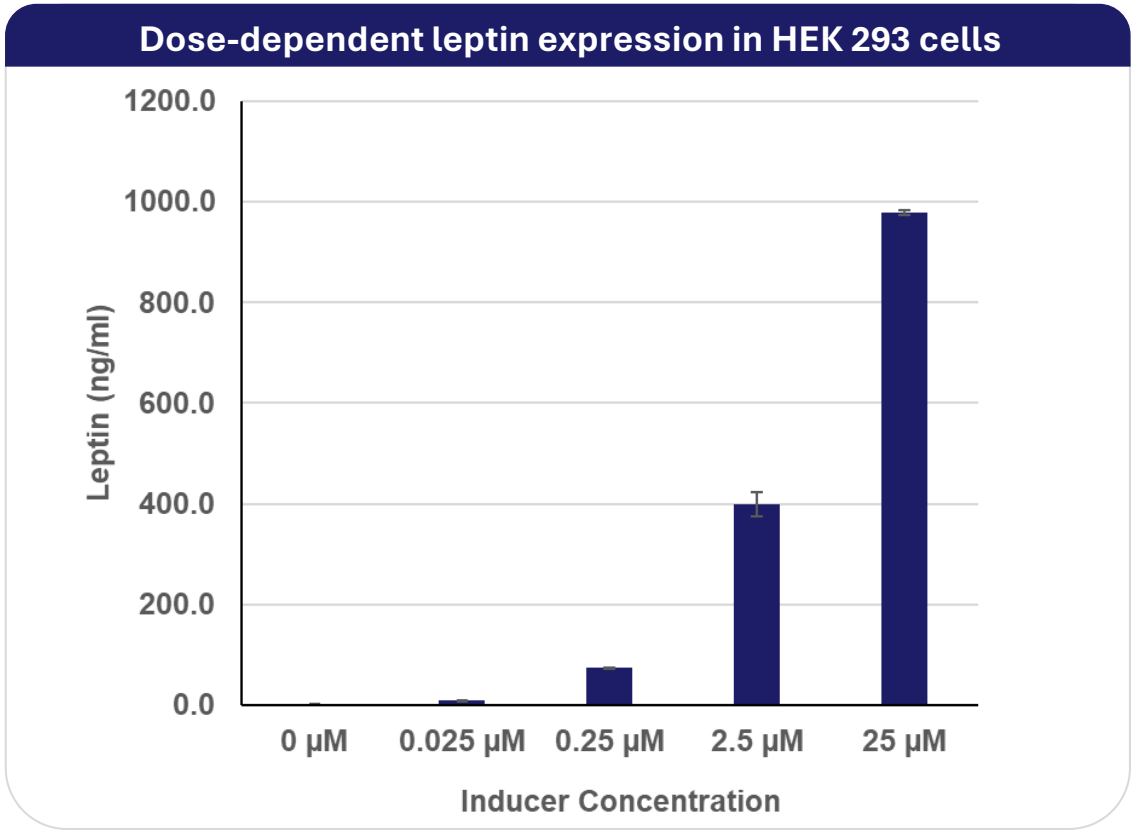
MeiraGTx is developing a new leptin therapy using its proprietary Riboswitch technology - to deliver native leptin to patients with a daily dose of an oral pill

- **riboLeptin offers meaningful potential advantages over current standard of care therapy (metreleptin):**
  - ✓ Reduced risk of immunogenicity (metreleptin carries a black box warning for ADAs)
  - ✓ Avoiding potential toxicity of metreleptin from supraphysiological surges on injection
  - ✓ Physiologically relevant production of native leptin by patient's own cells
  - ✓ riboLeptin is via convenient oral dosing (vs. daily injections)
  - ✓ Lower overall COGS (small molecule vs. recombinant protein production)
  - ✓ Pricing of of injectable metreleptin can be up to $1.3m/year[1]
  - ✓ riboLeptin allows broader access to larger populations at potentially considerably lower cost
- **In a widely accepted *in vivo* model of leptin deficiency (ob/ob mice), riboLeptin treatment led to complete correction of metabolic abnormalities associated with leptin deficiency with daily oral dosing, including:**
  - Dose dependent expression of native human leptin to physiological levels
  - Resolution of excessive food intake (hyperphagia) characteristic of leptin deficiency
  - Significant and durable weight loss - to normal levels
  - Significant reduction in body fat
  - Normalization of triglyceride levels and resolution of liver steatosis
  - Complete restoration of glucose tolerance and normal serum glucose levels

1- https://www.drugs.com/article/top-10-most-expensive-drugs.html

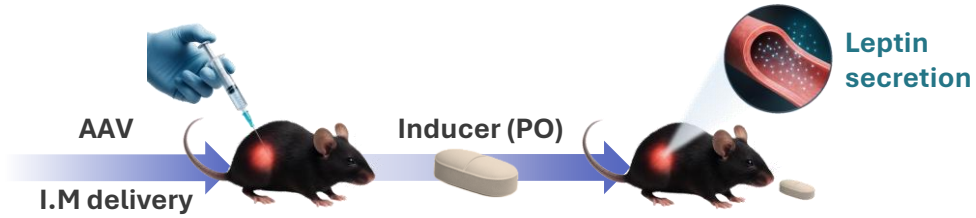
Riboswitch-regulated leptin demonstrates dose-dependent expression *in vitro* in mammalian cells

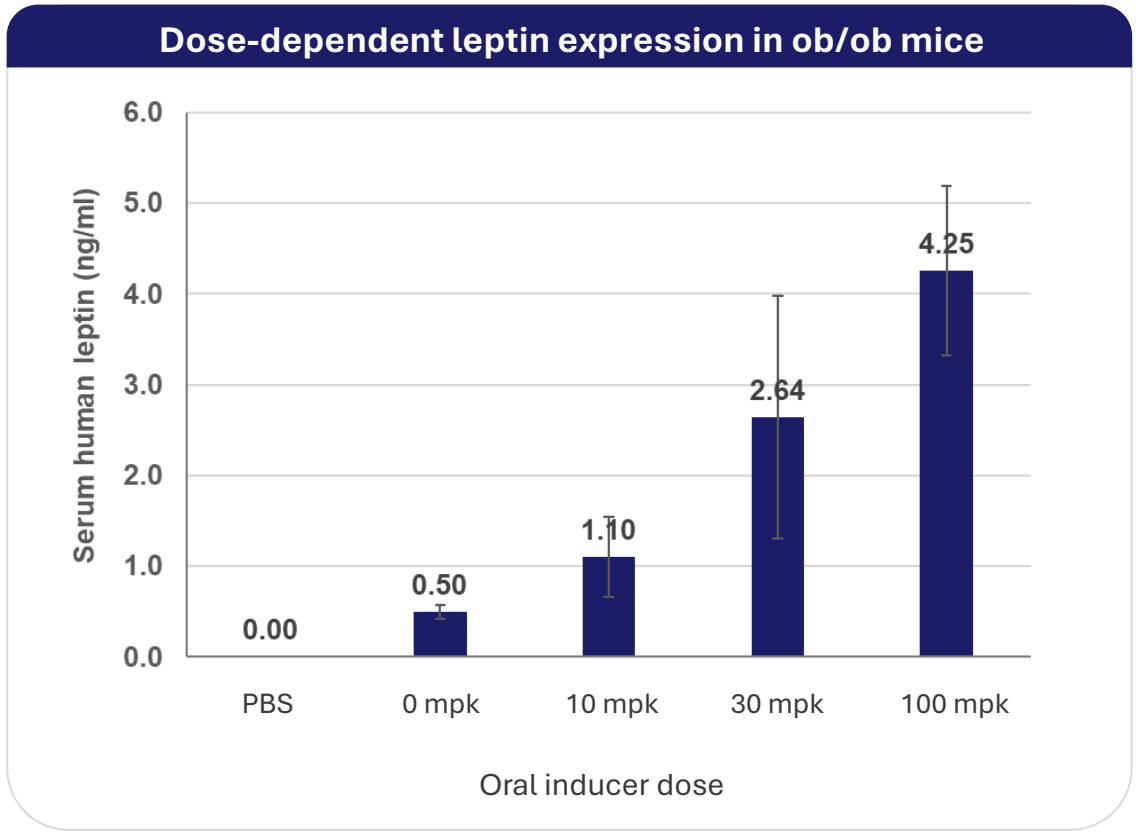




- Riboswitch gene regulation cassette was inserted in the coding sequence (CDS) of human leptin gene
- The construct was transfected into HEK 93 cells
- Transfected cells were treated with riboswitch small molecule inducer MXU-001at the indicated concentrations
- 48 hours after MXU-001 treatment, supernatants were collected and human leptin protein was measured using ELISA assay

Riboswitch-small molecule control of leptin demonstrates dose-dependent expression *in vivo* in leptin deficient ob/ob mice

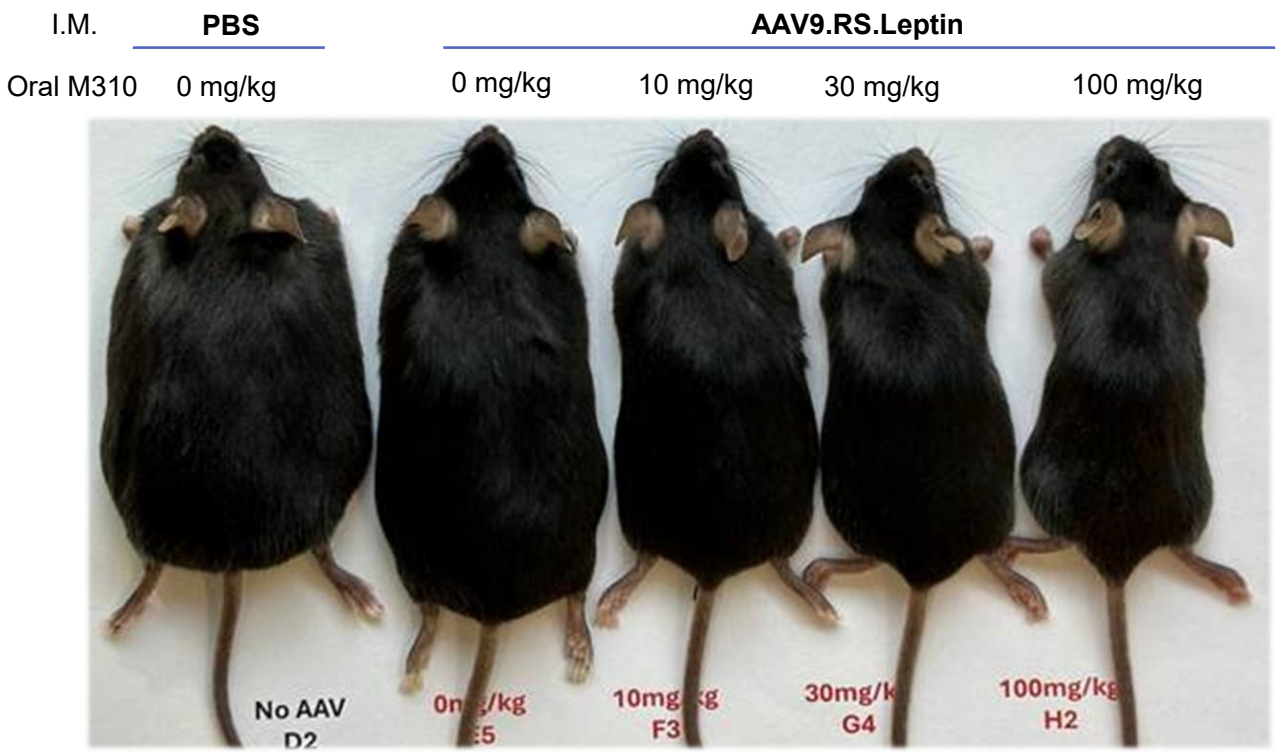




In leptin-deficient mice, leptin is expressed in a dose dependent manner in response to oral dosing with Riboswitch inducer, MXU-001, achieving physiological levels of leptin:

- AAV9 vector containing human leptin gene with Riboswitch cassette (AAV.RS.Leptin) at 1E11 vg/mouse, or PBS as control, was administered as a one-time local injection directly into the leg muscle of ob/ob mice
- 3 days post intramuscular injection, animals were orally dosed with the small molecule inducer M310 at the indicated doses. M310 was given daily for 6 days a week over 5 weeks
- On day 39 post the single IM AAV injection and 16 hours following the last dose of M310, blood samples were collected and the serum levels of circulating human leptin were determined by ELISA specific for human leptin
- Leptin expression levels directly corresponded to the dose of the orally administered inducer M310
- Leptin reached physiological levels in response to 30 mg/kg dose of inducer

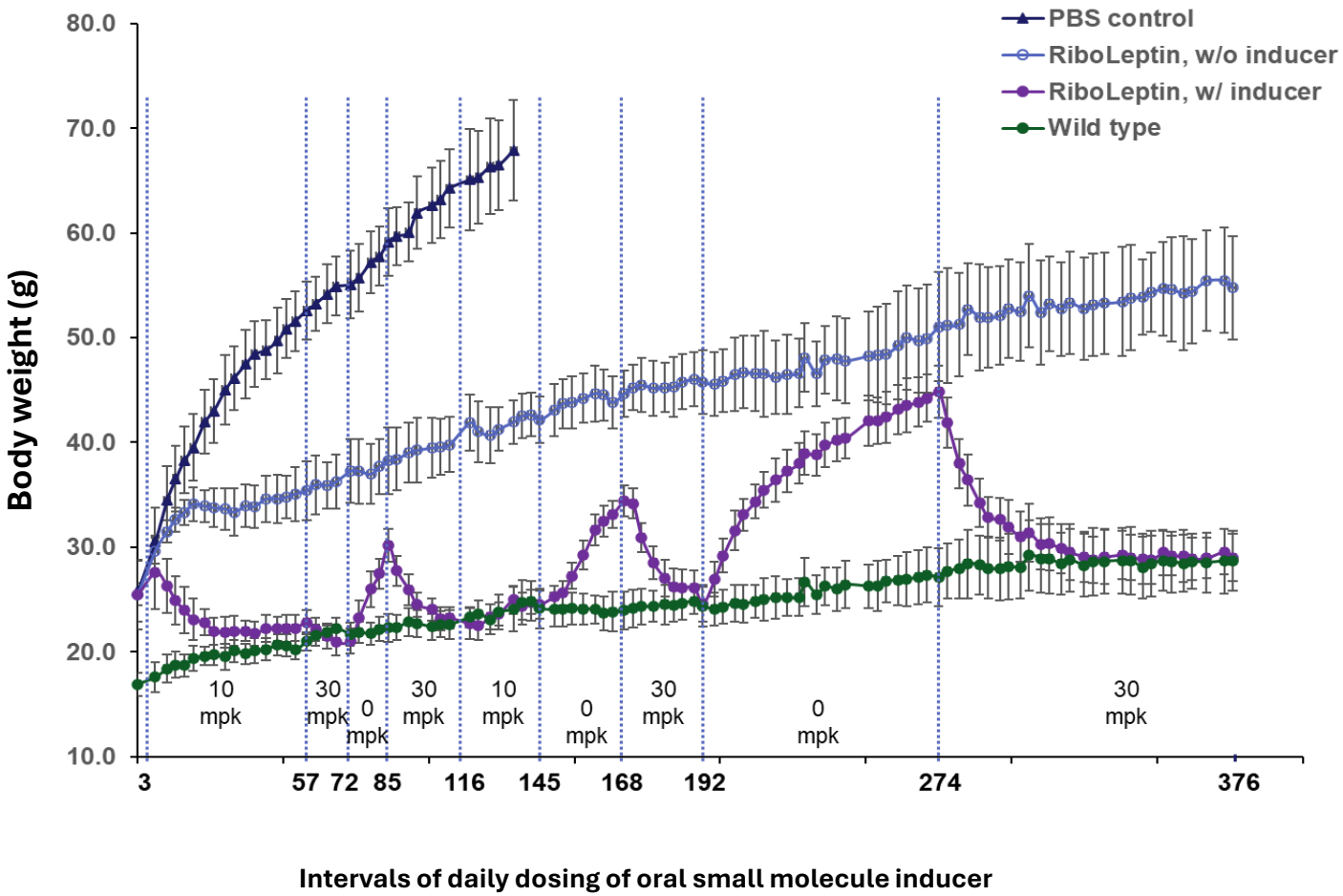
riboLeptin demonstrates dose-dependent weight loss in response to oral inducer dosing, preventing morbid obesity



riboLeptin normalizes body weight and prevents morbid obesity in leptin-deficient mice:

- AAV9 vector containing Riboswitch-controlled human leptin (AAV9.RS.Leptin) at 1E11 vg/mouse or PBS as control was administered as a one-time local injection into the leg muscle of ob/ob mice
- 3 days post intramuscular injection, animals were orally administered the small molecule inducer M310 at 0, 10, 30 or 100 mg/kg doses
- The oral dose of M310 was given daily for 6 days a week over 5 weeks
- On day 33 post the single IM AAV injection, photos of representative mice from each treatment group were taken, demonstrating the therapeutic effect of riboLeptin in normalizing body weight and preventing morbid obesity in leptin-deficient mice

Durable riboswitch-controlled production of leptin in ob/ob mice effectively treats leptin deficiency with daily oral small molecule dosing over a year after one-time IM injection of RiboLeptin



- 5.5 weeks old ob/ob mice were injected with PBS or 1E11 vg AAV9.RS.Leptin (RiboLeptin) into the muscle on Day 1
- 3 days post the single AAV injection, mice were treated with the indicated oral doses of small molecule inducer, daily (10mpk or 30mpk or no small molecule inducer) for consecutive days
- Daily morning dosing of the oral small molecule inducer resulted in rapid reduction in body weight in ob/ob mice to the weight of wild type mice
- When the small molecule was withheld, mice gained weight in the absence of production of effective leptin levels
- Repeated intervals of daily dosing with the small molecule inducer over a period of a year resulted in the same dynamics of leptin production and weight loss on reintroduction of the oral small molecule dosing, **showing long term durability of the riboswitch system**
- Wild type weight is currently being maintained in ob/ob mice with daily oral inducer dosing out past one year following the one-time injection of the Ribo-Leptin DNA template to the muscle

Riboswitch-regulated leptin therapy (RiboLeptin) - Summary

RiboLeptin resolved leptin deficiency following oral inducer treatment in ob/ob mice:

- Dose dependent expression of leptin to physiological levels
- Significant reduction in excessive food intake behavior (hyperphagia)
- Significant and durable weight loss - to normal levels
- Complete correction of body fat levels to normal levels
- Complete correction of glucose tolerance and serum glucose levels
- One-time local injection of gene vector followed by daily dose of oral small molecule
- Much decreased cost of goods, increasing the accessibility of leptin replacement, while replacing injection with a daily oral pill, and reducing toxicity and increasing safety

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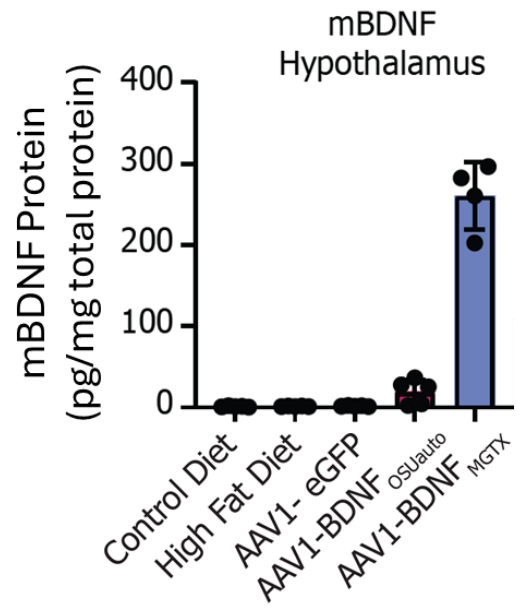
AAV-BDNF: small dose, locally delivered to hypothalamus to change dysregulated MC4R circuitry in the brain

IND Enabling: clear evidence of strong efficacy in animal models

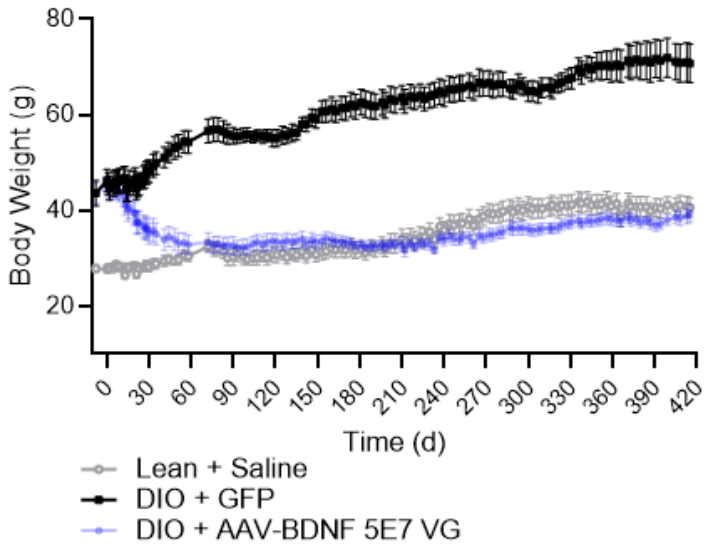
Treatment with AAV-BDNF leads to significant weight loss in obese mice, without muscle loss. Works downstream of MC4R to control weight.

Optimized, high expressing vector



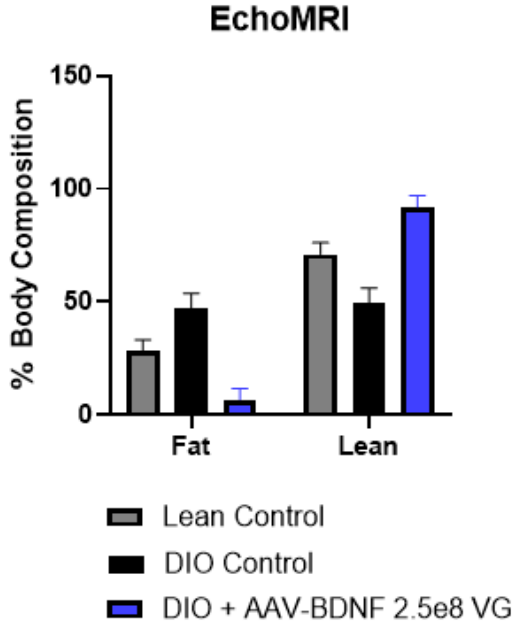
- Vector optimization by MeiraGTx's Vectorology group results in high expression of BDNF in mouse hypothalamus vs. unoptimized vector ("OSUauto"), allowing administration of ultralow vector dose to achieve therapeutic levels of BDNF

Meaningful and durable weight loss in DIO mice



- A single, ultralow dose of AAV-BDNF to the brain of obese mice causes significant weight loss that is stable throughout their lifespan (>14 months post treatment).

Significant fat reduction without affecting lean muscle mass



- AAV-BDNF treatment leads to significant fat reduction, while maintaining lean muscle composition

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Additional information available under CDA

MeiraGTx is leading the next wave of genetic medicines

Advanced and diverse pipeline of genetic medicines

- **4 pivotal stage programs:** Radiation-induced xerostomia, Parkinson's disease,, AIPL1 retinal dystrophy, X-linked retinitis pigmentosa
- **Diverse preclinical pipeline:** ALS, intractable neuropathic pain, obesity & diabetes, large ophthalmology indications such as Stargardt's, wet AMD and dry AMD
- **Multiple potential near-term BLA filings**

Powered by best-in-class genetic medicine technologies and unique industry leading end-to-end in-house GMP manufacturing:

Vector Design & Optimization Technologies

- ☑ Novel intravitreal capsids
- ☑ Proprietary promoters
- ☑ Sequence optimization
- ☑ Proprietary non-coding elements for increased potency

Riboswitch Platform

- ☑ Precise control of transgene expression with orally administered pills
- ☑ New approach to cell therapy, gene editing, metabolic disease

End-to-end GMP Manufacturing

- ☑ In-house plasmid and viral vector GMP manufacturing
- ☑ Commercially-licensed QC facility
- ☑ Fill & Finish
- ☑ Single use – flexible & scalable production


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