Company Overview

October 2019

Forward Looking Statements

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding expectations relating to meetings with global regulatory authorities and the FDA, product pipeline, anticipated product benefits, goals and strategic priorities, product candidate development and status and expectations relating to clinical trials, growth expectations or targets and pre-clinical and clinical data expectations in respect of collaborations, as well as statements that include the words “expect,” “intend,” “plan,” “believe,” “project,” “forecast,” “estimate,” “may,” “should,” “anticipate” and similar statements of a future or forward-looking nature. These forward-looking statements are based on management’s current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, our incurrence of significant losses; any inability to achieve or maintain profitability, acquire additional capital, identify additional and develop existing product candidates, successfully execute strategic priorities, bring product candidates to market, build-out the manufacturing facility and processes, successfully enroll patients in and complete clinical trials, accurately predict growth assumptions, recognize benefits of any orphan drug designations, retain key personnel or attract qualified employees, or incur expected levels of operating expenses; failure of early data to predict eventual outcomes; failure to obtain FDA or other regulatory approval for product candidates within expected time frames or at all; the novel nature and impact of negative public opinion of gene therapy; failure to comply with ongoing regulatory obligations; contamination or shortage of raw materials; changes in healthcare laws; risks associated with our international operations; significant competition in the pharmaceutical and biotechnology industries; dependence on third parties; risks related to intellectual property; litigation risks; and the other important factors discussed under the caption “Risk Factors” in our most recent quarterly report on Form 10-Q or annual report on Form 10-K or subsequent 8-K reports, as filed with the Securities and Exchange Commission. These and other important factors could cause actual results to differ materially from those indicated by the forward-looking statements made in this presentation. Any such forward-looking statements represent management’s estimates as of the date of this presentation. While we may elect to update such forward-looking statements at some point in the future, unless required by law, we disclaim any obligation to do so, even if subsequent events cause our views to change. Thus, one should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation. Unless otherwise stated or the context otherwise requires, the information herein is as of October 4, 2019.

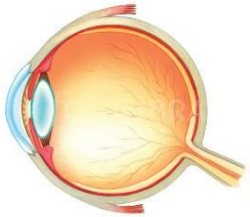
A Vertically Integrated, Clinical Stage Gene Therapy Company

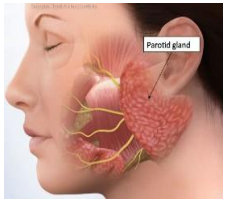
Developing a new pharmaceutical modality designed for the cost effective treatment of a broad range of serious disorders

Diversified Pipeline of Gene Therapy Candidates

6 ongoing clinical programs:

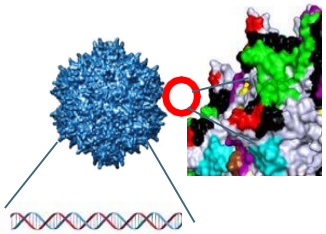
- Inherited retinal diseases
- Salivary gland
- Parkinson's Disease

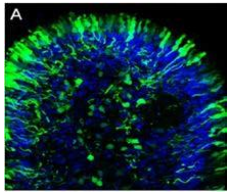




Platform of Core Viral Vector Engineering Capabilities

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



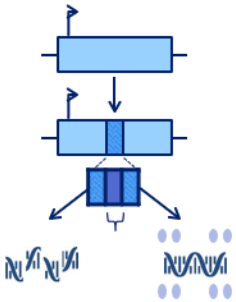


Manufacturing Capacity & Know-How

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

Next Generation Gene Therapy Riboswitch-Based Gene Regulation

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



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Gene Therapy Pipeline

Ocular, Neurodegenerative, Salivary Gland Programs

Multiple Therapeutic Targets

OCULAR

Clinical Development
- Genetic Inherited Retinal Disease (IRD) franchise: XLRP, achromatopsia, RPE65-deficiency, LCA4

Research
- Wet AMD, Dry AMD

Gene Regulation
- VEGFR2 Ab – eye drops

NEURODEGENERATIVE

Clinical Development
- Parkinson's disease

Research
- Amyotrophic Lateral Sclerosis (ALS)

Gene Regulation
- CNS expression with BBB penetrant small molecules

SALIVARY GLAND

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

Research
- Sjogren's Syndrome

Gene Regulation
- Peptide and hormone salivary gland delivery

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

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

Broad Clinical Pipeline

Product	Indication	Preclinical	Phase 1/2	Details
Ocular				
AAV-RPE65	RPE65-Deficiency	RPDD, Orphan Drug		
AAV-CNGB3*	Achromatopsia (CNGB3)	RPDD, PRIME, Fast Track, Orphan Drug		janssen
AAV-RPGR*	X-linked RP (RPGR)	Fast Track, Orphan Drug		janssen
AAV-CNGA3*	Achromatopsia (CNGA3)	RPDD, Orphan Drug		janssen
AAV-AIPL1	LCA4 (AIPL1)	Orphan U.S. & EU		EU Compassionate Use under Specials License
A006	Wet AMD (anti-VEGFR2)			
Neurodegenerative Disease				
AAV-GAD	Parkinson's Disease (GAD)			45 patient Phase 2 trial complete, regulatory path intended to be discussed with FDA in 2019
Salivary Gland				
AAV-AQP1	Xerostomia (hAQP1)	Orphan Drug		Phase 1 study at NIH ongoing; multi-site Phase 1/2 trial ongoing
AAV-AQP1	Sjögren's Syndrome (hAQP1)			

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

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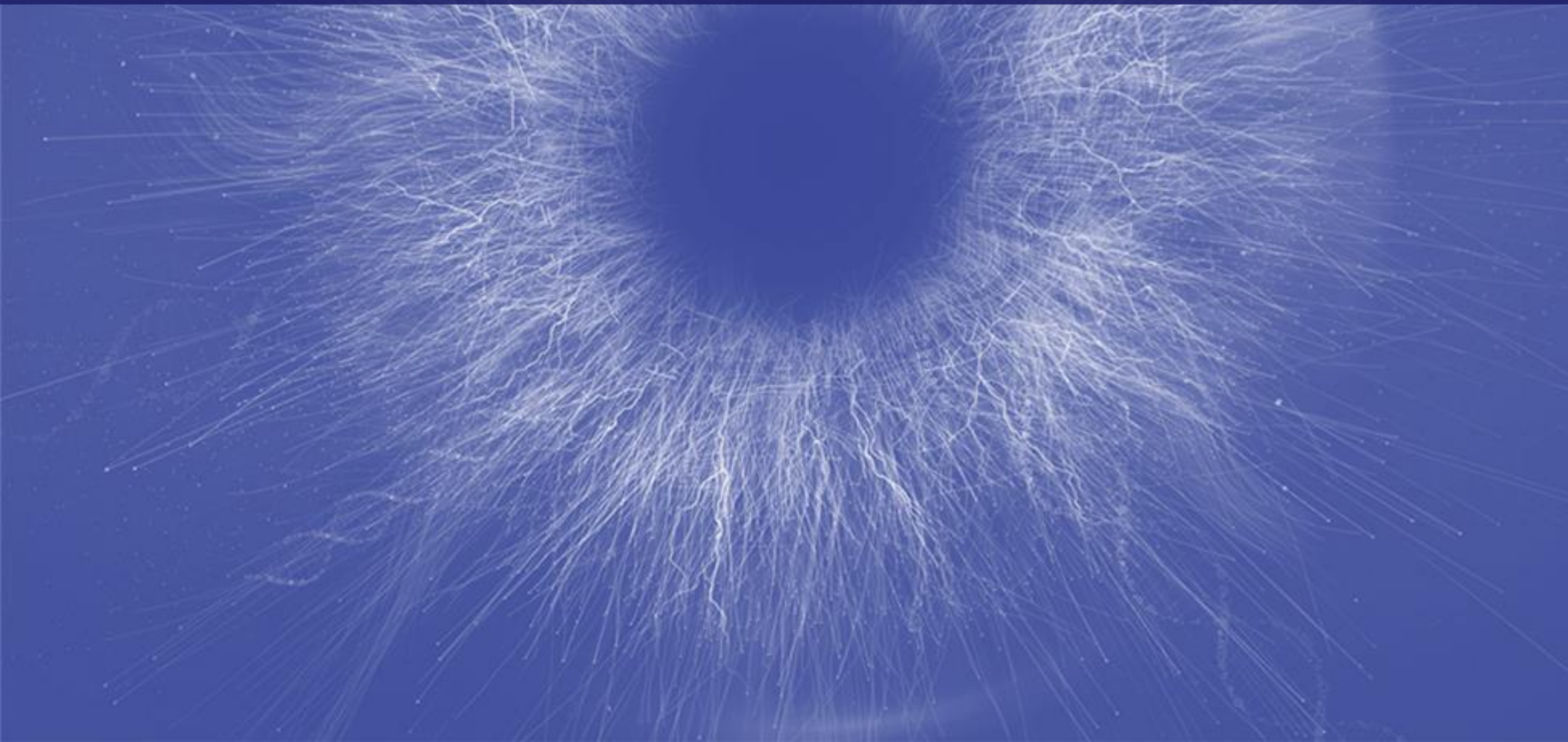
Ocular Franchise

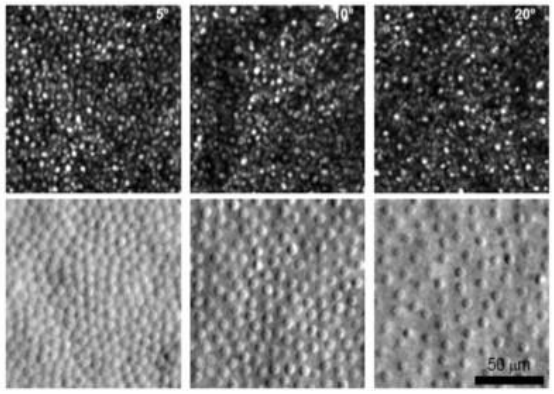


MeiraGTx Ocular Programs

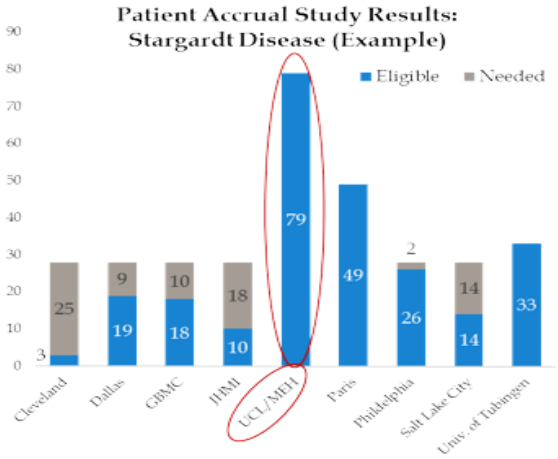
Ophthalmology Partners and Centers of Excellence

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

Our Partners Possess World Leading Imaging, Endpoint Development and Validation



Patient Access



Worldwide Strategic Collaboration

Janssen
PHARMACEUTICAL COMPANIES OF
Johnson & Johnson

Clinical development

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

Janssen commercial infrastructure

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

Pre-clinical IRD research

- Collaboration leverages MeiraGTx vector design and optimization technology to develop potential gene therapy treatments for multiple IRDs
- Janssen to receive exclusive rights to develop & commercialize programs from IRD research collaboration

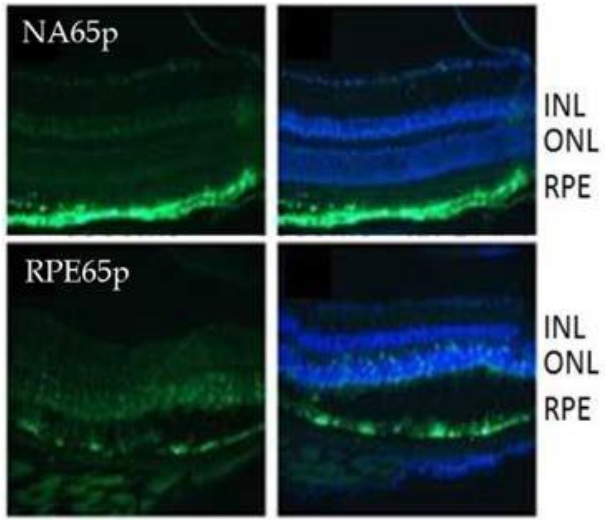
Manufacturing and process development

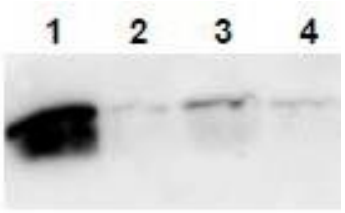
- Janssen accesses MeiraGTx advanced manufacturing capabilities with clinical and commercial supply agreements
- Joint development of novel AAV manufacturing technologies to expedite and optimize development

AAV-RPE65 Vector Construct Optimization

Optimization Details

- **Capsid changed from AAV2 to AAV5:** 4x improvement in transfection efficiency of RPE
- **Promoter optimization:** 20x increase in protein expression
- **Codon optimization:** 7x increase in protein expression in human cells
- **SV40 intron increases mRNA stability:** 2.5x increased mRNA levels



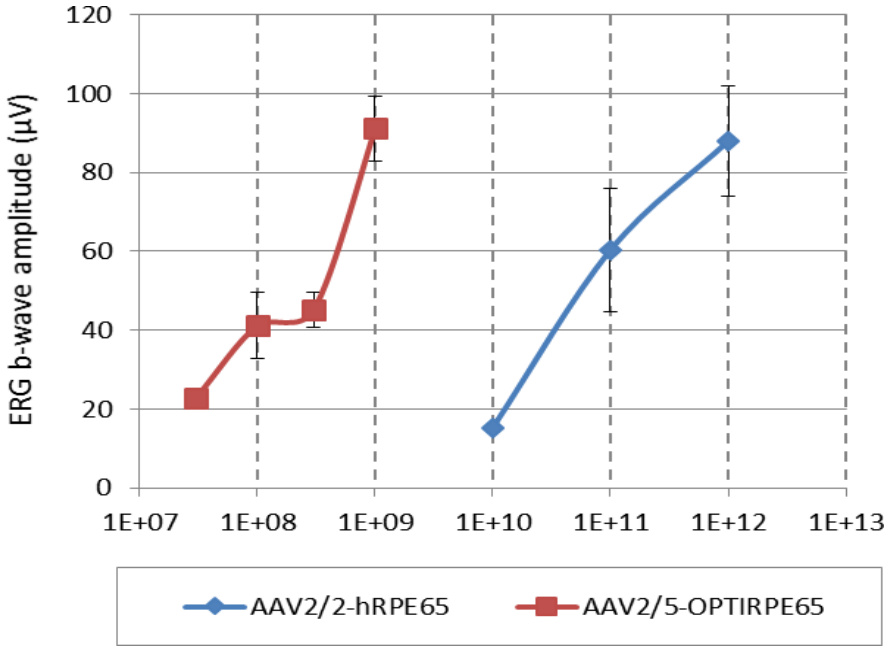


1: AAV. RPE65OPT.GFP
2: AAV. RPE65OPT.GFP (1:20 dilution)
3: AAV.BGL65p.GFP (alt promoter fragment)
4: AAV.hRPE65.GFP

Head-to-Head Comparison

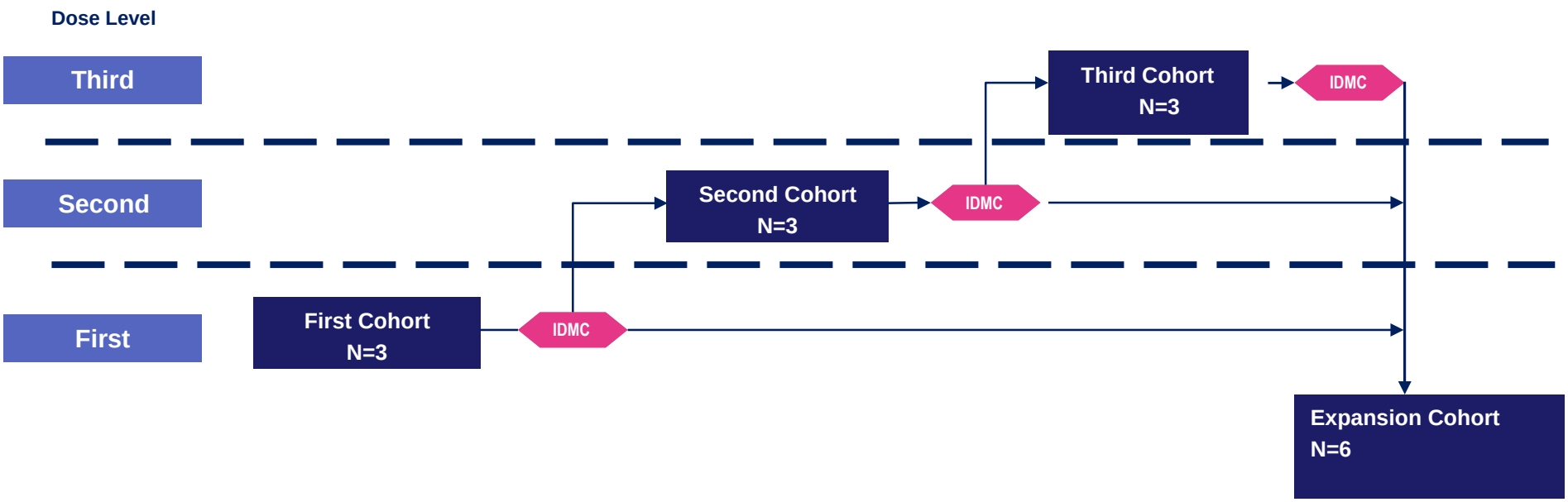
Head-to-head comparison in vivo of AAV2/5-OPTIRPE65 and AAV2/2-hRPE65, the vector used in the first UCL clinical trial

- After subretinal injection into RPE65-deficient mice, AAV2/5-OPTIRPE65 can restore retinal function at 300-1,000 fold lower doses than AAV2/2-hRPE65



Subretinal injection targeting the central retina
Volume of injection may be up to 1ml
Multiple retinotomies permitted

Phase 1/2 Trial of AAV-RPE65



- **Dosing complete:** 15 patients treated (nine adults in three dose escalation cohorts and six pediatric patients in an expansion cohort)
- **Six-month topline data released May 2019:** AAV-RPE65 was generally well-tolerated, with a safety profile consistent with other approved and investigational ocular gene therapies; statistically significant improvement across several secondary endpoints that assessed clinical activity.
- **Long-term follow up ongoing**
- **Natural History study ongoing:** >30 RPE65-deficiency patients well characterized

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

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

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

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

Achromatopsia (ACHM)

Retinal defect

- Complete absence of cone photoreceptor function from birth

Disease characterization

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

Prevalence and genes

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

Patient Experience

Normal

Achromatopsia

AAV-CNGB3
- Human cone arrestin promoter (hCARp)
- AAV2/8
- Human CNGB3 cDNA

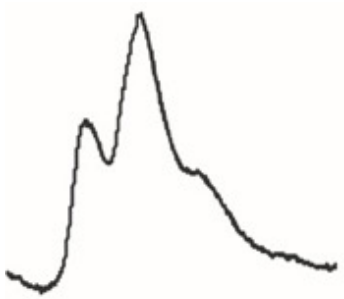
AAV-CNGA3
- Novel synthetic cone specific promoter (hG1.7p)
- AAV2/8
- Codon optimized human CNGA3 cDNA

AAV-CNGB3 Restored Function in Pre-clinical Models

Restoration of cone electrical function

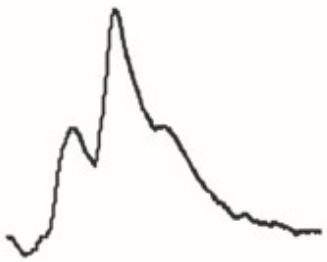
Bright light flash (photopic)

Normal Mouse

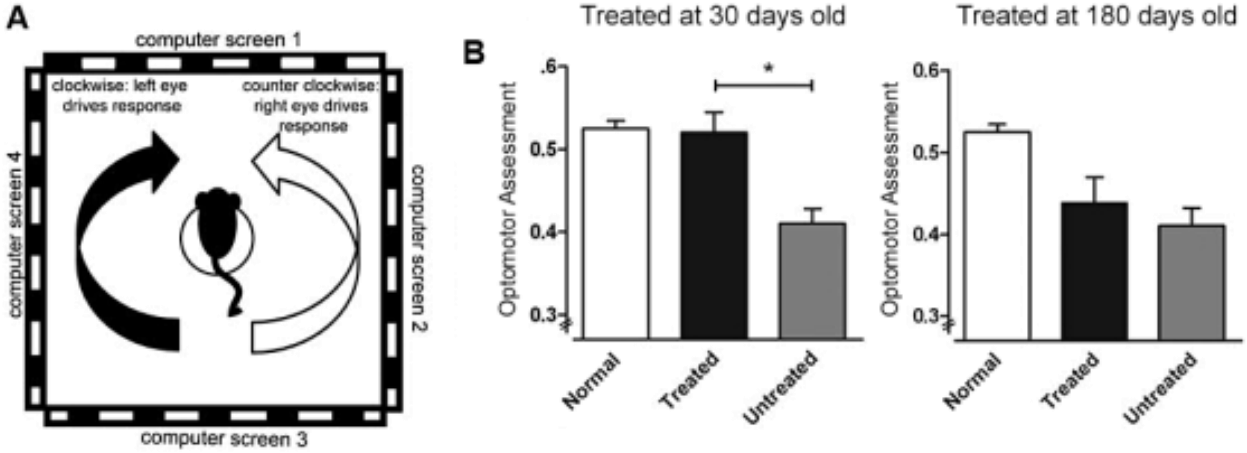


Untreated Mutant Mouse Lacking CNGB3

Treated Mutant Mouse Lacking CNGB3



Restoration of visual function



Carvalho L. Long-term and age-dependent restoration of visual function in a mouse model of CNGB3-associated achromatopsia following gene therapy, *Human Molecular Genetics*, 2011, vol. 20.

Phase 1/2 Trials of AAV-CNGB3 and AAV-CNGA3

- **CNGB3 dosing complete:** 23 patients treated
  - 11 adults in dose escalation cohorts; 12 children in pediatric expansion cohort)
- **CNGA3 clinical trial ongoing:** Enrolling children aged 3-15 years old
  - Dose escalation in progress, trial initiated Q3
- **ACHM Natural History study ongoing:** > 90 patients well characterized

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

XLRP

Retinitis Pigmentosa (RP)

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

Disease progression

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

Prevalence and genes

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

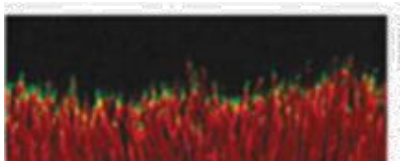
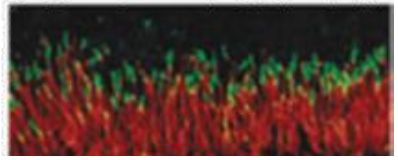
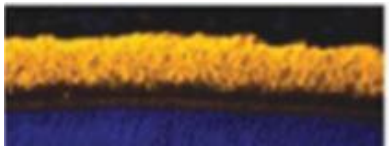
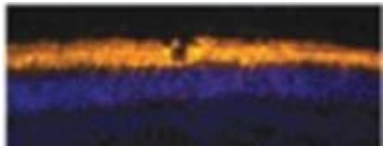
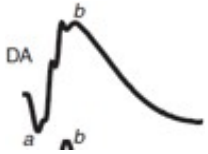
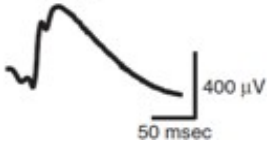
AAV-RPGR

- Human rhodopsin kinase promoter (RKp)
- AAV5
- $RPGR^{ORF15}$

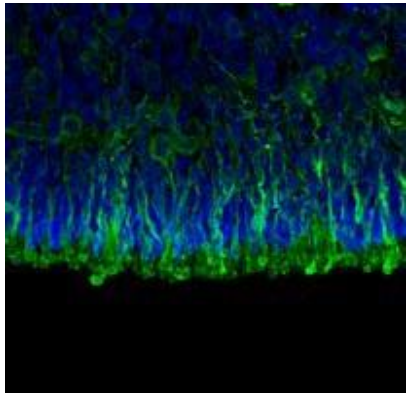
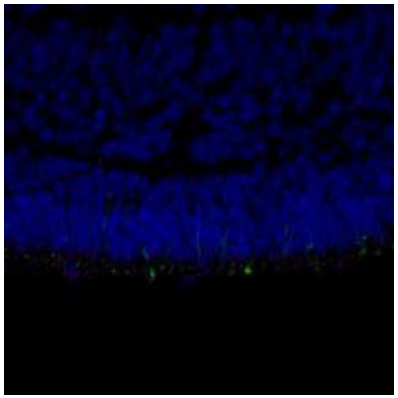
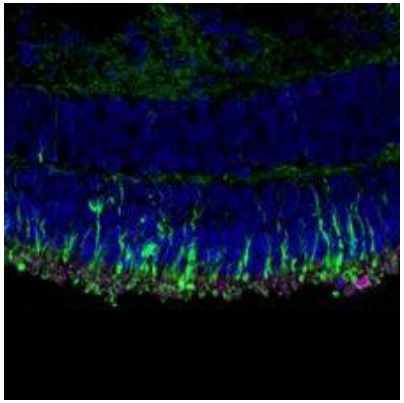
Patient Experience

AAV-RPGR Pre-clinical Data

Observations in wild type & RPGR-null mutant mice

	Normal Mouse	Untreated – RPGR Mutant	Treated – RPGR Mutant
RPGR Expression & Localization			
Rhodopsin			
Opsin			
ERG			

Observations in retinal organoids derived from RPGR Patients

Normal	Untreated – RPGR Mutation	Treated – RPGR Mutation
		

Phase 1/2 Trial of AAV-RPGR

- **Dose escalation complete:** 10 young adults (aged 18-30) treated in dose escalation, 3 children treated in pediatric expansion cohort
- **Randomized extension study ongoing:** Enrolling patients in the UK and U.S.
- **Natural History study ongoing:** > 100 XLRP patients well characterized

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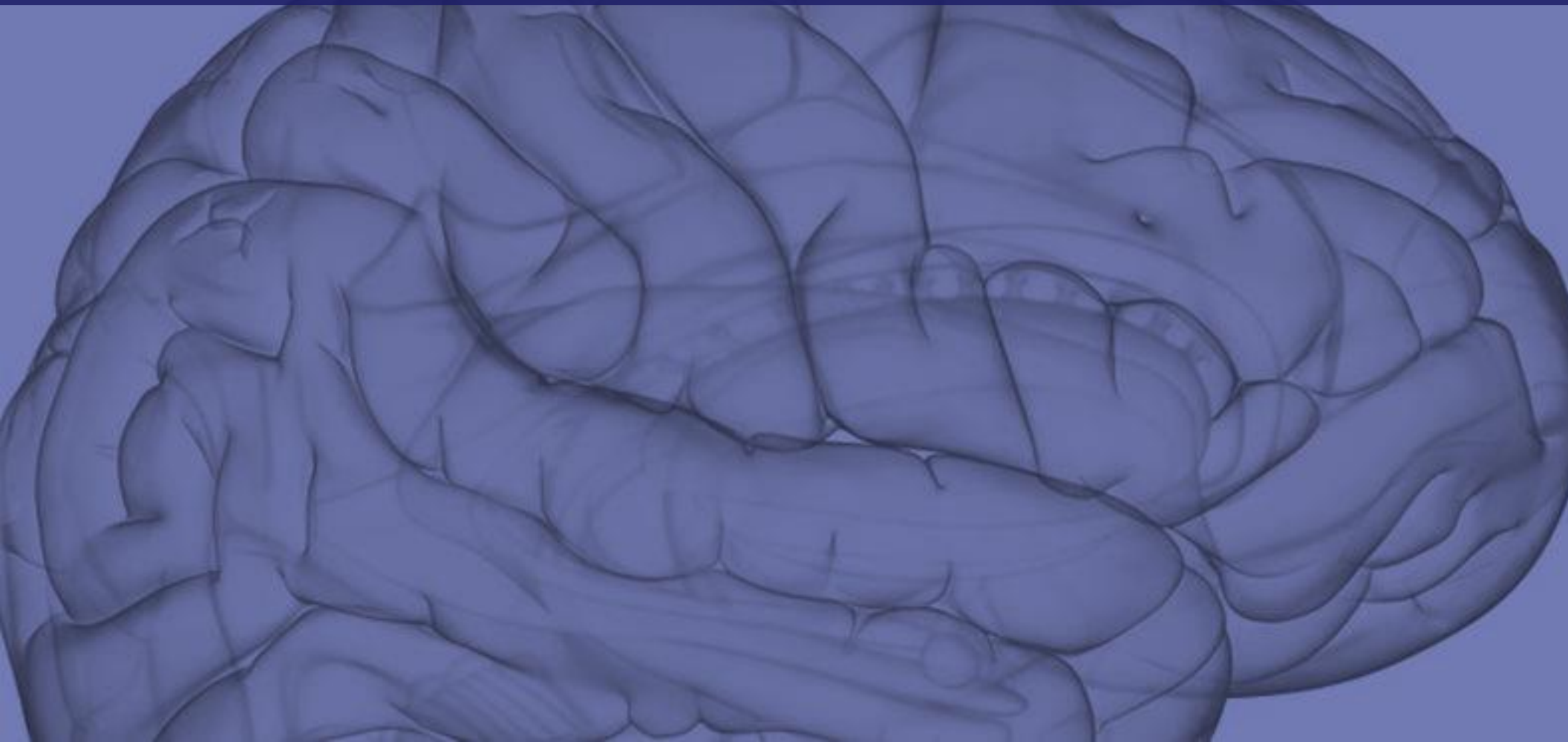
Neurodegenerative Diseases



AAV-GAD for Parkinson's Disease

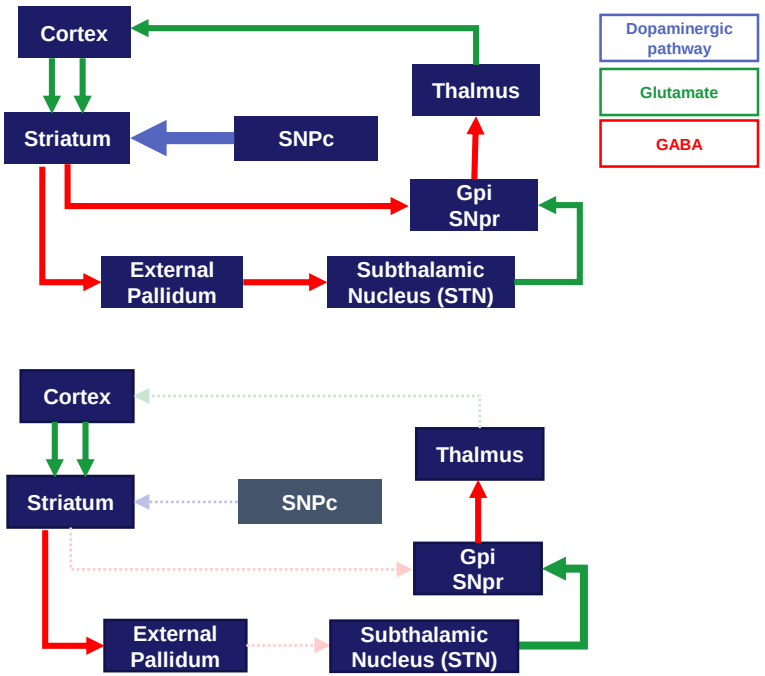
PD principally manifests as a movement disorder

The basal ganglia facilitate voluntary movements and the rejection of involuntary movements

- Subthalamic nucleus (STN) is a key modulator of motor circuitry

Parkinson's: dopaminergic neurodegeneration alters functional connectivity and metabolism

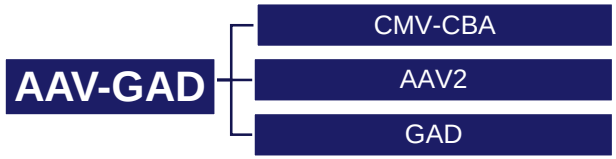
- Alterations cause hyperactivity of STN
  - Decreased GABAergic (inhibitory) inflow into STN
  - Increased glutamatergic (excitatory) outflow to the motor cortex
- STN surgical interventions can improve PD motor features
  - Surgical lesioning, Deep Brain Stimulation (DBS)



AAV-GAD gene therapy to rebalance excitation and inhibition

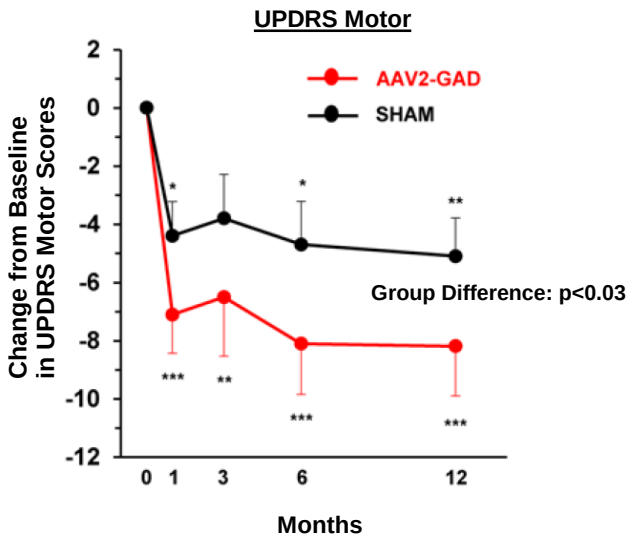
Glutamic Acid Decarboxylase converts glutamate (excitatory neurotransmitter) into GABA (inhibitory neurotransmitter)

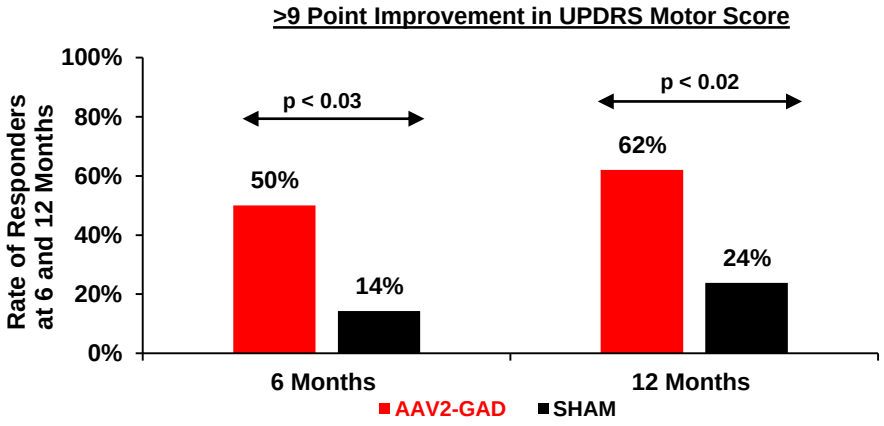
- Delivered directly into the STN, bypassing circuitry disrupted by dopamine loss
- AAV-GAD converts some STN neurons to inhibitory phenotype
  - Reduce STN hyperactivity
  - Restore normal neuronal firing
  - Restore normal basal ganglia outflow to the motor cortex



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

- **45 patients randomized 1:1 to bilateral infusion of AAV-GAD into STN or bilateral saline solution infusion into STN**
  - Primary endpoint: 6 month change from baseline in off-medication UPDRS motor score (UPDRS part III)
- **AAV-GAD was well tolerated**
  - No treatment-related SAEs
- **Met primary endpoint: 6 month change in UPDRS motor score**
  - 8.1 point improvement for AAV-GAD vs 4.7 point improvement for sham (p<0.03)
- **Responders with clinically meaningful 9 point or greater UPDRS motor score improvement**
  - 50% AAV-GAD response at 6 months vs 14% sham response
  - 62% AAV-GAD response at 12 months vs 24% sham response
- **Significant reduction in levodopa-induced dyskinesias**
  - At 6 months and 12 months for AAV-GAD patients





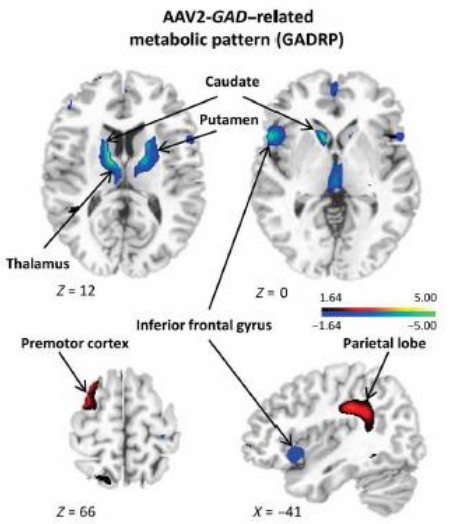
LeWitt PA. AAV2-GAD gene therapy for advanced Parkinson's Disease: a double-blind, sham-surgery controlled, randomized trial. *Lancet Neurology*, 2011.
Niethammer M. Long-term follow-up of a randomized AAV2-GAD gene therapy trial for Parkinson's disease. *JCI Insight*, 2017.

Metabolic Imaging Identified Biomarker of Activity

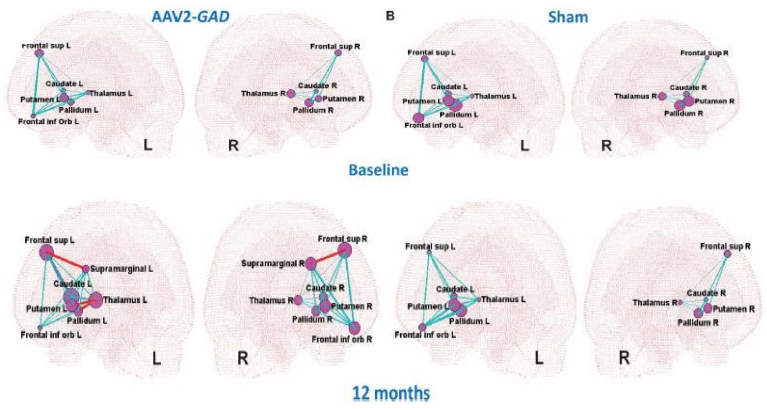
AAV-GAD reduces PD symptoms by reorganizing brain connectivity

- Metabolic imaging at baseline, 6 and 12 months
- AAV-GAD recipients developed unique treatment-dependent polysynaptic brain circuit (GAD related pattern, GADRP)
- GADRP reflects formation of new polysynaptic functional pathways linking the STN to motor cortical regions
- Statistically significant correlation between improvement in UPDRS motor ratings and GADRP expression ($p < 0.009$)
  - GADRP expression increased over time in AAV-GAD patients

This treatment-induced brain circuit is a novel endpoint to isolate true treatment-driven responses from placebo responses



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



New polysynaptic pathways connecting STN to motor cortex

Niethammer M. Gene therapy reduces Parkinson's disease symptoms by reorganizing functional brain connectivity. *Science Translational Medicine*, 2018.

AAV-GAD Summary

Regulatory discussions intended to be held in 2019 to discuss regulatory approval pathway

Novel approach to the treatment of PD

- Gene therapy delivered directly to STN to rebalance the basal ganglia output to the motor cortex

Encouraging safety and efficacy data consistently demonstrated across two clinical trials

- Well-tolerated
- No speech complications, neurophysical or cognitive declines
- Statistically significant improvement in motor symptoms
- Statistically significant reduction in medication complications
- Functional improvements persisted at 1 year
- Biomarker of activity identified

High unmet medical need

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

Surgical process convenient for patient, neurologist, neurosurgeon, hospital

- AAV-GAD delivery is into the same brain region as DBS, has no hardware or programming

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Salivary Gland

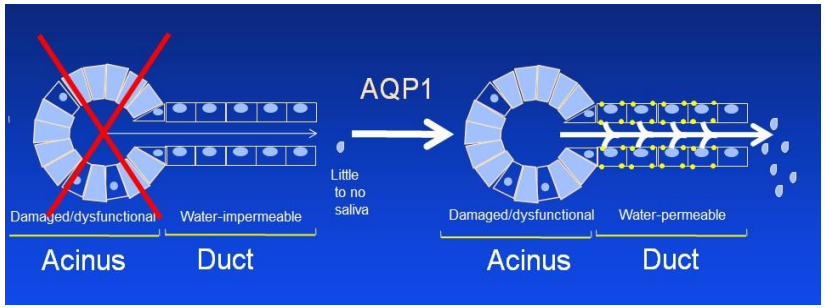
AAV-AQP1 for Radiation-Induced Xerostomia (RIX)

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

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

Strategy for the repair

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



Salivary gland as target for gene therapy

- Non-invasive: allows local administration and avoids systemic exposure
- Isolated and encapsulated
- Small volume of vector

AAV-AQP1
- CMV enhancer CBA promoter
- AAV2
- Human aquaporin 1 (hAQP1)

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

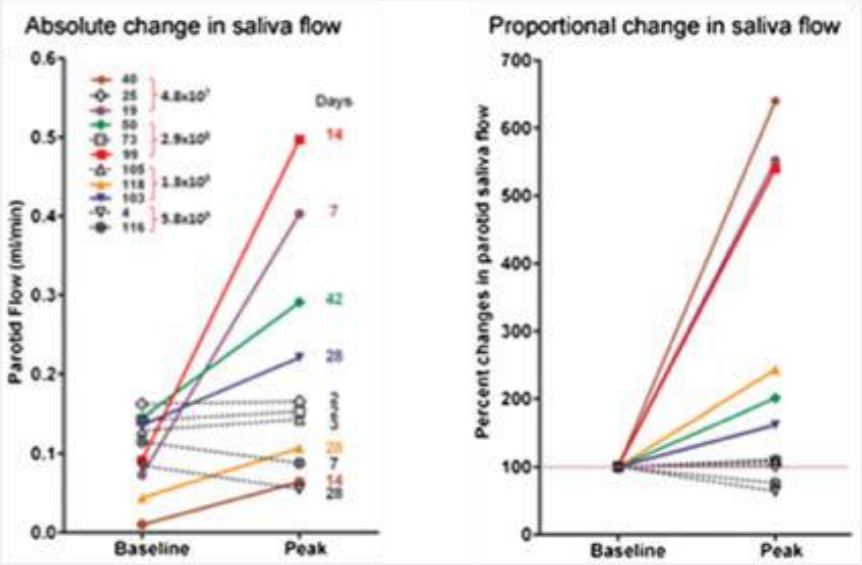
Adenoviral-mediated aquaporin-1 cDNA transfer for radiation-induced salivary hypofunction

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

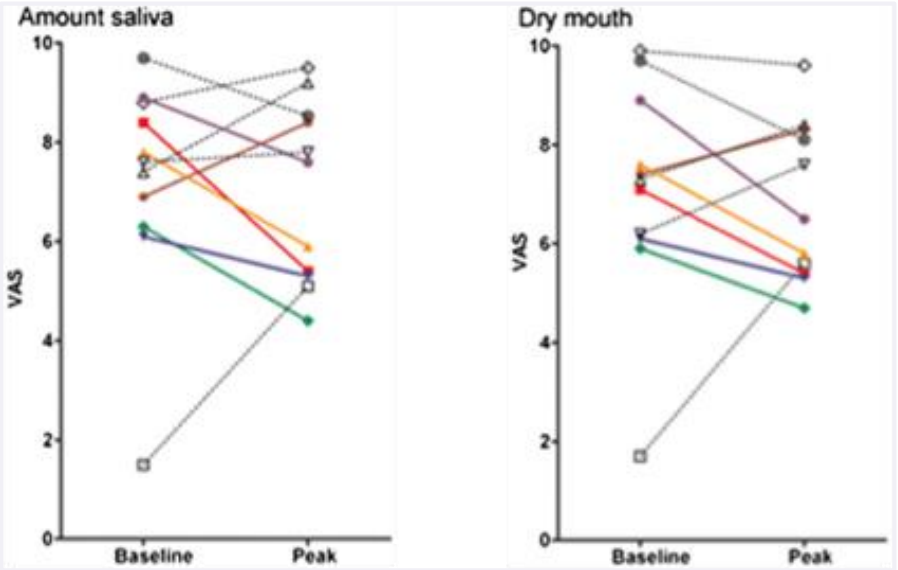
NIH

National Institute of Dental and Craniofacial Research

Change in parotid salivary flow rate



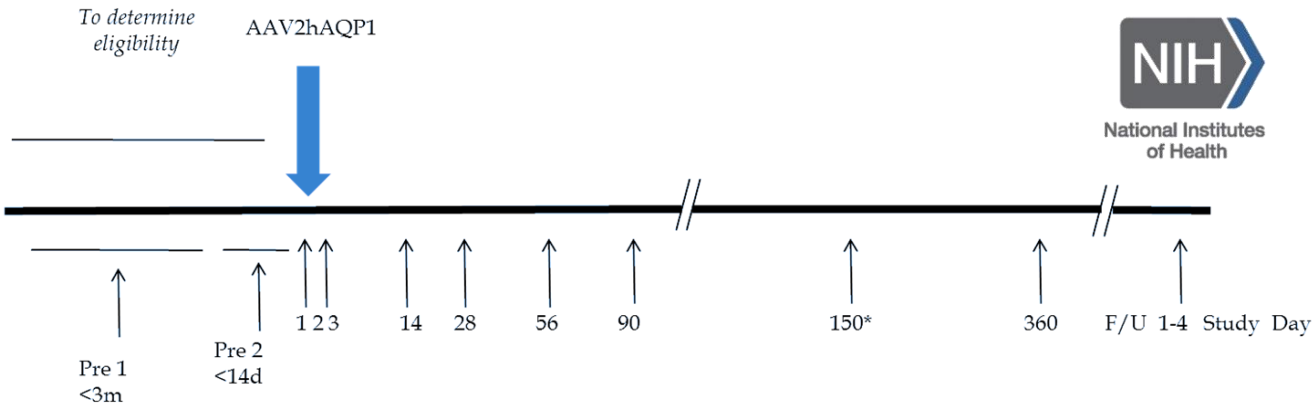
Visual analogue scale (VAS)



Baum BJ et al. *PNAS,* 2012.

AAV-AQP1 Clinical Trials Ongoing

AAV-AQP1 in patients with grade 2/3 xerostomia following IR for oral cancer



Dose Group	Vector Dose (Viral Particles per Gland)
*0	3×10^{9}
1	1×10^{10}
2	3×10^{10}
3	1×10^{11}
4	3×10^{11}
5	6×10^{11}

- **Primary endpoint:** safety
- **Secondary endpoint:** parotid gland salivary output
- **Dose escalation ongoing**
  - Single-site Phase 1 trial at NIH
  - Multi-site Phase 1/2 trial initiated Q3 2019

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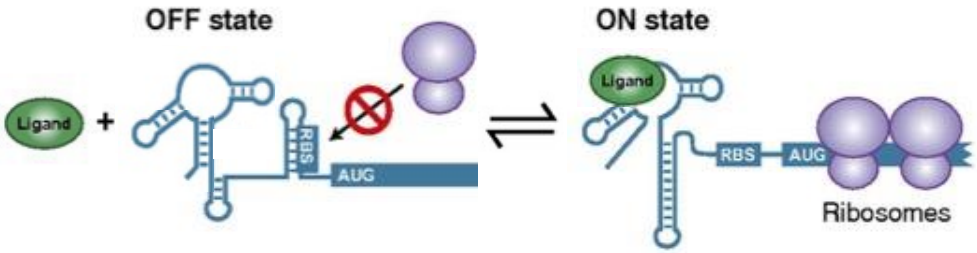
Gene Regulation

Next Generation Gene Therapy: Gene Regulation Platform

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

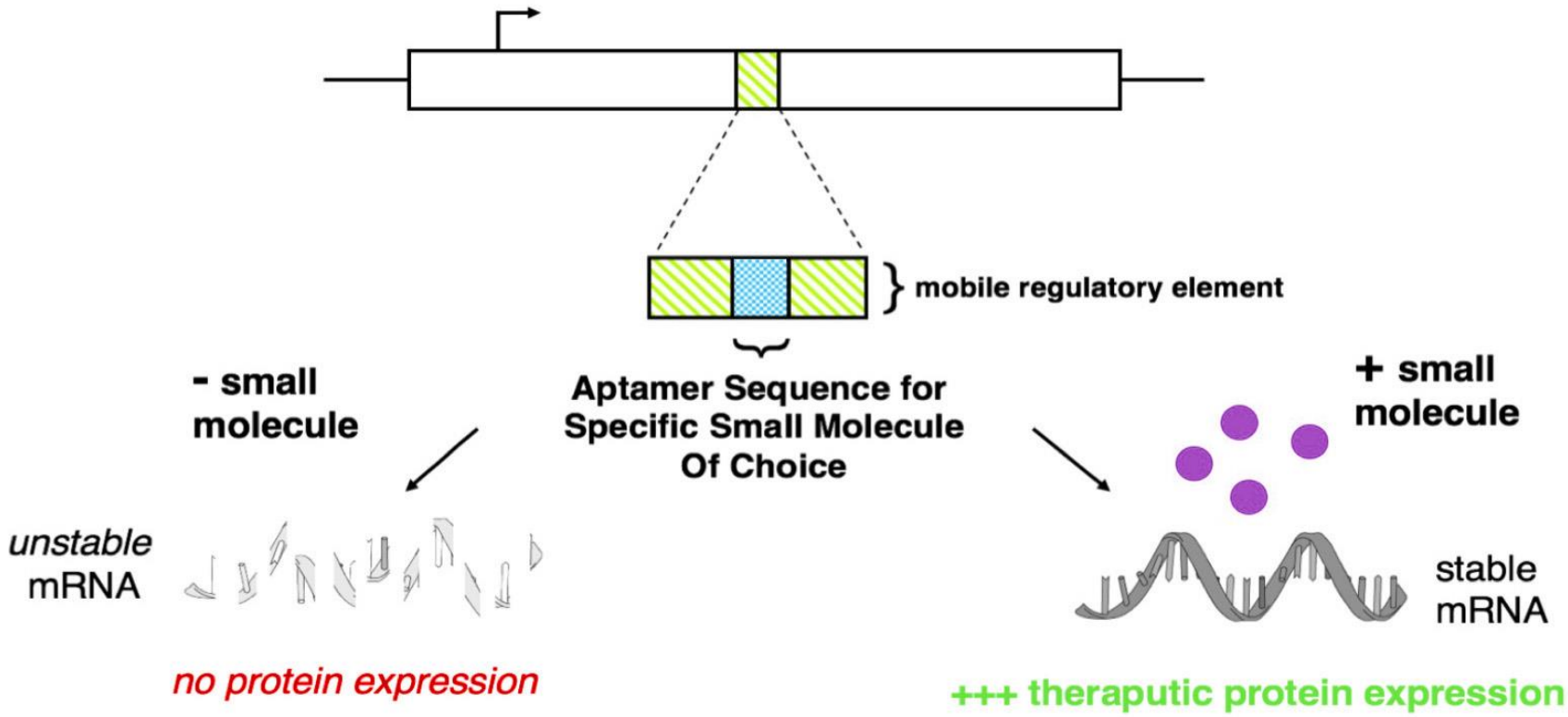
1 Insert the gene for a therapeutic protein

2 Oral small molecule for ongoing control of gene expression

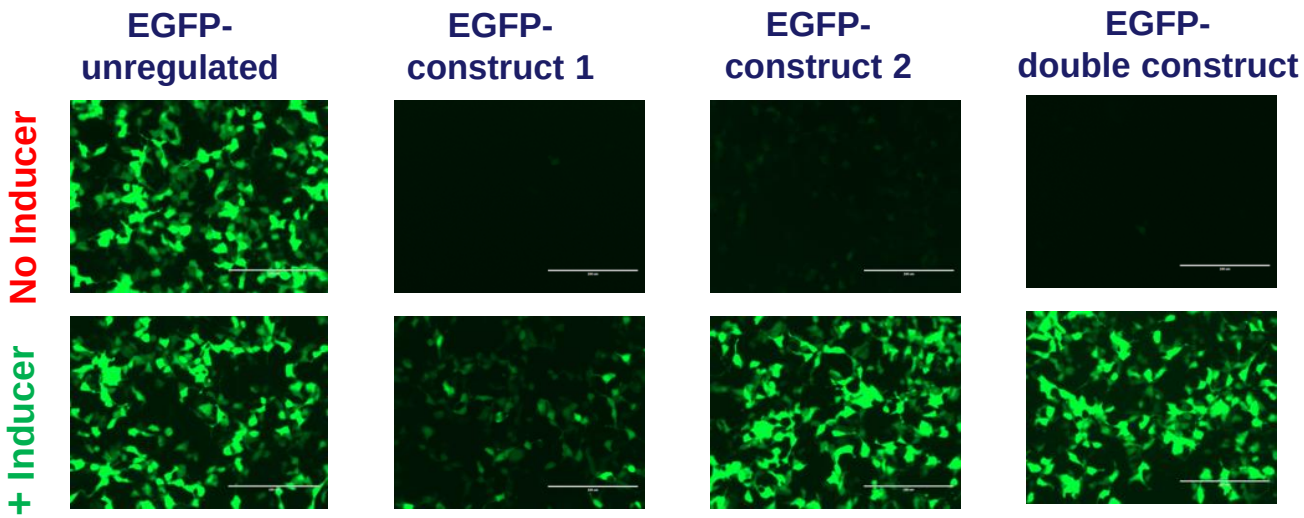


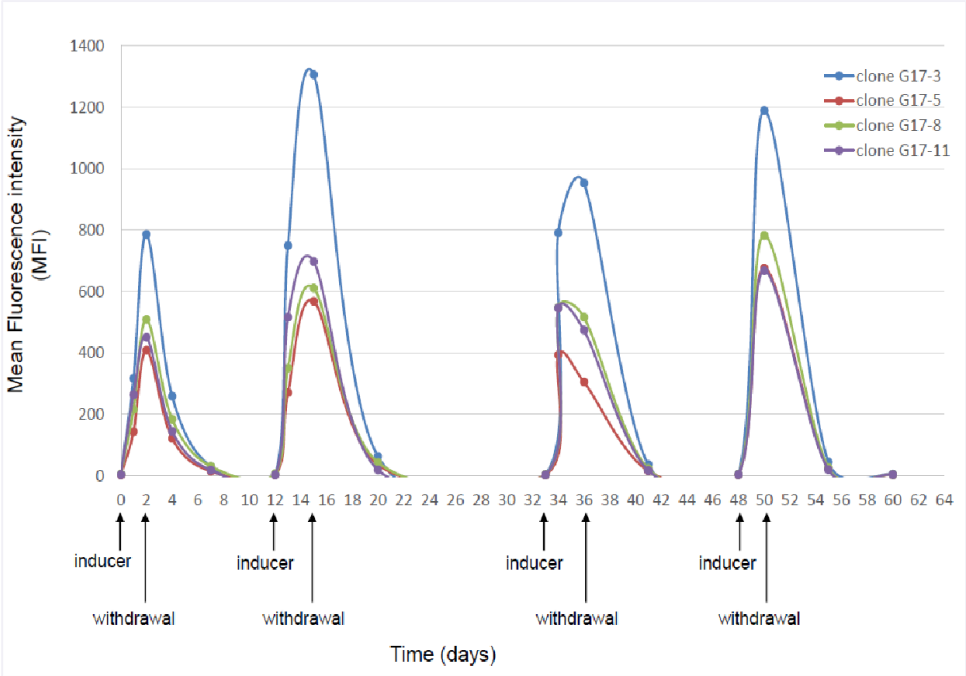
Regulation of Transgenes using Proprietary Riboswitch Technology

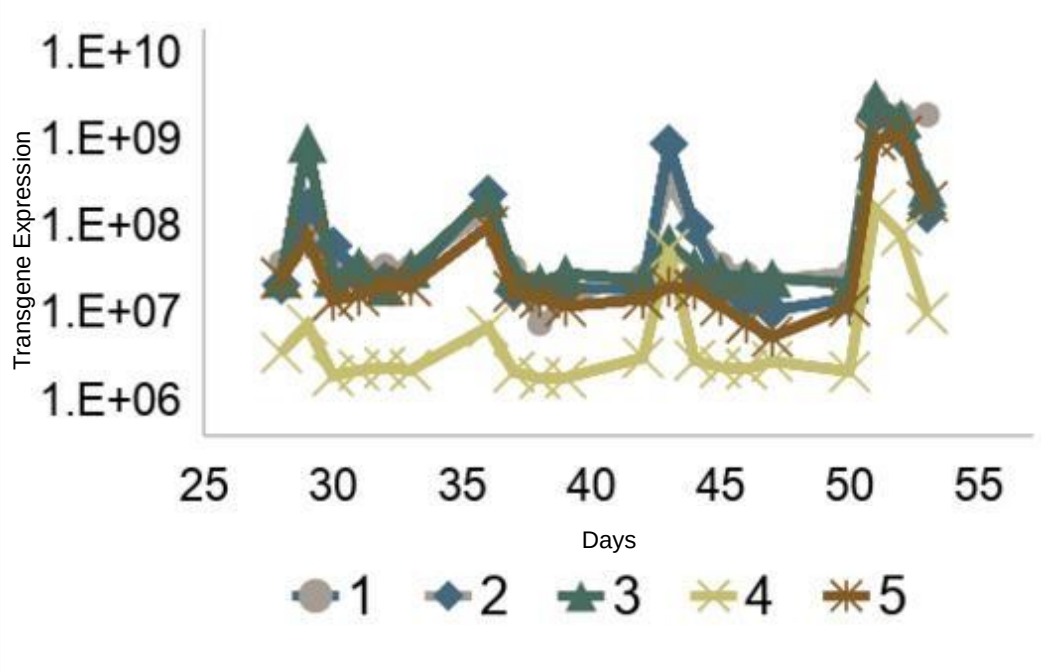
Regulation driven by specific small molecule / RNA binding driving functional changes in RNA configuration, splicing and translation



Regulation of Transgene Expression







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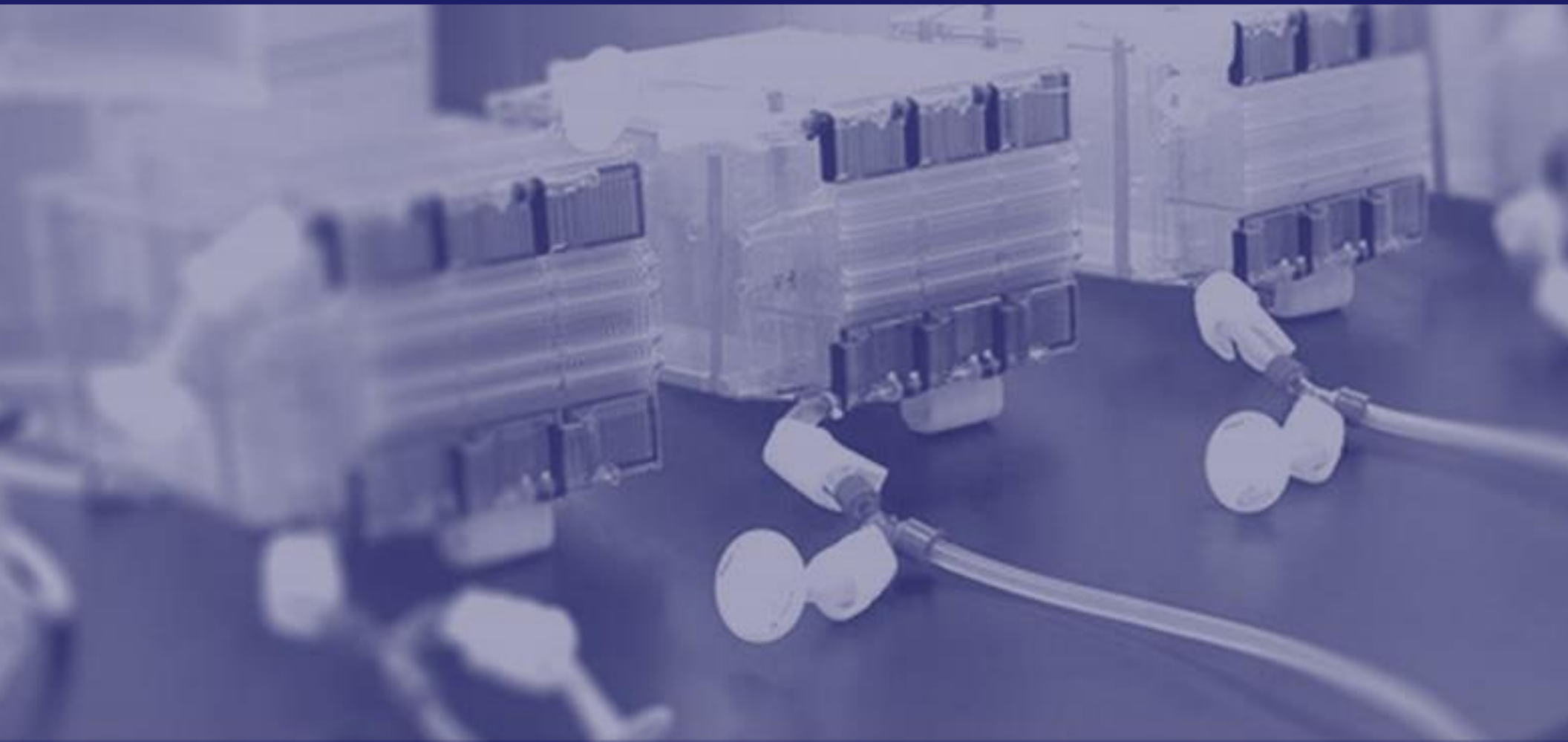
Manufacturing and Process Development



cGMP Certified Manufacturing Facility: Flexible and Scalable

Key Attributes

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

Plan