PYC Therapeutics

Life changing Science

PYC-001 for ADOA

November 2024

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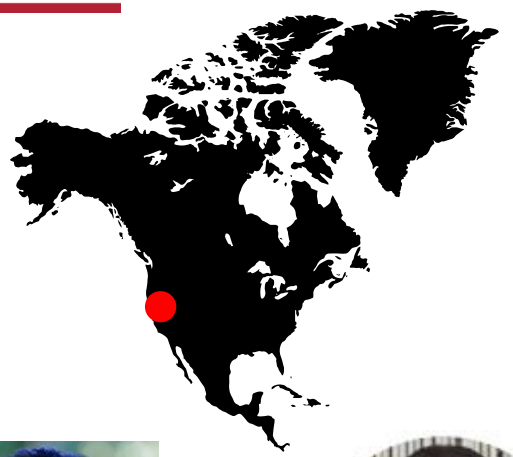
Who we are ?

PYC Therapeutics

Clinical Development

San Francisco, USA



Sri Mudumba
Chief R&D Officer

Clare Guerrero
Senior Director Operations

Our Vision

Create life-changing new medicines for those with severe disease and no treatment options available

Our Mission

Create first-in-class RNA drugs targeting root cause of a genetic disease.

Research & Development

Perth, Australia

Janya Grainok
VP of Discovery

Pipeline of first-in-class RNA drugs that target root cause of diseases

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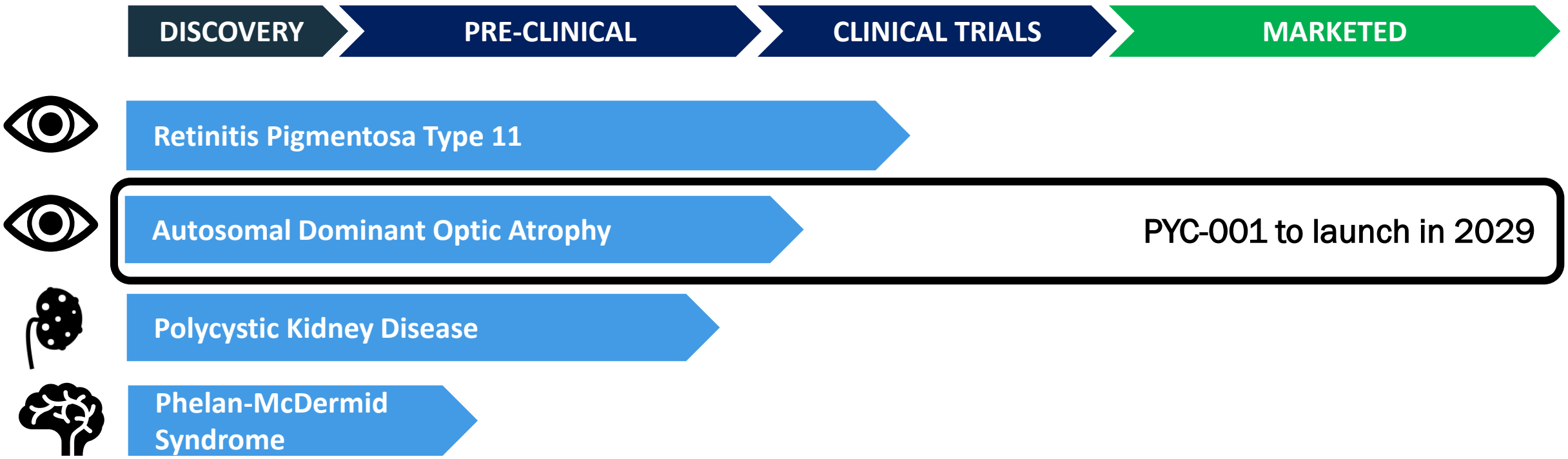
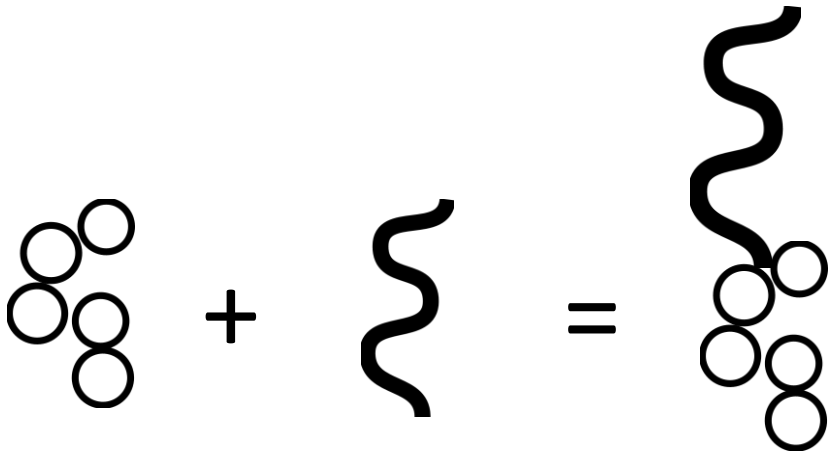


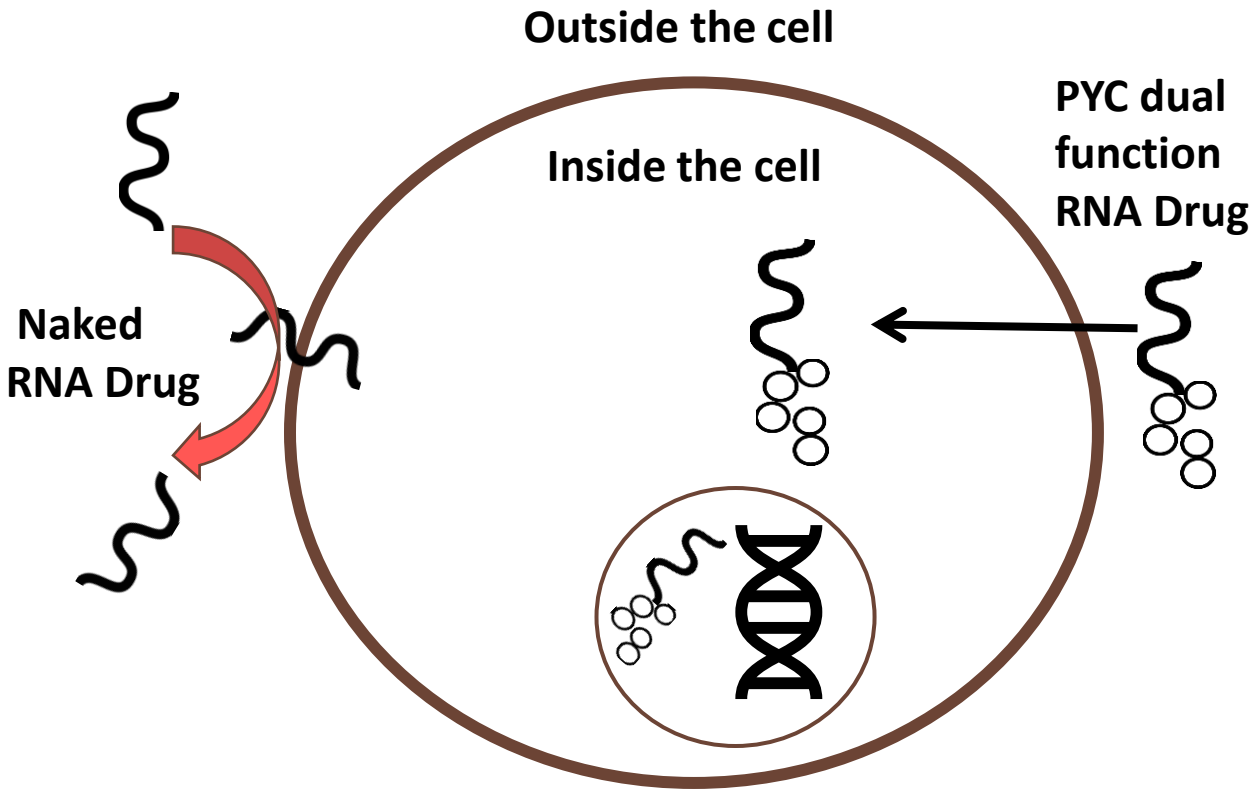
* PYC 96.2% ownership of VP-001 (3.8% ownership by Lions Eye Institute, Australia) and 100% ownership of all other pipeline programs
^ Market size is projected by multiplying patient prevalence per indication by the median orphan drug price of $150k p.a. EvaluatePharma. Orphan Drug Report. 2019.

PPMO drug delivery platform

- Non-Viral drug delivery platform
- Delivers drug inside target cells
- Drug can show better effect



Drug delivery peptide (CPP) + RNA drug (PMO) = PYC next generation dual function RNA drug (PPMO)



RNA therapy is preferred treatment for Ocular Disorders

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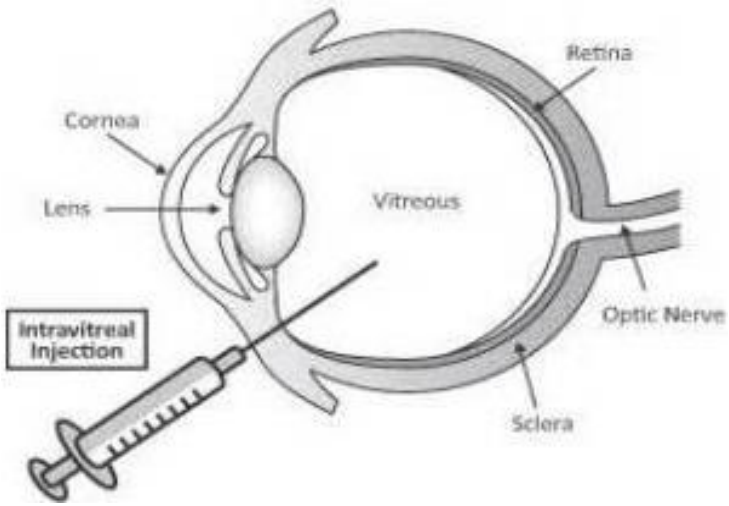
RNA Therapy with Peptide Delivery

- ✓ Reversible
- ✓ Keeps cell's own control over protein production
- ✓ Maintains natural balance of different isoforms or types of a particular protein
- ✓ Intravitreal injection (IVT) is routine and safe



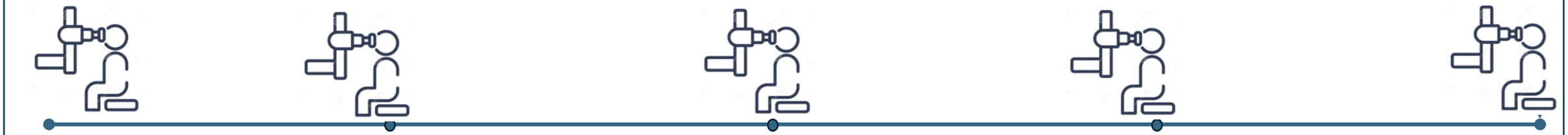
- 10-15mins procedure
- Feel pressure with little or no pain during injection

Gene Therapy with Viral Delivery

- X Permanent change in gene
- X Cell loses control of protein production
- X Loss of isoform balance
- X Risk of virus inserting into genome
- X Subretinal injection which has risks of retinal detachment
- X Risk of inflammation is higher
- X Multiple recent clinical failures

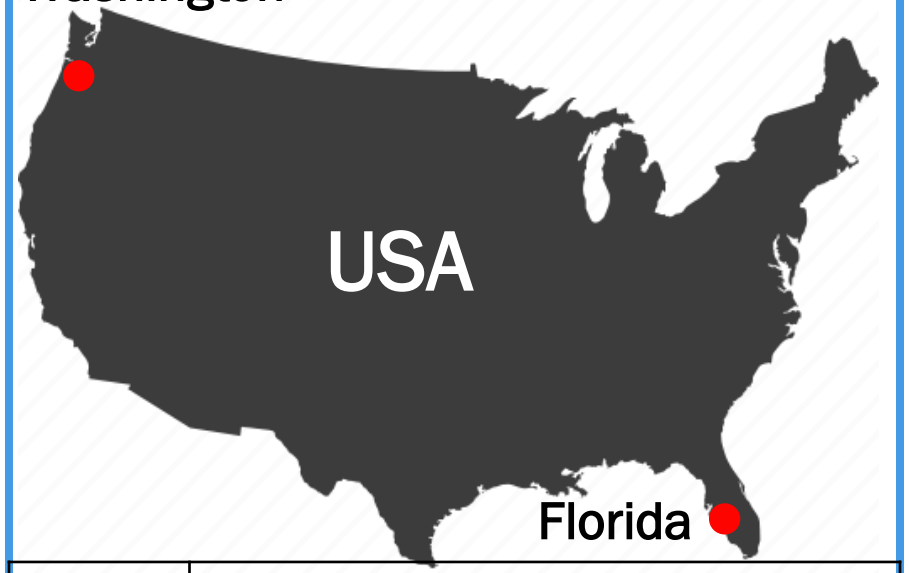
A Natural History Study of Patients with Genetically Confirmed Diagnosis of ADOA, caused by OPA1 Mutation- LEAD IN STUDY

Goal	Study the natural progression of ADOA disease over 2 years
Eligibility Criteria	8 years and above OPA1 mutation associated ADOA No systemic disease like ADOA plus BCVA of between 6/12 (20/40) (70 ETDRS) and 6/48 (20/160) (40 ETDRS)
Study type	Observational ONLY, 5 clinic visits over 2 years
Number of subjects	40 patients, 80 eyes, Male and Female included



BANKSIA Clinical Trial Sites

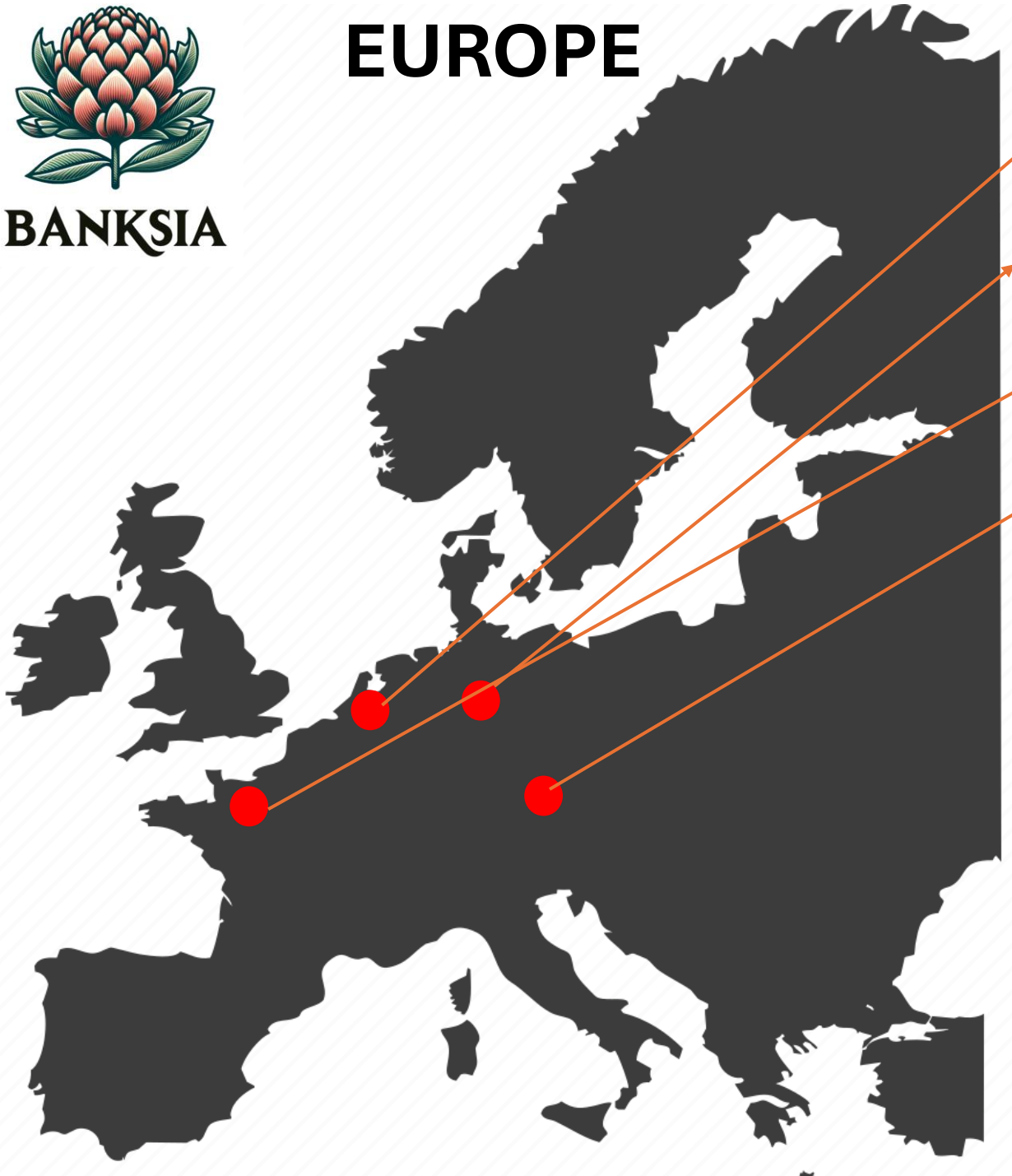
Location	Sydney, Australia
Site	Sydney Eye Hospital
Investigators	Dr. Clare Fraser Dr. John Grigg
Status	Currently Enrolling



Site 1	Dr.Byron Lam Bascom Palmer Medical Center, Miami, Florida
Site 2	Dr. Raghu Mudumbai University of Washington Medical Center
Status	Enrollment starts 1H 2025

BANKSIA

EUROPE



SITES

Netherlands	Dr. Camiel Boon Amsterdam University Medical Center
Germany	Dr. Karsten Hufendiek Hannover Medical School
France	Dr.Xavier Zanlonghi CHU de Rennes- Hospital Pontchaillou
Austria	Dr.Georghi Universitats-Augenklinik Medizinische Universitat Graz

STATUS

- Regulatory submission on going
- Expected Study start in 1Half 2025

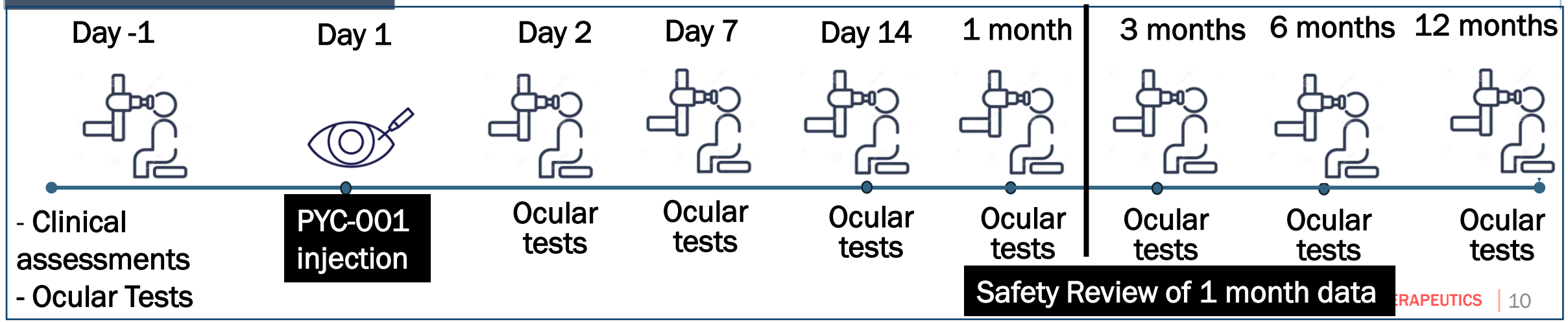
Interested to participate ?

Contact :

banksia@pyctx.com

SUNDEW: PYC-001 Interventional Clinical Trial in Patients with Genetically Confirmed Diagnosis of ADOA, caused by OPA1 Mutation

Goal	To study the safety of PYC-001 in treatment of ADOA
Eligibility Criteria	18 years and above OPA1 mutation associated ADOA No systemic disease like ADOA plus BCVA of between 6/12 (20/40) (70 ETDRS) and 6/48 (20/160) (40 ETDRS)
Study type	1 Intravitreal Injection in the eye, 10 clinic visits over 1 year
Number of subjects	9 patients , 9 eyes, male and female included
Dosing	3 cohorts of 3 patients each – low, mid, high dose



PYC therapeutics clinical studies in ADOA

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Natural History Study

BANKSIA

- Observational study
- 5 clinic visits over 2 years
- Currently enrolling in Sydney, Australia

Eligibility

8 years and above
OPA1 mutation associated ADOA
No systemic disease like ADOA plus
BCVA of between 6/12 (20/40) (70 ETDRS) and 6/48 (20/160) (40 ETDRS)

Enrollment begins in Europe in First half of 2025

Contact : banksia@pyctx.com

Further information: **ClinicalTrials.gov ID** NCT06140329

PYC-001 Interventional Trial

Sundew

- To Assess Safety of treatment with PYC-001
- 1 Intravitreal Injection in 1 eye,
- 10 clinic visits over 1 year
- 3 dose cohorts of 3 patients each

Eligibility

18 years and above
OPA1 mutation associated ADOA
No systemic disease like ADOA plus
BCVA of between 6/12 (20/40) (70 ETDRS) and 6/48 (20/160) (40 ETDRS)

Enrollment begins in Europe mid 2025

Contact : sundew@pyctx.com

Further information: **ClinicalTrials.gov ID** NCT06461286

APOLOGIES FROM PYC

Having posted information about upcoming Clinical Trials in public forums we could not respond to queries from Patients and their care-givers in a timely manner. We have since corrected the issue and would encourage everyone to contact us for information.

Please do not send us any personal history or medical records for privacy purposes. If you would like to talk to us , please share your contact details for us to call or email you.

banksia@pyctx.com
sundew@pyctx.com

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END

Backup slides

Structural & functional outcome measures in Phase1a/b studies to inform Pivotal Trials

VISUAL FUNCTION | FUNCTIONAL VISION

Disease Progression

Insufficient OPA1

Mitochondrial dysfunction

Apoptosis

RGC Loss

Optic Disc Atrophy

Central, Paracentral Visual Fields and Color Vision Defects

Markers

Structural

Functional

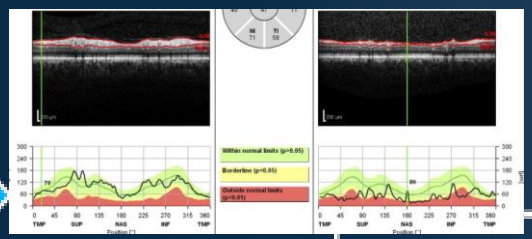
Sensitivity

RNFL, GCL Thickness

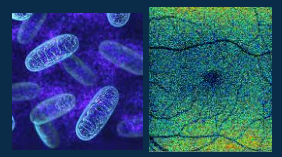
Optic Disc Volume

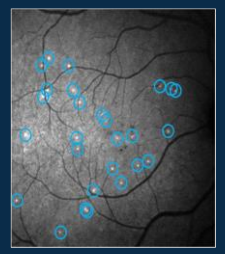
Flavoprotein Autofluorescence

Detection of Apoptotic Retinal Cells

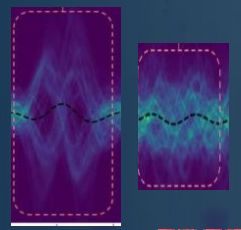


Visual Field Test, Color Vision, Contrast Sensitivity, LCVA





Mf VEP



1. Refer ASX Announcement: 4 October 2023 and 14 May 2024

PYC-001 addresses the root cause of ADOA - insufficient expression of OPA1 protein in the cells that form the optic nerve

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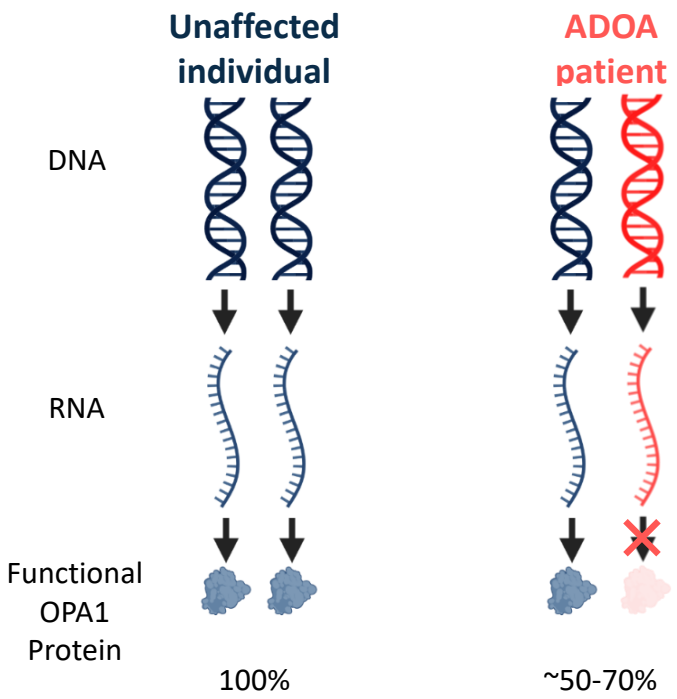
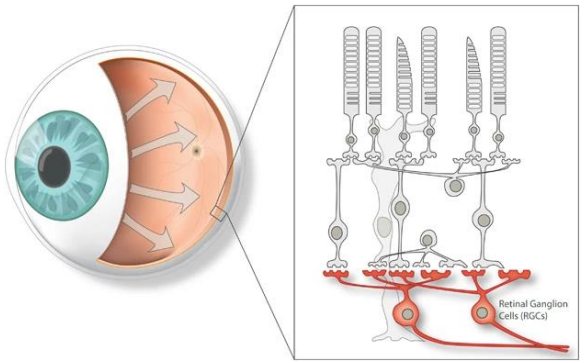
Mechanism of disease causation

ADOA patients have a mutation in one copy of the *OPA1* gene causing an **insufficient level of OPA1 protein in the RGCs**



In ADOA, the **retinal ganglion cells (RGCs),** that make up the optic nerve are affected

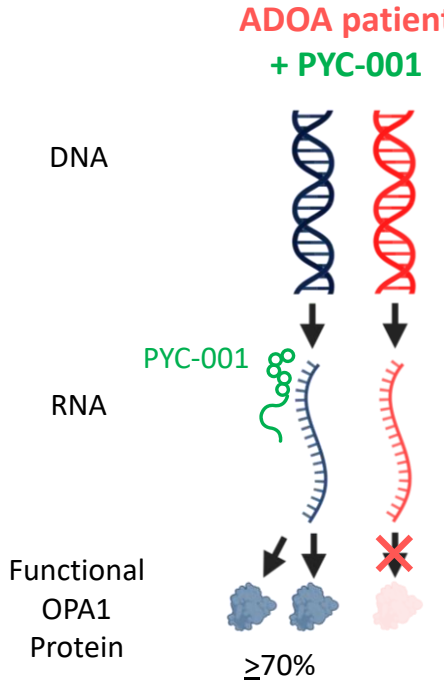


Decreased OPA1 protein leads to:

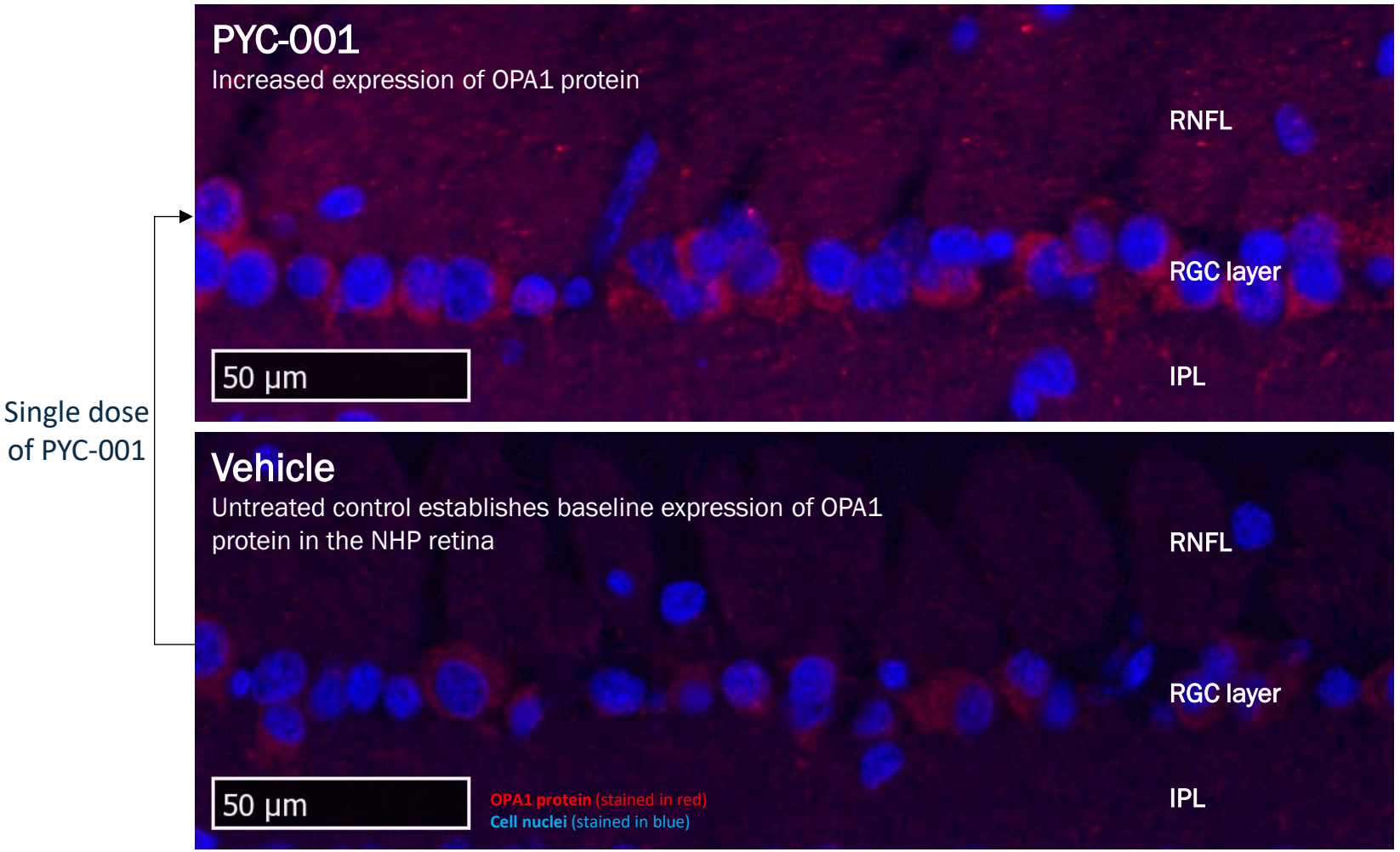
- Compromised mitochondrial function
- Reduced cellular bio-energetics
- Increased ROS and apoptosis
- RGC atrophy and vision decline

Treatment with PYC-001

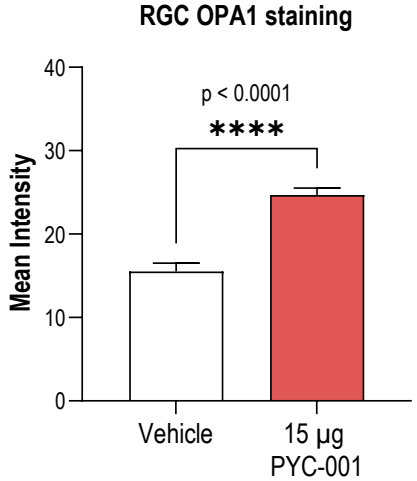
PYC-001 treatment **increases functional OPA1 protein expression** in a **mutation agnostic manner** while maintaining **OPA1 isoform balance**



PYC-001 increases OPA1 protein expression in the NHP retina



- A single 15 µg dose of PYC-001 increases OPA1 protein expression in NHPs in the two cellular layers affected by ADOA[1]
- This result was achieved with a dose of PYC-001 that is safe and well tolerated in NHPs[1]
- The 1.6-fold increase in OPA1 protein expression seen *in vivo* in NHPs[1] is associated with rescue of the functional deficits seen in ADOA patient-derived models *in vitro* [2]



1. Refer ASX announcement 4 October 2023
2. Refer ASX announcement 3 April 2023