# **CIRM OPHTHALMOLOGY CLINICAL PORTFOLIO**

# ICOC UPDATE MARCH 16, 2016



## Unmet medical need in eye disease

#### People who are at risk for blindness

People with genetic eye diseases People with eye diseases such as macular degeneration and glaucoma People with diabetes Stroke victims Eye surgery patients People who work with or near sharp objects or toxic chemicals Premature babies



# Anatomy of the eye





### Unmet medical need in eye disease

#### Genetic diseases of the eye

Stargardt macular dystrophy Usher syndrome Corneal dystrophies Retinitis Pigmentosa (RP) Leber's Congenital Amaurosis Type 2 Leber Hereditary Optic Neuropathy

#### Acquired diseases of the eye

Cataracts Age-related Macular degeneration (AMD) Corneal injuries Infections e.g. "River blindness" — caused by infection by a parasitic worm



### Age- related Macular degeneration (AMD)

- A leading cause of blindness in people over 55 years old
- Responsible for approximately 20% blindness in the U.S.
- Responsible for \$250B annual US healthcare costs
- Characterized by progressive loss of vision in central visual field
- Loss of vision is due to dysfunction of retinal pigment epithelium (RPE)









# Age-related Macular Degeneration: 2 types or stages

Normal





- Dysfunction of retinal pigmented epithelium (RPE)
- Degeneration of Bruch's membrane
- Accumulation of drusen

### Advanced AMD

Dry (atrophic) AMD 80-90%

Wet (exudative) AMD 10-20%

- Loss of photoreceptors
- Vision loss



# **Retinitis Pigmentosa (RP)**





 RP is a group of inherited diseases causing retinal degeneration

- People with RP experience a gradual decline in vision as photoreceptor cells (rods and cones) die
- Starts in **peripheral** visual field
- RP can be inherited in families but 40-50% of the time people with RP have no other affected family member





Normal Fundus



Retinitis Pigmentosa Fundus



Normal Visual Field





## Strategies for cell based therapies for eye diseases

- Cell Replacement Therapy: Pluripotent RPE cells
- Neuro-protective Therapy:
  - Pluripotent retinal progenitor cells
  - Genetically modified RPE cell therapy
- Gene Therapy



## **CIRM Ophthalmology Clinical Portfolio**

AWARD # PI, Institution	CIRM FUNDING (\$MM)	MODALITY	DISEASE/ INJURY	PROJECT GOAL	THERAPEUTIC APPROACH
DR3-07438 Humayun, USC	\$18.9	Cell Therapy + Scaffold	Age-related macular degeneration (dry form)	Ph 1/2a	Allogeneic RPE monolayers on synthetic substrate implanted sub-retinally surgically
DR2A-05739 Klassen, UC Irvine	\$17.3	Cell Therapy	Retinitis Pigmentosa	Ph 1/2	Allogeneic retinal progenitor cells injected intra-vitreally
CLIN1-08235 Wang, Cedars-Sinai	\$4.9	Cell Therapy	Retinitis Pigmentosa	IND	Allogeneic neural progenitor cells injected sub-retinally



#### Humayun/USC/ Regenerative Patch Technologies (RPT): hESC-derived RPEs on a scaffold for AMD

- Investigator: Mark S. Humayun MD, PhD, Professor of Ophthalmology, USC
  - Recipient of the National Medal of Technology and Innovation, December 2015
  - Member of the U.S. National Academies of Medicine
  - Co-inventor of the Argus Series retinal implants
- Scientific approach: Allogeneic RPE monolayers on synthetic substrate implanted subretinally
- Scientific Rationale: Sub-retinal implant designed to replace dystrophic RPE with healthy RPE stem cells
- Clinical indication: Geographic Atrophy- Severe dry AMD













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![](_page_13_Picture_1.jpeg)

![](_page_14_Picture_0.jpeg)

![](_page_14_Picture_1.jpeg)

![](_page_15_Picture_0.jpeg)

Remove vitreous humour

![](_page_16_Picture_0.jpeg)

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![](_page_19_Picture_0.jpeg)

![](_page_20_Picture_0.jpeg)

Make ~1mm incision in the retina

![](_page_21_Picture_0.jpeg)

Position patch injector

![](_page_22_Picture_0.jpeg)

Position patch injector

![](_page_23_Picture_0.jpeg)

Position patch injector

![](_page_24_Picture_0.jpeg)

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![](_page_30_Picture_1.jpeg)

Evacuate blister – reattach retina

#### Klassen/UCI/JCyte Retinal Progenitor cells for the treatment of Retinitis Pigmentosa

- Investigator: Henry Klassen, MD, PhD, Associate Professor Gavin Herbert Eye Institute, UC Irvine School of Medicine
- Scientific approach: Allogeneic human retinal progenitor cells injected intravitreally
- Clinical indication: Retinitis Pigmentosa (RP)
- Scientific Rationale:
  - Despite causative mutation, patients with RP
  - have functional photoreceptors and can see until the cells finally die
  - Transplanted progenitor cells rescue photoreceptors and vision

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![](_page_31_Picture_10.jpeg)

# Klassen UCI/J-Cyte Retinal Progenitor Cells for the treatment of Retinitis Pigmentosa

- Investigational New Drug Application submitted Dec 2014, cleared by FDA, April 2015
- Nine patients successfully enrolled as of Dec 2015
- Clinical Assessments & Follow up ongoing for the treated patients
- Continued Patient enrollment in progress

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# Shaomei Wang/Cedars-Sinai – Sub-retinal Delivery of human progenitor cells for the treatment of Retinitis Pigmentosa

- Investigator: Shaomei Wang, MD, PhD, Associate Professor -Biomedical Sciences Research Scientist, Board of Governors Regenerative Medicine Institute
- Scientific approach: Sub-retinal injection of allogeneic neural progenitor cells to delay retinal degeneration and preserve vision
- Scientific Rationale: to preserve the existing retinal structure and vision using a progenitor cell that migrates long distances along the retina adjacent to the photoreceptors and shows robust protection of the rods and cones
- Clinical indication: Retinitis Pigmentosa

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# Shaomei Wang/Cedars-Sinai – Sub-retinal Delivery of human neural progenitor cells for the treatment of Retinitis Pigmentosa

- Manufacturing of clinical grade cells is in progress
- Conduct of Mechanism of action studies is also in progress
- Design of preclinical studies with focus on:
  - Time and dose dependent spread and engraftment of the cells
  - Dose dependence of relief of retinal degeneration as assessed by functional methods
- Toxicology study enabling IND filing
- Refinement of Clinical protocol for IND filing

![](_page_34_Picture_8.jpeg)

![](_page_34_Picture_9.jpeg)

#### **CIRM Ophthalmology Clinical Portfolio**

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