Subretinal Human Retinal Progenitor Cells (hRPC) in Retinitis Pigmentosa (RP)

A Phase I/IIa update

Pravin U. Dugel, MD
Relevant disclosure

• Consultant to ReNeuron PLC

Full disclosures available in conference program
ReNeuron’s retinal progenitor cell (hRPC) therapy

- Cells isolated from fetal retina
- Can differentiate into retinal cells
- Cryopreserved with 9 month shelf life
- No immunosuppression required

Baranov et al (2014)
Mechanism of Action

Allogeneic transplantation in pigs @ 4 wks post-injection

Both integration and paracrine effects may contribute to efficacy

Subretinal hRPC

*Potential benefits*

1. *Direct delivery into subretinal space*
Subretinal hRPC

Potential benefits

1. Direct delivery into subretinal space

2. On demand shipment to site of care
Subretinal hRPC

Potential benefits

1. Direct delivery into subretinal space

2. On demand shipment to site of care

3. Treatment agnostic to genetic subtype of disease
RP Phase I/IIa clinical trial (NCT02464436)
Open-label, single, unilateral, subretinal injection of hRPC (worse eye)

Phase I study design

**Baseline:**
- ETDRS letters: 0-1***
- VA: LP - 20/800

***only 1 patient read 1 letter

**Dose:**
- 250K*, 500K*, 1M** cells

*fresh; **cryopreserved

**Safety Endpoint:**
- Good safety profile allowed progression into Phase IIa#

US Clinical Site:
- Massachusetts Eye & Ear, Boston, Jason Comander, MD, PhD

# Data presented by Dr. Comander in April 2019, at Retinal Cell and Gene Therapy Innovation Summit (Vancouver, BC).
RP Phase I/IIa clinical trial (NCT02464436)
Open-label, single, unilateral, subretinal injection of hRPC (worse eye)
Study ongoing

Phase IIa study design

Subjects (N=10)
Baseline: ETDRS letters: 9-56
VA: 20/640-20/80

Dose
1M cells in cryopreserved formulation

Primary Endpoint
Change in ETDRS letters read from baseline to 24 months post-treatment
(Interim visits: 1, 2, 3, 6, 9, 12, 18 months)

US Clinical Sites:
Massachusetts Eye & Ear, Boston, Jason Comander, MD, PhD
Retinal Research Institute, Phoenix, Pravin Dugel, MD
Surgical Procedure
Phase I/IIa safety

- N=22 subjects
- Dose escalation generally well-tolerated
- No evidence of inflammation or proliferative vitreoretinopathy
- 2 ocular SAEs reported – not related to drug product
  - Subject 4001 - progression of pre-existing epiretinal membrane requiring additional surgery
  - Subject 6003 - persistent subretinal fluid/patent retinotomy
Phase I/IIa safety

- 2 events leading to vision loss (one AE, one SAE) related to surgical procedure/patient selection
  - Subject 6001 – RPE tear
  - Subject 6003 – persistent subretinal fluid/patent retinotomy
ETDRS letters read: Phase IIa portion

*Change from baseline in treated eye*
## ETDRS letters read: Phase Ila portion

*Change from baseline in treated eye*

<table>
<thead>
<tr>
<th>Mean change: (per timepoint)</th>
<th>+8.3 (n=8)</th>
<th>+5.4 (n=8)</th>
<th>+6.1 (n=8)</th>
<th>+18.5 (n=4)</th>
<th>+12 (n=1)</th>
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### Days post-treatment

<table>
<thead>
<tr>
<th>30</th>
<th>60</th>
<th>90</th>
<th>180</th>
<th>270</th>
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### ETDRS letters read (Change from baseline)

- 5001
- 5002
- 5003
- 6001
- 6002
- 6003
**ETDRS letters read: Phase IIa portion**

*Change from baseline in untreated eye*

<table>
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<tr>
<th>Mean change: (per timepoint)</th>
<th>+1.6 (n=8)</th>
<th>+2.8 (n=8)</th>
<th>+6.8 (n=8)</th>
<th>+7.8 (n=4)</th>
<th>-1 (n=1)</th>
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```
30  60  90  180  270
ETDRS letters read (Change from baseline)
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5001  5002  5003
ETDRS letters read
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5001  5002  5003
Days post-treatment
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ETDRS letters read
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**ETDRS letters read: Phase IIa portion**

*Mean changes in treated eye vs untreated eye*

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**Graph:**
- **x-axis:** Days post-treatment
- **y-axis:** ETDRS letters read (mean change from baseline)
- **Legend:**
  - *treated eye*
  - *untreated eye*
ETDRS letters read: Phase IIa portion

Mean changes in treated eye vs untreated eye

Subjects with vision loss excluded

*excluding 6001, 6003

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<tr>
<td>+1.5 (n=6)</td>
<td>+3.5 (n=6)</td>
<td>+8.3 (n=6)</td>
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<tr>
<td>+28.7 (n=3)</td>
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* excluding 6001, 6003
Summary

• Acceptable safety profile
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• Biological efficacy signals
  • Very rapid and profound in some patients
  • Slower in other patients
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• These study results will provide a better understanding of optimal patient selection and surgical procedure standardization for future study design
Summary

• Acceptable safety profile
• Biological efficacy signals
  • Very rapid and profound in some patients
  • Slower in other patients
• These study results will provide a better understanding of optimal patient selection and surgical procedure standardization for future study design
• Potentially a promising new therapy for patients with RP