STRATEGY FOR CREATING INNOVATION
R&D MEETING 2016

Kenji Yasukawa Ph.D.
Senior Corporate Executive
Senior Vice President & Chief Strategy Officer
Astellas Pharma Inc.
December 8, 2016
Turn innovative science into value for patients by addressing unmet needs.
OPPORTUNITIES TO PURSUE & NEW STRATEGIES FOR DRUG DISCOVERY RESEARCH

Opportunities to pursue

- Innovative drug discovery in TAs with high UMNs
- New modalities such as cell therapies, gene therapies, etc.
- Increasing number of technologies with applicability in various fields
  ⇒ Opportunities to create innovative value for patients still exist

New strategies for drug discovery research

- Research with using strengthens in existing TAs + Advancing into new TAs
- Challenges in Rx business + α (new business): to provide medical solutions
- Utilization of external R&D resources through Network Research System: Best Science / Best Place / Best Talent
- Extensive input
- FASTEN (Multi-tracking of R&D process)

TAs: Therapeutic areas, UMNs: Unmet medical needs
FOUR PILLARS FOR ENHANCING CAPABILITIES TO DELIVER INNOVATIVE MEDICINES

① Extensive planting
② Fast fail
③ Quick win
④ Differentiation

POC: Proof of concept, E-med: Evolving medical solutions
OUTCOME OF R&D RESHAPING

- Sharply increased number of theme inputs
- Shortened timeframe of exploratory R&D stage by 30% after FASTEN implementation

*For illustrative purposes only *

- Confirmed a trend of cost reduction during exploratory R&D stage, also

GLP: Good Laboratory Practice
FOCUSED RESEARCH PROGRAMS

Existing TAs
- Urology
- Oncology
- Immunology
- Nephrology
- Neuroscience

New TAs
- Muscle Diseases
- Ophthalmology

Core technologies

New technologies, new modalities

Next-generation vaccines
- LAMP-vax
  - Institute of Medical Science, Univ. of Tokyo
- Muco-rice

Cell therapy
- AIRM

Gene therapy
- Oncolytic virus immunotherapy

Fusion protein
- KANYOS BIO

Small molecule Antibody
- Dana-Farber Cancer Institute
- Kyoto Univ. (AK Project)
AGENDA

I  Creating innovation

II  Therapeutic area: Oncology

III  Therapeutic area: Muscle Disease

IV  Therapeutic area: Immunology
CREATING INNOVATION

On the forefront of healthcare change to turn innovative science into value for patients

- Enhancing capabilities to deliver innovative medicines
- Advancing into new opportunities
  - Network-type research system
    - 3B (Best Science, Best Talent, Best Place)
  - Multitrack R&D project management
    - FASTEN
  - Renovate HR system to create innovation
    - aiPaths, DISC
Renovate HR system to create innovation

New HR program to encourage the creation of innovation from a personnel perspective aiPaths (Astellas Research Multi-Career Paths)

Career paths for researchers

Principal Investigator (PI)
The goal is to encourage researchers to ambitiously develop innovative ideas that were difficult to take on under existing systems and produce concrete R&D results in a timely manner. PIs will be given a certain degree of discretionary authority for personnel and budgets to initiate drug development for incorporating cutting-edge science.

Research Professional
The goal is strengthening research base by acquiring cutting-edge science and technologies through a range of specialties based on abundant knowledge and experience.

Recruitment for diverse researcher to create innovation

DISC (Drug Discovery Innovator Selection Camp)

Astellas has incorporated a unique program called DISC into the process of recruiting drug discovery researchers who are able to constantly create new forms of value with sharing of multifaceted values and solve issues by drawing upon all resources including specialized expertise, experience, knowledge, information and human networks.
AGENDA

I. Creating innovation

II. Therapeutic area: Oncology

III. Therapeutic area: Muscle Disease

IV. Therapeutic area: Immunology
ONCOLOGY

Building a portfolio of novel immuno-oncology therapeutics targeting tumor microenvironments to address tumor types unresponsive to anti-PD-1/PD-L1 Checkpoint Co-stimulatory signal Approaches targeting tumor micro environment

Targeting tumor-specific antigen
T-cell receptor like antibody

Low antigenicity, antigen presentation

Immune suppressive cells (Treg, MDSC, TAM) /mediators

Evoking anti-tumor immunity
Immuno-oncolytic virus
TIL increase

TIL activation
Novel checkpoint inhibitors, Co-stimulatory agonists

Reduced immunosuppressive environment
Blocking immunosuppressive cells / mediators

ONCOLOGY: Potenza Therapeutics COLLABORATION

A pipeline of novel checkpoint inhibitor, co-stimulatory agonist and modulator of immunosuppressive cells etc. for patients and tumor types unresponsive to PD-1/L1 blockers

Immunomodulatory mechanisms

Potenza program portfolio

<table>
<thead>
<tr>
<th>Program</th>
<th>Development Progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Checkpoint inhibitor</td>
<td>2017 IND scheduled</td>
</tr>
<tr>
<td>Treg modulator</td>
<td>2017 IND scheduled</td>
</tr>
<tr>
<td>Co-stimulatory agonist</td>
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</table>

PD-1: Programmed cell Death-1, PD-L1: Programmed cell-Death Ligand 1,
Treg: regulatory T cell, APC: Antigen Presenting Cell
ONCOLOGY: IMMUNO-ONCOLYTIC VIRUS APPROACH

Immuno-oncolytic virus with multiple trans-genes to evoke anti-tumor immunity (Collaboration)

NK cell: Natural Killer cell, DC: Dendritic Cell, APC: Antigen Presenting Cell
T-cell receptor like antibody, h8F4 against PR1/HLA-A2 which eliminates the target positive human AML cells

Anti-tumor mechanism of h8F4

Development progress

Expression of PR1/HLA-A2

AML: Acute Myeloid Leukemia, P3: Proteinase 3, NE: Neutrophil Elastase, ADCC: Antibody-Dependent Cell-Mediated Cytotoxicity
AGENDA

I. Creating innovation

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IV. Therapeutic area: Immunology
Create novel NMEs by innovation from research collaborations and in-house R&D capability based on the approach to improve muscle functions.
MUSCLE: Cytokineti cs COLLABORATION

Combat against muscle impairment/weakness with innovative approaches

Skeletal muscle biology-driven treatments for diseases

Advantages of Cytokinetics, Inc.
- Great expertise in muscle biology
- Broad technical platform to assess muscle functions in non-clinical/clinical studies
- Extensive human network in the muscle research field
- Experience in clinical development including ALS

Progress in the fast skeletal muscle activators

CK-2127107
- Fast skeletal troponin activator

CK-3672889
- Next-generation activator

<table>
<thead>
<tr>
<th>Program - Disease</th>
<th>Development Progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK-2127107</td>
<td>Pre-clinical</td>
</tr>
<tr>
<td>• SMA,</td>
<td>Clinical</td>
</tr>
<tr>
<td>• COPD</td>
<td>Ph2</td>
</tr>
<tr>
<td>CK-2127107</td>
<td>Pre-clinical</td>
</tr>
<tr>
<td>• ALS</td>
<td>Clinical</td>
</tr>
<tr>
<td>• ALS</td>
<td>Ph2 ready</td>
</tr>
<tr>
<td>CK-3672889</td>
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</tbody>
</table>

ALS: Amyotrophic Lateral Sclerosis
SMA: Spinal Muscular Atrophy, COPD: Chronic Obstructive Pulmonary Disease
CK-2127107 improves muscle contractility and exercise tolerance in a rat model of heart failure

CK-2127107 significantly increased isometric tension in LAD-HF plantarflexor.

CK-2127107 significantly increases running performance in LAD-HF rats with exercise intolerance.

(LAD-HF: Left Anterior Descending coronary artery Heart Failure)
Create novel NMEs for broad indications by Mitobridge's proprietary strength of mitochondrial biology and biotech-style research

Activation of mito. function by multiple biological approach

Strength of Mitobridge

Biology-based approach
- Research platform based on mitochondrial biology
- Plural research pipeline by multiple approach

Biotech-style research
- Agile research using enriched network
- Hybrid R&D with Astellas’ developmental capability

Scientific Advisory Board and talented researchers
- Research expertise based on mitochondrial biology
- Intake of newest science by prompt cooperation among researchers

Identify gene regulator “MTB-1” for clinical trial

TCA: TriCarboxylic Acid, NAD: Nicotinamide Adenine Dinucleotide
Candidate (MTB-1) for clinical development is now on preparation toward IND for Duchenne muscular dystrophy therapy.

Consultation with TREAT-NMD

Mitobridge had a meeting with TREAT-NMD advisory committee to discuss potential of MTB-1 for the treatment of DMD.

http://www.treat-nmd.eu/resources/tact/reviews/past/mtb-1/

Action of MTB-1 to activate mitochondrial function could be reasonable for the possible use in DMD treatment because mitochondrial dysfunction in muscle has been reported in DMD patients.

Additional experimental data to increase clinical benefits of MTB-1 and proactive investigation of regulatory guidance from the FDA and EMEA could accelerate early entry to clinical trials.

Development progress

<table>
<thead>
<tr>
<th>Program</th>
<th>Disease</th>
<th>Development Progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTB-1</td>
<td>DMD</td>
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<tr>
<td></td>
<td></td>
<td>Pre-clinical</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clinical</td>
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<tr>
<td></td>
<td></td>
<td>2017 IND scheduled</td>
</tr>
</tbody>
</table>

Other programs

TREAT-NMD: Translational Research in Europe-Assessment and Treatment of NeuroMuscular Diseases,
DMD: Duchenne Muscular Dystrophy
AGENDA

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IV Therapeutic area: Immunology
Develop an innovative platform which can achieve antigen-specific immune modulation, and create curative and safe therapeutics against allergy, autoimmune diseases and infectious diseases.

**Rice-Based oral vaccine**
Induce systemic and mucosal immunity
Stable at room temperature

**LAMP-vax DNA vaccine**
Next-gen DNA vaccine
Safe and short course of therapy

**Auto-antibody selective regulation**
Development of new platform

**Antigen-specific tolerance**
Innovative immune tolerance therapeutics

**ETEC; EnteroToxigenic E coli**
**LAMP: Lysosomal Associated Membrane Protein**
**T1D: Type 1 Diabetes**
LAMP-vax DNA vaccine platform

Revolutionary Technology
• LAMP-vax induce a robust Th1 immune response

High Safety and Convenience
• Short course curative therapy without systemic allergen exposure

Versatile platform
• Applicable to a wide variety of allergic diseases

Allergen-LAMP Fusion Protein
- Luminal domain: Glycosylation stabilizes antigen-LAMP fusion protein trafficking to MHC-II compartment
- Allergen Sequence: e.g. Cry I 1/Cry I 2, optimized for immunogenicity
- Cytoplasmic domain: Signal sequence YQTI directs fusion protein into the lysosome for MHC-II presentation to CD4 T-cells

No allergen leakage out of the cell

Th1-type immune reaction induction (Suppression of Th2 allergic response)
Versatile platform which can be applied to a wide variety of allergic diseases by changing inserted allergen DNA sequence.

**Food allergy**
- e.g. peanut, milk, wheat, egg, etc.

**Seasonal pollen allergy**
- e.g. cedar, cypress, ragweed, grass, etc.

**Perennial allergy**
- e.g. house dust mite, pet, mold, etc.

<table>
<thead>
<tr>
<th>Program</th>
<th>Development Progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASP0892 [peanut]</td>
<td>Pre-clinical</td>
</tr>
<tr>
<td>Other food allergies</td>
<td>Pre-clinical</td>
</tr>
<tr>
<td>ASP4070 [Japanese red cedar]</td>
<td>Pre-clinical</td>
</tr>
<tr>
<td>Other seasonal allergies</td>
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<tr>
<td>Perennial allergies</td>
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</table>
New platform for the induction of antigen-specific immune tolerance

- “Endogenous tolerogenic pathway” in liver and spleen is exploited to prevent autoimmunity
- The technology targets antigens to the surfaces of red blood cells in vivo; the associated antigens are processed to induce antigen-specific T cell deletion and Treg
- Applicable to a wide variety of autoimmune diseases whose pathogenic antigens are identified, including Type 1 Diabetes and Celiac Disease
- Additional tolerance induction platforms are being explored with Kanyos Bio
- Pre-clinical stage

Mechanism of action

- Antigen plus hook “anti-erythrocyte antibody”
- Binding to erythrocyte
- Acts as a tolerogen when cleared by the spleen and the liver
OUR JOURNEY

Turn innovative science into value for patients by

embodying outcome of Network Research System.
Robert Lanza, M.D.
Head of Astellas Global Regenerative Medicine and Chief Scientific Officer Astellas Institute for Regenerative Medicine (AIRM)
December 8, 2016
AGENDA

I Introduction

II Ophthalmology program
(Retinal pigment epithelium, Photoreceptor progenitors, Retinal ganglion progenitors and Corneal endothelium)

III Application in other fields
(Hemangioblast-derived MSCs and Vascular progenitors)

IV Joint research with academia in Japan

MSCs: mesenchymal stem cells
ADVANTAGE OF CELL THERAPY

Cell Therapy has a huge potential in clinical usage

Information: Cell >>> Biotherapeutics > chemical compound

- **Safe**: Cell is an ultimate “natural product” of human origin
- **Efficacious**: Efficacy is not limited to depressing progression, but complete recovery of function is expected theoretically
- **Responsive**: Only cells recognize its environment and respond ex. sugar sensor → insulin secretion by β-cells

Advantages of PSC-derived Tissues in Regenerative Medicine

- Virtually unlimited supply of cells
- Can be derived under GMP conditions pathogen-free
- Can be produced with minimal batch-to-batch variation
- Can be thoroughly characterized to ensure optimal performance

PSC: pluripotent stem cell
PLURIPOTENT STEM CELLS (PSCs) – THE BODY’S MASTER CELLS

Neurons for neurodegenerative disorders

Skin and/or hair follicles for wounds, ulcers & hair loss

Cardiac cells for heart disease

Hepatocytes for liver disease

Blood cell types for hematologic disorders

Retinal cell types for ocular diseases

Alveolar cells for lung diseases

Insulin-producing cells for diabetes

Intestinal cells for Crohn’s/irritable bowel syndrome

ADVANTAGE OF ASTELLAS INSTITUTE FOR REGENERATIVE MEDICINE (AIRM)

Advanced technology that can establish fully-differentiated cells from pluripotent stem cells (PSCs) and strengths in clinical studies and manufacturing for cell therapy

<table>
<thead>
<tr>
<th>Research</th>
<th>Development</th>
<th>Manufacturing</th>
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<tbody>
<tr>
<td>• Technology to establish differentiated target cells from PSCs that could provide functional replacement or trophic support to worn-out or dysfunctional cells and tissues</td>
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<tr>
<td>• Strong IP positions</td>
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<tr>
<td>• Cutting-edge science accepted by top journals</td>
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<tr>
<td>• Expertise in cell-based therapy for high and unmet needs in ophthalmology</td>
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<tr>
<td>• 38 patients treated safely to date</td>
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<tr>
<td>• Active programs currently for macular degeneration (dry AMD and SMD)</td>
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<tr>
<td>• Capabilities and track records to manufacture clinical grade cell product that was supplied to US and UK</td>
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<tr>
<td>• Strong process and analytical development capabilities (e.g. hypersensitive impurity cell detection method, novel cell formulation)</td>
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AMD: age-related macular degeneration, SMD: Stargardt’s macular dystrophy
### CURRENT R&D PROGRAMS

#### AIRM (US)

<table>
<thead>
<tr>
<th>Program</th>
<th>Potential Disease</th>
<th>Development Progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinal pigment epithelium (RPE)</td>
<td>• Dry AMD</td>
<td>Pre-clinical</td>
</tr>
<tr>
<td></td>
<td>• SMD</td>
<td>Clinical</td>
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<tr>
<td>Photo-receptor progenitors (PhRPs)</td>
<td>• Retinitis pigmentosa</td>
<td></td>
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<tr>
<td></td>
<td>• Macular degeneration</td>
<td></td>
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<tr>
<td>Retinal ganglion progenitors (RGPs)</td>
<td>• Glaucoma</td>
<td></td>
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<tr>
<td></td>
<td>• Optic neuropathies</td>
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<tr>
<td>Hemangioblast-derived MSCs (HMCs)</td>
<td>• Autoimmune diseases</td>
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<tr>
<td></td>
<td>• CNS/vascular indications</td>
<td></td>
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<tr>
<td>Vascular progenitors</td>
<td>• Critical limb ischemia</td>
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<tr>
<td></td>
<td>• Pulmonary hypertension</td>
<td></td>
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<tr>
<td>Corneal endothelium</td>
<td>• Corneal diseases</td>
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<tr>
<td></td>
<td>• Corneal injuries</td>
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</table>

#### DDR RML (JP)

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<thead>
<tr>
<th>Program</th>
<th>Potential Disease</th>
<th>Development Progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint research with Kyoto Univ. CiRA</td>
<td>• Kidney diseases</td>
<td></td>
</tr>
<tr>
<td>Joint research with Osaka Univ.</td>
<td>(non-disclosure)</td>
<td></td>
</tr>
<tr>
<td>Other programs</td>
<td>(non-disclosure)</td>
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</tbody>
</table>

ES cell: embryonic stem cell, iPS cell: induced pluripotent stem cell, CiRA: Center for iPS Cell Research and Application
OPHTHALMOLOGY PROGRAMS

- Corneal endothelium
  - Corneal diseases

- Retinal ganglion progenitors
  - Glaucoma/Optic neuropathies

- Retinal pigment epithelium
  - Dry AMD/SMD

- Mesenchymal stem cells
  - Immune/Inflammatory diseases

- Photoreceptor progenitors
  - Retinitis pigmentosa/Macular degeneration

Vision loss costs $3 Trillion worldwide

http://www.amdalliance.org/
RPE
RPE PROGRAM - TRACK RECORD

- **2003**: Start of human RPE program
- **2004**: Published first-ever paper describing the derivation and characterization of RPE from human pluripotent stem cells
- **2006**: Published first-ever paper showing hESC-RPE can prevent visual loss in animals
- **2010**: UK approval for Stargardt's trial
  - NCT01469832
- **2011**: FDA approval for Stargardt’s trial
  - NCT01345006
- **2012**: KFDA approval for Stargardt’s & dry AMD trials in South Korea
- **2014**: Study published showing hESC-RPE safe in Asian patients
- **2015**: Published first-ever report of the safety of pluripotent stem cells (hESC-RPE) in humans with any disease
- **2016**: Acquired Ocata Therapeutics
  - Changed the name to AIRM
Function of RPE Layer

- Provides critical nutrients, growth factors, ions and water
- Recycles photopigments & vitamin A
- Phagocytosis of photoreceptor fragments
- Detoxifies photoreceptor layer
- Prevents abnormal blood vessel growth
- Maintains Bruch’s Membrane
- Absorbs stray light and protects from UV

Modified from scienceofamd.org
AMD & SMD are the leading causes of adult & juvenile blindness in the developed world

- Number of people with AMD is projected to increase to 288 million worldwide by 2040
- SMD & dry AMD (which accounts for 80-90% of all AMD cases) are currently untreatable
- In US alone, the economic burden of vision loss/blindness is expected to reach $717B by 2050

http://www.preventblindness.org/cost-vision-problems-reach-717-billion-2050
AIRM RPE PROGRAM

AIRM successfully completed two Phase I/II clinical trials in the U.S. using RPE derived from hESCs to treat macular degeneration:

- Dry AMD
- SMD

Completed the only clinical trial in Europe using pluripotent stem cells hESC-RPE to treat SMD

RPE can be reliably generated from embryonic stem cells

- We have studied dozens of hESC lines – all reproducibly generate RPE lines that can be passaged, characterized, and expanded
- We have secured an extensive patent protection
NEXT STEPS FOR AIRM RPE PROGRAM

Take a new step toward product launch: Phase-Ib/II dose-ranging and proof-of-concept trial for dry AMD is planned to start with a new ES cell line and formulation in 1H/2017

Advantages of new cell line and formulation

- Comparable preclinical data to RPE cells derived from the previous ES cell line
- Fully comport with the FDA tissue donor compliance regulations revised in 2005
- Non-xenogeneic product which allows to eliminate patient blood sampling
- Larger cell bank which ensures a stable supply
- Longer shelf-life which enables centralized DP preparation
- Protective effect on cells which reduces cell loss during extrusion and debris at injection site
- More clinical trial feasibility

Phase-II PORTRAY study for dry AMD with the conventional cell line has been suspended due to cell line change

DP: drug product
RPE IMPROVE VISUAL ACUITY & RESCUE PHOTORECEPTORS IN ANIMALS

RCS Rats (d90)
hESC-RPE CLINICAL TRIALS

Treated 38 patients and confirmed safety

US Clinical Trial
Dry AMD
Thirteen patients treated (50K – 200K cells)
SMD
Thirteen patients treated (50K – 200K cells)

European Clinical Trial
SMD
Twelve patients treated (50K – 200K cells)

ClinicalTrials.gov
NCT01345006 and NCT01344993
During the 1-year follow-up period, patients in both the SMD and dry AMD clinical trials have shown significant improvement in visual acuity in the RPE-treated eyes:

- 8/18 (44%) patients improved >3 lines
- 3/18 (17%) patients improved 1-3 lines
- 6/18 (33%) patients remained stable
- 1/18 (6%) patients decreased >1 line

Untreated eyes did not show similar improvements in visual acuity during the same time period.

Overall Results:

- No safety issues related to the transplanted cells
- Clear signs of long-term engraftment & survival
Confirmed positive change in BCVA in AMD & SMD patients relative to baseline

**UPDATE:**
BCVA improvement continues to be sustained 2–3 years after transplantation in both AMD & SMD patients

BCVA: best-corrected visual acuity
Lanza and colleagues, Lancet 2015; 385:509-16
GENERATION OF NON-RPE RETINAL CELL TYPES FROM PSCs

- Human ES/iPS cells
  - Eye field progenitors (EFG)
  - Retinal neural progenitor cells (RNPC)
  - Photoreceptor Progenitors (PhRP)
  - Photoreceptors

- 3-4 month differentiation process from PSCs resulting in high purity (~95%) PhRPs
- 2 month differentiation process from PSCs resulting in high purity (~99%) RGPs
PHOTORECEPTOR PROGENITORS
Photoreceptor progenitors restore vision in completely blind animals

Graft-Host Connectivity
Synaptophysin is localized between the host and graft indicating synaptic transmission between the grafted cells & host retina (dashed line delineates the boundary between them).

Lanza and colleagues, Nature Scientific Reports 2016 Jul13;6:29784. doi: 10.1038/srep29784
RETINAL GANGLION PROGENITORS
RGP TRANSPLANTATION IMPROVES HOST RGC SURVIVAL IN MICROBEAD/MOUSE GLAUCOMA MODEL

RGPs enhance pSTR amplitude in glaucoma mice
pSTR is the most sensitive indicator of RGC function in the mouse
CORNEAL ENDOTHELIUM
Corneal endothelial cells (CECs) can be generated from hESCs that closely resemble normal adult CECs

- 10 million people with corneal blindness
- Cornea the most transplanted organ (1/3 due to endothelial failure)
- Solutions: Tx of whole cornea “Penetrating Keratoplasty”
  More popular: Tx corneal endothelium & Descemet’s membrane (DSEK)

Efficient Generation of Human Embryonic Stem Cell-Derived Corneal Endothelial Cells by Directed Differentiation

Washingtoneye.com
AGENDA

I. Introduction

II. Ophthalmology program
   (Retinal pigment epithelium, Photoreceptor progenitors, Retinal ganglion progenitors and Corneal endothelium)

III. Application in other fields
   (Hemangioblast-derived MSCs and Vascular progenitors)

IV. Joint research with academia in Japan
HMCs
HEMANGIOBLAST-DERIVED MESENCHYMAL STEM CELLS (HMCs)

HMCs more youthful (30,000X greater expansion than BM-MSCs) and potent than tissue-derived MSCs. Proof-of-concept demonstrated in six pre-clinical models

- Developed an efficient method of HMC generation
- HMCs are immunomodulatory/no need for immunosuppression
- Cells persist transiently/minimal risk of tumorigenicity
- Platform technology (therapeutic potential shown in 6 different indications

**HMCs superior to other clinically used MSCs**
- Greater therapeutic potency vs. BM & CB MSCs
- Better migratory properties vs. BM & CB MSCs
- Reduced IL6 levels vs BM & CB MSCs
- Unlimited (and non-variable) cell source

**Environmental stimuli**

MS: multiple sclerosis, BM: bone marrow, CB: cord blood
HMCs (BUT NOT BM-MSCs) DRAMATICALLY REDUCE CLINICAL SYMPTOMS IN EAE MODEL OF MS

- HMCs dramatically reduce clinical symptoms of EAE
  - both prophylactic and therapeutic inhibition
  - *In vitro* inhibition of T-cell function

- Differential cytokine expression (HMCs vs BM-MSCs)
- Differential ability to migrate into damaged tissues (hESC-MSCs vs BM-MSCs)

**EAE:** experimental autoimmune encephalomyelitis
HMCs HAVE POTENT THERAPEUTIC EFFECT IN ANIMALS WITH LUPUS AND CROHN’S DISEASE

Human embryonic stem cell-derived mesenchymal cells preserve kidney function and extend lifespan in NZB/W F1 mouse model of lupus nephritis
Austin Thiel, Gregory Yavanian, Maria-Dorothea Nastke, Peter Morales, Nicholas A. Kouris, Erin A. Kimbrel & Robert Lanza

Lanza and colleagues, Nature Scientific Reports 2015 Dec 2;5:17685. doi: 10.1038/srep17685.
POTENTIAL THERAPEUTIC APPLICATIONS FOR MSCs

- >100 autoimmune diseases
- Multiple Sclerosis
- Osteoarthritis
- Lupus
- Aplastic Anemia
- Crohn’s Disease/IBS
- Chronic Pain
- Limb Ischemia
- Heart Failure/MI
- Stroke
- Graft-versus-host Disease
- Spinal Cord Injury
- Liver Disease
- Kidney Disease
- Emphysema/Pulmonary Diseases
- Wound healing (ulcers/decubitus/burns)
- HSC engraftment/irradiated cancer patients
- Eye diseases (uveitis, retinal degeneration, glaucoma)

hES/hiPS-MSCs are ideal for clinical translation

- No need for immunosuppression
- Persist transiently
- Can be irradiated

VASCULAR PROGENITORS
VASCULAR REPAIR

Vascular progenitor cells generated from PSCs repair vascular injury

Hemangioblasts restore blood flow to ischemic limbs and cut mortality rate after severe MI in half

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IV. Joint research with academia in Japan
Explore the possibility to develop new cell-based therapies for renal diseases

Transplantation of human iPSC-derived renal progenitors ameliorated acute kidney injury (AKI) in mouse model

T. Toyohara et al, Stem Cells Trans Med 2015; 4:980-992
Osaka University and Astellas establish joint research chair for R&D on next-generation cell therapy

With a view developing fundamental technologies for next-generation cell therapies and bringing those technologies into practical use

• Develop cell sources
• Develop cell processing technologies
• Make cells highly functional
• Enhance therapeutic effects
OUR JOURNEY

Turn innovative science into value for patients by maximizing the potential of regenerative medicine.
CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING INFORMATION

In this material, statements made with respect to current plans, estimates, strategies and beliefs and other statements that are not historical facts are forward-looking statements about the future performance of Astellas. These statements are based on management’s current assumptions and beliefs in light of the information currently available to it and involve known and unknown risks and uncertainties. A number of factors could cause actual results to differ materially from those discussed in the forward-looking statements. Such factors include, but are not limited to: (i) changes in general economic conditions and in laws and regulations, relating to pharmaceutical markets, (ii) currency exchange rate fluctuations, (iii) delays in new product launches, (iv) the inability of Astellas to market existing and new products effectively, (v) the inability of Astellas to continue to effectively research and develop products accepted by customers in highly competitive markets, and (vi) infringements of Astellas’ intellectual property rights by third parties.

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