PROGRESS IN FOCUS AREA APPROACH

R&D Meeting - December 10, 2020
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 Pharma. 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.

Information about pharmaceutical products (including products currently in development) which is included in this material is not intended to constitute an advertisement or medical advice.
AGENDA

I Introduction
Kenji Yasukawa, Ph.D., President and Chief Executive Officer

II Primary Focus (PF) & PF Candidates (Primary Focus Lead)
- PF - Genetic Regulation: Ulf Tollemar
- PF - Blindness and Regeneration: Jotaro Suzuki, Ph.D.
- PF - Immuno-oncology: Peter Sandor, M.D.
- PF Candidate - Cancer Genomic Alteration: Peter Sandor, M.D.
- PF - Mitochondria Biology: Itsuro Nagase, Ph.D.
- PF Candidate - Immune Homeostasis: Shigetada Furukawa, Ph.D.

III Innovative Technology Platforms for Drug Discovery & Research to Support Focus Area Approach
Kenji Yasukawa, Ph.D.
PRIMARY FOCUS & PRIMARY FOCUS CANDIDATE
Primary Focus: Genetic Regulation

Developing potentially curative gene therapy treatments to transform the lives of people with genetic diseases

Ulf Tollemar
Primary Focus Lead, Genetic Regulation
SIGNIFICANTLY IMPROVING OUTCOMES FOR SERIOUS LIFE-LIMITING AND POTENTIALLY FATAL GENETIC DISEASES

Our mission is to identify, develop and deliver transformative gene-based therapies for patients with genetic diseases

~7,000 diseases

Often present from birth and affecting young children, nearly 7,000 human diseases are caused by mutations or deficiencies in genetic code ¹

- A single intervention could replace missing genes or regulate genes that are behaving abnormally, to significantly improve outcomes for serious, life-limiting diseases

- Alongside our world-renowned collaborators, we are building a Center of Excellence with competitive capabilities across the value chain for leadership in genetic regulation medicines

- We aim to develop life-changing medicines for diseases where no, or few, treatment options exist

Audentes Therapeutics, which became an Astellas company in January 2020, is developing genetic medicines with the potential to deliver transformative value for patients.

Based on their innovative scientific approach and industry-leading internal manufacturing capability and expertise, the company has become an Astellas Center of Excellence. Audentes is exploring several AAV-based gene therapy technologies to regulate genes; gene replacement, exon skipping gene therapy and vectorized RNA knockdown, with plans to expand focus and geographic reach under Astellas.
Astellas is the global leader in Genetic Regulation medicines with Audentes as its Center of Excellence (CoE)

**AAV Manufacturing**
- Continued global industry leadership in AAV manufacturing

**Integrated R&D Pipeline**
- Pipeline of transformative therapies, starting with rare disease with aspirations toward more common diseases

**Robust Research Capability**
- Focused on next-generation genetic regulation technologies

**Strong CoE infrastructure for sustained growth**

AAV: Adeno-associated virus, R&D: Research and development
AAV MANUFACTURING AT COE - A KEY STRATEGIC CAPABILITY ACROSS ASTELLAS

South San Francisco, California

- Internal AAV manufacturing capability provides self-sufficiency from research to commercial
- Capabilities to expand to support future AAV manufacturing and supply chain needs

AAV Drug Substance Manufacturing
- Suspension bioreactor systems at 1,000 L (2x500 L) scale
- AAV production supports clinical-stage GMP material with preparations in place for AT132 commercial launch
- Over 4 years of production experience
- Adding new Pilot Plant (2021) to expand development and IND-enabling material generation capacity, support tech transfer and new technology / innovation initiatives

AAV Drug Product (DP) Manufacturing
- All AAV DP batches filled in-house (no CMO reliance)
- Current semi-automated process will be augmented by new state-of-the-art automated fill line (2021)
- Capacity to support all CoE programs in the future

Plasmid Manufacturing
- Added internal plasmid manufacturing capability to supply research grade through GMP grade plasmid
- Move CoE toward controlling the supply chain of this critical raw material

Sanford, North Carolina

- This fully approved capital project is currently under construction
  - Scheduled to be operational and GMP ready by mid 2022
- First phase provides 4,000 L of bioreactor capacity
- Two future phases can bring the total bioreactor capacity to 20,000 L
- Plant can supply all CoE late stage clinical and commercial demand well into the future
- The building and site are expandable to support additional future demand

**RESEARCH CAPABILITY AT COE - ACCESS TO AND USE OF TECHNOLOGIES**

Our innovative use of technologies has the potential to transform outcomes for patients with rare, neuromuscular diseases

<table>
<thead>
<tr>
<th>AGENT</th>
<th>DELIVERY</th>
<th>MECHANISM</th>
<th>DISEASE TARGETS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gene → Protein</td>
<td></td>
<td><strong>Gene Replacement</strong>&lt;br&gt;Delivery of new functional gene copy to replace missing protein</td>
<td>XLMTM&lt;br&gt;Pompe disease</td>
</tr>
<tr>
<td>snRNA</td>
<td>AAV-based medicines&lt;br&gt;- Safe and efficient tissue transduction&lt;br&gt;- Tailored biodistribution leading to durable specific expression</td>
<td>Gene Regulation (Exon Skipping)&lt;br&gt;<em>In situ</em> production of a snRNA to induce exon skipping to correct translation to a functional protein</td>
<td>DMD&lt;br&gt;Myotonic dystrophy</td>
</tr>
<tr>
<td>miRNA</td>
<td></td>
<td><strong>Gene Regulation (RNA Knockdown)</strong>&lt;br&gt;<em>In situ</em> production of a miRNA to eliminate an unwanted toxic RNA or protein</td>
<td>Myotonic dystrophy</td>
</tr>
</tbody>
</table>

Access to new novel technologies will expand our potential to transform outcomes for patients with rare as well as more common diseases

# R&D PIPELINE
- CURRENT FOCUS ON MUSCLE DISEASES

<table>
<thead>
<tr>
<th>Compound</th>
<th>Mechanism</th>
<th>Target indication</th>
<th>Current phase</th>
<th>Origin/Partner</th>
</tr>
</thead>
<tbody>
<tr>
<td>AT132</td>
<td>MTM1 gene replacement</td>
<td>X-linked myotubular myopathy</td>
<td>Phase 2 - Pivotal (Clinical hold due to serious adverse events)</td>
<td>AUDENTES*</td>
</tr>
<tr>
<td>AT845</td>
<td>GAA gene replacement</td>
<td>Pompe disease</td>
<td>Phase 1 (Enrolling patients)</td>
<td>AUDENTES*</td>
</tr>
<tr>
<td>AT753</td>
<td>Vectorized exon 53 skipping</td>
<td>Duchenne muscular dystrophy</td>
<td>Preclinical (To enter into clinical phase in FY2021)</td>
<td>AUDENTES*</td>
</tr>
<tr>
<td>AT702</td>
<td>Vectorized exon 2, 1-5 skipping</td>
<td>Duchenne muscular dystrophy</td>
<td>Discovery</td>
<td>AUDENTES*</td>
</tr>
<tr>
<td>AT751</td>
<td>Vectorized exon 51 skipping</td>
<td>Duchenne muscular dystrophy</td>
<td>Discovery</td>
<td>AUDENTES*</td>
</tr>
<tr>
<td>AT466</td>
<td>Vectorized exon skipping / vectorized RNA knockdown for DMPK</td>
<td>Myotonic dystrophy</td>
<td>Discovery</td>
<td>AUDENTES*</td>
</tr>
<tr>
<td>GT0001X</td>
<td>ADAR2 gene expression</td>
<td>Sporadic amyotrophic lateral sclerosis</td>
<td>Preclinical</td>
<td>Gene Therapy Research Institution*</td>
</tr>
<tr>
<td>MDL-201</td>
<td>(Not disclosed)</td>
<td>Muscle disease</td>
<td>Preclinical</td>
<td>MODALIS</td>
</tr>
<tr>
<td>MDL-202</td>
<td>(Not disclosed)</td>
<td>Muscle disease</td>
<td>Preclinical</td>
<td>MODALIS</td>
</tr>
</tbody>
</table>

* Acquired (current programs classified as ‘in house’), ** Option agreement

R&D: Research and development, MTM: Myotubularin, GAA: Acid alpha-glucosidase, RNA: Ribonucleic acid, DMPK: Myotonic dystrophy protein kinase, ADR2: Adenosine deaminase acting on RNA2
AT845: DISEASE MODIFYING GENE REPLACEMENT THERAPY RESTORES THE KEY ENZYME IN POMPE DISEASE

DISEASE

- In Pompe disease, a deficient GAA enzyme causes glycogen build-up leading to tissue and organ damage predominantly in skeletal muscle, cardiac muscle and the nervous system.
- Infantile-onset Pompe disease is a severe condition with a high and early fatality rate, while the late-onset form of Pompe disease has less severe symptoms and a slower rate of progression.
- Current treatment is enzyme replacement therapy (ERT) which is limited by immunogenicity and its inability to penetrate key tissues affected by the disease.

MODALITY

- AAV is a non-pathogenic virus that has been engineered to carry and deliver functional genes into the nucleus of target cells.

BIOLOGY

- Gene replacement is achieved by AAV delivering a functional GAA gene to produce the missing GAA enzyme which breaks down glycogen into glucose in the lysosome.
- AT845 has the potential to generate GAA directly in the muscle to restore function in affected organs and reduce the need for chronic ERT treatment.

CURRENT STATUS AND NEXT STEPS

- Phase 1/2 open label, ascending dose “FORTIS” study in late-onset Pompe Disease is actively enrolling.

Breakdown of glycogen to glucose in the lysosome is impaired in Pompe disease.
**DMD FRANCHISE (AT702, AT751, AT753): VECTORIZED EXON SKIPPING, GENERATING FUNCTIONAL DYSTROPHIN TO TREAT DUCHENNE MUSCULAR DYSTROPHY (DMD)**

**DISEASE**
- Dystrophin is one of the largest proteins in humans, consisting of 79 exons, and is needed for muscle strength.
- In DMD, multiple genetic mutations on the dystrophin gene prevent functional dystrophin production causing deterioration and death of skeletal and cardiac muscle cells.
- Over time DMD causes muscle weakness and heart problems leading to disability and early death.
- There are limited treatments available, other than physical therapy. Many gene therapy studies are ongoing, mostly targeting the delivery of a truncated version of dystrophin.

**MODALITY**
- AAV is a non-pathogenic virus that has been engineered to carry and deliver a gene generating snRNA with antisense sequences into the nucleus of target cells.

**BIOLOGY**
- snRNAs are capable of regulating gene expression through exon skipping, bypassing faults in the dystrophin gene to enable cells to generate functional dystrophin protein.
- Increased functional dystrophin reduces deterioration of skeletal and cardiac muscle cells and may restore muscle strength and heart function.
- Range of mutations covered by the three lead assets affect up to 25% of the DMD population.

**CURRENT STATUS AND NEXT STEPS**
- Collaborative study with NCH ongoing, AT753 is on track to start a clinical study in FY2021.
- An efficient ‘umbrella’ clinical study protocol is being planned.

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**Exon skipping (AT751)**

<table>
<thead>
<tr>
<th>ATPase</th>
<th>DMD</th>
<th><strong>BIOLOGY</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>49 50 51 52 53</td>
<td>Pre-mRNA Deletion of exon 50</td>
<td>mRNA Reading frame disrupted</td>
</tr>
<tr>
<td>49 51 52 53</td>
<td>mRNA Reading frame restored</td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>Translation stopped prematurely</td>
<td>Translation continues</td>
</tr>
<tr>
<td>Non-functional dystrophin</td>
<td>Protein</td>
<td>Functional dystrophin</td>
</tr>
</tbody>
</table>

**AAV mechanism of delivery**
- snRNA causes skipping of exon 51
- AAV mechanism of delivery

**AAV: Adeno-associated virus, snRNA: Small nuclear ribonucleic acid, NCH: Nationwide Children’s Hospital**
Primary Focus:
Blindness and Regeneration

Developing revolutionary therapies to free patients from the fear of deteriorating vision and regain lost sight

Jotaro Suzuki, Ph.D.
Primary Focus Lead, Blindness and Regeneration
OFFERING POTENTIAL TO PROTECT AGAINST DECLINING VISION AND EVEN RESTORE LOST SIGHT IN PATIENTS WITH RETINAL DISEASES

Our mission is to identify, develop and deliver next generation treatments to restore sight for patients with retinal diseases

● Many diseases causing vision loss have few, or no, effective treatment options

● Utilizing our in-house ophthalmology expertise and rapidly expanding regenerative medicine capabilities, we are targeting transformational changes in the management of multiple devastating eye diseases

● Through revolutionary cell and gene therapies, we aim to restore and preserve the critical vision-supporting cells in the eye

Vision loss caused by diseases of the eye affects over 160 million people globally\(^1,2\) and can have a devastating long-term impact on quality of life

2: Data from the Foundation Fighting Blindness 2019 Annual Report.
We are combining truly innovative cell and gene modalities with a deep understanding of the biology of retinal diseases to establish a robust platform of regenerative medicine.
We are exploring innovative modalities to protect and/or restore degenerating cells important to visual function.

**Corneal endothelium:** Keeper of transparency

**Ganglion cell:** Electric wire to the brain

**Retinal pigment epithelium:** Guardian of photoreceptor

**Photoreceptor:** Converter of light into signal

**Retinitis pigmentosa**

**Glaucomatous optic neuropathy**

**Dry age-related macular degeneration**

- ASP7317
- ASP1361

**Modality**

- Pluripotent cell-derived cell therapy
- AAV-based gene therapy

**Corneal dystrophy**

**ASP7317** (Not disclosed)

**AAV:** Adeno-associated virus, mVChR1: Modified Volvox channelrhodopsin-1
## PIPELINE (2/2)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Modality/Mechanism</th>
<th>Indication</th>
<th>Current phase</th>
<th>Origin/Partner</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASP7317</td>
<td>RPE cell</td>
<td>Dry AMD, Other macular degeneration</td>
<td>Phase 1b/2 (Protocol to be amended to decouple PoC part)</td>
<td>Astellas Therapeutics (AIRM)</td>
</tr>
<tr>
<td>ASP1361</td>
<td>Gene therapy (AAV-mVChR1)</td>
<td>Retinitis pigmentosa</td>
<td>Preclinical (IND planned in 2021)</td>
<td>Quethera</td>
</tr>
<tr>
<td>(Not disclosed)</td>
<td>Gene therapy (AAV)</td>
<td>Glaucoma</td>
<td>Preclinical (IND planned in 2023)</td>
<td>Astellas Therapeutics (AIRM)</td>
</tr>
<tr>
<td>(Not disclosed)</td>
<td>Photoreceptor rescue cell</td>
<td>Retinitis pigmentosa</td>
<td>Discovery</td>
<td>Astellas Therapeutics (AIRM)</td>
</tr>
<tr>
<td>(Not disclosed)</td>
<td>Ganglion rescue cell</td>
<td>Glaucoma, Optic neuropathy</td>
<td>Discovery</td>
<td>Astellas Therapeutics (AIRM)</td>
</tr>
<tr>
<td>(Not disclosed)</td>
<td>Corneal endothelial cell</td>
<td>Corneal dystrophy</td>
<td>Discovery</td>
<td>Astellas Therapeutics (AIRM)</td>
</tr>
<tr>
<td>(Not disclosed)</td>
<td>Universal donor cell (UDC) RPE</td>
<td>Dry AMD, Other macular degeneration</td>
<td>Discovery</td>
<td>Universal Cells</td>
</tr>
<tr>
<td>(Not disclosed)</td>
<td>Gene therapy (AAV)</td>
<td>Dry AMD, Other macular degeneration</td>
<td>Discovery</td>
<td>University of Pittsburgh</td>
</tr>
</tbody>
</table>

* Acquired (current programs classified as ‘in-house’)
RPE: Retinal pigment epithelial, AIRM: Astellas Institute for Regenerative Medicine, AMD: Aged-related macular degeneration, AAV: Adeno-associated virus, mVChR1: Modified Volvox channelrhodopsin-1, IND: Investigational New Drug application
ASP1361: GENE THERAPY WITH THE POTENTIAL TO REVERSE VISION LOSS IN RETINITIS PIGMENTOSA

**DISEASE**
- Retinitis pigmentosa is a group of eye diseases caused by numerous gene mutations that cause photoreceptor cells in the retina to degenerate, leading to severe and permanent vision loss.
- Significant unmet needs exist for effective treatment options in ultra-low vision patients with retinitis pigmentosa due to lack of standard-of-care.

**MODALITY**
- AAV is a non-pathogenic virus that can be engineered to deliver functional genes to target cells.
- A mutation-independent gene therapy is a desirable approach.

**BIOLOGY**
- AAV2-mVChR1 can introduce the channel rhodopsin-1 gene (mVChR1) to retinal ganglion cells, rather than to the retinal photoreceptors that have been damaged as a result of gene mutations.
- This results in the expression of photosensitive ion channels in the retinal ganglion cells, restoring light sensitivity and visual function.

**CURRENT STATUS AND NEXT STEPS**
- IND submission planned in 2021 to start a clinical study in patients.

**ASP1361 mechanism of action**
- AAV2-mVChR1 can introduce the channel rhodopsin-1 gene (mVChR1) to retinal ganglion cells, rather than to the retinal photoreceptors that have been damaged as a result of gene mutations.
- This results in the expression of photosensitive ion channels in the retinal ganglion cells, restoring light sensitivity and visual function.

AAV: Adeno-associated virus, mVChR1: Modified Volvox channelrhodopsin-1, IND: Investigational New Drug application.
ASP7317:
PLURIPOTENT STEM CELL-DERIVED ALLOGENIC CELL THERAPY TO REPLACE RETINAL PIGMENT EPITHELIUM TO RESTORE LOST SIGHT

- Completion of 1st cohort in Phase 1b/2 study
- Phase 1b/2 study amendment aimed to optimize the overall development program has been submitted for FDA’s review (announced at the Q2/FY2020 earnings)
- Agreement by PMDA that new DS raw materials are acceptable for use in future clinical studies in Japan
- Completion of GMP DS manufacturing to support the future PoC supply
- Established cell manufacturing process to cover early commercial supply
- BLA is planned after completion of PoC study

FDA: Food and Drug Administration, PMDA: Pharmaceuticals and Medical Devices Agency, DS: Drug substance, GMP: Good Manufacturing Practice, PoC: Proof of concept, BLA: Biologics License Application
<table>
<thead>
<tr>
<th><strong>Enhancement of PSC lines and evolution of cell differentiation protocols</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Multiple clinical grade PSC lines with safety and quality assurance</td>
</tr>
<tr>
<td>• Develop the cells of interest by using the best PSC lines. Multiple INDs planned in 5 years from 2021</td>
</tr>
<tr>
<td>• Hundreds-fold increase of productivity of RPE cells</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Achievement of rejection-free allogenic cell therapy</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Multiple UDC-based PSC lines and establishment of master cell bank</td>
</tr>
<tr>
<td>• UDC-RPE is the leading program and multiple follow-on programs</td>
</tr>
<tr>
<td>• Research collaboration with panCELLa for Immune-cloaking technology</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Development of technology and infrastructure for GMP-level production</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Completion of the new facility with GMP-level production in US</td>
</tr>
<tr>
<td>• Selection of regulatory compliant raw materials for development in US / EU / JP</td>
</tr>
<tr>
<td>• Completion of GMP production of ASP7317 for PoC study</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Efficient logistics system for cell therapy</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Development of original and new formulation technology has advanced</td>
</tr>
<tr>
<td>• Optimization for each product candidate</td>
</tr>
</tbody>
</table>

**Steady progress since R&D meeting in 2018**

PSC: Pluripotent stem cell, IND: Investigational New Drug application, RPE: Retinal pigment epithelium, UDC: Universal donor cell, GMP: Good Manufacturing Practice, PoC: Proof of concept, R&D: Research and development
# ESTABLISH EFFICIENT LOGISTICS SYSTEM

<table>
<thead>
<tr>
<th>Feature</th>
<th>Current drug product</th>
<th>New drug product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feature</td>
<td>Cryopreservation of DS. Formulation into DP at GMP facilities for administration</td>
<td>Cryopreservation of DP. Reconstitution at the hospital just before administration</td>
</tr>
<tr>
<td>GMP DP production facility (or CMO)</td>
<td>Required for each region/country to manufacture final DP</td>
<td>Not required</td>
</tr>
<tr>
<td>Shelf-life of DP</td>
<td>Hours to days</td>
<td>Years</td>
</tr>
<tr>
<td>Timing of DP release</td>
<td>Just before the treatment (hours to days before the surgery). Risk of transportation problems</td>
<td>Flexible regardless of the surgery schedule</td>
</tr>
<tr>
<td>DP manufacturing scale</td>
<td>Frequent productions of only required number of units</td>
<td>Batch production (&gt; hundreds of vials)</td>
</tr>
<tr>
<td>Quality control of DP</td>
<td>Conduct at each DP GMP site for an individual DP</td>
<td>Conducted centrally at AIRM. Performed on batch-basis</td>
</tr>
</tbody>
</table>

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**Diagram:**

- **AIRM (GMP)**
- **EU (GMP)**
- **US (GMP)**

DS: Drug substance, DP: Drug product, GMP: Good Manufacturing Practice, AIRM: Astellas Institute for Regenerative Medicine
**Overview of New Facility**
- A complex of research, CMC/manufacturing, and clinical development, optimized for the promotion of cell therapy
- CMC/GMP manufacturing occupy half of 24,000 m²
- Central role in the manufacture of MCBs, investigational drugs and early commercial products
- 7 GMP clean rooms complied with US/EU/JP regulations. Expandable for future demands
- Independent air controlling system for clean rooms, enabling production of different cell types in parallel
- Seamless and fast GMP manufacturing by integration of Research and CMC

**Cell Drug Substance Manufacturing**
- 10 years’ experiences of PSC-derived cell therapy and GMP manufacturing cultivated as a pioneer
- Accumulated regulatory know-how accumulated through interactions with regulatory authorities
- Now promoting GMP manufacturing with protocols optimized for each cell type
- Established large-scale culture using bioreactors for non-ophthalmic cell therapy

**Cell Drug Product Manufacturing**
- Experience in supplying CTM to US and UK (total of over 40 doses)
- Plans to expand our capabilities as a center of future supply chain (DP shipping)

CMC: Chemistry, manufacturing and control, GMP: Good Manufacturing Practice, MCB: Master cell bank, PSC: Pluripotent stem cell, CTM: Clinical trial material, DP: Drug product
SNAPSHOT OF ASTELLAS CELL THERAPY
- CENTERS OF INNOVATION AND EXCELLENCE

Dedicated members at four sites in US and JP for our cell therapy

Universal Cells
- 2018 Universal Cells acquisition
- CSO: Dr. D. Russell
- Center of Astellas gene-editing
- Universal donor cell technology
- Contribution to industrial organization activities (ARM)

Xyphos Biosciences
- 2020 Xyphos acquisition
- CSO: Dr. D. Martin
- Center of next-generation cancer immunotherapy
- Unique ACCEL™ technology

AIRM Satellite Office
- Collaboration with internal function
- Collaboration with academia in Japan
- Contribution to industrial organization activities (FIRM)

AIRM
- 2016 Ocata acquisition
- CSO: Dr. R. Lanza
- Center of Astellas regenerative medicine
- Stem cell science and technology
- GMP manufacturing
- Clinical development for ophthalmology

TBRC
- CTM manufacturing for use in early stage clinical trial

CSO: Chief Scientific Officer, ARM: Alliance for Regenerative Medicine, GMP: Good Manufacturing Practice, FIRM: Forum for Innovative Regenerative Medicine, TBRC: Tsukuba Biotechnology Research Center, CTM: Clinical trial material
ORGANIC APPLICATION OF CELL THERAPY PLATFORM TO REALIZE MULTIPLE PF STRATEGY (1/2)

2018

- Ophthalmology
- PSC

2020

- Ophthalmology
- PSC + UDC
- Key modality platform of Astellas
- PF - Blindness & Regeneration
- PF - Immuno-Oncology
- PF Candidate - Immune Homeostasis
- PF - Mitochondrial disease
- Auto-immune disease
- Cancer
- Mitochondrial Biology

UDC technology

Universal Cells
(2018 acquisition)

OCATA THERAPEUTICS
(2016 acquisition; currently AIRM)

PF: Primary Focus, AIRM: Astellas institute for regenerative medicine, UDC: Universal donor cell, PSC: Pluripotent stem cell
Established cell differentiation protocols in multiple projects
Primary Focus: Immuno-oncology

Dedicating our collective strengths to find new ways to cure cancer globally

Peter Sandor, M.D.
Primary Focus Lead - Immuno-oncology
OUR GOAL IS TO DELIVER CURATIVE TREATMENT OPTIONS FOR PATIENTS WITH CANCER

EXPERTISE and EXPERIENCE in cancer biology and cancer drug development

ADVANCED TECHNOLOGY capabilities to develop and improve novel modality platforms

PARTNERING with the best minds in immuno-oncology research and industry to create new ways to treat cancer

Currently only approximately 20% of cancers respond to existing immuno-oncology treatments\(^1\)

WE ARE PASSIONATE ABOUT TURNING 20% into 100%

INNOVATIVE PIPELINE to **reinvigorate** the immune system’s ability to **discover**, **disarm** and **destroy** more cancers in more patients

We are allocating significant, sustained investment in understanding cancer biology and deploy this knowledge to establish multi-functional modality platforms and generate a broad, novel pipeline.

**Biology**
- Deep understanding of immune compromised cancer

**Multi-functional Modality Platforms**
- Bispecific immune cell engager
- Oncolytic virus
- Artificial adjuvant vector cell (aAVC)
- Allogeneic cell therapy

**Diseases**
- Deliver a sustainable pipeline of novel, differentiated candidates in multiple cancers with high unmet needs
Our early-stage platforms are built to trigger anti-tumor immune response by stimulating multiple immune functions at the same time.
## STRONG PROGRESS WITH THE IO PIPELINE SINCE Q3 FY19

<table>
<thead>
<tr>
<th>MODALITY</th>
<th>COMPOUND</th>
<th>MECHANISM</th>
<th>DISCOVERY</th>
<th>PRE-CLIN</th>
<th>PHASE 1</th>
<th>PARTNER</th>
</tr>
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<tbody>
<tr>
<td>Checkpoint</td>
<td>ASP1948</td>
<td>NRP1</td>
<td></td>
<td></td>
<td></td>
<td>Tottori University</td>
</tr>
<tr>
<td></td>
<td>ASP1951</td>
<td>GITR agonist</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oncolytic virus (OV)</td>
<td>ASP9801</td>
<td>OV IL-7, IL-12</td>
<td></td>
<td></td>
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<td>aAVC</td>
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<td>ASP0739</td>
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<td>convertibleCAR-NK</td>
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IO: Immuno-oncology, NRP1: Neuropilin-1, GITR: Glucocorticoid-induced TNFR-related protein, IL: Interleukin, aAVC: Artificial adjuvant vector cell, CAR: Chimeric antigen receptor, TCR: T-cell receptor, HiT: HLA (human leukocyte antigen)-independent TCR, NK: Natural killer
IMMUNE CELL ENGAGERS: REDIRECTING IMMUNE CELLS TO KILL TUMOR CELLS

Strong progress building a differentiated bispecific immune cell engager pipeline targeting solid tumors

Internal platform and pipeline development

2019 2020 2021 1st IND

Xencor partnership leveraging bispecific antibody technology XmAb (April 2019)

CytomX partnership leveraging Probody® T-cell engaging bispecific antibody platform (Mar 2020)

IND: Investigational New Drug application
COMBINING UNIVERSAL CELLS’ AND XYPHOS’ TECHNOLOGIES CREATES A DIFFERENTIATED CELL THERAPY PRODUCT CONCEPT

Universal Cells iPSC Platform

Scalable cell supply

Adaptive patient management

XYPHOS convertibleCAR Platform

PATIENT ACCESS
Potential to treat all eligible patients
Truly off the shelf

ECONOMY
Efficient and scalable manufacturing
Lower cost processes

FLEXIBILITY
Dynamically modulate cells without additional engineering
Directly address tumor heterogeneity within a patient and between patients

RELIABILITY
Standard product without variability
Single cell source

iPSC: Induced pluripotent stem cells
GENERATION OF FUNCTIONAL NK CELLS FROM UNIVERSAL DONOR CELL AND OPTIMIZATION OF *convertible* CAR FOR NK CELLS

Universal Donor Cell (UDC)  Optimized \textit{convertible} CAR (NK signaling)  \textit{convertible} CAR in UDC  Differentiated universal CAR on UDC

Optimization of CAR costimulatory domain with enhanced cytotoxicity in a NK cell line

**Generation of functional CD56+ NK cells from UDC**

- PBMC: 7.63%
- UDC derived-CD56+ NK cells: 97.7%

**Natural Cytotoxicity (K562 cells)**

- % Cytolysis
- Specific Lysis (%)

NK: Natural killer, PBMC: Peripheral blood mononuclear cells
**ConvertibleCAR RESILIENCE ENHANCES TUMOR TARGETING**

- Provides a **solution to directly address** tumor heterogeneity within a patient and between patients
- **Creates opportunities to dynamically modulate** cells without additional engineering to affect expansion, persistence, and tumor access

CAR: Chimeric antigen receptor
TARGETING DIFFERENT ANTIGENS WITH THE SAME convertibleCAR CELLS

Side-by-side demonstration of differential antigen targeting function with the same convertibleCAR-T cells to treat Non-Hodgkin's Lymphoma

- Sets the stage for multiplex targeting to reduce relapse due to antigen loss in patients
Center of Excellence will lead a holistic approach to developing novel allogeneic cancer cell therapy.
## EXPERIENCED TEAM TO DRIVE CELL THERAPY R&D AND MANUFACTURING WITH DIVERSE ACADEMIC AND INDUSTRY BACKGROUND

<table>
<thead>
<tr>
<th>Name</th>
<th>Title and Background</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAVID MARTIN MD</td>
<td>CSO of Cell Therapy CoE, UCSF-HHMI, Genentech, Du-Pont Merck, Chiron, Xyphos</td>
</tr>
<tr>
<td>DAVID RUSSEL MD PhD</td>
<td>CSO Universal Cell, University of Washington</td>
</tr>
<tr>
<td>KEITH BAHJAT PhD</td>
<td>Lead Scientist CoE, Providence Cancer Center, Medarex, BMS, Pfizer</td>
</tr>
<tr>
<td>TAKU YOSHIDA PhD</td>
<td>Head of IO Research, Eisai, Dana Farber Cancer Institute</td>
</tr>
<tr>
<td>QUNLI XU PhD</td>
<td>Head Translational Science, Roche, Eisai, Verastem, Takeda, Forma</td>
</tr>
<tr>
<td>ANDREW KRIVOSHIK MD PhD</td>
<td>SVP Head of Oncology TA, Mayo Clinic, Duke Univ, AbbVie</td>
</tr>
<tr>
<td>CARLOS YURASZECK</td>
<td>Executive Director, GMP Operations, Astellas Institute for Regenerative Medicine, Celgene, Pfizer, Pharmacia, and Merck</td>
</tr>
<tr>
<td>ALISON HAYLES</td>
<td>VP Regulatory Affairs, Oncology, Abbott Laboratories, Takeda</td>
</tr>
</tbody>
</table>

CSO: Chief Scientific Officer, CoE: Center of Excellence, IO: Immuno-oncology, TA: Therapeutic area, GMP: Good Manufacturing Practice, (S)VP: (Senior) Vice President
Introducing Primary Focus Candidate:
Cancer Genomic Alteration
Established a Primary Focus Candidate to develop novel pipeline targeting Genomic Alterations to overcome resistance to standard cancer therapies.

- Tumor Microenvironment
- Tumor Mutational Burden
- Neoantigens

WHAT’S NEXT? KEY PF IO MILESTONES IN FY2021

Pipeline
Continue to progress our key modality platforms and pipeline programs

Data Updates
Clinical data updates on ongoing Phase 1 studies

Clinical Initiation
Phase 1 study initiation
- ASP7517 and ASP0739 in advanced solid tumours

PF: Primary Focus, IO: Immuno-oncology
Primary Focus: Mitochondria Biology

Targeting mitochondrial function as an innovative new way of addressing diseases with high unmet needs

Itsuro Nagase, Ph.D.
Primary Focus Lead, Mitochondria Biology
OFFERING POTENTIAL TO CREATE AN ENTIRELY NEW WAY OF TREATING DISEASES WITH HIGH UNMET MEDICAL NEEDS BY TARGETING MITOCHONDRIA

Our mission is to become the global leader in discovering, developing and bringing to market mitochondrial biology-based medicine that provides clear value for patients, clinicians and healthcare systems.

- Mitochondria are present in almost all human cell types and play essential roles in energy production and in processes such as metabolism and cell signalling.
- Mitochondrial dysfunction is associated with diseases of the kidneys, liver, muscles, central nervous system, eyes and ears.
- Many of these diseases have significant unmet medical needs and few treatment options.

Mitochondria are specialized structures in cells that have their own maternally inherited DNA (mtDNA).

DNA: Deoxyribonucleic acid
STRATEGIC APPROACH

Allocating significant, sustained investment to mitochondria biology-based therapy development

FOCUS
- Mitochondrial biology, our unique and top-notch capability
- Diseases impacted by mitochondrial dysfunction

ENRICH
- Disease identification through deep understanding of the link between mitochondrial biology and disease pathophysiology
- New leads and innovative target molecules identified through phenotypic screening platform
- Faster understanding of molecules’ potential through selection of scientifically relevant indications for PoC/PoP

EXPAND
- Expansion into commercially viable indications after PoC
- Addition of mitochondrial cell therapy to modality approaches

Our early stage assets include candidates for:
- Mitochondrial stress response
  Mitochondrial stress signals are a key factor in cell damage and inflammation
- NAD+ enhancement and increased mitochondrial membrane potential
  Many clinical manifestations of mitochondrial diseases stem from the central role of bioenergetics in the cell
- Gene regulation & mitochondrial biogenesis
  Genetic regulatory factors are essential for mitochondrial biogenesis and function, playing a key role in cellular energy metabolism
- Mitochondrial fusion and fission
  Fusion and fission play a critical role in maintaining normal mitochondrial function

PoC: Proof of concept, PoP: Proof of principle, NAD+: Nicotinamide adenine dinucleotide
Build Primary Focus - Mitochondria Biology portfolio with various scientific approaches for multiple mitochondrial functions

Gene regulation and mitochondrial biogenesis
- ASP0367
- ASP1128

Research projects with Nanna Therapeutics

Mitochondrial stress response
- mtDNA
- ROS

Research projects

NAD+ enhancement and increased mitochondrial membrane potential
- Research projects including in partnership with Nanna Therapeutics

Mitochondrial fusion and fission
- Research projects

NUCLEUS Transcription ATP production

mtDNA: Mitochondrial deoxyribonucleic acid, ROS: Reactive oxygen species, ATP: Adenosine triphosphate, NAD+: Nicotinamide adenine dinucleotide
## PIPELINE (2/2)

Steady progress toward obtaining PoC / entering into the pivotal phase in PPARδ modulator programs

<table>
<thead>
<tr>
<th>Compound</th>
<th>Modality</th>
<th>Mechanism</th>
<th>Target indication</th>
<th>Current phase</th>
<th>Origin</th>
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</thead>
<tbody>
<tr>
<td>ASP1128</td>
<td>Small molecule (i.v. form)</td>
<td>PPARδ modulator</td>
<td>Cardiac surgery associated acute kidney injury</td>
<td>Phase 2 (Phase 2a PoC study FSFT in Nov 2019)</td>
<td>mitobridge *</td>
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<tr>
<td>ASP0367</td>
<td>Small molecule (oral form)</td>
<td>PPARδ modulator</td>
<td>Primary mitochondrial myopathy</td>
<td>Phase 2 (To start Phase 2/3 study in 1Q 2021)</td>
<td>mitobridge *</td>
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<tr>
<td>(Not disclosed)</td>
<td>Small molecule (Not disclosed)</td>
<td>(Not disclosed)</td>
<td>Duchenne muscular dystrophy</td>
<td>Phase 1 (To start Phase 1b study in patients in early 2021)</td>
<td>Discovery</td>
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<tr>
<td>(Not disclosed)</td>
<td>Small molecule (Not disclosed)</td>
<td>(Not disclosed)</td>
<td>(Not disclosed)</td>
<td>Discovery</td>
<td>Nanna Therapeutics *</td>
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</tbody>
</table>

* Acquired (current programs classified as ‘in-house’)

i.v.: Intravenous, PPARδ: Peroxisome proliferator-activated receptor delta, PoC: Proof of concept, FSFT: First subject first treatment
NANNA THERAPEUTICS

New approach to identify lead compounds / innovative target molecules that are directly associated with mitochondrial dysfunction

Focused Cambridge, UK-Based Team

Heart of European Biotech

- Unique medicinal chemistry for targeting mitochondrial biology
- Disease-relevant 'phenotypic' screens (patient-derived)
- World-leading mitochondrial scientists & medicine hunters
- Extensive world-class research & clinical network
- Connected to all major mitochondria patient advocacy groups

All Primary Mitochondrial Myopathies
- Pediatric
- Adult

Secondary Mitochondrial Diseases
- Spinal muscular atrophy
- Duchene muscular dystrophy
- Charcot-Marie-Tooth disease
- Amyotrophic lateral sclerosis
- Friedreich's ataxia

Rare Disease (Other)
- Life threatening viruses
- Co-treatments in oncology

Major Disease Areas
- Parkinson’s disease
- Oncology
MITOCHONDRIAL CELL THERAPY APPROACH

Combining Astellas’ unique capabilities and applying them to creating revolutionary mitochondrial cell therapy

New cell therapy approach focusing on mitochondrial transfer

Cell therapy platform at AIRM

Universal-donor cell technology at Universal Cells

Scientific knowledge on mitochondrial biology at mitobridge

AIRM: Astellas Institute for Regenerative Medicine
Primary Focus Candidate: Immune Homeostasis

*Developing potentially curative therapies for patients with immune-related diseases*

**Shigetada Furukawa, Ph.D.**
Primary Focus Lead, Immune Homeostasis
LAMP-vax, the key ASIM platform, has reached a stage of clinical validation, after completion of discovery research:
- ASP0892 for peanut allergy: Phase 1
- ASP2390 for house dust mite-induced allergic rhinitis: Phase 1

Exploration of next-generation immune modulation technologies led to identification of platforms with modalities distinct from ASIM.

To deliver innovative therapeutics, new in-house research (cell therapy) and research collaboration (Pandion Therapeutics) have been started.

The next generation research has been designated as a PF Candidate “Immune Homeostasis”
SPECIFICALLY SUPPRESSING DISEASE-RELATED IMMUNE RESPONSE WITHOUT IMPACTING THE BODY’S OVERALL IMMUNE SYSTEM

Our mission is to deliver safe and potentially curative therapies for patients suffering from immune-related diseases.

- Broad immune suppression can lead to debilitating and sometimes life-threatening side effects and increase susceptibility to infection.
- Immune homeostasis is the regulatory mechanism maintaining the balance between immunogenicity to pathogens and immune tolerance to self.
- Our aim is to develop innovative therapeutics to restore immune system equilibrium in patients whose immune system has become dysregulated due to autoimmune disease.

Current treatments for autoimmune diseases include general immunosuppressants and do not specifically target autoreactive immune cells.
STRATEGIC APPROACH

We are establishing competitive and innovative modalities that can restore immune homeostasis by leveraging our Immunology R&D experience and cell therapy capabilities

**FOCUS**
Focusing on the development of human hemangioblast-derived mesenchymal stem cells which have the potential to be recruited to the site of inflammation and stop the autoreactive inflammatory cascade

**ENRICH**
Leveraging our regenerative medicine and gene-editing expertise at AIRM and Universal Cells to develop novel immunoregulatory cell therapies

**EXPAND**
Engaging continually with the scientific community to expand our pipeline through partnering, collaboration and acquisition (e.g. collaboration with Pandion)

Our versatile platform technologies include:

- Pluripotent stem cell derived immunoregulatory cell therapy for autoimmune diseases
- Gene editing technology to enhance the immunomodulatory activity and increase disease specificity
- Innovative technology that can induce endogenous immunoregulatory cells, e.g. tissue-specific immune regulation by targeted immunotherapy
We are exploring innovative technologies and modalities that can eliminate disease-specific immune response and induce immune tolerance.

- Acquired (current programs classified as ‘in-house’)

Autoimmune diseases
- Type 1 diabetes
- Rheumatoid arthritis
- Inflammatory bowel disease

**Diagram**
- Autoantigen
- Dendritic cell
- Naive T cell
- Autoreactive T cell
- Mesenchymal Stem Cell (MSC)
- Hemangioblast-derived MSCs
- Immune modulation
- Tissue repair
- Targeted Immunotherapy
- Tissue-specific immune regulation
- Hemangioblast-derived MSCs
- Exert multiple immunomodulatory effects
- Hemangioblast-derived MSCs
- Immune modulation
- Tissue repair
- Autoimmune diseases
- Type 1 diabetes
- Rheumatoid arthritis
- Inflammatory bowel disease

**Legend**
- Innovative cell therapy to induce antigen-specific immune tolerance
- Regulatory T cell (Treg)
- Restore immune tolerance to self antigens
- **Universal Cells**
- Hemangioblast-derived MSCs
- Exert multiple immunomodulatory effects
- **AIRM** (Astellas Institute for Regenerative Medicine)
- **astellas**

* Acquired (current programs classified as ‘in-house’)

AIRM: Astellas Institute for Regenerative Medicine
INNOVATIVE TECHNOLOGY PLATFORMS FOR DRUG DISCOVERY & RESEARCH TO SUPPORT FOCUS AREA APPROACH

Kenji Yasukawa, Ph.D.
President and Chief Executive Officer
CREATING BREAKTHROUGHS IN DRUG DISCOVERY THROUGH SYNERGISTIC USE OF KEY METHODOLOGIES AND TECHNOLOGIES

**AI / Big Data & Robotics**
Finding a candidate

- Higher success rate in PoC
- Better selection of target patient
- More appropriate modality and dosage

**Human-mimetics**
Verifying a concept

**Visualization / Simulation**
Predicting an appropriate patient group and dosage

---

AI: Artificial intelligence, PoC: Proof of concept
IN SILICO SCREENING
WITH AI AND MACHINE LEARNING

Molecular structure

Virtual library \geq 100 \text{ million}

Hit identification from \textit{vast virtual library}

Conventional method: 300k chemical library that has not cover various chemical spaces
Maholo
Perform complicated /long-term processes exactly the same every time

Complex system reflecting patho-physiology

Screening station
Obtain huge image data from vast amounts of samples

Conventional method:
Simple model that cannot evaluate complex cellular processes

Hit identification considering complex mechanism
Human-mimetics

ORGANOID ALLOWS TO DETECT BIOLOGICAL INTERACTION BETWEEN HUMAN AND MEDICINES

Three dimensional organ-like structures derived from stem cells

* Modified from Int. J. Mol. Sci. 2020, 21, 2032
QSP MODEL ENABLES US TO PREDICT VARIOUS CLINICAL OUTCOMES

Visualization / Simulation

QSP (Quantitative Systems Pharmacology)

Mathematical model describing interaction between biological system and drug(s)

Virtual clinical trial (Computer simulation)

Generating virtual patients with various background

Prediction of biological response and clinical outcome

Can incorporate various mechanism of actions (MoA)

Can describe biological inter individual differences in healthy/disease states

Mathematical model describing interaction between biological system and drug(s)

Simulating of various combination therapies / different regimens

Can predict outcomes in various patient subpopulations and combination effect of drugs with different MoA

CREATING BREAKTHROUGHS IN DRUG DISCOVERY THROUGH SYNERGISTIC USE OF KEY METHODOLOGIES AND TECHNOLOGIES

AI: Artificial intelligence, iPS: Induced pluripotent stem, QSP: Quantitative systems pharmacology, RNA: Ribonucleic acid, MPS: Micro physiological system, IHC: Immunohistochemistry