



Cell and Gene Therapies

-Transforming New Treatments into Patient VALUE-
Brochure for scientific community

Version 1, August 2021

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1

Approach for Cell and Gene Therapy to Deliver VALUE to Patients

Cell-based therapeutics and gene therapies have tremendous potential to satisfy unmet patient needs across a broad range of disease areas. This potential puts cell and gene therapies at the heart of Astellas' VISION: Be on the forefront of healthcare change to turn innovative science into VALUE for patients. There is still so much to explore and develop in terms of both where the science can go and how it can help patients, particularly those for whom no other treatment exists.



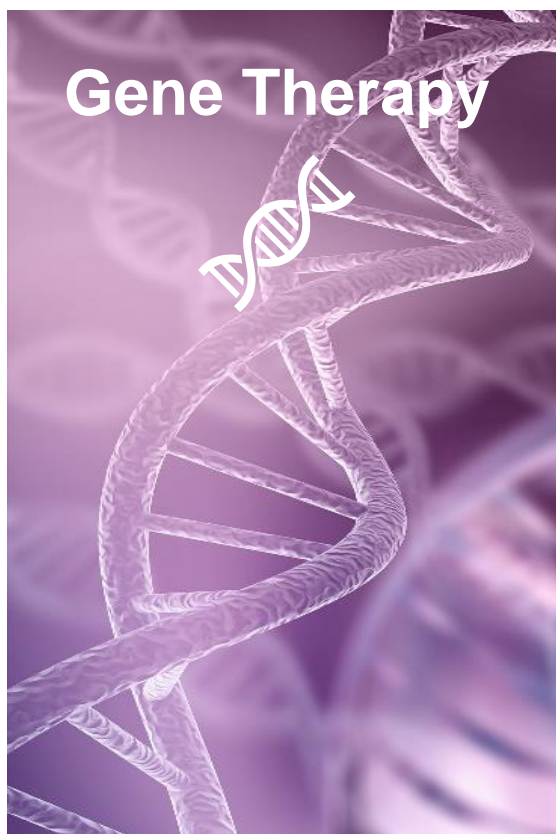
Innovative Cell and Gene Therapy to bring VALUE to PATIENTS

Cell Therapy



- We fully explore the potential of cell therapy to repair, replace or restore function to tissues damaged by injury or disease, and target / kill specific cancer cells, particularly in patients with high unmet need
- We are applying the latest technologies to the development of these therapies which allows us to stay at the forefront of breakthroughs in this fast-paced and emerging new field
- We are developing “off-the-shelf” cell-based therapies that can be used in any patient by using allogenic pluripotent stem cell (PSC)-derived differentiated cells
- We are working at the intersection of cell science and genetic regulation technologies to develop the cell-based therapies of the future

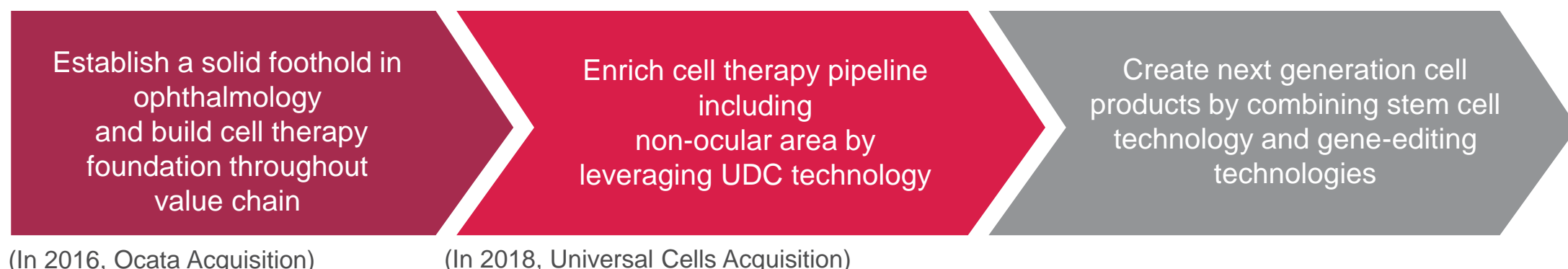
Gene Therapy



- We are dedicated to develop gene therapy treatments to potentially transform the lives of people with genetic and some non-genetic diseases, even with a single administration
- We pursue to develop life-changing gene-based therapies for patients with diseases where no or few treatment options exist
- A single intervention could replace missing genes or regulate genes that are behaving abnormally, to significantly improve outcomes for serious, life-limiting diseases
- We take an approach to achieve our goal for utilizing various genetic regulation technologies such as adeno associated virus that enables the delivery of functional genes into the nucleus of target cells

2 Astellas' Cell Therapy Platform and Capabilities

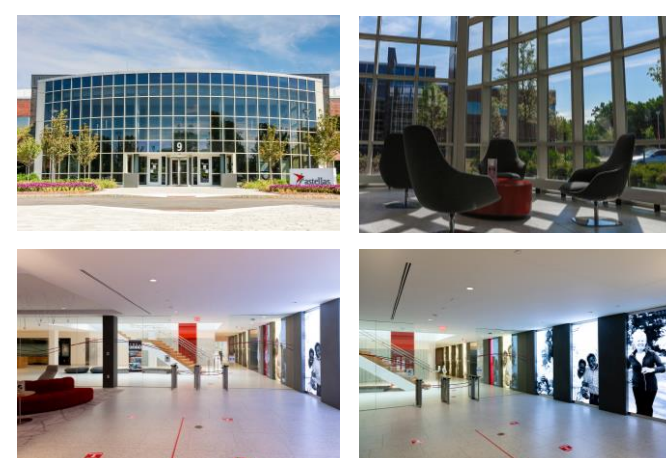
Strategic Approach for Cell Therapy



Capabilities for Cell Therapy

Research Capability

- Established cell differentiation protocols for approximately 20 cell types
- Own safe Pluripotent Stem Cells (PSC) line / banks compliant with regulations
- Efficient differentiation protocols for desired cell types
- Immune rejection avoidance
- Establish expertise and infrastructure for GMP cell manufacturing
- State of the art laboratories located in innovation hubs of Seattle and Boston



Manufacturing Capability

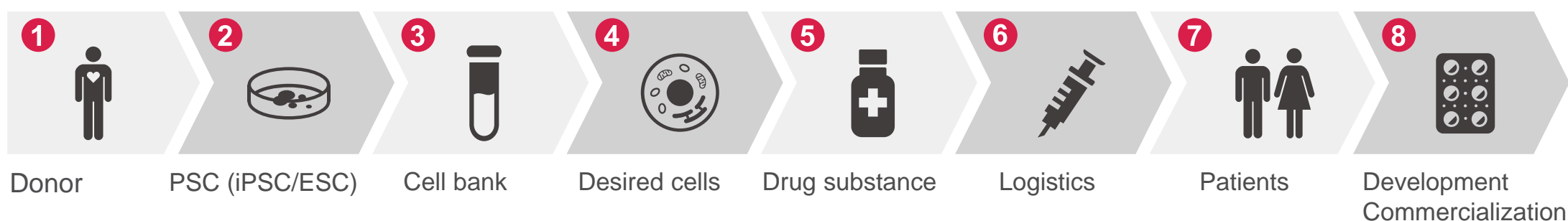
- Capable of supplying all the clinical demand of drug substance and drug product for all the cell therapy programs
- cGMP Manufacturing facility with up to 10 GMP manufacturing suites, allowing for independent production of multiple products
- Multiproduct facility with the ability to perform clinical and commercial production
- On-site QC laboratories provide full support for product and environmental testing
- Campus setting allows for facilitated transfer of information among research, development and GMP personnel
- Experienced management staff have a proven track record of GMP compliance and successful regulatory approval of other unique biologics

What is UDC Technology?

Universal Donor Cell (UDC) technology is an approach for creating cell therapy products that can be administered to any recipient without the need for Human Leukocyte Antigen (HLA) matching based on gene editing by rAAV (recombinant Adeno-Associated Virus) and cell engineering of pluripotent stem cells. UDC has a potential to avoid immune rejection.

We are building end-to-end capabilities in Cell therapies

Challenges for commercialization



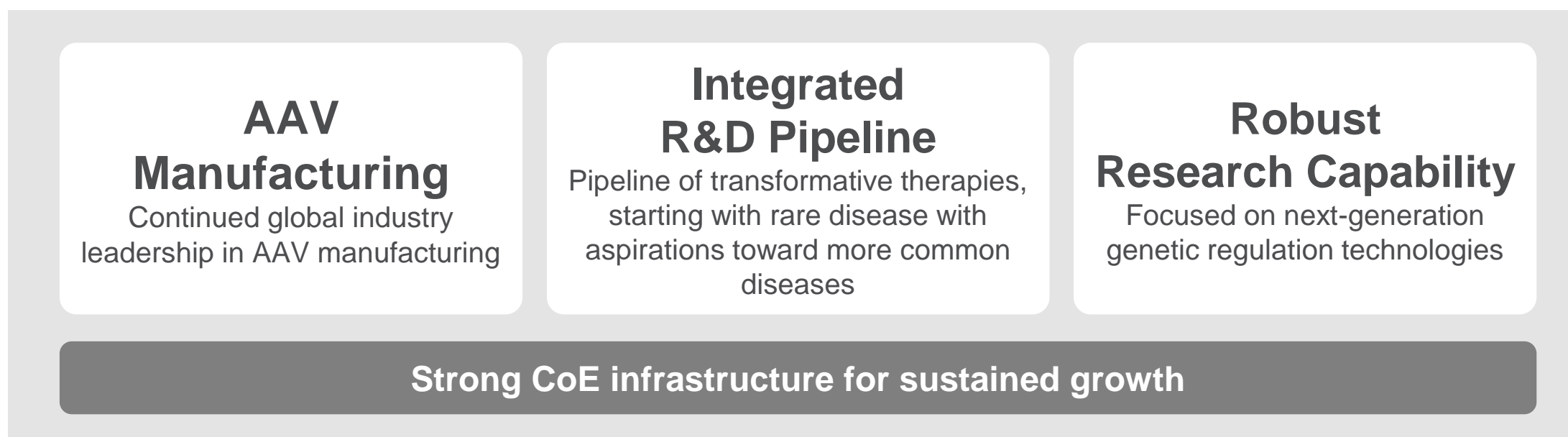
GMP: Good Manufacturing Practice
 cGMP: current Good Manufacturing Practice
 QC: Quality Control
 iPSC: Induced Pluripotent Stem Cell
 ESC: Embryonic Stem Cells

3

Astellas' Gene Therapy Platform and Capabilities

Strategic Approach for Gene Therapy

Astellas is the global leader in Genetic Regulation medicines
With Astellas Gene Therapies as its Center of Excellence (CoE)



Capabilities for Gene Therapy

Strong CoE Infrastructure

- We integrated our wholly owned subsidiary, Audentes Therapeutics, and established “Astellas Gene Therapies” within the organization
- Astellas Gene Therapies serves as the Gene Therapy Center of Excellence operated through three divisions specializing in gene therapy research including technical operations, medical and development, and future commercialization of gene therapy programs

Research Capability

- We acquired innovative genetic regulation technologies from Audentes
- Our innovative use of technologies has the potential to transform outcomes for patients with rare, neuromuscular diseases

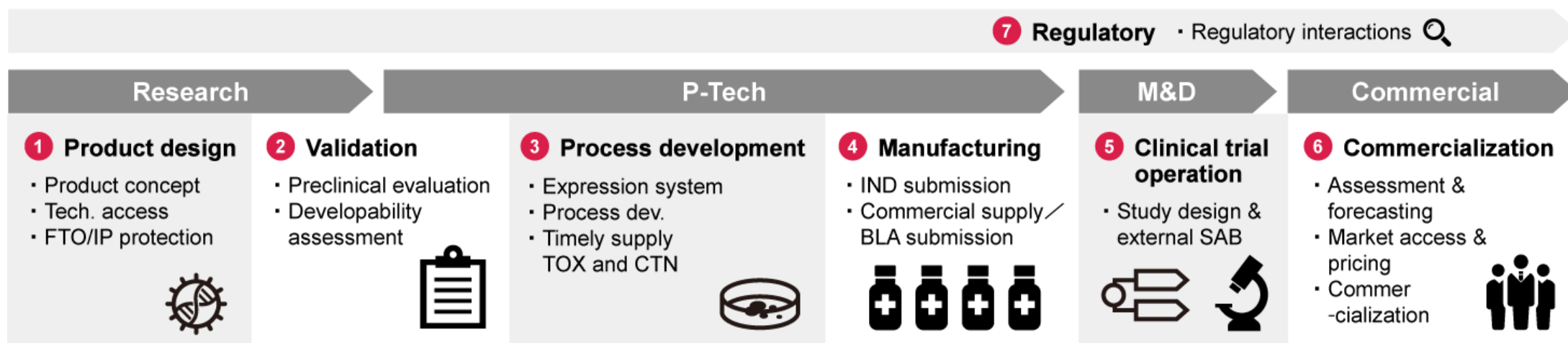
AAV Manufacturing Capability

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

What is AAV technology?

AAV vectors that utilize AAV, which is a non-pathogenic virus, are a type of viral vector that can deliver the target gene to the nucleus of the target cell. Using this gene transfer tool, the target functional gene can be introduced into the nucleus of the target cell, and the target gene replacement and gene regulation can be performed.

We are building end-to-end capabilities in Gene therapies



4

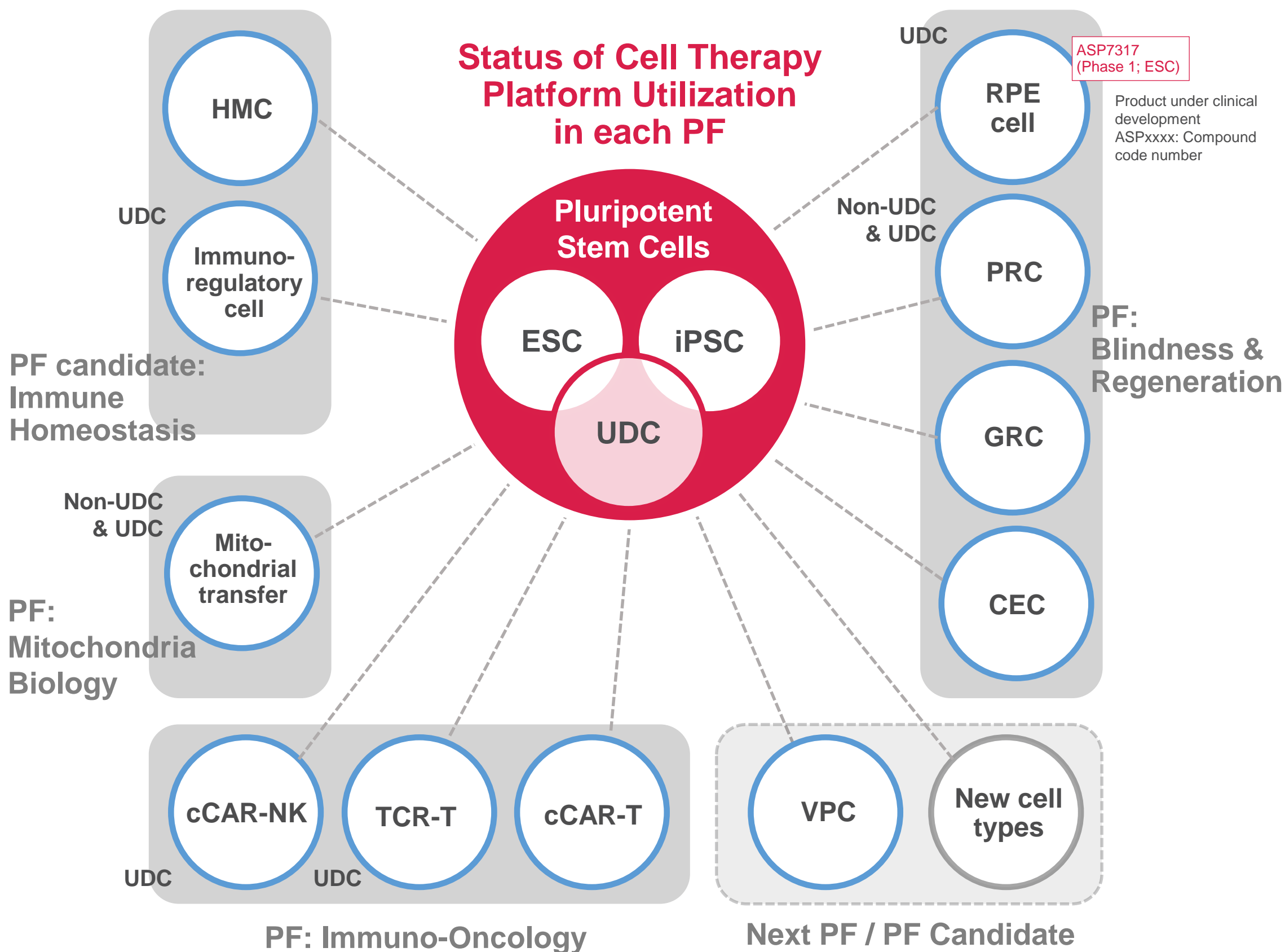
Organic Application of Cell Therapy Platforms

Astellas has evolved our cell medicine technology and is utilizing it in each Primary Focus (PF) * area selected by our strategic approach to research and development. The graphic below outlines the status how each PF utilizes the cell therapy platform. We are utilizing various cell types and have already established cell differentiation protocols for approximately 20 cell types. With the progress of such research, we would like to provide a treatment option of cell therapy to patients with a wide variety of diseases in the near future.

Primary Focus:

Astellas has established a Focus Area Approach for its research and development strategy. Based on a Focus Area approach, we concentrate our R&D investments on Primary Focus, and work to develop innovative treatments.

<https://www.astellas.com/jp/en/science/focus-area-approach>



● Cell differentiation protocols established as of May 2021

PF: Primary Focus, AIRM: Astellas Institute for Regenerative Medicine, ESC: Embryonic stem cell, UDC: Universal donor cell, iPSC: Induced pluripotent stem cell, HMC: Hemangioblast-derived mesenchymal stem cell, RPE: Retinal pigment epithelium, PRC: Photoreceptor rescue cell, GRC: Ganglion rescue cell, CEC: Corneal endothelial cell, VPC: Vascular progenitor cell, CAR: Chimeric antigen receptor, cCAR: convertibleCAR, TCR: T-cell receptor, NK: Natural killer

5 Organic Application of AAV-based Technology Platform

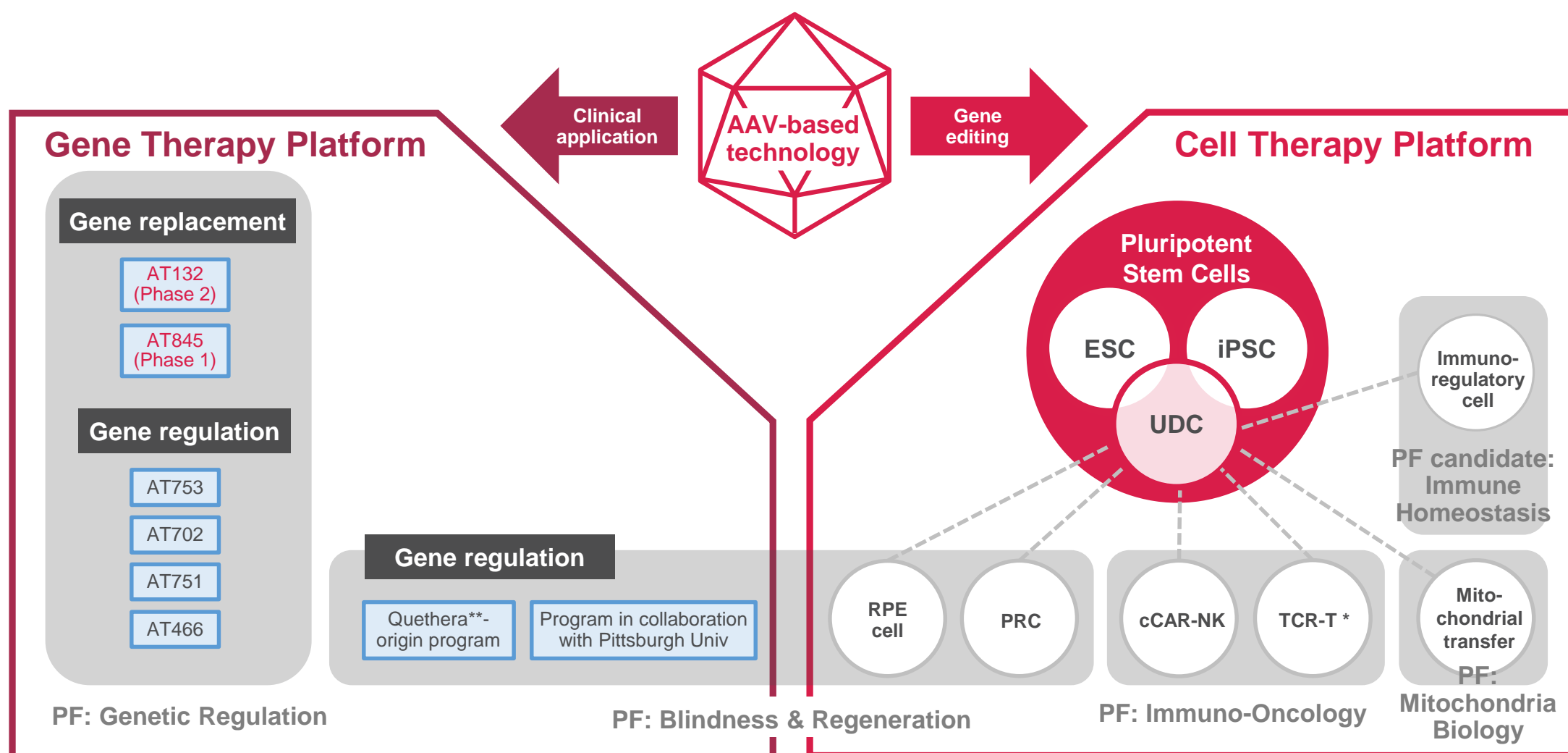
Astellas has evolved AAV technology as our genetic technology and is utilizing it in each Primary Focus (PF) * area selected by our strategic approach to research and development. The graphic below outlines the status how each PF utilizes AAV technology. AAV technology is widely used not only for clinical application of gene therapy platforms (left in the graphic), but also for cell therapy platform (right in the graphic) as gene editing technology. As a gene therapy platform, we especially apply "gene replacement" and "gene regulation" technologies to many programs. Through these attempts, we would like to provide therapeutic options that utilize AAV technology to patients with a wide range of diseases.

Primary Focus:

Primary Focus: Astellas has established a Focus Area Approach for its research and development strategy. Based on a Focus Area approach, we concentrate our R&D investments on Primary Focus, and work to develop innovative treatments.

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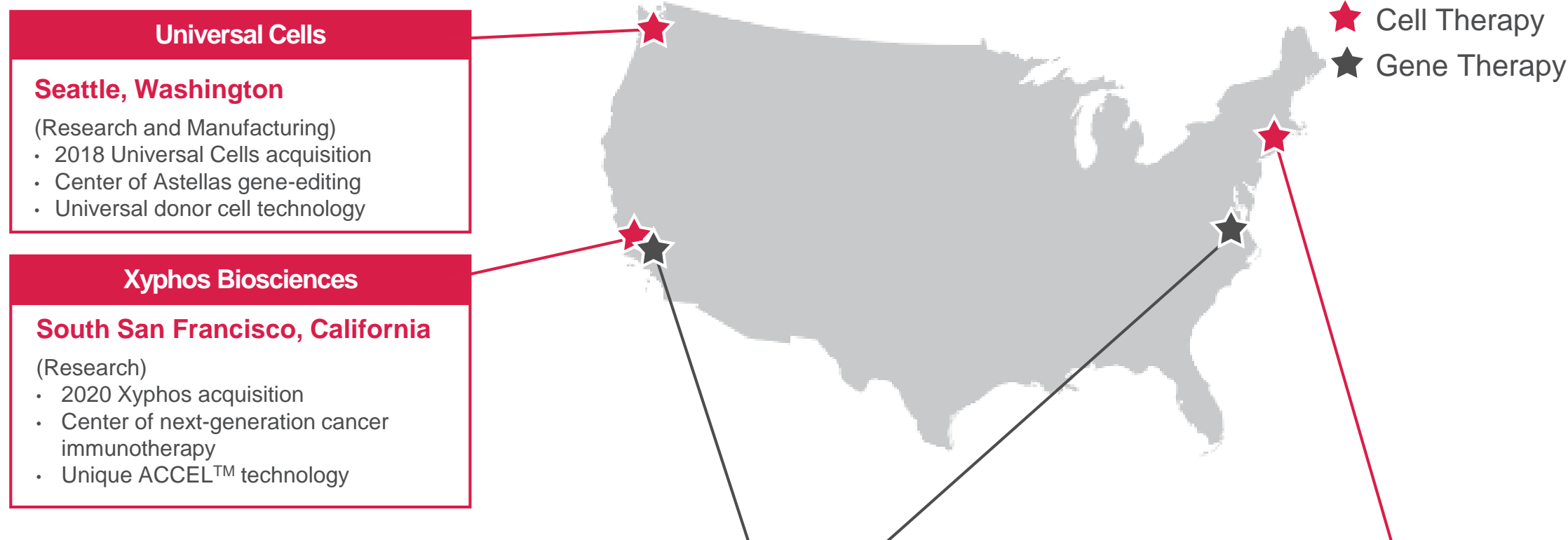
Status of AAV technology application to each PF



... Projects under research and clinical development
 ATxxx: Compound code number
Red; under clinical development
Black; Preclinical stage

6

Main Sites of Research and Manufacturing



Astellas Gene Therapies / AAV manufacturing




South San Francisco, California
 (Research and Manufacturing)
 • Preclinical research
 • Internal AAV manufacturing capability provides self-sufficiency from research to commercial
 • Capabilities to expand to support future AAV manufacturing and supply chain needs
 • Capabilities include:
 ♦ AAV Drug Substance Manufacturing
 ♦ AAV Drug Product (DP) Manufacturing
 ♦ Plasmid Manufacturing



Sanford, North Carolina
 (Manufacturing)
 • Currently under construction - scheduled to be operational and GMP-ready by 2022
 • Plant can supply all CoE late-stage clinical and commercial demand well into the future
 • Building and site are expandable to support additional future demand

Tsukuba, Ibaraki
 (Research and Manufacturing)
 • Preclinical research
 • Process & analytical development

Astellas Institute for Regenerative Medicine (AIMR) / Cell Therapy Research and Manufacturing



Westborough, Massachusetts
 (Research and Manufacturing)
 • 2016 Ocata acquisition
 • Center of Astellas regenerative medicine
 • Stem cell science and technology
 • Capable of supplying all the clinical demand of drug substance and drug product for all the cell therapy programs
 • GMP manufacturing
 • Clinical development for ophthalmology

AIRM Satellite Office

Tsukuba, Ibaraki
 (Research)
 • Collaboration with internal function
 • Collaboration with academia in Japan
 • Contribution to industrial organization activities (FIRM)

TSUKUBA BIOTECHNOLOGY RESEARCH CENTER (TBRC)

Tsukuba, Ibaraki
 (Manufacturing)
 • CTM manufacturing for use in early stage clinical trial



AAV: Adeno-associated virus
 GMP: Good Manufacturing Practice
 FIRM: Forum for Innovative Regenerative Medicine
 CTM: Clinical trial material