Primary Focus: Genetic Regulation

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

Our Mission

Our mission for Primary Focus Genetic Regulation is to **identify, develop** and **deliver transformative gene-based therapies** for patients with genetic 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, which aims to develop life-changing medicines for diseases where no, or few, treatment options exist.

~7,000 diseases

Background

Often present from birth and affecting young children, nearly 7,000 human diseases are caused by mutations or deficiencies in genetic code.[1] By replacing missing genes, or by regulating genes that are behaving abnormally, we can, in a single intervention, **significantly improve outcomes** for **serious**, **life-limiting** and **potentially fatal diseases**.

Strategic Approach

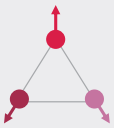
We are building a new multidisciplinary franchise for Astellas, investing in world class end-to-end capabilities across the entire gene therapy innovation process:

FOCUS

Focusing on rapidly developing adeno-associated virus (AAV)-delivered gene replacement and regulation treatments for diseases with high unmet need, caused by the absence or dysregulation of a gene.

ENRICH

Developing end-to-end discovery, development, manufacturing and commercial operations to build a portfolio of candidates; starting in neuromuscular diseases with an aspiration to expand to other organs and more common diseases.



EXPAND

Working closely with our biotech and academic partners to access tools and technologies to expand our portfolio of competitive projects.

Lead program (AT132)
Candidate targeting X-linked myotubular myopathy, a serious life-threatening neuromuscular disease

Integrated facilities
Fully integrated, in-house manufacturing and laboratory facilities in South San Francisco, California and under construction in Sanford, North Carolina, U.S.

Effective delivery of multiple programs
Establishing a Center of Excellence, combining a deep understanding and capability for using AAV technology, with the agility and tenacity of a biotech and Astellas' global experience and strengths

aAVC: Artificial adjuvant vector cells

Spotlight: Audentes Therapeutics

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.

AAV: Adeno-associated virus, RNA: Ribonucleic acid

Research Capabilities

Our innovative approach and access to novel technologies has the potential to transform outcomes for patients with rare, neuromuscular diseases, as well as more common diseases.

AGENT	DELIVERY	MECHANISM	DISEASE TARGETS
Gene → Protein	**AAV-based medicines** • Safe and efficient tissue transduction • Tailored biodistribution leading to durable specific expression	**Gene Replacement** Delivery of new functional gene copy to **replace** missing protein	**XLMTM** **Pompe Disease**
snRNA		**Gene Regulation (Exon Skipping)** *In situ* production of a snRNA to induce exon skipping to **correct** translation to a functional protein	**DMD** **Myotonic Dystrophy**
miRNA		**Gene Regulation (RNA Knockdown)** *In situ* production of a miRNA to **eliminate** an unwanted toxic RNA or protein	**Myotonic Dystrophy**

RNA: Ribonucleic acid, snRNA: Small nuclear RNA, miRNA: Micro RNA, AAV: Adeno-associated virus, XLMTM: X-linked myotubular myopathy, DMD: Duchenne muscular dystrophy

Pipeline – Current Status†

Current focus on muscle diseases:

Compound	Mechanism	Target indication	Current phase	Origin/partner
AT132	MTM1 gene replacement	X-linked myotubular myopathy	Phase 2 - Pivotal	AUDENTES An Astellas Company *
AT845	GAA gene replacement	Pompe disease	Phase 1	AUDENTES An Astellas Company *
AT753	Vectorized exon 53 skipping	Duchenne muscular dystrophy	Preclinical (to enter into clinical phase in FY2021)	AUDENTES An Astellas Company *
AT702	Vectorized exon 2, 1-5 skipping	Duchenne muscular dystrophy	Discovery	AUDENTES An Astellas Company *
AT751	Vectorized exon 51 skipping	Duchenne muscular dystrophy	Discovery	AUDENTES An Astellas Company *
AT466	Vectorized exon skipping/ vectorized RNA knockdown for DMPK	Myotonic dystrophy	Discovery	AUDENTES An Astellas Company *
GT0001X	ADAR2 gene expression	Sporadic amyotropic lateral sclerosis	Preclinical	Gene Therapy Research Institution **
MDL-201	Not disclosed	Muscle disease	Preclinical	MODALIS
MDL-202	Not disclosed	Muscle disease	Preclinical	MODALIS

† Accurate as of January 2021. * Acquired (current programs classified as 'in house'), ** Option agreement
MTM: Myotubularin, GAA: Acid alpha-glucosidase, RNA: Ribonucleic acid, DMPK: Myotonic dystrophy protein kinase, ADAR2: Adenosine deaminase acting on RNA2

REFERENCES: 1. U.S. Department of Health & Human Services. Rare Diseases FAQ, Version 11/30/2017.

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