Primary Focus: Genetic Regulation

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

Our Goal

Our goal 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

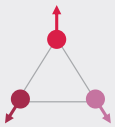
We are building a new multidisciplinary franchise for Astellas, investing in world class end-to-end capabilities across the entire gene therapy innovation process:

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

Pipeline

Our innovative research pipeline has the potential to transform outcomes for patients with rare, neuromuscular diseases.

AUDENTES An Astellas Company

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**

snRNA: Small nuclear RNA, miRNA: Micro RNA, XLMTM: X-linked myotubular myopathy, DMD: Duchenne muscular dystrophy

Spotlight: Audentes Therapeutics, Inc.

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.

Current Status†

Current status of our Center of Excellence AAV-based programs in neuromuscular diseases:

Compound	Modality/mechanism	Origin/partner	Target indication	Current stage		
				Discovery	IND enabling	Clinical
AT132	MTM1 gene replacement	AUDENTES*	X-linked myotubular myopathy			
AT845	GAA gene replacement	AUDENTES*	Pompe disease			
AT753	Vectorized exon 53 skipping	AUDENTES*	Duchenne muscular dystrophy			
AT702	Vectorized exon 2, 1-5 skipping	AUDENTES*	Duchenne muscular dystrophy			
AT751	Vectorized exon 51 skipping	AUDENTES*	Duchenne muscular dystrophy			
AT466	Vectorized exon skipping/ vectorized RNA knockdown for DMPK	AUDENTES*	Myotonic dystrophy			

AAV: Adeno-associated virus, IND: Investigational New Drug, MTM: Myotubularin, GAA: Acid alpha-glucosidase, DMPK: Myotonic dystrophy protein kinase.
† Accurate as of June 2020, * Acquired (current programs classified as 'in-house').

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

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