Getting More Common: The Growing Reach of Gene Therapy

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Increased comfort among key stakeholders, advances in gene delivery, and identification of novel genetic targets are key drivers for expansion of gene therapy into common diseases*

Key Factors Driving Development of Gene Therapy in Common Diseases

Experience with Gene Therapy (GTx)

Clinical and commercial stakeholders' comfort with GTx continues to grow, alongside a steady rise in FDA/EMA approved gene targeted agents and increasing utilization

Greater market receptivity and increased strategic thinking surrounding GTx

Advances in Vector Technology

Novel viral/non-viral delivery methods evade issues with immunogenicity, which is a key challenge with current vectors that excludes ~50% of the population and does not allow redosing

Broader applicability independent of antibody status and potential redosing

Stronger Understanding of Human Genomics

An increasing body of genetics data and functional genomics allows for a deeper understanding of key genetic interactions with therapeutic potential beyond those causing monogenic diseases

Increase viable GTx targets, including causal mutations, as well as key disease drivers with broader applicability

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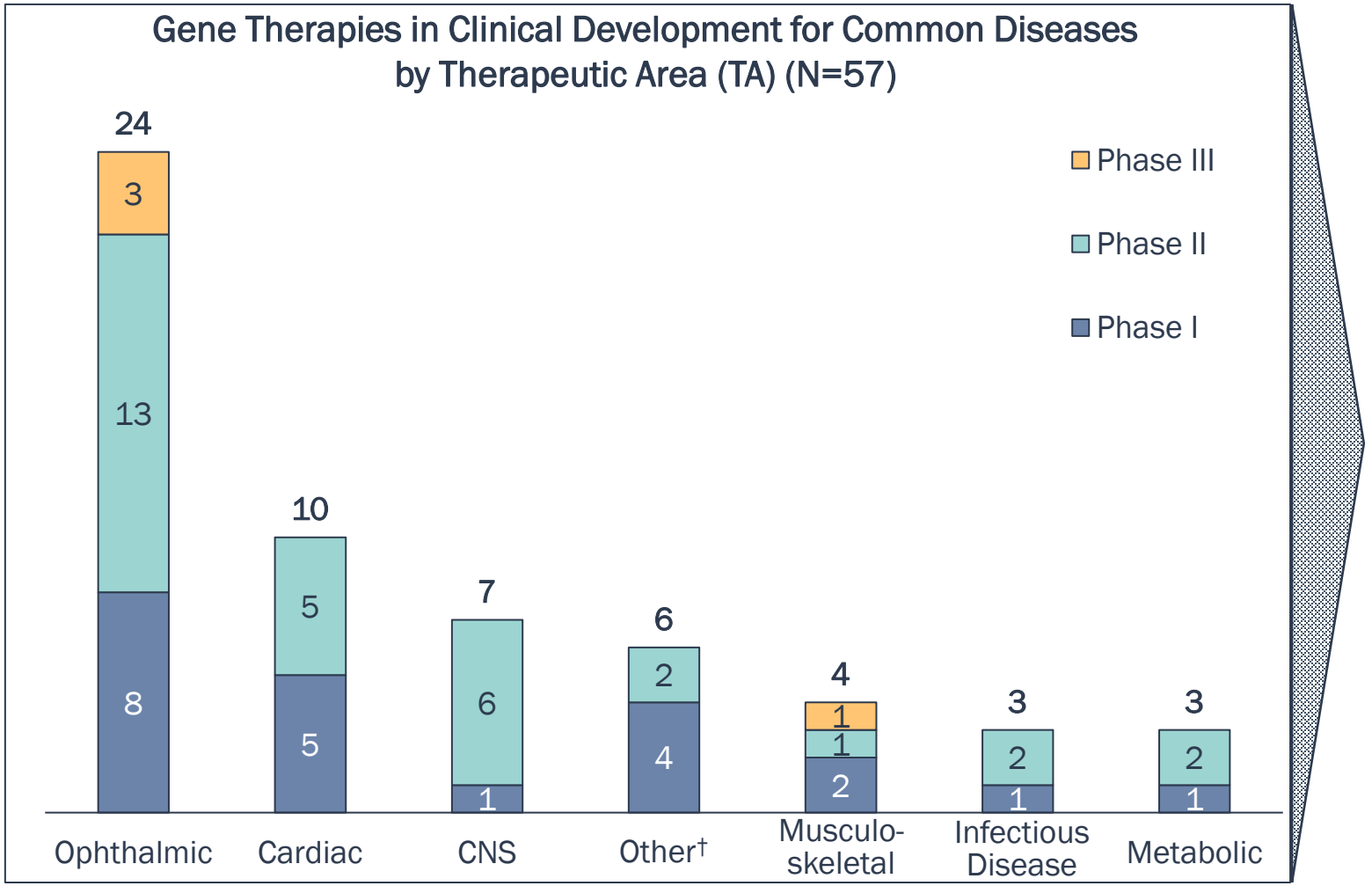
*Any diseases that affects >200,000 individuals in the U.S. is classified as a common disease

Source: Bluestar Analysis

The majority of GTxs for common diseases are in early-/mid- stage development and focus on ophthalmology and cardiology

Clinical Development of Gene Therapies for Common Diseases



- The majority of assets are in Ph I/II clinical trials with only 4 assets in Phase III development
- 15 assets have been granted fast-track designation by the FDA
- Ophthalmology is a key area of focus (e.g., AMD, glaucoma, AMD, dry eye) followed by cardiac diseases (e.g., heart failure)
- Higher selectivity of common delivery vectors towards cardiac tissue and ease of access to the eye likely influence current TAs in focus

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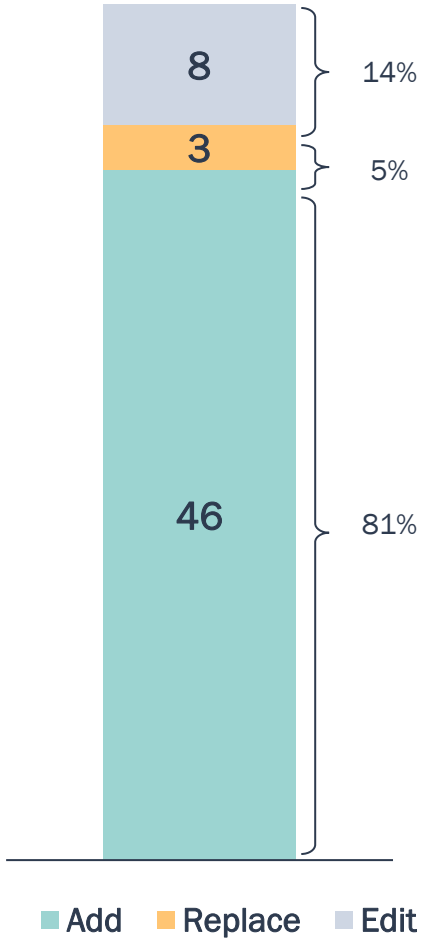
†other includes otolaryngology, and dermatology
Source: PharmaProjects

Common diseases are most amenable to gene addition compared to editing/replacement methods, which have stronger applicability in rare, monogenic diseases

GTx Common Disease Pipeline, by Approach



	Goal of GTx Approaches in Common Diseases	Example in Common Disease	Trends in Development and Most Common Addressable Patient Populations
Gene Editing	Modify DNA to correct a disease-related genetic mutation	EXCISION: EBT-101 (Ph II) for the treatment of HIV	**Dependent on disease-causing mutation** *While both approaches are more applicable to genetically-defined, monogenic diseases (~80% rare), there are some common diseases with defined and targetable causes; minority are in common disease*
Gene Replace-ment	Replace missing/faulty gene with a functional copy	REGENERON: DB-OTO for OTOF-deficient hearing loss	
Gene Addition	Addition of a gene that is non-specific to a disease-causing mutation	ocugen: OCU-410 for Dry AMD	**Agnostic to disease-causing mutation** *Not restricted to diseases with defined genetic origins; majority are in common disease*

Typically Rare Diseases

Narrower Applicability

Broader Applicability

Typically Common Diseases

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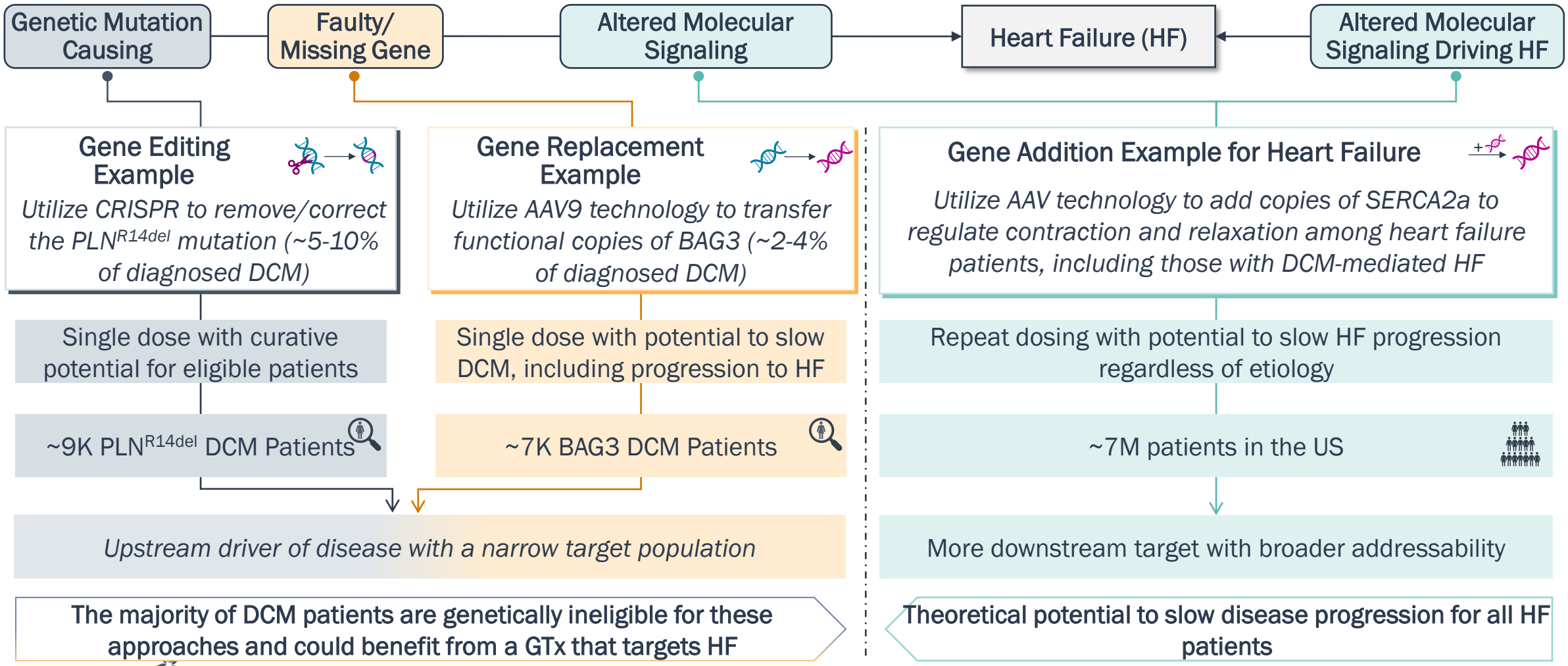
Gene addition approaches often utilize targets, like SERCA2a in HF, with potential to slow disease progression and mitigate symptom development without targeting causal mutations

Potential Applications of GTx Approaches in Dilated Cardiomyopathy (DCM) and Heart Failure (HF)



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Potential expansion of gene therapy into the common disease space further highlights the importance of monitoring the rapidly evolving landscape

Historical Trends Among Approved Gene Therapies

Adoption

- High receptivity towards GTx among key stakeholders (i.e., physicians, patients, caregivers, advocacy groups)
- Due to the novelty and complexity associated with GTx administration, only select centers are equipped to deliver approved GTxs, thereby limiting capacity

GTx Value Proposition

- Provide treatment for high unmet need patient populations (e.g., rare, high disease burden)
- Offer significant clinical benefit, including curative potential and typically one time administration

Pricing

- Drug prices for approved GTxs are largely driven by value proposition (e.g., curative potential, disease modifying) and small patient populations
- Particular emphasis on HEOR reducing long-term costs to the healthcare system

Key Considerations for Understanding the Broader Implications of GTx Use in Common Diseases

How does potentially lower efficacy affect market receptivity?

What actions will be necessary for GTx administration in a broader set of centers?

How does repeat dosing for gene addition approaches compare to other chronic treatments?

How will advancements to vector technology impact the potential for GTx in common diseases?

How will value proposition for GTxs in common diseases be viewed by payers?

How will payers influence GTx use in common diseases that may have more treatment options?

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