Gene Therapy at the Inflection:

Reading the Signal Through the Noise

Prof. Luk Vandenberghe, PhD

Grousbeck Gene Therapy Center | Harvard & Mass General Brigham

London | 2026

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Introduction

Prof. Luk H. Vandenberghe, PhD
Director, Grousbeck Gene Therapy Center, Mass Eye and Ear, Mass General Brigham
Harvard Medical School, Boston, MA, USA

ACADEMIC

KU LEUVEN → Penn University of Pennsylvania →

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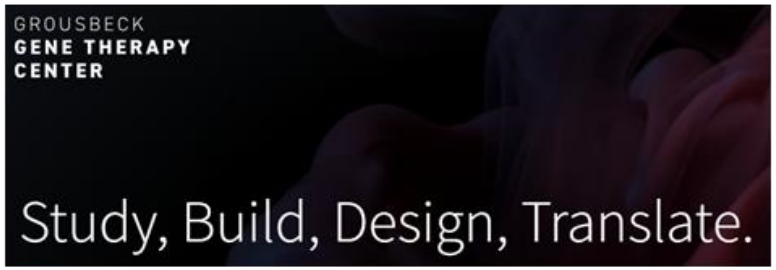

MASSACHUSETTS EYE AND EAR · Mass General Brigham · BROAD INSTITUTE · HARVARD MEDICAL SCHOOL

INDUSTRY

GenSight BIOLOGICS · Odylia · LUMEVOQ

Euronext · *Non-profit*

AAV9 · zolgensma® · NOVARTIS

+ 15 Ph1/2/3

Anc80 · AKOUOS

Acquired by Eli Lilly for $487M (2022) Lilly

affinia™ THERAPEUTICS

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ciendias.bio

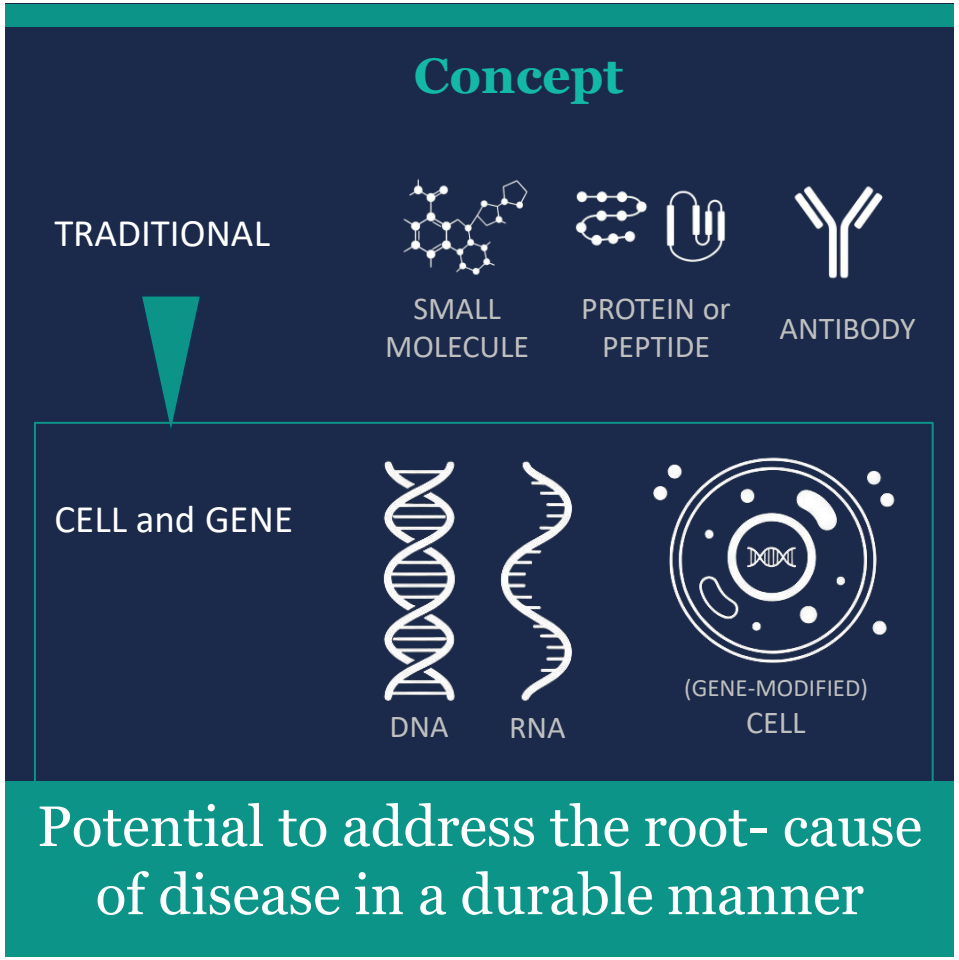
NewCo 1

NewCo 2

Seed Stage

1 Cell and Gene Therapy in a Nutshell

'the gene as a drug'



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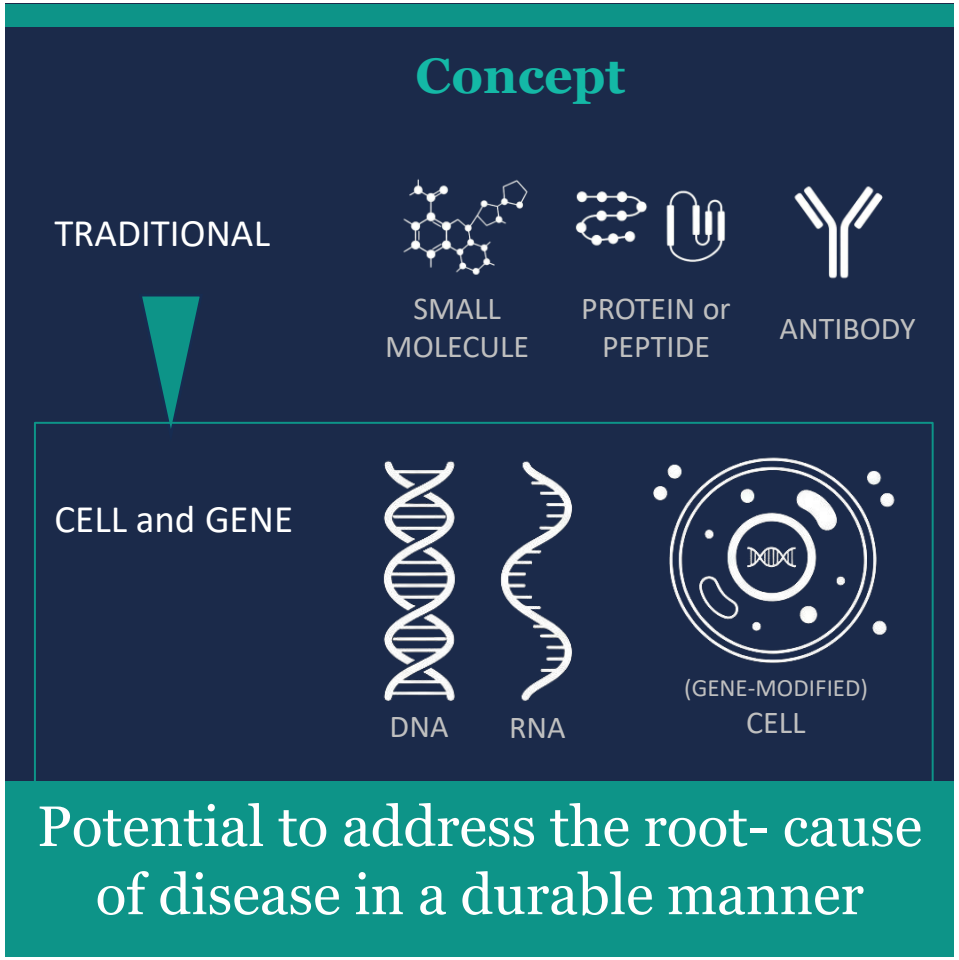
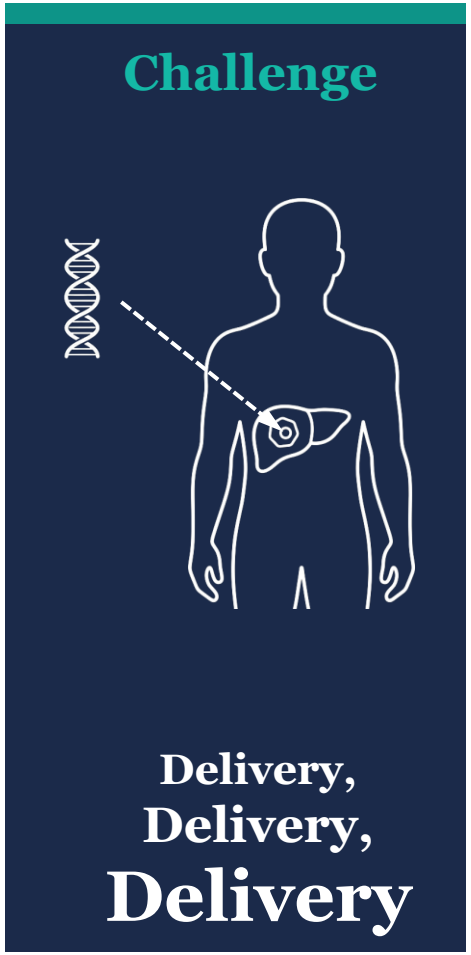


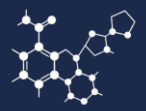


1 Cell and Gene Therapy in a Nutshell

'the gene as a drug'

Concept

TRADITIONAL

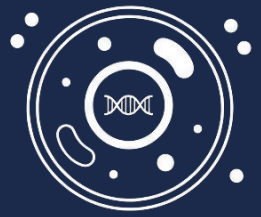

SMALL MOLECULE


PROTEIN or PEPTIDE


ANTIBODY

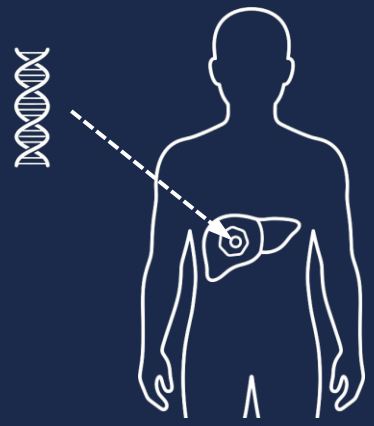
CELL and GENE


DNA RNA


(GENE-MODIFIED) CELL

Potential to address the root- cause of disease in a durable manner

Challenge

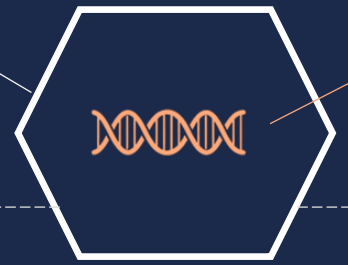


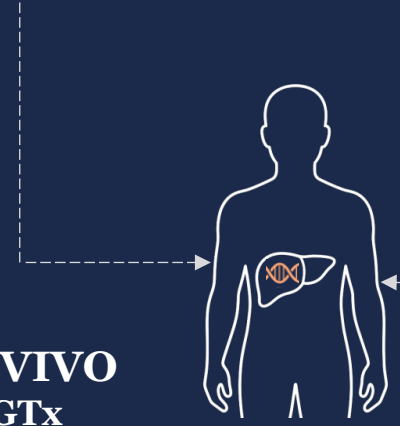
Delivery, Delivery, Delivery

Solution

(Viral) Vector

Therapeutic Cargo





IN VIVO GTx

EX VIVO GTx

2 Potential for transformative treatment effects

MIRACLE GENE JAB Blind babies to have eyesight restored by revolutionary £613,000 gene therapy available on the NHS

Shaun Wooller
4 Sep 2019, 0:34 | Updated: 4 Sep 2019, 0:35

LUXTURNA™ voretigene neparvovec-rzyl for subretinal injection

Ghent, Belgium March 19, 2026

Gene Therapy Shows Promise For A Growing List Of Diseases

November 29, 2017 · 7:40 AM ET
Heard on Morning Edition

ROB STEIN

zolgensma® (onasemnogene abeparvovec-xioi) suspension for intravenous infusion

Emily Whitehead: A Young Girl Beats Cancer with Immunotherapy

KYMRIAH® (tisagenlecleucel) Suspension for IV infusion

'Oscar of science' awarded to team behind gene therapy that restores lost vision

Married couple Jean Bennett and Albert Maguire developed Luxturna, which helped a patient see their child's face for the first time

The Guardian

Ian Sample *Science editor*
Sun 19 Apr 2026 08.00 CEST

The New York Times

Gene Therapy Allows an 11-Year-Old Boy to Hear for the First Time

The genetic treatment targeted a particular kind of congenital deafness and will soon be tried in children who are younger.

By Gina Kolata

Jan. 23, 2024

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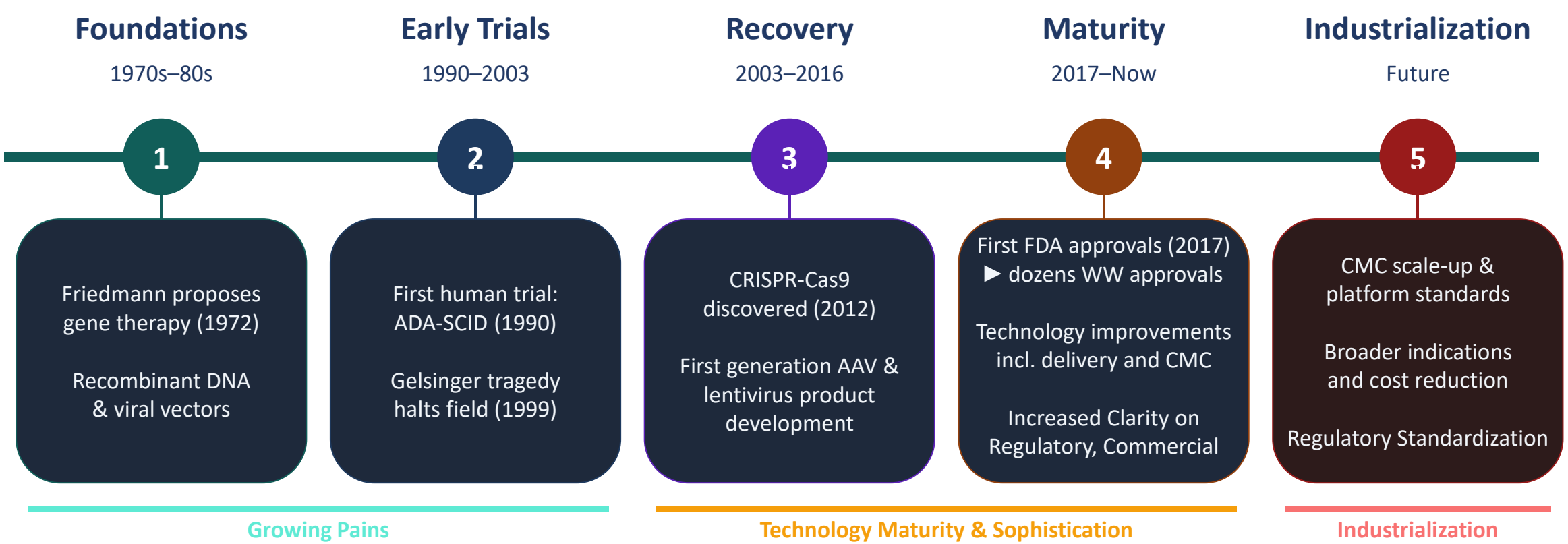
The evolution of gene therapy

From concept to industrialization



From early setbacks to a maturing ecosystem — gene therapy enters its industrial era

Source: ASGCT, FDA, PMC/NIH

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CGT at an inflection point

From delivering on potential to commercial execution

Delivering on the Promise

- Transformative efficacy in inherited diseases
- Growing portfolio: 38 approved products globally
- Durable clinical outcomes (5+ yr data emerging)
- Investment and revenue growth across CART, NMD, ophthalmology

Setbacks in Context

- Commercial: pricing, reimbursement, market access hurdles
- Safety signals in high-dose systemic programs
- Manufacturing complexity remains a bottleneck
- Biotech/Pharma pipeline rationalization

5

A New Foundation Beneath Gene Therapy

Technology Caught Up to the Ambition

The Opportunity

- Delivery:
  - Step-change in improved and novel vectors for safety and efficacy
- Cargo:
  - Expanding toolkit for sophisticated and precise control over gene therapy
- Access:
  - Complex, expensive indiv. Tx ► more economical, off-the-shelf

Safer, more efficacious products

Unlocked indications

Broader Patient Impact

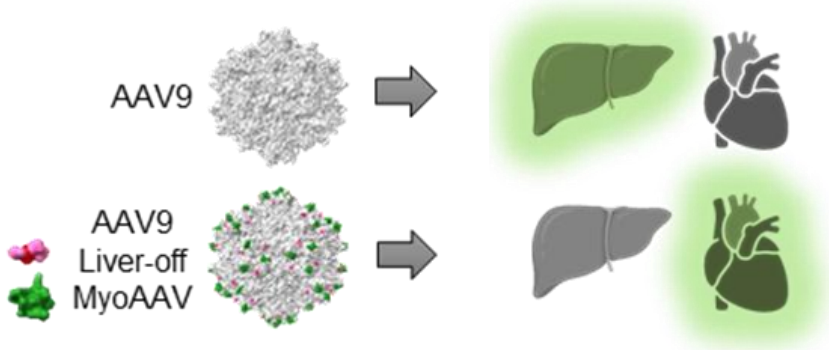
5 Novel Vectors: Improved Targeting

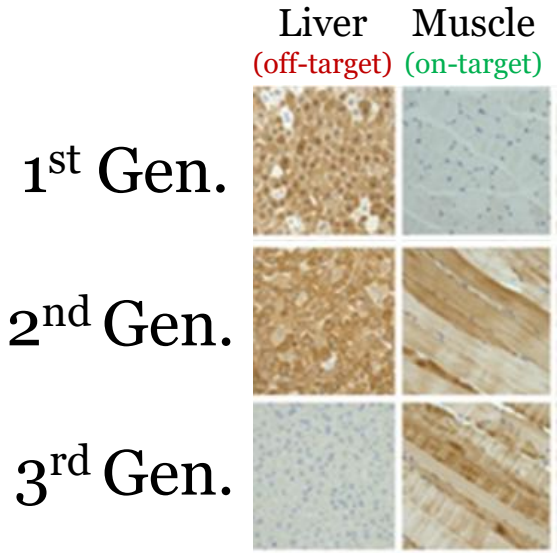
Advances in vector technology markedly increases control over safety and efficacy

1st Gen: Liver-targeting AAVs, even for non-liver indications (e.g. SMA, DMD)

- Limited on-target tropism
- Dose-limiting toxicity

2nd & 3rd Gen: Muscle-targeted, Liver-sparing AAV

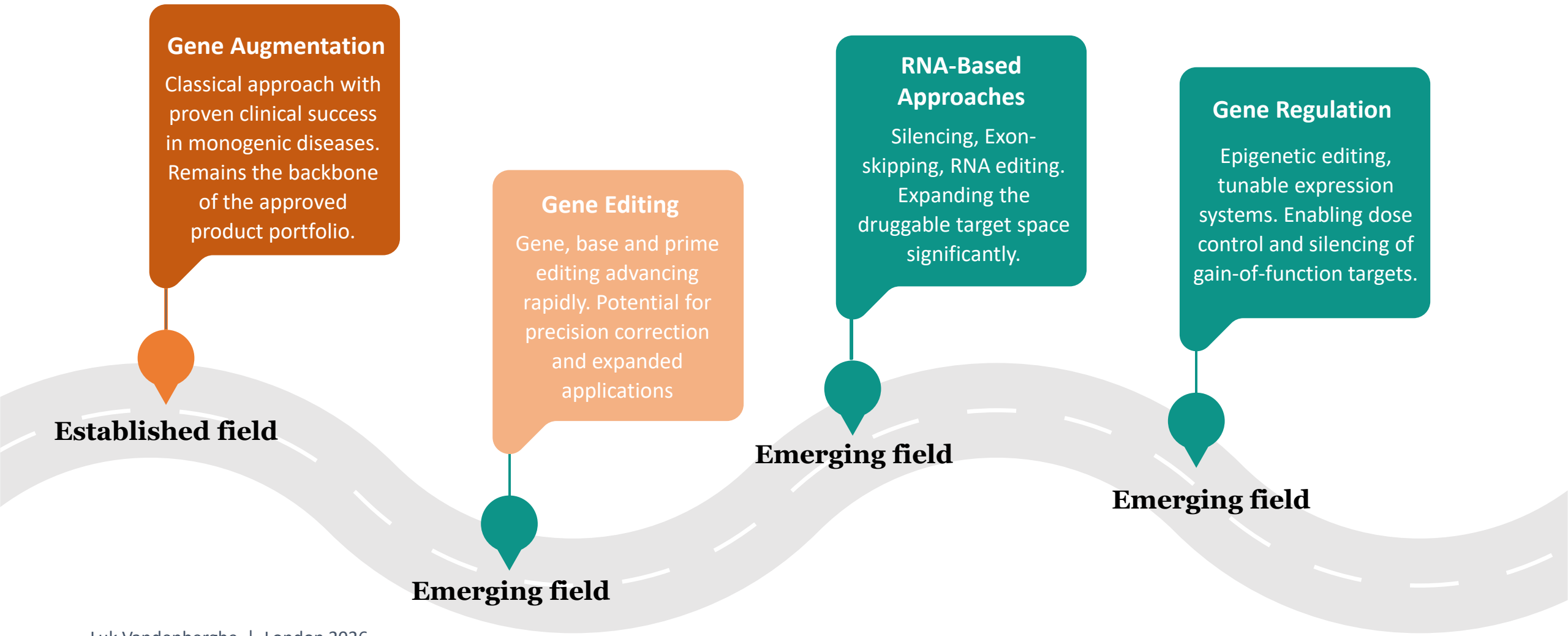




Decades of investment, combined with powerful methods (incl. AI) provides new vector tools aiming to minimize safety concerns and maximize efficacy

5 Sophisticated Cargo: Precise Genetic Control

Beyond gene replacement — an expanding therapeutic toolkit to reach more patients



6 The Gene Therapy Opportunity Beyond Science

Regulatory, Commercial, and Structural Advantages

The Opportunity

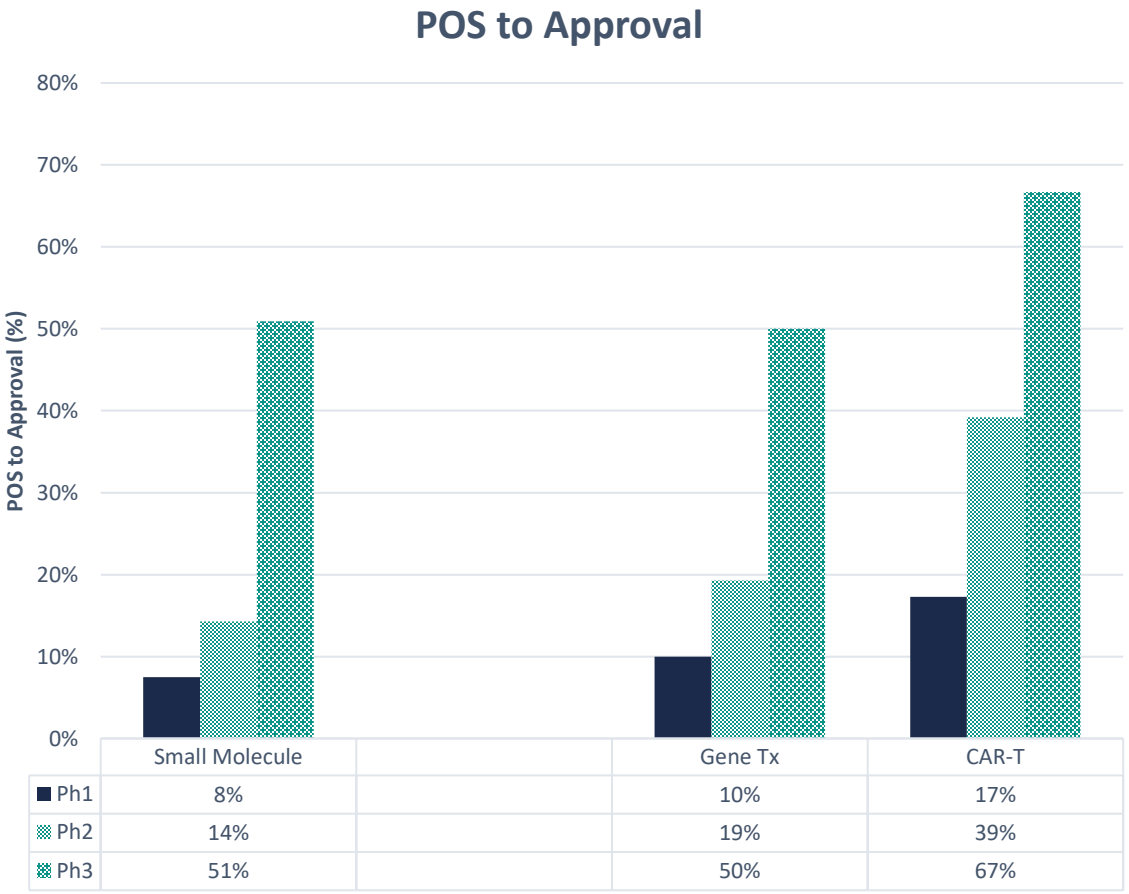
- Pathways for accelerated approval
- Potential for expansion in earlier line of treatment
- Probability of success in development high and increasing
- Concept of platform approval is maturing

Faster approvals

Early focus on Scale, Adaptability, Regulatory Robustness and Execution

Key reliance on CMC-partners

6 Probability of success is high and increasing



	Small Molecule		Gene Tx	CAR-T
Ph1	8%		10%	17%
Ph2	14%		19%	39%
Ph3	51%		50%	67%

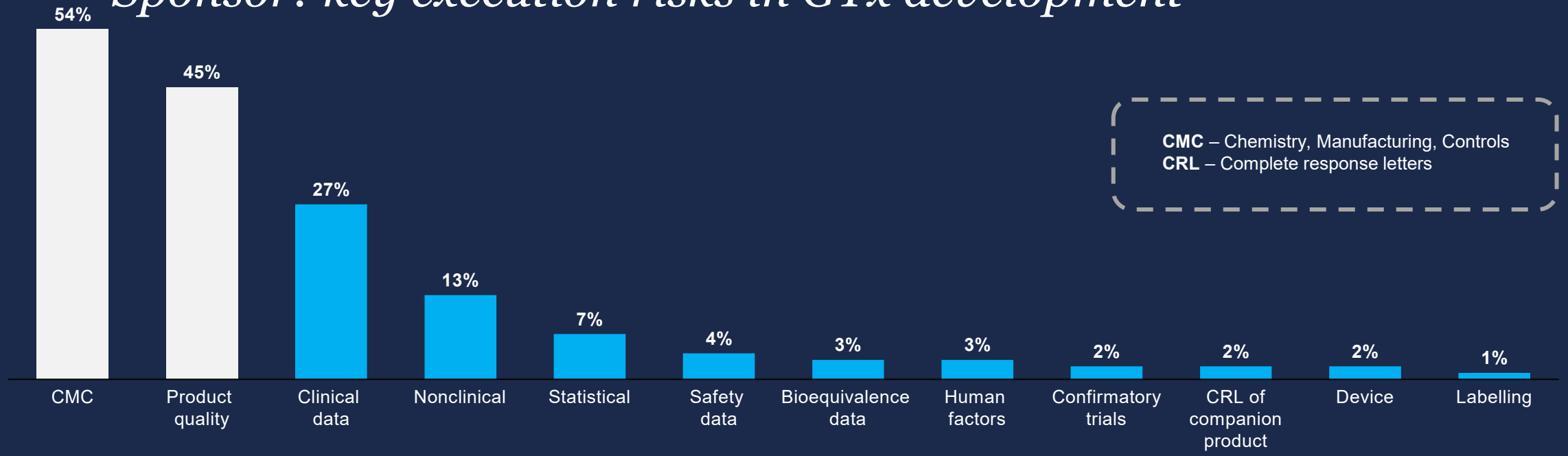
- ❖ Biological Precision Tools
- ❖ Targeted Disease Mechanisms
- ❖ High-Impact Biomarker Usage
- ❖ Stronger Proof-of-Concept
- ❖ Regulatory and Competitive Advantages
- ❖ Development and Clinical Experience ↗

Clinical Development Success Rates and Contributing Factors 2011–2020 BIO, PharmaIntelligence, QLS 2021

7 The Outsized Importance of Manufacturing & CMC

> *Regulator: 50% of the drug is CMC* — FDA perspective on GTx products

> *Sponsor: key execution risks in GTx development*



Sources: Jefferies Analyst Report, September 2025

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Excellence in Execution

Where do specialized CDMOs fit?

Speed

Accelerated timelines from process development to clinical supply

Time-to-IND as competitive advantage

Scale

Ability to transition from clinical to commercial volumes

Platform scalability across programs

Robustness

Consistent manufacturing

Reliable batch success

Reproducible quality attributes

Flexibility

Multi-platform capability

Accommodate novel vectors, formulations, and evolving regulatory requirements

Gene therapy manufacturing demands deep specialization requiring a focused CDMO

Questions?

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