NORD
National Organization for Rare Disorders

Rare Disease Scientific Symposium

Access and Coverage: Data and Clinical Development

Pamela Gavin
NORD
(Moderator)

Ravi R. Pathak, PhD, MBA
Takeda

Mark Trusheim, MS
Tufts Medical Center

Margarita Valdez Martinez
ASGCT

Danny Yeh, PhD
AESARA

TuftsMedicine
Tufts Medical Center

Financial Considerations for Rare Disease Cell and Gene Therapies

NORD RDSS
Access and Coverage: Data and Clinical Development
April 15, 2026

Mark Trusheim
Senior Strategy Advisor, NEWDIGS
Mark.Trusheim@TuftsMedicine.org

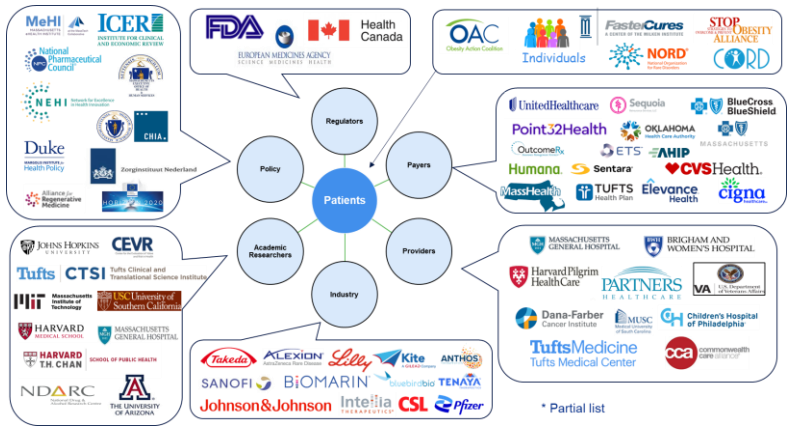
NEWDIGS

NEWDIGS @ Tufts Medical Center

Our Mission

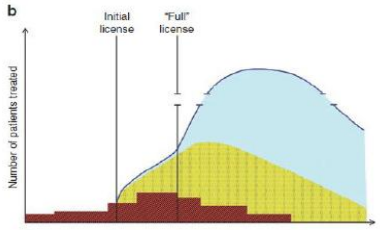
Improve health outcomes by accelerating appropriate, timely, and equitable access for patients to biomedical products in ways that are scalable and sustainable for the system.

Our Approach: Collaborations



Our Areas

Adaptive Licensing



Financing Cures FoCUS

RWE Learning Ecosystem

Obesity Disease Management

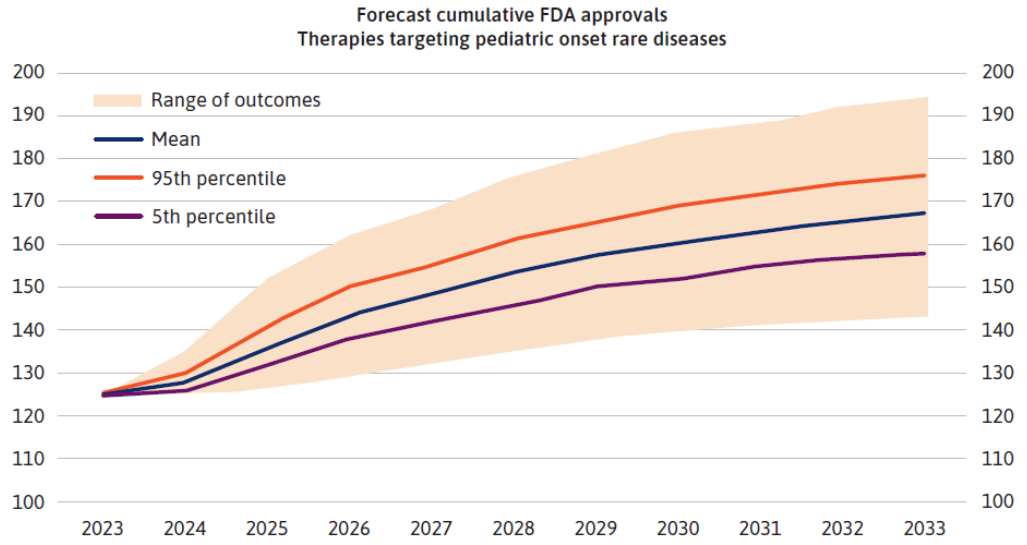
Alzheimer's Disease Care

The Total Pediatric Rare Disease Pipeline Yields Products But Limited Revenues

The challenge is not FDA Approval

~45 new FDA product-indications by 2033

FIGURE 2 Baseline US Projected Product Approvals 2023-2033



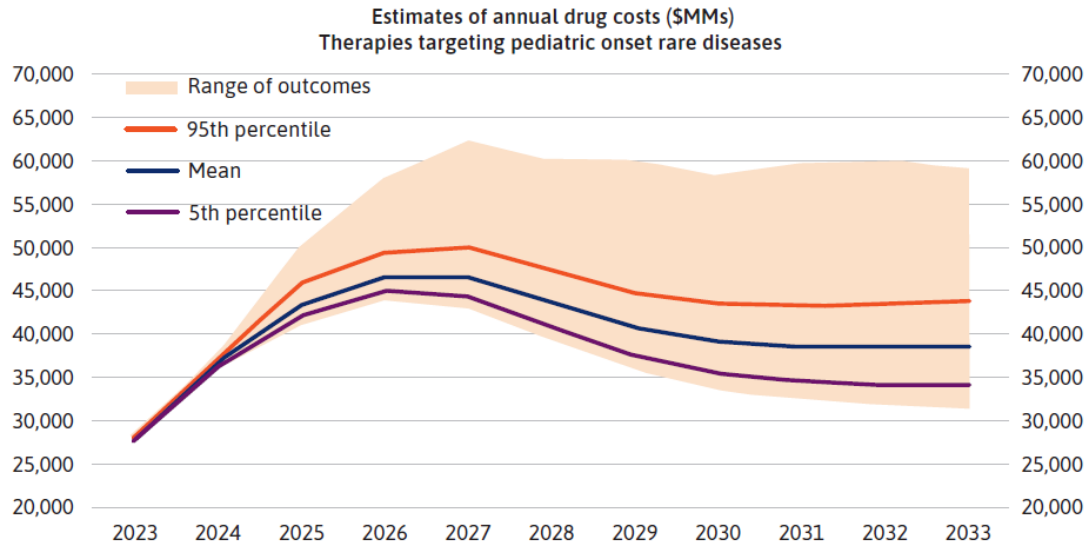
FDA = US Food and Drug Administration.

We projected all treatments for 113 nononcologic, pediatric-onset rare diseases with approved or candidate therapies in trials

The revenue challenge is low adoption or very few patients

~$11B New Annual List Price Therapy Spending (Peak $18B))

FIGURE 3 Baseline US Projected Annual Revenues 2023-2033



Young CM, Phares SE, Kennedy A, Sullivan J, McGowan B, Trusheim MR. Pediatric-onset rare disease therapy pipeline yields hope for some and gaps for many: 10-year projection of approvals, treated patients, and list price revenues. Journal of Managed Care & Specialty Pharmacy. 2025 May;31(5):491-8.

Therapy Utilization is Less Than Hoped (by some)

Many individual factors, mechanisms, and decisions lead to this result;
But most have roots in uncertainty.

Investors | FDA | Payers | Patients / Providers

Development → Approval → Launched

Population

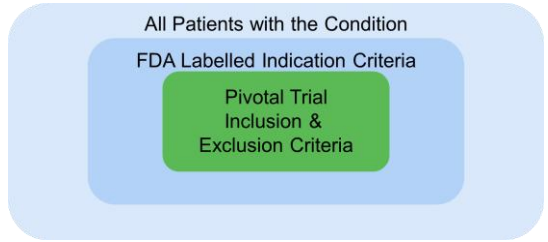
Small Trials

Late Line Or Step Therapy

Patient Reluctance

Value

Endpoints



Coverage to RCT not Label

Provider Incentives

Total Population Cost

Uncertainty is the Root Cause of Low Utilization

And Uncertainty falls into only a few types

Social benefits (carers, employers, gov't)

Effectiveness (patient)

Effectiveness (health system)

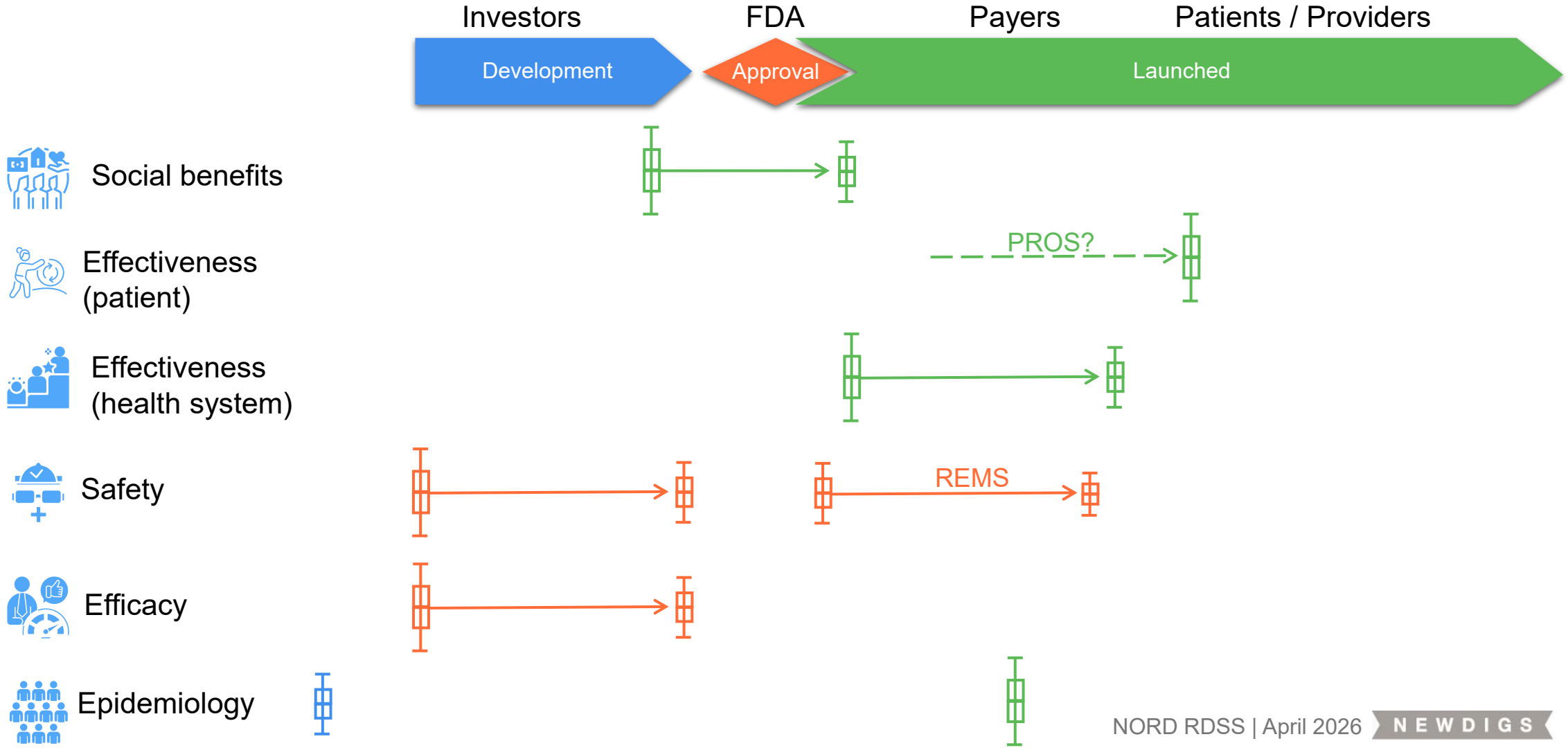
Safety

Efficacy

Epidemiology

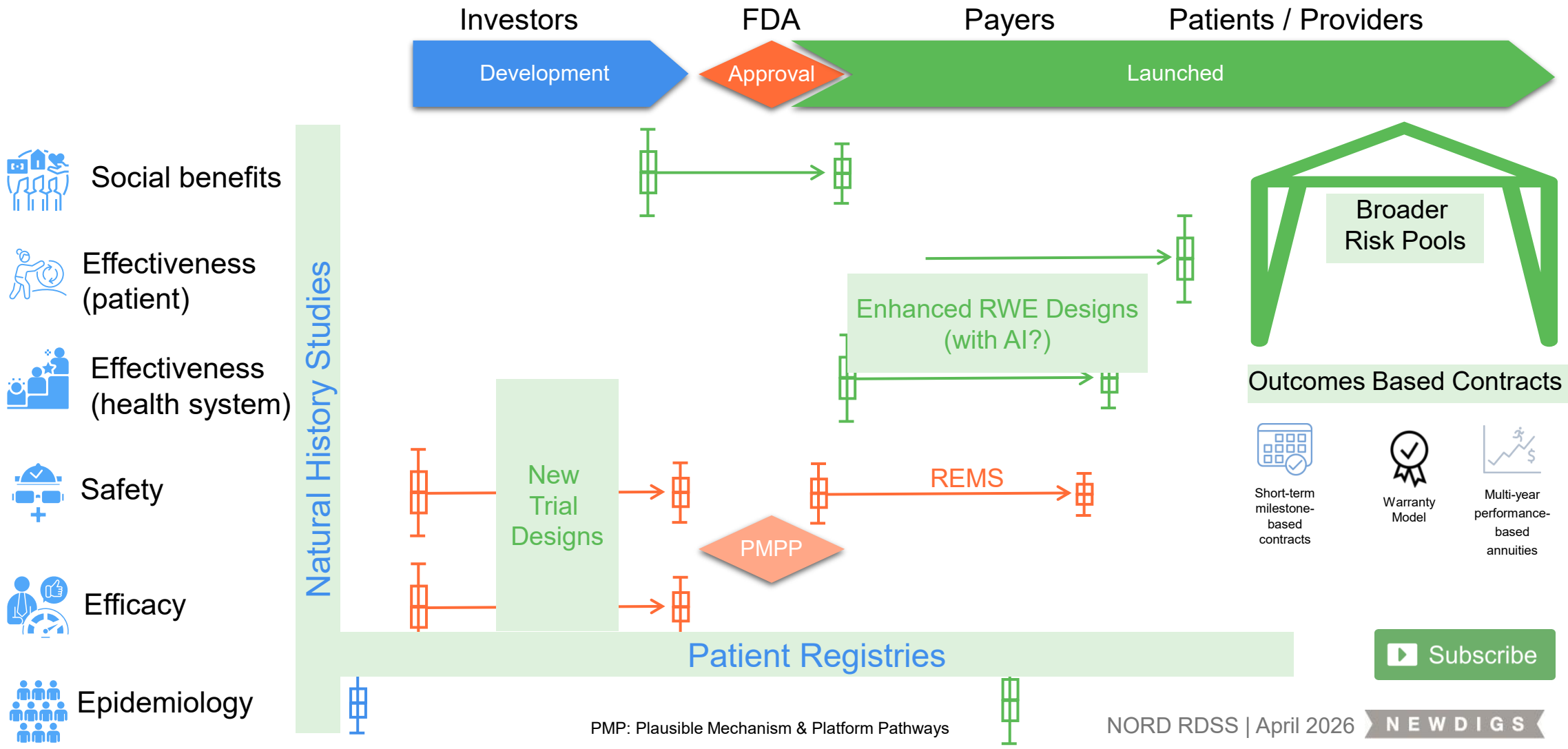
Unfortunately, Evidence is Developed Unevenly

Currently, evidence development is driven by FDA requirements with less attention to downstream decision makers



Evidence Creation & Uncertainty Management Tools Exist to Systematically Change Therapy Utilization

The challenges are costs of coordination & data as well as value sharing



PMP: Plausible Mechanism & Platform Pathways

TuftsMedicine
Tufts Medical Center

THANK YOU

NORD RDSS
Access and Coverage: Data and Clinical Development
April 15, 2026

Mark Trusheim
Senior Strategy Advisor, NEWDIGS
Mark.Trusheim@TuftsMedicine.org

NEWDIGS

NORD RARE DISEASE SCIENTIFIC SYMPOSIUM| Panel Discussion

From Evidence Generation to Evidence Translation

Designing Real-World Data That Translates Evidence into Access

Ravi Ramesh Pathak PhD, MBA
Takeda Pharmaceuticals

Speaker Declaration & Conflict of Interest Statement

Employment & Affiliation

I am a full-time employee of Takeda Pharmaceutical Company Limited. My participation in this panel discussion is in a personal and professional capacity as a subject matter expert. Takeda has not directed, reviewed, approved, or endorsed the content of this presentation.

Views & Opinions

All views, opinions, and statements expressed in this presentation are solely my own and do not represent, reflect, or constitute the official position, policy, or endorsement of Takeda Pharmaceutical Company Limited or any of its affiliates, subsidiaries, or partners.

Financial Interests

As a Takeda employee, I hold standard employee compensation and may hold equity in Takeda Pharmaceutical Company Limited. No additional financial relationships relevant to this presentation exist.

Off-Label Use

This presentation does not discuss, promote, or reference any unapproved or investigational use of any medicinal product. No product-specific promotional content is included.

This disclosure is made in accordance with applicable industry codes of practice, including the PhRMA Code on Interactions with Healthcare Professionals and the EFPIA Code of Practice. Questions regarding this disclosure may be directed to the speaker.

Rare disease therapies are approved faster than ever. So why do so many patients still struggle to access them?

What Regulators Accept

- Single-arm trials with synthetic controls
- Surrogate / biomarker endpoints
- Accelerated & conditional approvals
- Small, heterogeneous patient populations
- Natural history as external comparator

GAP

What Payers Still Ask For

- Comparative effectiveness vs. standard of care
- Long-term outcomes & durability data
- Healthcare resource utilization data
- Quality of life in real-world populations
- Evidence of value beyond the trial window

Source: Dayer et al., Orphanet J Rare Dis 2024; FDA RWE Guidance Series 2019–2024

THE ROOT CAUSE

We built our evidence for one audience.
Payers are a different audience with different questions.

Organizational Silos

- Regulatory teams drive late-stage development with one destination: submission and approval.
- Market access and HEOR teams board the bus too late to shape the evidence architecture.

Registry Structural Failures

- Inconsistent data capture.
- Rigid protocols requiring regulatory approval to update.
- Access restricted to participating PIs.
- Dissemination controlled through periodic industry publications.

The Fragmented Patient Journey

- A rare disease patient navigates multiple specialists, institutions, and EMR systems - many non-electronic.
- Their clinical odyssey is less visible to current RWD infrastructure.

Payers report they seldom receive the RWE on disease burden, treatment patterns, and HRU that would most inform their coverage decisions.
Dayer et al., Orphanet J Rare Dis 2024

The rare disease clinical odyssey generates the richest possible evidence. Almost none of it is captured.

What Current RWD Infrastructure Misses:

- Fragmented EMRs across institutions - often non-interoperable, sometimes non-electronic
- Family and caregiver observations - the most longitudinal dataset that exists, completely uncaptured
- Patient-reported outcomes - underrecognized as first-class RWE in both regulatory and payer submissions

AI can aggregate across fragmented systems but cannot replace the clinical context that only specialists, families, and patients can provide.

Newborn screening is identifying rare disease patients before they have a single symptom.

The SMA Case Study

- NBS identified infants presymptomatically
- Treatment existed and was proven effective
- 39% of providers delayed treatment beyond 3 weeks
- Primary barrier: insurance authorization process
- Treatment window for CNS protection: days, not weeks

Natural History Data

Historical symptomatic cohorts are no longer valid comparators for presymptomatic treated patients.

Registry Design

Registries must follow NBS-identified patients from Day 1 of life. Current designs were not built for this.

Coverage Authorization

Prior authorization timelines designed for chronic therapy cannot accommodate biological urgency in newborns.

Outcomes Measurement

How do you demonstrate value to a payer for a child who never became sick because they were treated at Day 10?

Source: Glascock et al., Int J Neonatal Screen 2024; Varone et al., Front Neurol 2025

Three forces are reshaping what is now possible.

AI-Augmented RWD

✓ Aggregates fragmented data across non-interoperable EMRs, claims, genomics, and imaging. 75% of pharma firms now integrate AI tools with RWD (2025).

Consider:

Cannot replace clinical context from specialists, families, and patients. Garbage in, garbage out data quality remains the foundational challenge.

Adaptive Registries & Digital Health

✓ Digital health technologies enable continuous longitudinal patient monitoring outside clinical sites. DHT adoption in rare disease trials nearly doubled from 2017–2020 to 2021–2024.

Consider:

Registries must evolve from PI-restricted data silos to open, interoperable platforms accessible to researchers, payers, and patient communities.

Outcomes-Based Contracts

✓ CMS Cell & Gene Therapy Access Model is now live covering 84% of Medicaid sickle cell disease beneficiaries through outcomes-based agreements as of early 2026.

Consider:

Frameworks for presymptomatic NBS-identified cohorts do not yet exist. Payers have no established methodology for valuing prevention of disease never manifested.

Payer-aligned evidence planning starts at Day 1, not at approval.

Evidence Element	Traditional Approach	Payer-Aligned Approach
Registry Design	Regulatory-submission focus; PI-restricted access	Open, interoperable; captures NBS cohorts from Day 1; PROs embedded from launch
Trial Endpoints	Biomarker / surrogate outcomes chosen for regulatory fit	HTA-relevant endpoints co-designed with HRU, QoL, and long-term function measures
Natural History	Symptomatic population; historical controls	Pre-symptomatic arms; NBS-identified cohorts; family-reported observations
Evidence Dissemination	Periodic industry publications; restricted to academic channels	Independent governance; payer-accessible dashboards; real-time registry insights
PRO / Family Data	Optional; collected inconsistently	First-class RWE; systematically collected, validated, and submitted

The shift is not just methodological, it is organizational. Evidence strategy must be a shared function from Phase II onwards.

THE PATH FORWARD

Every stakeholder in this room has a role.

Industry

Integrate payer-aligned endpoints and PRO collection from the first day of late-stage development planning. Make registries open, independently governed, and NBS-ready.

Researchers

Co-design natural history studies that capture presymptomatic NBS cohorts. Validate patient-reported outcome measures as primary endpoints, not secondary add-ons.

Payers & HTA

Develop coverage frameworks for presymptomatic patients and one-time interventions. Outcomes-based models are the right direction and implementation needs to accelerate.

Patient Advocates

Hold all of us accountable. Demand that evidence programs include family-reported data. Require transparent, independent governance of the evidence we generate together.

" The evidence that gets a rare disease therapy approved and the evidence that gets patients access are not the same thing - closing that gap is our most important unfinished job. "

CMMI Models for CGTs

Margarita Valdez Martínez, Chief Advocacy Officer,
American Society of Gene & Cell Therapy
April 15, 2026

American Society of Gene + Cell Therapy

Background

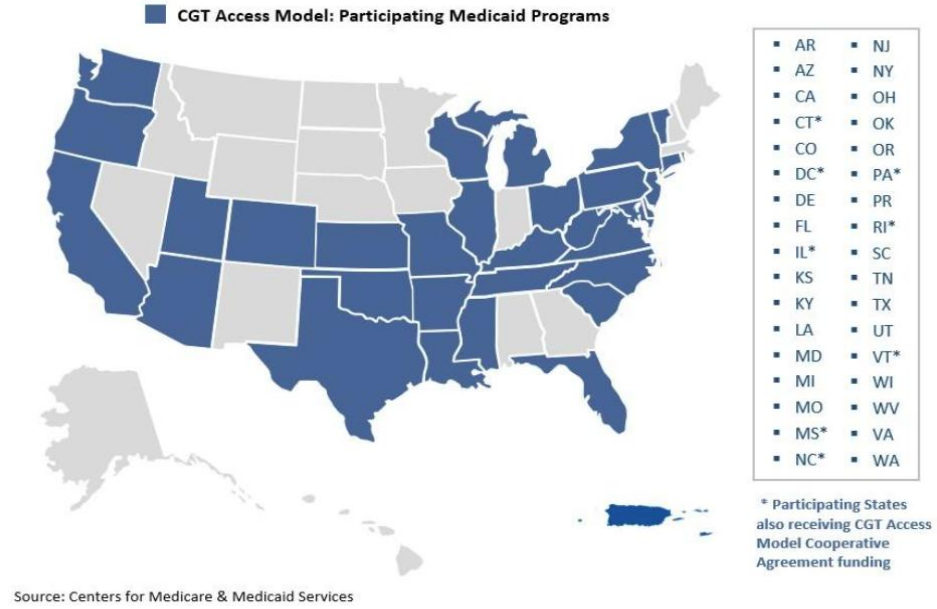
- The Center for Medicare and Medicaid Innovation (CMMI) was established by Congress in 2010.
- CMMI develops new payment, and service delivery models.
- The purpose is to lower spending for Medicare, Medicaid, and CHIP while simultaneously:
  - ✓ Improving patient care
  - ✓ Lowering costs
  - ✓ Aligning patient systems to promote patient-centered practices
- CGT (Cell and Gene Therapy Access) Model announced February 14, 2023.
- Two gene therapies for SCD approved on December 8, 2023, by FDA.

- Initial focus of the model on access to gene therapy treatments for people living with SCD.
- Multi-year, voluntary model for states and manufacturers.
- Some Medicaid programs opted to only offer one of the available therapies.
- “Rolling start” in January 2025; states could choose to begin participation at a time of their choosing between January 2025 and January 2026.
- Performance period is anticipated to conclude December 31, 2035, unless terminated earlier.

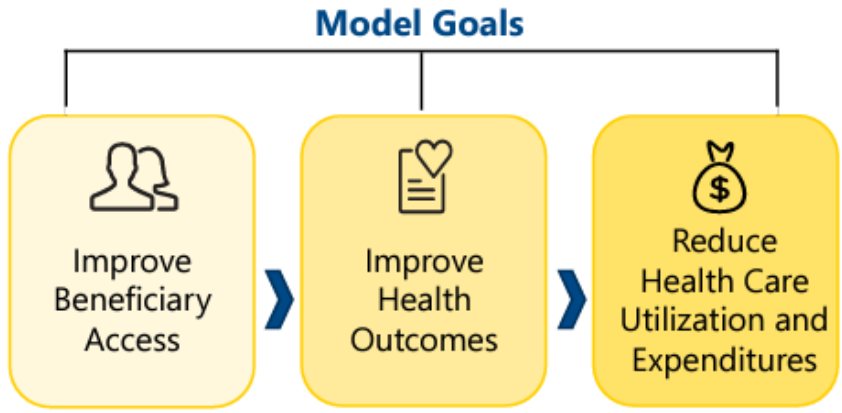
Cell and Gene Therapy Access Model

CMMI Demonstration Model

The CGT Access Model has released the list of participating states – 34 + Washington DC and Puerto Rico. This initiative empowers the Centers for Medicare and Medicaid Services (CMS) to negotiate outcomes-based agreements (OBAs) with manufacturers, with a focus on CGT treatments for sickle cell disease.



Source: Centers for Medicare & Medicaid Services



COST

Lower the cost of CGTs and enable more people with Medicaid to access potentially transformative treatment.

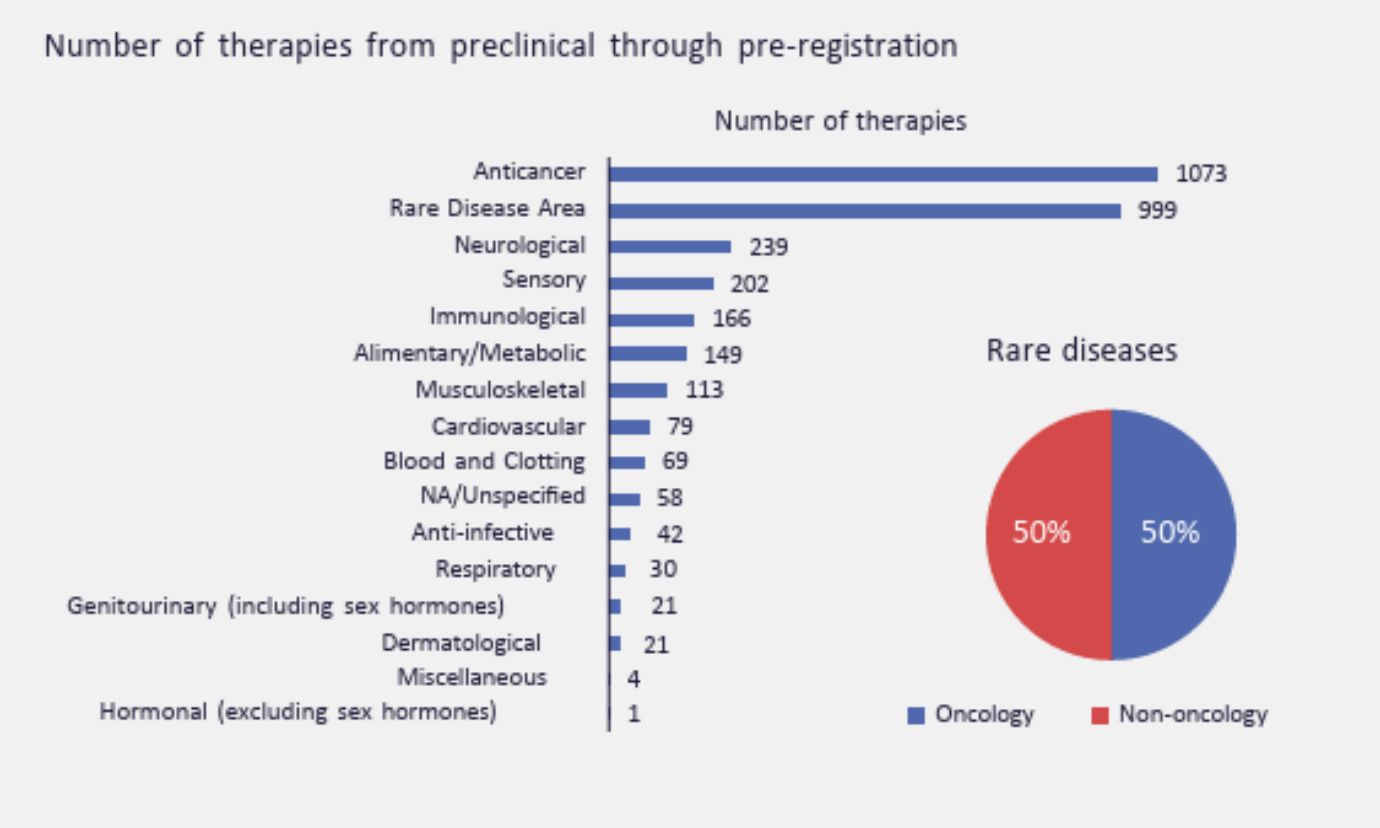
HEALTH DISPARITIES

Increase access to potentially transformative therapies for all individuals with SCD, including groups who have experienced historic disparities associated with this disease.

ACCESS BARRIERS

Offer states funding for activities that reduce access barriers for people with Medicaid. Require manufacturers to cover certain fertility preservation services, because the care journey for SCD CGT typically results in infertility. Lack of access to fertility preservation services presents a significant access barrier to individuals considering CGT.

Gene therapy pipeline: most commonly targeted therapeutic areas



https://www.asgct.org/news-publications/landscape-report

- ✓ Oncology and rare diseases remained the top areas of gene therapy development in both the overall pipeline (preclinical to pre-registration) and in the clinic (Phase I to pre-registration).
- ✓ Development for rare diseases was split equally between oncology and non-oncology rare diseases, with oncology representing two percentage points lower than the previous quarter.

American Society of Gene + Cell Therapy

The Cell and Gene Therapy Access Model — A Vision for Future Development

Authors: Abe Sutton, J.D., Corinne Alberts, M.P.P., Andrew Xuan, M.P.H. , Nicholas Minter, M.P.P., and Abigale Sanft, M.A. Author Info & Affiliations

Published March 7, 2026 | N Engl J Med 2026;394:1046-1048 | DOI: 10.1056/NEJMp2513320 | VOL. 394 NO. 11

- ✓ CMS intends to expand the model to new indications.
- ✓ These expansions will not include treatments for rare diseases with small populations.
- ✓ CMS is interested in improving reimbursement and billing for treatment centers to improve uptake.
- ✓ CMS intends to explore broadening the model to include Medicare patients.
- ✓ CMS intends to explore alternative financing mechanisms, including pay-over-time arrangements and subscription-based models.

- ✓ CMS is interested in supporting competition in the marketplace for cell and gene therapies.
- ✓ The new model may cover existing therapies or therapies in the pipeline.
- ✓ The model may not include an opportunity for cooperative agreement funding due to low uptake for the CGT access model.
- ✓ CMS is interested in supporting competition in the marketplace for cell and gene therapies.
- ✓ New model may be announced summer 2026.

American Society of Gene + Cell Therapy

ASGCT Open Access Publications

Providing timely updates

The Patient Press Newsletter – *Bimonthly*
Resources, events, rare disease news relevant for the patient community

The Advocate Newsletter – *Monthly*
ASGCT's actions to advance CGTs and related policy news

Gene, Cell, & RNA Therapy Landscape Report
Quarterly with ASGCT + Citeline
Field-wide report covering the therapeutics pipeline, clinical targets, and industry trends

Family of Journals

Open access journals with the latest scientific findings:

- ✓ Molecular Therapy
- ✓ Nucleic Acids
- ✓ Molecular Therapy Oncology
- ✓ Methods & Clinical Development

https://www.asgct.org/

American Society of Gene + Cell Therapy

CHANGE BEFORE CHANGE™

We are a woman and minority owned business.
We support human rights and cherish diversity.

Evidence Generation for Access in Rare Diseases

Aligning Value and Affordability

Danny Yeh, PhD, VP, Rare Disease, AESARA

April 15, 2026

10th AESARA

© 2026 AESARA Inc. All rights reserved.
CONFIDENTIAL AND PROPRIETARY
DO NOT DISTRIBUTE

DISCLAIMER:
The information contained in this presentation and any attachments is for general informational purposes only and does not constitute legal, financial, or professional advice. Some content may have been created with AI assistance; however, all content has been reviewed and approved by AESARA. AESARA disclaims all liability for any direct, indirect, incidental, or consequential damages arising from or related to the use of this presentation.

Image was generated by AI and refined by AESARA iDX

What Do Payers Do?

- Manage a **fixed budget across many diseases**
- Make tradeoffs across **existing and new treatments**
- Focus on **population-level impact**, not individual patients

Regulators ask: *Is the new treatment safe and efficacious?*

Payers ask: *Is the new treatment worth it and can we afford it?*

© 2026 AESARA Inc. All rights reserved.
CONFIDENTIAL AND PROPRIETARY
DO NOT DISTRIBUTE

Two Questions Drive Decisions — Evidence Must Answer Both

Value
Is it worth it?

- Meaningful patient benefit
- Magnitude and durability of effect

Evidence of Value

- Clinically meaningful outcomes
- Patient-relevant benefits
- Durability of effect
- Comparative effectiveness

Affordability
Can we afford it?

- Number of eligible patients
- Total budget impact

Evidence of Affordability

- Size of eligible population
- Treatment uptake and duration
- Healthcare resource use
- Budget impact over time

Payers need evidence that clearly demonstrates both **value** and **affordability**.

© 2026 AESARA Inc. All rights reserved.
CONFIDENTIAL AND PROPRIETARY
DO NOT DISTRIBUTE

First Treatment – Defining the Standard

Build the Value Story

- Natural history and disease burden
- Consequences of no treatment
- Endpoints that reflect real patient benefit

Build the Affordability Story

- Define the treatable population
- Epidemiology to quantify scale
- Early view for budget impact

You define what “**value**” means and what “**affordable**” looks like.

© 2026 AESARA Inc. All rights reserved.
CONFIDENTIAL AND PROPRIETARY
DO NOT DISTRIBUTE

Not First: Prove Incremental Value

Incremental Value

- What is better than existing options?
- Is benefit more meaningful or durable?
- Does it address remaining unmet need?

Affordability Impact

- Incremental budget impact
- Changes in treated population
- Reducing uncertainty over time

Better outcomes alone are not enough. **Affordability** must also improve or be justified.

© 2026 AESARA Inc. All rights reserved.
CONFIDENTIAL AND PROPRIETARY
DO NOT DISTRIBUTE

Closing Evidence Gaps Beyond Trials

What is already working

NORD → advancing patient registries to build natural history evidence

FDA → promoting Voice of the Patient to capture disease impact

Where the biggest gaps remain

1. Translating trial benefit into real-world value

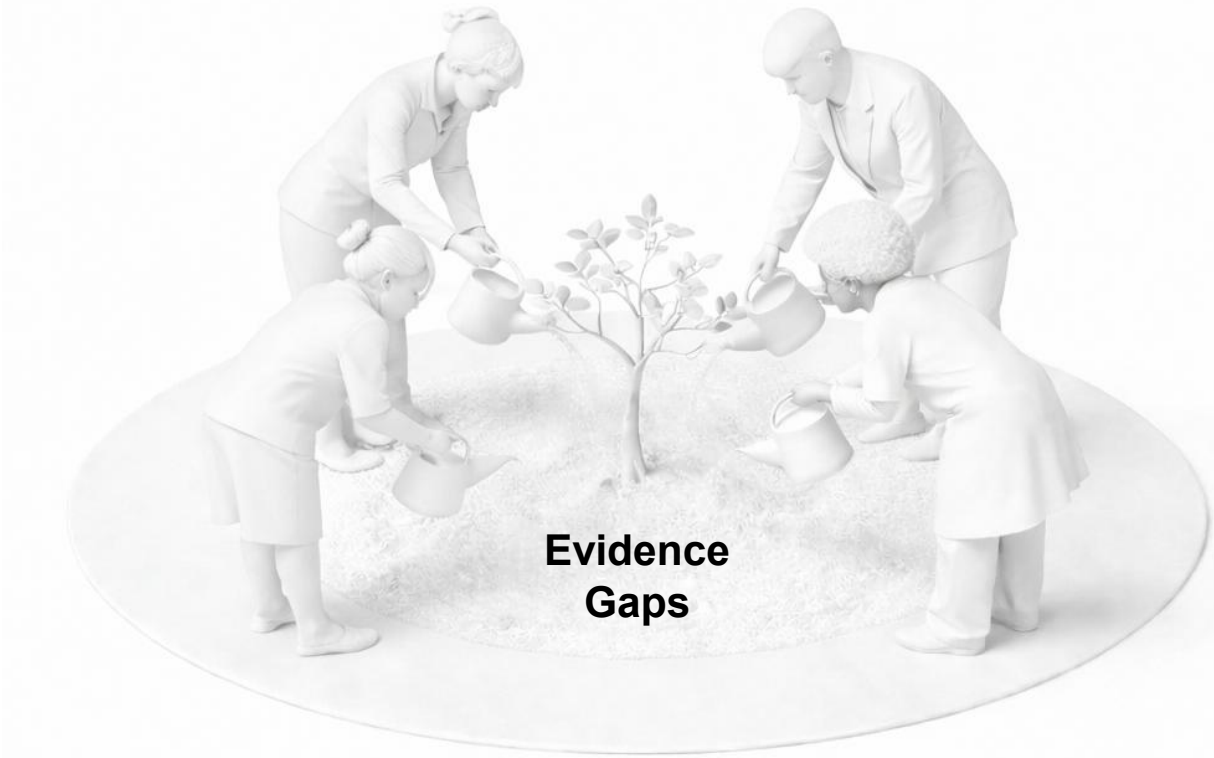
- What do trial results mean over the long term?
- How durable is benefit in real life?
- Payers must make decisions under long-term uncertainty

2. Certainty in addressable patient population

- Lack of reliable incidence and prevalence
- Many rare diseases lack accurate or consistent coding
- High uncertainty in budget impact

Patients & Advocacy (NORD)
Define meaningful outcomes

Sponsors
Generate & invest in evidence



Payers
Signal evidence needs early

Researchers & Clinicians
Design & validate studies

© 2026 AESARA Inc. All rights reserved.
CONFIDENTIAL AND PROPRIETARY
DO NOT DISTRIBUTE