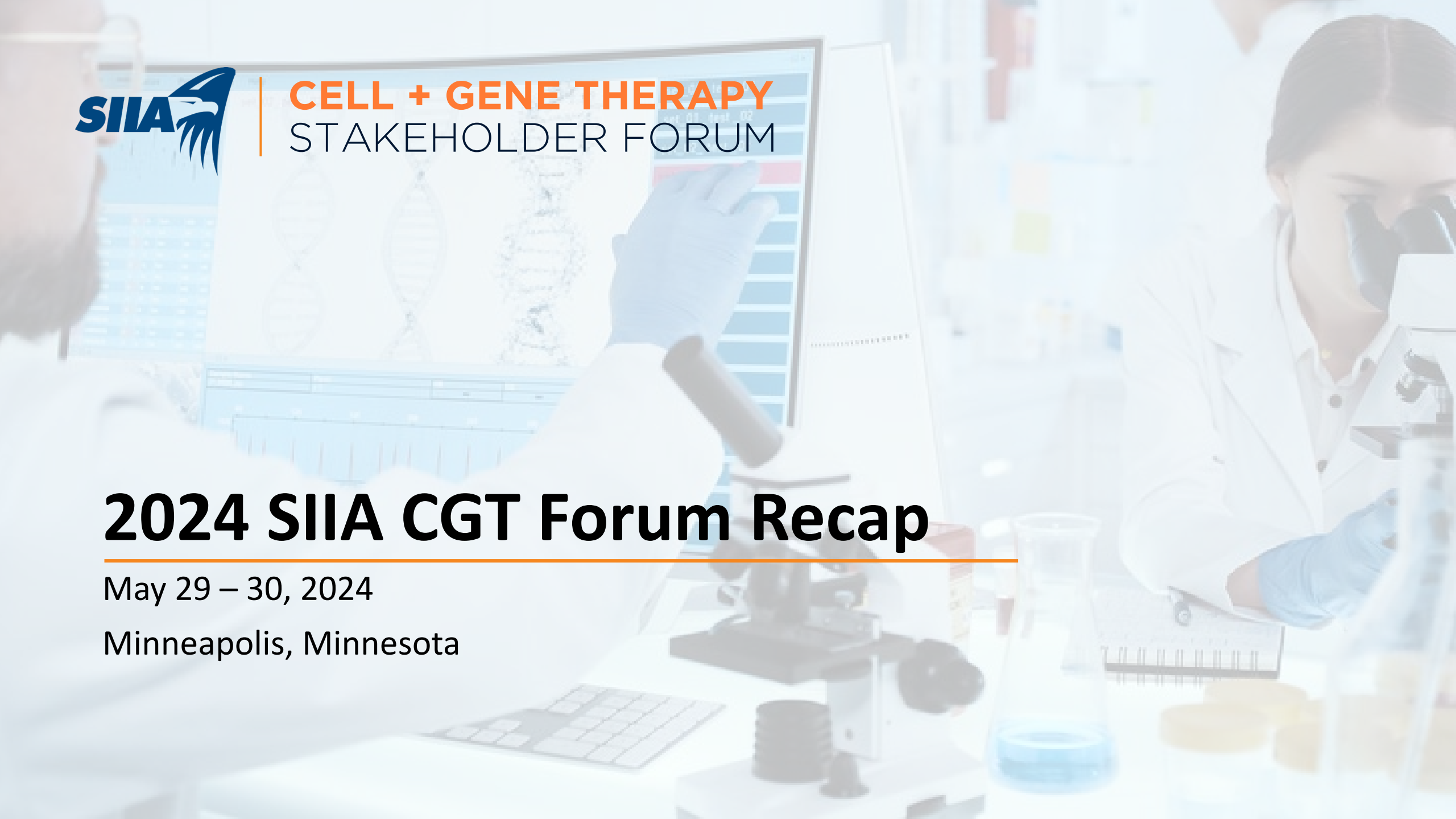


CELL + GENE THERAPY
STAKEHOLDER FORUM

2024 SIIA CGT Forum Recap

May 29 – 30, 2024

Minneapolis, Minnesota

2024 SIIA Cell & Gene Therapy Forum Topics

1. Welcome & SIIA Cell & Gene Therapy Task Force Update
2. Approval Pathways and Effects on Coverage
3. The Manufacturer's Perspective
4. Marketplace Solutions for Self-Insured Payers – What's Working?
5. One Patient's Story with Cell & Gene Therapy Treatment
6. CGT & Financial Risk Transfer Considerations
7. Provider Experience
8. Share, Ask & Answer

Welcome & SIIA Cell & Gene Therapy Task Force Update

Shaun Peterson, VP Head of Worksite Solution Pricing & Stop Loss Product, Voya Financial, and Chairperson, SIIA Cell + Gene Therapy Task Force

Key Takeaways

SIIA established a new Cell & Gene Therapy Task Force in early 2024 to identify potential opportunities to assist association members.

- Input was collected and resulted in potential workstreams in four key areas:
  - Performance guarantees
  - Pipeline & forecasting
  - Best practices
  - Education & resources

Welcome & SIIA Cell & Gene Therapy Task Force Update

Shaun Peterson, VP Head of Worksite Solution Pricing & Stop Loss Product, Voya Financial, and Chairperson, SIIA Cell + Gene Therapy Task Force

Key Takeaways

US cell & gene therapy market updates since the previous 2023 conference:

- Catastrophic claims are growing at rate far faster than overall medical claims and claims in excess of $1M are growing even faster as a percent of catastrophic claims.
- Fortune 100 Employers say medical spend / medical coverage is significant worry to solve.
- Key drivers are gene therapies, GLP-1's, and provider recovery challenges such as staffing.
- Focus for this discussion is on cell & gene therapies ranging from $300,000 to over $4M.
- Catastrophic claims are growing, coming close to 3% of catastrophic claims being in excess of $1 billion (from 1% in 2012), and continuing to grow.
- Expectation that downstream should have offset when eliminate accumulated long-term costs.
- PMPM values are also increasing, from about $2 PMPM in 2012 to ~$10 in 2022. The growing number of therapies in the pipeline means more therapies to increase these values even more.

US FDA Approved Therapies with Condition, Date & Cost*

Therapy Brand Name	Condition(s)	Approval Date	Therapy List Cost†
Cell Therapies – *Chimeric antigen receptor (CAR) T-cell*			
Kymriah®	Acute lymphoblastic leukemia	August 2017	$581,895
Yescarta®	Diffuse large B-cell lymphoma, follicular lymphoma	October 2017	$462,000
Kymriah®	Diffuse large B-cell lymphoma	May 2018	$456,941
Tecartus®	Mantle cell lymphoma	July 2020	$462,000
Breyanzi®	Diffuse large B-cell lymphoma, follicular lymphoma	February 2021; May 2024	$487,477
Tecartus®	Acute lymphoblastic leukemia	October 2021	$462,000
Kymriah®	Follicular lymphoma	May 2022	$456,941
Breyanzi®	Chronic lymphocytic leukemia or small lymphocytic lymphoma	March 2024	$487,477
Abecma®	Multiple myeloma	March 2021; April 2024	$498,408
Carvykti™	Multiple myeloma	February 2022; April 2024	$522,055
Breyanzi®	Mantle cell lymphoma	May 2024	$487,477
Cell Therapies – *Tumor-infiltrating lymphocytes (TIL)*			
Amtagvi™	Metastatic melanoma	February 2024	$515,000
Cell Therapies – *Other*			
Rethymic®	Congenital athymia	October 2021	$2,729,500
Omisirge®	Hematologic malignancies (Blood cancers)	April 2023	$338,000
Lantidra®	Diabetes Type 1	June 2023	Not available

Therapy Brand Name	Condition(s)	Approval Date	Therapy List Cost†
Gene Therapies (*in vivo*)			
Luxturna®	Biallelic *RPE65* mutation associated retinal dystrophy	December 2017	$456,875 per eye ($913,750 both eyes)
Zolgensma®	Spinal muscular atrophy	May 2019	$2,322,044
Hemgenix®	Hemophilia B	November 2022	$3,500,000
Adstiladrin®	Bladder cancer	December 2022	$60,000 per instillation
Elevidys®	Duchenne muscular dystrophy	June 2023; June 2024	$3,200,000
Roctavian®	Hemophilia A	June 2023	$2,900,000
Beqvez™	Hemophilia B	April 2024	$3,500,000
Gene Therapies (*ex vivo*)			
Zynteglo®	Transfusion-dependent beta-thalassemia	August 2022	$2,800,000
Skysona®	Cerebral adrenoleukodystrophy	September 2022	$3,000,000
Casgevy™	Sickle cell disease	December 2023	$2,200,000
Lyfgenia™	Sickle cell disease	December 2023	$3,100,000
Casgevy™	Transfusion-dependent beta-thalassemia	January 2024	$2,200,000
Lenmeldy™	Metachromatic leukodystrophy	March 2024	$4,250,000
Gene Therapies – *Topical*			
Vyjuvek™	Dominant and recessive dystrophic epidermolysis bullosa	May 2023	$631,000** ($900,000 maximum†)

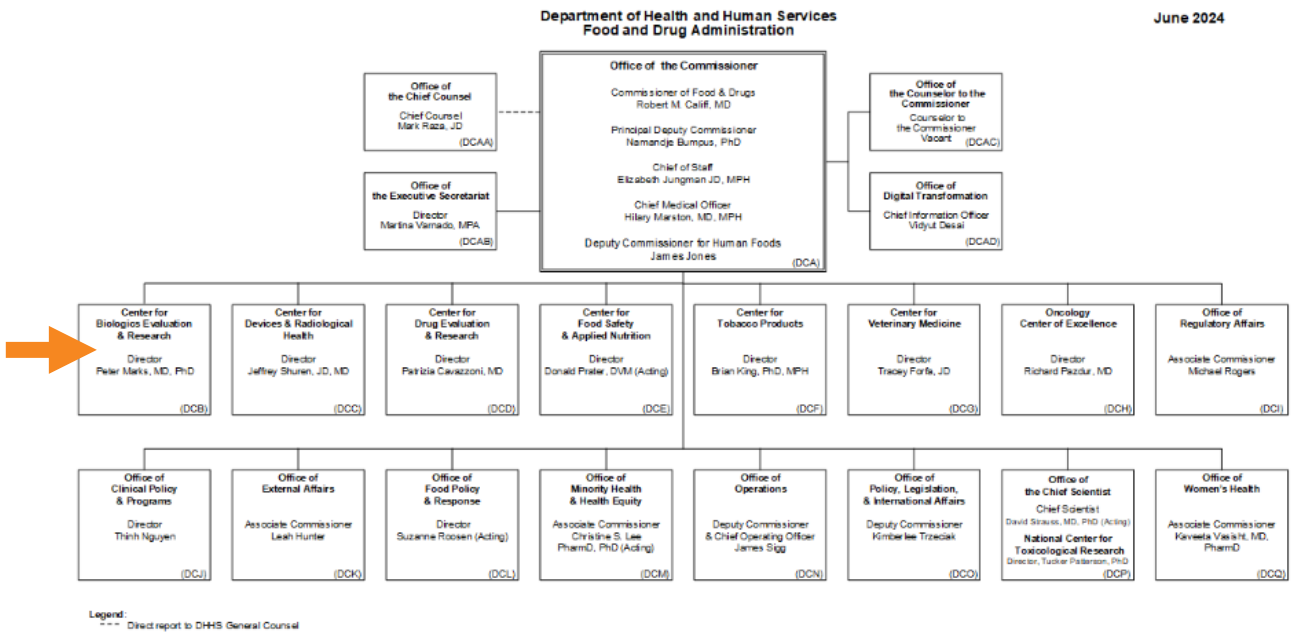
Please note that list cost for cell & gene therapies does not include any of the care needed to deliver the therapy, such as costs before and after delivery. Administration and associated hospitalizations can range from $300,000 to $800,000.

*US Food and Drug Administration (FDA) approved; Prices as of June 2024, and subject to change.**Expected average annual cost per patient after induction and based on per vial cost of $24,250 for 26 weeks; commercial members capped at $900,000 with manufacturer terms.

Approval Pathways and Effects on Coverage

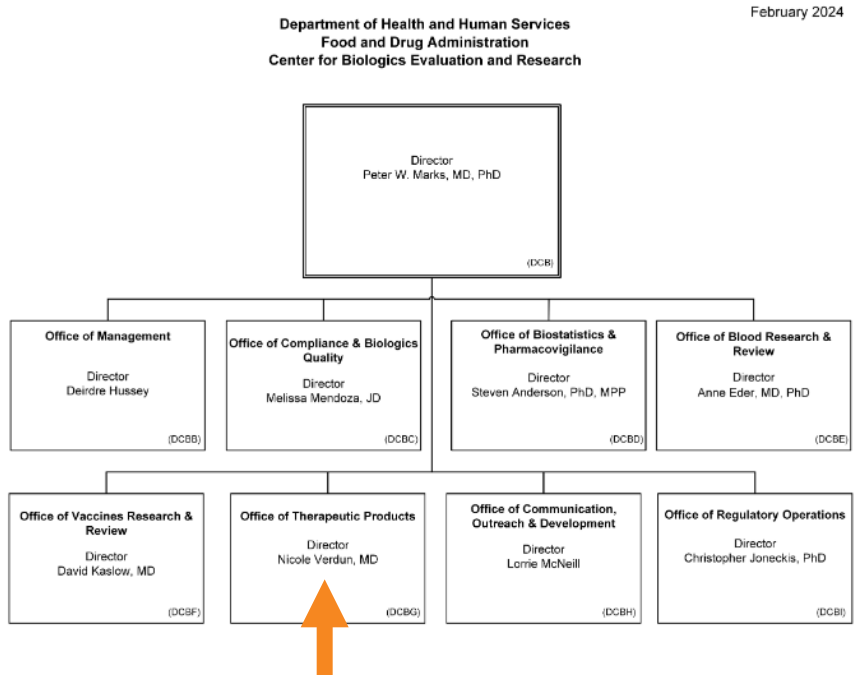
Rachael Anatol, Deputy Super Office Director, Office of Therapeutic Products, Food & Drug Administration

FDA Overview Organization Chart



https://www.fda.gov/about-fda/fda-organization-charts/fda-overview-organization-chart

Center for Biologics Evaluation and Research Organization Chart (CBER)



https://www.fda.gov/about-fda/fda-organization-charts/center-biologics-evaluation-and-research-organization-chart

Approval Pathways and Effects on Coverage

Rachael Anatol, Deputy Super Office Director, Office of Therapeutic Products, Food & Drug Administration

Key Takeaways

- Cell & gene therapies are the future of medicine, driven by hope for patients.
- Of 2600 active Investigational New Drug (IND) applications, most are for cell & gene; +300-500 meeting requests/year.
- The US Food & Drug Administration (FDA) has approved over 32 cell and gene therapy products, most for rare disorders (defined as less than 200,000 people).
- Rare disease Product Development is a CBER 2024 priority.
  - Around 80% of rare diseases have a genetic cause. (Centers for Disease Control, The landscape for rare diseases in 2024, June 14, 2024.)
- There are two Biologic License Application (BLA) approval pathways:
  - ***Traditional Approval*** requires a positive, clinically meaningful effect, which means that the product has a positive effect on how an individual feels, functions, or survives. Requires substantial evidence of effectiveness.
  - ***Accelerated Approval*** is based on an intermediate clinical endpoint, or surrogate endpoint, that is reasonably likely to predict a positive effect on how an individual will feel, function, survive, and it still requires confirmatory evidence of positive effect. Requires substantial evidence of effectiveness.
- With the increasing number of approved treatments, self-insured employers must now make more cell and gene therapy coverage decisions at a faster pace.

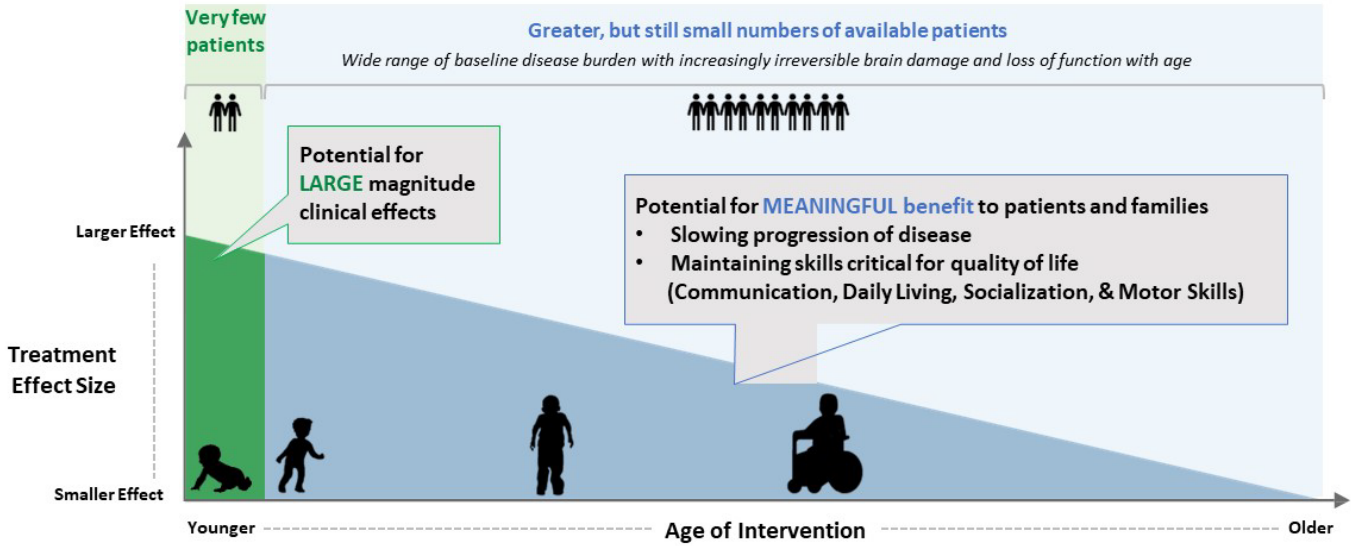
https://doi.org/10.1016/S2214-109X(24)00056-1

Approval Pathways and Effects on Coverage

Rachael Anatol, Deputy Super Office Director, Office of Therapeutic Products, Food & Drug Administration

Why Accelerated Approval?

- Time – the earlier treatment done, more meaningful the effect
- Patient need
- Both require FDA to determine a substantial evidence of effectiveness.
- Speed allows FDA to "approve drugs sooner than possible for diseases in which it can take extended time to determine impact on how an individual feels, functions, or survives"
- Flexibility (controls, efficacy, use of end point)



Source: Dr. Cara O'Neill, Reagan-Udall Foundation Meeting, Qualifying Biomarkers to Support Rare Disease Regulatory Pathways https://reaganudall.org/sites/default/files/2024-02/Biomarkers%20Website%20PDF.pdf

The Manufacturer's Perspective

Mark Trusheim, Strategic Director, NEWDIGS, Center for Biomedical System Design, Tufts Medical Center
Jay Newman, SVP & Head of Commercial Development, Pricing & Reimbursement, Spark Therapeutics, Inc.
LeeAnna Hoskins, VP Payer Access & Reimbursement, Sarepta Therapeutics
Susan Serrano, Senior Director, Contracting and Payer Marketing, bluebird bio

Key Takeaways

- The manufacturer session focused on discussions related to gene therapies and their impact on patients, healthcare systems, and pricing strategies.
- Panelists delved into key topics such as the approval process, monitoring patient outcomes, interfacing between FDA and CMS, rare diseases transitioning to more common conditions, and the challenges of financing expensive treatments.
- Noteworthy points included detailed descriptions of Duchenne muscular dystrophy progression, the urgency felt by organizations like Sarepta in addressing patient needs promptly, innovative gene therapy treatments like Luxturna improving functional vision significantly with real-world examples shown through videos.
- Pricing models were also a significant focus with discussions on eliminating markups for costly drugs and implementing value-based payment structures for better access.
- With cell & gene, a challenge is the huge upfront cost, like a mortgage – like buying a condominium instead of paying rent on an apartment.
- Outcomes-based agreements are not for every customer or for every product, and really need to be tailored to the unique needs of both the disease/product as well as the customer.
- Questions were related to payment models, buy and bill alternatives, Medicaid access model, durability, collaboration potential with qualified treatment centers on rates or rebates, logistics and timing, understanding of risk and how this is handled in industry, potential to reduce US pricing, potential for cost limitations, transparency of pricing, quality of care and experience. The panel also addressed pricing implications, value-based payments, warrantees, and patient access considerations.

TuftsMedicine
Tufts Medical Center

CGTs: Where We've Been, Are, and Going

SIAA Cell and Gene Therapy Stakeholder Forum
May 2024

Mark Trusheim
Mark.trusheim@TuftsMedicine.org

NEWDIGS

NEWDIGS – Helping the System Catch Up With the Science

Drive more value faster to patients, in ways that work for all stakeholders

- Safe haven **"think & do" tank**
- Track record of **real-world impact**
- Interactive methods/tools for **multi-stakeholder design**
- Bold, transformational system innovations **for 14 years**
- Founded at MIT, joined Tufts Medical Center in July 2022

NEWDIGS "Adaptive Licensing" Project fueled timely action & impact in Europe from regulatory science innovation…..

STATE OF THE ART — nature publishing group *Open*

See COMMENTARY page 378

Adaptive Licensing: Taking the Next Step in the Evolution of Drug Approval

H-G Eichler[1,2], K Oye[2,3,4], LG Baird[2], E Abadie[5], J Brown[6], CL Drum[2], J Ferguson[7], S Garner[8,9], P Honig[10], M Hukkelhoven[11], JCW Lim[12], R Lim[13], MM Lumpkin[14], G Neil[15], B O'Rourke[16], E Pezalla[17], D Shoda[18], V Seyfert-Margolis[14], EV Sigal[19], J Sobotka[20], D Tan[12], TF Unger[18] and G Hirsch[2]

… and Illuminated a Broad Set of Principles for Accelerating Sustainable Patient-Centered Innovation

LEAPS

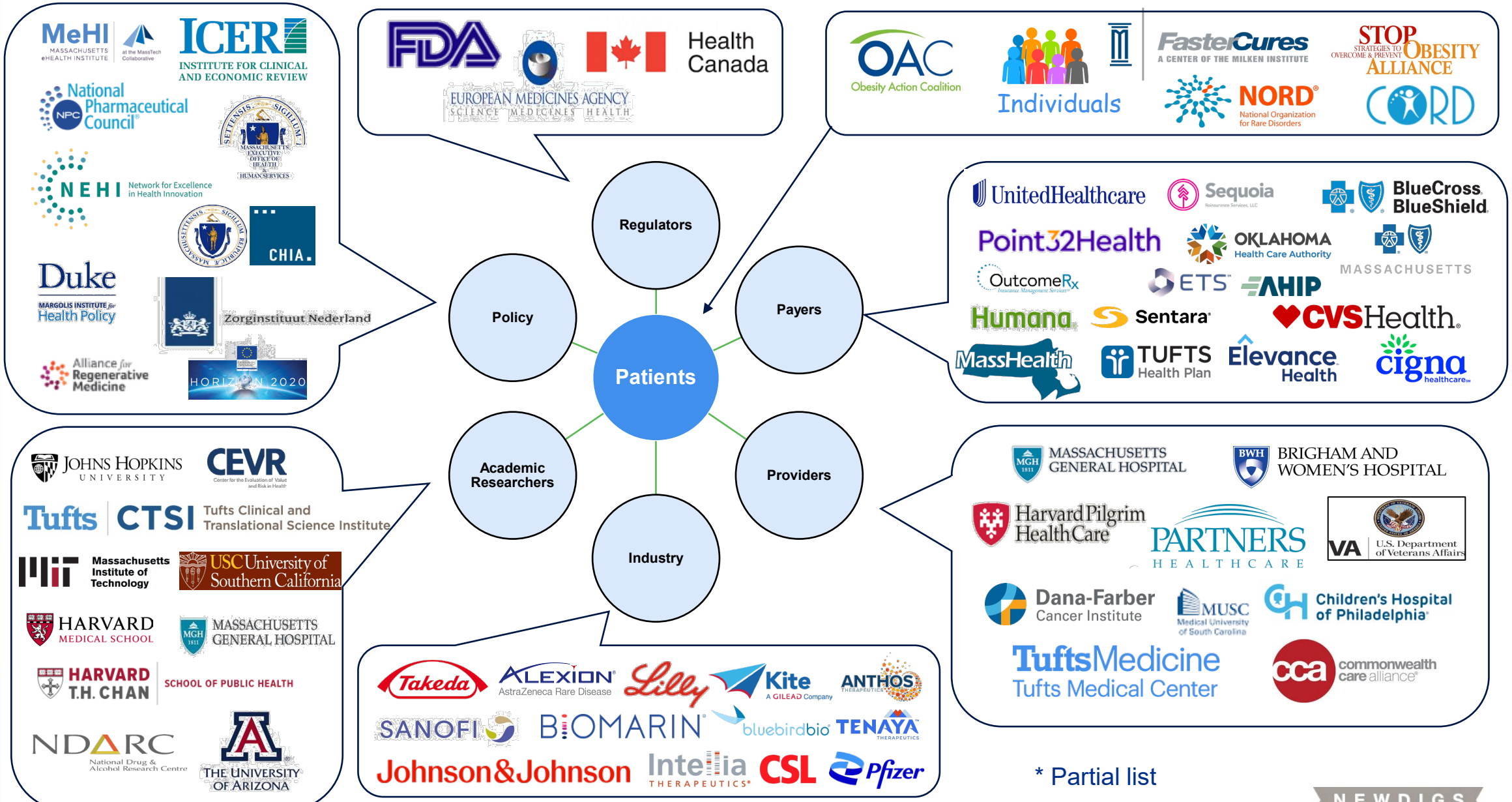
Learning Ecosystems Accelerator for Patient-centered, Sustainable innovation

FoCUS

Financing and Reimbursement of Cures in the US

Clinical Pharmacology & Therapeutics (2012); **91** 3, 426–437. doi:10.1038/clpt.2011.345

NEWDIGS Collaborators* are Designing the System



* Partial list

Where we were: Pre-Pandemic Near term treatments
(US, As of mid-2019)

4 Currently available

Oncology CAR-T therapies:

Kymriah®, Yescarta® Currently approved for acute lymphocytic leukemia (ALL) and diffuse large B-cell lymphoma (DLBCL)

Ultra-rare disease treatments

Luxturna®- for Retinitis pigmentosa & Leber's congenital amaurosis (both RPE65)

Zolgensma® - for Spinal muscular atrophy

Other possible treatments within 5 years

Hematological conditions

Hemophilia A & B

Sickle Cell anemia

β-thalassemia

Additional ophthalmological treatments

RP & LCA (other genetic mutations)

One or more other conditions possible

Neurological conditions – one or more

Higher prevalence disease treatments

Macular degeneration possible

Most Durable Gene Therapies Use Innovative Payment Models

Therapy Brand Name	Condition(s)	Therapy List Cost**	Payment Model
Oncology Cell Therapies			
Kymriah®	Acute lymphoblastic leukemia	$508,250	No invoice if poor 30 day response
Yescarta®	Diffuse large B-cell lymphoma, follicular lymphoma	$424,000	Milestone-based
Kymriah	Diffuse large B-cell lymphoma	$399,110	Traditional
Tecartus®	Mantle cell lymphoma	$424,000	Traditional
Breyanzi®	Diffuse large B-cell lymphoma, follicular lymphoma	$447,227	Traditional
Abecma®	Multiple myeloma	$457,255	Traditional
Tecartus®	Acute lymphoblastic leukemia	$424,000	Traditional
Carvytki™	Multiple myeloma	$465,000	Traditional
Kymriah	Follicular lymphoma	$399,110	Traditional

Therapy Brand Name	Condition(s)	Therapy List Cost**	Payment Model
Gene Therapies (*in vivo*)			
Luxturna®	Biallelic *RPE65* mutation associated retinal dystrophy	$425,000 per eye ($850,000 both eyes)	Milestone-based (90 day & 30 month)
Zolgensma®	Spinal muscular atrophy	$2,125,000	Milestone-based, Evolving
Hemgenix®	Hemophilia B	$3,500,000	Warranty
Elevidys®	Duchenne muscular dystrophy	$3,200,000	Traditional
Roctavian®	Hemophilia A	$2,900,000	Warranty / Milestone-Based
Gene Therapies (*ex vivo*)			
Zynteglo®	Transfusion-dependent beta-thalassemia	$2,800,000	Graduated 2 year
Skysona®	Cerebral adrenoleukodystrophy	$3,000,000	Traditional
Casgevy®	SCD & Beta Thal	$2,200,000	Details Not Disclosed
Lyfgenia®	Sickle cell disease	$3,100,000	Graduated 3 year
Lynmeldy®	Early-onset Metachromatic Leukodystrophy (MLD)	$4,250,000	VBC. Details Not Disclosed

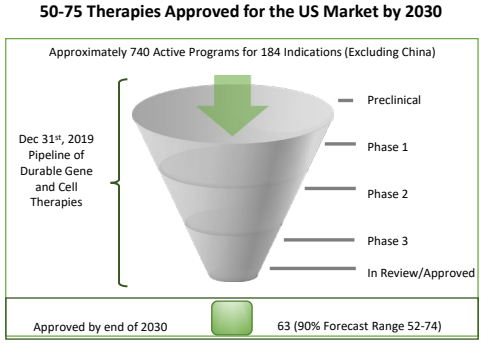
***US Food and Drug Administration (FDA) approved; Prices as of January 2024 and subject to change.**
****Please note that list cost for cell & gene therapies does not include any of the care needed to deliver the therapy, such as costs before and after delivery. Administration and associated hospitalizations can range from $300,000 to $800,000 based on ETS proprietary calculations.**

Paying-For-Cures Resources

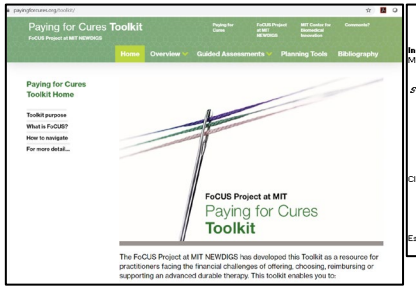
Go to https://newdigs.tuftsmedicalcenter.org/paying-for-cures/

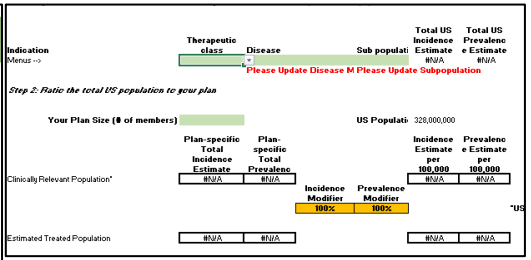
Research Briefs and Peer-Reviewed Publications

Unique Gene and Cell Therapy Pipeline Impact Modeling



On-line Toolkit to Educate and Support Practitioners Developing Financing Solutions





Public Speaking Engagements

Educational Events

Design Labs

Marketplace Solutions for Self-Insured Payers – What's Working?

Richard Fleder, CEO, ELMCRx Solutions (Moderator)
Ashley Hull, Executive Vice President, ParetoHealth
Brooks Wildasin, Co-Founder & Chief Underwriting Officer, OutcomeRx Insurance Management Services, LLC
Ramesh Jayasuriya, Head of Digital Health, Evio
Joe Sabol, Senior Vice President, DW Van Dyke

Key Takeaways

Like it has done when faced with past challenges, the self-insurance industry is adapting to evolving cell & gene therapy realities, with companies bringing new solutions to market and working to develop additional solutions for future introduction.

1. Employers (most) are excluding cell & gene therapy coverage, however, in the future, most employers will have to cover it.
   - With life-saving and life-changing therapy stories in the news, people are paying attention; believe we can expect to see more self-funded covering it, pushing risk down to stoploss carriers and secondary/reinsurance.
   - Excess risk is not being thought of enough; not enough tools to support advantages; not just look at the numbers but look at the adjustments and indications – over time, have moved up the funnel (used to worry about bottom, now at top).
2. Stoploss carriers (SLC) are protected for a bit longer but will not be able to treat as business as usual – such as reduction of lasers. When it comes, it will hit SLC – either point solutions or excess. Similarities with organ transplant.
3. Rebates shifting to outcomes-based rebate if outcomes achieved, require data capture; versus warranties, which are easier to administer, based on claims data. Some of complexity is around data collection, structure/administration of contracts, affordability, prior auth process, etc.
   - Care and navigation is critical to be there – even if pay the claim, patient experience is key.
4. Small / medium-sized companies are transitioning from structured (fully-insured) environment to self-insured.
   - GLP-1 (glucagon-like peptide 1) drugs: how are small/medium employers dealing with and will this take from CGT? Have claims data on these drugs, but not on gene therapies; reinsurers have tools to cover, whether cost effective is question.
   - Work with small to mid-size employers looking for a product like a carve-out for transplant, competitive, driven to stay with vendor, ability to move between SLCs.

One Patient's Story with Cell & Gene Therapy Treatment

Rae Blaylark, President & CEO, Sickle Cell Foundation of Minnesota
Erica Barnes, Executive Director, Minnesota Rare Disease Counsel

Key Takeaways

- With her extensive experience in healthcare systems and advocacy for sickle cell disease, Rae brings firsthand knowledge and passion to highlight the challenges faced by patients, particularly regarding racial disparities, biopsychosocial impacts, barriers to care, and the need for improved pain management.
    1. Impact of Racial Disparities
        - Racial disparities in healthcare affect care quality and outcomes for sickle cell patients, necessitating systemic changes for equitable treatment.
    2. Biopsychosocial Effects
        - Sickle cell disease causes chronic pain, psychological stress, and social challenges, requiring holistic care approaches.
    3. Barriers to Accessing Care
        - Patients face socioeconomic, trust-related, and geographic barriers to care, requiring solutions for improved access and outcomes.
    4. Addressing Pain Management
        - Patients, including those with sickle cell disease, face stigma as drug seekers, necessitating compassionate pain management reforms.
    5. Community Engagement in Gene Therapies
        - Early and proactive engagement is crucial, addressing awareness gaps and providing trusted information for informed decision-making.
- Her insights underscore the importance of community engagement and informed decision-making, especially concerning gene therapies and clinical trials in the context of sickle cell disease.

CGT & Financial Risk Transfer Considerations

Raj Gulati, Senior Vice President, Risk Strategies
Theresa Galizia, SVP & CUO, Berkley Accident and Health
Mike Remeika, President, Accident and Health Division, Skyward Specialty Insurance
***Crystal Kauder,* ASA, MAAA, Chief Pricing Actuary, US Health, PartnerRe America Insurance Company**
Thomas Brown, Senior Broker, Locke & Reed

- Industry Evolution and Adaptation: The reinsurance industry has undergone significant changes, especially with the advent of gene and cell therapies. Adapting to these changes has been crucial but challenging, due to the unpredictability in drug approvals and market uptake.
- Rise in Therapy Approvals: There has been a notable increase in the number of gene and cell therapy drug approvals since 2020, with expectations of continued growth. This surge has necessitated new approaches in pricing and risk management.
- Challenges in Predictive Modeling: The industry initially struggled with predictive models for these therapies, leading to adjustments in product offerings and client engagements over time. Stability in pricing and fewer major reactions to new therapies are now being observed.
- Impact on Reinsurance: Reinsurers are facing challenges such as high claim costs for therapies like gene and cell treatments. Strategies like drop-down deductibles and transparent pricing agreements are being explored to manage these costs effectively.
- Future Considerations: Key uncertainties remain around therapy uptake rates and pricing adequacy, particularly for therapies to treat conditions such as Duchenne muscular dystrophy and sickle cell disease. The industry is moving towards more transparency in pricing and leveraging AI to enhance risk assessment capabilities.

Provider Experience

Claire White, MSN, RN, Policy Analyst, Cellular Therapy & Transplant Section, Children's Hospital of Philadelphia
Stephan Grupp, MD, PhD, Medical Director, Cellular Therapy & Transplant Section Chief, Children's Hospital of Philadelphia
Amy Emmert, MScPH, Executive Director, External Affairs HSCT & Cellular Therapy Service Line, Dana-Farber/Brigham Cancer Center
Stephanie Farnia, Principal, Nimitt Consulting

Key Takeaways

As new therapies receive approval, physicians and facilities face several challenges that may affect patient access:

- Know what the drugs cost, need to get back all the money paid for the biologic, and don't want to mark it up just to get cost back.
- Incur significant new costs/investment for providing cell & gene therapies such as physical building changes, new data systems, training, addressing antiquated systems, etc.
- Know these are high-risk, multi-step, new therapies, sometimes time-sensitive, all of which can create perfect storm from financial standpoint.
- Post-marketing information data needs, following the patients in commercial setting, and need to determine who pays, where does data go.
- Need a financial clearance process to push these through quickly; may not be codes yet.
- Medical necessity and payer communications, administrative policies from payers and payment policy issues, plus regulatory obstacles.
- How to get 'yes' on paper when systems are not set up to agree is requiring new level of payer outreach and communications.
- Supporting patients appropriately with multi-disciplinary program approach with all teams involved through intake, onboarding and product choice, feasibility, patient risk, administration, etc.
- For outpatient, when possible, needing model for outpatient care – for high-capacity providers to create model to educate providers of in-home care; for inpatient, challenge to have enough beds, lodging, etc.

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Thank You