manatt

How Can Pharma Balance Gene Therapy's Promise and Price?

November 16, 2016

Speaker Bios

Jon Glaudemans
Managing Director

Sandy W. Robinson
Managing Director

Melinda J. Dutton
Partner

Attendee Polling Question - 1

Which of the following best describes the organization you represent?

A. Regulator/Policy Official/Staff

B. Life Sciences (Pharmaceutical, Biopharmaceutical, Device, etc.)

C. Payer/Health Insurer

D. Provider/Medical Center/Delivery System

E. Other (i.e., Healthcare services company, consultant, etc.)

Agenda

Introduction & Landscape

Patient Journey

Private Insurance Coverage & Payment

Medicaid Payment

Payment Models

Attendee Polling Question - 2

Which one of the following areas are you *most closely* tracking with respect to gene therapy products?

A. Basic science

B. Clinical trials and outcomes

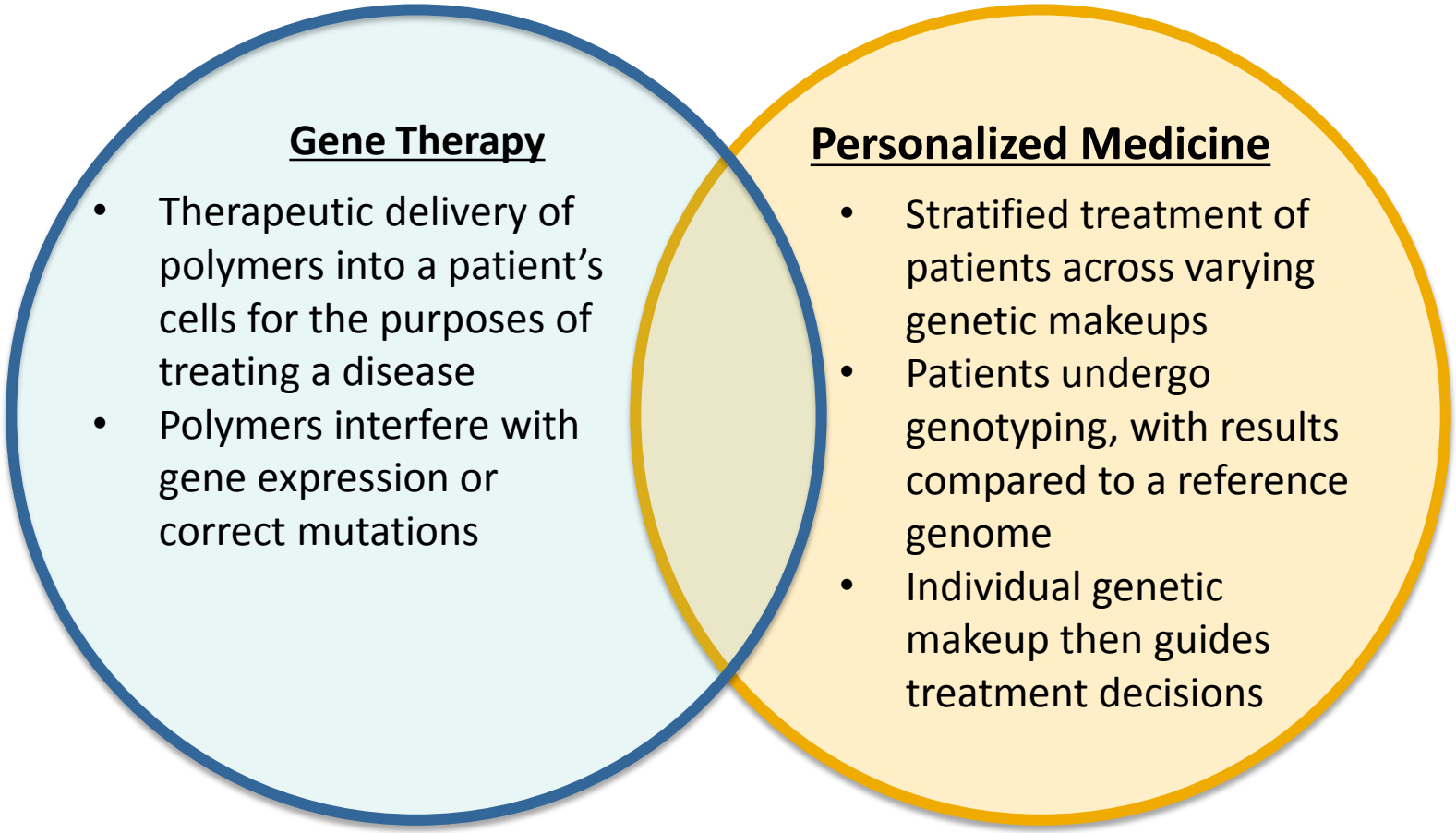
C. Patient impact

D. Legal and regulatory issues?

E. Reimbursement

Gene Therapy vs. Personalized Medicine

Gene therapy and personalized medicine are distinct areas of medicine, with today focused on gene therapy.

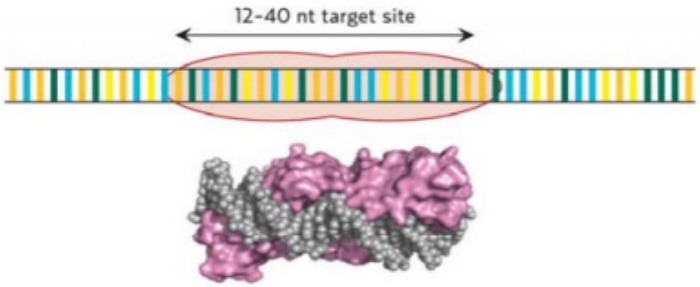


Gene-editing Technologies[1]

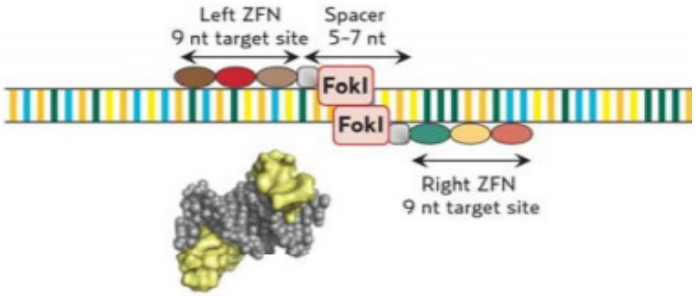
- **Meganucleases** and **Zinc-Finger Nucleases** were the first tools developed for nuclease-based genome editing
- These processes were both labor intensive and costly

First Generation

Meganucleases



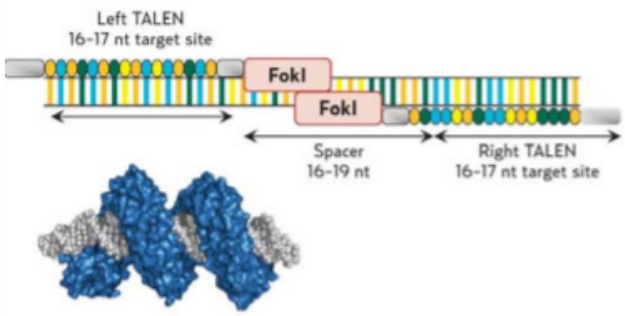
Zinc-Finger Nucleases



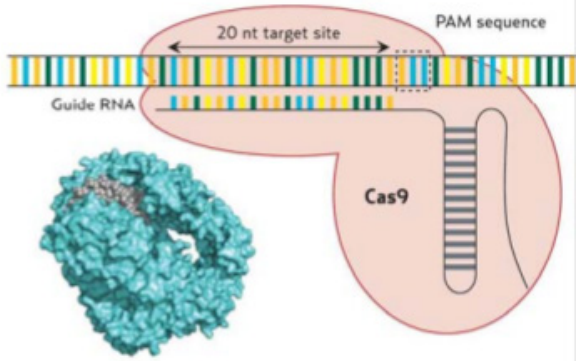
- **Transcription Activator-Like Effector (TALE) nucleases** and **Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) nucleases** are the latest innovations in the field of genome editing
- TALE and CRISPR are considerably easier to use and less costly

Second Generation

TALE



CRISPR



Uses of Gene Therapy

First generation gene therapy pipeline products tend to address rare genetic disorders and diseases.

Examples

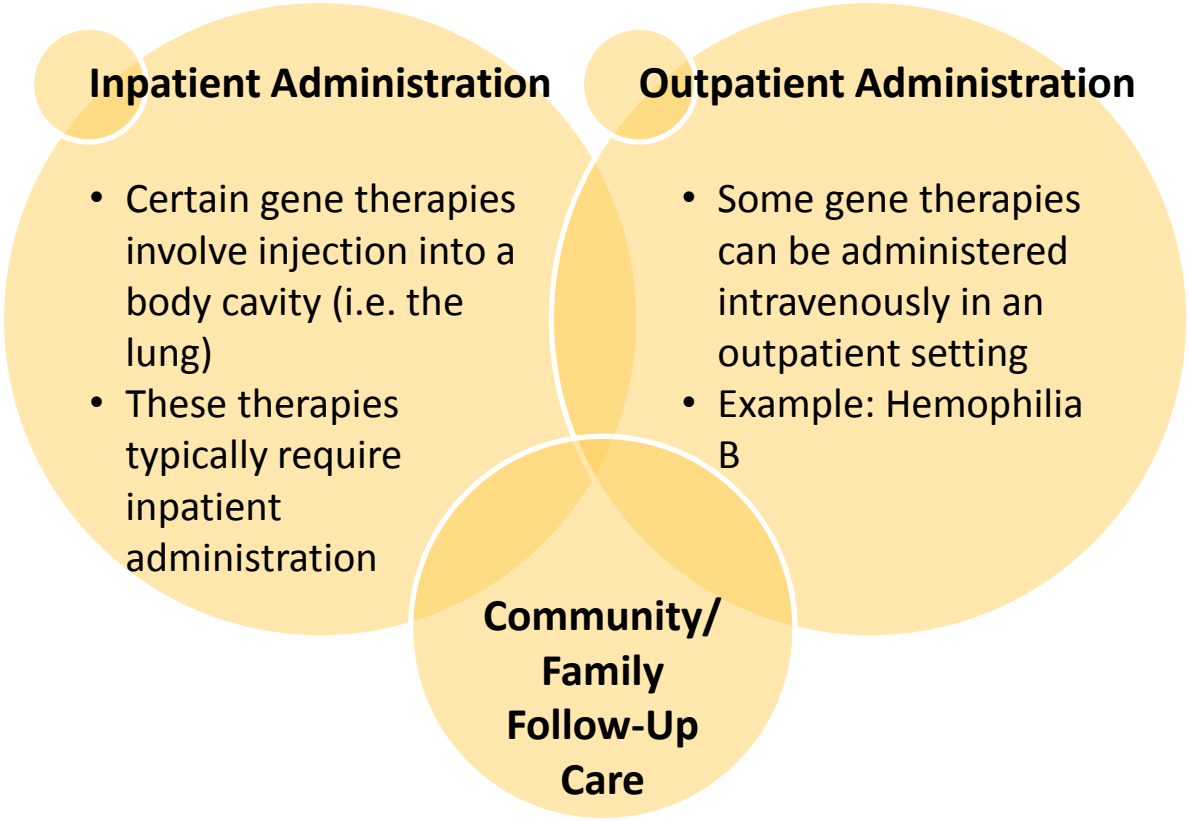
- Leber's congenital amaurosis[2]
- choroidemia[3]
- X-linked SCID[4]
- chronic lymphocytic leukemia[5]

Delivery System Implications

Gene therapy administration requires coordinated treatment across multiple sectors of the healthcare ecosystem[6,7]

Gene Therapy Laboratory

- Genetic material is packaged into a vector, which carries it into the nucleus of target cells
- Vectors can be administered into the affected tissue directly, into a surrogate tissue, or into the blood stream or intraperitoneal cavity
- The method of administration has implications for delivery systems



Considerable Complexity and Uncertainty for Innovators

Gene therapies implicate multiple settings of care, payers, and payment models, requiring new approaches to reimbursement.

Medicare

Medicaid

Commercial

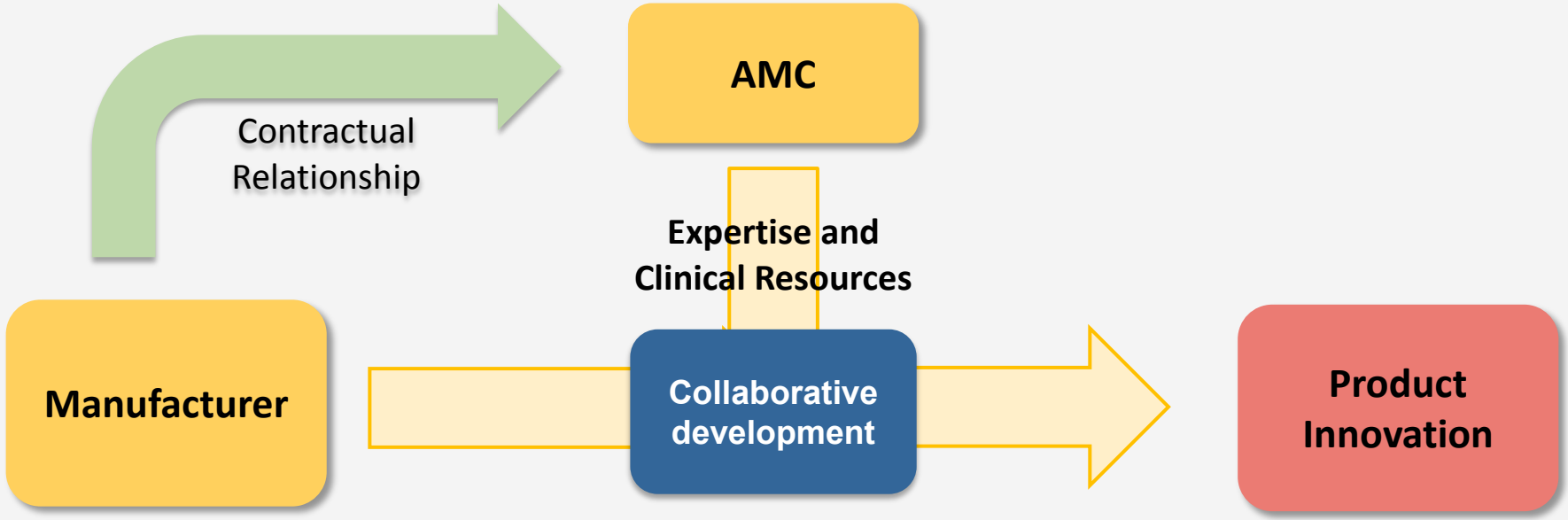
Fee For Service

Pay-for -Performance

Capitated Payments

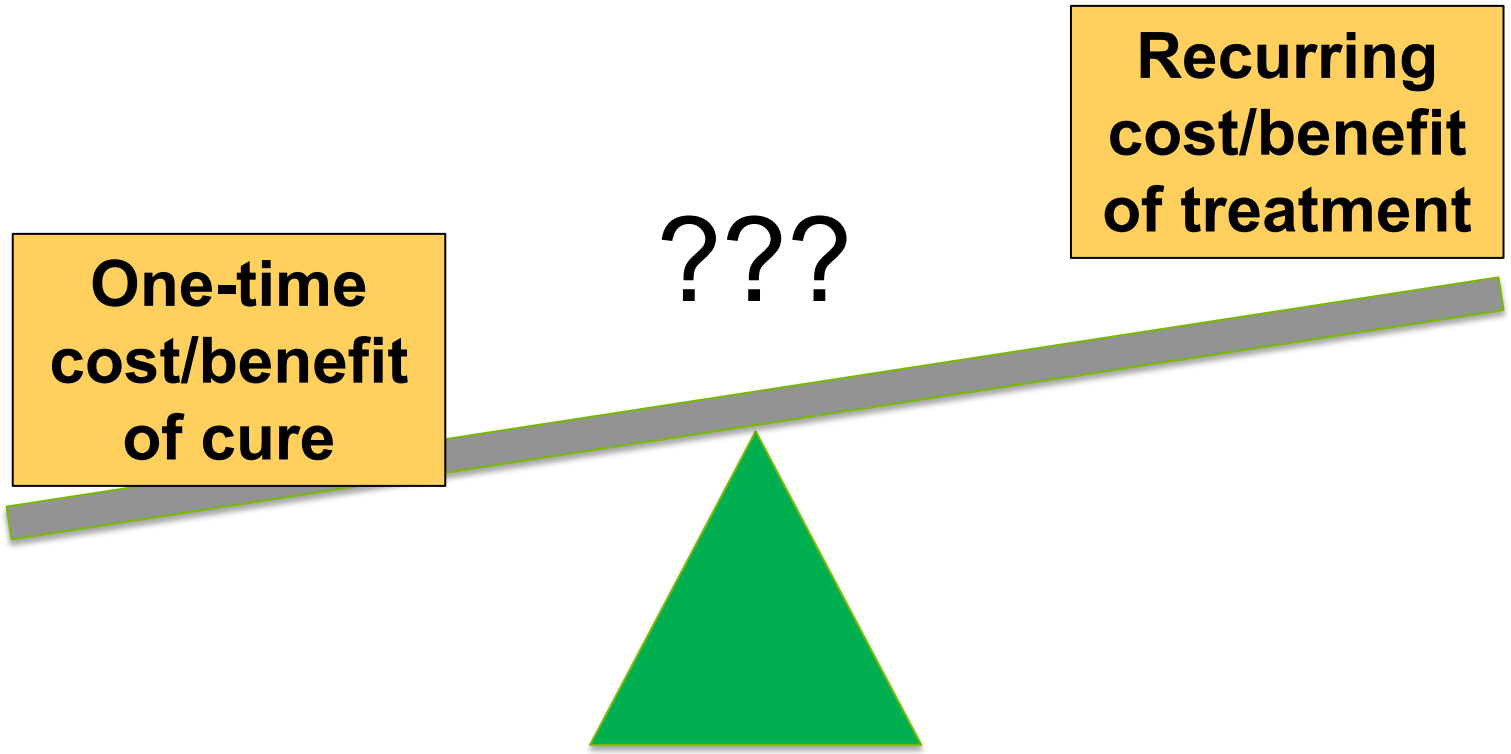
Emerging Partnership/Collaboration Opportunities

Innovative academic medical center partnerships are emerging, reflecting the hybrid nature of gene therapy science and delivery.[8]



Pricing Challenges

Gene therapies also face the challenge of pricing to value, given their curative potential and likely high cost.



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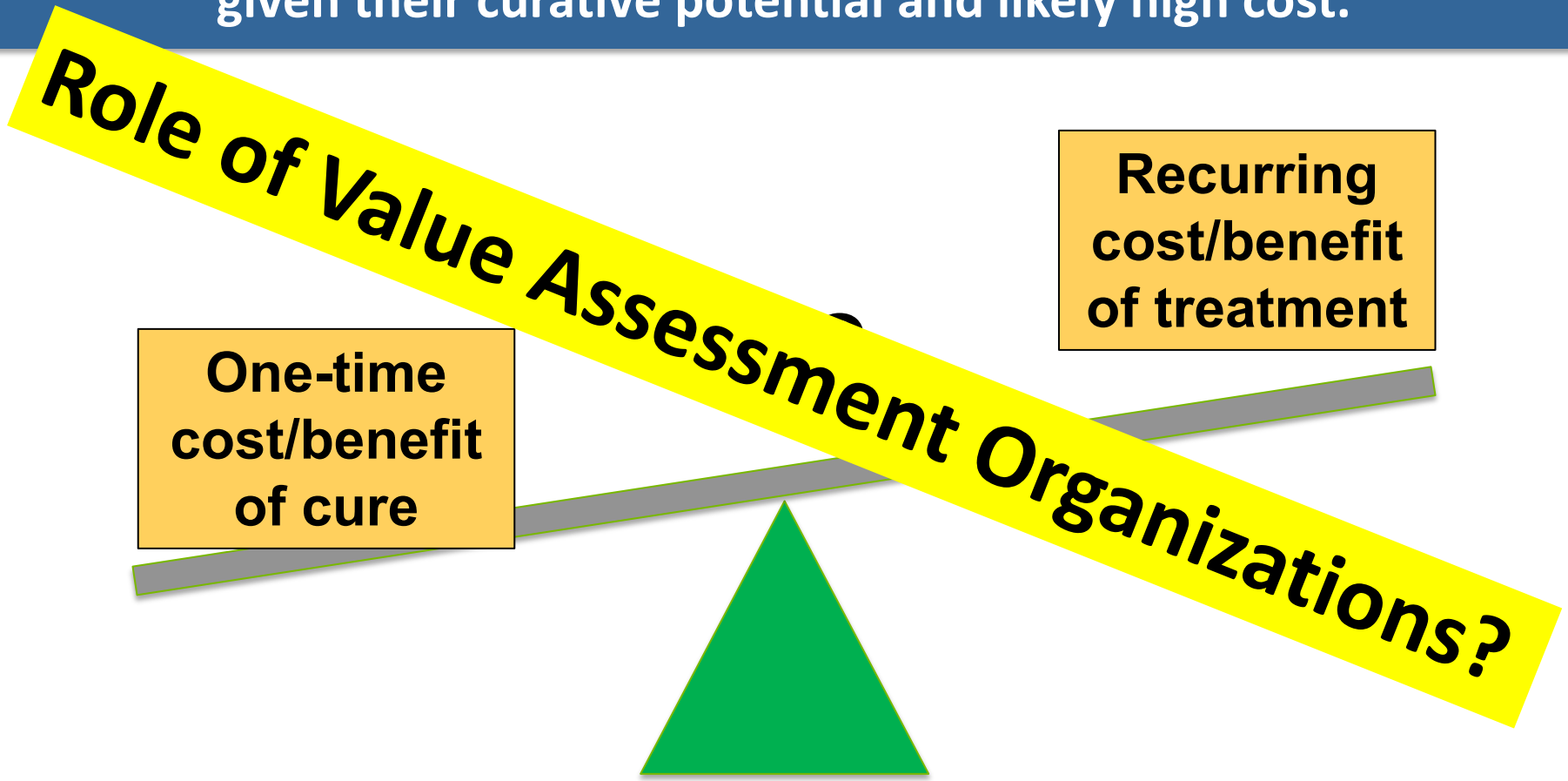
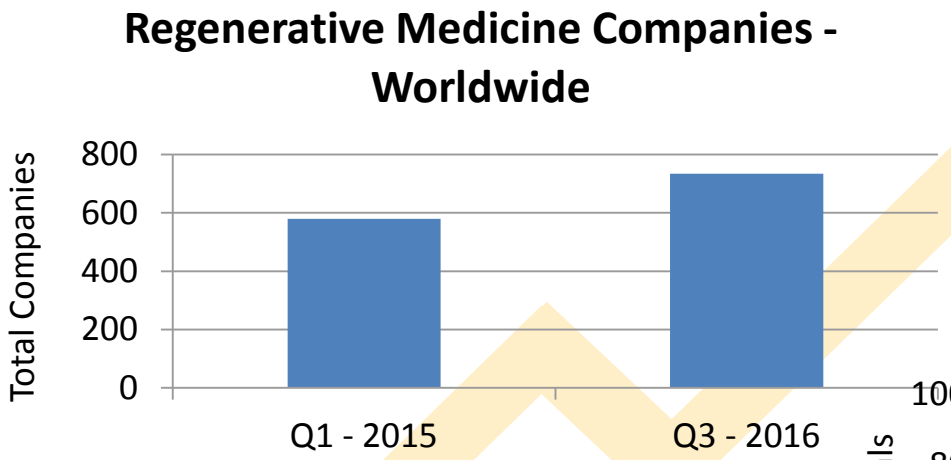
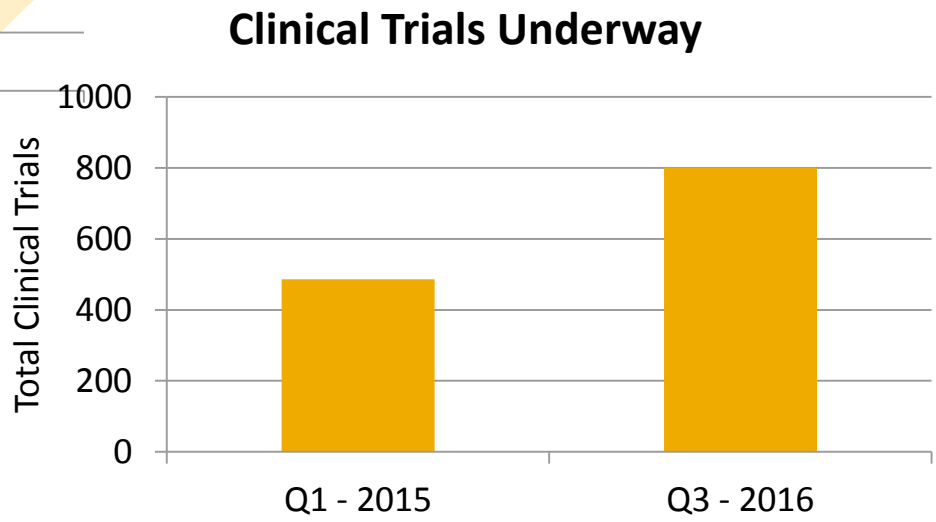


The number of regenerative therapy market participants is increasing, with recent rapid growth in clinical trials [9, 10]



ALLIANCE for Regenerative Medicine



Robust Pipeline, Including All Regenerative Therapies[11]

Current Clinical Trials by Therapeutic Category: Q3 2016

- More than 43% of current clinical trials are in oncology
- More than one in 10 are in cardiovascular

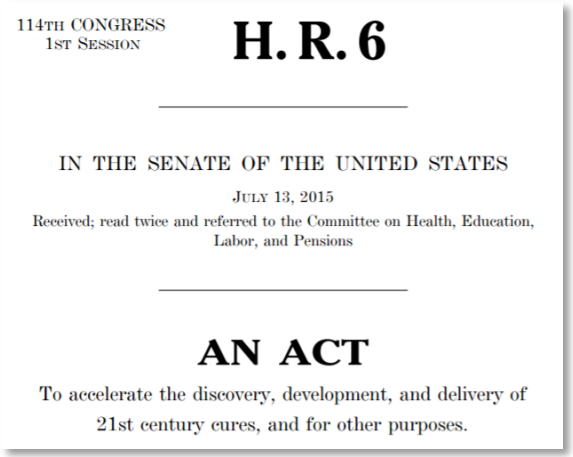
Gene therapy market to be shaped by legal/regulatory issues

Ongoing Patent Challenges[12]

Ethical Issues[13]

The National Academies of SCIENCES · ENGINEERING · MEDICINE

21st Century Cures Act[14]



114TH CONGRESS
1ST SESSION

H. R. 6

IN THE SENATE OF THE UNITED STATES

JULY 13, 2015

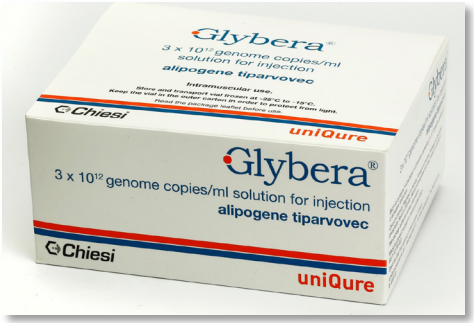
Received; read twice and referred to the Committee on Health, Education, Labor, and Pensions

AN ACT

To accelerate the discovery, development, and delivery of 21st century cures, and for other purposes.

International Lessons are Mixed, with Focus on "Guarantees"

The EU has approved 2 gene therapies, one of which has fallen well short of expectations, while the 2nd embraces outcome-based pricing



Strimvelis

Glybera[15]

- First approved gene therapy in EU(2012)
- Priced at $1 million
- Required arduous prior-authorization process; only paid for and used commercially once
- Manufacturer forced to drop plans for approval in the US and sold rights

Strimvelis[16]

- Second approved gene therapy in EU
- Priced at $665,000
- Expected to treat approximately 8 patients per year
- Manufacturer adopts innovative pricing models, including staggered pricing and outcome-based, full or partial money-back guarantees

Agenda

Introduction & Landscape

Patient Journey

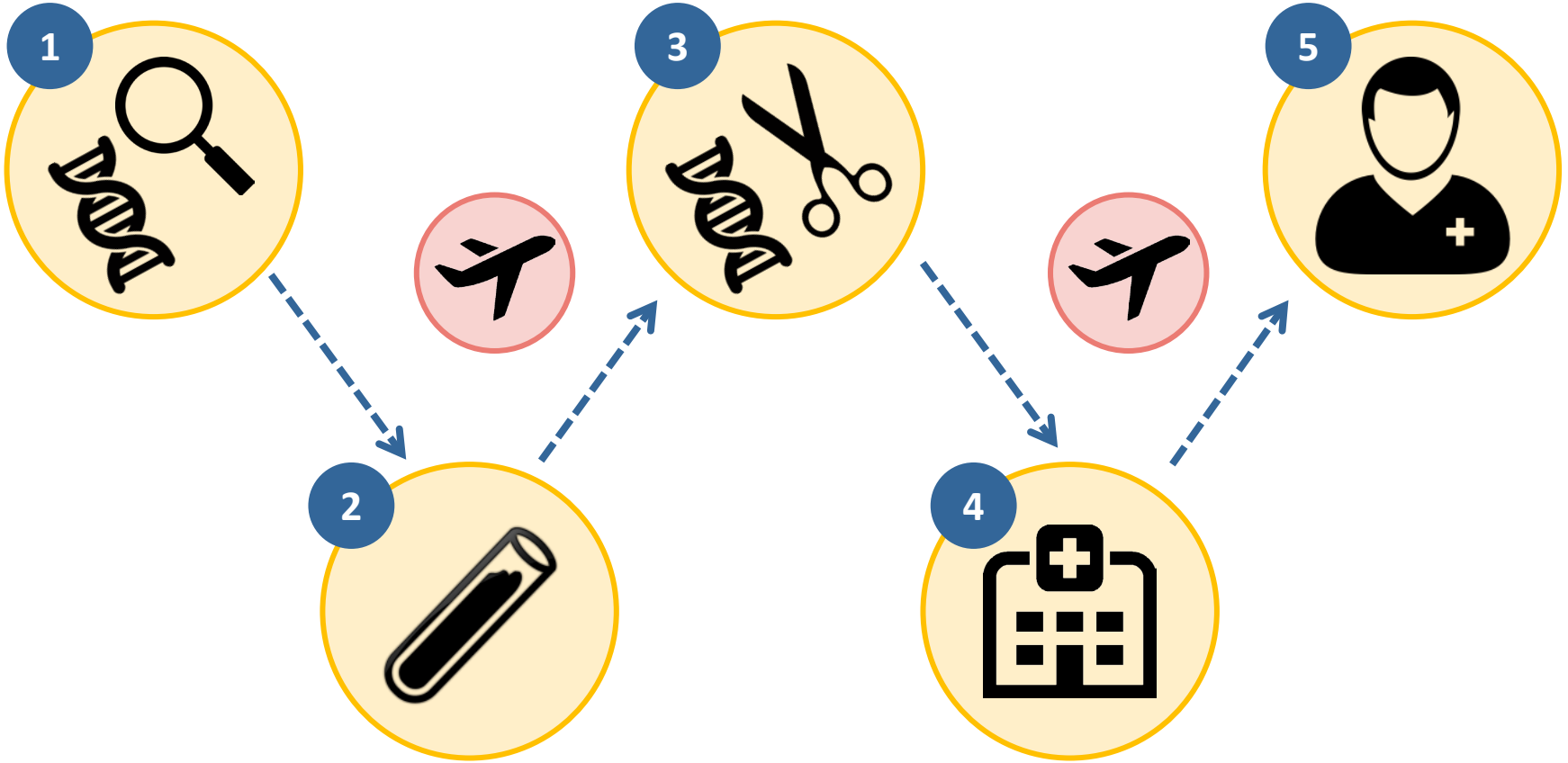
Private Insurance Coverage & Payment

Medicaid Payment

Payment Models

Patient Journey and Challenges to Access

The patient journey presents several challenges to access because it spans multiple treatment settings, types of providers and varying payment methodologies.



Agenda

- Introduction & Landscape
- Patient Journey
- **Private Insurance Coverage & Payment**
- Medicaid Payment
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Attendee Polling Question

In 2014, what percentage of children were covered under private insurance?

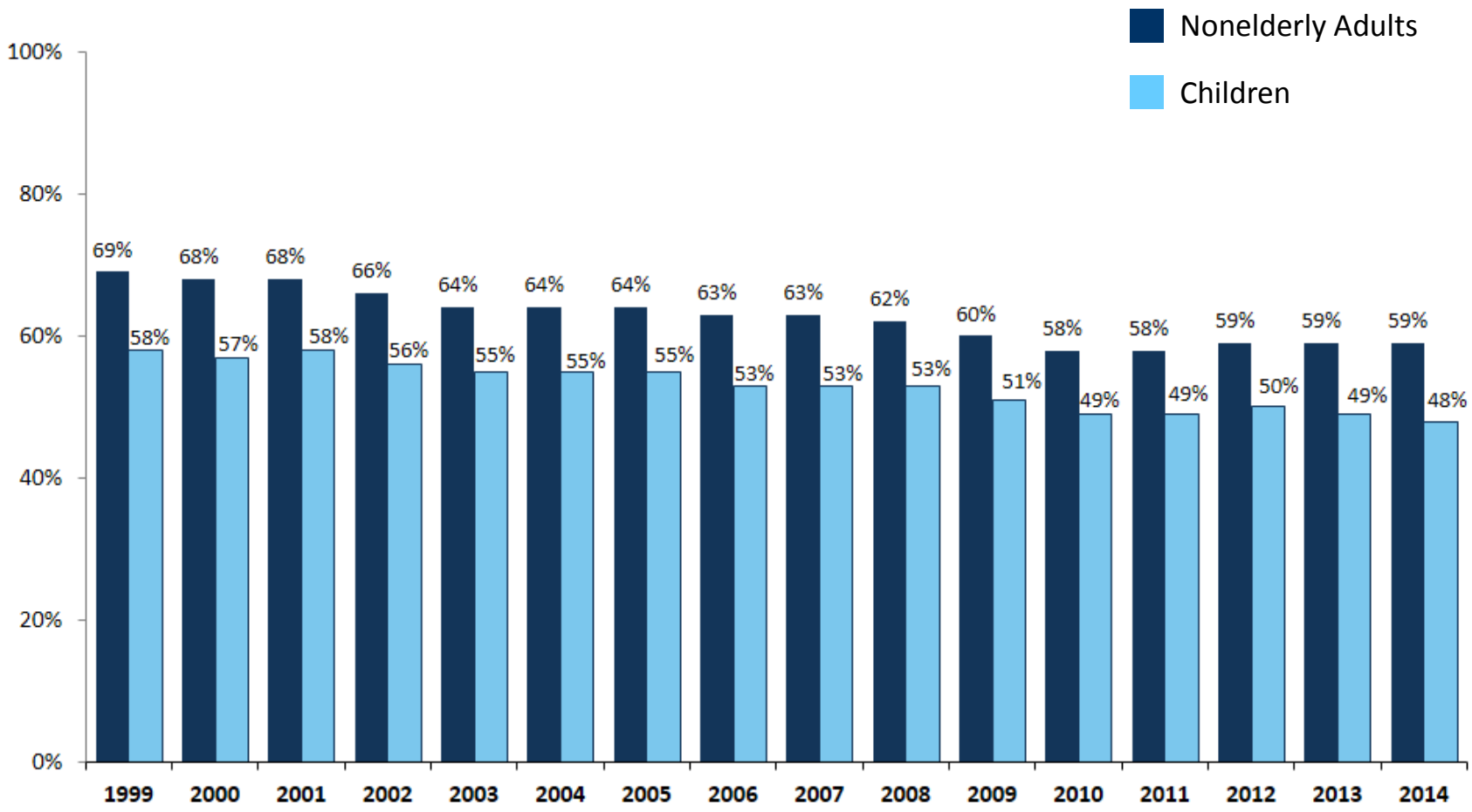
A. 34%

B. 48%

C. 62%

D. Not sure

Percent of Nonelderly Adults and Children Enrolled in Employer-Sponsored Coverage, 1999-2014[1]



1. Kaiser Family Foundation analysis of the National Health Interview Survey, 1999-2014.

Coverage & Adequate Payment of Gene Therapy and Transplantation is Not Guaranteed Under Private Insurance

Both will be subject to medical necessity and coverage criteria determinations.

aetna℠

- *"…considers allogeneic hematopoietic cell transplantation medically necessary for individuals with intermediate-risk or high-risk myelodysplastic syndrome (MDS), and who have not responded to prior therapy and have an available human leukocyte antigen (HLA)-compatable donor."*[1]

OPTUM®

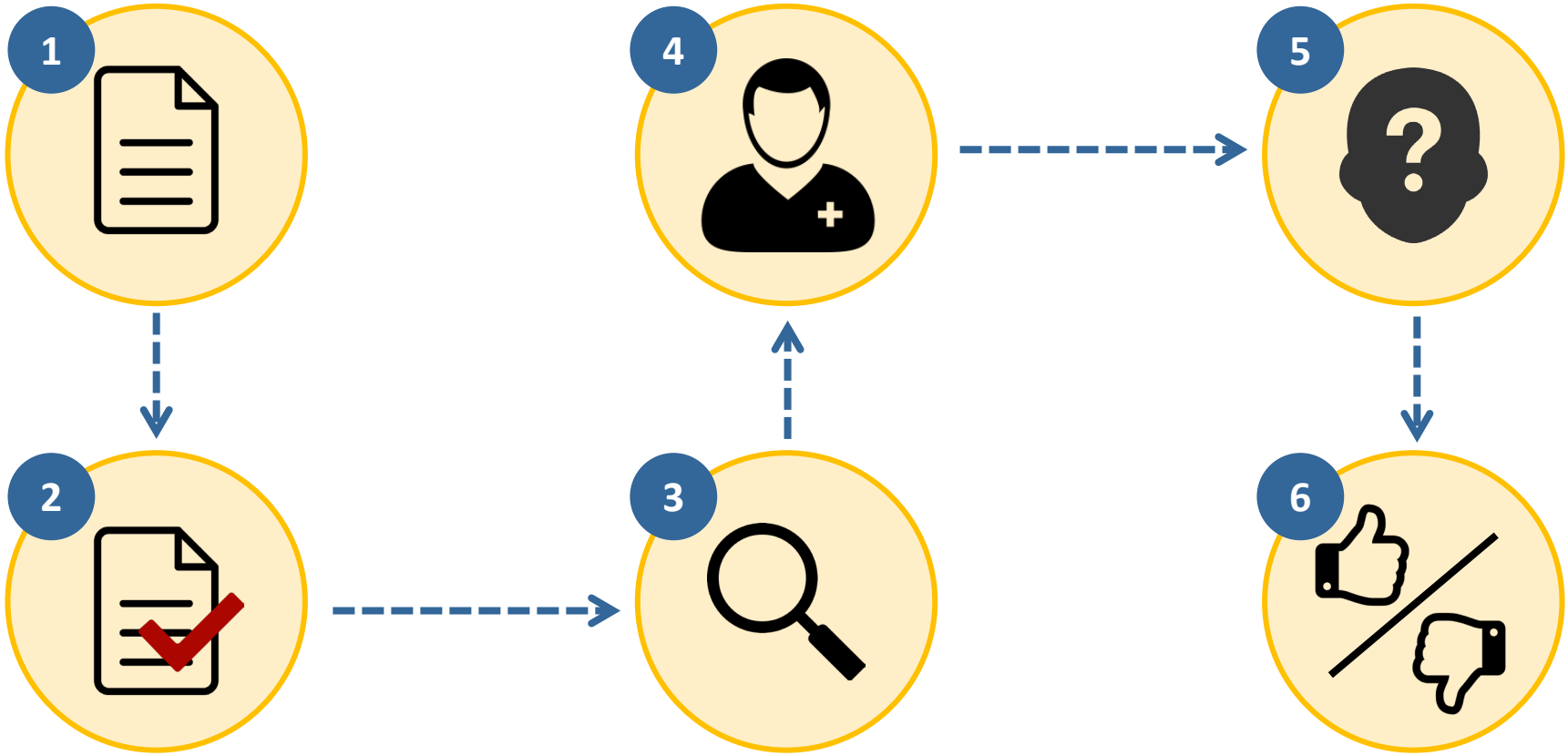
- *Autologous hematopoietic stem cell transplantation for treatment of individuals with multiple myeloma is a covered indication for single auto and tandem (auto followed by auto).*[2]

Cigna®

- *"…covers an autologous hematopoietic stem-cell transplantation (HSCT) for the treatment of active multiple myeloma (MM) as medically necessary for EITHER of the following indications: after response to primary therapy or refractory to primary therapy in an individual with relapse or progressive disease."*[3]

1. Hematopoietic Cell Transplantation for Myelodysplastic Syndrome. Aetna.
2. Transplant Review Guidelines: Hematopoietic Stem Cell Transplantation. Optum.
3. Cigna Medical Coverage Policy. Stem-Cell Transplantation for Multiple Myeloma, POEMS Syndrome and Amyloidosis. Cigna.

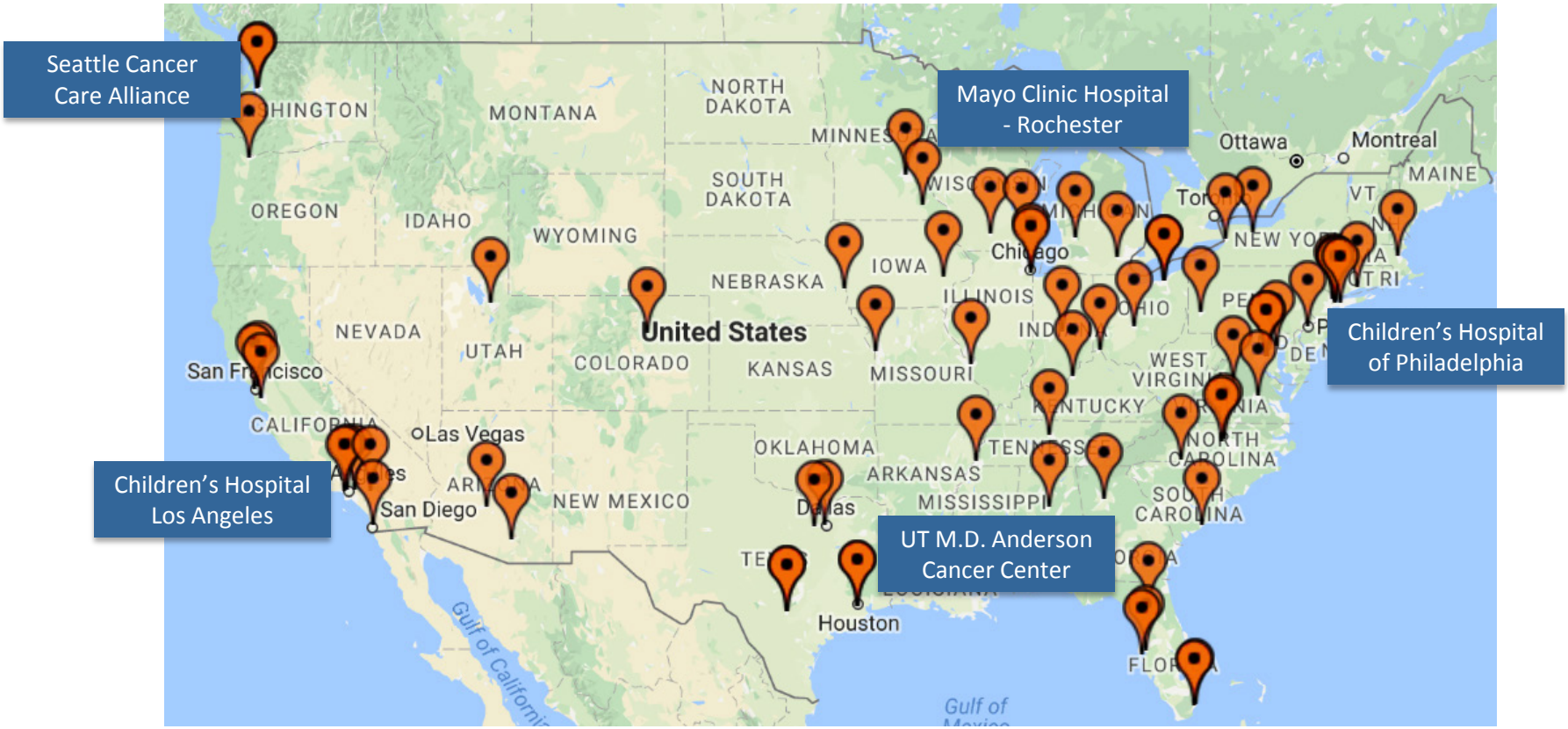
Most Transplants are Reviewed on a Case-By-Case Basis



Expect gene therapy to be reviewed on a case-by-case basis as well.

Optum's Commercial Pediatric Transplant Centers Of Excellence (COE) Network

Optum has 69 pediatric COEs in the United States.[1]



1. Optum's Commercial Pediatric Transplant Centers of Excellence Network as of November 10, 2016.

Examples of "In Network" with Certain Private Payers

Typically contracts are bundled, which will present challenges for the added cost of gene editing.

Memorial Sloan Kettering Cancer Center™

In Network:
Aetna, Blue Cross Blue Shield, Cigna, UnitedHealthcare, EmblemHealth, HealthSmart, MagnaCare[1]

SEATTLE CANCER CARE ALLIANCE

Fred Hutchinson Cancer Research Center
UW Medicine
Seattle Children's

In Network:
Premera Bluss Cross, Community Health Plan of Washington, UnitedHealthcare Charter Plans HMO, Group Health HMO[2]

1. https://www.mskcc.org/insurance-assistance/insurance-billing
2. http://www.seattlecca.org/becoming-patient/insurance-coverage-and-bills-0

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Attendee Polling Question

In 2014, what percentage of young children (age 0-3) had Medicaid/CHIP coverage?

A. 27%

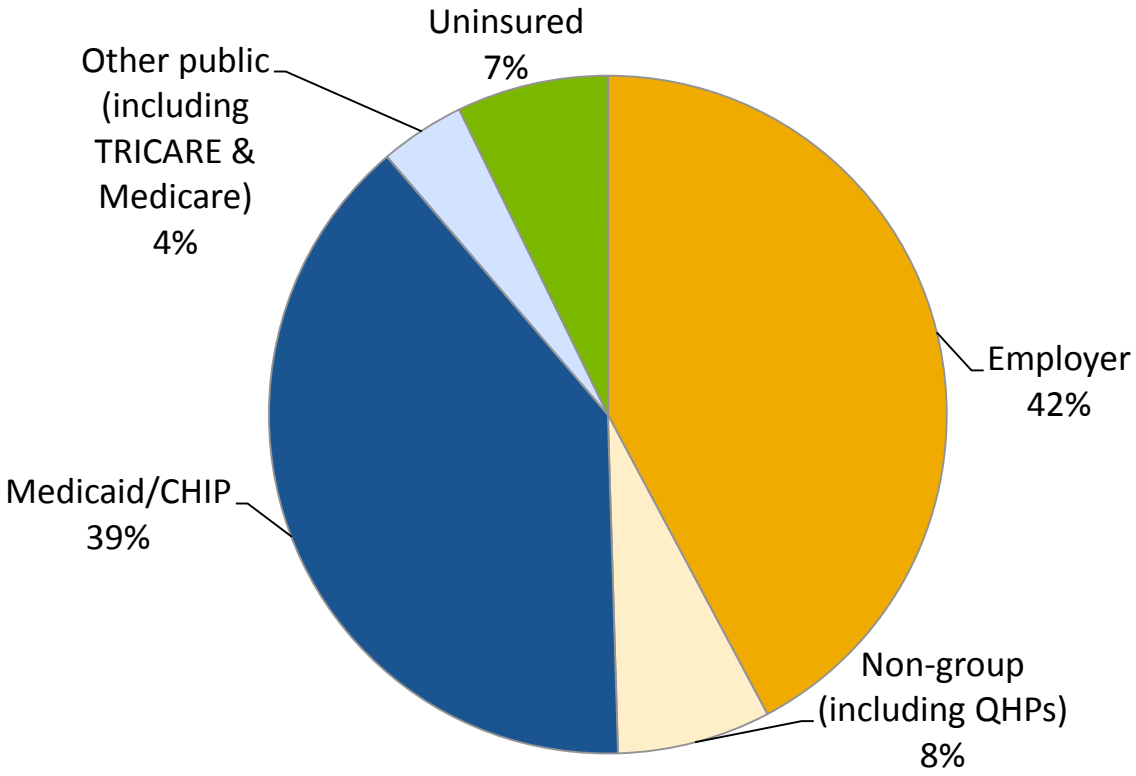
B. 39%

C. 47%

D. Not sure

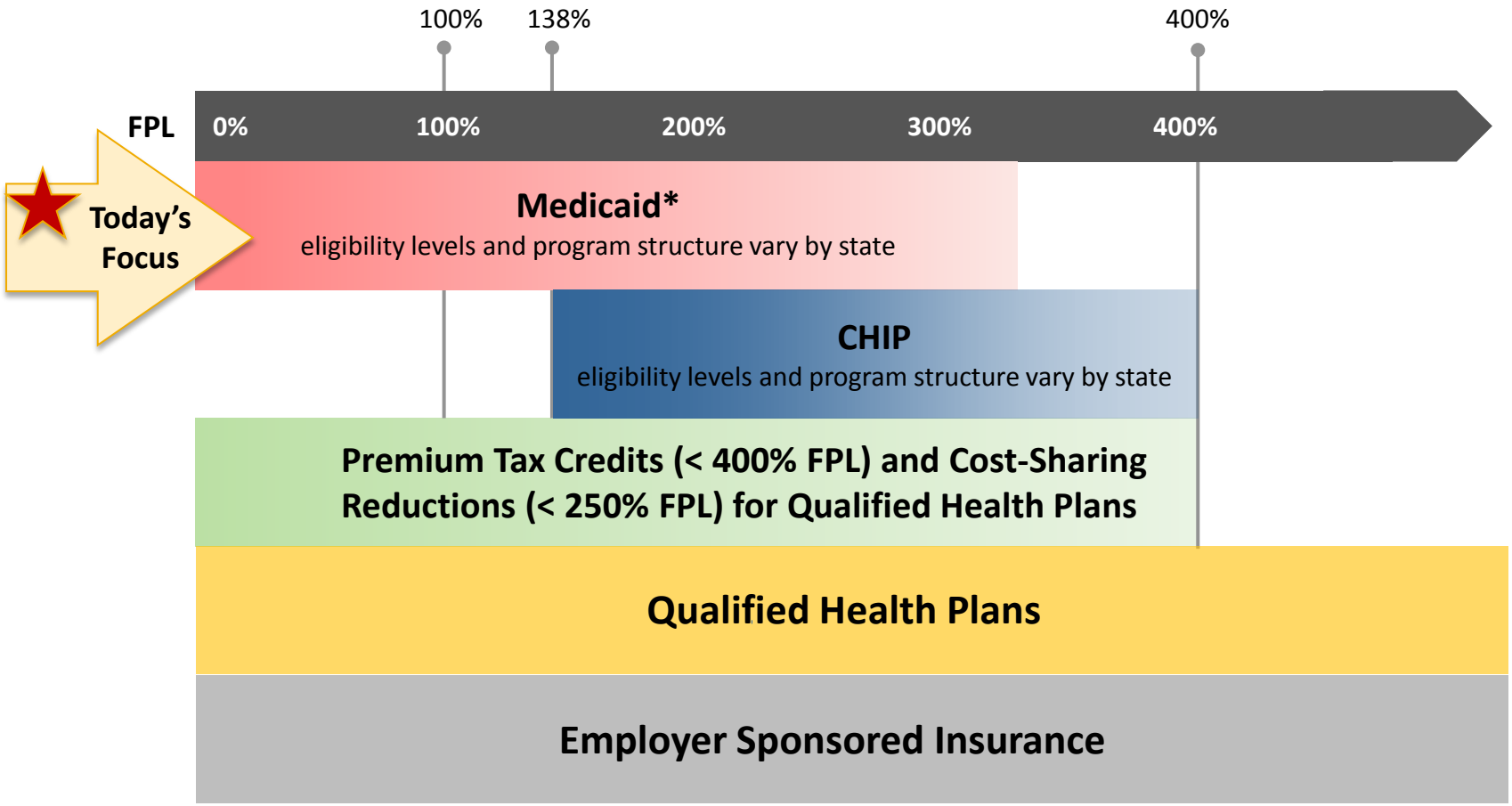
Young Children's Coverage Today (0-3 years old, 2014)

93% of the U.S.'s 12 million young children have health insurance coverage



Source: U.S. Census, Current Population Survey (2014), http://www.census.gov/hhes/www/cpstables/032015/health/hi08.xls

Coverage Continuum & Eligibility Levels for Young Children (0-5)



**Optional state Medicaid programs may provide coverage for children beyond those categorically eligible for Medicaid as low-income children. Alternative coverage may include the Medically Needy program, the Home and Community-Based Services program, and Institutional Medicaid.*

Source: Medicaid and CHIP eligibility levels: http://kff.org/health-reform/state-indicator/medicaid-and-chip-income-eligibility-limits-for-children-as-a-percent-of-the-federal-poverty-level/

Medicaid Coverage for Low-Income Families

Benefits Covered under Medicaid

- **States must cover certain services under Medicaid**, including:
  - Hospital care,
  - Nursing facility services,
  - Physician services,
  - Clinic services,
  - Laboratory and x-ray services, and
  - Family planning services.

Prescription drug coverage is an optional benefit, but all states provide such coverage.

- States must also **cover Early Periodic Screening, Diagnostic, and Treatment (EPSDT)** services.

Includes health care and treatment necessary "to correct or ameliorate" conditions, interpreted by courts to mean all medically necessary services for children, even if not for adults.

- Medicaid must **provide all medically necessary services** to children.

States are not required to cover experimental services; with new treatments, a critical issue is determining when a treatment is medical necessity vs. experimental.

- While services may be subject to utilization management (such as prior authorization), **states may not impose service caps on children**.

Medicaid Coverage of a Low-Income Child's Gene Therapy

Medicaid sets payment rate for child's treatment.

Hospital and gene therapy maker negotiate payment rate for gene therapy.

Hospital administers gene therapy.

Child endures a 6 month hospital stay in the course of the gene therapy. Medicaid provides full coverage for the gene therapy and related hospitalization. The family owes no cost sharing.

Many Children With or Without Private Insurance May Qualify for Programs under Medicaid

If children are not income-eligible for Medicaid, they may be eligible for coverage under another Medicaid program.

Medicaid for Low-Income Children

If children are not income-eligible for Medicaid, they may qualify for one of the following Medicaid programs.

Alternatives to Medicaid

- **Medically Needy Program**
- **Home and Community-Based Services (HCBS) and Katie Beckett Waiver Programs**
- **Institutional Medicaid Coverage Program**

Children, who are eligible for these alternative Medicaid programs, also may have employer-sponsored insurance (ESI) coverage, which acts as the first payor.

Under all three alternatives, children generally are not subject to premiums and cost sharing.

Coverage under Medicaid Medically Needy Program

Medically Needy Program

Optional state program that extends Medicaid eligibility to individuals with high medical expenses whose income exceeds the maximum threshold, but who otherwise would be eligible for Medicaid.

In 2009, 740,000 non-disabled children were enrolled in a state medically needy program, representing 2.4% of all medically needy enrollment.[1]

Qualifying for Medically Needy Option

1. Individuals with income below state-established Medically Needy levels but above categorically needy income levels.

2. Persons must incur sufficient medical costs (the "spend down" or "share of cost") so that their remaining income falls below a state's Medically Needy income level.

Calculating a family's "spend down":	Subtract the state's monthly Medically Needy income level of $1,390 from the family income's, assumed to be $6,000/month; the family's "spend down" would be $4,610/month.

1. Kaiser Commission on Medicaid and the Uninsured and Urban Institute estimates based on data from FFY 2009 MSIS, 2012.

Coverage under Medicaid Medically Needy Program, cont.

Child may qualify for Medicaid coverage through his state's Medically Needy program.

- **Proceed with gene therapy treatment**
- **Spends down income to make child Medicaid-eligible**

Family <u>first</u> must incur monthly medical costs equal to the difference between the family income and the Medically Needy income level.

Note: The family's spending on child's ESI premium counts toward spend down.

Medicaid sets payment rate for child's treatment.

Hospital and gene therapy maker negotiate payment rate for gene therapy.

Hospital administers gene therapy.

Child endures a 6 month hospital stay over the course of treatment:

- **ESI covers all services not related to the gene therapy.**
- **Family liable for $27,660 against the spend down.***
- **Medicaid covers all remaining costs related to the gene therapy.**

*Some states offer assistance to help pay for medical bills, which may count towards the medically needy spend down, but is not counted toward family income.

Coverage under Home and Community-Based Services (HCBS) and Katie Beckett Waiver Programs

HCBS Waiver Program

- Optional state program that provides Medicaid coverage to individuals who require a facility level of care but instead opt-to receive care at home.
- Parental income and resources are not considered eligibility.
- Not all HCBS programs are applicable to gene therapy.

The Katie Beckett program is similar but often has less strict eligibility criteria than HCBS; however, most states do not have a Katie Beckett program.

Coverage under HCBS Program

- **Child needs a facility level of care but that care can be provided at home.**
- **Child meets state's HCBS program criteria for physically disabled children, and enrolls in Medicaid under that program.***

After 2 months of home care, child is hospitalized and family proceeds with gene therapy treatment.

Medicaid sets payment rate for child's gene therapy treatment.

Hospital and gene therapy maker negotiate payment rate for gene therapy.

Hospital administers gene therapy.

Child receives home care for 2 months prior to gene therapy and endures a 6 month hospital stay in the course of his treatment:

- **ESI covers all services not related to the gene therapy.**
- **Medicaid covers all costs related to the gene therapy and the cost sharing child owes under ESI (up to the Medicaid fee schedule amount).**

Note: After a month in the hospital, child's Medicaid would likely transition from HCBS coverage to institutional coverage.

*Alternatively, some children may be eligible for Medicaid under the Katie Beckett program (for children with disabilities or complex medical conditions), which may have less strict requirements than the HCBS programs.

Coverage under Institutional Medicaid

Institutional Medicaid Coverage Program: Children who are institutionalized for more than 30 days may be determined Medicaid eligible without considering family income and resources. States provide full benefits, including EPSDT.

Doctors determine that child must remain in the hospital after birth due to his condition.

After 30 days, child can qualify for Medicaid without regard to his family's income.

Child's parents apply for Medicaid on his behalf, and he is enrolled in Medicaid.

Child's family proceeds with gene therapy treatment.

Medicaid sets payment rate for child's treatment.

Hospital and gene therapy maker negotiate payment rate for gene therapy.

Hospital administers gene therapy.

Prior to gene therapy, child lives in the hospital for 2 months; he endures a 6 month hospital stay in the course of his treatment:

- **ESI covers all services not related to the gene therapy.**
- **Medicaid covers all costs related to the gene therapy and the cost sharing that child owes under ESI.***
- **Family owes no cost sharing under Medicaid, but will pay cost sharing, up to $10,000, under ESI for costs related to the first 30 days of hospitalization.**

*ESI cost sharing for the first month in the hospital would not be covered by Medicaid. Medicaid will cover cost sharing up to the applicable amount on the Medicaid fee schedule.

Medicaid Appeals Rights

Consumers have due process rights if Medicaid denies gene therapy coverage for children

Families may:

- Pursue an administrative appeal of Medicaid's denial of coverage through a fair hearing and, if necessary, litigation;

  and/or

- Work with advocacy groups and gene therapy makers to pressure Medicaid to revise their findings.

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Innovative Models

There are few analogues in the marketplace that serve as predictors of how gene therapy might be covered and paid for by key payers.

1. Non-Traditional Financial Models
2. Risk Sharing With Transplant Facility
3. Pay for Outcomes

Thank You!

Questions?

Jon Glaudemans
jglaudemans@manatt.com

Sandy W. Robinson
swrobinson@manatt.com

Melinda J. Dutton
mdutton@manatt.com

Section One - Notes

1. https://www.bcgperspectives.com/Images/BCG-New-Era-Precision-Gene-Editing-10Sept15.pdf
2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2829748/
3. http://www.nejm.org/doi/full/10.1056/NEJMc1509501#t=article
4. http://www.nature.com/ni/journal/v11/n6/full/ni0610-457.html
5. http://www.nejm.org/doi/full/10.1056/NEJMoa1103849
6. http://www.oncolink.org/cancer-treatment/immunotherapy/gene-therapy-the-basics
7. http://www.asgct.org/general-public/educational-resources/faqs
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9. http://alliancerm.org/press/alliance-regenerative-medicine-releases-quarterly-data-report,-highlighting-key-sector-trends
10. http://alliancerm.org/page/arm-q3-2016-data-report
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12. http://www.sciencemag.org/news/2016/10/dramatic-twists-could-upend-patent-battle-over-crispr-genome-editing-method
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