Rare Disease as a Use Case for Access and Affordability

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CIRM
CALIFORNIA'S STEM CELL AGENCY

Roadmap to Access & Affordability Strategies

DELIVER A ROADMAP FOR ACCESS AND AFFORDABILITY OF REGENERATIVE MEDICINE FOR ALL CALIFORNIA PATIENTS

Facilitate Reimbursement and Limit Patient Expenses	Support New Payer Models	Address State Policy Issues	Build Clinical Resources
Patient Support Services	Engagement with Payers	Creation and/or endorsement of new State policy for C&GT	Alpha Clinics and CCCE
Alpha Site Coordination and Alignment	Performance-Based Models	Treatment across state lines	Patient and post-marketing Registries and Data (RWE, HEOR)
Patient Navigator at CCCEs	Introduce New Payer Mechanisms for Orphan Products	Inpatient vs. Outpatient reimbursement	Accelerate Advocacy at community level; Medical Education
Coverage Analysis, Insurance Support, Co-Pay Assistance, Access and Appeals	Risk Pools/Coalition Partners	Align to Gov Plan on Office of Health and Affordability	State and Federal authorized treatment centers

Today's Focus

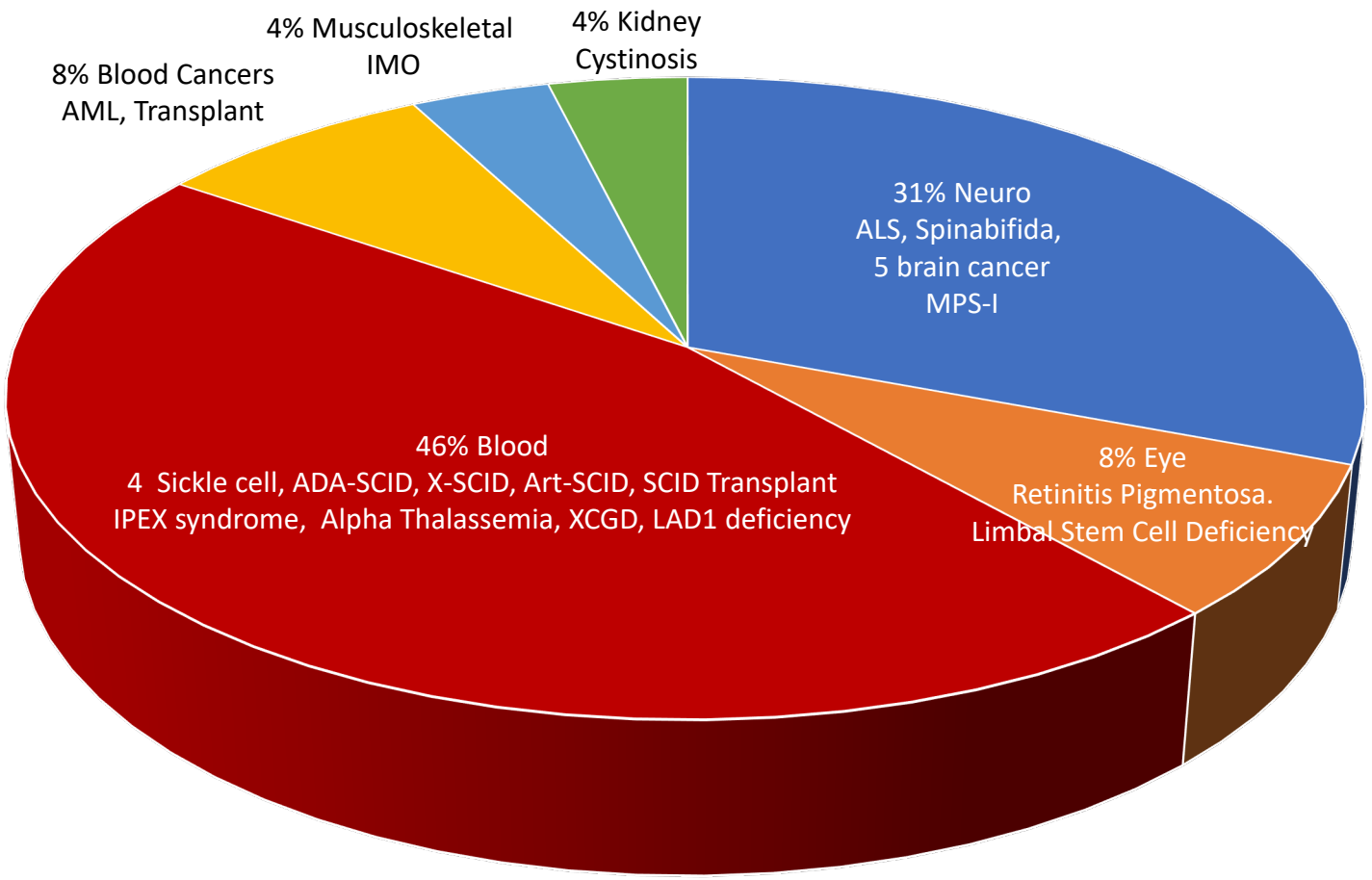
Use Rare Disease as a use-case for discussion of the roadmap to Access and Affordability

Why?

Approximately half of CIRM's portfolio is in rare disease and are advancing to later stages in the clinic.

There are ~7,000 rare diseases in the United States affecting an estimated 25 to 30 million people of which >50% are children.

Active Clinical Trial Portfolio in Rare Diseases



Active Rare Disease Clinical Trial Awards as of 2/27/23

- Affecting Children and Adults
- Utilizing State of the Art Technologies
- Advancing Towards Registration

  20 Phase 1

  5 Phase 1/2

  1 Phase 2
- Total 26 Active Clinical Trials

Active Rare Diseases Grants with Accelerated Designations

Clinical Phase	Disease Area	Investigator	Institution	FDA Designation
1	Blood disorder (Artemis SCID)	Cowan Morton	UCSF	RMAT
1	Blood disorder (All SCID)	Pang, Wendy	Jasper Pharma	RMAT
1/2	LAD-1 Deficiency	Patel, Kinnari	Rocket Pharma	RMAT
1/2	Blood disorder (ADA SCID)	Kohn, Donald	UCLA	Breakthrough
1/2	Blood disorder (X SCID)	Gottschalk, Stephen	St. Jude	RMAT

RMAT: Regenerative Medicine Advanced Therapies

CIRM is Strategically Aligned with FDA/NIH's focus on Rare Diseases

FDA's Center for Biological Evaluation and Research (CBER) is expanding Rare Disease with Operation Warp Speed for C&GT.

Center for Drug Evaluation and Research (CDER) - Accelerating Rare Disease Cures (ARC) Program (2022) designed to speed development of treatments for Rare Diseases.

CIRM joined the Accelerating Medicines Partnership® (AMP®) program (part of the Bespoke Gene Therapy Consortium) which is a public-private partnership between the National Institutes of Health, the U.S. Food and Drug Administration, and multiple public and private organizations.

Delivery of Therapies for Rare Disease has been Uniquely Challenging

Clinical

MDs unfamiliar with the disease state
Poorly understood underlying Disease Mechanisms
Difficulty designing Study Endpoints

Data Generation

Limited number of Patients
Health Institutions not Equipped
HCPs and Health Personnel not trained in Administration of Complex Therapies

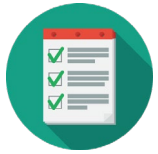
Manufacturing

Small batch production
GMP-requirements not up to speed
Difficulty upscaling Production

Regulatory

Difficulty in Determining Standards for Approval
Safety and Efficacy standards
Approval duration due to accelerated approval

Post-Marketing Requirements



Post-Marketing Commitments extending up to 15 Years
Long-Term Safety Studies (Phase IV)
Long-Term Efficacy Studies (Phase IV)

Commercial

Pricing Hurdles
Small Target Populations
Increased capital expense
Prescriber confusion over appropriate use

Payer/Reimbursement

Unclear Processes for Determination of Reimbursement at Insurance Agencies
Lack of Comparators to determine clinical and economic benefit of Novel Therapies
Restrictive policies limiting access

Why Post-Marketing Commitments are Important

- Per FDA, all commercially approved cell and gene therapies require the manufacturer to oversee post-marketing commitments for up to 15 years.
- In addition to mandated safety reporting, post-marketing data has become instrumental for reimbursement through value-based agreements with payers.

Rare Disease Drug Development – Post-Marketing Considerations

Phase IV (Longitudinal)

Opportunities

- Studies to determine the safety profile in the larger or in a specific patient population
- Real World Data Research to determine areas of greatest impact
- HEOR to determine the medical-economic benefits
- RWD and HEOR to aid in establishing reimbursement Structures

Phase IV (Reimbursement/Health Economic Impact)

Phase IV (Long-Term Safety and Tolerability)

Phase IV (Evaluate if Contributing to Significant Clinical Outcomes compared to other therapies)

Phase IV (Study to Evaluate Cost-Benefit vs. Existing Therapies)

Phase IV (Long-Term Efficacy and Attenuation of Effect

Phase IV (HEOR & RWD – Therapy Optimization)

Why it's Important to Fund Post-Marketing Commitments for CIRM Programs

Real World Evidence is playing an increasing role in Healthcare Decisions and provides clinical evidence regarding the usage, benefits and risks of a medical product.

Health Economics and Outcomes Research (HEOR) generates evidence for the value of a new therapy for reimbursement and healthcare payers.

Benefits of Investing in Post-Marketing Infrastructure can bridge the gap to RWD and HEOR

Real World Evidence

Broader insights into drug safety and efficacy

Creates a diverse set of real-life data to study

Identify feasibility and access hurdles

Enhanced and Targeted Research

Will meet FDA's framework for RWE under 21st Century Cures Act

HEOR

- Support for Coverage Decisions (value-based contracting)
- Cost Effectiveness and Utility
- Quality-of-Life Data
- Patient Reported Outcomes

Summary of Access and Affordability Topics

- Patient Support Service
- New Payer Models
- Inpatient to outpatient setting (e.g., CAR-T)
- State and Federal Policy (e.g., CCEA)
- Alpha Clinics and Community Care Centers of Excellence (CCCE)
- Real World Data
- Health Economics Outcomes and Research (HEOR)
- **Next Topic: Coverage Analysis, Access and Appeals, Co-Pay, Risk Pools**

Thank you and Discussion