Alliance *for* Regenerative Medicine

VALUING TRANSFORMATIVE THERAPIES

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#ASGCT20

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Access the Reports Cited in this Presentation:

Navigating Cell and Gene Therapy Value Demonstration & Reimbursement in U.S. Managed Care

CLICK HERE TO ACCESS

Getting Ready: Recommendations for Timely Access to ATMPs in Europe

CLICK HERE TO ACCESS

A Transformative Therapy Value Model for Rare Blood Diseases

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About ARM

- **International advocacy organization**
  - Dedicated to realizing the promise of safe and effective regenerative medicines for patients around the world
  - Cell and gene therapy, tissue engineering
- **350+ members**
  - Small and large companies, non-profit research institutions, patient organizations, and other sector stakeholders
  - Across 25 countries
- **Priorities:**
  - Clear, predictable, and harmonized **regulatory** pathways
  - Enabling market access and value-based **reimbursement** policies
  - Addressing industrialization and **manufacturing** hurdles
  - Compile sector data, **educate** media and other stakeholders

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ARM's Work in Market Access

- **Build** the value story for regenerative medicine products through evidence collection, including case studies, framework development, coverage criteria, and external stakeholder engagement.
- **Secure** supportive coverage and payment policies for cell and gene therapies and other regenerative medicine products.
- **Analyze** current and potential payment and financing models to facilitate and improve access and adoption.
- **Break down** barriers to the adoption of new, innovative payment and financing models, drive value-based payment reform, and address core challenges to enable payments over time.

Policymakers, Others Seeking Guidance on Value-Based Care

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ARM's Recent Comments, Letters, & Testimony	Recipient	Date
Response to CMS's RFI: Coordinating Care from Out-of-State Providers for Medicaid Eligible Children with Medically Complex Conditions	CMS	March 2020
Joint letter with BIO to requesting guidance to hospitals regarding appropriate charges for CAR-T therapies	CMS	March 2020
Letter to Reps. DeGette and Upton in response to their RFI for a Cures 2.0 initiative	US House Committee on Energy & Commerce	Dec 2019
Joint letter with BIO on 'Request for MS-DRG Reclassification for Certain Cases Involving Use of CAR-T Therapies'	CMS	Nov 2019
Response to ICER's RFI on the '2020 Value Assessment Framework'	ICER	Oct 2019
Comments on ICER's 'Value Assessment for Single or Short-Term Transformative Therapies: Proposed Adaptions to the ICER Value Assessment Framework'	ICER	Sept 2019
Comments on the HIPPS for Fiscal Year 2020	CMS	June 2019
Comments on the Proposed Rule on the Removal of Safe Harbor Protection for Rebates Involving Prescription Pharmaceuticals	HHS OIG	April 2019
Comments on proposed National Coverage Decision (NCD) for Chimeric Antigen Receptor (CAR) T-cell Therapy	CMS	March 2019
Comments on ICER's RFI: Evaluation of Potentially Curative Treatments and for Translating the Results of Cost-Effectiveness Analyses into Recommendations for Value-Based Price Benchmarks	ICER	Feb 2019

Regenerative Medicine & Value

All reports available at www.alliancerm.org

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Patient Impact of Recently Approved Products

Therapy Name	Product Developer	Response
Zynteglo	bluebird bio	• **75%** of patients with TDT without β0/β0 genotype treated achieved transfusion independence
Zolgensma	AveXis, a Novartis company	• **93%** of SMA Type 1 patients treated were alive without permanent ventilation at 24 months post-treatment
LUXTURNA	Spark Therapeutics	• **93%** of patients treated showed an improvement of at least 1 light level from baseline
Yescarta	Kite Pharma, a Gilead company	• **58%** of patients with R/R B-Cell NHL treated experienced a complete response
Kymriah	Novartis	• **40%** of patients with R/R DLBCL treated experienced a complete response • **82%** of patients with R/R B-Cell ALL treated experienced complete remission or complete remission with incomplete hematologic recovery

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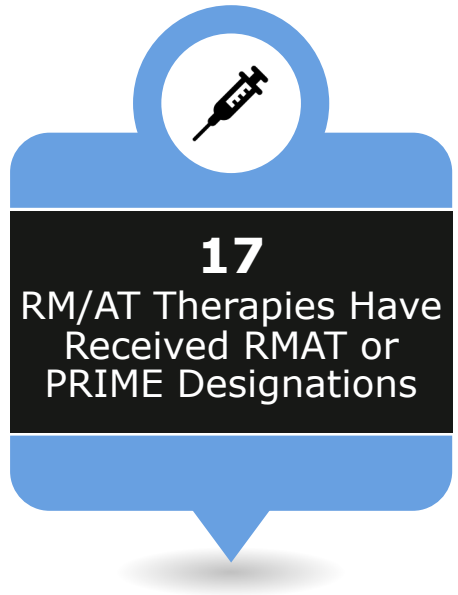
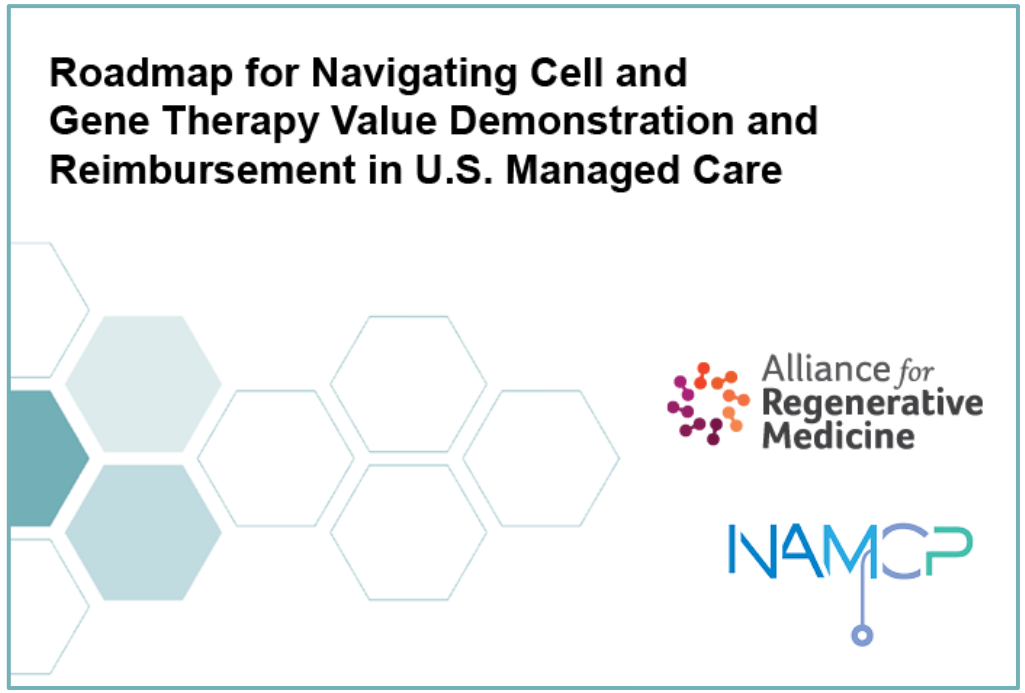


The need for innovative value models will only increase as the field progresses.

Medical Directors' Perspectives on Value & Reimbursement



Released September 2019

- Roadmap for Navigating Cell and Gene Therapy Value Demonstration and Reimbursement in U.S. Managed Care
- Joint study by ARM and NAMCP
- Bringing Manufacturers and Payers together
- Survey results from 44 medical directors in the US, representing preeminent commercial MCOs (Aetna, Cigna, WellPoint, United Healthcare) as well as health system and provider organizations
- Discussed the integration of cell and gene therapies into the existing system, including existing gaps and potential solutions.

Access the report

Key Findings

01 **Reducing barriers to coverage will be critical** for equitable patient access to cell and gene therapies.

02 **Improving stakeholder alignment** on evidence requirements and a value framework for cell and gene therapies is key to support more rapid coverage and access decisions.

03 **Lack of appropriate fit into existing coding and payment systems** creates significant risks for provider adoption and patient access.

04 **Cell and gene therapy manufacturers must think comprehensively** and not take anything for granted in developing a value demonstration strategy.

05 It is critical for commercial payers to **actively engage in solutions** for making truly transformative therapies available to patients in an affordable manner.

Common Value Mistakes

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Payers indicate that the following mistakes are often made by developers building a value story around gene and cell therapy development:

- Insufficient focus on **linking surrogate endpoints to "harder" outcomes** (mortality, morbidity, health resource utilization) that payers care most about
- **Unclear rationale for the target patient population** and positioning (e.g., based on epidemiology data, biomarker data and other rationale)
- **Unclear burden of disease**, natural history, or Standard of Care impact
- Basing the entire value proposition on **minimalist or surrogate endpoints** for a cell and gene therapy that is anticipated to have transformative or curative effect
- **Lack of comparative effectiveness** of the therapy compared to Standard of Care

Getting Ready: Recommendations for Access to ATMPs in Europe

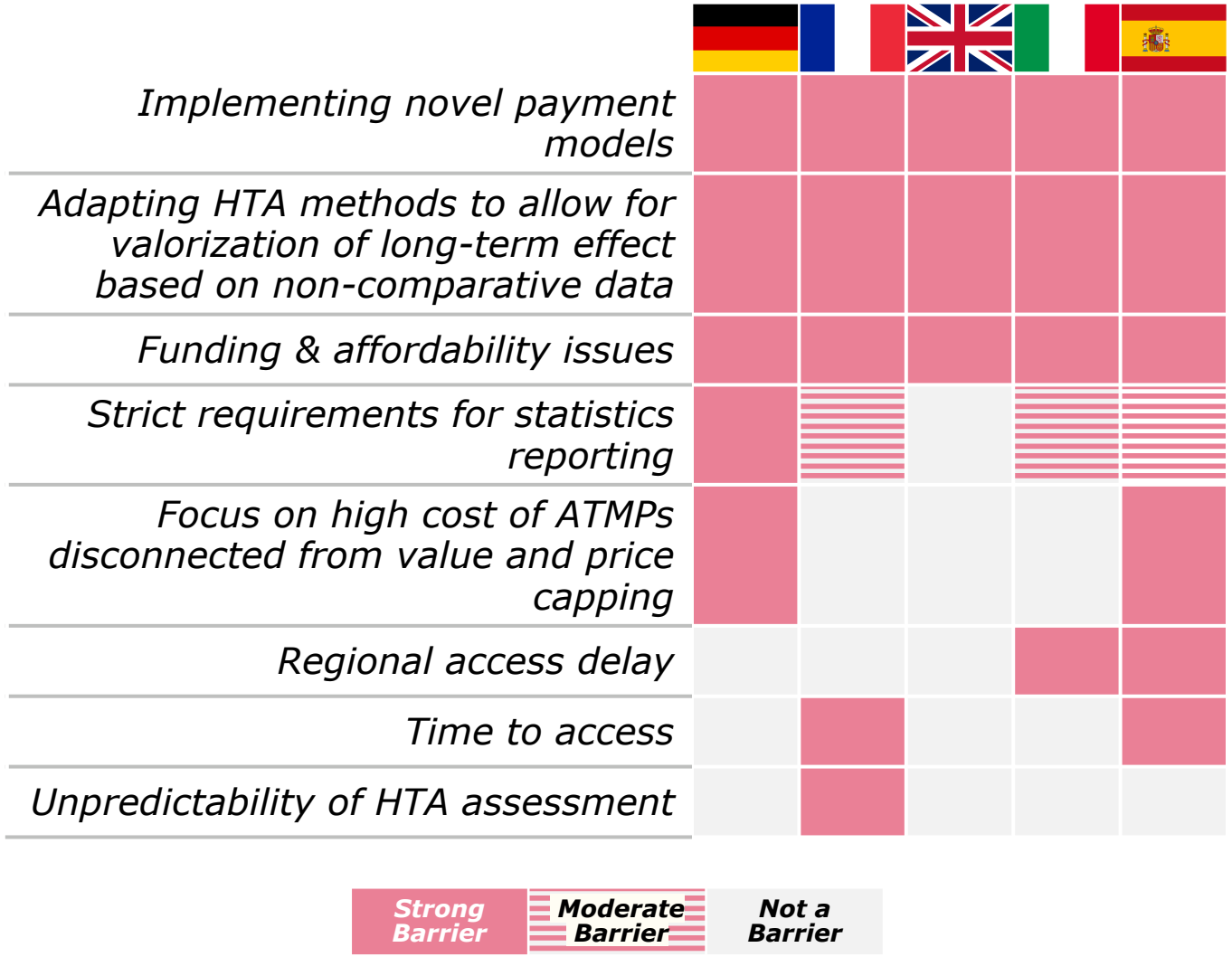
Released July 2019

- Assessment of current regulatory and market access frameworks in six European countries: France, Germany, Italy, Spain, Sweden and the United Kingdom
- Identifies hurdles to adoption and makes EU-wide policy recommendations to address those challenges
- The report brings together the views of multiple European policy makers and experts:

EUCOPE efpia EHC EuropaBio EURORDIS RARE DISEASES EUROPE NICE

Access the report

Challenges Faced by ATMP Developers in EU5



Main Challenges for ATMP Market Access

Need for Innovative Payment Models
Need to implement outcomes-based payments, annuities, and other innovative financing models

Rigidity of HTA Requirements
HTA bodies require head-to-head RCTs and long-term data at time of launch

Affordability
There is a lack of funding for ATMPs

Recommendations to Improve Access to ATMPs in Europe

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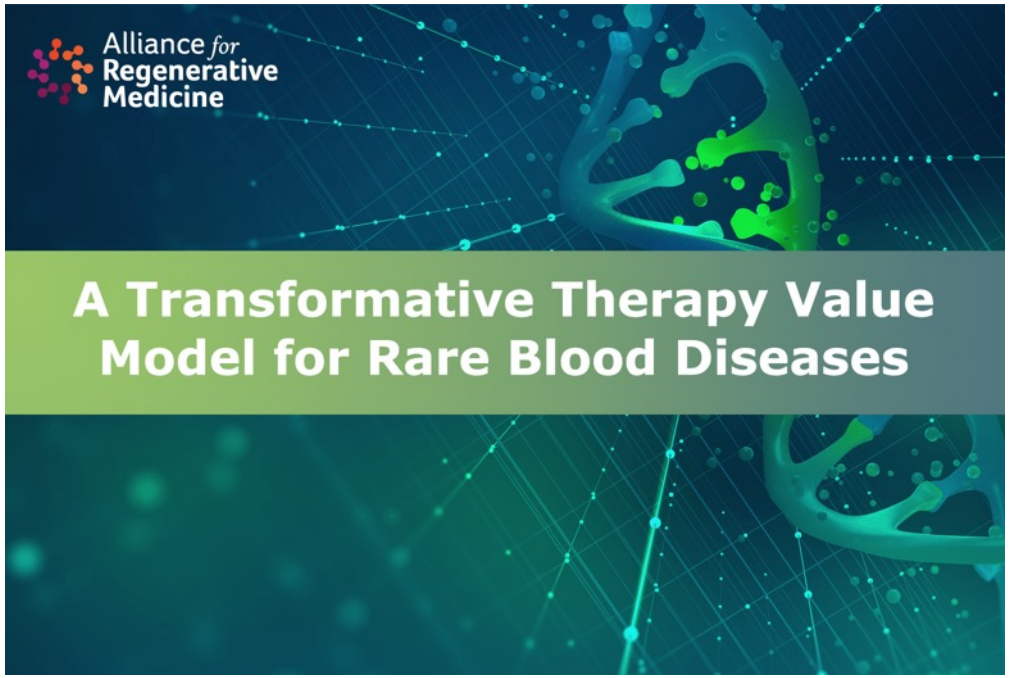
01 Wider application of **conditional reimbursement schemes** to help mitigate uncertainty

02 **Better adapt HTA frameworks for ATMPs** by allowing the use of surrogate endpoints and indirect comparisons; development of natural history datasets; and adopting changes in economic modeling

03 Develop **pan-European initiatives** to promote RWE infrastructure; early-dialogue opportunities; and access to cross-border healthcare

04 Favor wider application of **innovative access and funding arrangements**, such as pay-for-performance, annuity payments, and special funds for high-value medicines

New Analysis of 10 Year Cost Impact of Cell & Gene Therapy

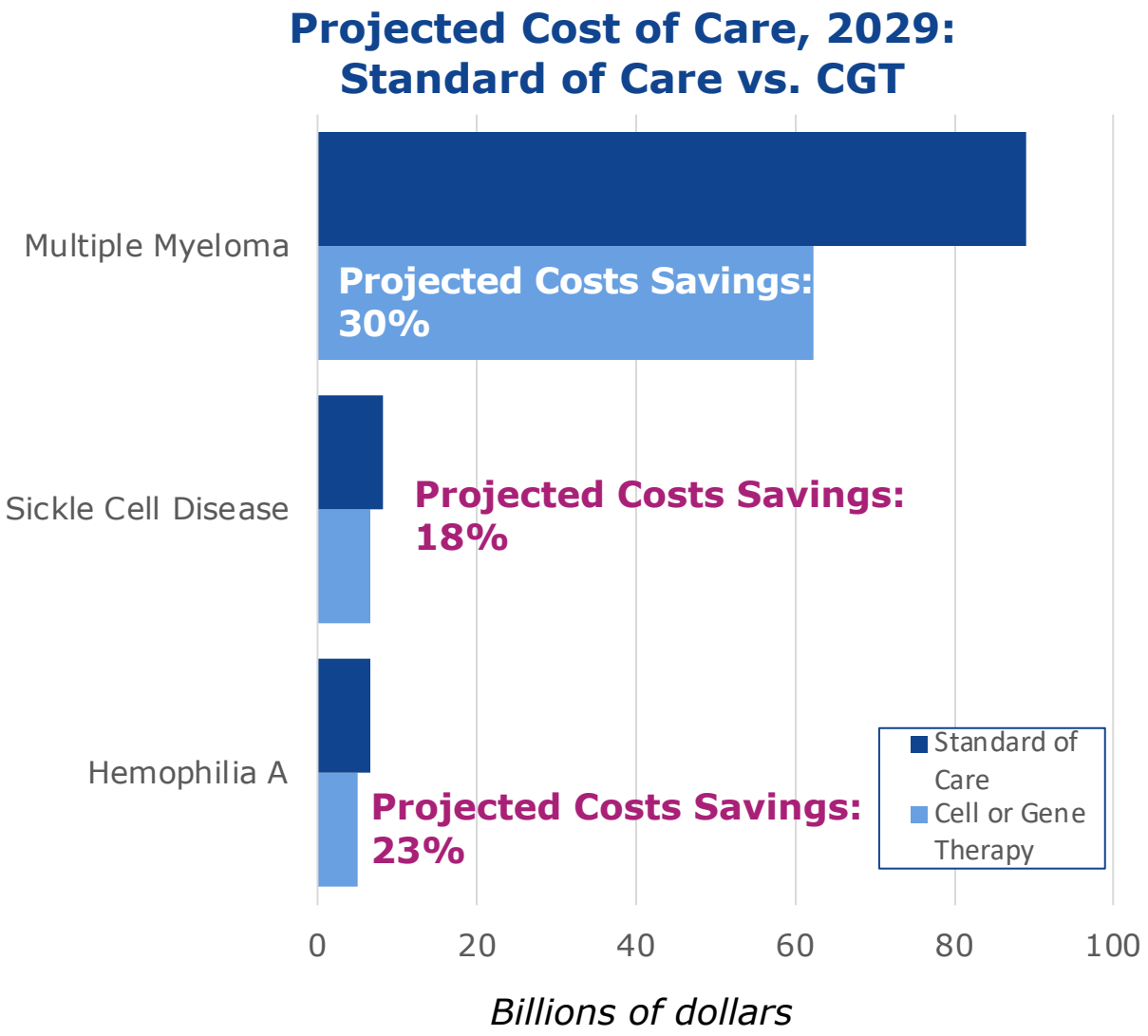


Released January 2020

- Produced by the Marwood Group with support from ARM
- A Transformative Therapy Value Model (TVM): first-of-its-kind refined model developed to evaluate long-term value of regenerative medicines
- Employs 10-year timeframe used by US Congressional Budget Office to calculate long term cost-savings
- Utilizes sickle cell disease, hemophilia A, and multiple myeloma as case studies

Access the report

Long Term Cost Savings



- Model shows **18 to 30% in total potential savings** from cell and gene therapies
- This represents an **aggregate cost savings of more than $33B** by 2029.
- Modeled cost savings were highest in multiple myeloma patients ($27B in cumulative savings per year by 2029) due to:
  - High cost of the current standard of care
  - Greater productivity losses experienced by the adult children caregivers of older patients.

The Need for a New Value Analysis Framework

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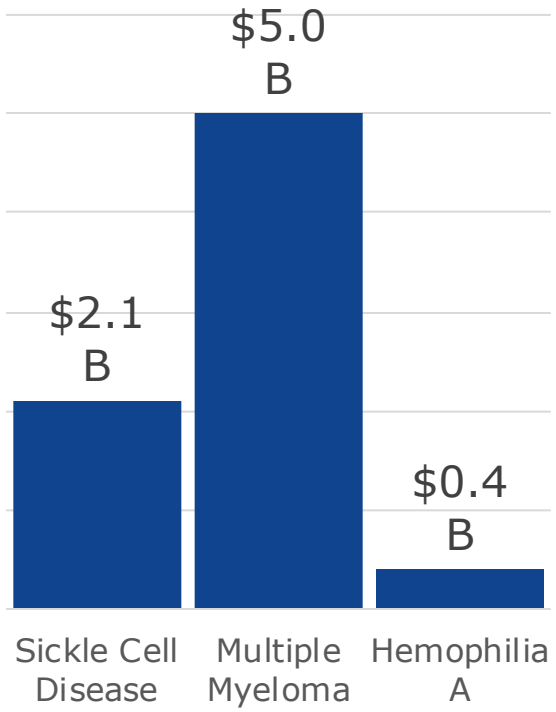
- Current value-based models often **undervalue the gains in productivity** provided a cell or gene therapy with a durable, potentially curative benefits
- Many existing models rely on focus on cost per QALY gained, but may miss the full benefit that a durable therapy could provide
- These benefits **extend beyond patients to family members**, who are often the primary caregiver for patients with a rare disease
    - Significant numbers of caregivers reduced their work hours, took time off or a leave of absence, turned down a promotion, or gave up working entirely
- Standard cost-effectiveness models **do not account for both patient and caregiver QALYs gains** in their base case analysis.
- Through the TVM, **payers can project trends in their own disease populations** to assess these durable therapies, adjusting wage productivity for their covered lives.

Cumulative Loss in Productivity, 2020-2029



*The cumulative value of productivity gains for patients and caregivers from 2020-2029 totals **more than $7B**.*

The ARM Foundation

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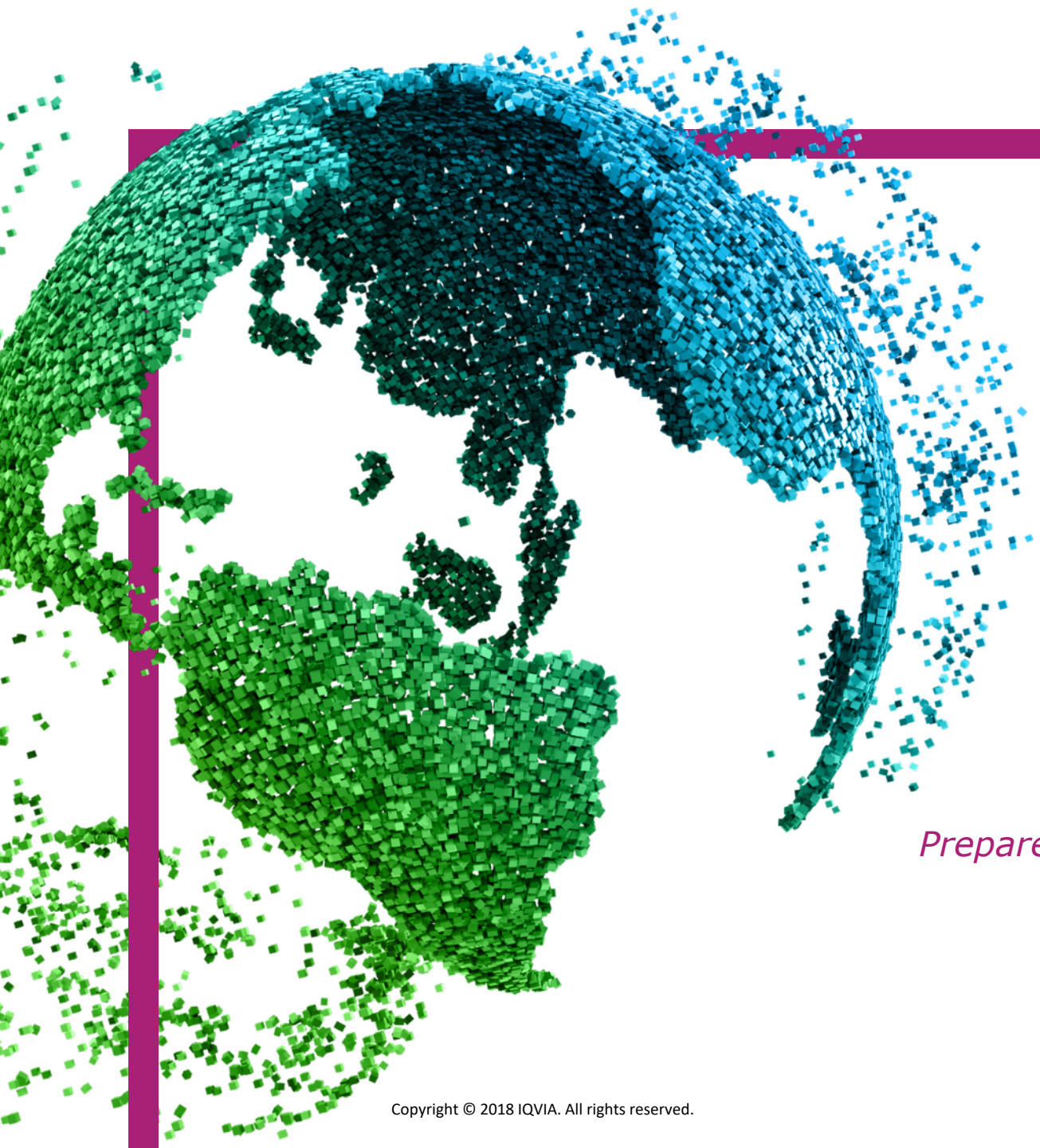

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Regenerative Medicine/ Advance Therapeutics (RM/ATs) Landscape Assessment

June 2018

Prepared by the IQVIA Cell And Gene Therapy (CATG) Center

Payer Archetypes

Most countries have leveraged traditional archetypes and frameworks that are not suitable for RM/ATs

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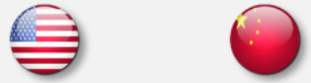
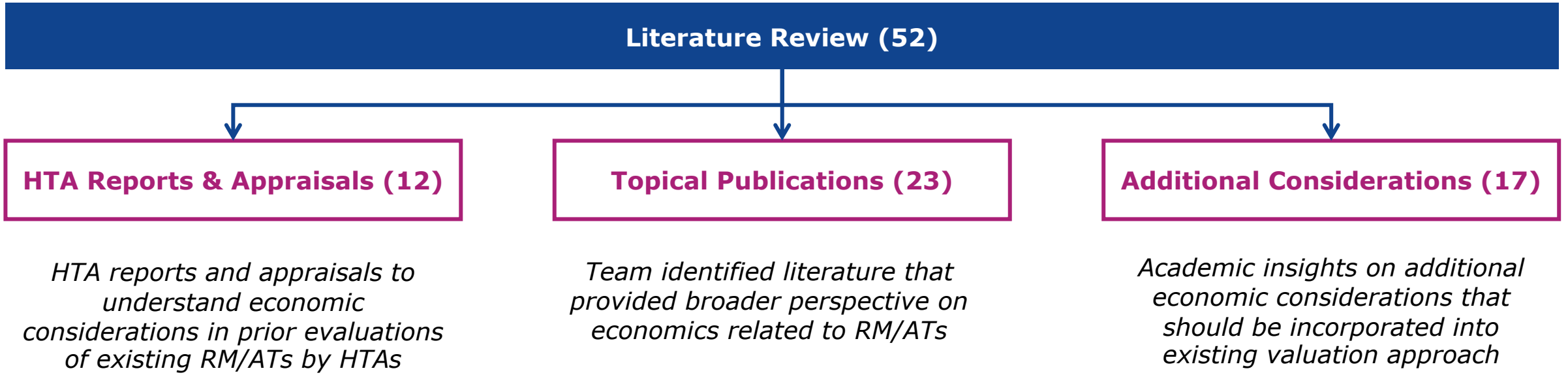
Payer Archetypes

	Pharmacoeconomic	Therapeutic Referencing	Willingness-to-pay
Definition of value:	*Value is considered in the context of utility that a treatment brings to stakeholders and/or the ability to implement that treatment with constrained resources*	*Value is considered as the therapeutic benefit that a product brings over the standard of care and/or other therapeutic alternatives*	*Value is influenced by the complex dynamics of competition on both the supply and demand side of the payer equation, reflecting both willingness and ability to pay*
Countries:			
Key test of value:	• *Cost-effectiveness (usually by ICER)*	• *Clinical benefit relative to comparator(s)*	• *Clinical and non-clinical benefit; unmet need* • *Cost / budget impact*
Issues for RM/ATs:	• *Difficult to meet current QALY thresholds due to small patient populations*	• *Challenging to compare clinical superiority and cost savings against non-curative comparator*	• *Difficult to justify non-clinical benefit to payers focused on clinical value* • *Fragmented systems make it difficult to pay upfront*

IQVIA

Literature Review: Existing & Suggested Economic Considerations for RM/ATs



The CAGT team utilized findings from literature review to generate additional economic considerations to more comprehensively capture value of RM/ATs

Additional Economic Considerations

The considerations would allow HTAs & payers to better assess the net economic benefits of RM/ATs

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Inputs from HTA Models*

Population size
Small patient populations lead to higher prices to offset development costs

Lifetime horizon
Shifting focus from traditional short-term budgetary cycles to assess long-term cost-effectiveness

Patient indirect costs (during treatment)
Costs associated with loss of productivity

Patient & caregiver non-medical costs (during treatment)
Costs associated with transport, home care, counseling, etc.

Inputs from Literature Review

Age of onset
Younger patients will gain significantly larger value from curative treatments across all inputs

Additional value for curative nature
Modifying CE thresholds or budget impact considerations for curative therapies

Patient & caregiver indirect medical costs (lifetime)
Costs associated with loss of productivity

Real world evidence
Valuing subpopulation data, indirect comparisons vs. SoC, follow-up data, etc. from RWE

Innovative payment models / contracting**
Reducing payer uncertainty surrounding high cost / budget impact

Inputs from CAGT Center

Societal economic impact
Costs to employers, government, etc. due to loss of productivity and chronic care

Patient centered endpoints
Ascribing greater value to PCEs to better understand non-clinical / clinical benefit of RM/ATs for patients

Patient & caregiver non-medical costs (lifetime)
Costs associated with transport, home care, counseling, etc.

Although these inputs will help uncover additional value of RM/ATs, they will require different levels of resource investment and involve different stakeholders across health systems

**These inputs are derived from assessments conducted by HTAs, however they are not currently included in most HTA / payer approaches*
***Will not impact value of overall product, but will reduce budget impact and improve market access*

Health & Economic Impact Model

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1 OBJECTIVE

Characterize the ***health and economic impact*** of cell and gene therapies in terms of treatment, quality of life, cost and other impacts

2 APPROACH

Economic analysis using flexible & globally accepted DICE modelling framework **across multiple disease areas** to assess aggregate benefit

3

Globally relevant, annually updatable framework to assess impact of cell & gene therapy

WHY DO WE NEED THIS?

- **No credible, quantitative global impact argumentation is available** to move cell & gene acceptance & uptake where they need to go to be SOC
- **Currently, developers addressing an asset-at-a-time** across multiple markets with different approaches to cell & gene value assessment
- Following COVID-19, **acceptance may be even more challenging**:

"Given where we are with the pandemic and the impact on the economy, in the next 3-5 years there's going to be marked pressure on those employers still able to remain in business and what they're able to afford." – BCBS Medical Director

IMPACT FOR DEVELOPERS

Single quantitative framework for communicating impact of cell & gene therapy w/ one voice:

- **Aggregates impact across different disease areas**, w/o going to disease- or asset- level
- Focuses on **benefit and impact**; does not pivot on pricing
- Leverages **familiar, credible modeling method to reduce stakeholder heterogeneity** in cell & gene value assessment

DICE = Discretely Integrated Condition Event; AE = adverse event

Evidera | PPD

Top-Line Project Approach

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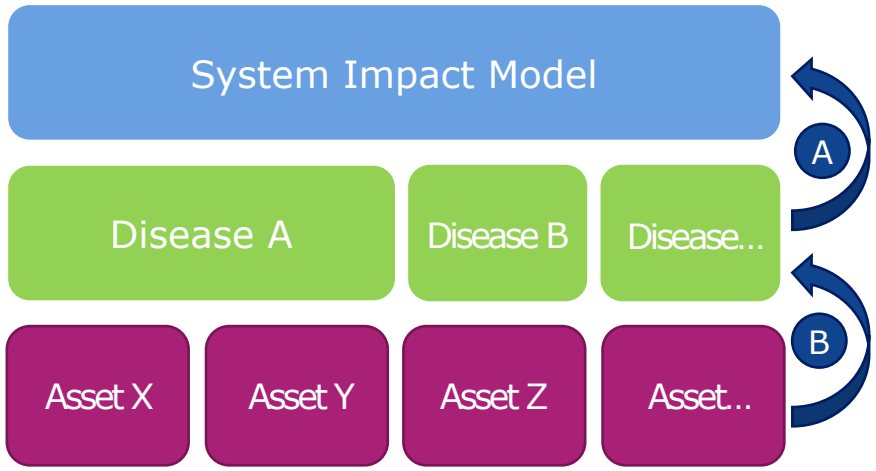
Process for getting to System Impact of Cell & Gene Therapy



Example Outputs:

- System/national level impact to society
- May include adaptation to state level
- Evaluation of key drivers of benefit
- Highlight early success stories
- Explore uncertainties in benefit assessment

Increasing standardization of RM/AT value assessment

- Leverage relationships built around DICE methodology to gain feedback from ICER, NICE, other EU HTAs on model standards and drive **greater consensus on uncertainty areas** of cell & gene value
- Leverage one voice + global analysis to help encourage changes to global assessment & reimbursement systems

- Leverages data from asset or disease models to flow SOC data into system impact model
- Focus: quantify benefits of transformative/curative therapy beyond current SOC
- Does not include asset or disease level "read out" from system impact model (they are only source of SOC data), but may include archetype level (e.g., slow progressing rare disease) "read out"
- System impact to be quantified at direct, indirect and humanistic impact level with qualitative discussion of other aspects of system impact

Evidera | PPD

Summary

- Cell and gene therapies provide an unprecedented durable therapeutic benefit to patients. The pipeline is robust and growing
- The upfront cost of these therapies can create a considerable burden for existing reimbursement practices, but early analysis show these therapies can provide significant economic benefits to patients, systems, and society over time.
- Adaptation of standard value assessments to the current realities of transformational therapies is critical to ensuring patients can access these life-changing therapies in a timely manner. This challenge exists across geographies and all payer types.
- New payment models like pay-for performance can facilitate the adoption of transformative therapies and address data gaps and uncertainties.
- Urgent need for solutions to mitigate barriers to patient access.

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Thank You!

These slides and the referenced ARM reports can be found at www.alliancerm.org

Along with additional resources:

- Quarterly sector data reports
- Upcoming near-term clinical trial milestones & data readouts
- Access to slides, graphics, and figures from ARM presentations
- Our weekly sector newsletter, a robust round-up of business, clinical, scientific, and policy news in the sector
- Commentary from experts in the field

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