Valuation of Regenerative Medicine/Advanced Therapies (RM/ATs): challenges and opportunities for creating a better framework

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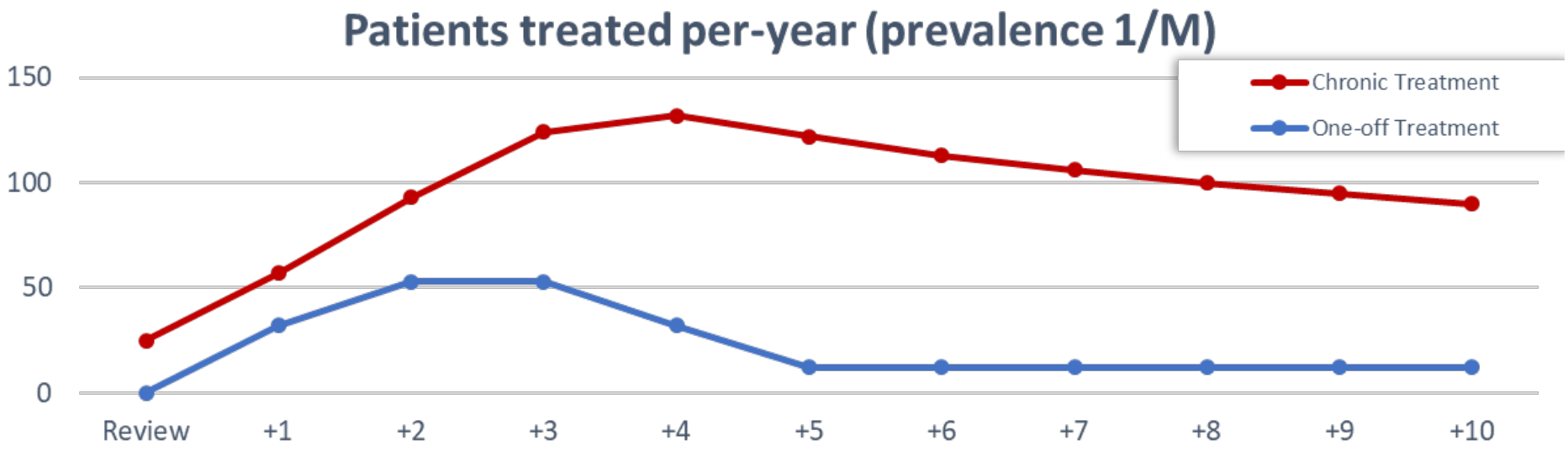
Overview

- Economics of Gene Therapy and other Advanced Therapies
  - Analysis from Diego Ardigo, Chiesi and Therapies Committee chair of IRDiRC
- Value Frameworks for Advanced Therapies and Regenerative Medicines
  - Analysis from IQVIA, ARM Foundation and CIRM project led by John Doyle (now at Pfizer)
- What does this mean for Pfizer and our evidence and access planning?
  - Me

Gene Therapy vs Chronic Treatments

Patients treated over time

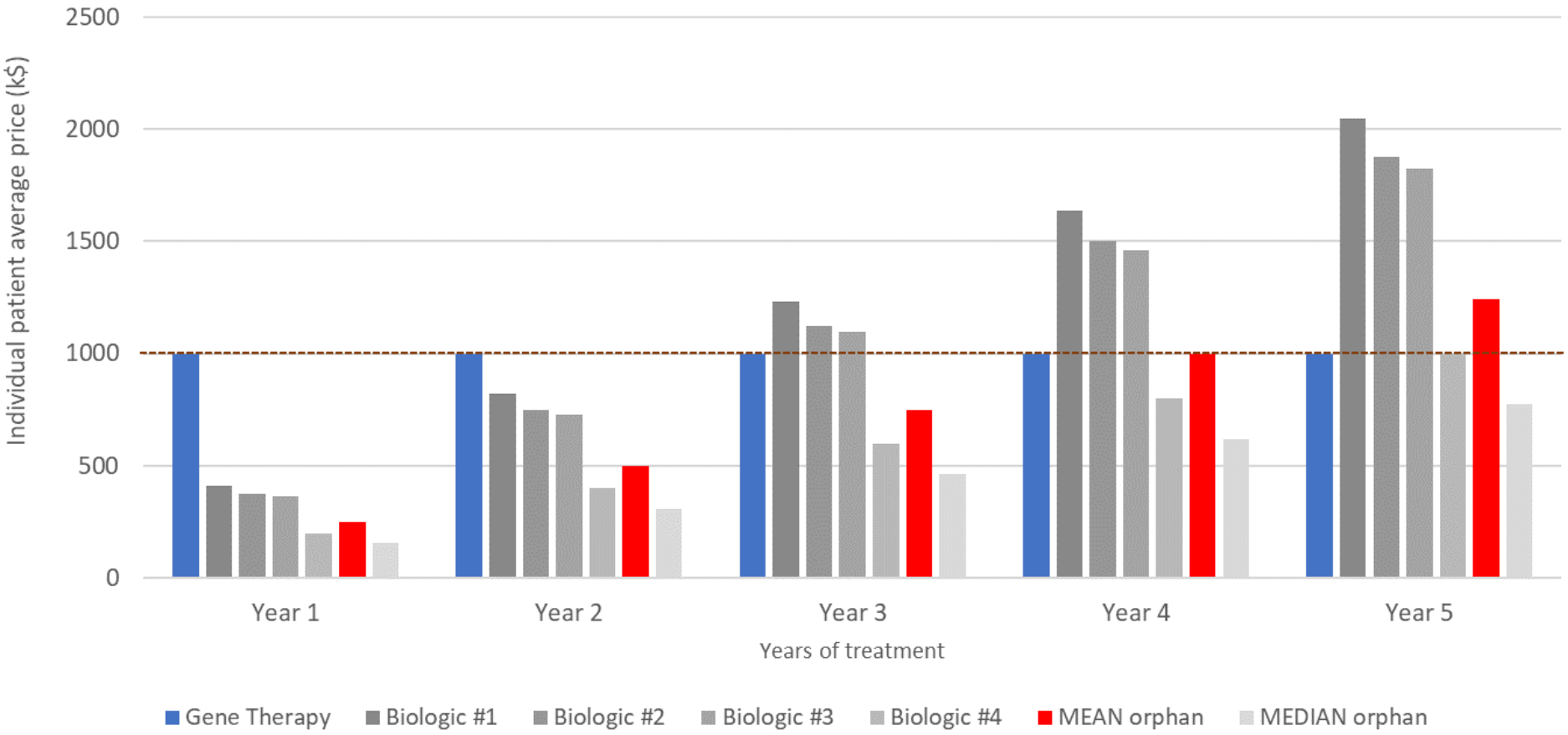


Key Assumptions

- Prevalence = 1 / million inhabitants (~500 prevalent cases in EU)
- Proportion eligible to treatment = 50%
- Eligible patients undergoing treatment = 50%
- Yearly incident cases = 1/10th of prevalent cases
- Adherence to treatment = 85% (drop out of 15%/ year)
- Prevalent cases treated within the 4th year from launch

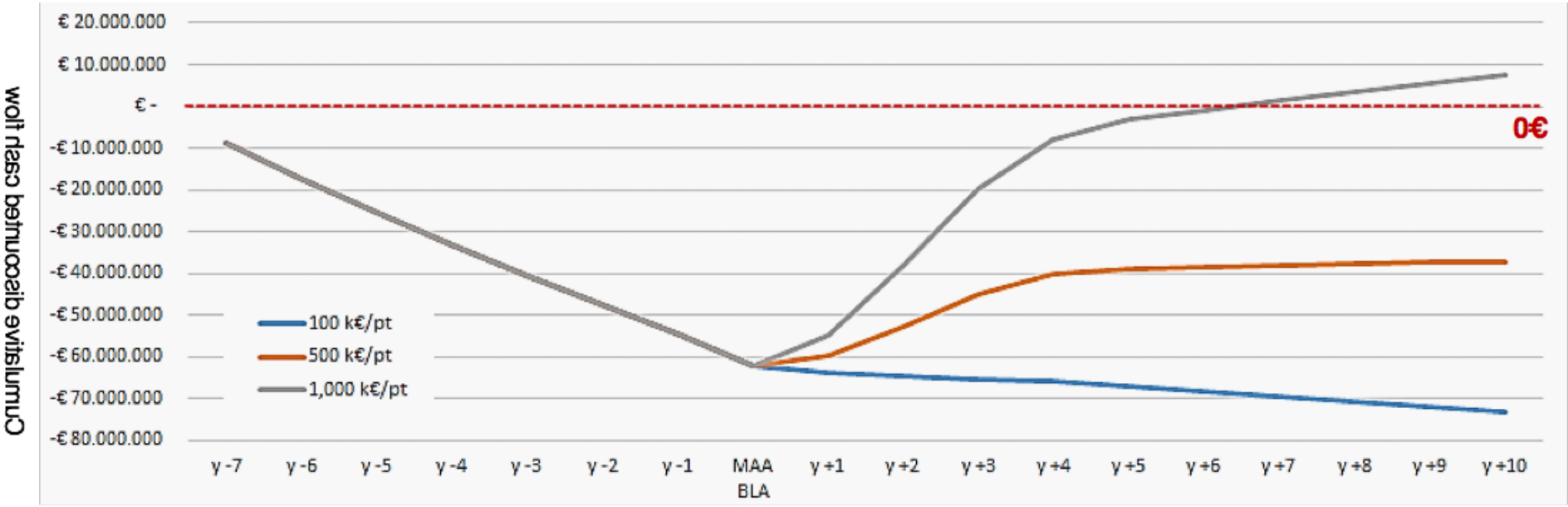
Gene Therapy vs Chronic Treatments

Spending per patient



R.o.I. for a Hypothetical ATMP

"Fictional example with unrealistically conservative cost assumptions"



Key Assumptions

Treatments → Prevalence = 1/M; Incidence = 1/10th of prevalence; Proportion of eligible = 50%; Eligible treated = 50%; Prevalent cases treated in 4 years from launch; No commercial expenses

Research and Development → 100M € pre-approval (all inclusive) [*TuftsCenter = 2.7B$; Prasad = 648M$]*; 7 years development; 1M €/ year after approval

Cost of goods = 50K €/ treatment **PRICE per-patient =** 100K € | 500K € | 1,000K €

DiMasi JA et al. J Health Econ. 2016 *Prasad V et al. JAMA Intern Med 2017;*

Value Frameworks for Advanced Therapies

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Advanced Therapies face specific challenges to demonstrate value to stakeholders

Patient / Caregiver

- Patients face **high access barriers** due to **enormous co-pays** for RM/ATs and **small number of accredited centers** for treatment

HTA / Payers

- Payers **skeptical** of **long-term clinical efficacy** due to **lack of statistically significant, head-to-head trials**
- RM/ATs often not cost-effective as payers typically **prioritize short-term, direct impact**; they **do not completely capture long-term, indirect / non-medical benefits** of RM/ATs
- Payer **3-5 year budgetary cycles cannot handle high upfront cost** of RM/ATs

Manufacturer

- Difficult to **demonstrate clinical superiority** as **small** target **patient populations** make it **difficult** and **expensive** to conduct **RCT**, **head-to-head** studies
- Difficult to **demonstrate short-term cost-effectiveness vs. non-curative comparators**

Providers / Hospitals

- **Lack of uniform assessment** of RM/ATs causes hospitals / providers to **struggle to obtain reimbursement**
- Hospitals **assume high financial risk** of RM/ATs due to **prolonged reimbursement timelines** caused by payers struggling to absorb budget impact of RM/ATs

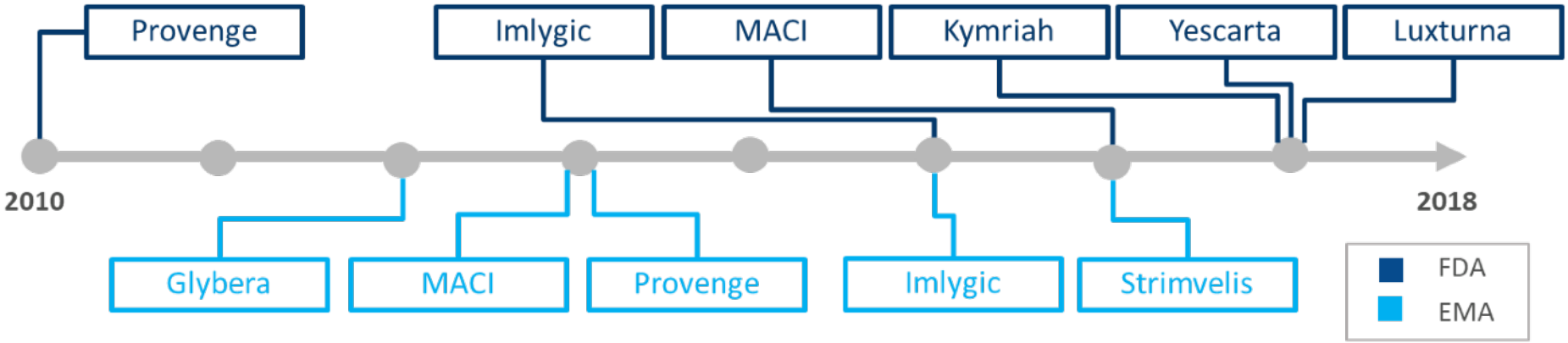
"First of Its Kind" Economic Impact Landscape Analysis of regenerative medicine advanced therapy. CIRM, ARM Foundation, IQVIA 2019

Case studies highlight some common problems

Many RM/ATs have struggled to meet market expectations due to challenges in value determination

Common challenges across RM/AT commercial success include

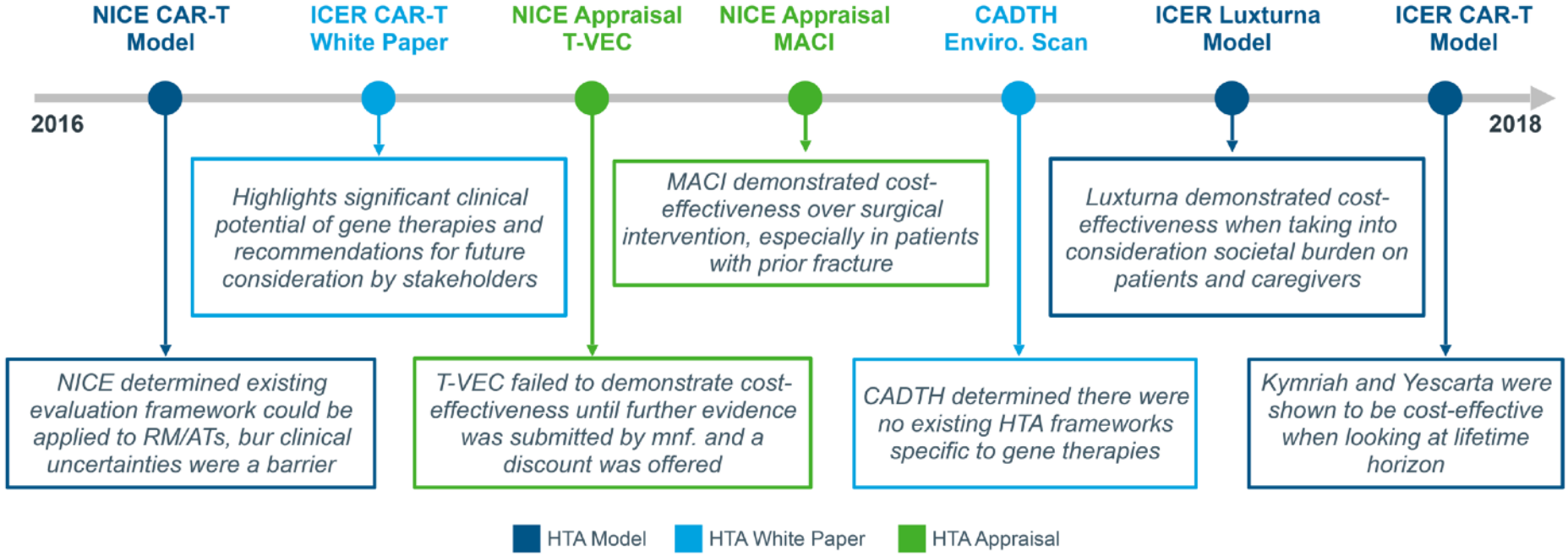
- Stakeholder scepticism of high upfront costs of RM/AT therapies with uncertain economic value
- Unclear models and inputs for economic assessments by regulators & payers
- Suboptimal patient access and reimbursement schemes compared to traditional therapies
- Unclear long term therapy benefit of potentially curative therapies



Adapted from "First of Its Kind" Economic Impact Landscape Analysis of regenerative medicine advanced therapy. CIRM, ARM Foundation, IQVIA 2019

No specific value frameworks for RM/ AT

Some initial appraisals and assessments of value have been conducted



HTA Reports & Appraisals

NICE and ICER cost-effectiveness models begin to demonstrate importance of expanding economic inputs taken into consideration during evaluation of RM/ATs

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What metrics are HTAs including for RM/AT?

Emerging efforts to demonstrate value by including a more comprehensive set of metrics on economic impacts

HTA Models and Economic Inputs				
Framework Inputs	**Pivotal Stakeholders**	**NICE CAR-T (2016)**	**ICER Luxturna (2018)**	**ICER CAR-T (2018)**
Cost of acquisition				
Healthcare utilization costs				
Population size				
Administration and monitoring				
Health-related QoL				
Lifetime horizon				
Hospital markup				
Innovative payment models / contracting				
Loss of productivity (during treatment)				
Nursing home care				
Caregiver burden				
Non-medical costs (during treatment)				

Patient and caregiver inputs are less commonly considered than other considerations

Providers / hospitals · HTA / Payers · Patient / caregiver · Manufacturer

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Different kinds of payment model have been critical to ensure access

Innovative payment models have been critical to help overcome HTA/payer uncertainties about high upfront costs

Payers skeptical of long-term efficacy of RM/ATs

- **Kymriah** — P4P contract with CMS
- **Imlygic** — P4P contract with NICE
- **Strimvelis** — P4P contract with AIFA
- **Luxturna** — P4P contract with Harvard Pilgrim and Express Scripts

Manufacturers are guaranteeing clinical efficacy of their products through outcomes-based contracting agreements

Payers unable to absorb large budget impact of high-cost RM/ATs

- **Luxturna** — Annuity-based contracting model with CMS, with payments tied to outcomes

Spark is reducing budget impact by allowing CMS to spread payment over several years

Although innovative contracting and payment models reduce payer skepticism and budget impact, issues remain:

- *Lack of infrastructure to track patients and link clinical outcomes to claims*
- *Innovative payment models reduce immediate budget impact and/or spread risk but do not improve long-term sustainability*

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Role of real world evidence generation

Real world evidence generation will play a key role in reducing stakeholder uncertainty over long-term effectiveness and safety

Historical Challenges – examples include

- Insufficient comparative clinical data with SoC to differentiate
- Poorly established natural progression of disease
- Failure to identify sub-populations where benefit may be greater

Historical Successes – examples include

- RWE leveraged to identify natural progression of disease and burden of illness in patients
- RWE used to highlight significant benefits to patients where only single arm trial data available

Application of RWE Strategies to RM/ATs

Retrospective data analyses

- Define historical treatment landscape, patient journey, burden, and generate data for SoC/ comparators
- RWE will characterise how product will address disease burden and fulfil gaps in treatment, differentiating it from SoC

Prospective observational studies (cohort)

- Track safety and effectiveness before, during and after treatment of patients
- Identify potential subpopulation benefits to differentiate product
- Demonstrate durability of effect and safety after launch

Registry studies

- Continue to demonstrate real-world durability of effect/safety
- Capture outcomes to support innovative payment models/contracting agreements
- Identify potential sub-populations and follow-on indications

Adapted from: First of Its Kind" Economic Impact Landscape Analysis of regenerative medicine advanced therapy. CIRM, ARM Foundation, IQVIA 2019

Emerging conclusions from landscape analysis

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Inclusion of additional economic considerations will allow HTA/payers to better assess the net economic benefits of RM/ATs

Inputs from HTA Models*	Inputs from Literature Review	Inputs from CAGT Center
Population size *Small patient populations lead to higher prices to offset development costs*	**Age of onset** *Younger patients will gain significantly larger value from curative treatments across all inputs*	**Societal economic impact** *Costs to employers, government, etc. due to loss of productivity and chronic care*
Lifetime horizon *Shifting focus from traditional short-term budgetary cycles to assess long-term cost-effectiveness*	**Additional value for curative nature** *Modifying CE thresholds or budget impact considerations for curative therapies*	**Patient centered endpoints** *Ascribing greater value to PCEs to better understand non-clinical / clinical benefit of RM/ATs for patients*
Patient indirect costs (during treatment) *Costs associated with loss of productivity*	**Patient & caregiver indirect medical costs (lifetime)** *Costs associated with loss of productivity*	**Patient & caregiver non-medical costs (lifetime)** *Costs associated with transport, home care, counseling, etc.*
Patient & caregiver non-medical costs (during treatment) *Costs associated with transport, home care, counseling, etc.*	**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*	

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

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What does this mean for evidence and access planning?

1. For many rare diseases where RM/AT could transform lives, manufacturers will have little pricing flexibility

- Crunch times for economic viability will often be in a few early years immediately after launch
- We need to be really sure as a community that we have ways to properly and fully assess value or investment may go elsewhere

2. Landscape analysis has identified some positive changes that could be made in the following areas:

- Valuation frameworks and inclusion of new metrics including patient centric measures;
- Contracting & payment models; and
- Evidence generation, esp RWD.

3. Some issues that arise are familiar statistical and evidence quality questions around small populations and RWD. Others feel rather new and may have aspects specific to RM/AT:

- Lifetime horizon; and
- Patient end points beyond impacts on clinical measures or health system utilisation.