Will regenerative medicines (RMs) change the way we evaluate evidence, determine value, and fund innovation?

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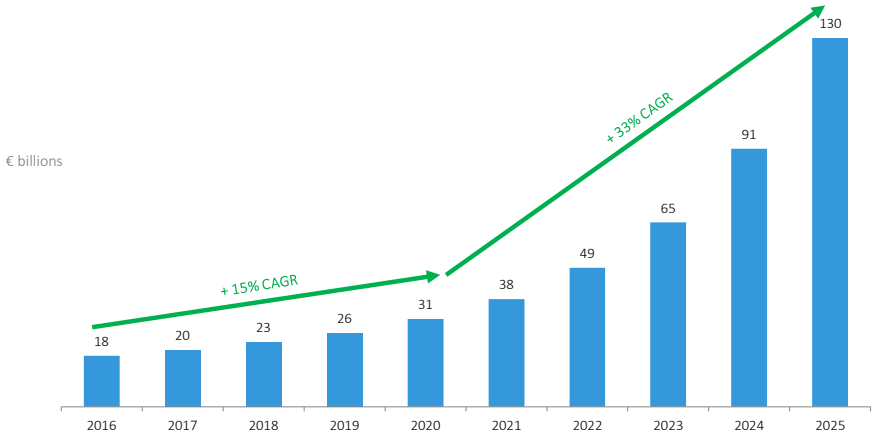
RM market substantial, growing; growth expected to accelerate

Global regenerative medicine market volume & expected growth, 2016-2025



There are currently 985 trials involving 287 gene or cell therapies, including 82 Phase 2/3 or 3 trials involving 44 therapies

Abbreviations: RM = regenerative medicine, CAGR = compound annual growth rate
Column chart source: Roland Berger, Focus: Regenerative Medicine, September 2017
Pipeline statistics source: Citeline search conducted 4 October 2018

However, PRMA outcomes and uptake challenging to date

- ***Regulatory.*** 2010 FDA approval, 2013 EMA approval
- ***HTA/payer.*** DE: "unquantifiable added benefit" from IQWiG; UK: not cost-effective
- ***Commercial.*** Uptake extremely low due to: price (US: $93K per course), uncertainty about reimbursement, complex administration, manufacturing issues, launch of Zytiga & Xtandi → 2015 Dendreon bankrupt
- 2015: EMA approval withdrawn at request of Dendreon
- 2018: US share very low (7-8%) despite access

- ***Regulatory.*** 2012 EMA approval; Chisei decided FDA requirements were too onerous
- ***HTA/payer/commercial.*** FR: SMR insufficient; DE: hospital product, 1 sick fund paid €900K for 1 patient; elsewhere in Europe: not reimbursed / commercialized
- 2017: Chisei decided to allow MAA to expire

2009 2010 2011 2012 2013 2014 2015 2016 2017 2018

- ***Regulatory.*** 2015 EMA & FDA approval
- ***HTA/payer.*** UK: CE with PAS & restricted beyond label; DE: IQWiG & G-BA no added benefit; ES: reimbursed; /FR/IT: no agreed price yet / not marketed; US: access
- ***Commercial***. Intra-tumoral admin. insufficient for visceral lesions → disease progression → modest sales, behind CPIs as monotherapy → studying in combo with CPIs…

- ***Regulatory.*** 2016 EMA approval
- ***HTA/payer.*** IT: innovative, pay €594K-by results, installment payment; UK: NICE HST positive, 5-year budget impact ~ £2.4 M; FR/DE/ES not yet assessed
- ***Commercial***. Only offered at 1 center, in Milan; handful of patients treated; sold by GSK to Orchard

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Note: not exhaustive of all RMs with regulatory approval; illustrative only

For debate: HTA/payer approach to evidence evaluation will change

- Increasing acceptance of adaptive trial designs?
- Increasing acceptance of surrogate endpoints (e.g., MRD, PFS 2)?
- Increasing acceptance of modified intent to treat analysis (e.g., CAR-T)?
- Increasing payer use of RWE, to confirm claims of "cure," e.g., to update beliefs about product with only single-arm, open-label Phase 2 trial?

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For debate: methods of value determination will change

- Increasing focus on budget impact, shifting away from use of ICER threshold?
- Increasing utilization of indication-based pricing?
- "Academic" products, not industrial products, used as price benchmarks (e.g., CAR-Ts)? How can this be stopped if it's one shot?
- Increased expectation that manufacturers will assume/accept financial risk (e.g., CAR-T cell therapy produced for patient who dies before infusion)?
- Precision medicine, cream skimming and 'social contract': is there a fix?
- What if a one-shot RM replaces a chronic drug therapy (e.g., haemophilia)? Is there a "value formula" (e.g., price of one shot = price of x years of chronic therapy)?

For debate: funding pathways will change

- In multiple-payer markets like US and DE, single taxpayer-funded risk pool could be an option
- Legal barriers to flexible contracting may fall (e.g., Medicaid best price, restrictive German laws)
- Will New DRG/HRG/T2A be developed and set to incentivize use of "academic" cells, putting massive pressure on "industrial" cells?
- Will HTA bodies evolve from considering some therapies to be drugs, to considering them to be procedures (e.g., CAR-Ts)? (e.g., in DE, allowing bypass of national HTA process in favor of contracting between company and sickness funds)?