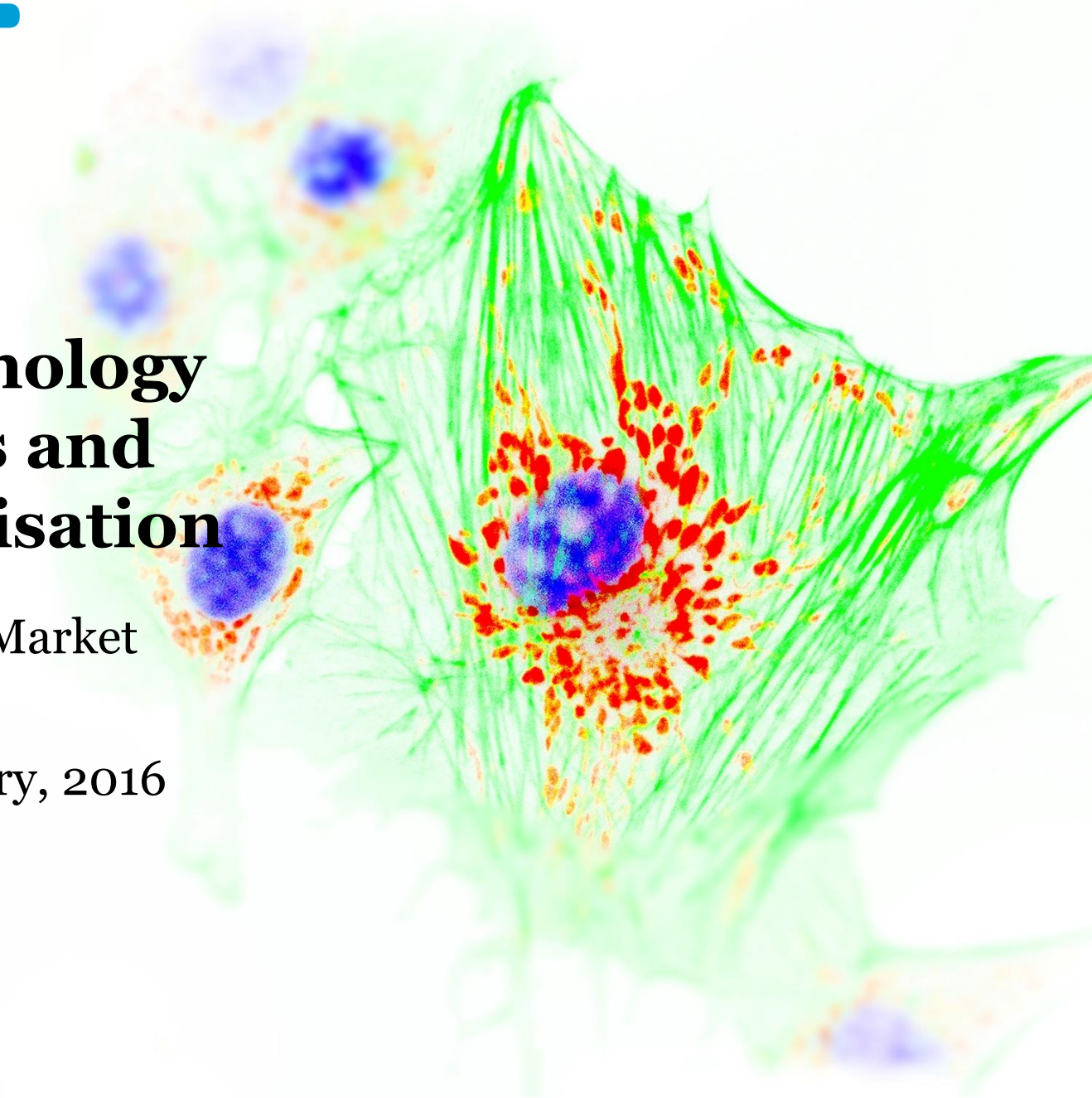
CATAPULT
Cell and Gene Therapy



Health technology assessments and commercialisation

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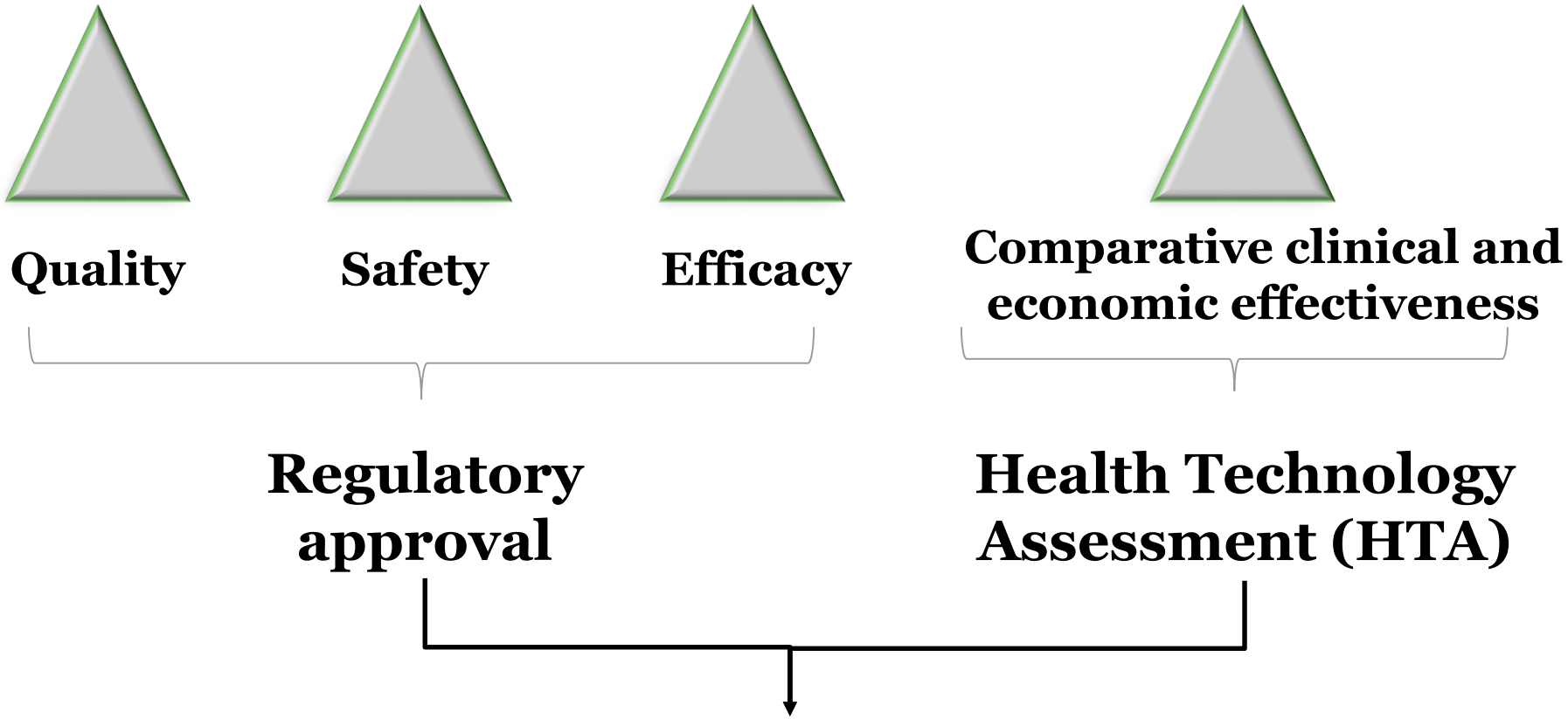
London, 23 February, 2016

Two hairy hurdles, one overall objective – therapy adoption



Understanding HTA methodologies and stakeholders is crucial for therapy adoption

- Some central concepts in ensuring therapy adoption:
  - What are the structural features of the healthcare system?
    - Existing funding mechanisms, available infrastructure (both in terms of diagnostics, skills and technology needed for delivery), etc?
    - Who makes the decisions?
      - At national level, regional level, local level?
  - What evidence do they base their decisions on?
    - Improvement in efficacy vs. the existing standard of care (SOC)
    - Health economics: Cost-effectiveness (cost-utility), budget impact, etc?
      - Threshold values?
  - What grade of evidence will demonstrate the greatest product value?
    - Trial design (endpoints, size, control vs. one-arm), magnitude of benefit, statistical significance, etc?
  - How does regulatory status, indication or therapeutic positioning impact the reimbursed price potential?

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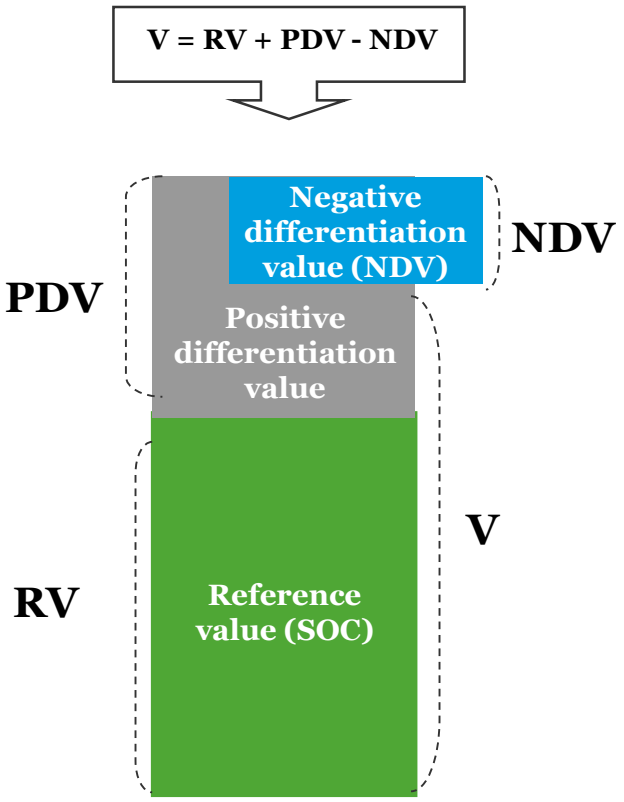
Value-based assessments link price potential to the novel therapy's added value

PRINCIPLES OF VALUE-BASED ASSESSMENTS



Differentiating Value

- Added value defined in terms of clinical and economic terms
- Comparative data against the SOC **per country** is required:
  - Gold-standard: H2H RCT
  - Indirect comparisons can be leveraged
  - Comparative evidence can be based on modelled data to address e.g.
    - Trial imbalance (observational vs. RCT)
    - Treatment switching/cross-over
    - Extrapolations
- For a given indication, "V" varies depending on therapeutic positioning

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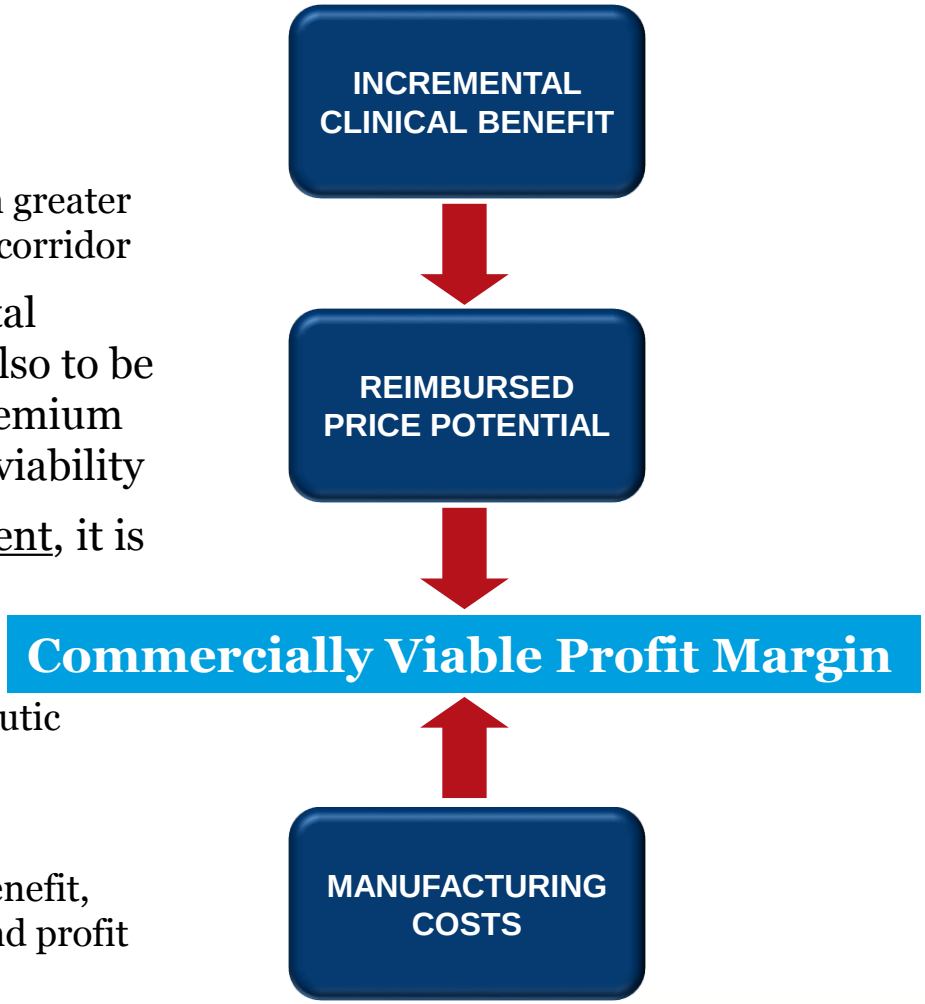
The high cost of ATMPs necessitates earlier consideration of reimbursement matters

- For small molecules demonstration of statistically and clinically significant improvement over SOC could suffice
  - Lower manufacturing costs provide much greater flexibility over commercially viable price corridor
- However for cell therapies the incremental benefit not only has to exceed MID but also to be proportionate to the substantial price premium (over the SOC) required for commercial viability
- Prior to embarking on clinical development, it is important to understand:
  - Room for innovation
  - Value maximising indication and therapeutic positioning
  - Key HE drivers to inform TPP
  - Interrelationship between incremental benefit, reimbursed price, manufacturing costs and profit margins
- Inform clinical and manufacturing strategy
- Ongoing re-assessment as evidence is generated



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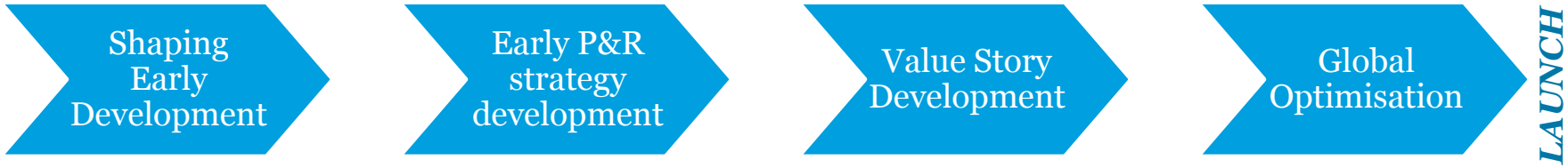
Planning for reimbursement should start prior to clinical development



- Early HE analysis
  - Identification of clinical and HE value drivers
  - Room for Innovation
  - Indication and therapeutic position prioritisation
- Identify incremental benefit and manufacturing cost thresholds
- Define TPP; plan evidence generation to substantiate claims
- Go/no-go criteria for the "stage-Gate" process

Planning for Reimbursement

- Engagement with key market access stakeholders to explore:
  - Key value drivers
  - Likely positioning, pricing, & reimbursement
  - Supporting data requirements
- Develop Value Story
  - Test credibility and impact
- Address evidence gap between RCT data and value proposition
  - Modelled data
- Finalise HE models
- Develop Value Dossier
- Identify price corridor:
  - Revenue maximising price per market
  - International price referencing
  - Launch sequence
- Contingency planning and risk-sharing schemes
- Planning for post-launch evidence generation