New Targets for Innovative Diagnostics and Treatment

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Introduction

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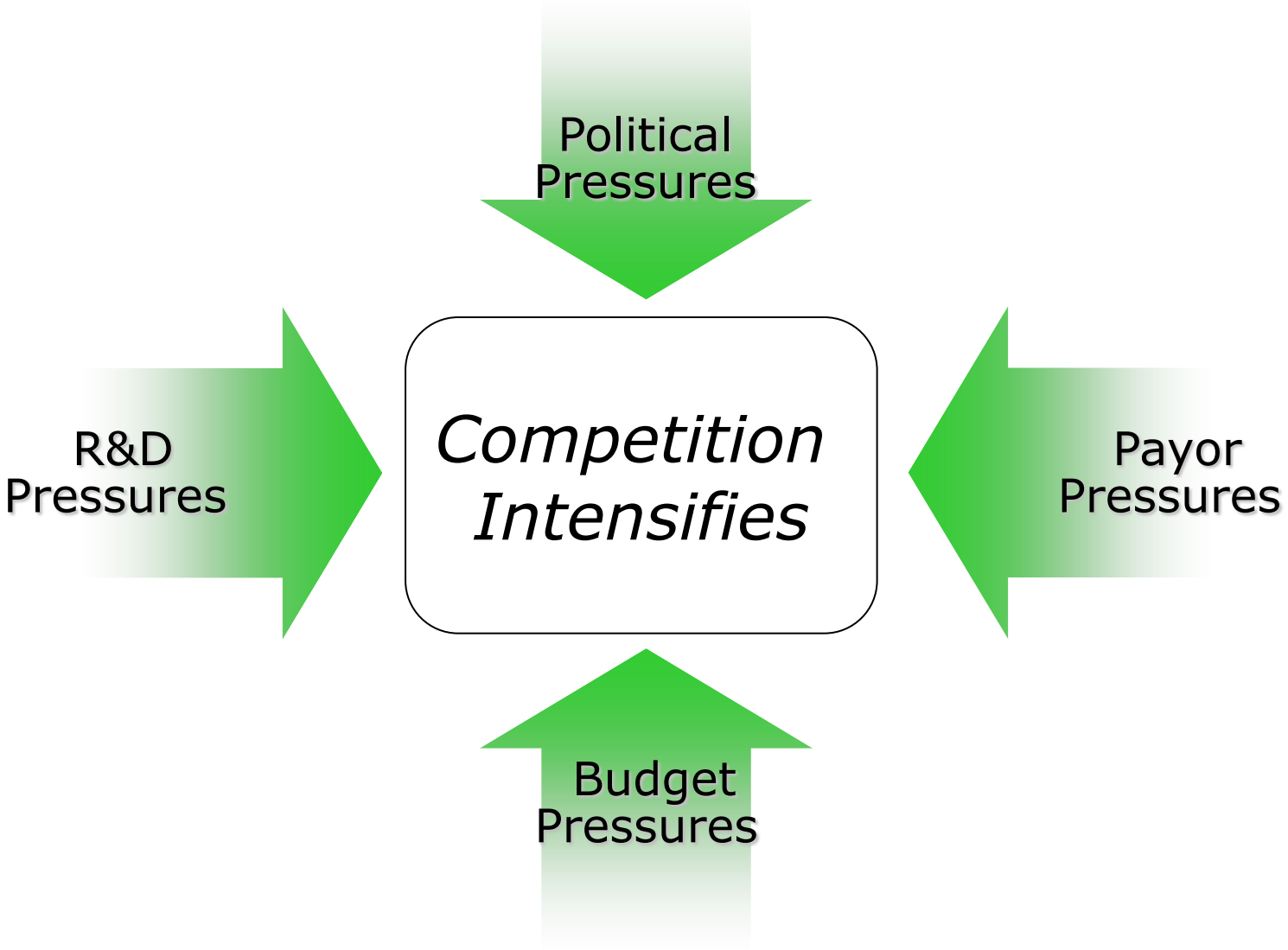
Hanna, living with Epilepsy

The pharmaceutical industry faces rising cost containment and increasingly demanding payers



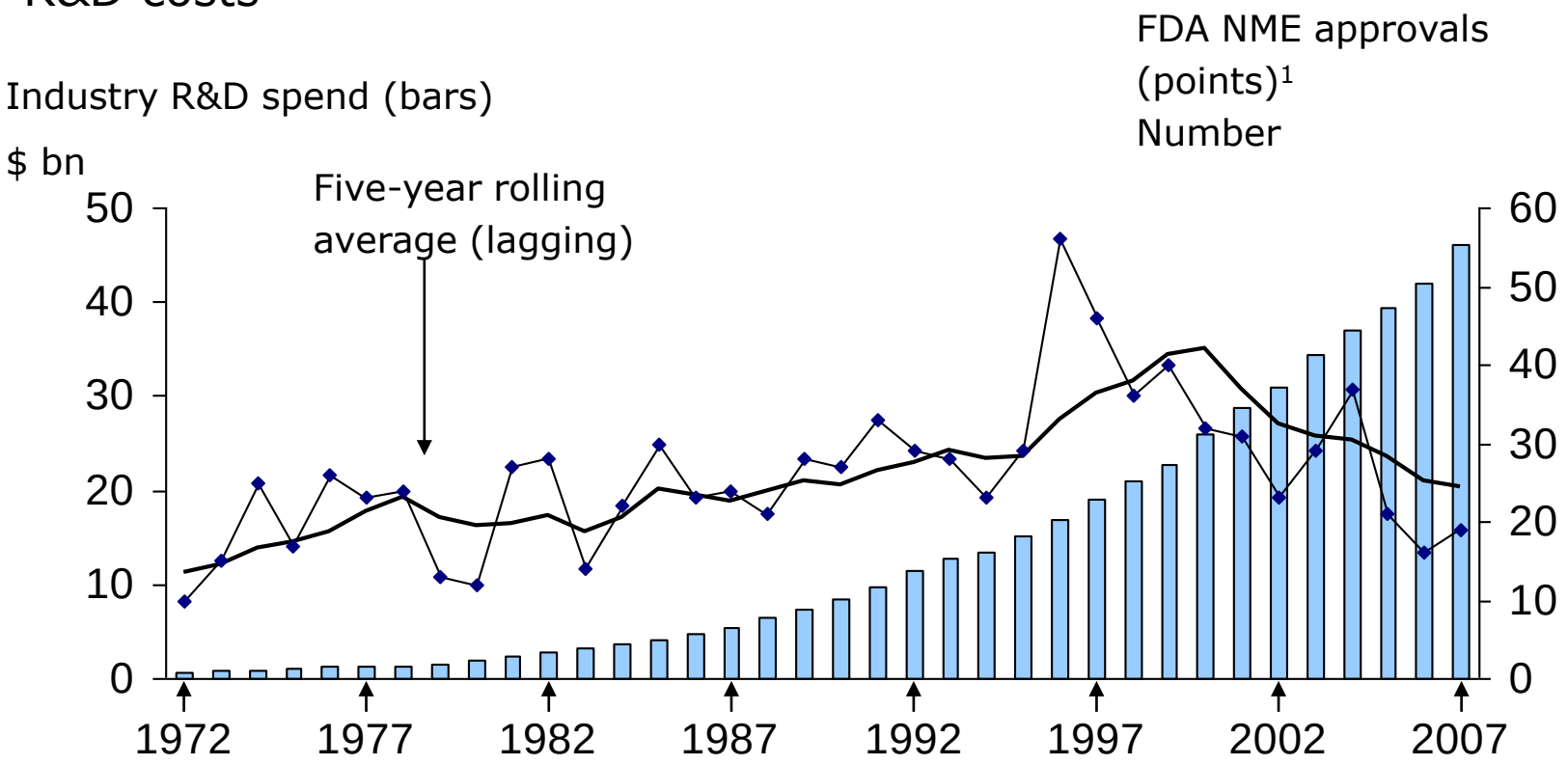
The Future Business Perspective of the Pharmaceutical Industry

Focus on diseases with strong value proposition and high likelihood for successful execution of R&D

- **Strong value proposition:**
  - High unmet medical need
  - Significant promise for superior efficacy compared to standard of care
- **Successful execution:**
  - Novel, validated and drugable targets
  - Predictive value of preclinical models
  - Availability of relevant biomarkers
  - Viable patient population for clinical trials
  - Robust and registerable endpoints

R&D spend of the pharmaceutical industry is increasing exponentially, but FDA approvals are not …

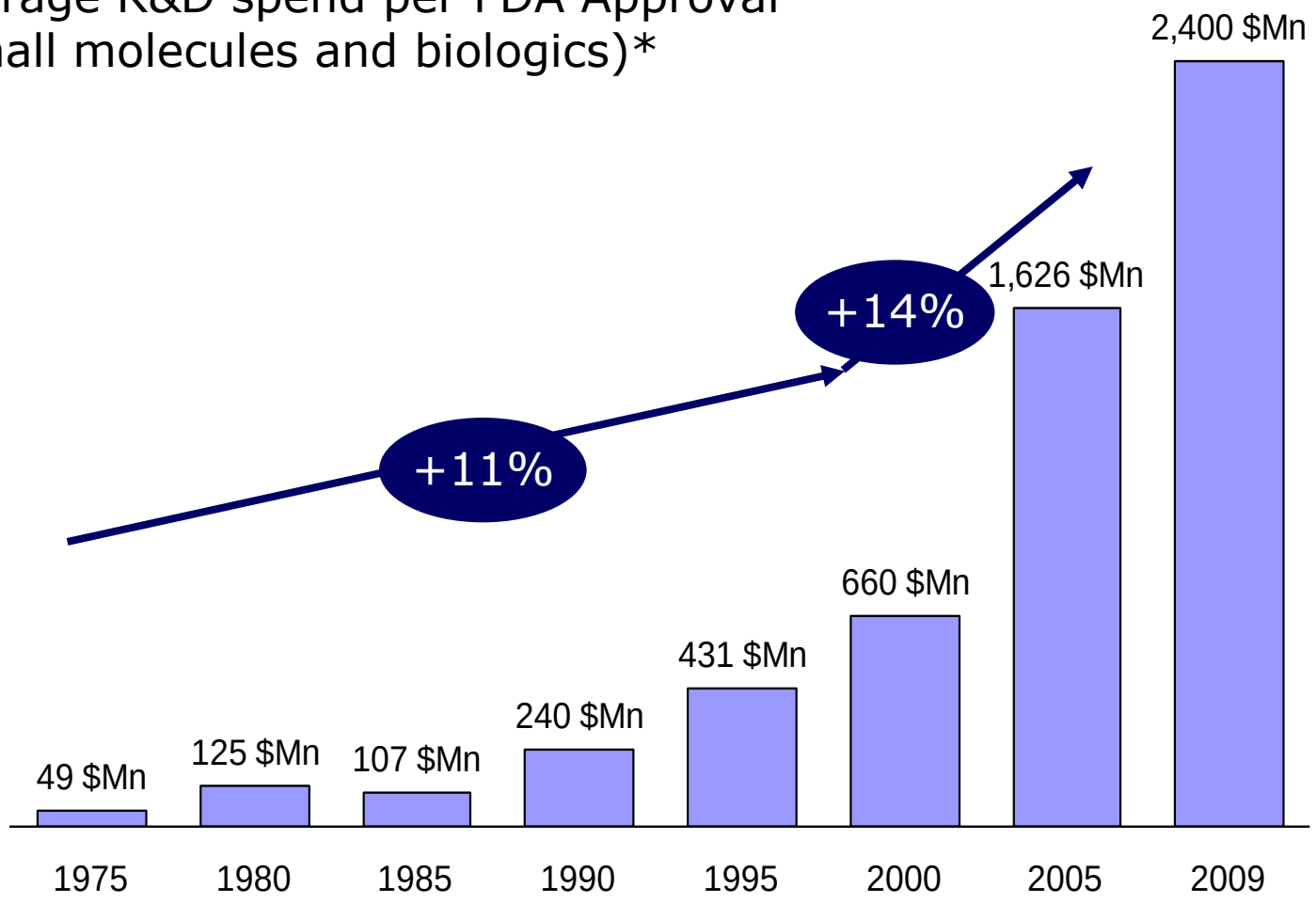
NME approvals over the last 30 years driven by exponential growth in R&D costs



1. Includes NCEs and BLAs. BLAs include 1986 onward; biologics approvals in prior years assumed negligible
Source: Peltzman, *in Journal of Political Economy* v. 81, no. 5; P.B. Hutt, Health Affairs ; Parexel, *Pharmaceutical R&D Statistical Sourcebook* 2007/2008; Food and Drug Administration; Pharmaceutical Research and Manufacturers of America

Significantly increasing average R&D spend per new therapy of the pharmaceutical industry

Average R&D spend per FDA Approval
(small molecules and biologics)*

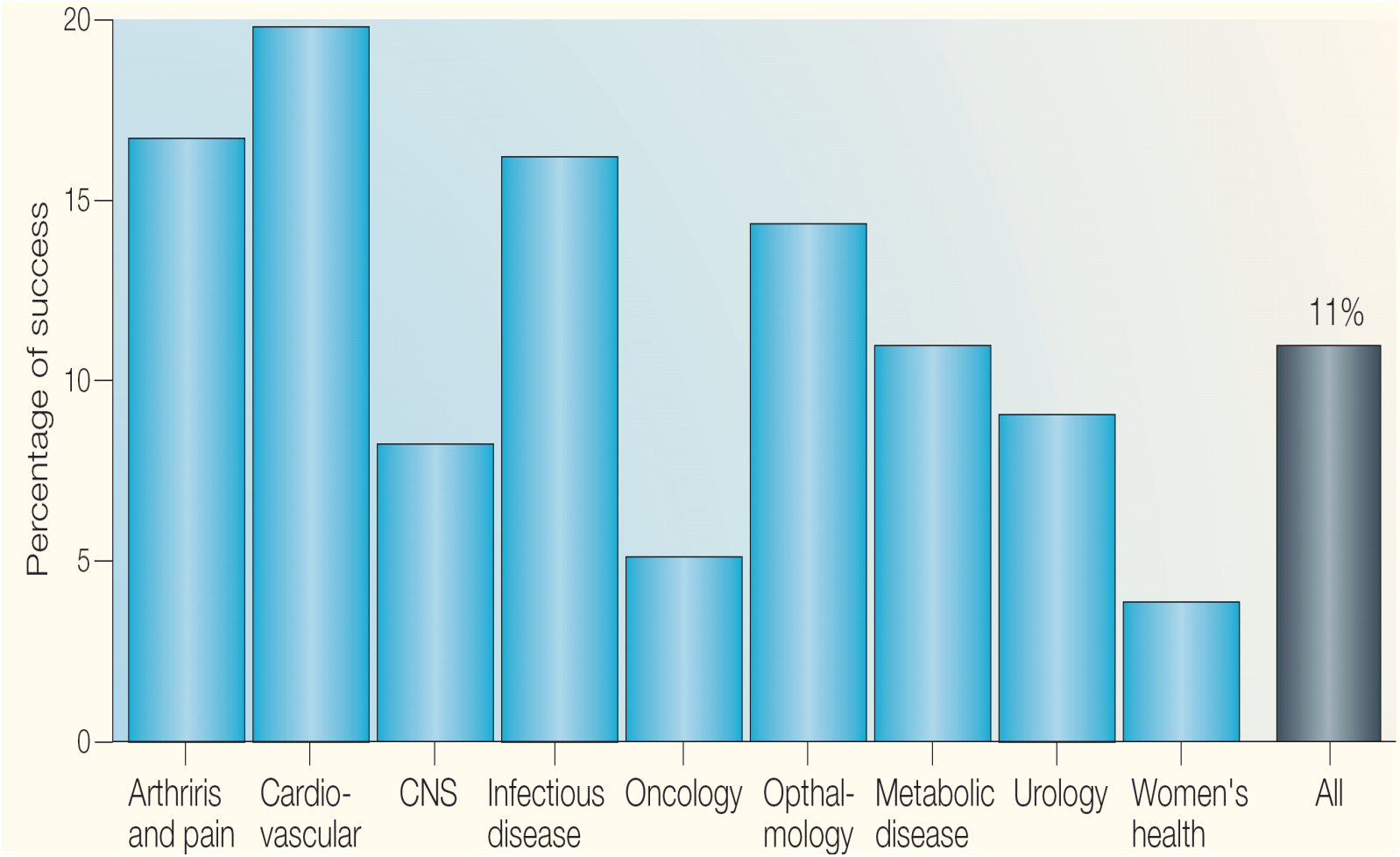


* Average R&D spend per NME defined as 5 year lagging average R&D spend divided by sum of present period NME and BLA approvals

Note: Biologics included only from 1986 onward, biologics approvals assumed negligible in prior periods

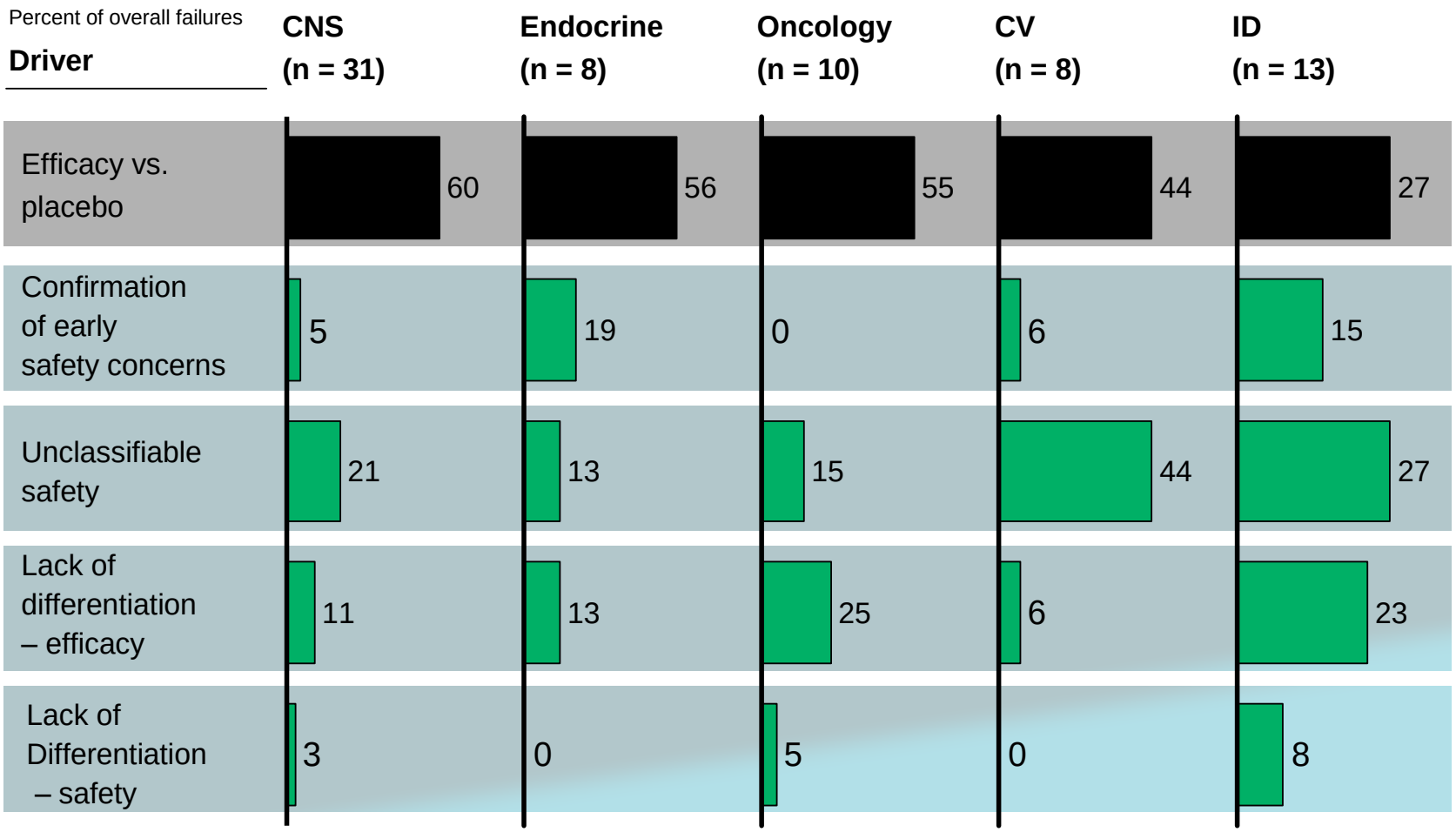
Source: McKinsey analysis, NME data from multiple publications and statistical sourcebooks Industry R&D spend data from the Pharmaceutical Research and Manufacturers of America, PhRMA Annual Membership Survey, 2006.

Attrition is an issue the pharmaceutical industry needs to address, especially in some therapeutic areas



Ismail Kola & John Landis (2004). *Nature Reviews: Drug Discovery 3 : 711 - 715*

Root causes of phase III failures vary by TA, but still largely an efficacy issue



Note: All figures are rounded

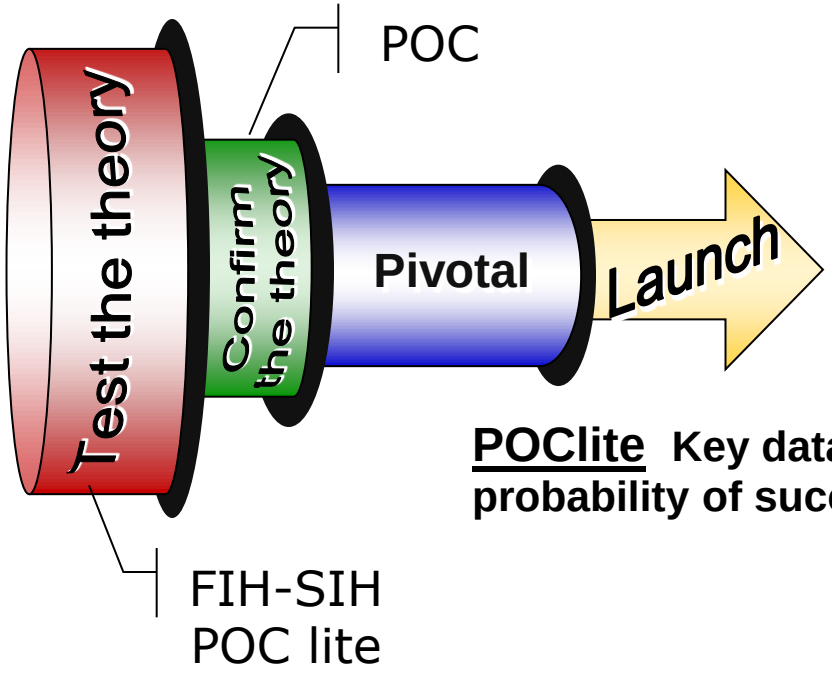
Source: McKinsey; Evaluate; Pharmaprojects; Factiva; PubMed; literature search; team analysis

Future AED discovery – based on novel and validated targets

- Target identification by creative scientists taking inspiration from ...
  - existing and novel hypotheses (transporter, target, network,...)
  - research on genetics, transcriptomics and epigenetics
  - mechanisms from other therapy areas
  - emerging technologies

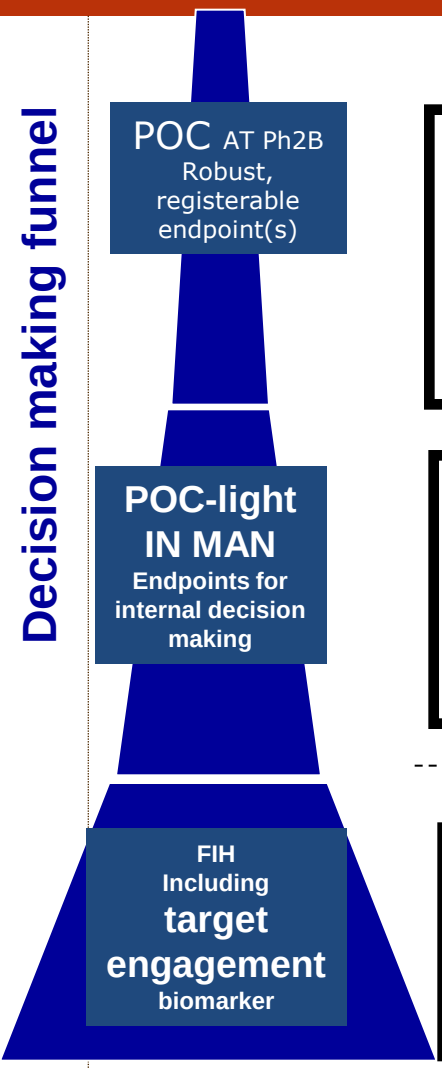
- Proof of concept studies providing target validation using genetic and pharmacological validation

Future AED development – continuum of proof of concept approaches important to de-risk evelopment



POClite **Key data that de-risks the project and increases probability of success**

Future AED development – relevant biomarkers key to increase probability of success



Type: 6	Readout/surrogate biomarker for Regulatory endpoint
Type: 5	Readout/biomarker of a clinical benefit
Type: 4	Readout/biomarker of disease activity
Type: 3	Physiological System or Biological Process downstream from target
Type: 2	Exposure: in the right tissue
Type: 1	Target engagement activity*

Biological Effect Biomarkers and/or clinical readouts

Target/Drug Specific

* Or as proximal to the target/drug interaction as possible

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Key to address remaining unmet medical need in epilepsy!