Addressing attrition in neurosciences

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Inspired by patients.
Driven by science.

Disclaimer and safe harbour

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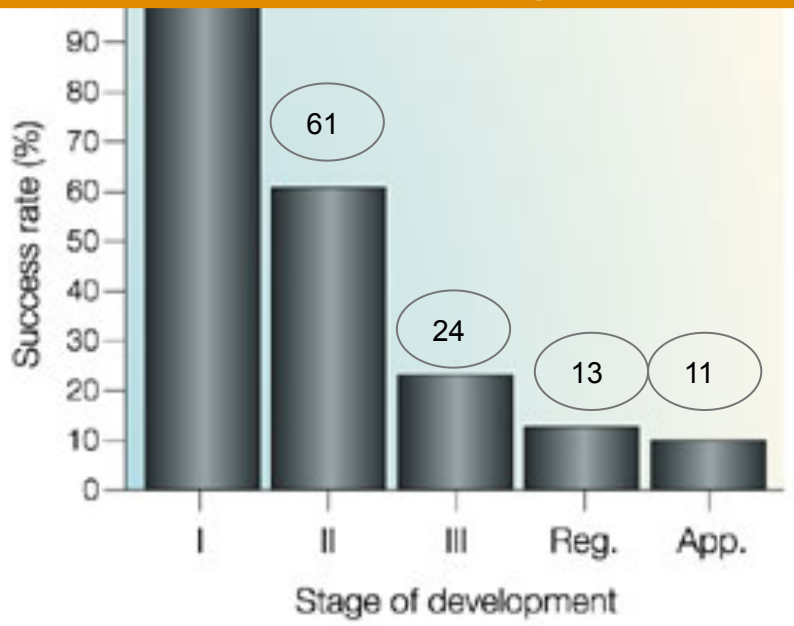
Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical pricing and reimbursement.

Inspired by **patients.**
Driven by **science.**

The pharmaceutical industry has certainly been effective…but not efficient in either regulatory or commercial terms

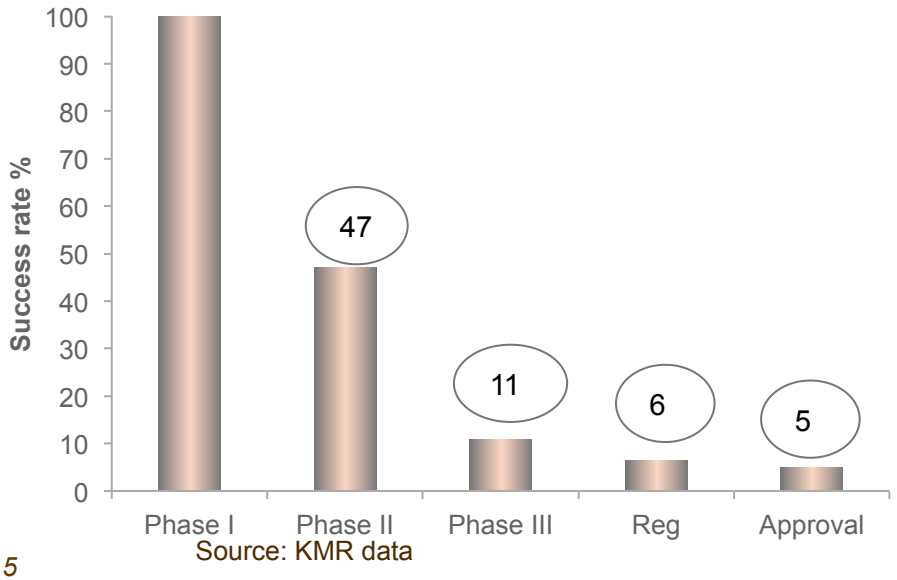
Regulatory success

1990-1999: 43% of Phase III trials fail
11% of Phase I molecules gain approval



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

2006 -2010: 54% of Phase III trials fail
5% of Phase I molecules gain approval



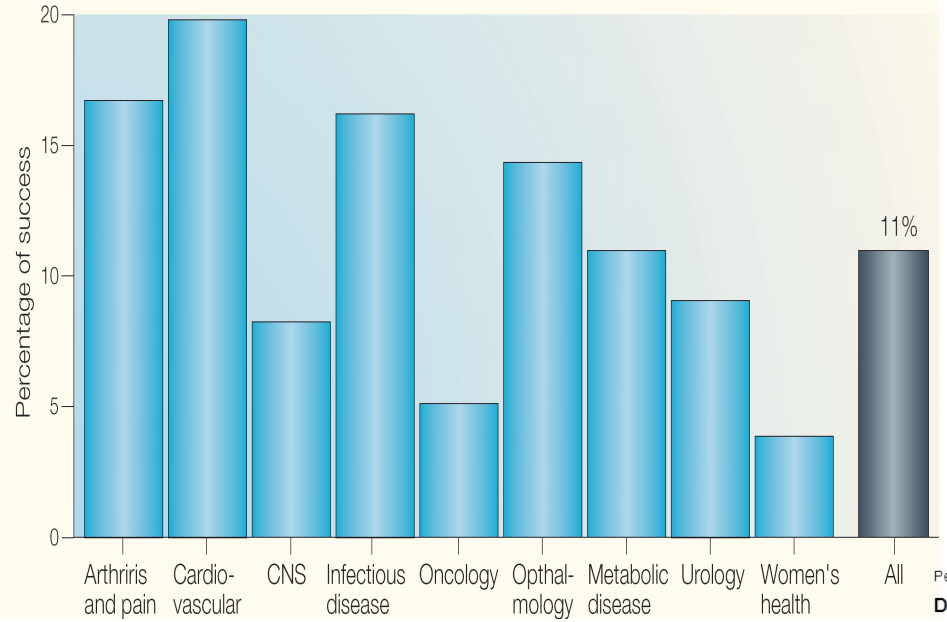
Source: KMR data

Meanwhile development costs continue to rise exponentially

And **commercial success** remains a challenge: even in the 90s only 30% of products recouped their initial investment

# of successful compounds from original 100 in Ph 1

Attrition is an issue our industry needs to address, especially in some therapeutic areas such as CNS



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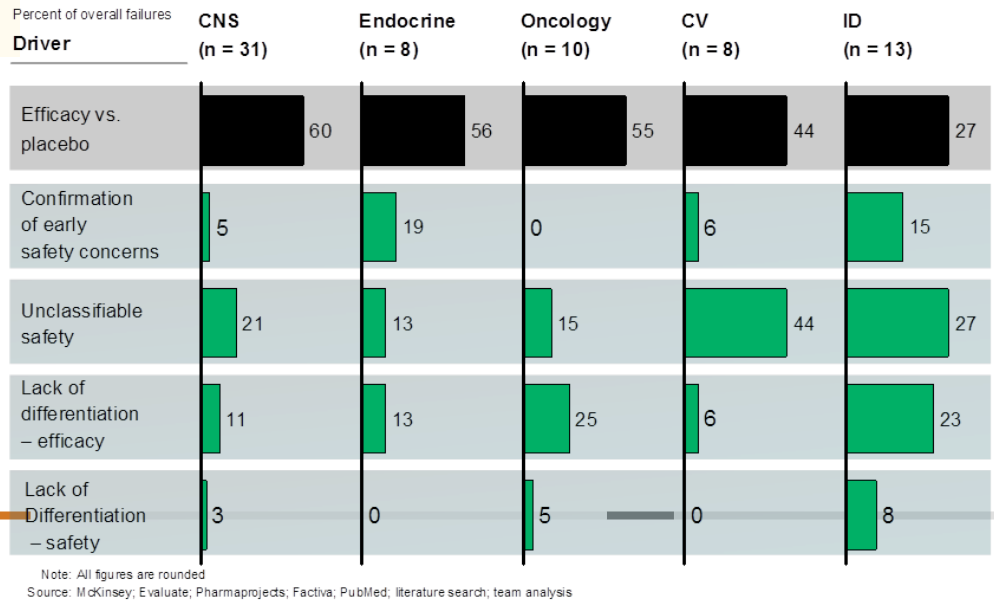
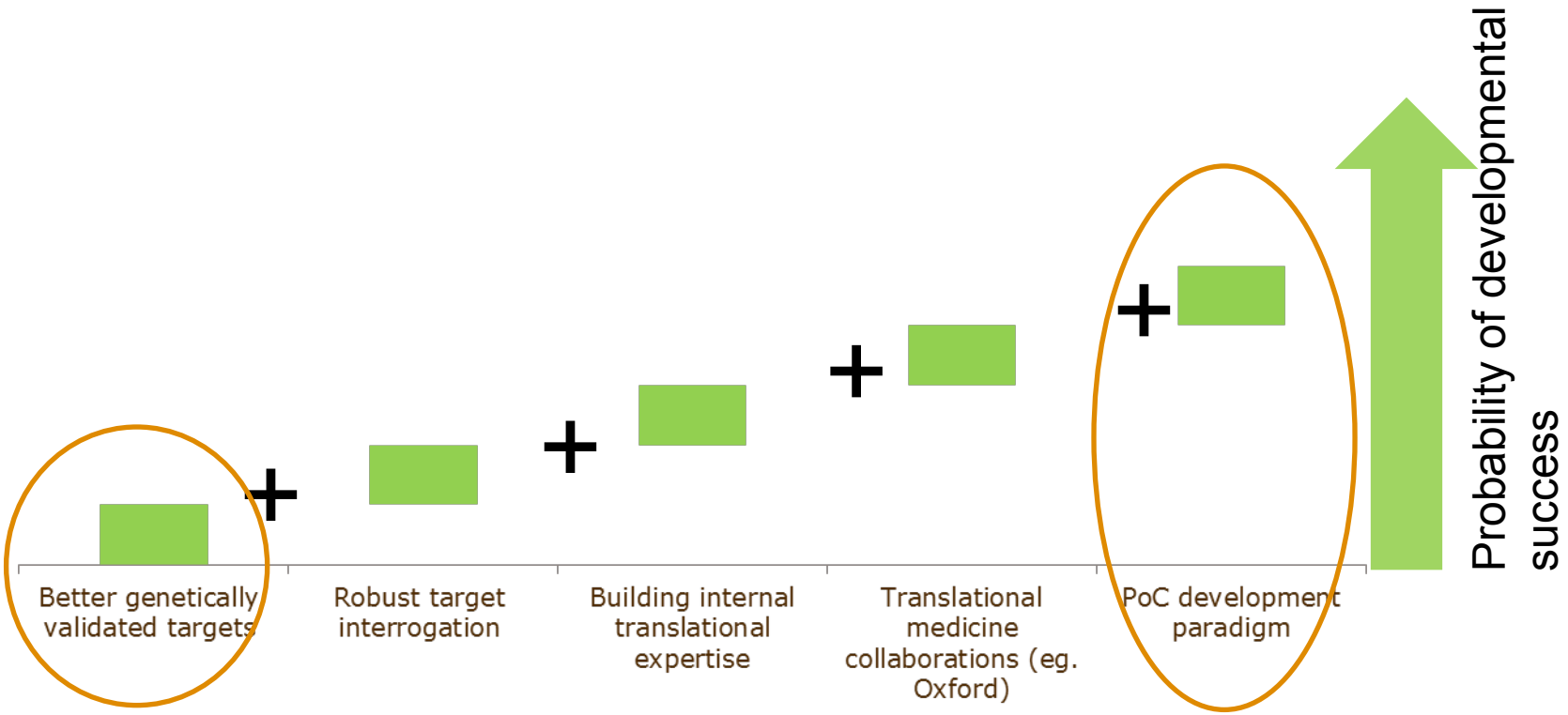


Source: McKinsey analysis

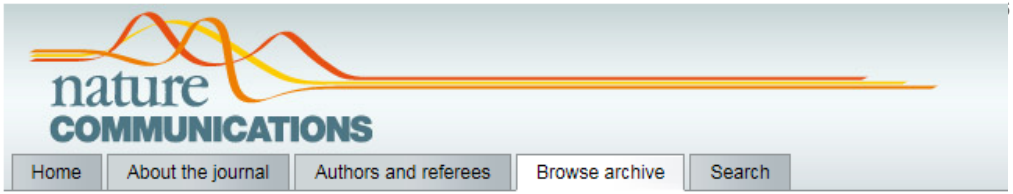
Levers to pull to reduce attrition rates



Actions to improve probability of success of innovative targets

Right target → Right molecule → Right indication → Right patient

Lever 1: Better genetically validated targets



Systems genetics identifies Sestrin 3 as a regulator of a proconvulsant gene network in human epileptic hippocampus

ORIGINAL RESEARCH ARTICLE | Genetics inMedicine

Open

Whole-exome sequencing in undiagnosed genetic diseases: interpreting 119 trios

Xiaolin Zhu[1], Slave Petrovski[1,2], Pingxing Xie[1,13], Elizabeth K. Ruzzo[1], Yi-Fan Lu[1], K. Melodi McSweeney[1], Bruria Ben-Zeev[3,4], Andreea Nissenkorn[3,4], Yair Anikster[3,4], Danit Oz-Levi[5], Ryan S. Dhindsa[1], Yuki Hitomi[1,14], Kelly Schoch[6], Rebecca C. Spillmann[1], Gali Heimer[3,7], Dina Marek-Yagel[8], Michal Tzadok[3,4], Yujun Han[1], Gordon Worley[6], Jennifer Goldstein[6], Yong-Hui Jiang[6,9], Doron Lancet[5], Elon Pras[3,10], Vandana Shashi[6], Duncan McHale[11], Anna C. Need[1,12] and David B. Goldstein, PhD[1]

[Q3]

COMMENT

Towards reforming the taxonomy of human disease

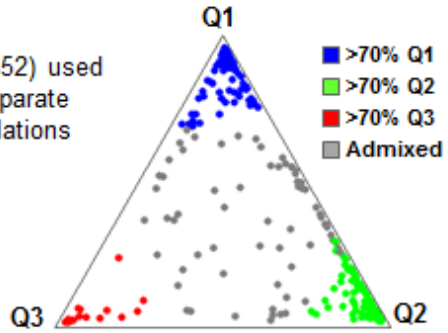
Martin Hofmann-Apitius[1], Marta E. Alarcón-Riquelme[2], Chris Chamberlain[3] and Duncan McHale[3]

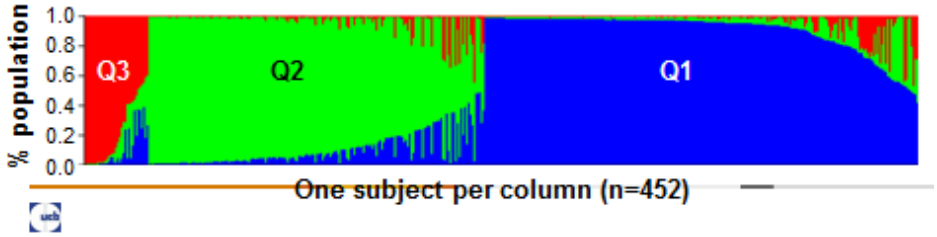
Consortia have begun to establish 'mechanism-based taxonomies' for inflammatory and neurodegenerative diseases that could aid drug development and personalized therapy.

Better genetically validated targets

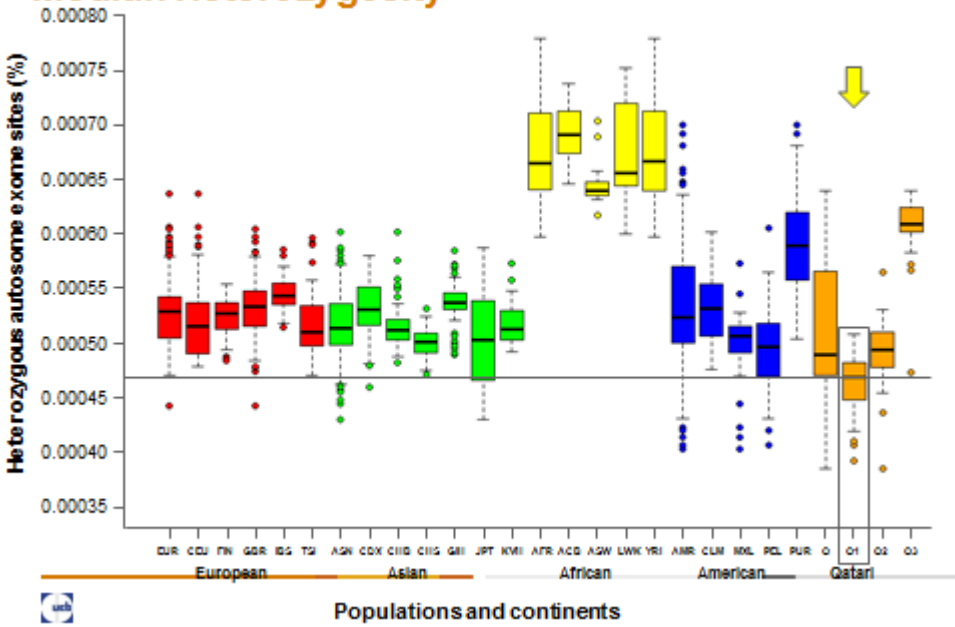
Overall Qatari Genome Structure

- 500K SNP microarray (n=452) used to identify 48 SNPs that separate Qataris into 3 distinct populations
  - Q1 Arab
  - Q2 Persian
  - Q3 African





Q1 Bedouin Qataris Have the Lowest Worldwide Median Heterozygosity

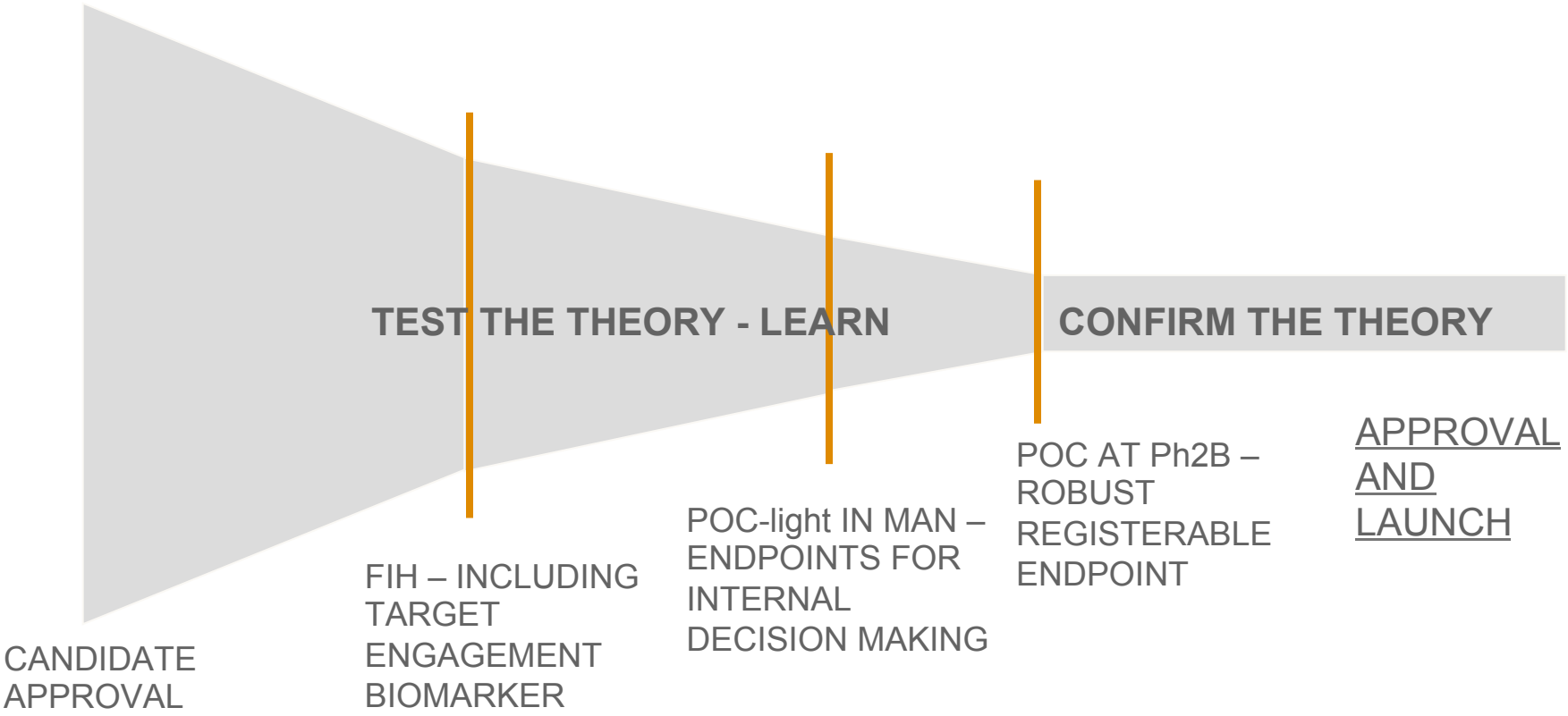


Potential families

- Systemic lupus erythematosus (n=4)
- CNS dx (9)
- Cardiac (3)
- Immunodeficiency (1)
- Rheumatology other than SLE (4)
- Joint (1)
- Bone malformations (1)
- Charcot foot (1)
- Mitochondrial (1)
- Miscellaneous (2)

Lever 2: Development paradigm

Robust biomarkers and endpoints, courageous decision-making



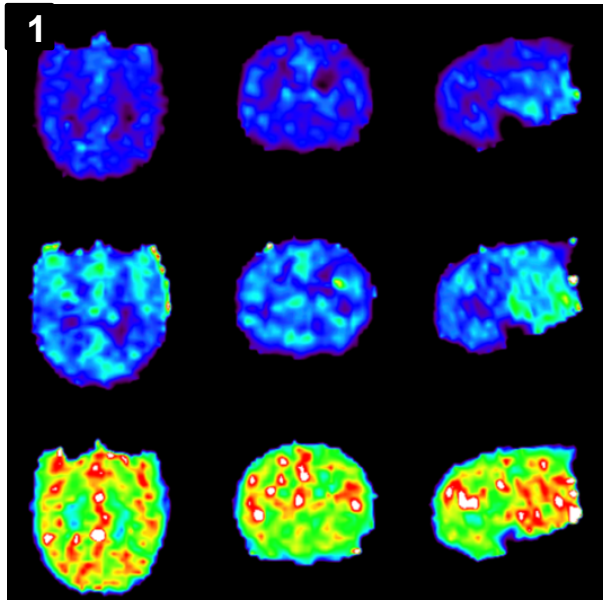
Right target → Right molecule → Right indication → Right patient

LPS-induced neuroinflammation

Reducing neuroinflammation may be disease-modifying in neurodegenerative disorders

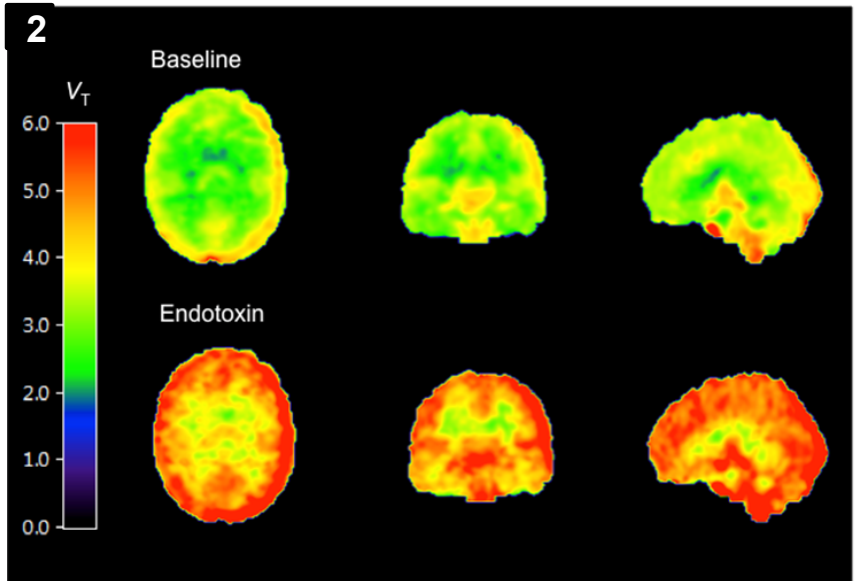
A novel PET paradigm was developed to allow testing of the attenuation of microglial activation as proof of pharmacology

Pre and post LPS in baboons



Endotoxin-induced neuroinflammation measured by PET imaging in baboons (from Hannestad et al., 2012)

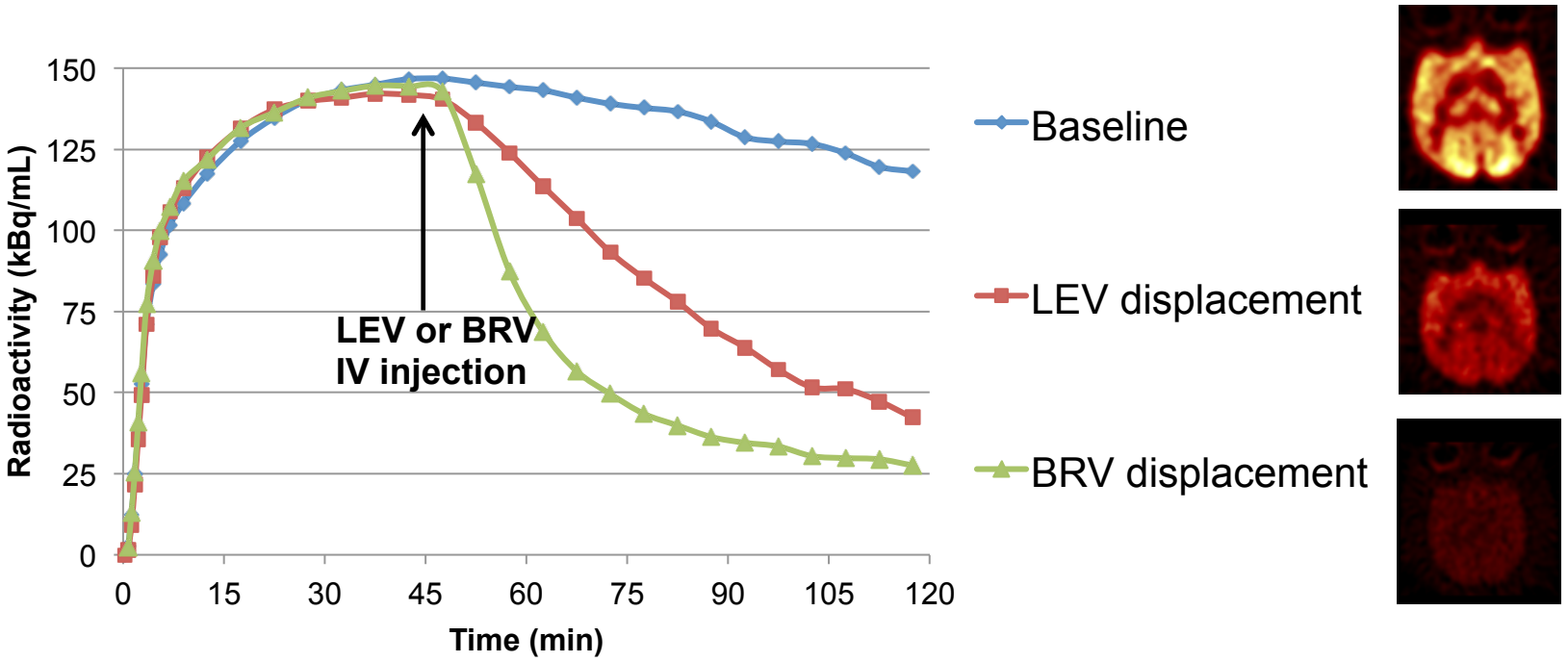
Pre and post LPS in humans



Translation of this novel biomarker to humans (from Sandiego et al., 2015)

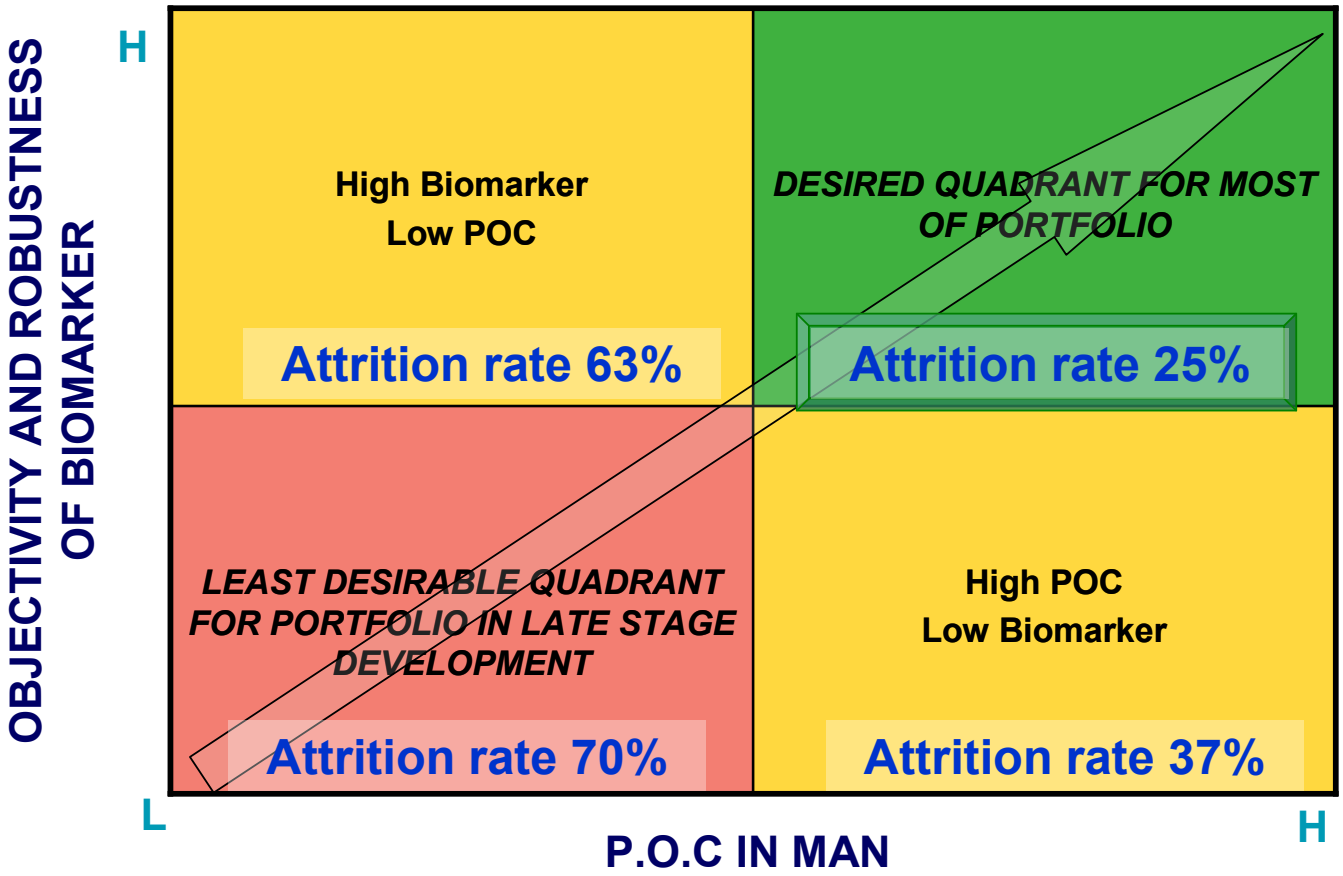
[^{11}C]UCB-J: a PET ligand for SV2A

Levetiracetam and brivaracetam differed markedly in the time course of the displacement of [^{11}C]UCB-J in nonhuman primates, confirming BRV's faster brain penetration.



Displacement of [^{11}C]UCB-J after IV administration of LEV (red) or BRV (green) shows that BRV enters the brain 5 times faster than LEV in rhesus macaques (from Hannestad et al., 2014)

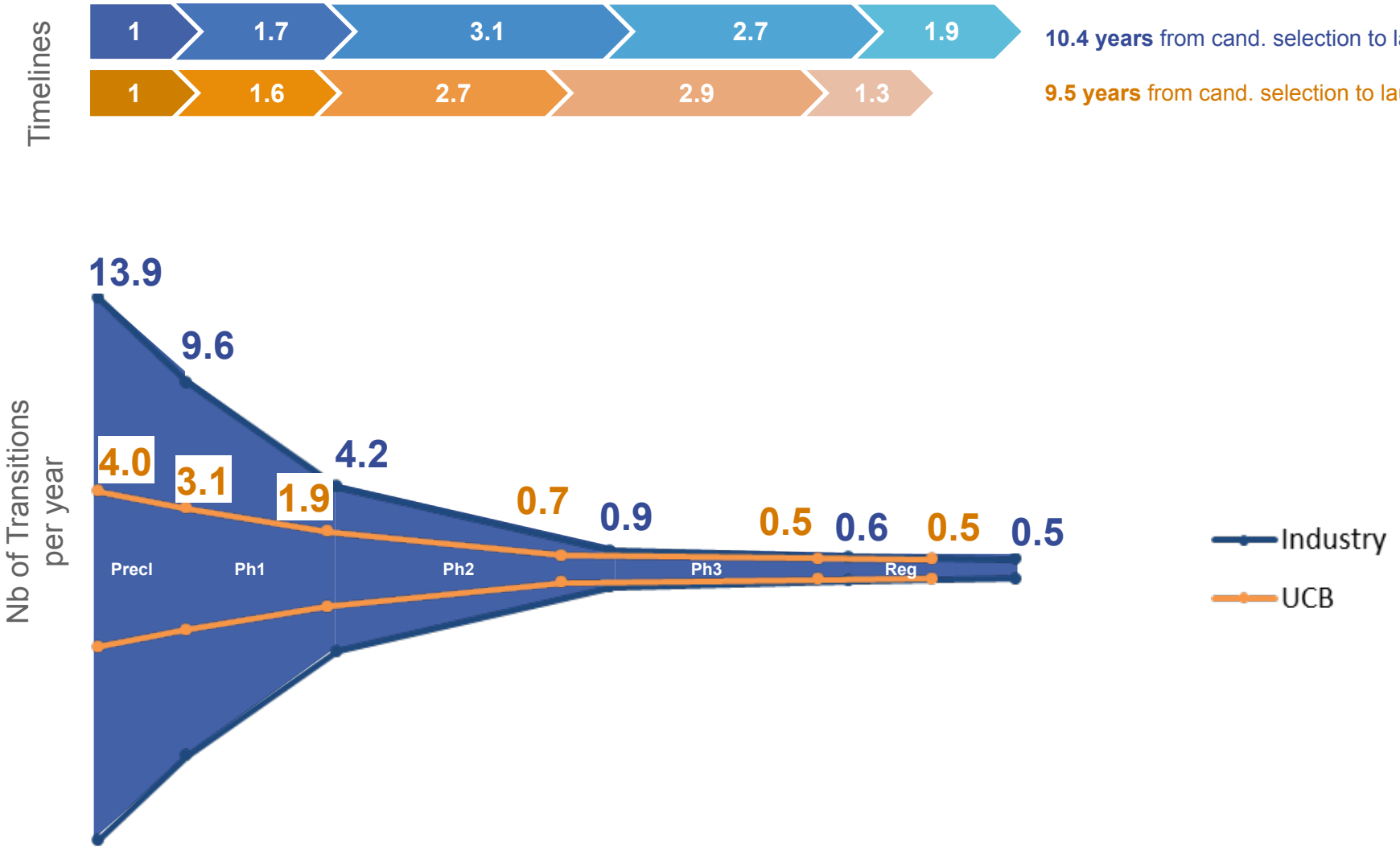
Impact of the PoC development paradigm



Source: Evaluate; Pharmaprojects; Factiva; literature search; McKinsey analysis; I. Kola

Note: Includes aggregate attrition rates for following TAs: CNS, Endocrine, CV, ID, Oncology, and Respiratory. All figures are rounded

This model can secure leading R&D productivity



Source of Industry timelines : McKinsey July 2014
Source of Industry Nb of Transitions : calculation done on KMR 2007-2011 PoS

Questions?