Drug discovery in an academic setting
- the best of both worlds?

Dr Simon Ridley, Alzheimer's Research UK

ELRIG Research and Innovation 2015

Alzheimer's Research UK

The Power to Defeat Dementia

Independent , fundraising charity

- **Fund** biomedical dementia research to accelerate / facilitate the discovery of therapeutic interventions / preventions in Alzheimer's and other dementias
- Work with others to make dementia research a **national and international priority**
- Provide **evidence-based information** to the public about dementia and dementia research

Current portfolio of research grants / initiatives worth a total of £27m

- Main charity funder of biomedical dementia research in the UK; second globally to (US) Alzheimer's Association

Long-established UK remit, widening globally

Fund research through mixed models

- 17 different regular funding streams covering Projects, Training, Resources
- Wide range of strategic initiatives

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G8 Dementia Summit Declaration: London, December 11th 2013

BBC NEWS HEALTH — G8 'will develop dementia cure or treatment by 2025'

Challenges of researching dementia

- Disorder of the brain

- Not a single disease -
  a syndrome with many possible causes

- Mixed dementia pathologies common
  e.g. neurodegenerative (AD) plus vascular

- Results from a complex mix of genetic and environmental
  risk factors which interact over a lifetime

- Complicated by other processes or conditions
  which can also accompany the ageing process

- Long preclinical phase

- Unlikely to have a single, universal 'cure all' or prevention

- Relatively small pool of researchers; seen as an unattractive area
  – *difficult, poorly-funded,*
  few opportunities in academia and industry

Clinical development in AD has been challenging

Mangialasche et al. Lancet Neurol 2010; 9: 702–16

"Amyloid is the wrong target"

"AD is just too difficult as a therapeutic area"

"We shouldn't trial any drugs until we understand more basic science"

- Were the drugs tested too late in the disease process ?

- Many trial subjects didn't actually have AD

- Did the Phase II data really warrant Phase III trials ?

- Need to develop better detection / prognostic/ "theragnostic" markers, especially for preclinical or early disease

- Need to understand more fundamental biology/pathology

- Identification & pre-clinical validation of new targets and associated drug discovery – where will this come from?

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Translational science

- There is a large gap in 'translation' as pharma retreats

- Academia and other not-for-profit organizations can be very successful in producing new medicines

- Scientific excellence is required to find drugs

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- The current model for drug discovery and development is under significant strain, with many companies pulling out of R&D for challenging diseases – such as dementias

- New models have to emerge that will address the problems of high cost and lack of innovation

- A way of *promoting* the translation of basic research that we fund currently into patient benefit is a key objective for ARUK

- Drug discovery work is not always provided for by regular grant funding schemes

- Academics often do not have access to high quality drug discovery expertise

- **ARUK is involved with, or leading several different partnership models**

A new VC-funded model supported by UK Dept. of Health, Pharma partners, ARUK

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Dementia drug research aided by $100 million venture capital fund

BY BEN HIRSCHLER

LONDON | Tue Mar 17, 2015 10:04am GMT

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(Reuters) - The world's first venture capital fund dedicated to finding new ways to prevent and treat dementia has raised more than $100 million with the backing of the British government and several of the world's leading drugmakers.

The global Dementia Discovery Fund ↗ is unique in focusing on a single difficult to treat disorder and in bringing together industry and government.

Drug companies involved include GlaxoSmithKline, Johnson & Johnson, Eli Lilly, Pfizer and Biogen Idec.

The initiative, announced by Britain's health minister Jeremy Hunt at a meeting in Geneva

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Neuro-MAP: a global charity-funded programme

- To identify existing projects (that have been stalled, shelved or parked) and invest in them.

- To work with industry to help them get potential new treatments to clinical trial and see new drugs launched.

The Dementia Consortium: a charity – Pharma partnership

The aim of the Dementia Consortium is:

- To provide a mechanism (funding and expertise) to enable promising, early-stage academic research to progress to Pharma-standard drug discovery through Pharma-standard preclinical target validation.

- To de-risk targets for the pharmaceutical industry and to help provide the scientific substratum upon which they can build drug discovery programs.

DEMENTIA Consortium

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- Up to £2m funding
- Knowledge of the field
- Academic research networks

MRC-T
- Tech transfer, IP expertise
- Managing application and review
- Project management of awards
- Expertise and facilities in drug discovery
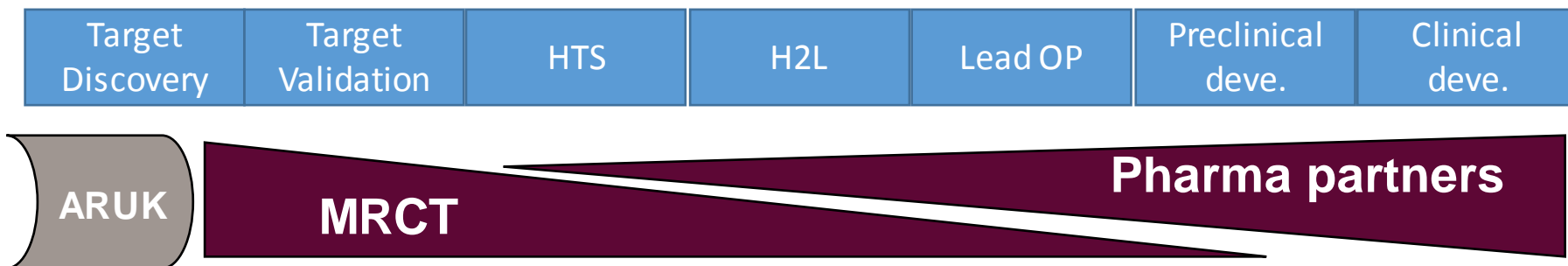- Global research networks

Pharma Partners
- Up to £1m funding
- Expertise in drug discovery and dementia
- Option to pursue targets for drug discovery (beyond pre-clinical validation or pre-competitive tool compound)

£3m - pooled resource to be expended over 3 years

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The Dementia Consortium route: to and through the clinic

3-5yr ←————————→ ~1.5yr   5-10yr

| Target Discovery | Target Validation | HTS | H2L | Lead OP | Preclinical deve. | Clinical deve. |

ARUK

MRCT

Pharma partners

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DRUG DISCOVERY ALLIANCE

Cancer Research UK:
Martin Drysdale, Donald Ogilvie,
Ian Waddell, Allan Jordan

How to translate basic science into drug discovery projects to deliver patient benefit

- Access to excellent scientists and fundamental scientific research into disease mechanisms

- Access to clinicians who know the disease and treat patients

- Access to patients and patient material (genome, fluids, samples, biomarkers, brain banking)

- 4 attributes needed for drug discovery success

   - Hire talented people

   - Provide good resources and stable funding

   - Set a clear mission

   - Allow time for knowledge and expertise to develop

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The ARUK Drug Discovery Alliance of three Drug Discovery Institutes

- Embedding dedicated, Pharma-level drug discovery expertise within academic centres of excellence to work on dementia.

- Focus away from current Pharma targets; less risk-averse

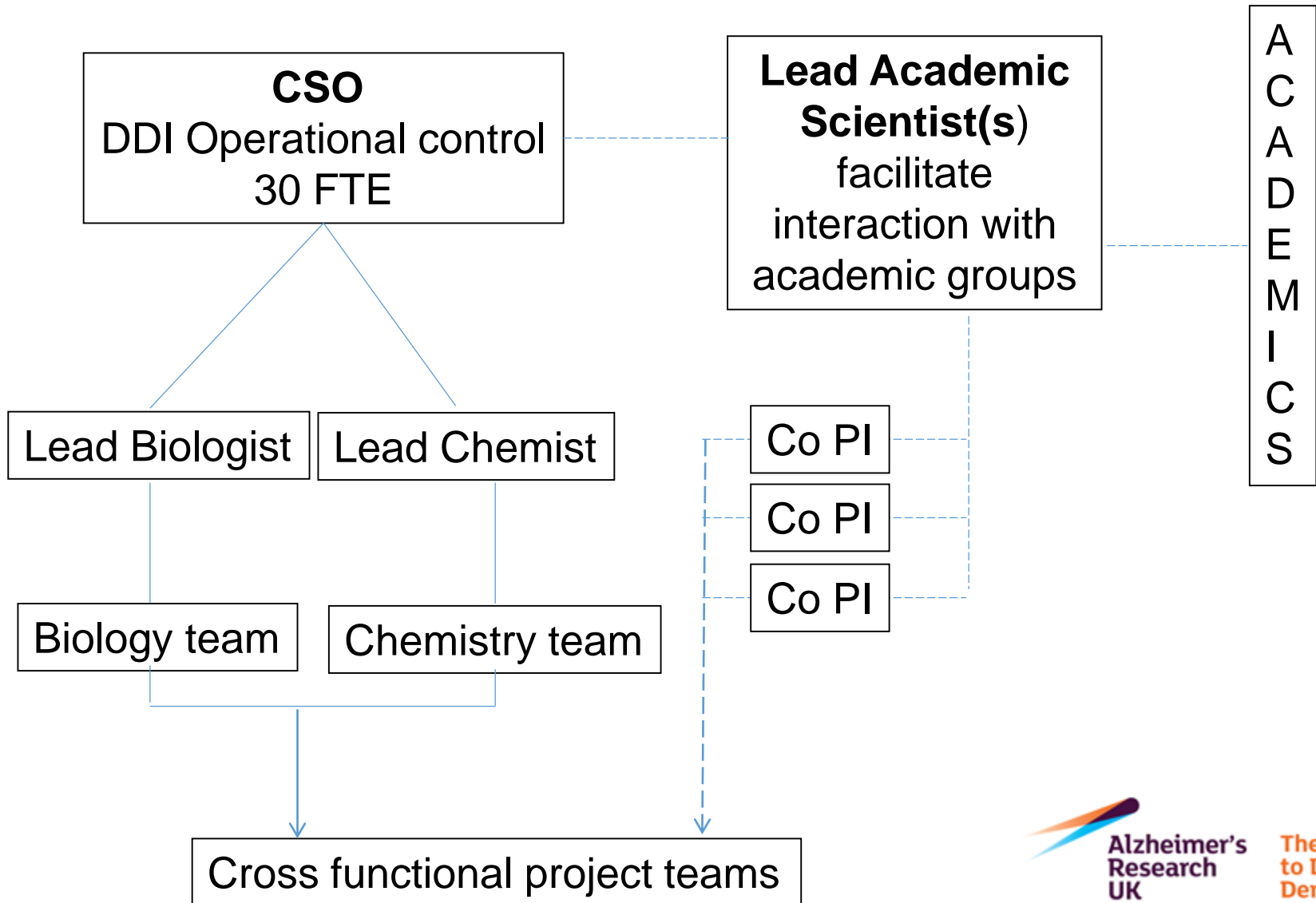|	UNIVERSITY OF CAMBRIDGE DDI	UNIVERSITY OF OXFORD DDI	UCL DDI
Five-year funding	£10m	£10m	£10m
Lead Academic Scientists	Rubensztein	Lovestone, Bountra	Schaivo, Hardy, de Strooper

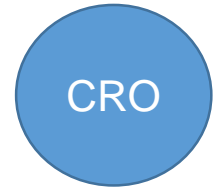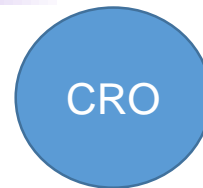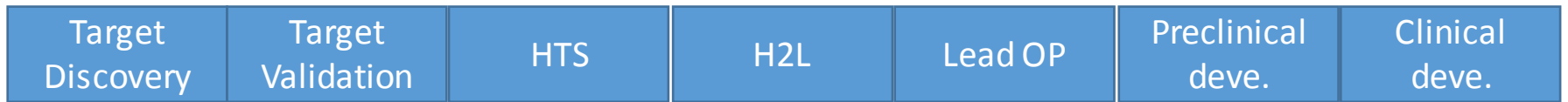Alzheimer's Research UK — The Power to Defeat Dementia

Operational model for each DDI

Operational model for the DDI Alliance

- Cooperation between DDIs facilitated by 3 CSOs and overseen by ARUK
  - Avoid duplication
  - Pool expertise and resources when appropriate

- Quarterly progress meetings with ARUK;

- Annual and Five-Year Reviews with external Advisory Group

- Expectation over first five years:
  - Establishment, embedding and integration of DDIs within their Universities
  - Development of pipelines
  - 1-2 Lead molecules /DDI

Thank you