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

Dr Simon Ridley, Alzheimer’s Research UK

ELRIG Research and Innovation 2015
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
G8 Dementia Summit Declaration: London, December 11th 2013

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
“Amyloid is the wrong target”

“We shouldn’t trial any drugs until we understand more basic science”

“AD is just too difficult as a therapeutic area”

- 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?
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
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.
Dementia drug research aided by $100 million venture capital fund

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

(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,...
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.
Alzheimer’s Research UK
- Up to £2m funding
- Knowledge of the field
- Academic 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)

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

£3m - pooled resource to be expended over 3 years
The Dementia Consortium route: to and through the clinic
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
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

Five-year funding

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<th>University</th>
<th>Five-year funding</th>
<th>Lead Academic Scientists</th>
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<tbody>
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<td>University of Cambridge</td>
<td>£10m</td>
<td>Rubensztein</td>
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<td>University of Oxford</td>
<td>£10m</td>
<td>Lovestone, Bountra</td>
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<tr>
<td>UCL</td>
<td>£10m</td>
<td>Schaivo, Hardy, de Strooper</td>
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Operational model for each DDI

CSO
DDI Operational control
30 FTE

Lead Biologist
Lead Chemist

Biology team
Chemistry team

Cross functional project teams

Lead Academic Scientist(s)
facilitate interaction with academic groups

Co PI
Co PI
Co PI

ACADEMICS

Alzheimer's Research UK
The Power to Defeat Dementia
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
<table>
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<tr>
<th>Stage</th>
<th>Timeframe</th>
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<tbody>
<tr>
<td>Target Discovery</td>
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<td>Clinical deve.</td>
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<td>ARUK DDIs</td>
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<tr>
<td>PARTNER FUNDING &amp; LICENSING</td>
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**CRO**
Thank you