AD mission in the U.K.

By Lauren Martz, Staff Writer

The U.K. government is responding to calls for a dementia therapy by 2025 by securing nearly £120 million (\$205 million) from U.K.-based organizations for a series of research initiatives that span R&D from discovery to the clinic. Reaching the target might require international coordination to incentivize investors.

In the last few years, several governments have responded to the looming healthcare crisis in Alzheimer's disease (AD) by launching

or joining public-private partnerships with pharmas, not-for-profit organizations and academic organizations (see Table 1, "Dementia public-private partnerships").

The field has been held back by numerous late-stage clinical failures that prompted several pharmas to pull out and others to rethink their strategies from target selection to trial design. Clinical trials for AD are difficult because the disease progresses slowly, there are no biomarkers to indicate whether a therapeutic is working and the most widely studied target— β -amyloid ($A\beta$)—has thus far proven fruitless.

Mike Hutton, CSO of neurodegeneration at **Eli Lilly and Co.**, told SciBX that "dementia is a set of slowly progressing diseases, and it is very difficult to design trials that tell us if a drug is working. We don't usually know if a drug is working until we get to Phase III trials, which usually last 18 months, include more than 1,000 patients and are very expensive."

As the incidence of the disease grows with the aging population, several governments have concluded that the problem might not be solved if left to the private sector alone.

In the U.K., Prime Minister David Cameron first spoke out in March 2012 for a national dementia challenge—a call to governments, industry

Table 1. Dementia public-private partnerships. Selected public-private partnerships focused on dementia research initiated over the past five years.

Date	Title	Companies	Institutions	Funding amount	Description
February 2008	Coalition Against Major Diseases (CAMD)	At least 23 industry partners	Alzheimer's Association; Alzheimer's Foundation of America; Brookings Institution; Critical Path Institute; Parkinson's UK; USAgainstAlzheimer's; European Medicines Agency; FDA; Foundation for the National Institutes of Health; National Institute of Neurological Disorders and Stroke; National Institute on Aging (NIA); 16 university partners	Unknown and/or undisclosed	Identify biomarkers that signal the onset of Alzheimer's disease (AD) and/or Parkinson's disease (PD)
January 2010	Prediction of cognitive properties of new drug candidates for neurodegenerative diseases in early clinical development (PharmaCog)	At least 19 industry partners	20 university partners; funded as part of the EU's Innovative Medicines Initiative (IMI)	€27.7 million (\$37.6 million)	Funded as part of IMI to accelerate identification of new neurodegenerative disease therapeutics
January 2011	Alzheimer's Disease Neuroimaging Initiative 2 (ADNI 2)	At least 22 industry partners	NIA; Alzheimer's Association; Canadian Institutes of Health Research; Alzheimer's Drug Discovery Foundation; Foundation for the National Institutes of Health	\$62 million	ADNI 2 is the third stage of the ADNI project that uses neuroimaging studies to identify biomarkers and study pathology
February 2014	Accelerating Medicines Partnership Alzheimer's Disease	AbbVie Inc. (NYSE:ABBV); Biogen Idec Inc. (NASDAQ:BIIB); GlaxoSmithKline plc (LSE:GSK; NYSE:GSK); Eli Lilly and Co. (NYSE:LLY)	NIH; Alzheimer's Association; Alzheimer's Drug Discovery Foundation; Foundation for the National Institutes of Health; Geoffrey Beene Foundation; USAgainstAlzheimer's	\$129.5 million	A U.S. public-private partnership to identify disease biomarkers and validate the targets in human brain tissue
Proposal accepted December 2013; not yet launched	European Platform for Proof of Concept for Prevention in Alzheimer's Disease (EPOC-AD)	Not applicable	Not applicable	Not applicable	An IMI-funded collaboration to improve patient selection and clinical trial design. The initiative will also conduct an adaptive clinical trial using the UK Dementias Research Platform's patient registry

and charities to contribute more funding to improve awareness, research and care for patients with dementia. He committed to increase the annual dementia research funding available to the **National Institute for Health Research, Medical Research Council (MRC)** and **Economic and Social Research Council** from £26.2 million (\$44.9 million) in 2009–2010 to £66.3 million (\$113.5 million) in 2014–2015.

Last December, G-8 countries gathered for a dementia summit in London, at which they discussed health care for AD and produced the 2025 goal for a disease-modifying therapy.

In June, Cameron announced plans to double the funding again by 2025.

Now, U.K. organizations have answered the call with a series of dementia initiatives aimed at addressing the holes in the development process. Those holes include a lack of new targets, low predictive value of *in vitro* and *in vivo* models, a dearth of biomarkers and poorly designed clinical trials.

Coordinated discovery

Alzheimer's Research UK is leading the drive with five new programs announced since the start of the year that cover sequential stages in drug development, starting with discovery stage research (see Table 2, “Dementia research initiatives in the U.K.”).

Four of the new programs were announced in June, as part of its £100 million (\$171 million), 5-year Defeat Dementia campaign. The

largest of the programs is a £30 million (\$51.3 million) plan to establish Drug Discovery Institutes—a network of institutes for validating drug targets identified in academia and designing targeted therapeutics.

“These institutes will actually bring early drug discovery capabilities including medicinal chemists and biologists into academic centers to advance translational science and support new ways of thinking and innovating,” said Simon Ridley, head of research at Alzheimer's Research UK. Ridley hopes they will set up three institutes within three years.

George Vradenburg, founder and chairman of **USAgainstAlzheimer's**, told *SciBX* that the structure of the networks of Drug Discovery Institutes creates an innovative way to get research out of the lab and into the marketplace. He said that there are no similar initiatives in the U.S. **USAgainstAlzheimer's** is a not-for-profit organization committed to mobilizing groups affected by AD to find a cure by 2020.

The Drug Discovery Institutes complement the U.K. Dementia Consortium, a discovery-oriented partnership set up in January by Alzheimer's Research UK with **Eli Lilly**, **Eisai Co. Ltd.** and **MRC Technology**. The consortium supports academic projects to validate drug targets and identify therapeutics, and it brings industry expertise to help translate the targets and therapeutics to the clinic.

“Academics or small- and medium-sized enterprises come to the consortium with ideas. MRC Technology and Alzheimer's Research UK

Table 2. Dementia research initiatives in the U.K. Select U.K.-based dementia research initiatives launched during the past year. **Alzheimer's Research UK** is contributing a total of £102 million (\$174 million), including £100 million (\$170.6 million) from the Defeat Dementia fundraising campaign that will be spread between at least 5 research initiatives. The charity organization is also contributing £2 million (\$3.42 million) to a stem cell research consortium that also has £1 million (\$1.71 million) from company partners.

Date	Title	Companies	Institutions	Funding amount	Description
January 2014	Dementia Consortium	Eli Lilly and Co. (NYSE:LLY); Eisai Co. Ltd. (Tokyo:4523)	MRC Technology ; Alzheimer's Research UK	£3 million (\$5.19 million) including £2 million (\$3.42 million) contributed by Alzheimer's Research UK and £1 million (\$1.71 million) total contributed by Eli Lilly and Eisai	Identify and validate new dementia drug targets from academia
June 2014	Drug Discovery Institutes	None	Alzheimer's Research UK	£30 million (\$51.34 million) from the Alzheimer's Research UK's Defeat Dementia campaign	Drug discovery to translate basic science to drug identification
June 2014	Defeat Dementia's Global Clinical Development Fund	None	Alzheimer's Research UK	£20 million (\$34.25 million) from the Defeat Dementia campaign	Funding is for clinical trials in dementia by small and medium enterprises in the U.K.
June 2014	Alzheimer's Research UK Stem Cell Research Centre	None	Alzheimer's Research UK; The Gurdon Institute at the University of Cambridge ; University College London	£2 million (\$3.42 million) from trust as part of the Defeat Dementia campaign	Develop human <i>in vitro</i> neuronal models of dementia based on stem cell research
June 2014	Prevention Fund	None	Alzheimer's Research UK	Undisclosed funding from the Defeat Dementia campaign	Funding for projects that analyze existing epidemiologic data to identify ways to prevent dementia
Program renewal Fall 2014	Alzheimer's Research UK Research Network	None	Alzheimer's Research UK; 15 academic centers in the U.K.	Undisclosed funding from the Defeat Dementia campaign	A network comprised of 15 universities that unites established and prospective dementia researchers
June 2014	UK Dementias Research Platform	MedImmune LLC ; Janssen R&D LLC ; GlaxoSmithKline plc (LSE:GSK; NYSE:GSK); Araclon Biotech S.L. ; Ixico plc (LSE:IXI); SomaLogic Inc.	Cardiff University ; University of Cambridge ; University of Edinburgh ; Imperial College London ; Medical Research Council (MRC) ; Newcastle University ; University of Oxford ; Swansea University ; University College London	£16 million (\$27.40 million) from MRC and undisclosed funding from industry partners	A 5-year study on about 2 million participants to identify biomarkers, stratify patients for clinical trials and create a patient registry for dementia trials

will work with the academics on selected projects to validate the biology and that the targets are druggable, and the pharmas will give input into that process,” said Lee Dawson, head of open innovation at Eisai. He added, “This initiative really goes both ways. We will work with the academics who come to us with ideas to discuss the science and what can be done moving forward even on the projects we don’t select.”

Justin Bryans, director of drug discovery at MRC Technology, added, “If we can identify suitable projects and develop them to such a point that our pharma partners bring them into their research and development portfolios, then I think this will have been a success.”

Eli Lilly and Eisai have a right of first refusal to partner further at the end of the consortium project.

Clinical cooperation

In addition to closing the discovery gap, Alzheimer’s Research UK is seeking to address problems that have hampered clinical development.

Defeat Dementia launched the Global Clinical Development Fund with £20 million (\$34.25 million) for clinical trials by U.K.-based small and medium enterprises. The goal is to get candidate compounds to patients more quickly and decrease the time required for clinical trials by using improved patient stratification and innovative trial design.

The program was launched alongside the UK Dementias Research Platform, a five-year public-private partnership coordinated by the MRC. The platform is funded with £16 million (\$27.4 million) from the MRC and undisclosed amounts from the six participating companies including **GlaxoSmithKline plc** and **AstraZeneca plc’s MedImmune LLC** unit. It will create and analyze a cohort of about 2 million patients with dementia and controls.

“The cohorts include patients who were healthy at the time of enrollment, some of whom have since developed dementia, and patients at all stages ranging from preclinical dementia to advanced disease,” said Simon Lovestone, a professor of translational neuroscience at the **University of Oxford**. The cohorts have been following patients for between about 5 years and more than 65 years, with some of the cohorts dating back to the 1940s. Lovestone said that the goal of the platform is to generate new experimental medicine programs including the identification of biomarkers that might help diagnose patients, stratify patients or assess therapeutic efficacy.

Paul Wren, director of neurodegeneration at GlaxoSmithKline, said that the program aims to collect a comprehensive set of data from the patients. “Multiparameter data such as clinical history, genetics, cognitive performance, fluid and physiological biomarkers and neuroimaging scans will be collected to enable well-characterized clinical cohorts to be made available for research purposes, clinical trial readiness and experimental medicine studies.”

Iain Chessell, head of the neuroscience group at MedImmune, told *SciBX*, “The advantage of this platform is the scale and the consolidation of multiple partners under a single conductor. This is a much bigger initiative that dwarfs any other imaging initiative.”

By comparison, the U.S. Alzheimer’s Disease Neuroimaging Initiative has collected neuroimaging data from over 1,000 patients.

Chessell added that because the platform is a government-backed initiative, the resulting information will be made public; however, the industry partners will have access to the data before their release.

The Dementias Research Platform will also be used to develop a regulated registry of 10,000 patients who have been characterized in detail and have given permission to be approached for clinical trials. Eli Lilly’s Hutton said, “For a four-year, Phase III trial, we spend a year and a half recruiting patients. Working toward a patient registry makes trials more efficient.”

Going global

Although the U.K.’s investments have drawn praise for coordination between programs, it might need to go further afield to create a sustainable program for advancing new therapies. Indeed, efforts to engage in international collaboration are already under way.

“What distinguishes this effort in the U.K. is the size of the platform, which is very large and very advanced, the tight linking of each of the elements and the strong commitment to creating dementia-friendly communities,” Vradenburg told *SciBX*. He said that the U.K. Department of Health is directly coordinating the efforts of both government and privately funded initiatives. Vradenburg added that in the U.S., there is some organization on a national level with an advisory committee, but the country is much larger and there are a lot of independent initiatives.

He said that maintaining momentum for the U.K. initiatives could be difficult and might best be tackled with a globally unified effort. That could be done via the World Dementia Council, which was formed in the wake of the G-8 summit to create an internationally unified framework for dementia progress.

Europe’s **Innovative Medicines Initiative (IMI)** is also linking up to the U.K. programs via the European Platform for Proof of Concept for Prevention in Alzheimer’s Disease (EPOC-AD), a planned program to promote resource sharing between different companies. “The IMI’s EPOC adaptive trial will advance dementia research by testing therapeutics from multiple companies in one rolling trial. The trial will use the Dementias Research Platform’s Biobank cohort, as well as other cohorts in Europe, directly integrating this IMI initiative with the U.K. programs,” said Lovestone.

Vradenburg added that a key element for success will be getting international agreement on new regulations to improve pharma incentives. “We need a global approach to increase incentives for industry and investors such as changes to market exclusivity, pricing or reimbursement. We need a way to decrease business and investor risk through tax incentives or improvements to clinical trial infrastructure,” he said.

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COMPANIES AND INSTITUTIONS MENTIONED

Alzheimer’s Research UK, Cambridge, U.K.
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