UniQuest Submission to the McKeon Review with specific reference to Commercialisation

A Strategic Review of Health & Medical Research in Australia

Summary

Australia has excellent medical research, but is falling down in translating the outcomes of that research into products and services that benefit the community. This translation process generally requires commercial funding to provide the very significant investment required to undertake the late stage clinical trials, approval process and manufacturing development. However, a much of Australia's research is not attracting such funding and remains in the lab or goes no further than publications.

There is a lack of both the capabilities and early stage funding necessary to develop and package the research outcomes to the stage where commercial funding can be obtained. This gap should be bridged by programs that support commercial proof of concept, translation to the clinic, clinical trials and most importantly, the development of effective commercialisation capabilities in clusters of critical mass to undertake this process and attract commercial funding.

The following recommendations would, if funded and designed appropriately, address the gap in translating Australia's medical research into products and services that benefit the community.

Specific Recommendations:

1. Proof-of Concept Funding – a critical step in translating innovations from universities and research institutes is to be able to provide proof-of-concept funding to projects with commercial application where an idea emanating from a research grant funded project can be tested at a prototype or reduction to practice step, such as the generation of *in vivo* data in a relevant animal model of disease so that the innovation is sufficiently developed to attract translation grants or industry financial support for the following development stages necessary to bring it to market. Proof

of concept funding should form part of the funding support available for translational research.

2. Pre-Clinical and Clinical Drug and Device Development Funding – The translation research strategy enacted by the Medical Research Council (MRC) in the UK should be emulated within Australia to provide commercially focussed, milestone-based, grant funding to span the valley of death in medical device and therapeutic drug and vaccine development. This would span pre-clinical and clinical development with grants that provide end to end continuous funding as development milestones are met.
3. Clinical Trial Support - Australia has an established network of clinical service providers in the clinical trial space. However, there is a need to provide specific grant funding for conducting clinical trials of new therapeutic drugs, vaccines and medical devices specifically for drugs developed from Australian research.
4. Technology Transfer – Many research innovations are not progressing beyond the lab because of the lack of expertise and resources to prepare them for investment in the development process. To improve the effective commercialisation of health research outcomes there needs to be improved resourcing and funding of technology transfer offices. The centralisation of these resources would allow for best practice through the provision of a critical mass of commercially experienced professionals, which ideally should be in the order of 20 – 30 people for maximum effect. In the UK, funding is provided to the universities to be used for technology commercialisation to champion translational research outcomes and facilitate knowledge exchange in its broadest context. Ideally they should have access to the research continuum from basic research within the universities and research institutes through to clinical applied research in neighbouring teaching hospitals, like the University College London Business (UCLB) case study discussed below. Smaller institutions could apply for funding to support commercialisation collaborations and outsourcing, with the outcomes being measured and funding awarded on the basis of impact KPIs as is the case with third stream funding in the UK as discussed below.
5. NHMRC Development Grants – These grants should be phased out and replaced with more effective translational grant funding as noted above.

Introduction:

It is well recognised that Australia's investment in the commercialisation of research is poor by international standards and lacks a co-ordinated strategy and long-term vision. This is particularly the case in regards to the commercialisation of health and medical research. Previous and current commercialisation programs have not been adequate in addressing the funding gap that exists between competitive research grant funded projects through proof of concept and into commercial development. This "valley of death", as it is termed, must be overcome to achieve knowledge exchange with impact that adds value to research and teaching and promotes economic growth and benefits to the Australian population. In healthcare, this involves the fundamental underpinning of reducing healthcare costs and improving patient outcomes, through more effective disease prevention, diagnosis, treatment and management.

The biotechnology and pharmaceutical industry can and does play an important role in commercialising leading medical and health research outcomes. The traditional technology transfer approach to commercialising these outcomes has been to license the intellectual property protecting the technology from universities and research institutes to industry for further development and, ultimately, new products and services are brought into the market. However, in the case of medical and health research outcomes in Australia these are generally at a very early stage of development and generally are too immature to license or, if they are licensed, the financial terms that are negotiated provide a very poor return to the licensor. This has led many Australian technology transfer offices to choose instead to license the intellectual property into a start-up company for equity alongside a pre-seed venture investor's capital for equity. The invested capital is then used by the start-up company to further the development of the underlying technology which, when more mature and technically de-risked, is often licensed out of the start-up to a biotechnology or pharmaceutical company. This provides additional national benefit, developing expertise and potentially allowing the start up to develop a second invention to a later stage before out-licensing.

Australia has had a poor success rate in forming start-up companies from our medical research institutes and hospitals and has fared somewhat better from its universities. The

reasoning behind this predominantly stems from the lack of technology transfer resources within the medical research institutes and hospitals that can identify, protect, package, secure investment and ultimately manage the asset going forward. Universities with generally better resourced technology transfer offices have been able to achieve relatively more success in this regard. A combination of a lack of both pre-seed capital and follow on capital with a lack of experienced management and Board Directors compounds this problem. The Australian Federal Government's Industry Innovation Funds (IIFs) have addressed in part the pre-seed funding gap with funds like the Medical Research Commercialisation Fund (MRCF) receiving their support in later funding rounds. The Global Financial Crisis has significantly reduced the amount of capital available for follow on investments as venture capital funds have been largely unable to raise funds due to pension and superannuation funds totally withdrawing from venture investments.

The formation of start-up companies as a commercialisation vehicle for the development of a potential new therapeutic drug, vaccine or medical device is also not ideal from the perspective that the amount of capital required to develop the technology is often not available and the companies are left stranded short of an exit milestone. Many Australian start-up biotechnology companies were left with little alternative but to try and raise capital on the public markets and went to IPO and failed to raise sufficient capital and have to a large extent performed poorly as an investment. In the past, the Federal Government had a funding scheme for start-ups to assist with the development of such technologies called the Commercial Ready program, which was very beneficial in providing leveraged funding alongside venture investment. However, this scheme was withdrawn and has not been effectively replaced by the Commercialisation Australia program which generally does not fund pre-clinical and clinical development programs.

There is a role for R&D tax incentives to assist with the progression of technologies within start-up companies, however, these are generally not sufficient to encourage new investors to invest in early stage start-up companies. In the UK there is the highly effective Enterprise Investment Scheme which provides for a 40% reduction in the personal tax rate for the invested capital from angel investors. The net result of this is that many start-ups in the UK are generated from investments from an asset class that is not readily incentivised in Australia.

Additionally, as the technologies are spun out early from research institutes, hospitals and our universities the parent shareholder suffers considerable dilution of their shareholding across the life of the start-up. This is in part due to the fact that they hold common stock from their licensing in of the IP relative to the venture investor, who benefits from holding preference stock across multiple rounds of further capital investment which the parent shareholder is unable to participate in. The net result of this practice is that the retention of value by our institutes, hospitals and universities is low. Hence they are often unable to generate free cash flow to fund additional research, protect intellectual property and fund commercialisation activities.

Lessons from the United Kingdom

The UK government has recently attempted to address the valley of death through a House of Commons Science and Technology Committee review entitled *Bridging the "Valley of Death": Improving the Commercialisation of Research*. David Willetts, the UK Minister for Universities and Science has made a preliminary announcement about the findings of the review and has stated that there would be increased funding of innovation to span the valley of death through mid and late-stage research of the kind that leads to commercial products. It is the UK Government's view that its research councils, the Higher Education Funding Council for England (HEFCE), the Medical Research Council (MRC) and the Biotechnology and Biological Sciences Research Council (BBSRC) stop funding much earlier than is done in the US. Minister Willetts quotes that "the National Institutes of Health and the National Science Foundation continues to fund closer to the market and we in the UK are surprised when venture capitalists don't step in and it is legitimate for Government to take some of that risk". UniQuest has met with a number of the key groups that have made submissions to the UK review and has formed some views as to best case exemplars of how best to overcome the valley of death that are further explored below.

<u>The UK Medical Research Council Translational Research Strategy</u>

The Medical Research Council Translational Research Strategy was recently introduced in response to Sir David Cooksey's 2006 report, 'A review of UK health research funding', which looked at funding schemes that would result in an increase in the rate of uptake of the translation of fundamental research and is paraphrased below. It generally seeks to

reduce the economic burden that poor health imposes on society through the improved diagnosis, treatment and management of disease. The funding of the MRC's 'translational research' program in the UK Governments Comprehensive Spending Review was provided to the tune of an additional £132 million to the MRC for the period 2008-2010. The National Institute for Health Research (NIHR) (the body through which the Department of Health delivers the UK Government's R&D strategy) works in collaboration with the MRC and together this is a formidable funding partnership. The NIHR has replaced the National Health Service (NHS) Innovation hubs, which were generally found to have had little practical impact in identifying and implementing health care innovations within the NHS.

The UK now has co-ordinated strategies, built around the advice, priorities and needs of the NIHR, the MRC and the NHS. These strategies encompass translational, public health, e-health records and methodology research and human capital. They are additionally supported by the very strong basic research carried out in the UK (http://bis.ecgroup.net/Publications/Science/Science.aspx The major funding body for biological research is the BBSRC through its comprehensive program of grants and eight centres of research excellence as detailed in their 2010-2015 Strategic Plan entitled :The Age of Bioscience".

It is important to note that the MRC's Translational Research Strategy builds on existing translational activities and schemes that provided a backdrop of both translational research workforce and infrastructure. There was already substantial funding available for clinical and pre-clinical research on healthcare innovations, support for MRC and NIHR clinical trials, other initiatives and programmes, work within the MRC's own units, institutes and centres and research funded through UK universities. The UK government, through the MRC, "provides continued investment in fundamental basic and clinical research that underpins the translational agenda, which is recognised as the engine room of healthcare innovation".

A major focus of the MRC's strategic funding is in 'experimental medicine' – targeted programmes that support early-stage clinical discovery work. The overall approach of the MRC is to ensure that there is an integrated way of supporting research, developing the infrastructure and ensuring that the highly trained people required to deliver this agenda are available.

The MRC leads in implementing a strategy for the discovery and exploratory development of fundamental research towards patient benefit. The aims of this strategy include:

- accelerated development of novel therapeutics, devices and diagnostics;
- faster determination of pathways of disease leading to the identification of targets for therapeutic intervention;
- increased skills base to deliver high quality research for greater health and economic benefits; and
- increased partnership with industry.

To deliver this plan, the MRC has created dedicated funding streams, specific targeted initiatives, support for key facilities, coordination of existing infrastructure and capacity development.

The MRC already supports a substantial amount of fundamental, hypothesis-led basic and clinical research through its research funding boards. These are now augmented with a new funding stream, specifically aimed at accelerating the process of research and development of promising discoveries through the support of milestone-driven, goal-oriented research.

To support and underpin experimental medicine research, the MRC has launched a series of strategic initiatives, targeted at specific points in the process. These initiatives are in biomarkers (surrogate indicators of a biologic state or process), human and animal disease models and disease-based sample collections. They are achieved through the support of relevant investigator-initiated research proposals, as well as specific calls for proposals in defined areas with earmarked funding. There are further initiatives in drug safety science.

There are opportunities for partnership funding for certain initiatives, from charities and industry, as well as from the Technology Strategy Board (TSB) – the executive non-departmental public body which promotes innovation in the UK. THE TSB's report entitled "Concept to Commercialisation - A Strategy for Business Innovation 2011-2015 outlines its approaches to funding innovation. A key feature of the TSB programs is the Knowledge Transfer Partnerships which resources academic and industry collaborations through a training scheme to improve "competitiveness and productivity through the better use of knowledge, technology and skills that reside within the UK knowledge base". The TSB also

manages the Small Business Research Initiative (SBRI) which is modelled on the highly successful US Small Business Innovation Research scheme whereby SME's are offered grants to fund key technology problem solving activities. The latest major scheme introduced by the TSB is the Catapult program of National centres of excellence for technology and innovation that seek to "transform the UK's ability to create new products and services in priority areas, and drive future economic growth." An example of a priority area is the newly announced Catapult centre for Cell Therapy.

There is already significant support by the MRC and NIHR for infrastructure that underpins translational research but levels of support are still being reviewed. Potential gaps in UK research facilities are identified and are being filled.

It was recognised that increasing the UK's capabilities in translational research would require increased numbers of scientists trained in relevant areas of science. The MRC has enhanced training and career opportunities in translational areas, such as clinical research training, pharmacology, toxicology, informatics, methodology, and biostatistics, together with industrial collaborative studentships.

The MRC is leading in methods research and the development of new and improved systems and theories for health research. Its aim is to develop a high-quality national platform in methodology research and establish the UK as a world leader in innovation in this area.

The NIHR leads on evaluative research and clinical trials and its activities should increase the amount of high-quality research conducted in the UK. Through the NIHR, the MRC provides funding for clinical trials that assess potential new treatments and their underlying mechanisms of action, and continues to support intervention trials in global health.

MRC Translational Research Funding Schemes

The Developmental Pathway Funding Scheme/Developmental Clinical Studies scheme (DPFS/DCS) supports the translation of fundamental discoveries toward benefits to human health. It funds the pre-clinical development and early clinical testing of novel therapeutics, devices and diagnostics, including "repurposing" of existing therapies. These grants are totally non-dilutive and do not require co-funding from industry or venture investment.

The DPFS/DCS scheme combines the previous individual translational funding schemes, permitting a more flexible and integrated approach to the development of new interventions and diagnostics. The DPFS/DCS scheme has an annual budget of over £40m per year. Applications need to be substantive and have as a minimum £250k in costs. There is no formal upper limit on project costs but applicants are required to justify costs based on the needs of the individual project. Likewise, duration is based on the needs of the project, for example pre-clinical projects are likely to be around 2 years in duration, with clinical projects frequently requiring support for a longer period.

Awards are subject to up to four key milestones (go/no-go decisions). This allows risk to be managed appropriately, and enables projects to be supported when later stages of the work are dependent on the success of earlier stages. Failure to meet a milestone may lead to early termination of funding.

The commercial focus of these grants and the milestone-tranched funding which is the norm in venture financed start-up funding provides focus and ensures there is accountability for the funding.

Additional Translational Research Support Schemes

In addition to these funding schemes, the UK government assesses the quality of translation from higher education institute and university research in a similar way to the Australian Government's ERA for Research Excellence. The benefits of this are twofold- an awareness and support for translating research into products and services that benefit the population by the researchers themselves and funding, which is provided to the universities to underpin and encourage the provision of translation and commercialisation services by the university, which can be undertaken though a specialised team in the case of larger institutions or through contracting a larger commercialisation group. This ensures sufficient critical mass and adequate commercialisation skills.

The UK Government has also introduced via the TSB a £180m BioCatalyst fund which provides matched funding to venture and industry funded health research projects emanating from small to medium enterprises (SMEs). This provides an additional route for

the commercialisation of health research. The difference between this and Australian support for SME's through the programs of Commercialisation Australia (CA) is that CA is generally unwilling to fund pre-clinical and clinical development therapeutic and device projects from start-up companies. The recently introduced R&D Tax Incentive scheme in Australia provides a very welcome backdrop for start-up companies to engage in R&D activities across the translational health research spectrum and this scheme mirrors effective tax incentive schemes in the UK.

Third Stream Funding

In the UK by 1997 the public funding of teaching per student the so called "unit of resource" had fallen by 36%. This led higher education institutions (HEIs) to seek to generate additional income from non-government sources. This funding was termed "third stream" funding in that it was in addition to the primary sources for teaching and research.

The Higher Education Funding Council for England commenced third stream funding in 1999. These funds were to support institutions increase their capacity to respond to the needs of business and the wider community and result in wealth creation. Third stream activities assume that some knowledge or expertise flows between HEIs and users. The first specific funding scheme was the Higher Education Reach out to Business and the Community initiative (HEROBAC) sponsored by the Department for Education and Science and the Department of Trade and Industry. An important feature of this funding is that it was available to the HEIs through a competitive bidding process. The initial third stream funding was followed by successive rounds of the Higher Education Innovation Funds (HEIF) principally provided by the Science Budget. Similar schemes were administered by analogous government bodies in Wales, Scotland and Northern Ireland.

Public funding support for third stream activities is not easy to design. Third stream activities need to remain very diverse as each university responds to its external needs in its own way and this focus should not be narrowed by funding metrics. The policy goal for third stream activities should remain broad so as to enhance the social and economic impact of universities. The overarching policy objective should be to instil economic and social impact as "values" within HEIs. The UK government set such a policy in the Science and Innovation Investment Framework in response to the *Lambert Review of Business*–

University Collaboration. This was reinforced in the 2007 report by Lord Sainsbury *The Race to the Top* and in the Innovation White Paper produced by the Department for Innovation, Universities and Skills in 2008.

The impact of third stream funding has been assessed in a report to the HEFCE by the Public and Corporate and Economic Consultants and the Centre for Business Research, University of Cambridge. These are some of the key observations:

- Total committed third stream funding between 2000/01 and 2010/11 amounts to £1 billion pounds (at 2003 prices).
- In the period 2002/03-2003/04, some 31% of third stream funding went to dedicated knowledge transfer staff rising to a planned 52.3% in the latest HEIF 4 funding round.
- Relatively small amounts of funding have gone to proof-of-concept and seed funding (5.4%) and investment in spin-out companies.
- The synergies between knowledge exchange activities and teaching and research result in very little displacement.
- Income generation is becoming increasingly important as a long-term goal for knowledge exchange activities.
- Small and medium-sized enterprises (SME's) are the most frequent target for third stream activities but for the top six (Imperial College London, King's College London, University College London, University of Cambridge, Manchester University and the University of Oxford) and for higher research institutions large corporations and the public sector are important.
- Some 74% of engagements with industry are still initiated without the involvement of the knowledge exchange offices.
- Knowledge exchange offices face a number of constraints on their growth, namely their ability to attract suitably qualified staff, shortage of finance and negative attitudes of academics.
- Knowledge exchange activities of higher education institutions generated £1.94 billion in income in 2007, growing by 12% over the period 2001-07.

- Income from non-commercial organisations such as public sector and charities constitutes the largest proportion of knowledge exchange income, with SME's generating the least income.
- HEIs believe that between 28% and 41% of knowledge exchange income can be attributed to HEFCE third stream funding.
- The injection of £592 million by HEFCE for third stream funding in the period 2001-07 has generated between £2.9 billion and £4.2 billion of gross additional knowledge exchange income over the same period.

An overall observation of the effectiveness of third stream funding is that the implementation of the scheme through competitive bids by HEIs led to what has been termed "initiativitis" in that many small initiatives were instigated as pilots but largely failed to be rolled out across other HEIs. A significant outcome of third stream funding is, however, that HEIs technology transfer offices were resourced appropriately and this directly increased the commercialisation outcomes particularly in translational research. A recent trend in the provision of third stream funding in the UK is that its effectiveness is assessed in terms of its impact and that the impact measure is used as part of a formula to determine the funding provided to the university by HEFCE.

It is interesting to note that in 1980 in the US the Stevenson-Wydler Technology Innovation Act was introduced at the same time as the better known Bayh-Dole Act and this Act specifically requires that all Federal Laboratories actively participate in and budget for technology transfer activities such that they could capture the value of translational research outcomes.

Third stream funding is not available to Australian university, research institutes and hospital technology transfer offices. This has a significantly negative impact on the ability of these offices to deploy adequate and effectively trained staff to identify and protect intellectual property and bring about its commercialisation. The New Zealand Government provides a Pre-Seed Accelerator Fund (PSAF) across their universities and research institutes endeavouring to achieve greater scale and critical mass through a collaboration termed KiwiNet. The PSAF requires 50/50 matching direct funding from the technology transfer office but it is non-dilutive and is relatively effective except that it is limited by the funding

requirement of poorly funded- technology transfer offices that receive no equivalent third stream funding.

In Australia, proof of concept funding is seldom available to universities, research institutes and hospitals which results in a poorer innovation pipeline as ideas are not tested as the generation of prototypes and translation of *in vitro* to *in vivo* results and disease model studies are not generally grant funded. The Queensland Government has provided very welcome proof of concept funding to several universities within the State but this program is now on hold while the new government decides on its strategy.

Best Case Exemplar – University College London Business

University College London Business PLC (UCLB) is the commercialisation and enterprise arm of the University College London. In the health sciences space, it covers the identification and management of commercialisation projects and resultant contracts stemming from basic research undertaken within the university and its collaborative translation at the neighbouring NHS hospitals (University College, Royal Free, Whittington, Moorfields Eye, and Great Ormond Street).

UCLB has been very successful in bridging the valley of death in drug development through use of the DPFS/DCS schemes in conjunction with additional Wellcome Trust (available in Australia, if invited) TSB and NIHR grants. These grants have been used to fund early stage proof-of-concept demonstrations through to formal pre-clinical drug development. These value-added opportunities can then be partnered through licensing to biotech and pharmaceutical companies and quality returns made on subsequent commercial development and product success. This type of funding is very difficult to obtain in Australia, and many healthcare innovations do not progress beyond the laboratory. In Australia, this type of funding can occasionally be provided by external investors, but that is rare and often results in the innovation and the value being taken from the institution. The UK type approach not only allows a significant pipeline of research to be commercialised efficiently but also encourages the researchers themselves, as they are more involved in the outcomes and impact of their research.

Third stream funding allowed the UCLB team to be resourced appropriately and enabled them to develop the skills and talent to effectively commercialise translational research.

Summary

The UK government, through a number of over-arching schemes but particularly through the MRC strategic grant funding provides continued investment in fundamental basic and clinical research that underpins the translational agenda, which is recognised as the engine room of healthcare innovation. The introduction of third stream funding which is not currently available in Australia has significantly enhanced the ability of the UK technology transfer offices to be more effective in commercialising translational research outcomes.

Australia could do well to heed the best case exemplars that these UK strategies, initiatives, policies and funding schemes have produced that effectively capture the value of translational health research.

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