February 2016

Encouraging the ideas boom in biosciences through collaboration

Key points

- MSD Australia welcomes the Prime Minister's recent announcement of a National Innovation and Science Agenda.
- Australia has a long heritage in making medical breakthroughs but our track record in commercialising biomedical research is poor.
- Consistent with the National Innovation and Science Agenda, MSD believes that the following would greatly enhance Australia's innovative output in the biosciences:

    1. Leverage the local presence of business development functions of global bioscience companies, potentially through the Medical Technologies & Pharmaceutical Growth Centre
    2. Involve more leaders with commercial experience on NHMRC grant panels
    3. Further encourage private companies to participate in NHMRC and MRFF research
    4. Recognise the potency of clinical trials in generating expertise in cutting edge science
    5. Streamline the approval and improve the co-ordination of clinical trials
    6. Support fair and transparent reimbursement policies
    7. Consider the benefits of extending data exclusivity provisions for Australian science
    8. Reduce the red-tape associated with registering innovative medicines.

Introduction

Australian scientists have played a leading role in bioscience research for over 80 years, from Florey's pioneering work in penicillin production, through Don Metcalf's discovery of the first therapeutic proteins to Ian Frazer's invention of cancer vaccine technology.

While Australia punches above its weight in basic research, its performance in commercialising biomedical discoveries is poor. The 2013 Global Innovation Index ranked Australia 116th out of 142 countries in innovation efficiency. As IP Australia has noted, we have the right ingredients for innovation but are ineffective in capitalising on these inputs when it comes to innovative output.[1]

The global pharmaceutical industry funds much of the research that translates scientific discovery into new medicines. The industry invested US$137 billion in R&D globally in 2013, equivalent to 19% of the industry's sales[2]. Pharmaceutical R&D investment in Australia amounts to A$1 billion per year[3], less than 5% of sales[4]. There is clearly scope for Australia to expand its share of this activity.

In this context, the Prime Minister's recent announcement of a National Innovation and Science Agenda is a very welcome development. The Agenda will be of great value in furthering Australia's ability to translate its biomedical capabilities into commercial success. In particular, it rightly identifies collaboration as a key pillar supporting future innovation. In addressing this pillar, the Agenda focuses on funding collaborative university research, research infrastructure and commercialisation through the Biomedical Translation Fund and the CSIRO Innovation Fund.

MSD has drafted this white paper to stimulate discussion on how NISA and other policy initiatives can help to realise the full potential of Australia's world leading capabilities in the biosciences. The paper explores how deeper partnership between Australian bioscience organisations and the global pharmaceutical industry could help to commercialise Australian research, through the following recommendations:

- Deepen the bioscience sector's engagement with global companies
- Increase Australian researchers' participation in global research programs
- Ensure the local environment supports innovative medicines

[1] IP Australia (2014). Australian Intellectual Property Report 2014, page 25. http://www.ipaustralia.gov.au/uploaded-files/reports/intellectual-property-report-2014-low-res.pdf Accessed 04/02/2016

[2] Medicines Australia (2015). Facts Book – Fourth Edition, page 9. https://medicinesaustralia.com.au/wp-content/uploads/sites/52/2010/11/MAFactsBook4_update2015.pdf Accessed 04/02/2016

[3] Medicines Australia (2014).Submission to the Senate Economics References Committee's Inquiry into the Australian Innovation System. Page 1. https://medicinesaustralia.com.au/wp-content/uploads/sites/52/2010/02/33.pdf Accessed 04/02/2016

[4] Medicines Australia (2015). Facts Book – Fourth Edition, page 34. https://medicinesaustralia.com.au/wp-content/uploads/sites/52/2010/11/MAFactsBook4_update2015.pdf Accessed 04/02/2016

1. Deepen the bioscience sector's engagement with global companies

1.1. Leverage the local business development presence of global biomedical companies

MSD has supported Australian research and biotechnology companies for over thirty years. In the 1980s, MSD was the leading commercial partner of both Australia's top biotech companies at the time, CSL and AMRAD. These partnerships led to major research collaborations.

CSL licensed Ian Frazier's "virus like particle" technology from the University of Queensland in 1995 and quickly on-licensed it to MSD[5]. This technology was critical to the development of the HPV vaccine GARDASIL®. MSD has subsequently spent over US$1 billion in developing GARDASIL and the University of Queensland and CSL have earned substantial royalties from GARDASIL sales.

In 2003, MSD entered into a US$112 million collaboration with AMRAD, to develop therapeutic drugs for asthma, respiratory diseases and cancer[6].

More recently, MSD has announced two major collaborations with Australian biotech companies, as summarised in the accompanying case studies[7].

Some common threads are evident in MSD's experience in commercialising Australian research. Our most successful collaborations have arisen from long-standing relationships. In addition, small initial ventures often lead to bigger, sustained investments as an opportunity develops. A critical component of building relations and making early connections is having a local business development presence.

While MSD Australia has full time business development capacity, MSD has established business development centres in Shanghai, London, San Francisco and Boston. These centres help to embed MSD within the bioscience ecosystem, developing understanding of the research being done, building relationships and making discrete

MSD Case Study 1 - Bionomics

Earlier this year, MSD announced a $12.5m investment in the Adelaide based Bionomics for the discovery and development of drug candidates for the treatment of chronic and neuropathic pain. This investment builds on a collaboration agreement concluded in 2013, also related to pain therapy worth US$172m and an agreement on cognitive impairment research worth up to US$506m. In announcing the agreement, Dr Iain Dukes Senior VP, Business Development & Licensing Merck Research Laboratories noted that "establishing strong long-term external collaborations is central to our business development strategy".

[5] Janelle L. Grimes (2006). HPV vaccine development: A case study of prevention and politics. Biochemistry and Molecular Biology Education. Volume 34, Issue 2, pages 148–154. http://onlinelibrary.wiley.com/doi/10.1002/bmb.2006.49403402148/full Accessed 04/02/2016

[6] http://www.lifescientist.com.au/content/biotechnology/news/amrad-in-research-collaboration-with-merck-sharp-dohme-459056448 Accessed 04/02/2016

[7] http://www.bionomics.com.au/upload/investors/asx-announcements/4736/ASX731%20Bionomics%20Merck%20investment%20and%20pain%20collab%20extension.pdf, http://www.bionomics.com.au/upload/investors/asx-announcements/4736/ASX679%20AGM%202014%20Final%20Presentation.pdf, http://www.vaxxas.com/news/vaxxas-initiates-program-with-merck-to-optimize-delivery-of-next-generation-vaccines/ Accessed 04/02/2016

investments in medical research institutes, national research organisations and promising biotech companies in these locations. These centres also help build our own skills in due diligence and working with partners to progress promising bench research into clinical trials.

MSD already conducts outreach work with biotechs and research institutions through our existing relationships and networks. There would be significant value in exploring collaborative ways of deepening this engagement, possibly in conjunction with groups like the recently announced Medical Technologies and Pharmaceuticals Growth Centre.

MSD Case Study 2 – VAXXAS

In 2012 MSD initiated a research collaboration with Brisbane-based VAXXAS to evaluate, develop and commercialize VAXXAS' Innovative Nanopatch™ vaccine delivery platform. MSD also agreed to provide funding to VAXXAS to conduct research evaluating the potential of using Vaxxas' Nanopatch platform for vaccine candidates. The Nanopatch technology also originated at The University of Queensland and was initially commercialised by the university's commercialisation arm, UniQuest.

1.2. Involve more leaders with commercial experience on NHMRC grant panels

A challenge that MSD faces in Australia is finding ways to collaborate in NHMRC funded projects. Academic institutions dominate both the decision making process for NHMRC grant dispersal and the pool of recipients. Scientific leaders with biotech or global pharma experience are not often represented on grant panels and consequently translational research projects are rarely favoured in grant allocations.

As a case in point, of the $630 million in NHMRC grants announced in November 2015[8], only a small proportion was for projects that could be regarded as translational research.

1.3. Further encourage participation of private companies in publically funded research

Of additional concern are the conditions attached to commercial participation in government funded research programs. For example, the collaborative research grants provided through the Australian Research Council and the Department of industry require partner organisations to contribute a significant proportion of overall funding. This can hamper involvement in those small initiatives which could be instrumental in building the relationships and collaboration necessary for bigger joint projects.

Given these points, we are very heartened that NISA has put such emphasis on translational research including the establishment of the new $250m Biomedical Translation Fund. Together with other recently established funding sources such as the Medical Research

[8] https://www.nhmrc.gov.au/_files_nhmrc/file/media/151109_ley_mr_nhmrc_grants_announcements.pdf Accessed 04/02/2016

Commercialisation Fund, this will greatly assist in developing promising Australian research to the point of commercialisation.

Another important development in research funding was the government's announcement last year that a Medical Research Future Fund would be established to support research that enables game-changing medical innovations and improves the health of Australians. The fund is expected to distribute $10m in 2015-16 and $400m over the next four years.

Legislation for MRFF was passed in August 2015 and the Health Minister Sussan Ley has announced that the announcement of an eight person board of governors will follow shortly[9]. Encouragingly, the Minister announced that this board will include governors with expertise in commercialisation and the translation of research into health applications. Hopefully the MRFF can fund research that increases collaboration across academia, biotechs and global companies that will spawn bigger development and commercialisation projects.

2. Increase Australian participation in global research programs

2.1. Recognise the potency of trials in generating expertise in cutting edge science

Clinical trials are a critical means of nurturing innovation in Australia through closer collaboration between industry and scientists. MSD supports approximately 70 trials ongoing at any one time in Australia, costing around $60 million (over three years). The company has seen a significant increase in recent years in the early phase clinical research conducted in Australia. This is important because it gives Australian clinicians and scientists exposure to the newest and most complex part of pipeline. It also gives Australians the opportunity to influence how future research will be conducted, given the world leading expertise that Australia has in many therapeutic areas. One example would be melanoma where Australia participated in the Phase I study for MSD's KEYTRUDA® (pembrolizumab) and this led to participation in more than five further trials in Phase II-III due to the success of the Phase I study and the high quality data submitted by our Australian sites.

Clinical research can also add significant value to early Australian research. For example, the Sydney based biotech Viralytics recently announced that it would be jointly researching a combination of its investigational cancer immunotherapy CAVATAK™ with KEYTRUDA®[10]. The Phase 1b clinical trial will evaluate the safety and efficacy of this novel immunotherapy combination in patients with either advanced stage non-small cell lung cancer (NSCLC) or metastatic bladder cancer. The trial will begin in 2016.

[9] http://www.health.gov.au/internet/ministers/publishing.nsf/Content/770C94E11F5BE7FCCA257E9F001AA120/$File/SL101.pdf Accessed 04/02/2016

[10] http://www.viralytics.com/wp-content/uploads/2014/05/151106-FINAL-release-Viralytics-Merck-combination-study.pdf Accessed 04/02/2016

2.2. Streamline the approval and improve the co-ordination of clinical trials

Unfortunately, despite recommendations from the Clinical Trial Action Group and the McKeon review to streamline trial administration, Australia is still a difficult market in which to conduct trials. The consequence of this has been a decline in the number of new trials conducted here, from a high of 865 trials in 2007 to 681 in 2013[11]. Although we have seen some growth in new trials in 2014 and 2015, the unpredictability and high costs of local research prevents Australia from even greater participation in global clinical trial programs.

The most critical recommendations that government should continue to act on include:

1. Streamlining the requirements for research governance (RGO) approval – insisting on parallel RGO and ethics committee approvals.
2. A single national ethics submission application form, a single national CTRA and national accreditation of committees, that is recognised by all states and territories, that avoids the redundant re-review of applications/approvals or different template expectations between tertiary hospitals around the country.
3. Looking to host a forum between the Hospital Chief Executives and Research officers from the major research hospitals around the country, so that a single conversation of how to increase global trial participation can be had to transcend the barriers of the state and federal legislation and procedures that prevents this from happening now.

3. Ensure the local environment supports commercialisation & investment

3.1. Support fair and transparent reimbursement policies

Investments in medical science by governments and companies ultimately only make sense if patients stand to benefit from the resulting advances. Australian innovation has already delivered substantial benefits to local patients. For example, Australia has achieved one of the highest coverage rates in the world with GARDASIL, which has already brought tremendous benefits. A recent study showed that in the five years after GARDASIL was added to the national immunisation program in Australia, the occurrence of genital warts in women under 21 fell by 93%[12].

Unfortunately, many PBS and other policies in Australia systematically undervalue innovative medicines. The most recent of these – implemented as part of the 2015 PBS Access and Sustainability Package – imposes indiscriminate price cuts on patented medicines that have already undergone rigorous assessment for cost-effectiveness. Another policy that restricts funding for innovative medicines is the requirement that any new PBS spending must be funded

[11] Medicines Australia (2015). Facts Book – Fourth Edition, page 12. https://medicinesaustralia.com.au/wp-content/uploads/sites/52/2010/11/MAFactsBook4_update2015.pdf Accessed 04/02/2016

[12] Ali et al. (2013). Genital warts in young Australians five years into national human papillomavirus vaccination programme: national surveillance data. British Medical Journal. http://www.bmj.com/content/346/bmj.f2032 Accessed 04/02/2016

through offsets, yet the billions of dollars in savings that government has secured through generic price reductions and pharmaceutical rebates cannot be used for this purpose.

Such policies are ultimately a self-defeating means of securing budget savings for the Australian government. Not only do they reduce the probability that innovative new medicines will be listed on the PBS in future, they also reduce the incentive to develop any new medicines in the first place. The US, Japan and other developed markets provide a disproportionate share of incentives for biomedical innovation and Australia, through its reimbursement policies, effectively free-rides on the contributions of other payers.

3.2. Consider the benefits of extending data exclusivity provisions for Australian science

Australia also falls short in the provision of data exclusivity for medicines where patent protection is not available. Most developed countries provide eight to twelve years of such protection, whereas Australia only provides five. This disadvantages not only global companies but also Australia firms that have less incentive to complete the development work needed to commercialise products that do not have patent protection.

3.3. Reduce the red-tape associated with registering innovative medicines

Regulatory red-tape is a further barrier to commercialising biomedical research. The recent Review of Medicines and Medical Devices includes a number of recommendations to streamline and accelerate the regulatory approval of innovative medicines. These could greatly enhance both the speed and predictability of the approval process in Australia.

Specific recommendations that MSD would support include introduce an expedited review process for breakthrough medicines, streamlining the TGA variations process and exploring opportunities to enhancing real time pharmacovigilance through e-health.