GUIDE TO LIFE SCIENCES INVESTING

First Edition

AusBiotech
AUSTRALIA'S BIOTECHNOLOGY ORGANISATION

MTPConnect
MedTech and Pharma Growth Centre

Australian Government
Department of Industry, Innovation and Science

Industry Growth Centres

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FOREWORD

By Glenn Cross, CEO, AusBiotech

AusBiotech is committed to promoting the sustainable growth of the Australian life sciences sector. This includes connecting the life sciences industry, investors and researchers to spark collaboration and innovation; influencing and supporting the development of industry policy; driving outreach and access to markets; and representing and advocating for members in Australia and around the world.

As part of an initiative aimed at increasing the competitiveness of Australian life sciences research and commercialisation in the global marketplace, AusBiotech is actively educating potential investors in life sciences companies about the unique ecosystem, particularly in the medical technology and pharmaceuticals (MTP) sector in Australia.

This *Guide to Life Sciences Investing* will provide potential investors in life sciences companies with consolidated, factual, relevant and independent information about the sector. It builds on general investment guidance by featuring key considerations for the life sciences sector. It will be accompanied by complementary seminars to equip potential investors with knowledge of the basic operations and products of life sciences companies, including the terminology, time lines and regulatory frameworks in the sector, as well as how securities trade on the market. These seminars will be delivered nationally.

As industry momentum, policy settings and healthy levels of confidence remain a work in progress, AusBiotech is optimistic about the environment that life sciences companies operate in. The *Guide to Life Sciences Investing* is one of the four main projects within the 'Comprehensive Global Investment Program for the Australian Life Sciences Sector – companies, investors and researchers' (funded by the MTPConnect Project Fund Program), and is a collaboration between Australian Securities Exchange (ASX), KPMG, Dentons and WE Buchan. We acknowledge the generosity and expertise of MTPConnect, the consortium members and various life sciences industry experts for their contributions in developing and delivering this valuable program.

CONTENTS

ONE About this Guide

Guide to Life Sciences Investing (the Guide) explains the unique ecosystem of the life sciences sector to potential investors in life sciences companies, particularly in the medical technology and pharmaceuticals (MTP) sector in Australia.

Aimed at investors with little experience in the life sciences sector, this Guide outlines the factors particular to life sciences companies that potential investors should consider. This specialised knowledge is not generally available from mainstream investment resources.

This Guide:

- consolidates factual, relevant and independent information about the life sciences sector, such as the unique regulatory requirements, terminology, time line and business cycle of these companies;
- builds on general investment guidance by featuring the important considerations for the life sciences investor;
- explores general paths and scenarios but does not cover all possible options within the very diverse MTP sector.

Monetary amounts are given in Australian dollars unless otherwise specified.

This Guide is not investment or financial product advice and is not intended to be used as the basis for making an investment decision. This document has been prepared without taking into account the investment objectives, financial situation or needs of any particular person and does not purport to contain all of the information that may be required to evaluate a potential investment. Readers who are considering an investment in a life sciences company should seek appropriate professional advice in light of their particular circumstances.

This Guide is part of a larger program to educate investors, both private and institutional, about the industry and provide life sciences companies with the skills to better source, connect and communicate with potential investors.

Educating potential investors about the industry will ensure more and higher quality investment, increase investors' participation in the wider life sciences community and drive long-term sustainable growth. Our goal is that Australian and overseas investors increasingly see Australian life sciences research and small-to-medium enterprises (SMEs) as viable and attractive investment options.

TWO Why consider the life sciences sector?

The life sciences sector is among the most innovative in the global economy and is a major contributor to research and development (R&D) both internationally and within Australia. With scientific and technological advances in medical treatments, growth in healthcare expenditure fuelled by increasing demand from an ageing population and efforts to tackle chronic and infectious diseases, investor interest in the life sciences sector is growing.

The life sciences sector comprises universities, other research organisations, small and large local and multinational companies, investors, service providers, industry organisations, regulators, policymakers, and funders.

Scientific and technological innovation

Basic biomedical research, including the fields of genomics, epigenetics, the microbiome, neuroscience, immunology, and cellular and molecular biology, is constantly improving our understanding of the human body and how it works – in health and in sickness or ageing. We can peer inside cells to see the complex processes controlled by genes and non-coding DNA, and we can trace the roles of particular molecules within cells. This knowledge provides insight into the biomolecular causes of many diseases and conditions, and may help scientists uncover novel strategies for diagnosis, prevention and treatment.

At the same time, technological advances, such as in genome sequencing, microscopy, drug delivery, gene editing, labs on a chip, 3-D printing and bionic devices, are transforming healthcare, facilitated by advances in information technology (IT) and mathematics. The ability to handle huge electronic datasets (big data), and to analyse the data with mathematical and statistical techniques (bioinformatics), has given healthcare providers, researchers and leaders in the MTP sector valuable and actionable patient insights.

Advances in medical services

New and evolving technologies are also being applied directly to medical services and healthcare: the Australian Government announced in the 2017 Budget that electronic health records would be created for every Australian from 2018; hospitals are moving towards sophisticated electronic medical records rather than patient charts; wearable healthcare devices are becoming available; and data analytics techniques allow for the collection and use of real-world evidence (that is, data from patient and health service records outside clinical trials).

As hospitals embrace big data, healthcare providers can match individual patients with the best treatment for their diseases, personalising their care and treatment. It is anticipated that, with these policy changes and advances in technology, along with increased life expectancy and cultural shifts, people will take a more active role in their health management in the future.

Engagement will increase as patients begin to better understand their own condition, and they have better informed conversations with their healthcare provider.[1]

Initiatives to share information on health and disease within the research community can also accelerate and increase the effectiveness of new drugs and treatments.

The combination of research, big data and advances in healthcare has enabled the emergence of new applications and digital products to empower patients, carers and clinicians. Studies have demonstrated a global demand from patients for access to high quality digital health services that cater to their needs. Start-ups in the digital health field have emerged to fill this demand.

A growing healthcare sector

Growth in the life sciences sector is closely linked to global healthcare expenditure, and this is rising as populations age and as governments tackle chronic and infectious diseases. With increases in healthcare spending, there is also a rising demand for novel medical technology and pharmaceutical solutions that can help reduce costs while also delivering a higher standard of care.

The Deloitte *2017 global life sciences outlook: thriving in today's uncertain market* report provides an overview of the current state of the global life sciences sector.[2] Overall, the report found an increase in global healthcare expenditure due to the rising prevalence of chronic and communicable diseases as well as increased life expectancy. The findings from this report are adapted in Figure 1.

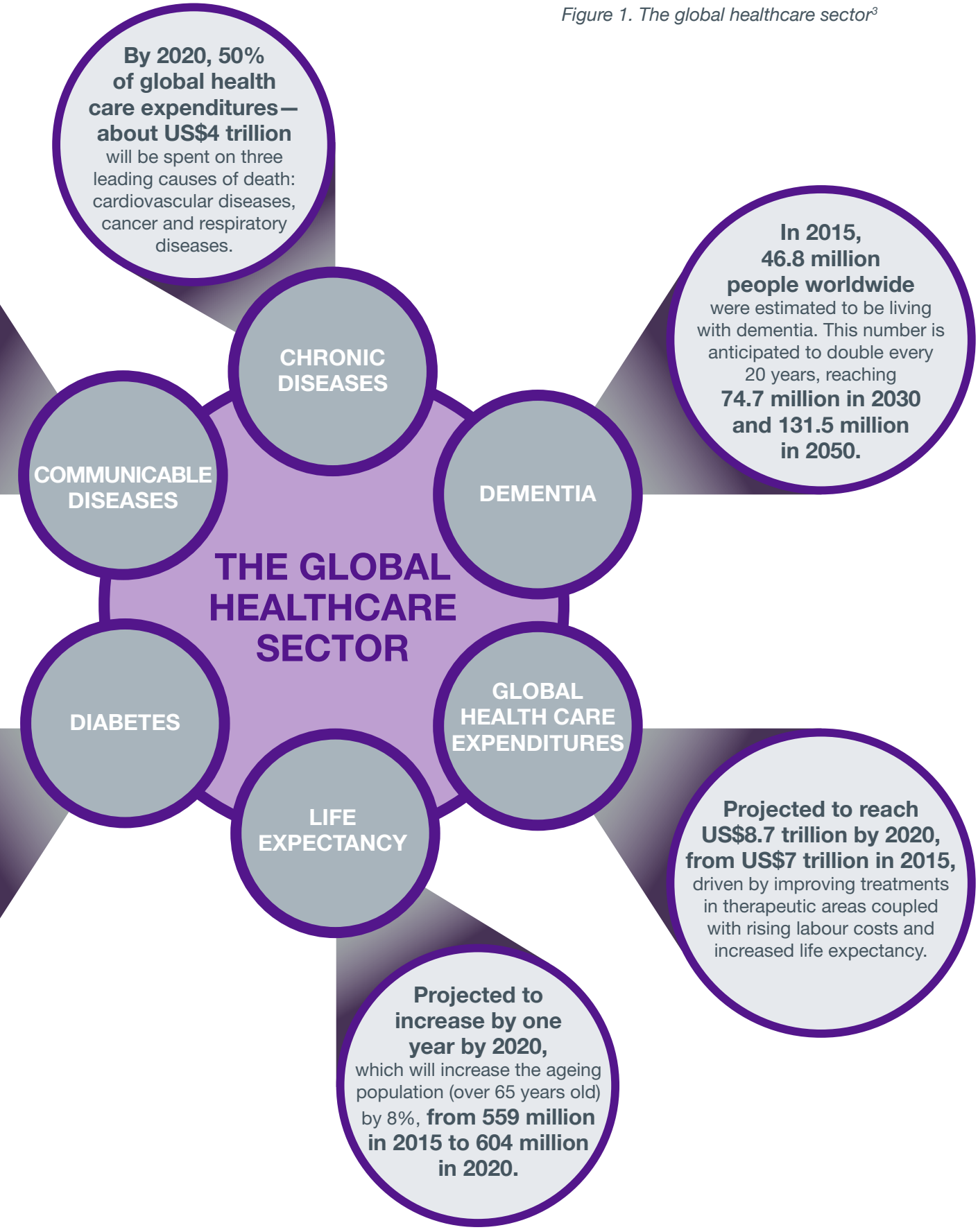
HIV-AIDS continues to affect **36.9 million people worldwide, with around 70% of them living in Sub-Saharan Africa.** The Zika virus and associated upsurge in microcephaly are major threats in Latin America.

China and India have the largest number of diabetes sufferers in the world, at around **110 million and 69 million, respectively.** Globally, the number is expected to rise from the **current 415 million to 642 million by 2040.**

1 Australian Digital Health Agency website, 'Welcome to my health record' https://myhealthrecord.gov.au/internet/mhr/publishing.nsf/content/home

2 Deloitte, 2017, *2017 global life sciences outlook: thriving in today's uncertain market*, Deloitte https://www2.deloitte.com/content/dam/Deloitte/global/Documents/Life-Sciences-Health-Care/gx-lshc-2017-life-sciences-outlook.pdf

Figure 1. The global healthcare sector[3]



3 Ibid.

Improved economic activity in key regions, such as developing nations in the Middle East and Asia, continuing industry consolidation and collaboration, and new business models enabled by scientific and technology advances are all potential growth drivers.

Global revenue for the healthcare sector is expected to rise from US$1,652 billion in 2015–16 to US$2,696 billion in 2025, with a compound annual growth rate of 5.6 per cent.[4] North America and Europe are currently the most significant markets for the sector, but emerging economies are rapidly increasing in buying power. North America is expected to lose its largest healthcare market tag to Asia in the next decade.

Interest in life sciences investment

The developments discussed above have fuelled investor interest in the life sciences sector, including some extremely large players. In September 2012, the Wellcome Trust, the world's second-largest biomedical charity, established an investment unit to back life sciences start-ups in the medical technology, therapeutics, diagnostics and digital health industries; Syncona Partners limited liability partnership (LLP) began with £200 million of initial capital. In December 2016, Battle Against Cancer Investment Trust acquired Syncona Partners LLP to form an investment company valued at more than £850 million, with the aim of addressing the capital shortage for commercialising life sciences research.[5,6] In another example, Google Ventures in 2015 invested about one-third of its funding into companies in the life sciences sector.[7]

Recent reports suggest an optimistic overall outlook for investments, although some investors and industry thought leaders have expressed concern that growth in the sector may not continue at the same pace.[8,9]

Investors choose the life sciences sectors for a variety of reasons, including:

- the sector's potential for explosive capital growth;
- benefit to the community; for example, through new medicines or improved processes;
- the fact that equities in life sciences are less affected by broader economic conditions than are equities in some other sectors;
- to diversify or balance an investment portfolio;
- a demand for 'high risk, high reward' investments.

4 Ibid.

5 Syncona website, 'About Syncona' http://www.synconaltd.com/about/

6 Wellcome Trust website, 2016, 'Syncona to join forces with leading investment trust' https://wellcome.ac.uk/news/syncona-join-forces-leading-investment-trust

7 Enriquez, J, 2016, 'Google ventures betting big on medtech, biotech, digital health', Med Device Online website https://www.meddeviceonline.com/doc/google-ventures-betting-big-on-medtech-biotech-digital-health-0001

8 McGovern, B, 2017a, 'Biotech stocks still gaining despite drug price regulation fears', Life Science Investing News website http://investingnews.com/daily/life-science-investing/biotech-investing/biotech-stocks-gaining-despite-pricing-regulation-fears/?as=1&nameplate_category=Life+Science+Investing

9 McGovern, B, 2017b, 'Report suggests the biotech industry is still thriving despite political unrest', Life Science Investing News website http://investingnews.com/daily/life-science-investing/biotech-investing/report-suggests-the-biotech-industry-is-still-thriving-despite-political-unrest/?as=1&nameplate_category=Life+Science+Investing

Performance and risk

Index performance tracking on ASX has shown that the health sector has outperformed other sectors, including IT and mining, in recent years.

However, investing in the life sciences is considered by many to be high risk. Overall, life sciences companies have a 5 to 15 per cent success rate on products they attempt to commercialise.[10] Successful life sciences companies take about 10 to 15 years to achieve commercialisation, longer than the average in other sectors, and most businesses operate for long periods of time before they achieve any measurable revenue.[11]

Like investors in the mining industry, investors in the life sciences sector tolerate high levels of risk, but may also enjoy high returns when investments are successful.

Early shareholders of companies such as Amgen and Biogen have made massive profits as those entities have grown significantly over the years. Investors in life sciences start-ups may also receive substantial returns when larger firms acquire the entity or license its technology to add to their own product offerings.

In addition to the inherent uncertainties of dealing with human or animal health, life sciences companies must navigate unique challenges around regulatory compliance, clinical and operational innovations, customer and consumer engagement, and cost and pricing.

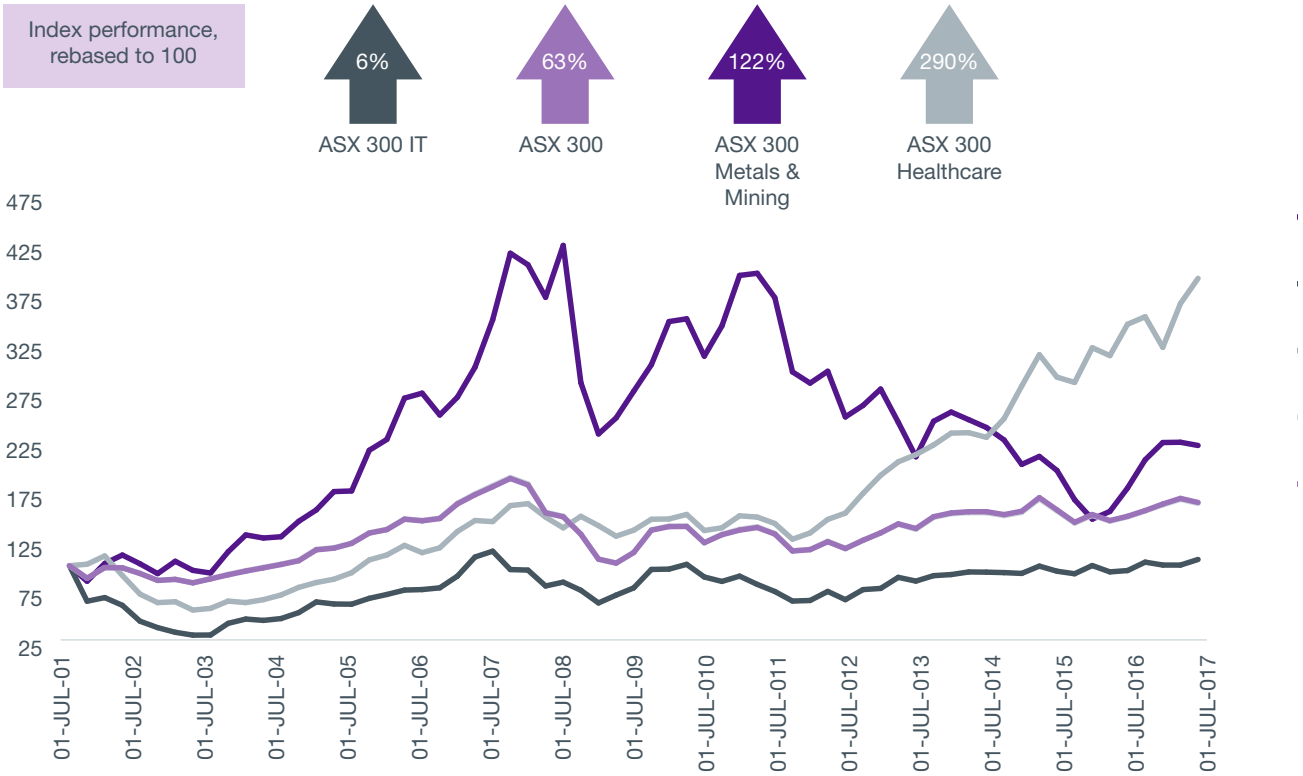


Figure 2. ASX health sector performance July 2001 – June 2017 (data provided by ASX)

10 Thomas, DW, Burns, J, Audette, J, Carroll, A, Dow-Hyeglund, C & Hay, M, 2016, *Clinical Development Success Rates 2006–2015*, Bio, Biomedtracker & Amplion https://www.bio.org/sites/default/files/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf

11 AusBiotech 2013, *Guide for Life Science Company Directors*, 1st edition https://www.ausbiotech.org/documents/item/334

THREE The Australian life sciences investment landscape

Australia is ranked in the top 10 Organisation for Economic Co-operation and Development (OECD) member nations for its total expenditure on R&D.[12] Australian scientists are doing cutting-edge research; Australian research findings are regularly cited in many of the world's leading publications, and Australia has world-class research institutions and a well-educated workforce. A global leader in life sciences research, Australia offers investment opportunities ranging from discovery research through to product development partnerships in medical technology and pharmaceuticals, biotechnology and digital health areas.

Investors can benefit from:

- research excellence and a collaborative culture;
- accessible world-class research infrastructure;
- a track record of commercial success;
- an ideal market for testing new innovative medical products and technologies;
- Australia's trade, investment and cultural ties to the fast-growing Asia–Pacific region;
- Australia's strong but flexible regulatory regime, including strong intellectual property (IP) protection, fast-tracked clinical trials, tax incentives and a supportive business culture for undertaking R&D.

Australia's life sciences sector

Australia represents a very small market, with approximately 1 per cent of global MTP sales[13], but is well placed to capitalise on the rapid growth of its densely populated neighbours. Australia has a thriving research industry. The National Health and Medical Research Council (NHMRC) reports that Australia contributes 3 per cent of the world's published biomedical research.[14] Between 2001 and 2010, Australia ranked sixth in the world in terms of overall output of health and medical publications.[15] Australia ranked fifth globally in biotechnology in *Scientific American Worldview* 2016.[16]

The MTP sector, a vibrant ecosystem of start-ups and established companies, is a significant contributor to the Australian economy, generating approximately $4.4 billion in gross economic value added and $4.0 billion in annual exports from manufacturing in 2016.[17] In 2017, it was found that the sector employs more than 100,000 people across medical technology, biotechnology and pharmaceuticals, and health and medical research.[18]

There are approximately 325 medical technology companies and 281 pharmaceutical companies currently operating in Australia.[19]

12 Australian Trade and Investment Commission website, 'Innovation' https://www.austrade.gov.au/International/Invest/Why-Australia/Innovation

13 L.E.K. Consulting Pty Ltd, 2016, *Medtech, biotechnology and pharmaceutical sector competitiveness plan*, MTPConnect, Clayton https://www.mtpconnect.org.au/SCP

14 NHMRC website, 'Measuring up 2013' https://www.nhmrc.gov.au/guidelines-publications/nh164

15 MTP Connect website, 'MTP sector facts and stats' https://www.mtpconnect.org.au/Category?Action=View&Category_id=87

16 Scientific American Worldview website, 'The 2016 *Scientific American Worldview* overall scores' http://www.saworldview.com/scorecard/the-2016-scientific-american-worldview-overall-scores/

17 L.E.K. Consulting Pty Ltd, 2016, op.cit., p.10

18 AusBiotech website, 'Australia's Life Sciences Sector Snapshot 2017' https://www.ausbiotech.org/documents/item/389

19 Ibid.

Over 160 medical technology, biotechnology and pharmaceutical companies are listed on ASX, with a combined market capitalisation of $50 billion, and in 2015 over 500 medical technology companies with products are listed on the Australian Register of Therapeutic Goods (ARTG).[20,21]

In 2015, the NHMRC and Australian Research Council (ARC) awarded approximately $775 million in grants for R&D projects in the life sciences sector.[22] Industry R&D spending is estimated at $630 million per year.

Despite the availability of research funding, shortfalls in funding at the pre-clinical and early stages of clinical development are common; attracting private capital during these early stages is difficult. Some potential innovations do not get past the pre-clinical and clinical stages of development because of challenges in attracting funding. These early exits from the innovation process detract from the long-term success of the sector. Recognising this, the Australian Government has established programs, such as the $250 million Biomedical Translation Fund, to attempt to bridge the commercialisation gap.

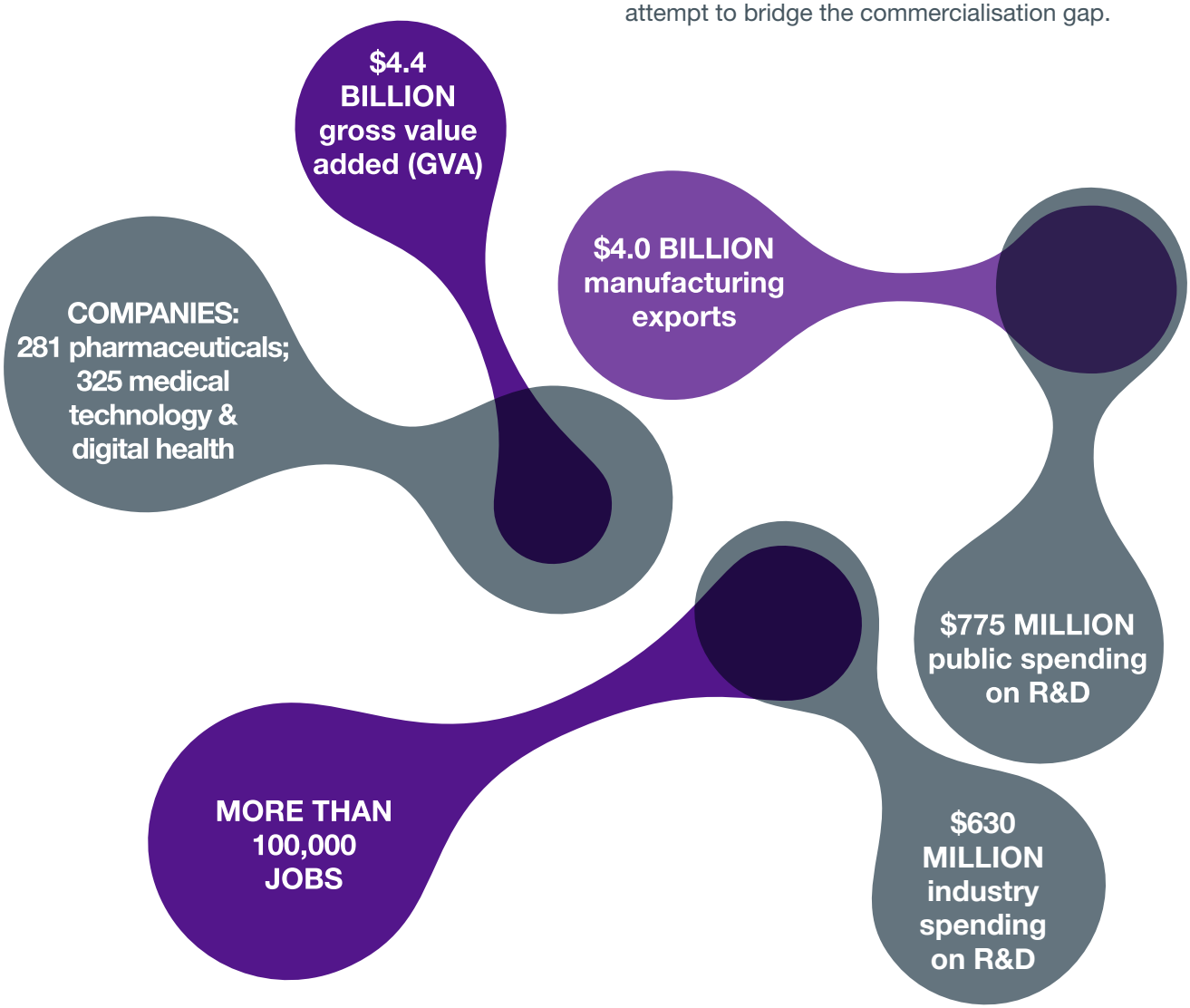


Figure 3. The Australian life sciences sector[23,24]

20 Medicines Australia, 2015, *Facts book*, 4th edition, Medicines Australia, Deakin, ACT

21 AusBiotech website, 'Biotechnology industry' https://www.ausbiotech.org/biotechnology-industry/fast-facts

22 L.E.K. Consulting Pty Ltd, 2016, op.cit., p.10

23 Ibid.

24 AusBiotech, 2017, op.cit., p.10

Successful Australian research–industry collaborations

Australian researchers and institutions have played pivotal roles in the discovery of a number of treatments. Some of the most notable commercialisations have come about through collaboration between scientists in universities and research organisations and industry.

A drug that targets cancer cells in leukaemia patients[25,26]

Cancer is an abnormal proliferations of cells, long believed to be caused by excessive cell growth. In 1988, scientists from the Walter and Eliza Hall Institute of Medical Research (WEHI) discovered that in some cancers the excessive cell numbers result from unwanted cells not dying when they should – and that this was caused by the Bcl-2 gene. This new perspective on cancer was hailed as a major milestone. The team then discovered small molecules (called BH3-mimetics) that bind to Bcl-2, stopping it working and allowing the usual cell death to occur. The institute then established a collaboration with pharmaceutical companies AbbVie and Genentech. The drug venetoclax (ABT-199) was developed for clinical use, and patients with chronic lymphocytic leukaemia in Melbourne were the first to receive treatment in 2011. In 2016–17, drug regulatory bodies in the United States of America (US), European Union (EU) and Australia approved venetoclax for treating certain forms of chronic lymphocytic leukaemia. In 2016, Reuters forecast that 2020 sales of venetoclax would reach US$1.477 billion.

The Gardasil vaccine against cervical cancer[27]

Cervical cancer is the second most common cancer in women globally, killing approximately 275,000 women annually. Many cervical cancers are caused by the human papilloma virus (HPV). The main barrier to the successful development of a vaccine was that the virus cannot be cultured without living tissue. In 1990, researchers at the University of Queensland (UQ) developed virus-like particles that could mimic the HPV virus, technology that would later be used to develop the Gardasil vaccine. The HPV technology was patented in 1991 and faced a complex patent dispute against competing researchers from the US, under the (now abolished) 'first to invent' rules in the US. In 2006, the United States Food and Drug Administration (FDA) approved Gardasil; in 2007, the US Federal Court ruled in favour of UQ. After several years of sales, Gardasil continues to dominate the global HPV vaccine market, reaping sales of more than US$1 billion annually.

25 Walter and Eliza Hall Institute, 'Venetoclax: towards a cure for cancer' https://social.shorthand.com/WEHI_research/nge4mUouhGc/venetoclax

26 Thomson Reuters, 2016, *Drugs to watch 2016*, Thomson Reuters http://images.info.science.thomsonreuters.biz/Web/ThomsonReutersScience/%7B14407903-e8d2-45ec-845d-38e68caf0bca%7D_tr_drugs_watch.pdf

27 HPV Vaccine website, 'The HPV vaccine' http://www.hpvvaccine.org.au/the-hpv-vaccine/vaccine-background.aspx

Mesoblast: an Australian-based regenerative medicine company[28,29]

Mesoblast was established in Melbourne, Australia, in June 2004 by its Chief Executive Officer, Professor Silviu Itescu. Mesoblast's vision is to develop a range of therapeutic applications to treat inflammatory ailments, cardiovascular disease and back pain using mesenchymal precursor cells (MPCs), which are connective tissue cells that are capable of differentiating into multiple cell types. Mesoblast listed on ASX six months after its establishment, raising $20.7 million. Mesoblast undertook further funding, raising $78.4 million from 2006 to 2010. In 2010, Cephalon, a US-based biopharmaceutical company acquired a 19.99 per cent equity stake in Mesoblast at a 45 per cent premium along with a $129 million up-front cash payment and milestone payments of up to US$1.7 billion, amounting to a deal worth more than $2 billion. Mesoblast received Therapeutics Goods Administration (TGA) approval in July 2010 allowing it to manufacture its MPCs and supply them to doctors and hospitals around Australia. Mesoblast has leveraged its proprietary technology platform based on the mesenchymal lineage adult stem cells (MLCs) to establish a broad portfolio of late-stage product candidates. In particular, its investigational product candidate MPC-06-ID is currently being developed to treat patients suffering from moderate to severe chronic low back pain due to moderately degenerated discs. The treatment is currently in Phase 3 trial in the US with an estimated completion date of February 2020.

Spinifex Pharmaceuticals[30,31,32]

Spinifex Pharmaceuticals, a US–Australian biotechnology company developing new drug candidates for the treatment and management of pain, was established in 2005. It was a privately held development stage company focused on developing a peripheral approach to treat neuropathic pain (which is caused by disease or injury affecting the nerves on the skin or inside the body). Spinifex's investors were Novo A/S, Canaan Partners, GBS Venture Partners, Brandon Capital Partners, Uniseed and UniQuest. In 2015, Spinifex was acquired by Novartis for US$200 million plus undisclosed clinical development and regulatory milestone payments. Positive results from Spinifex's Phase 2 clinical trial have been published in *The Lancet*.[33] They show the efficacy of their new drug (EMA401) in treating post-herpetic neuralgia, a painful condition that develops in some people following shingles. No central nervous system side effects or any serious adverse events were observed in the study.

28 Department of Industry, Innovation and Science, 2011, *Mesoblast case study December 2011* https://industry.gov.au/innovation/reportsandstudies/Documents/MesoblastcasestudyDecember2011.pdf

29 Mesoblast website, 'Overview' http://www.mesoblast.com/company/overview

30 Jane Prentice website, 'Another medical research success story out of UQ' http://www.janeprentice.com.au/News/ID/2268

31 Fierce Biotech website, 'Updated: Novartis takes a pain med in $700M buyout deal for Spinifex' http://www.fiercebiotech.com/biotech/updated-novartis-takes-a-pain-med-700m-buyout-deal-for-spinifex

32 Cision PR Newswire website, 'Spinifex Pharmaceuticals to be Acquired by Novartis', http://www.prnewswire.com/news-releases/spinifex-pharmaceuticals-to-be-acquired-by-novartis-510575371.html

33 Rice, A et al., EMA401, an orally administered highly selective angiotensin II type 2 receptor antagonist, as a novel treatment for postherpetic neuralgia: a randomised, double-blind, placebo-controlled phase 2 clinical trial. *The Lancet*, 2014, 383(9929):1637–1647

FOUR Understanding life sciences companies

Investors in life sciences companies should understand the characteristics of such companies, in terms of the nature of their assets, their product development pathways, and the regulatory and policy environments controlling their development and commercialisation.

In contrast to companies selling services or non-regulated products, which may be able to generate revenue within weeks or months, life sciences companies typically generate no revenue or operate at a loss for a long time. Developing life sciences products entails large risks, including the possibility that clinical trials will fail or that regulatory approval will be denied. Even if those hurdles are passed, it may take 10 to 15 years for a product to reach market, and commercial success is not guaranteed.

Intellectual property assets

The long lead time in life sciences product development means that most of the value of start-up life sciences companies is derived from their IP assets. For companies whose business model involves licensing their product to third parties in return for royalties and other payments, a broad and secure IP position is necessary for business success. Even before a product starts to generate revenue from licensing or sales, IP assets can offer exclusivity and/or other competitive advantages that may help attract investment and capital for technology development. Examples of IP assets are:

- Patents for inventions, such as drugs, devices and methods of treatment
- Trade secrets and know-how, including proprietary processes, procedures, cell lines and information
- Trademarks, brand names and logos
- Copyright materials, such as promotional materials and website content
- Regulatory exclusivity, such as data or market exclusivity

Patents

Patents are the most common method of protecting IP in life sciences, and a life sciences company's patent portfolio is arguably its most important IP asset. Patents provide exclusive commercial rights to a defined invention for a specified period of time; they are granted on a country-by-country basis. The patent holder has the exclusive right to exploit the invention during the term of the patent, and to authorise one or more third parties to exploit the invention. A patent may be granted when it is shown that a device, substance, method or process is new, inventive and useful. In return for the grant of exclusivity, patent applicants must publicly disclose a full description of how their invention works, which can provide the basis for further research by others. There are two types of patents in Australia[34]:

STANDARD PATENT

Provides long-term protection of up to 20 years for an invention

INNOVATION PATENT

Provides protection for up to eight years for inventions that are innovative rather than inventive

34 IP Australia website, 'Types of patents' https://www.ipaustralia.gov.au/patents/understanding-patents/types-patents

Innovation patents are rarely used for life sciences inventions because of their short exclusivity period and the fact that they are granted (but not enforceable) without substantive examination. In August 2017, the Australian Government released its response to the Productivity Commission Inquiry into Intellectual Property Arrangements, supporting the recommendation that the innovation patent system be abolished.[35] The Australian Government will seek legislative amendments to the *Patents Act 1990* (Cwlth) to abolish the innovation patent system, with appropriate arrangements to maintain existing rights.

Patent protection gives companies in the life sciences sector the power to set their own prices, in comparison to, for example, the mining sector where prices are at the mercy of commodity fluctuation.

In a number of countries, including Australia, patent laws provide for an extension of the term of a patent where a significant portion of the patent life has been used up in lengthy regulatory processes.[36] The term of an Australian pharmaceutical patent may, if strict criteria are met and strict procedures are followed, be extended from the usual 20-year term to up to 25 years, if the date of regulatory approval was at least five years after the date of the patent.[37]

Trade secrets

Trade secrets are information, processes or formulas used in production that are kept confidential by a company or inventor. For example, while the composition of a product and the ways in which it can be used may be published in patent specifications, its manufacturing processes may be a closely guarded trade secret.

Trade secrets are protected by maintaining confidentiality. This may be achieved through contractual obligations of confidence, and by taking practical means to limit access to the knowledge. By keeping them confidential, trade secrets can be protected indefinitely, but they may lose their value if they become known.

Regulatory exclusivity

Products that have gained regulatory approval may also benefit from a period of some type of exclusivity, depending on the country in which regulatory approval has been granted:

- Data exclusivity specifies a period of time during which generic competitors cannot use data generated by the innovator to secure regulatory approval under the *Therapeutic Goods Act 1989* (Cwlth) for a generic or biosimilar version of the innovator drug.
- Market exclusivity is the protection given by the patent system that prevents a competing generic product from entering the market. Unlike the more limited protection afforded to novel drugs by data exclusivity, market exclusivity prevents a competing pharmaceutical company from generating its own data and submitting a new application for regulatory approval.
- Orphan drug status is a category used by the FDA for medications used to treat rare diseases and conditions. It gives a manufacturer specific financial incentives and market exclusivity to develop and provide such medications.[38]

35 Department of Industry, Innovation and Science website, 'Australian Government Response to the Productivity Commission Inquiry into Intellectual Property Arrangements' https://www.industry.gov.au/innovation/Intellectual-Property/Documents/Government-Response-to-PC-Inquiry-into-IP.pdf

36 Attorney-General's Department, 2012, *Intellectual property manual* (version 2), Commonwealth of Australia http://aspheramedia.com/wp-content/uploads/2014/10/intellectualpropertymanual-1.pdf

37 Australian Patent Office website, Manual of Practice and Procedure, '3.12 Extension of term of standard patents relating to pharmaceutical substances' http://manuals.ipaustralia.gov.au/patents/opposition/ext_of_term/3.12_Extension_of_Term_of_Standard_Patents_Relating_to_Pharmaceutical_Substances.htm

38 USFDA website, 'Designating an Orphan Product: Drugs and Biological Products' https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/HowtoapplyforOrphanProductDesignation/default.htm

The regulatory environment and developmental pathways

The development and commercialisation of new medical technologies and pharmaceuticals are controlled by a rigorous framework of local and international regulations. The sector is also affected by government policies on reimbursement and procurement, and tax and IP laws, all of which affect the length of time and investment involved in the commercialisation pathway.

The life cycle of a life sciences company is not typical of companies in many other sectors. The development pathway for pharmaceuticals is between 10 and 15 years, and the risk-adjusted average cost of bringing a new vaccine or medicine to market is US$1.5–2.6 billion.[39]

Products must be commercialised at an international scale to deliver the required return on investment, and most Australian pharmaceutical revenue is earned by multinational pharmaceutical companies that sell products developed for the global market. While research and early development often begin locally, the commercialisation pathway frequently involves the out-licensing or divesting of Australian innovations to a global partner during the pre-clinical or clinical development phases. This is required to bring in the development, regulatory, sales, marketing and distribution capabilities and resources needed to maximise the product's global reach and value.

A formal application to national regulatory bodies is required to gain approval to market in a particular country. A successful application requires a comprehensive set of data on quality, safety and efficacy gained through a series of pre-clinical and clinical trials over many years.

The major Australian regulatory authority is the TGA, which assesses and monitors activities to ensure that goods with therapeutic claims available in Australia are of an acceptable standard. The TGA administers the Therapeutic Goods Act, which provides a framework for a risk management approach that allows the Australian community to have timely access to therapeutic goods which are consistently safe, effective and of high quality. Before being supplied in Australia, all products must be listed, registered or included in the ARTG.[40]

Many Australian life sciences companies use the US and/or EU regulatory path as the benchmark for their product development. In the US, the FDA is responsible for protecting public health by ensuring the safety, efficacy and security of products, such as human and veterinary drugs, biological products, vaccines and medical devices; the FDA has regulatory authority over these products. In Europe, the European Medicines Agency (EMA) acts as the European Agency for the Evaluation of Medical Products (EMEA) to coordinate the evaluation of the safety, efficacy and quality of medicinal products within the EU.[41] In order to sell medical devices in the EU, companies must obtain or apply 'Conformité Européene' (CE) Marking for their products; this indicates that the product complies with EU regulations and allows the product to be marketed in 32 European countries.[42]

In this Guide, we focus on the FDA regulatory path as it is the most used pathway.

39 Thomas, 2016, op. cit., p.9

40 Therapeutic Goods Administration website, 'Australian Register of Therapeutic Goods' www.tga.gov.au/industry/artg.htm

41 European Medicines Agency website http://www.ema.europa.eu/ema

42 Emergo website, 'European CE Marking strategy for medical devices' https://www.emergogroup.com/services/europe/ce-certification

Drug development pathway

Trials approval

Following toxicology trials on animals (sometimes called Phase 0 trials), new drugs need to be tested on humans. An Australian company wishing to initiate human clinical trials for pharmaceuticals in the US must file an investigational new drug (IND) application with the FDA. The company may choose to meet with the FDA at a pre-IND meeting to discuss the requirements for initiation of the first human study under this application. These early discussions are also used to discuss appropriate regulatory paths.

Clinical trials

Human clinical trials typically proceed through four phases:

1 PHASE 1 CLINICAL TRIAL

Phase I clinical trials are done to test a new biomedical intervention for the first time in a small group of people (around 20–80) to evaluate safety (for example, to determine a safe dosage range and identify side effects).

2 PHASE 2 CLINICAL TRIAL

Phase 2 clinical trials are done to study an intervention in a larger group of people (several hundred) to determine efficacy (that is, whether it works as intended) and to further evaluate its safety.

3 PHASE 3 CLINICAL TRIAL

Phase 3 studies are done to study the efficacy of an intervention in large groups of trial participants (from several hundred to several thousand) by comparing the intervention to other standard or experimental interventions (or to non-interventional standard care). Phase 3 studies are also used to monitor adverse effects and to collect information that will allow the intervention to be used safely.

4 PHASE 4 CLINICAL TRIAL

Phase 4 studies are done after an intervention has been marketed. These studies are designed to monitor the effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use over longer periods of time. They may also be used to investigate the potential use of the intervention in a different condition, or in combination with other therapies.[43]

A key part of the IND application process is a meeting that occurs at the end of a Phase 2 clinical trial. The primary focus of the meeting is to determine whether the company has adequate safety and efficacy data to proceed into a Phase 3 clinical trial. The design and protocols for Phase 3 human studies will also be discussed with the FDA, and any additional information that may be required to support the submission of the new drug application (NDA) or biologics license application (BLA) is identified. Upon successful completion of Phase 3 clinical trials, the sponsor meets with the FDA in a pre-BLA/NDA meeting to discuss the presentation of data in support of the NDA.

Regulatory approval

After reviewing the NDA, the FDA will either issue an 'approvable' letter (for those drugs suitable to go to market) or a 'complete response letter' (for applications that are not approved in their present form). The approvable letter may contain a list of correctable deficiencies and may request commitments to do certain post-approval studies. The sponsor may request a meeting with the FDA to discuss these issues.

Reimbursement approval

To have a successful product launch, life sciences companies need to consider reimbursement requirements (that is, who is paying for the final product) throughout the product development process. Early consideration of and research into the final pricing, as well as prospects for pricing and reimbursement, will allow for the creation of a well-differentiated product that is profitable.

43 Source: National Health and Medical Research Council https://www.australianclinicaltrials.gov.au/what-clinical-trial/phases-clinical-trials

Opportunities for pricing and reimbursement will differ depending on the country and structure of the healthcare system in each country. Investors should investigate whether the company has an achievable strategy to seek reimbursement in key markets.

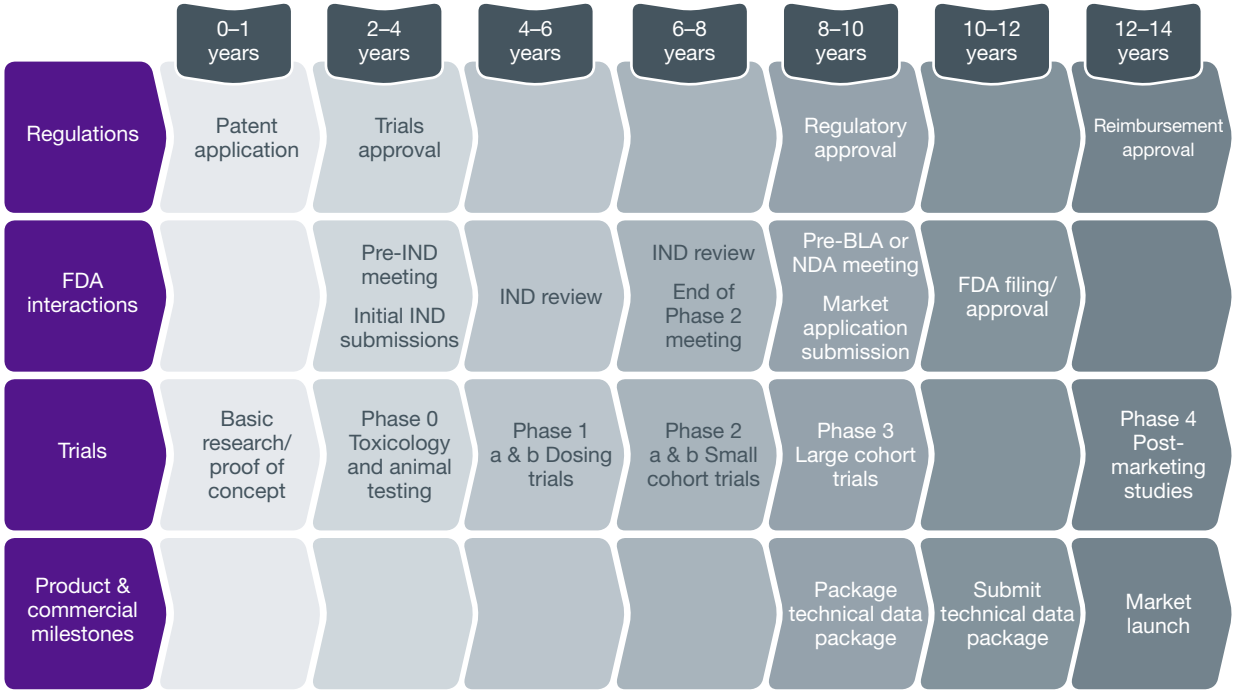


Figure 4. Drug development and approval pathway[44]

Medical technology product development pathway

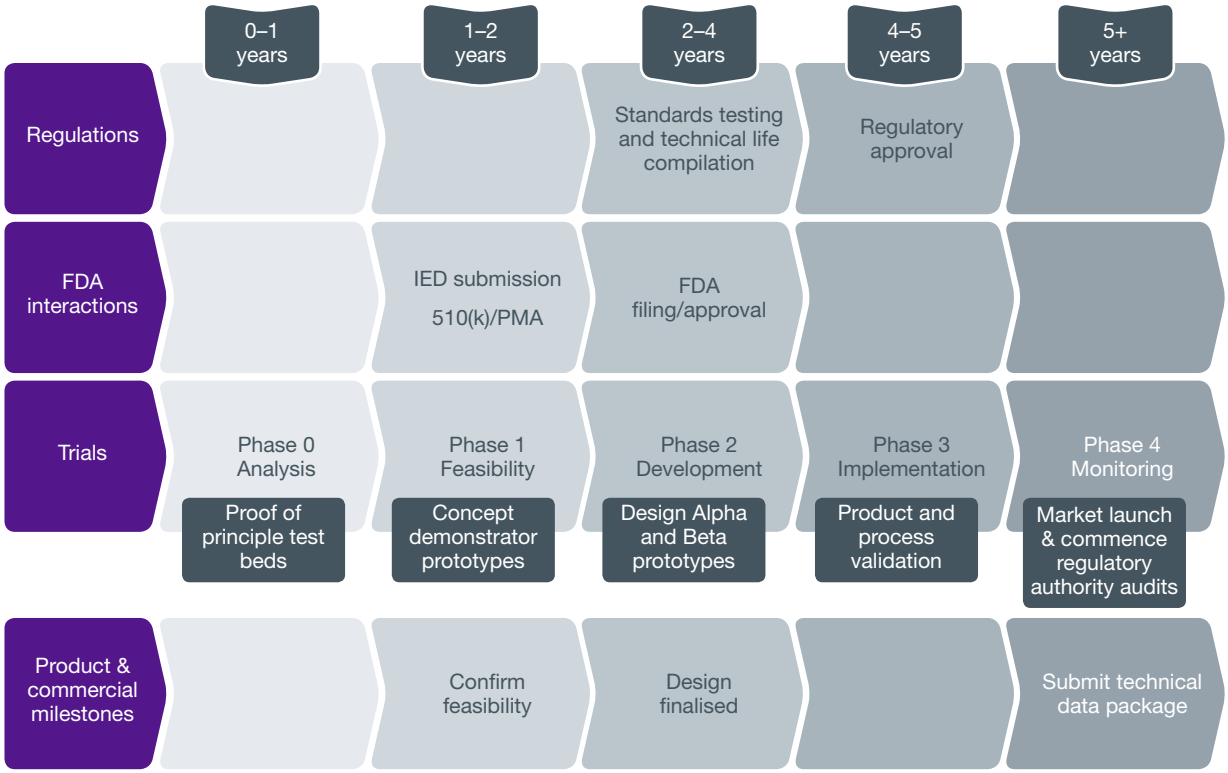
The development time frame and costs for medical technology products are frequently shorter, and the product life cycle and investment return period less, than for new drugs. For instance, in the US, it generally takes between four and ten years to bring a product to market, and costs US$30–150 million.[45] As a result, it is easier for small and mid-sized medical technology companies to launch a product into the market than it is for similarly sized pharmaceutical companies.

However, a company will need to access global markets to realise the full value of a product.

An investigational device exemption (IDE) allows an investigational device to be used in a clinical study to collect the safety and effectiveness data required for a premarket approval (PMA) application or a premarket notification (510(k)) submission to the FDA. Clinical studies with devices must be approved by both FDA and an institutional review board (IRB) before the study can begin.

44 AusBiotech, 2013, op. cit., p.9

45 L.E.K. Consulting, 2016, op. cit., p.10



Note: This figure outlines the FDA approval route; the CE Mark route in Europe is substantially different.[46]

Figure 5. Product development and approval pathway[47]

46 Wellkang Tech Consulting website, 'How to obtain CE Marking for my product?' http://www.ce-marking.org/how-obtain.html

47 AusBiotech, 2013, op. cit., p.9

FIVE Funding sources and time lines

Availability of sufficient capital poses a significant risk for a life sciences company, especially if the company is in the pre-revenue phase of development and applying for regulatory approval. As previously mentioned, a life sciences company may have to spend tens of millions of dollars, sometimes hundreds of millions or even billions, on R&D and clinical trials before it has the opportunity to earn revenue from its product. Investors provide critical support in these early stages of product development.

A life sciences company may need to regularly raise funds to meet each milestone, such as the next phase in a trial, thus its ongoing operation will depend on its ability to raise capital. This, in turn, depends on:

- internal factors, such as the strength of the board and management team and IP assets;
- external factors, such as changes in regulatory requirements or views of key opinion leaders, success or failure of competitor products in development, the health of economies and stock markets globally and the international currency exchange rates.

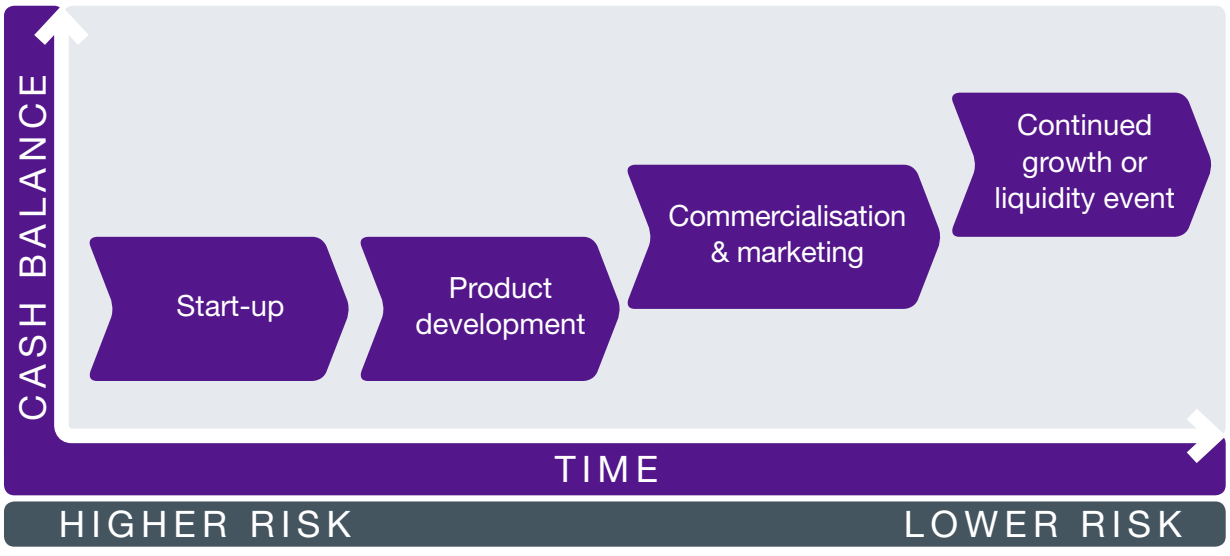


Figure 6. The relationship between cash resources and risk over the life of a company

Sources of funding along the company life cycle

Start-up

Start-up or spin-out companies are often based on one promising innovative technology or platform. Generating funding and capital during the pre-clinical and early stages of clinical development is difficult and is a common problem faced by start-ups.

Activities

- Prototype design/proof-of-concept trial.
- Establishment of legal structures, such as registering a company and determining a governance structure, for example, establishing a board.

- Establishment of some IP assets, such as provisional patents – these are often acquired/ secured from academic institutions prior to start-up.[48]

Investor considerations

This stage is considered high risk and, commonly, the predominant driver for investing is to support the inventor/founder who has the vision. As such, funds are typically sourced from friends and family. Seed investors, angel investors and government grants are also good sources of capital at this stage.

Potential MTP developments often do not progress past these early stages due to challenges in funding, and such failures hinder the long-term success of the Australian MTP sector. The government has recently announced programs, such as the Biomedical Translation Fund, in an attempt to bridge these funding gaps. The R&D Tax Incentive is of particular relevance to eligible loss-making companies, as it can provide significant funding for eligible activities. Appendix B has detailed information on funding mechanisms and sources that MTP companies can access to deliver greater returns to investors.

Product development

The product development phase (the R&D phase) may include clinical or field trials. The product development stage is typically the highest risk period for the company, as it has no revenue and large costs.

Activities

- Expansion of proof-of-concept testing, toxicology studies, commencement of clinical trial program.
- Increased focus on regulatory requirements, IP management, commercial considerations and the attraction of enough capital to fund development to the next stage.

Investor considerations

For investors, there is now more data available to analyse and make a more informed investment judgement. Investors tend to distinguish between companies in the early and late stages of clinical development; the distinction being whether the company has successfully completed Phase 2 clinical trials.

Sources of funding for this stage are typically angel investors, government grants, venture financing, private equity or partnership. Also, some companies may pursue an initial public offering (IPO). An IPO allows a company to raise funds from a wide pool of investors, including institutions and retail participants, to provide it with the working capital needed to fund its next phase of growth. Once listed as a public company, it trades in the secondary market where its shares are bought and sold. Public companies can issue additional shares (for example, through placements to selected new or existing shareholders or by rights issues to existing shareholders) in order to raise more funds, also known as follow-on capital or secondary offerings. One of the key advantages of going public is the ability for companies to 'tap' the market, in a relatively short time frame, for additional fundraising.

Many companies fail to take off in this stage due to lack of capital to fund the next stage of the commercialisation process.

Commercialisation and marketing

Commercialisation may be achieved by licensing or selling IP assets and technology to a larger company for further development, or by taking the technology to market. Both cases involve an injection of cash into the company.

Activities

- Injection of cash into the company from up-front milestone and royalty payments or revenue streams – achieving regulatory approval is pivotal.
- Reimbursement is ideally secured before product launch and marketing occurs.
- Due to Australia's small market size, an Australian company will need a strategic approach as to which overseas markets to enter and in what priority. Regulatory approval in other countries is required for access and export to those markets.

48 IP Australia website, op. cit., p.14

Investor considerations

Expansion capital is a different risk profile at this stage as the company is established and technology risk is low. However, the ultimate test and determinant of success is if the customer, typically doctors, will use the final drug or product.

Funding comes from strategic partners or capital markets, such as ASX.

Continued growth or liquidity event

After launching in the market, a company will continue to support its product or platform generally for the life of its patent portfolio.

Activities

- The company may be able to use the revenue to accelerate development of earlier stage technologies or license in new technologies to develop.
- It may also choose to strategically set up, and sometimes spin out, a subsidiary company to specialise in a new technology or group of technologies, which may attract a different pool of investors and commercial partners.

Investor considerations

At this stage, the development of several assets within a company provides diversity of risk for investors.

Types of early stage funding

The type of early stage funding will affect the company's ownership structure and investor returns.

Dilutive financing

Dilutive financing is capital received by a company that also diminishes ownership.[49] This includes:

- funding agreements with angel investors or venture capitalists where a portion of equity is given up to gain access to capital;
- any public or private rounds of funding whereby company shares are issued to new investors.

These are viable ways of getting access to large sums of cash, but there are risks associated with losing a stake in company ownership.

Dilutive financing might be sourced during early stages of the development cycle or towards the later stages in order to rapidly expand. If the company is properly funded, the dilution will be outweighed by value creation.

The Early Stage Innovation Company (ESIC) tax incentive scheme, which came into effect 1 July 2016, is designed to foster investment in early stage innovation companies in Australia by providing investors with generous tax incentives (see Appendix B). While it is a tax incentive for investors, it is also dilutive in the sense that the investor acquires a share in the company.

Non-dilutive financing

There are a range of options for generating cash flow that are available at different stages of a life sciences company's maturity (Table 1).

49 Nelson, A, 2016, 'Dilutive vs non-dilutive financing', Business Finance.com website http://www.businessfinance.com/articles/dilutive-vs-non-dilutive-financing.htm

Table 1. Non-dilutive funding options available to life sciences companies

Funding options	Business maturity			
	Start-up/invention	Early stage commercialisation	Commercialisation	Growth/operation
R&D tax incentive				
Accelerating commercialisation				
Business management and connections				
Foundations (philanthropic, non-government organisations, non-profit organisations etc.)				
Industry partnerships				
Venture debt				
Revenue				

See Appendix B for further details regarding Australian Government programs.

How securities are traded

Public companies shares are traded via an exchange. In order to trade securities in a public company you need to have a brokerage account with a brokerage firm that is connected to the exchange. In Australia, retail brokerage accounts are quick to set up and execution is relatively inexpensive. Shares in public companies trade on business days on ASX, between the hours of 10 am and 4 pm. During this time you are able to buy shares of listed companies via your broker; settlement occurs two business days later.

ASX is a highly active capital market across many sectors; over the past three years, 36 healthcare IPOs have collectively raised $5 billion.[50] The ASX healthcare sector is diverse; according to the Global Industry Classification Standard (GICS) definition: 28 per cent of companies are in biotechnology, 21 per cent in healthcare equipment and supplies, 16 per cent in pharmaceuticals, 10 per cent in healthcare technology, 6 per cent in life sciences tools and services, and the remainder are healthcare providers and services.[51]

Trading in a listed entity does not guarantee a favourable return on that investment. Company performance, market sentiment, prevailing economic conditions and other factors out of one's control can influence share prices. It is important to remember that share prices can fluctuate. The attraction of shares in a listed company, compared with other forms of investment, is liquidity – you have the option of buying more shares, or selling any shares, and your shareholdings can be valued based on the market price for those shares.

Investors can diversify their portfolio by purchasing shares in companies operating across different sectors. This reduces the likelihood of losing money compared with investing all your funds into a single venture or sector. Owning shares also entitles you to vote at an annual general meeting (AGM) and receive dividends if applicable.

50 HealthInvestor Asia website, 'Analysis: why float on the ASX' http://www.healthinvestorasia.com/ShowArticle.aspx?ID=2949&AspxAutoDetectCookieSupport=1

51 ASX, 2017, Health care & biotechnology sector profile, ASX Limited http://www.asx.com.au/documents/resources/00176_Health_Care_and_Biotechnology_Sector_Profile_03_FINAL.pdf

What should you look for in a life sciences investment?

MARKET OPPORTUNITY

How big is the overall addressable market?

What are the market trends, e.g. growing, shrinking, competition, patent expiry?

What are the high-priority sub-markets, e.g. geographical, disease state, customer type?

What are the current competitive environment and the availability of competitive drugs or devices, e.g. differentiators, advantages and drawbacks?

What is the point of difference, e.g. efficacy, price, superior safety?

Is the company or product supported by key opinion leaders?

SCIENTIFIC BASIS

What is the body of early stage research?

Where does the science come from, and who is behind it today?

Are there any peer-reviewed publications that validate the science?

Is any clinical faculty or industry partner supportive of the program and participating in its development?

PIPELINE

How many drugs or devices being developed by the entity are currently in the approval process, and what is their order of priority? Are any already licensed to, or the subject of collaborations with, third parties?

If the technology is a 'platform', which uses of the platform are being prioritised?

What stage in development has the product reached in terms of regulatory approval? How long will it take to reach the next inflection point (or key developmental milestones), e.g. data collection, deals, approvals, launches?

What is the likelihood of full regulatory approval?

BOARD AND MANAGEMENT

Do board members and management have a history of commercialisation, or experience in larger entities in the same or similar areas of focus?

Does the company have a diversity of skills, e.g. scientific/technical, clinical, sales, strategy, regulatory, reimbursement?

Are the managers' objectives (markers of success) in alignment with investors' objectives?

Can the company market itself effectively to investors, e.g. effectively articulate the value proposition?

INTELLECTUAL PROPERTY

What products and technologies fall within the scope of patent and other IP rights?

Does the company own or sufficiently control those IP rights?

How likely is it that (if not already granted) those rights will proceed to registration and remain valid?

Does the company have the freedom to exercise those rights and commercialise those technologies?

If patents have been granted, what is the duration of patent rights?

SALES AND MARKETING

Is the company's sales and marketing plan effective?

How will the company access sales capabilities, e.g. recruit an in-house sales force, fully outsource or adopt a hybrid approach?

How will the company engage with clinicians and patients to encourage adoption?

Does the company have marketing agreements with large pharmaceutical companies, medical device distributors and so on?

FINANCIALS

What is the current balance sheet, in particular, cash on hand?

What is the monthly rate of cash burn (negative cash flow)?

What is the expected rate of cash burn until regulatory approval (if necessary) or next inflection point?

Does the company have a pathway to profitability?

CAPITAL STRUCTURE

What is the current capital structure?

Who are the major shareholders?

Are there any institutional shareholders? If so, what proportion of the share register do they take up?

What equity or shares are held by management, board members and employees, and how are they remunerated?

What is the spread of existing investors?

Are there any convertible note holders and/or options granted?

REGULATORY

Where will the company obtain the initial regulatory approval for their product?

In which jurisdictions are they seeking regulatory approval, and in what order?

Are there markets with expedited pathways?

Will approval in one market assist approval in other markets?

Who is, or will be, manufacturing the product?

Do sufficient data exist to satisfy the regulatory requirements and approvals process?

How has the company engaged with regulators in the area of clinical trial design?

REIMBURSEMENTS

What are reference prices in the major markets, e.g. US, Europe, Japan, China?

What is the pathway for reimbursement, e.g. via government programs such as Australia's Pharmaceutical Benefits Scheme or health insurers?

For pharmaceutical products, what is the current or potential future state of generic or biosimilar competition?

SIX Key considerations when investing

Despite the risks and complexities, investing in life sciences can be extremely rewarding from both commercial and social perspectives. Investing in life sciences companies offers the potential for rewarding financial returns from the select group of companies that achieve commercial success, and investors are also investing in products and research that could potentially save lives, cure diseases and improve quality of life.

Investing in the life sciences is a 'high risk, high reward' activity, and it is important to be clear about the risks, and what information you can use to maximise your chances of successful investment.

Rates of success

A study of clinical development success rates for new drugs[52] found that, in the 10 years to December 2015, 63.2 per cent of companies registered in the FDA approval process successfully transitioned from Phase 1 to Phase 2. Phase 1 clinical trials commonly have the highest success rate, as they are typically testing for safety, and efficacy need not be demonstrated for advancement. Phase 1 success rates may also be exaggerated by reporting bias, as some larger companies may not deem failed Phase 1 clinical trials to be material; consequently, they may not report them in the public domain.

Consistent with other studies, Phase 2 success rates (30.7 per cent) were found to be far lower than any other phase. Phase 2 clinical trials are generally the first time that proof of concept is deliberately tested in human subjects.

It is at that point in development that industry must decide whether to pursue the large, expensive Phase 3 clinical trials or terminate development.

The second-lowest phase transition success rate was found in Phase 3 (58.1 per cent). This is significant as most company-sponsored Phase 3 clinical trials are long and very expensive. However, once a company successfully completes this phase and files an application for regulatory approval, it has an 85.3 per cent success rate.

Multiplying these individual phase components to obtain the overall probability of progressing from Phase 1 to regulatory approval reveals that only 9.6 per cent of drug development programs successfully bring a product to FDA approval. This is particularly important in the context of cost and time of unsuccessful clinical trials.

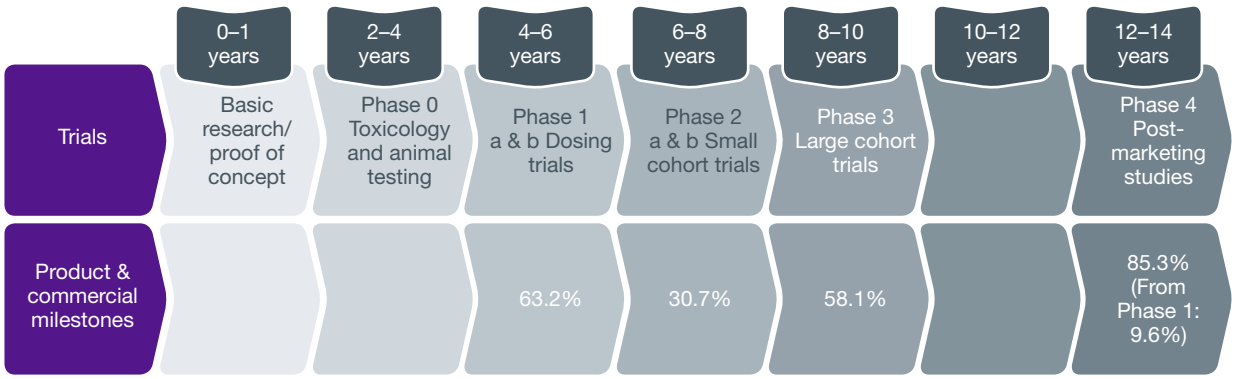


Figure 7. Phase transition success rates[53]

52 Thomas, 2016, op. cit., p.9

53 Ibid.

Contributing factors

Both clinical factors and factors related to regulation may influence success rates. Clinical factors include the patient population and selection strategy; the complexity of the clinical trial, for example, whether additional safety and efficacy studies were required; and the difficulty of obtaining clinical validation of a target, drug class or mechanism of action. Clinical validation requires demonstrating within a clinical trial that there is a statistically meaningful therapeutic benefit and acceptable safety when engaging with the target for a given indication or disease.

Broader business issues also come into play, for example, lack of funding to complete a clinical trial; shifting priorities in the portfolio and the broader market; the success or failure of trials of similar therapies; the emergence of competition products; and litigation concerning the company's or a competitor's IP portfolio.

Key considerations

Investors looking to the life sciences sector should be aware that the further along a company's product is in clinical trials, the greater its chance for success. You should conduct your own independent research to increase the odds of making a profitable decision. It is critical to investigate a company's financial health and consider managerial performance and stability, along with additional factors that are specific to the sector.

A potential investor will assess a company's value based on the likelihood it will meet milestones in a timely fashion and achieve value inflection points along the development path. You should also seek information on any other factors that may influence success, such as the existence of collaborative development pathways with other companies or partners; the receipt of grants; news of an accelerated development pathway; or interest expressed by a potential acquirer of the company's technology.

Investors should look for opportunities to invest in value-creating milestones for a company, rather than simply investing in ongoing operating expenses and salaries. You should focus on companies that have a genuine 'shot on target' with a realistic set of proposals that will create value; for example, a company that is running trials that are not under an IND approval, and in a less-developed country, is likely to have a poorer outcome. Look to invest in a company where the amount of funding invested and the milestones achieved should increase its value.

Some key considerations are outlined below.

Figure 8. Key considerations in selecting an investment

Due diligence

Undertaking due diligence on a life sciences company involves assessing both the business plan and the financial projections of the company, and whether the product is scientifically sound.[54] You should investigate whether the company is well managed, has appropriate financial strategies in place and is developing a truly innovative product that fulfils an unmet need. You should find out what the company's core business is, and whether their IP covers that core business (it may not if the company's direction has changed), whether the IP is protected with patents and whether it allows them to make and sell the product.[55] It is also important to understand the regulatory landscape, and how that will affect development and approvals processes.

Valuation, risks and the development pathway

As discussed in Chapter 5, life sciences companies may never generate commercial revenues but may still have tradeable assets in IP or R&D. These assets are difficult to value, and it is well worthwhile getting advice from a specialist who is familiar with the development pathways of life sciences companies.

The potential return to an investor is greatly influenced by how far along the development pathway a company is. For example, risks are higher the earlier in the process a company is (and more funding may be needed along the way), but potential returns are greater (although early investors could find their assets diluted).[56]

Return on investment

Many investors in life sciences companies only receive a return on their investment when the company holds an IPO or when the company is sold to a larger pharmaceutical company.[57] Large pharmaceutical companies may also boost their portfolio and speed their internal development time lines by buying spin-offs of drug-discovery or R&D organisations that have developed IP or undertaken significant R&D. The sale price will be optimised if a number of potential buyers compete in a bidding process.[58]

Company attributes

Size

Investors in early stage life sciences companies should expect to sit with uncertainty for 10 to 15 years. The types of risk and the mix of risks a company is exposed to, as well as the level of such risks, will change over the life cycle of a company. As we saw above, the risk profile of a start-up company with only one technology and no revenues will be vastly different from that of a mature company with a broad portfolio, including products on the market and cash reserves. The failure of a clinical trial to meet its endpoint could cause the demise of a start-up company, whereas for a mature company developing multiple assets it may be no more than an unwelcome, but only partial, setback.

Smaller companies may look attractive as the investment may be at a lower valuation price, with the potential to generate high returns. But many small companies in the MTP sector have no revenue as their products are usually still in research and pre-clinical trial phase. In addition, smaller listed stocks in the life sciences sector usually experience greater price fluctuations and lower liquidity, either due to listing too early, R&D outcomes or investor perception. As such, investing in smaller companies is considered high risk, in what is already considered a high-risk sector, but there is the potential to generate massive returns if the company is successful.

Investors who are less tolerant of risk should consider investing in large cap, established MTP companies. A company with multiple products in development and in the market is more likely to possess the funds to cover failed development efforts, thus making their stocks more stable.

54 Neophytou, S, 2016, 'Investing in life sciences: the importance of sector experience', Deepbridge website http://www.deepbridgecapital.com/news-and-events/investing-life-sciences-importance-sector-experience

55 Booth, P & Mooi, L, What to know before investing in life sciences, *Managing Intellectual Property* 2005 06:1

56 Neophytou, 2016, op. cit., p.28

57 Ben-Joseph, O, 2016, 'Where the bodies lie', Bioentrepreneur doi:10.1038/bioe.2016.8 http://www.nature.com/bioent/2016/160801/full/bioe.2016.8.html

58 Neophytou, 2016, op. cit., p.28

As these companies have been public for longer, investors can also more easily obtain information about previous performance, such as clinical trial results and profitability, which are key to predicting the future performance of stocks.

Table 2. Key differences between small and large companies for investors[59]

SMALL COMPANIES	LARGE COMPANIES
Lower valuation price, potential for high returns	Stocks are more stable, greater transparency
Often have no product to sell	Higher valuation price, less likely to see explosive growth

Listed or unlisted

Investors have a choice between listed and unlisted companies.

Table 3. Key differences between listed and unlisted companies for investors

LISTED	UNLISTED
Investors can increase or sell down their holding with relative ease, because there is a market.	Limited opportunities to buy or sell unless a trade sale is negotiated.
Value of shares is known day-to-day because market sets the price.	No external indicators of value are readily available.
Must publish financial information at least half-yearly and in some cases quarterly.	May not be required to publish financial information but may agree with shareholders to provide financial information.
Must promptly inform the market of new matters which could affect share price positively or negatively.	Not usually required to make public disclosure (some unlisted public companies have disclosure obligations equivalent to the continuous disclosure regime because they have raised capital through a prospectus or similar document). Information flow to shareholders is governed by constitution or shareholders' agreement.
Company is prohibited from selective briefing of investors beyond clarification of what has been disclosed publicly.	Some shareholders may have access to greater information than others, e.g. through board representation.
Listing rules mandate that certain material transactions, including transactions with directors and significant issues of new capital, are subject to shareholder approval.	Constitution or shareholder's agreement may or may not provide equivalent protection to shareholders.

59 Pratt, C, 2016, '3 ways to invest in biotech', Biotech Investing News http://investingnews.com/daily/life-science-investing/biotech-investing/3-ways-to-invest-in-biotech

Investing in unlisted companies is generally a more complex endeavour than investing in listed companies. One common issue is the general lack of information about an unlisted company as they are not subject to ASX reporting requirements. Unlisted companies also tend to reinvest their profits to fund growth instead of paying them out as dividends. In general, investors that invest in unlisted companies are usually more experienced, long-term investors and are familiar with a particular company or sector.

Good managers

Investors may want to see that the management team of a company of interest are aligned with the investors in success; for example, that the managers are remunerated more for performance (such as in stock options) than in salary. In addition, investors should seek companies whose board members have expertise in governance as well as domain expertise in the life sciences sector, whether as key opinion leaders, investors or executives.

Diversifying your investments

As has been made clear, companies in this sector can take considerable time to develop a product to a point where the company is generating revenue or an exit may be possible; during this period it may be difficult to value progress. That is one of the reasons why investors should consider a portfolio approach rather than investing in a single company. A portfolio approach allows investors to diversify; spreading out funds across different asset classes may help investors ride out the fluctuations of the financial markets. While diversification does not guarantee gains or protect against losses, selecting a mix of investments and managing the risk–reward trade-off will improve the likelihood of more consistent returns over time.[60]

It is worth emphasising that diversification only works if the portfolio is composed of companies with genuine prospects, and investments need to be carefully selected.

60 MoneySmart, ASIC, website 'Diversification' https://www.moneysmart.gov.au/investing/invest-smarter/risk-and-return/diversification

SEVEN How life sciences companies are valued

The valuation methods for life sciences companies, and their assets, are quite different to other sectors. Assets in the area of the life sciences are usually non-tangible; valuation of these assets is an important and highly specialised area, often requiring independent expert advice.

The information provided in this section is meant to be an introduction to some of the methodologies used to value life sciences companies. It is by no means exhaustive and is not investment or financial product advice. Readers who are interested in learning more about the different valuation methods for life sciences companies and assets should seek appropriate professional advice from valuation experts.

Life sciences companies can be valued several ways. There is no one right methodology and it makes sense to approach things from different perspectives. Below are three valuation methods commonly used to value life sciences companies.

- Discounted cash flow (DCF) – this method uses a company's future positive and negative free cash flow projections discounted to the present value.[61]
- Market comparable – this approach uses data from public, peer-group companies to determine multiples that are used for calculating the value of a company.[62]
- Sum of parts – this method estimates the total net present value of a company by adding the risk-adjusted net present value (rNPV) of lead product(s) in development to the discounted cash flow of all other company operations.[63,64]

Risk-adjusted net present value (rNPV) product valuation

The rNPV valuation approach is based on the classical discounted cash flow with some special adjustments for the MTP sector. This method factors in the success rates of therapeutic products in pharmaceutical development, and the probability of failure is then used to discount the yearly free cash flows over the entire life cycle of the product.

61 Corporate Finance Institute website, 'Guide to the Discounted Cash Flow Formula' https://corporatefinanceinstitute.com/resources/knowledge/valuation/dcf-formula-guide/

62 Global Arbitration Review website, 'Market Approach or Comparables' http://globalarbitrationreview.com/chapter/1076605/market-approach-or-comparables

63 Stewart, JJ, Allison, PN &, Johnson, RS, Putting a price on biotechnology, *Nat Biotechnol*., 2001, 19:813–817, doi: 10.1038/nbt0901-813

64 Stewart, JJ &, Bonifant, B, The valuation high ground, *Nat Biotechnol*., 2009, 27(11):980–983, doi:10.1038/bioe.2009.9

Case study: LEO acquires Peplin[65,66]

Acquisitions like the 2009 purchase of Peplin Operations, Australia, by Leo Pharma A/S (LEO), a global pharmaceutical company headquartered in Denmark, provide very good examples of how valuation metrics work, and also show that often it is not just about price. This case study analyses the valuation of Peplin at that time.

In November 2009, LEO acquired Peplin for approximately US$287.5 million in cash. Peplin's lead product candidate was the PEP005 gel, which was in Phase 3 clinical trials for actinic (solar) keratosis (AK), a common pre-cancerous skin lesion. Results from Peplin's first Phase 3 AK trial, REGION-I, were announced in May 2009 and the Phase 3 clinical trials were planned to be completed by the end of 2009. Peplin was planning to file an NDA application in mid-2010, and also had a Phase 2 clinical trial ongoing for PEP005 gel in superficial basal cell carcinoma and preliminary data in squamous cell carcinoma and cutaneous warts.

The rNPV calculation can be split into four different elements:

- development phase;
- market phase;
- risk adjustment;
- discounting to present value.

These four parts allow for the development of a free cash flow model looking 15 years into the future.

Development phase

The development phase looks at the cost and time line for bringing the product to the different markets. For Peplin, the product was already in Phase 3 clinical trials in the US with aims for a US market launch in 2011. While the results of Peplin's first Phase 3 AK trial, REGION-I for the treatment of non-head locations were positive, they were not outstanding.[67] The complete clearance rate of 27.4 per cent did not compare favourably to the 44 per cent rate found in Peplin's previous PEP005–006 Phase 2b study.[68] Neither did it compare favourably to other topical treatments on the market, which have generally shown complete clearance rates of around 45 per cent. Peplin did, however, have the advantage of a much shorter duration of treatment. The FDA suggested, and Peplin agreed to, a second Phase 3 study of non-head sites. As such, some additional registration costs in the US would be considered. As AK is a growing problem globally, it can be assumed that other markets will be taken into consideration. Therefore, the costs for additional registration and time frame until expected market entry should also be considered.

Market phase

For the market phase, it is important to consider the prevalence of the disease (its frequency in a population), drug pricing in different markets, competition and development time lines to determine when the product can be sold on the different markets.

65 LEO Pharma, 2009, 'LEO Pharma to acquire Peplin for $US287.5m', media release 3 September 2009 http://www.leo-pharma.com/Home/LEO-Pharma/Media-centre/News/News-2009/2009-sep-03-LEO-Pharma-to-Acquire-Peplin-for-US$287.5m.aspx

66 Walsh, L, 2009, Peplin cancer gel tests help boost drive, The Courier Mail, 25 May 2009 http://www.couriermail.com.au/business/peplin-cancer-gel-tests-help-boost-drive/news-story/09fdbfcbec8858c25cde8b630be59c46?sv=44854b20c62fa1bd8b4c2517b3e29a9b

67 Biotech Daily, 2009, Marc Sinatra's bio-guide brief: Peplin not a 5-banger, any more, Daily news on ASX-listed companies, 3 September 2009 http://www.biotechdaily.com.au/media/sinatra/Peplin%20Brief%20September%203.pdf

68 Peplin, 2009, Positive results for Peplin's first Phase III AK trial, ASX and media release, 17 May 2009 https://www.sec.gov/Archives/edgar/data/1408808/000119312509117567/dex991.htm

The number of patients with AK is rapidly growing, especially in Europe, the US and Australia.[69] According to the Skin Cancer Foundation, AK affects about 58 million Americans and is the most common form of pre-cancer.[70] In the UK, around 3.6 per cent of males aged between 40 and 49 years, and 20 per cent of patients over 60 years, have at least one AK lesion.[71,72] Peplin's current and potential competitors include the mainstream cream Aldara, an immune response modifier and pain reliever[73], as well as the traditional treatment of freezing off lesions.

Based on this information, a revenue projection that takes into account prevalence, pricing and competition can be generated. This can be applied to different scenarios, using different prices and different market shares for different markets. However, it should be clear, despite all the calculations and scenarios, the valuation is ultimately based on assumptions and expectations.

Risk adjustment

Compared with a DCF valuation, the risk in an rNPV is split into two parts:

- product-specific attrition risk (risk adjustment);
- general business risk (discounting).

For risk adjustment, it is possible to use historical information of the success rate for a product to move successfully from one phase to the next. Table 4 shows the average success rate for oncology (solid tumours). From Phase 1 to the market, the chance of success is 4 per cent. There is a 34.2 per cent chance of successfully completing a Phase 3 clinical trial. Based on this standard assumption, Peplin had a 27.3 per cent chance of reaching the market in the US.

Table 4. Average success rate – oncology (solid tumours)[74]

Phase 1	Phase 2	Phase 3	FDA/EMEA	Cumulative
64.1%	23%	34.2%	79.6%	4.0%

The yearly cash flow is then risk adjusted according to the product's likelihood of reaching the US market. Generally, the likelihood for the cost of the registration phase is 100 per cent as the company needs to spend the money to know if the product will pass the phase successfully. Thus, the revenues in the US could be adjusted with a 27.3 per cent likelihood of success.

Discounting to present value

The next step is to take the general business risk into account and calculate the present value of the future expected risk-adjusted cash flows. This step uses a discount rate, which can vary from below 10 per cent to over 26 per cent depending on the company involved. The discount rate reflects the cost of capital and the general business risk. The cost of capital and the general business risk are substantially lower for large companies compared to smaller companies. As a result, larger companies may be able to pay more for a product or company because their cost of capital and associated business risk are much lower.

69 Ulrich, M, Drecoll, U & Stockfleth, E, Emerging drugs for actinic keratosis, *Expert Opin Emerg Drugs, Dec 2010, 15(4):545-–555*

70 Skin Cancer Foundation website, 'Skin cancer facts & statistics' http://www.skincancer.org/skin-cancer-information/skin-cancer-facts

71 Harvey, I, Frankel, S, Marks, R, Shalom, D, Nolan-Farrell, M, Non-melanoma skin cancer and solar keratoses. I. Methods and descriptive results of the South Wales Skin Cancer Study, *Br J Cancer*. Oct 1996, 74(8):1302–1307

72 Memon, AA, Tomenson, JA, Bothwell, J, Friedmann, PS, Prevalence of solar damage and actinic keratosis in a Merseyside population, *Br J Dermatol*., Jun 2000, 142(6):1154–1159

73 Drugs.com website, 'Aldara' https://www.drugs.com/aldara.html

74 Thomas, 2016, op. cit., p.13

The value of the products as estimated with the rNPV method is added to the DCF of other company operations, assuming that there is more than one product under development, to obtain the total value of the company. Whereas the discount rate used for the DCF takes into account other company risks, such as management risks, the discount rate used in the rNPV only includes the risks specific to the specific project. Consequently, the discount rate used for DCF is usually significantly higher than that for the rNPV.

Market comparable valuation

Another frequently employed valuation method is the comparison of companies against a relevant peer group to assess relative value. This can be a helpful 'sanity check' for companies without earnings or in instances where rNPV is difficult or problematic to undertake. Comparing valuations against peers can help identify undervalued and overvalued opportunities.

Comparisons may be made by assessing the market capitalisations, and preferably the enterprise values, of peers within the same disease area or at the same stage of development. The sample size within a peer group can be expanded by including relevant peers listed on other exchanges, noting that this is often the source of valuation arbitrage. Other metrics for comparison could also include price to number of employees (P/employees) and price to R&D expense (P/R&D); these metrics estimate the potential of the company to carry on projects as well as its potential for future growth, respectively.

Notably, a liquidity discount should be applied when valuing private companies using comparable public companies, which takes into account that private companies shares are more difficult to sell.

Table 5. ASX-listed market valuation for life sciences companies at the different development stages

	Pre-clinical	Phase 1	Phase 2	Phase 3	Commercial
Total market valuation	$144,886,709	$148,471,937	$1,204,440,222	$1,618,596,586	$28,039,494,235
Average company valuation	$36,221,677	$29,694,387	$80,296,014	$404,649,146	$1,401,974,712

Note: This table is intended as a rough guide for generalist investors and should not be considered as valuation advice. As market valuations fluctuate, this table is relevant as of August 2017.

Table 5 shows the ASX-listed market valuation for life sciences companies at different development stages as of August 2017. The average company valuations were calculated based on the total market valuation. The guiding principles for including companies in the analysis in Table 5 are:

- The company is developing a proprietary product i.e. the company has full ownership of the product.
- The proprietary product is the main value driver of the company.
- CSL is excluded as an outlier as it is significantly bigger than other companies.

Based on the table above and the same guiding principles, investors can compare the valuations of companies that they might be interested in investing in against peers in the same development stage to identify undervalued and overvalued opportunities. Once an investor has done the initial assessment via market comparable valuations, a specialist may be engaged to conduct a more in-depth analysis.

EIGHT Glossary of terms

Big data

Big data refers to the huge digital datasets of information relevant to healthcare, including clinical records (such as electronic health records, digitised images and data from medical devices), health research data and medical management records (such as billing and costs). Requiring high-end computing to manage the data, it has the potential to deliver personalised medicine, increased healthcare efficiencies and improved medical outcomes.

Bioinformatics

Bioinformatics is the multidisciplinary field of using statistical, mathematical and software techniques to analyse big datasets in the life sciences, particularly in molecular biology.

Biologics license application

A company seeks FDA approval to introduce, or deliver for introduction, a biologic product through a biologics license application (BLA) process. The FDA will review submitted information on the product and manufacturing process, results from pre-clinical and clinical studies as well as product labelling.

Biotechnology

Biotechnology is technology based on living systems or processes; it is used in agriculture, industry and medicine. In medicine, biotechnology is used to improve diagnosis and produce and deliver drugs, vaccines and other therapies.

Commercialisation

In the context of health and medical research, commercialisation is the process of bringing the research into the market, where the resulting drugs or products can be sold in a profit-making business.

Data exclusivity

The *Therapeutic Goods Act 1989* (Cwlth) gives a five-year period of data exclusivity for protected (confidential) information provided in an application to register therapeutic goods. That prevents other companies who may be developing a similar product from using that information in their application, unless consent has been given by the first company.

Digital health

Digital health is the capturing of and connecting health records from the whole range of agencies involved in healthcare; and using digital software and tools, such as telehealth and health apps, to communicate and share information.

Due diligence

Due diligence is taking reasonable steps to investigate a company or person, especially a company that you are considering investing in. It involves making an assessment of the company's assets, liabilities and commercial potential. A company would also undertake due diligence before acquiring another company.

Electronic health record

An electronic health record is an online record of a person's health information (such as allergies, medical conditions, medicines and pathology reports), collated into one place and accessible to authorised healthcare providers. The Australian Digital Health Agency has established My Health Record as the digital healthcare system.

Electronic medical records

Electronic medical records are a computerised version of a hospital patient's paper charts. They make the data more easily accessible to all medical practitioners involved in a patient's care, and can also raise alerts, such as to potential errors in medication.

Free cash flow

Free cash flow assesses a company's financial performance by measuring the amount of cash that is available to use after excluding capital expenditures. This excess cash can be used to develop new products, expand production, pay dividends and reduce debt.

Gene therapy

Gene therapy is a collection of techniques that use genes to treat or prevent disease. Generally, they work by replacing a mutated gene that would otherwise cause a genetic disease with a corrected copy. Gene therapy is a new field and largely still experimental, but some conditions have been successfully treated.

Genomics

Genomics is the study of the genome (the full suite of an organism's genes and other genetic material) to understand their structure and functions, the proteins they code for and the influence of environmental factors.

Immunotherapy

Immunotherapy is a range of drug treatments for cancer that stimulate the ability of a person's immune system to find and kill abnormal cells.

Intellectual property

In biotechnology, intellectual property (IP) is the rights of the creators or inventors of new drugs or products, which can be protected by law. IP is generally protected by patents, copyright and trademarks, which allows companies to reap financial rewards from their investment in research and development.

Investigational device exemption

An approved investigational device exemption (IDE) shows that approval has been given by the IRB (or FDA for devices with significant risk) for the device under investigation for be tested in a clinical study assessing its safety and effectiveness.

Investigational new drug application

An investigational new drug (IND) application is required under US federal law before clinical trials begin (strictly speaking, it permits a drug to be transported across state borders, as is usually needed for trials). Thus, it is the first step in the FDA approval process. There is some scope for fast-tracking IND approval in emergency situations.

Large cap

Large cap companies are those with large market capitalisation values, such as over $1 million. Market capitalisation is the current market value of a company's outstanding shares. Thus, it is calculated by multiplying the current share price by the number of shares on the open market (including those held by company insiders).

Licensing

A company can license another company to use its intellectual (or actual) property, usually in return for payment. Licensing agreements are a way that life sciences companies can commercialise their invention, and they can be a valuable asset.

Life sciences

Life sciences comprise the branches of science relating to living organisms and life processes.

Medical technology

Medical technology refers to the use of novel technology to develop highly sophisticated electronic products or medical devices for application in healthcare markets.

New drug application

A company seeks approval to market a new drug in the US through a new drug application (NDA) to the FDA. The FDA will review data from animal studies and human clinical trials to determine the safety, efficacy and cost–benefits of the new drug, as well as its proposed labelling and the quality of its manufacturing process.

Patent

A patent is a legally enforceable right granted for a specific length of time to use and commercially exploit a discovery or invention.

Pharmaceuticals

Pharmaceuticals are compounds manufactured for use as medicines or drugs in healthcare.

Premarket approval application

Under US federal law, companies must seek regulatory approval before marketing medical devices. For Class III devices (where failure is of highest risk to human life, such as a heart valve or implantable middle ear devices), companies must submit a premarket approval (PMA) application.

Premarket notification 510(k)

The 501(k) premarket notification is an alternative to the premarket approval application above. It applies to applications for US regulatory approval for medical devices in Class I and Class II, where the risks are lowest or moderate, respectively. Companies are required to demonstrate that their new device is substantially equivalent to another device already on the US market. Products requiring 510(k)s include X-ray and dialysis machines.

Provisional patent

Provisional applications are filed prior to a full patent application. The provisional application is used to establish a priority date and is an inexpensive way of signalling intent to file for a full patent application at a later date. It also allows the applicant time to determine whether to proceed with a full patent application. Filing a provisional application does not grant the applicant patent protection and a full patent application must be made within 12 months of the provisional patent filing in order to claim priority date.

Real-world evidence

Real-world evidence is clinical evidence drawn from data collected outside traditional clinical trials. This includes digital health data, case reports, public health surveillance and registries, and administrative and billing records.

NINE Abbreviations

ACRONYM	FULL NAME
510(k)	Premarket notification 510(k)
ABN	Australian business number
AGM	Annual general meeting
ARC	Australian Research Council
ARTG	Australian Register of Therapeutic Goods
ASX	Australian Securities Exchange
BLA	Biologics license application (under the FDA)
CE	Conformité Européene
CTN	Clinical Trial Notification
CTX	Clinical Trial Exemption
EMA	European Medicines Agency
EMEA	European Agency for the Evaluation of Medical Products
ESIC	Early Stage Innovation Company
DCF	Discounted cash flow
FDA	Food and Drug Administration (US)
GICS	Global Industry Classification Standard
HPV	Human papilloma virus
IDE	Investigational device exemption
IND	Investigational new drug

ACRONYM	FULL NAME
IP	Intellectual property
IPO	Initial public offering
IRB	Institutional Review Board
LLP	Limited liability partnership
MTAA	Medical Technology Association of Australia
MTP	Medical technology and pharmaceuticals
NDA	New drug application
NHMRC	National Health and Medical Research Council
OECD	Organisation for Economic Co-operation and Development
OGTR	Office of the Gene Technology Regulator
PMA	Premarket approval
QIC	Queensland Investment Corporation
R&D	Research and development
rNPV	Risk-adjusted net present value
SMEs	Small-to-medium enterprises
TGA	Therapeutic Goods Administration
UQ	University of Queensland
WEHI	Walter and Eliza Hall Institute of Medical Research

TEN Contributors

This Guide was developed by an Advisory Committee convened by AusBiotech.

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Sincere appreciation is extended to these individuals as well as to the members of the Advisory Committee.

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Josh is responsible for developing ASX's domestic and international listings business. Prior to joining ASX, Josh spent nearly a decade in various roles within the investment banking industry at both Morgan Stanley and Nomura. Josh holds a Bachelor of Property Economics from the University of Technology, Sydney, and

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CEO, AusBiotech

Glenn is the Chief Executive Officer of AusBiotech. He was appointed Chief Executive Officer and Executive Director of AusBiotech Ltd in September 2016. AusBiotech is Australia's industry body for life sciences, with over 3,000 members. Glenn has spent the last decade as Chief Operating Officer, where he has been responsible for business development, finance and general operations. He has over 30 years' experience in the life sciences sector and has held senior executive roles in both multinational and Australian companies.

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Liz has over 16 years' experience in grants, funding and incentives advisory, taxation, project management, research, advocacy and innovation advisory in Australia and the UK. Liz's unique experience as a research scientist looking at therapeutic agents for neurological conditions, combined with her business experience, make her well placed to provide in-depth funding strategies to biotechnology companies.
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Patrik is founder and CEO of Venture Valuation AG, Switzerland. He started the company over 14 years ago when, during a collaboration with Novartis Venture Fund, he noticed a need for independent valuation services in high-growth areas; Novartis Venture Fund became his first client. Since then he has been involved in over 250 valuations for investors as well as for biotech, pharma and medtech companies. Patrik graduated from the Business University of St Gallen, Switzerland, and completed his PhD thesis, *Assessment and valuation of high growth companies,* at the Swiss Federal Institute of Technology, EPFL Lausanne, Switzerland. Patrik's articles have been published in a number of scientific journals including *Nature Biotechnology* and *Chimia,* and business publications, *Starting a business in the life sciences: from idea to market* and *Building biotechnology: starting, managing, and understanding biotechnology companies.*
He has lectured at Seoul National University, South Korea, EPFL Lausanne, and the University of St Gallen, and gives regular workshops on valuation.

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Lawrence is the Chief Investment Officer and Founder of Scientia Capital, a specialised global investment fund focused exclusively in life sciences. With 15 years of experience in investing and banking, Lawrence has expertise in all areas of investment management and deep roots in the scientific and biotech communities. Prior to Scientia, Lawrence was responsible for the largest biotechnology investment portfolio in Australia as the institutional biotechnology analyst at QIC (the Queensland Investment Corporation), an investment fund with over $60 billion under management. He previously worked as the senior biotechnology analyst in the equities team at Foster Stockbroking, and gained corporate finance experience advising life sciences companies at Deloitte. Lawrence currently serves as a director on the boards of Prana Biotechnology (NASDAQ: PRAN), Seattle-based Nohla Therapeutics and Gyder Surgical. He holds a Bachelor of Science with Honours (in immunology) from the University of Melbourne.

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Aitana joined Venture Valuation in 2013, and she is currently senior consultant. She previously worked as a pharma equity research analyst for Kepler Cheuvreux in Zurich, Switzerland; as a consultant on projects on market access, pricing and reimbursement, and on budget impact model for Stratas Partners in Basel, Switzerland; and as an investment analyst for London-based hedge fund Carval Investors, as part of the Non-performing Loans team, where she assisted in the pricing and performance analysis of investments across several geographies. Aitana holds a PhD in evolutionary genetics from the University of Groningen, Netherlands, and is a Chartered Financial Analyst Level II candidate.

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James has over 15 years' experience in financial markets in Australia and overseas. Since joining ASX in 2012, he has been responsible for developing the listings and capital raising business, both domestically and internationally. He works with companies from a broad range of industry sectors, including healthcare, technology and resources. James formerly worked for NYSE Euronext in London in the capital markets and trading businesses, most recently as Managing Director, International Listings.

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Michael has over 18 years' experience in senior leadership roles in the life sciences industry as an investor, advisor, and investment banker. Most recently, Michael served as Interim Chief Executive Officer of Nohla Therapeutics, Inc., during which time he successfully spearheaded its start-up and guided its transformational Series A financing in November 2016. He was the Director and Head of life sciences investment banking at Bell Potter Securities from June 2014 until he joined Nohla. Prior to Bell Potter, he was the Founder and Senior Portfolio manager of the Meditor Cobra fund, a €500 million Healthcare Hedge fund based in London. From 1997 to 2003, Michael served as Director and Global Head of Healthcare at DWS Investments, Deutsche Bank, overseeing €6billion of direct investments in the public and private markets. Michael holds an Master's of Science (in biochemistry) from the University of Oxford, UK.

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Hans joined to KPMG in 2016 with over 20 years in life sciences through working with various Fortune 500 companies, such as Novartis and Amgen. He is a commercially focused senior executive with extensive finance, sales and marketing and general management experience in the biotechnology, healthcare and pharma sectors. He is passionate about designing innovative and transformational solutions that greatly enhance the strategic capabilities of clients and deliver competitive advantage in fast-changing external healthcare environments.

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Kyahn is a specialist in financial and corporate communication and leads the investor communication practice at WE Buchan. Kyahn has a depth of experience in working with life sciences companies in drug development, medical technology and early stage commercialisation. She has extensive networks in investment markets and media, and experience in managing complex stakeholder engagement and investor relations programs across a wide range of scenarios, including mergers and acquisitions, initial public offers and regulatory issues. Kyahn has been with WE Buchan for almost 12 years and has a Bachelor of Arts (Public Relations) from RMIT and a Diploma in Investor Relations from Australasian Investor Relations Association.

Mr Steven Yatomi-Clarke
CEO and Managing Director, Prescient Therapeutics

Steven was appointed CEO and Managing Director of Prescient Therapeutics in 2016, having previously been a non-executive director of the company. He was responsible for refocusing Prescient's clinical and commercial strategy as well as recapitalising the company. Under his stewardship, Prescient has also built an experienced operational team and made significant progress in its clinical programs.

Steven has over 17 years' experience in investment banking specialising in biotechnology, where he was consistently one of the most prolific and successful bankers in the sector. Steven has also been a collaborator on clinical trials conducted in Australia and the US in cancer immunotherapy.

Dr Janet Yeo
National Projects Manager, AusBiotech

(Guide to Life Sciences Investing Project Manager)

Janet is responsible for the management and delivery of national projects at AusBiotech. Prior to joining AusBiotech, Janet worked in research management at the University of Melbourne, supporting the delivery of the University Chancellery's Research Infrastructure Strategy objectives. She holds a PhD in biochemistry/ medical biology from the Walter and Eliza Hall Institute of Medical Research and University of Melbourne. Janet is also the program manager for the MedTech-Pharma stream of the Industry Mentoring Network in STEM (IMNIS) program.

Appendices

Appendix A. Regulatory authorities

In Australia, regulatory authorities include the following:

- Therapeutic products – the Therapeutic Goods Administration, www.tga.gov.au;
- Gene technology and genetically modified organisms – the Office of the Gene Technology Regulator (OGTR), www.ogtr.gov.au;
- Clinical trials conducted in Australia with unapproved therapeutic products are regulated by the TGA through the Clinical Trial Exemption (CTX) and Clinical Trial Notification (CTN) schemes, www.tga.gov.au/industry/clinical-trials.htm.

Appendix B. Sources of funding for life sciences

Government grants

A number of government grants and funding opportunities are made available by federal, state, and local government bodies to assist life sciences companies to innovate, commercialise and grow.[75] The type of grant and amount of funding available varies, with some programs involving a competitive process to seek an award and/or only being offered in rounds or at specific times of the year.

Australian Government programs include:

- Biomedical Translation Fund – $250 million funds in aggregate, managed by Brandon Capital, BioScience Managers and OneVentures, that makes venture capital investments in early stage companies that are developing and commercialising biomedical discoveries. More information at https://www.business.gov.au/assistance/biomedical-translation-fund;
- Cooperative Research Centres Projects grants – provides up to $3 million and supports short-term industry-led collaborations to develop important new technologies, products and services. More information at https://www.business.gov.au/assistance/cooperative-research-centres-programme/cooperative-research-centres-projects-crc-ps;
- Accelerating Commercialisation – provides guidance and grants of up to $1 million to assist small and medium businesses, entrepreneurs and researchers to commercialise novel products, services and processes. More information at https://www.business.gov.au/assistance/accelerating-commercialisation.

Foundations

Australian philanthropic foundations contribute millions of dollars to the life sciences sector, based on the alignment of projects to the ideals of their founders. These grants are often less restrictive than government grants as foundations are not accountable to the government and do not use taxpayers' money. Grants from foundations are often made to encourage business growth, and may only last for a few years. Foundations are also more likely to support groups that have deductible gift recipient status with the Australian tax office.[76]

75 Funding Centre website, 'Government, philanthropic and corporate grants: three different paths to grant application success' https://www.fundingcentre.com.au/help/three-paths

76 Ibid.

Industry partnerships

Industry partnerships involve agreements to foster collaboration between the Australian research sector, industry partners and other organisations. The ARC Linkage grants are specifically designed to increase collaboration between academia and industry or other partners. Increased collaboration between academia and industry will facilitate more efficient delivery of innovative research to areas where it is most needed. This also allows research students to gain experience within relevant industries through their research training. The combination of government funding and partner contributions allows larger scale projects to be undertaken, and often provides significant return on investment.[77]

Venture debt

Venture debt is a form of debt financing available for venture-backed start-ups when they cannot finance themselves through debt with traditional banks because they lack the assets or cash flow. Specialised banks or non-bank lenders provide venture debt to fund working capital or capital expenses, such as new equipment. Venture debt has a number of advantages, including flexibility, less dilution of ownership, and being a less costly form of risk capital than equity. Companies may seek venture debt in between milestone stages, where they can expect to attract venture capital.

Revenue

If the company is making money, it can reinvest part of its revenue back into the company. These reinvestments (also known as retained earnings) may generate further revenue in the form of increased sales or by attracting investors. High levels of revenue reinvestment may be interpreted in different ways by potential investors: some may see it as a positive sign of company success. In contrast, other investors would see a high level of dividend payouts (rather than retained earnings) as a positive indication of confidence.

R&D Tax Incentive (Australia)

The R&D Tax Incentive encourages companies to undertake R&D that benefits the Australian economy by providing financial benefits in the form of a tax offset or cash rebate and has the following two options:

- a 43.5 per cent refundable tax offset for eligible entities with an aggregated turnover of less than $20 million – with the exception of those controlled by tax exempt entities;
- a 38.5 per cent non-refundable tax offset for all other eligible entities.[78]

The refundable tax offset is applied after all other tax offsets (with the exception of franking deficit tax offsets).[79] When a company's tax liability is reduced to zero and there is an excess of tax offsets, a company may be entitled to a cash refund.[80]

The non-refundable tax offset is applied prior to refundable tax offsets and franking deficit tax offsets but after all other tax offsets.

77 Australian Research Council website, 'Industry collaboration' http://www.arc.gov.au/industry-collaboration

78 Australian Taxation Office (ATO) website, 'About the program' https://www.ato.gov.au/business/research-and-development-tax-incentive/about-the-program/

79 ATO website, 'R&D refundable and non-refundable tax offsets' https://www.ato.gov.au/Business/Research-and-development-tax-incentive/In-detail/Fact-sheets/Refundable-and-non-refundable-tax-offsets/

80 Ibid.

Examples of the varying benefits (dependent on a company's turnover and tax position) for FY17 are listed below:

Turnover	<$10m	<$10m	$10m -<20m	$2m -<20m	>20m
Tax rate	27.5%	27.5%	30%	30%	30%
Profit/loss	Loss	Profit	Loss	Profit	Profit or loss
R&D expenditure	$100,000	$100,000	$100,000	$100,000	$100,000
R&D benefit	43.5% cash refund	43.5% tax offset	43.5% cash refund	43.5% tax offset	38.5% tax offset
R&D permanent benefit ($)	$16,000	$16,000	$13,500	$13,500	$8,500
R&D timing benefit ($) 'cash out losses'	$27,500		$30,000		
Total R&D benefit ($)	$43,500	$16,000	$43,500	$13,500	$8,500

Companies in a tax loss position with turnover below $20 million derive significant non-dilutive benefit from the R&D Tax Incentive program.

Early Stage Innovation Company

The Early Stage Innovation Company tax incentive scheme, which came into effect on 1 July 2016, is designed to foster investment in early stage innovation companies in Australia by providing investors with generous tax incentives.[81] While it is a tax incentive for investors, it is also dilutive for the investee in the sense that the investor acquires a share in the company.

The scheme provides investors in a qualifying ESIC company with an up-front 20 per cent non-refundable tax offset (capped at $200,000 per investor per year for 'sophisticated investors' and $50,000 for other investors), as well as a 10-year capital gains tax exemption for investments held for at least 12 months. A company will generally qualify as an ESIC if it meets the early stage and innovation requirements.

The early stage test assesses the company's eligibility against criteria related to company expenditure ($1 million or less in the previous income year), assessable income ($200,000 or less in the previous income year), stock exchange listing and date of incorporation or Australian business number (ABN) registration date. The innovation limb assesses the company's involvement in innovation, and is measured against a number of criteria which fall under either a principles-based test or an objective test. Companies can choose to apply for a private ruling from the Australian tax office about whether they qualify as an ESIC.

81 ATO website, 'Qualifying as an early stage innovation company' https://www.ato.gov.au/Business/Tax-incentives-for-innovation/In-detail/Tax-incentives-for-early-stage-investors/?page=2

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