Article

Australian Biotechnology: Promissory Expectations And Ecosystem Performance Far From The Global Superclusters

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ABSTRACT

Australia is an interesting case study of biotechnology ecosystem development. Despite its distance from the US biotechnology superclusters, the country has had high expectations for its potential development into a biotechnology superpower. These expectations have not been met over the last two decades. Despite generous R&D tax incentives and a robust network of public research organizations (PROs), the local biotechnology industry has remained small and weak, without a single 'big biotech' emerging. Cluster analysis over 11 years of all private and public DBFs indicated that the PRO network output failed to translate to the development by the local biotech industry of drug candidates that could attract Big Pharma deals. Analysis of the investor returns over 15 years from all public drug development biotech firms (DDBs) showed that not a single firm produced attractive long-term investor returns and the sector overall generated negative returns for investors. Despite high promissory expectations, favorable government policies and an inflated view of the quality of the country's science output, Australia has failed to create a sustainable biotechnology ecosystem. Some of the reasons are identified and suggestions are offered for changes in government policy that could improve value creation by the local biotech sector.

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INTRODUCTION

Governments worldwide have embraced the idea of biotechnology clusters as essential to building ecosystems with the critical mass needed to foster a robust bioeconomy. The US biotechnology sector is the exemplar of a successful bioeconomy, where the so-called 'superclusters' in the Boston area and San Francisco areas have been central to building critical mass and driving the remarkable growth of the US biotech sector.

In seeking to emulate the US success, other countries have embraced the idea of clusters as a key to building critical mass and creating a sustainable ecosystem. Australia is no exception: In 2001, the Australian Federal Government launched an 'innovation action plan for the future', highlighting biotechnology as a key opportunity area, because of the country's alleged prowess in the life sciences.[1,2]

The optimism was high, as echoed in a *New Scientist* article in 2002: "Once upon a time, Australia was the Cinderella of the commercial biotech world. But now the continent is set to blossom as the belle of the ball."[3] These aspirations were cheered on by the national industry body, AusBiotech, which over the last two decades has consistently proclaimed Australia's international biotechnology leadership, often referring to Australia's disproportionately large number of public biotech firms and the country's high ranking in the *Scientific American* "Worldview Biotechnology Scorecard".[4]

This paper examines whether the promissory expectations for the Australian biotechnology ecosystem have been realized over the last 20 years. It highlights recent studies that have sought to objectively measure the performance of the sector and empirically assesses the efficacy of the government policies and corporate strategies

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aimed at building a successful biotechnology ecosystem in Australia.

PROMISSORY EXPECTATIONS

There is no doubt that the expectations for an Australian biotechnology industry have been high.[5] Since the early 2000s, the rhetoric has been universally celebratory and unrelenting, especially from AusBiotech. The AusBiotech website homepage states[i]:

> *Biotechnology is widely recognised as a "game-changer" and foundation stone of our future. It is anticipated that biotechnology will underpin our economy and provide solutions to disease, climate change, fuel alternatives and food security – in addition to improving our quality of life.*

In a 2016 article, titled 'Australian biotechnology packs a powerful punch',[6] AusBiotech reported that: "Australia is a world-leading location for biotechnology, boasting the largest listed biotechnology sector as a proportion of GDP in the world. It has one of the largest and fastest-growing public markets for biotechnology and yields some of the greatest public revenues across the globe." A 2017 *Industry Position Survey* by AusBiotech[7] stated: "Australia currently has around 100 ASX-listed life sciences companies, with a market capitalisation of $93.74 billion." The consistent message has been that Australia has been successful in creating a vibrant biotechnology ecosystem. Another consistent message from AusBiotech and some State governments has been that Australia is a world biotechnology leader, based on its high ranking in the *Scientific American* "Worldview Scorecard".[4]

From 2009 to 2016, *Scientific American* published its annual Worldview Scorecard of the global biotechnology industry. The 2016 Worldview Scorecard measured the comparative performance of 54 countries with respect to biotechnology activity, based on 27 metrics around: Productivity, Intellectual Property Protection, Intensity, Enterprise Support, Education/Workforce, Foundations, and Policy & Stability. Over the years, the Worldview Scorecard has been cited by governments and industry bodies to promote their biotechnology prowess on the world stage, the attractiveness of their country as a home for biotechnology firms, and the potential for partnering their biotechnology outputs. Australia has been particularly active in this regard[4,8,9]. The Worldview Scorecard has also been used as input to public policy [10,11].

A number of the metrics for the scorecard were derived from public biotechnology company data published each year in *Nature Biotechnology* (NBT). For a number of years, at least until 2016, the NBT datasets included the revenue, market cap and employment numbers for the Australian pharmaceutical firm, CSL. As noted in a recent study and as long recognized by most CEOs in the local biotech sector, CSL is a century-old and previously government-owned pharmaceutical manufacturing business that has low R&D intensity and was never a biotech firm[12]. However, with 2015 revenues of $5.5 billion, a market cap of $36 billion and 14,000 employees, its inclusion in the NBT dataset served to dramatically inflate the numbers for Australia's biotechnology performance and elevate its ranking on the Worldview Scorecard.

From 2016, after a critical review by NBT of their inclusion criteria, CSL was removed from the NBT dataset (along with several other large firms incorrectly classified as biotech firms), reducing Australia's reported 'biotechnology revenues' from $5.7 billion in 2015 to $0.4 billion in 2016, and biotechnology market valuation from $37.8 billion to $2.8 billion. Nevertheless, the historical 'top five' ranking of Australia on the Worldview Scorecard continues to be promoted by AusBiotech[ii] and in news articles about Australian biotechnology.[13]

COLLABORATIONS, CLUSTERS AND NETWORKS

A study in 2008[14] focused on Australia's networks and clusters and questioned whether clusters far from the world superclusters are viable, noting they "are little more than the combination of research institutions and spinout biotechnology firms…[and] there is good reason to question whether the ambitions of regional governments are realistic." In Australia's case, the study identified the 'tyranny of distance' as a major obstacle to the development of the Australian biotechnology ecosystem. It concluded: "regional governments face an immense challenge in creating viable biotechnology clusters far from the world hubs."

A 2010 study[15] compared the clusters in Australia's three largest cities – Melbourne, Sydney and Brisbane – with San Diego, and concluded that the Australian cities lacked many of the features needed for a US-standard biotechnology ecosystem. Specifically, Australian cities suffer from inadequate investment intensity, support a relatively shallow research portfolio, and generate

i <https://www.ausbiotech.org/biotechnology-industry/biotech-is-a-game-changer> accessed October 21, 2020

ii <https://www.ausbiotech.org/biotechnology-industry/fast-facts> accessed October 22, 2020

research outputs of low average quality and low commercial significance.

The most extensive and robust study of Australian biotechnology clusters and networks was only recently completed and published.[16] The design of the study drew heavily upon the landmark research by Powell and colleagues in the US, which mapped the trajectories of US biotech firms, clusters and networks from 1988 to 2002[17-20]. The Australian project similarly mapped the development of all Australian biotechnology firms (public and private), as well as cluster and network formation from 2003 to 2014; 2003 was used as the baseline year because in that year Australian DBFs (dedicated biotechnology firms) overall were approximately the same age, size and scale as the DBFs in the US superclusters in 1988[16]. Like the US study, DBFs were defined as 'independently operated, profit-seeking entities involved in human therapeutic and diagnostic applications of biotechnology' in line with the definitions applied by Powell and colleagues.[17]

The study identified the three critical challenges for biotechnology firms as: access to new knowledge and intellectual property, early-stage fund-raising for the timely development of a viable product, and commercial efforts aimed at bringing a product to market. In the US, firms pursue 'multiconnectivity' to meet these challenges.[17] The Australian study sought to assess the degree to which such mutliconnectivity occurred in Australia and its efficacy in meeting all three challenges. It employed descriptive analyses and data visualizations, as well as statistical modelling. For statistical modelling, the study used three dependent variables, each aligned with these three challenges.

In relation to new knowledge and acquiring a science base, the study used the *number of patent applications* in a given year as a proxy for DBF inventive productivity. While patent applications do not necessarily reflect product development output or commercialization, they are a useful indicator of new knowledge creation.[21] With regard to early-stage fund-raising, whether or not a DBF was able to forge a *risk capital deal* was used as a dependent variable. This was coded as 1 for each year that a DBF secured a deal with a financial partner (or listed on ASX). Finally, with respect to commercialization, *deals with Big Pharma* (in a given year), was used as the dependent variable.

The results showed that collaborations between DBFs and PROs underpinned Australian clusters and domestic networks throughout the period. Indeed, PROs appeared to produce more connectivity in Australian clusters during the period than was the case in the US superclusters during the 1990s[22]. It appeared that the regional science base in Australia generated positive network effects consistent with the experience of the world superclusters and consistent with the opportunity to create the 'virtuous cycle' needed to support a viable biotechnology ecosystem.

In relation to the second challenge, the results showed that provision of early-stage funding for DBFs in Australia was dominated by domestic partnerships with financial entities. These included government funding, such as the Innovation Investment Fund and grants through the federal agency, AusIndustry. The results indicated that ties with Australian PROs, domestic DBF collaborations and financial collaborations positively influenced early-stage funding and thereby confirmed the potential for PROs to be anchor tenants for Australian biotechnology, extending beyond knowledge creation to early-stage funding. In summary, it appeared that the collaboration networks helped Australian DBFs in meeting the second challenge of accessing early-stage funding for development of a viable product. However, it was in the third step – commercialization – that the process came to a dead end.

For the final challenge of commercialization, the focus of the study shifted from domestic to international collaborations, mainly because of the absence of multinational pharmaceutical companies in Australia, apart from CSL. Descriptive and visual analyses showed that as DBFs became more mature, not unexpectedly, they formed relatively more international collaborations, but unlike domestic collaborations, they were thinly spread and gave rise to sparse networks and very few Big Pharma deals. Overall, the local collaborations and networks failed to translate into international network effects necessary for partnering and commercialization.

In summary, Australian PROs served as anchor tenants in meeting the first two challenges. However, in not facilitating the third, they failed as anchor tenants for the development of an effective biotechnology ecosystem in Australia. This finding was consistent with other studies that highlighted the limitations of PROs as anchor tenants.[23,24] As noted by the authors (p. 14):

> *The challenge of securing deals with Big Pharma can partly be understood in terms of the 'tyranny of distance' (Gilding, 2008), but it is much more than this. It requires attention to institutions, facilities and practices that mitigate geographic distance, extending the reach of local and domestic organizations and their absorptive capacity. This might include local observatories (as found in the superclusters), international exchange programs between PROs and Big Pharma (designed to make PROs more robust anchor tenants), or incentive schemes for more mature DBFs to forge collaborations with start-ups (following the example of the superclusters).*

They noted that the public investment, bipartisanship and patience needed to nurture such initiatives were inconsistent with the partisan Australian industry policy climate, short election cycle times and the government's narrow understanding of market failure. The authors concluded[16] (p. 14):

> *In conclusion, our analysis suggests that advocates of the innovation economy – politicians, policymakers, scientists and industry players – have overstated their case for biotechnology as a prospective industry for countries far from the world biotechnology superclusters and Big Pharma. In close connection, the literature on 'territorial knowledge dynamics' is excessively optimistic about the prospects of navigating distant collaborations and combinatorial knowledge across 'multi-location milieu' (Butzin and Widmaier, 2016; Crevoisier and Jeannerat, 2009). Distant collaborations cannot seamlessly substitute for local deficits. Regional public research organizations struggle to catalyze collaborations with diverse partners across the entire value chain. Strategies to build absorptive capacity and embed distant capabilities are poorly understood. Collaborations do not automatically translate into virtuous cycles, and may become dead ends. The ambitions of regional policymakers and industry players have been mostly disappointed. We need a better understanding of network failure in order to fashion new industries far from the world advanced-technology hubs.*

INVESTOR PERFORMANCE

Another recent study examined the effectiveness of the Australian biotechnology ecosystem from the perspective of investor performance over a 15-year period.[12] The study focused on public biotech firms and specifically those involved with drug development, which is by far the dominant application and the historical standard bearer of biotechnology. To distinguish these firms from DBFs, which includes diagnostics firms, the term 'DDB' or drug development biotech was deployed. This term was preferred over 'biopharma', because the latter is a broader term that has been used to embrace large pharmaceutical firms as well as biotech firms, as in the 'biopharma industry'.[25-27] Also 'biopharma' has led to confusion with the term 'biopharmaceutical', which is restricted to biologic drugs that are the product of bioprocessing[28].

According to the study, outside the US, almost all DDBs remain as pre-commercial entities that are consistently loss-making and reliant on ongoing investor funding. Investors invest in these firms for the capital value growth arising from changes in the perceived value of the DDB's pipeline as it progresses candidate drugs towards a pharmaceutical license or sale. In the absence of cash flow from operating profitability, a DDB will not be able to progress its R&D pipeline or even survive without ongoing investor support. This makes investors crucial stakeholders and gives them a substantial 'captaincy' role in firm birth and survival. Therefore, the delivery of long-term investor returns is a relevant measure of the performance of individual DDB firms and crucially important to the health and sustainability of a country's biotech sector, for which the DDB sector is a proxy[12,29].

For public DDB firms, especially in Australia, maintaining investor confidence and securing regular ongoing funding is crucial to building value and survival. In turn, growth in the value of a DDB's share price is crucial to investor confidence. Accordingly, the research sought to answer the question: Do Australian public DDB firms deliver attractive investor returns, consistent with building a robust biotechnology ecosystem that is adequately supported by investors?

The study[12] focused on all 40 public DDB firms that existed (and had a minimum of five years' operation) in Australia from 2003 through 2018. As a principal performance metric, it measured overall sector investor return by treating the portfolio of 40 firms as if it were a venture capital (VC) portfolio and calculated the gross pooled internal rate of return (IRR) over the 15 years.

In addition to overall sector IRR, the study measured the performance of individual firms using a similar IRR calculation, which was equivalent to annualized share price growth. Apart from investor performance, it also collected data on the average levels of cash held by firms and their R&D expenditure (RDE) to assess whether these variables had any predictive value with respect to investor performance for individual firms.

The results showed that the overall sector returns were abysmal: The portfolio lost 51% of the invested principal over the period, representing a sector IRR (annualized loss) of – 6.2%. The individual firm results were equally disappointing: Only nine firms (22.5%) produced a positive investor return over the period, but the highest return was only 8.5%, which was well below investor expected returns for this high-risk sector. The more telling result was that 31 firms (77.5%) produced negative average annual returns, with the vast majority losing more than 80% of their investors' principal over the period[12].

The study also examined whether the results were an artifact of an unusually negative terminal year for the final return calculation, but the opposite was the case: 2018 proved to be a year of modest positive value growth for the sector and choosing any other recent ear for the

Table 1. NBT 2017 data for global biotech industry

Country	Number of public biotech firms	Total MV US$ mill	Total RDE US$ mill
United States	337	878,133	41,153
Australia	43	3,550	261
France	39	19,403	1,301
UK	32	55,968	2,346
Sweden	30	9,276	278
Canada	28	4,152	483
Germany	18	8,280	393
Israel	15	1,736	201
Switzerland	11	5,763	389
Denmark	10	31,019	765
Other countries (21)	63	65,254	1,716
Total	626	1,082,534	49,286

Source: Morrison, C. and Lähteenmäki, R. (2018) Public biotech in 2017 – the numbers.
Nature Biotechnology 36(7):576-84 (supplementary table 1).

terminus actually worsened the results. It was apparent that since the 2008/09 recession, the underlying value of the sector had been in steady decline, with 2018 potentially being a modest silver lining, due to substantial value increases for two firms, one of which was sold in 2018.

Public biotech firm metrics reported by NBT were compared for Australia and other countries. This data is in Table 1, showing countries ranked by the number of public biotech firms.

The US accounts for around half of all biotech firms globally, but an overwhelming 81% of market value and 83% of R&D spend globally. Australia has a relatively large number of public biotech firms for its population, but this is due to the low valuation and listing hurdles for the ASX and the opportunity for expedited listing without the involvement of VCs or institutional funds (discussed below). However, as a result, the public biotech sector is weakly funded and small, based on valuation and RDE. The study concluded that the Australian biotech sector is fundamentally small and weak and any view that Australian biotech 'punches above its weight', at least in the core area of drug development biotech, is groundless[12].

While inadequate commercialization skills, lack of venture capital funding and the 'tyranny of distance'[14,30] have been blamed for Australia's weak biotechnology performance, the study results suggested that the quality of the science underpinning these companies also may be part of the problem. The study observed, however, that regardless of the causes of the poor investor performance, the sector's history of negative investor returns and the absence of a big biotech success story will make it very difficult for Australian biotechnology to attract future private funding.

WHERE TO FOR AUSTRALIAN BIOTECHNOLOGY?

Australia is an interesting case study because it appears to have a lot going for it as a place to build a bioeconomy. Firstly, it has a Federal government with an expressed commitment to growing a world-class biotechnology ecosystem. While government policies and financial support for biotechnology may have waxed and waned over the last 20 years, through its various systems of grants and the tax incentives, the government has been a major investor in Australian biotechnology. In the DDB sector, the amount of the government funding over the last 15 years has been estimated to be around $2 billion, which is almost as much at the total funding from private investors.[12] The R&D tax incentive (RDTI) alone is extremely attractive, in that qualifying RDE receives a 43.5% cash rebate. Effectively, it halves the cost of R&D for Australian biotechnology firms. Australia's commitment to biotechnology has been reinforced by a highly active industry group, AusBiotech, dedicated to promoting the benefits of Australia as a world-leading site for biotechnology innovation, lobbying for favorable government policies, and otherwise fostering industry development.

Another often-cited attraction for Australian biotechnology firms is that Australia is a favorable location for conducting Phase I human trials, because of its expedited CTN (clinical trial notification) system. This compares with the much more burdensome and time-consuming US IND (Investigational New Drug application) process. Combined with a favorable exchange rate, this has led to the proliferation and growth of local CROs (contract clinical research organizations) dedicated to running such trials, mostly for foreign pharmaceutical clients. However, the real benefits of the CTN system for the local biotechnology sector are indeterminate. Also, it should be recognized that while Phase I trials are useful to establish initial human safety and drug pharmacokinetics, it is the more expensive and risky Phase II trials, aimed at establishing dosage, efficacy and safety in patients, that are the real trigger for pharmaceutical deals; and to have deal-making currency, these generally need to be done in the US, under an IND.

Although not often promoted by AusBiotech or the government, another feature of Australia as a location for biotechnology firms is the low barrier to public listing on the ASX, compared with many other jurisdictions including the US. In many ways, an ASX listing provides

a substitute for venture capital for early-stage Australian firms[31]. As such, it represents an attractive mechanism for early-stage funding of technologies that might otherwise not receive VC funding, either due to a lack of VC funding – as is often claimed in Australia – or because the program does not meet the type or quality of program sought by the VCs. Indeed, it has been argued that VCs cherry-pick the highest quality projects and leave the lesser-quality programs to compete for an ASX listing, obtaining their 'venture capital' from less-discerning retail investors.[31] Regardless, there is no doubt that the low listing hurdles in Australia are an advantage for Australian biotechnology firms.

Apart from the initial funding at IPO, an ASX listing opens access to ongoing public funding through institutional placements (referred to as PIPEs in the US), share purchase plans (SPPs) and other public equity sales through brokers and investment bankers. Due to the early-stage of most biotechnology programs at IPO and the relatively modest initial raises, most firms rely on ongoing equity sales to continue to fund their R&D; however, this comes at the cost of shareholder dilution and the negative impact that that has on investor returns.[12]

ASX listing is such an attractive funding mechanism for early-stage projects that it has been exploited by entrepreneurs to fund foreign technologies that have been unable to secure funding in their home countries. For example, the most valuable ASX-listed DDB in 2018 was Clinuvel, which was built on drug technology from the University of Arizona, not an Australian PRO. Indeed, up to a third of all recent DDB ASX listings were based on foreign technology.[12] This must bring into question the quality or accessibility of the output of Australia's much lauded PRO network? It should also cause the Australian Government to question its substantial investment in RDTI (R&D tax incentives) where the firm is simply a vehicle for funding of foreign technology rather than the output of a local PRO.[12]

In addition, many other recent ASX listings have been simple repurposing of existing technology or products, rather than scientific breakthroughs, whether from Australian PROs or not. Possibly the most opportunistic in this regard have been the cannabis-related companies, with 14 of them listing on the ASX in the last several years. Indeed, it is difficult to find any Australian public DDB firms that are exclusively built on Australian PRO drug discovery research.

Ironically, a feature of the Australian biotechnology landscape that has been heavily promoted by the government and AusBiotech is the quality of its PRO research output, with the long-standing and rarely-questioned assertion being that the country "has punched well above its weight in terms of scientific breakthroughs".[6,32] However, one study has suggested otherwise,[15] concluding that Australia's research output is of mediocre quality, compared to a US cluster like San Diego. Another recent study also questions the quality of Australian science as a basis for building a DDB sector.[12]

If Australia does indeed 'punch above its weight', then the science base and network of PROs should provide a solid springboard for a globally-competitive drug discovery ecosystem. However, the cluster study described earlier[16] suggested otherwise and indicated that the activities of the network of Australian PROs fail to translate into commercially-relevant products, at least as measured by Big Pharma deals. The fact that there are few if any public DDBs on the ASX that are primarily built on Australian PRO breakthroughs reinforces this.

Even when the PRO research output is categorically world-class, there may be another cause for the disconnection between PROs and local industrial exploitation. The one major recent drug research breakthrough from an Australian PRO – the research by Walter and Eliza Hall Institute that led to the billion-dollar anti-cancer drug, venetoclax – was licensed directly from the PRO to Big Pharma (Genentech/Roche and AbbVie), at a very early stage and without any local Australian development beyond drug discovery and patenting by the PRO. Ultimately, the PRO sold off its royalty rights to its Big Pharma partners for a relatively modest $325 million, with the funds mostly directed to expansion of the PRO's facilities.[12]

There is no shortage of cancer-focused DDB firms in Australia and had the venetoclax discovery been licensed to one of these companies and clinical-stage value added in Australia prior to its licensing to Big Pharma, there is little doubt that the net present value of the licensing deal would have been in the tens of billions of dollars. More importantly, the country would have created its first home-grown 'big biotech' by now.

The country may have also obtained preferred, low cost access to this important drug. Instead, the PRO circumvented the Australian biotech industry to pocket a small payout, while – egregiously – this expensive cancer drug is now re-imported into Australia and subsidized on the Pharmaceutical Benefits Scheme, with the exorbitant treatment cost borne by Australian taxpayers. Incongruously, this has been celebrated by the PRO and the government as a great victory and a testament to Australian scientific prowess.[iii] The reality is that it was

iii <https://www.wehi.edu.au/news/illuminate-newsletter/september-2017/venetoclax-annoucement#:~:text=The%20Institute%20has%20made%20a,the%20anti%2Dcancer%20treatment%20venetoclax.> accessed October 30 2020.

a squandered opportunity to decisively bolster the DDB sector and pivotally leverage the government's multi-billion dollar investment in grants and tax credits to the biotechnology sector.

Apart from the 'venetoclax syndrome', there may be another insidious cause of the broken bridge between PROs and local industrial realization. During the early 2000s there was considerable interest by various Australian VC groups in funding Australian biotechnology projects. Indeed, Australian VCs backed three firms, which all progressed to listing on the ASX: Pharmaxis, Alchemia and Qrxpharma. Unfortunately all three later crashed emphatically, due to clinical trial or regulatory failures. Since 2010, not a single VC-backed biotech has progressed to listing on the ASX.[12] No doubt the three high-profile failures were dissuasive, but the other factor was the two-year escrow (post-listing) and other constraints imposed by ASX, which made it unattractive for VCs to list portfolio companies on the ASX.

One way or another, VCs moved their focus to private DDB firms, cherry-picking high potential programs from PROs with the goal of a trade sale and explicit avoidance of any projects where the founders wanted to build a sustainable company or list on the ASX[iv]. For example, the VCs backed several private PRO spinouts, such as Hatchtech, Spinfex and Fibrotech, and then on-sold them to pharmaceutical partners at the earliest opportunity, thereby liquidating their investments without an IPO.[12] The overall trade sale values obtained were in the hundreds of millions of dollars, which accrued to the benefit of the small number of high net worth investors in the VC funds (and to some extent the PROs), but like the venetoclax syndrome, the opportunity to contribute to the sustainable development of the DDB sector was squandered.

The venetoclax syndrome and VC cherry-picking are examples of behavior that have led to value leakage rather than value creation in the context of building a robust local biotechnology ecosystem that has any chance of reaching critical mass. The ultimate culprit is the financialized model of biotech funding.[33,34] This model promotes 'value extraction' rather than 'value creation' and the early monetization of drug development programs – typically in trade sales – rather than building a sustainable biotechnology sector. The Australian VCs have explicitly pursued this and the venetoclax syndrome shows that Australian PROs are complicit. The urgency to extract value at the earliest opportunity is a constant brake on growth and leads to leakage of value creation and depletion of the assets needed to reach ecosystem critical mass. In the face of this challenge, a recent study concluded[12]:

> *Potentially, Australia has neither the funding ecosystem nor the technology quality to support a globally-competitive DDB sector that can reach the critical mass needed to spin out one or more big biotech firms, and on which a bioeconomy could be anchored.*

As the author of that conclusion and the self-confessed promoter and perpetrator of value extraction events for public DDBs, I now demur. I believe that if the forces causing the leakage of assets can be understood and tamed through government policy and ASX changes, it may be possible for Australia to reach the critical mass needed to generate its first big biotech and build a world-class bioeconomy.

Key to that goal must be the recognition that the health of the public DDB sector is the key measure of ecosystem success. ASX listing by DDB firms brings with it, not only funding opportunities, but a public profile that drives aspirations for drug breakthroughs, determines investor sentiment, and shapes the country's overall perception of the efficacy of its biotechnology output. Public biotech firms should be vehicles for the 'best of the best' of Australian biotechnology commercialization opportunities – the standard bearers for Australian successful drug development. If the public biotech sector fails then the ecosystem fails. For the last 20 years, it has failed, but it can be salvaged by removing the drivers of value leakage and moving the value creation opportunities into the hands of ASX-listed biotech firms. This may finally give the sector the critical mass it needs to spin out its first big biotech.

Stemming the value leakage would require government policy aimed at ensuring that any drug discovery or development research generated by PROs is offered to Australian DDBs (or used to spinout a new Australian DDB) and that the 'venetoclax syndrome' is never repeated. It would also require policy that prevents Australian VCs from exiting private DDB programs through trade sales, at the same time incentivizing VCs to not only increase their investment in drug development projects (specifically), but also to exit only through ASX listing. Finally, ASX listing of foreign technology should be dissuaded by preclusion of any RDTI for companies that list based principally on foreign technology. Above all, ASX listing must not be viewed solely as a funding mechanism for companies, but as a responsibility to carry the standard for Australian technology and to contribute to a sustainable biotechnology ecosystem, not drive to an early exit.

iv Based on personal communications with VC firms between 2012 and 2016.

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