Questions on notice: Joint submission to the Economics References Committee's Inquiry into the Australian Manufacturing Industry

To: Committee Secretary, Economics References Committee, Department of the Senate, PO Box 6100, Parliament House, CANBERRA ACT 2600. Via email: Economics.Sen@aph.gov.au

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AusBiotech, Cell Therapies Pty Ltd, MTPConnect and Research Strategies Australia, are pleased to provide responses to three questions posed by the Committee in the Inquiry into the Australian Manufacturing Industry.

Question 1. *Your submission has argued that Australia has an opportunity to harness and leverage a growing and active global regenerative medicines industry, which could potentially be worth $6 billion per year in annual revenue by 2035 and 6,000 new high-value jobs. You've argued that Australia's potential competitive advantage in this space comes from our pre-existing reputation for high-quality, complex, and safe medical products as well as our already significant base of highly skilled workers in comparable sectors.* ***Given that we do have some of the building blocks in place, how quickly do you think we could scale-up a regenerative medicine industry within Australia, and what support would be needed from the federal government to make that happen?***

<u>Timing</u>

To realise, and in turn capitalise, on the current and emerging opportunities of the regenerative medicines (RM) sector, Australia needs to invest in and build an end-to-end solution for the RM industry, including sovereign large-scale and commercial manufacturing capability and capacity, and the solidification of an export market for RM products.

Australia has highly-evolved competencies and a distinct competitive advantage in RM, which includes world-leading research, a harmonised regulatory framework, and incentives to onshore biotech companies for further R&D at preclinical stages (the R&D Tax Incentive).

An industry gap currently exists within the Australian RM ecosystem at the translation and commercialisation stages of product development. More specifically the lack of available commercial infrastructure unique to RM therapy manufacture, and incentives for attracting commercial programs onshore for manufacturing is a current challenge for the ecosystem but importantly a significant opportunity for the sector and Australia's sovereign capabilities.

Investment should and can track to the development pipeline of RM products meaning that in the next **three to five years, commercial manufacturing capacity could be scaled to meet the new wave of therapies forecast to reach Australian shores. Whilst Australia is a relatively small consumer of these therapies, the geographical proximity of our country to the Asia Pacific (AP) region will lend itself to becoming a regional manufacturing hub for advanced RM therapies.**

<u>Federal Government</u>

The Federal Government can: A) support large-scale and commercial manufacturing capital infrastructure to complete the end-to-end RM industry in Australia; B) incentivise the onshore manufacture of commercial programs; C) develop policy to enable access to an export market for the AP region and rest-of-world; and D) support the development of the highly-skilled workforce pipeline.

A) Capital infrastructure for large scale commercial manufacturing. RM product manufacturing is sophisticated and complex and requires expensive, bespoke manufacturing equipment, the costs of which are difficult for CMOs (contract manufacturing organisations) to incur and carry prior to signing program contracts, and a need for a diverse mix of large "big pharma" clients and local smaller companies to amortise the significant operational costs of such programs. Having larger clients means that there is scale, expertise and capability, including international regulatory approval (Japan, Singapore, South Korea, Taiwan and Hong Kong) which provide substantial benefits, including lower entry prices to smaller local developers of these new products.

B) Incentives for onshore manufacturing of commercial programs. Pharma/biotech developers identify the cost of technology transfer from their global bases in the US and EU to local CMOs as a major consideration in their 'Make' (in their US/EU base) or 'Buy' (Australian CMO domiciled manufacturing) decision making. We have observed how sovereign government support of tech transfer costs in other jurisdictions such as Singapore or Germany can incentivise companies to 'Buy' and onshore their manufacturing to those jurisdictions. Therefore, Australian Federal Government support for tech transfer costs can encourage pharma/biotech developers to onshore their manufacturing to reputable Australian manufacturers. Of course, this relies on existing sovereign manufacturing capacity, credibility and capability, and the capacity to export to the AP region, in recognition that the Australian market is in itself small and the real opportunity is to use Australia as an exporter of these high cost, highly specialised bespoke products to the region. As most products are tied to a patient cell collection locally there are compelling reasons for a large company to have a regional presence, however the risk is that this opportunity is all too susceptible to other inducements from other regional jurisdictions who wish to displace Australia as a regional supplier of RM products.

C) Policy development to open the export market for RM therapies. Current legislation is not responsive to the new RM sector and is a major barrier to the export of RM products manufactured by TGA-accredited GMP manufacturers. A consultation is open now, and modification of this legislation can ensure an open and accessible export market for RM therapies. This will encourage large "big pharma" clients to establish Australian manufacturing programs that can rely on Australia's reputable production of safe complex medical products, therefore establishing Australia as the manufacturing hub for the region. Taken from the TGA consultation page: *'Currently, biologicals included in the Australian Register of Therapeutic Goods (ARTG) can be exported, but they are not permitted to vary from the product supplied in Australia. This means that 'export only' biologicals cannot have different indications, release specifications, or labels to the product approved by the TGA, even if the importing country has assessed and approved the product independently.'* Biologicals manufactured within Australia, and that meet the requirements of the country of export where the product has been registered, should be allowed to be exported regardless

of what is registered in Australia and listed on the ARTG. TGA manufacturing licenses should of course still be in place regardless of whether the facility is performing export-only activities.

D) Grow the highly skilled workforce pipeline. Support the development of an in-depth, industry leading nationally accredited training program utilising the existing onshore expertise in the commercial GMP manufacture of RM products. Support industry engagement with tertiary education such as internships and integration of RM advanced manufacturing within curriculums. *See answer to Question 2 for more information on 'How'.*

Background

The RM product development pipeline – Cellular Immunotherapies:

Cellular immunotherapies are currently the largest market and one of the major drivers of growth in the RM sector. These include Adoptive T cell and NK cell therapy, such as CAR-T, TCR, and CAR-NK products for cancer treatment. In 2020, the global T cell market size was valued at USD 4.6B[1]. At the forefront of the adoptive T cell therapy market are chimeric antigen receptor-T cell (CAR-T) therapies. A personalised one-time treatment, CAR-T is revolutionising cancer treatment and the healthcare system in Australia, where it has just been made available commercially, and globally, with access to these treatments in North America, Europe, Japan, and China.

To date, five CAR-T therapy products have reached the market, all of which are approved for the treatment of specific subsets of blood cancers. These marketed products are just the tip of the iceberg and across the globe there is a robust pipeline of adoptive cell therapies at various stages of clinical trial (Figure 1). Therapies to treat solid tumours (90 percent of the cancer patient population) are yet to enter the market and are at various stages of development, representing ~23 percent of total CAR-T clinical trials[2].

[1] T-cell Therapy Market Size & Share Report, 2021-2028, *Grand View Research*.

[2] Global CAR-T Cell Therapy Market, Market Size, Forecasts, Trials and Trends, 2021, *BioInformant*.

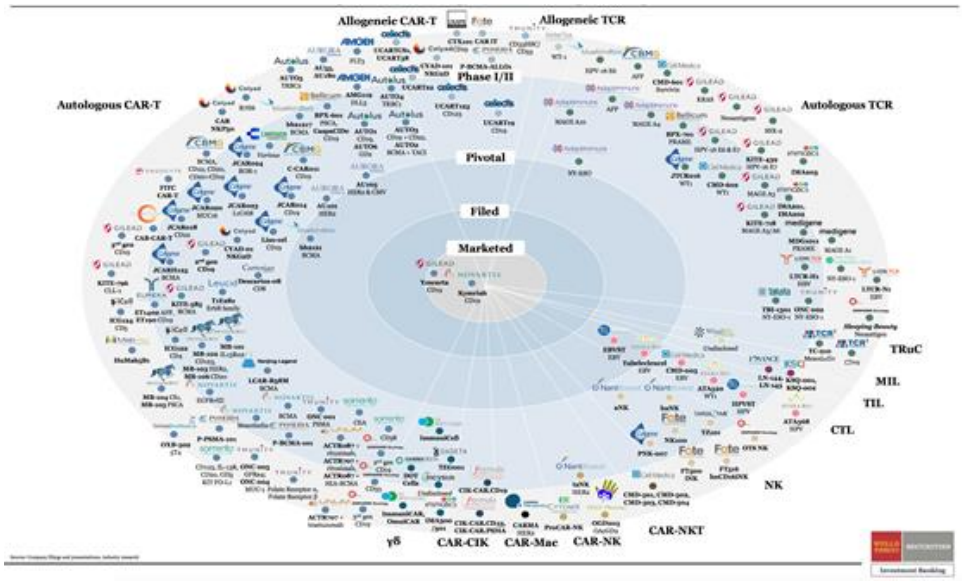

Figure 1. Adoptive Cellular Therapy Immuno-Oncology Landscape. Development pipeline of adoptive cell therapies at various stages of clinical trial and marketed in 2018. As of May 2021, there are five marketed autologous CAR-T therapy products: Kymriah® (Novartis), Yescarta® (Kite/Gilead), Tecartus® (Kite/Gilead), Breyanzi® (BMS/Celgene/Juno), Abecma® (BMS/Celgene). Imaged adapted from Wells & Fargo, 2018

In 2017 the first CAR-T therapy was approved by the US FDA. Kymriah® from Novartis for acute lymphoblastic leukemia (ALL) and diffuse large B-cell lymphoma (DLBCL) as a third-line treatment, after two or more previous standard treatment lines have failed. Kymriah® was TGA approved for ALL and DLBCL in December 2018 and is reimbursed via the Medical Services Advisory Committee (MSAC). Australia is fortunate to have a single site for sovereign Kymriah® manufacturing in Cell Therapies Pty Ltd, one of only six manufacturing sites globally.

The sector is gaining momentum and since the first CAR-T therapy product entered the market in 2017, another four CAR-T therapies have been FDA approved, three of which have been approved in the last year, with one gaining TGA approval in 2020 (Table 1).

The distinct risk is that we now have a once in a generation opportunity to onshore this capability whilst other jurisdictions are aggressively courting the larger “big pharma” sponsors to consider their jurisdictions as a preferred production site. Now that companies such as Novartis have engaged Cell Therapies Pty Ltd in Melbourne as a fully-credentialled regional supplier, there is a unique opportunity to onshore other products from other sponsors for both our local patients, but also to cement Australia as supplier for the region. With this comes a capacity to better support local companies and establish the long-desired RM ecosystem, which will also benefit access to innovative, potentially curative, trials for our patients.

THERAPY	INDICATION	APPROVALS
Novartis **Kymriah®** (tisagenlecleucel)	ALL R/R DLBCL	US August 2017 **AU December 2018** EU June 2018
Gilead/Kite **Yescarta®** (axicabtagene ciloleucel)	R/R DLBCL R/R FL	US October 2017 EU June 2018 **AU February 2020** US March 2021 (FL) China June 2021
Gilead/Kite **Tecartus®** (brexucabtagene autoleucel)	R/R MCL	US July 2020
BMS/Celgene/Juno **Breyanzi®** (lisocabtagene maraleucel)	R/R DLBCL	US February 2021 JP March 2021
BMS/Celgene **Abecma®** (idecabtagene vicleucel)	R/R MM	US March 2021

Table 1. Summary of Marketed CAR-T Products. BMS, Bristol-Myers Squibb; ALL, Acute Lymphocytic Leukemia; R/R, relapsed/refractory; DLBCL, diffuse large B cell lymphoma; FL, Follicular Lymphoma; MCL, Mantle Cell Lymphoma; MM, Multiple Myeloma

***Question* 2.** *Your submission argued that central to the development of this industry would be the development of a high performing workforce pipeline, but that this was compounded by the fact that current graduates from the university sector have had very little exposure to commercial-scale operations within this sector, due to its nascent stage of development. One solution could of course be to simply import the global talent we need, but assuming that our goal is to develop our own home-grown talent, then it might be that the only way to give today's students access to that sort of environment would be to embed into our courses a component of industry placement abroad, but this itself runs the risks of*

creating a situation where our graduates simply move offshore following university. ***So how do you think we can start to build that link between today's students and this new industry that we're trying to build, and to do so in a way that keeps the product of our investment in Australia and contributing to the growth of this industry?***

The development of a highly skilled workforce pipeline that can be trained in Australia, and remain in Australia, relies on there being an onshore end-to-end RM industry, and the resultant career path for the workforce. Most highly skilled jobs in the RM sector will lie in translational and commercial manufacturing, and indeed it is this segment of the end-to-end RM industry that requires further development and support to realise the true potential.

One of the skills gaps identified in the REDI Skills Gap Reports is the lack of GMP trained and qualified staff. This skills gap covers pharmaceutical, biotechnology and regenerative medicine (cell and gene therapies) manufacturing and impacts new entrants up to senior GMP managers. REDI has released a Request for Proposal (that closed 30 November 2021) to find suitably-qualified companies to deliver training programs to close the GMP skills gaps with courses for new entrants and also for experienced staff.

Investment in sovereign manufacturing, which includes access to the high-end processes and equipment, will establish an end-to-end solution for RM product development with a commercial outcome (and capacity to enter a large export market) that will simultaneously generate a RM career path from which new jobs will ensue.

To support potential employees, an industry-leading nationally accredited training program is required. The program must be industry-led and include training within GMP-certified facilities to produce industry-ready candidates, but there are many evident opportunities to partner with vocational and university training and education to build contemporary and industry-ready training that is grounded in the modern manufacturing behind these commercial RM products.

Question* 3.** *Your submission highlighted a "chicken or egg" problem where Australia needs to attract manufacturers to have a local regenerative medicine industry, but manufacturers will not come until there is an established industry to service. You note that other countries such as the United Kingdom and United States have invested significant money to overcome this hurdle and are now starting to reap rewards from that investment.* ***Are there any specific models that exist abroad which you think could serve as a model for the Australian context, and what sort of support would be required from the federal government to get something like this up and running?

The Regenerative Medicine Catalyst Project surveyed the global landscape and identified principles that can inform government support.

Background

The role of government at this stage is paramount in building the conditions for attracting greater investment – be it local or global – into RM manufacturing. Government investment and support for the RM manufacturing industry needs to be carefully matched to the stage of development of the local sector to maximise its impact. It is difficult to 'import' models that are used in other jurisdictions because they are operating at different stages of development. Examples from other jurisdictions point to the important role for PPPs, such as the Vaccines Manufacturing and Innovation Centre (VMiC) in the United Kingdom, the UK Cell and Gene therapy Catapult and the 'Cellicon Valley' concept in Philadelphia. Such approaches will work at the right time.

Government support does not need to be in place longer term, but providing support to establish and coordinate what is needed will be key assist in creating a vibrant platform that can then continue with existing support mechanisms (e.g., R&D Tax incentives, Accelerating Commercialisation grants, etc.).

The establishment of manufacturing has begun but needs to be nationally coordinated by a catalytic body that can drive the growth and development for the current early stages to establish the structural elements, where they are needed. As noted in our submission, AusBiotech and Medicines Australia are co-leading an 'expression of interest' process to gather funding needed to progress this work under the auspices of a 'Cell and Gene Catalyst' – as no single suitable organisation currently exists to drive this work. The Catalyst aims to support the Australian RM industry to see it thrive and drive benefits to the health of its people and Australia's economy. It is not yet funded and therefore progress is uncertain. Establishing a foundation fund to enable the work to determine what exactly is needed, develop the strategic plan and coordinate this work would enable Australia to address a significant opportunity.