JCB Boardroom/Bioentrepreneurship Industry Perspectives

"A Conversation on How we can Accelerate Innovation in Biopharma and Life Sciences Through Global Collaborations and Alliances"

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ABSTRACT

We note and reflect on the power of international partnering and collaborations that led to many of the innovations that were brought to market extremely quickly and successfully during the Covid-19 pandemic. These collaborative global approaches suggest the potential for developing broader, open innovation models in more extensive regional and global collaborations for other biopharma and life science market segments. In this article, we adopt a 'virtual panel discussion format' to frame and discuss potential issues and models that would need to be designed, developed and tested, with the purpose of engaging emerging global regions as equal partners. We also consider similar challenges for regions within countries – even in the US – that lack significant sources for capital across the company life cycle. Several recent open innovation alliance approaches or models are discussed as potential models. They are: the Eli Lilly FIP Net (fully integrated pharmaceutical network); the Enlight Bioscience alliance developed by Pure Tech Ventures; the Harrington Project linking academia to industry; and, the Corporate Accelerator model notably recently expanded globally by Illumina. We outline a proposal to create a guiding coalition, or "think tank" to further test and develop the proposals discussed herein.

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INTRODUCTION

This is an unusual article that started as "a virtual conversation" between the authors, following publication of the recent issue of JCB that was focused on ecosystems and clusters [**Vol. 26, No. 1 (2021); Building and Leveraging Ecosystems and Clusters**]. Peter Molloy in Australia and Art Boni in the US, discussed implications taken from the recent analysis (by Molloy, Johnson and Gilding) of the poor financial performance over the last decade of the nascent biotech industry in Australia, against the overwhelming dominance of the US in the global biotechnology industry, and in contrast to the locally-held belief that Australia excels in biotechnology. This led us to ask the question: how can Australia, other similar "emerging" countries, and even regions within countries, all outside the US 'Superclusters', leverage their core biotechnology competencies and create value in the global ecosystem, while building strong regional ecosystems and clusters locally? We recognized the central role that the US and European pharmaceutical companies play as a 'market' for biotech firms, and that value creation at a country and regional level can only be maximized by building bridges to that market, while leveraging local competencies, such as science and technology generation and launching of startups locally. Could we envision and operationalize this connected, global ecosystem, consisting of geographically distributed clusters working collaboratively to optimize access to the 'market', and at the same time to build up local ecosystems and clusters?

This was the start of a discussion that we thought might have the potential to empower broader development of a globally-integrated ecosystem that could enhance the value creation of non-US clusters. We first reflected on the success of global partnerships that have

been implemented in multi-firm global alliances associated with Covid-19 innovations. These alliances employed creative, internet/digital technologies to facilitate the effectiveness of these collaborative teams that spanned the globe – US, Europe, India, etc. Serendipitously, Rich Bendis and Brian Darmody invited Art Boni and Moira Gunn to discuss our recent Special Edition of JCB on Ecosystems and Clusters (Vol. 26, No. 1, 2021 at the annual meeting of the Association of University Research Parks (AURP). In a panel discussion (covered below) it was noted that there are also regions in the US that struggle to attain critical mass to build and sustain biopharma ecosystems and clusters. In other words, the critical mass problem is not just outside the US. These, typical non-coastal states and regions in the US are often referred to as "flyover regions" by venture capitalists. This confluence suggested the need to consider the creation and implementation of a region-to-region network in the US. Then, extrapolating internationally, why not a network of nation-to-nation partnerships to include, US, Europe and international partners in Asia and Australia.

As our emails and Zoom discussions continued, and the discussion evolved, we added comments from a few more of our colleagues who contributed to the Ecosystems and Clusters edition (Volume 26, No.1, 2021) – notable with Susan Finston on the EU perspective. So, this paper evolved in an unusual way amongst a small cohort of "experts" in the business of biotech who collectively believe that an evolved and collaborative global ecosystem can be formed by creatively connecting ecosystems globally and nationally. This paper is intended to document our discussions and explore ideas as a basis for further discussion and research, rather than as a systematic analysis with a clear conclusion.

THE START OF A CONVERSATION ON THE STATE OF THE AUSTRALIAN BIOTECHNOLOGY INDUSTRY

Peter Molloy

My PhD research focused on value creation and investor performance in the Australian public biotech sector over a 15-year period through 2018. Surprisingly to many in the local industry, it showed that the sector failed to create value and the investor returns were consistently negative and the sector had failed to spin-out a single big biotech since its inception in 1985. We recently did a follow-up analysis of the 10-year period from 2010 to 2020, to take out the impact of the global financial crisis, which is published in this edition of JCB. Like the previous research, it confirmed the poor investor performance of the public biotech sector, at least when it comes to drug development. This poor investor performance was in stark contrast to the locally-held view that Australia is a world leader in biotechnology.

The reality is that the US accounts for half of all public biotech firms worldwide and a monumental 81% of global biotech firm value. Relatively, the public biotech sector in Australia is very small and weak in comparison. Australia and other similar countries aspiring to build world-class biotech ecosystems clearly need to develop a different approach for creating value and building the critical mass needed for successful and sustainable biotech ecosystems.

In looking at the success in the US, the key factors underpinning the US Superclusters have been identified as (mostly from Owen, ref. Financial Times, p. 9, 2016):

- high quality universities where biomedical research is massively funded by the US Federal Government;
- efficient mechanisms for licensing or spinning out companies from these universities;
- a deep-pocketed venture capital community funded by a large population of high net worth individuals looking for high returns (and almost exclusively US geographically focused, not international);
- the US being the world's single largest domestic pharmaceutical market without centralized drug price controls.
- plus widespread availability of grant funding under the Small Business Innovation Research (SBIR) program and access to National Institutes of Health (NIH) grants

This unique admixture in the US spins out and creates many companies per year (including historically Genentech, Amgen, Gilead, Biogen, etc.) and feeds the ambitions of others and whets the appetite of US investors, by signaling the high investor returns achievable from the partnered or alliance based biotech business model. No other country has this, yet every other country wants to create big biotechs partnered with the international pharmaceutical sector to underpin a sustainable biotech sector locally. I'm sure that if the Australian investor performance analysis were repeated in countries like Germany, UK, Canada, etc., we would see the same pattern and poor performance as Australia. Australia is not uniquely problematic, it is just one with loud promissory expectations.

So, this assessment led Art Boni to reach out to Susan Finston to get her perspective on the EU. She

wrote an article on the EU ecosystem in the recent JCB Special Edition on Ecosystems and Clusters globally noted above.

Susan Finston

In evaluating the EU Biopharmaceutical Strategy, we wrote about the first-ever European comprehensive strategy for the pharmaceutical sector, based on explicit recognition that "the pharmaceutical industry is of key importance for the EU's economy." Biopharmaceuticals remain of central importance for the European bio-economy, responsible for the lion's share of value creation through research and development of health-care products that generate social and economic benefit. The European Commission seeks to improve the enabling environment for product development – the "D" in R&D. (c.f. article taken from JCB Q1 edition on Ecosystems and Clusters; Vol. 26, No. 1, 2021 by Finston and Thompson).

- In recent years we have seen the growth of local or regional European bio-clusters, with focus on niche emerging technologies – e.g., immunotherapies, brain and neuronal technologies, metabolic disorders, so-called advanced medical technologies, vaccines[1] and microbiome therapies.[2] France's successful development to a microbiome R&D bio-cluster makes for a particularly interesting case study given the traditional and historic roots of fermentation and microbial technologies in the French bioeconomy. Prior to Brexit, the UK attracted the lion's share of life sciences investment – approximately 25% of all EU R&D investment, i.e., equal to French and German R&D combined, and this shows no signs of showdown. In fact projections for 2021 indicate another banner year for the UK bioeconomy, with record high levels of investment.[3]
- More broadly, recent events relating to delays and U-turns relating to national COVID-19 vaccine campaigns demonstrate the challenges of implementation among and between Brussels and EU Members, even for something as critical as the COVID Pandemic. Even in 2021 EU Governments should be expected to place national interests ahead of EU priorities.

Editor's Note: We also note that in the UK, no longer part of the EU, three organizations have recently *merged to create a nationwide life sciences ecosystem, helping early-stage British businesses compete on a global stage; https://www.epmmagazine.com/news/merger-creates-uk/.* BioCity Group, an accelerator and venture investor; Knowledge Factory, which manages science parks; and Trinity Investment Management, which owns a portfolio of science parks, have formed We Are Pioneer Group. The new firm will operate across 10 science parks across England, Scotland and Wales, hosting 650 businesses – 10% of the country's life sciences ecosystem. The deal has been funded by Trinity and global real estate investor firm Harrison Street, which own the underlying real estate through their existing joint venture. We will talk more about Science Parks later in this article.

Art Boni

At this point, we started discussing the role of collaborative innovation and the factors present for success in the US. We recognized that collaborative innovation is (and always will be) a hallmark ingredient of the business model of the broad and growing biopharma industry – including med tech, and digital medicine. It is well

1 Franck Le Deu and Jorge Santos da Silva,"Biotech in Europe: A strong foundation for growth and innovation," *McKinsey & Company (August 2019), available online at* https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/biotech-in-europe-a-strong-foundation-for-growth-and-innovation.

2 Will Chu, "France forms Alliance to Promote Microbiome based Innovation," NutraIngredients.com (7 May 2021) *available online at* https://www.nutraingredients.com/Article/2021/05/05/France-forms-alliance-to-promote-microbiome-based-innovation

3 Julia Collewe, "Investors flock to life sciences as UK sector breaks funding record", The Guardian (2 May 2021) *available online at https://www.theguardian.com/business/2021/may/02/investors-flock-to-life-science-as-uk-firms-break-funding-record* ("UK drugmakers, diagnostics, medical equipment and other life sciences companies have raised £10.6bn from private funding rounds and stock market flotations in the first three months of the year, more than half of last year's record total, according to a report.")

known that the pharmaceutical industry has sustained the innovation pipeline (both small molecule and then genetically based therapeutics) through partnering and M&A activity, resulting in what we refer to today as the biopharma industry. We suggest that this approach could well be extrapolated to cross trans-national boundaries. And, there are examples of that which have emerged during Covid-19; e. g. India – Serum Institute of India and potential collaborations beyond India, including the US yet to be determined; and, Ocugen as a US-based (Philadelphia company) in partnership with an Indian biotech company). Also the Pfizer/BioNTech alliance, the alliances formed by Moderna, and others that have been created in parts of the value chain beyond the vaccine itself, e.g. PPE, diagnostics.

Rich Bendis and Brian Darmody have recently published in our Ecosystems and Clusters issue (JCB, Vol. 26, No. 1, 2021) and comment below. They provided the following success factors for any region: 1) Strong Leadership; 2) Significant Industry Engagement; 3) Experienced Talent; 4) Access to Capital; 5) Research Assets and Facilities; and, 6) Market and Brand Awareness.

These factors were highlighted and further discussed by Rich Bendis in a panel discussion moderated by Brian Darmody at the annual meeting of the **University Association of Research Parks** annual meeting held in June 2021. As noted above, that panel included Art Boni and Moira Gunn who highlighted the JCB issue on Ecosystems and clusters. At the UARP meeting Moira Gunn and I summarized our slightly longer list of the necessary conditions for building successful ecosystems. There is of course some overlap with Bendis and Darmody (reference their quotes above and the article in the Q1 issue for more detail).

Art Boni and Moira Gunn

Our necessary conditions for a region to have a successful ecosystem are as follows:

1. The region needs to embrace and reward an entrepreneurial culture, with strong leadership in both the public and private sectors, which work collaboratively with a shared long range vision (at the national, regional, and local levels)
2. Has **strong universities and world class hospital systems** to provide an educated workforce and a source of technologies and spinoffs
3. Attracts people who want to live in the region, since **it's a great place to live** and raise a family – and is affordable
4. Has the ability to grow and/or attract leadership for biopharma, med tech and digital medicine (or health) organizations across the life cycle
5. Home to a **full spectrum financial industry for sources of risk capital across the company life cycle** to start, grow and build strong industry clusters
6. Has, or is building, one or more world class **anchor organizations** to serve as role models and attractors
7. **Well-connected and networked to collaborate with other regions in the US and internationally**
8. The region is patient and persistent, and has "the grit" to prevail over the long period required to develop and grow the regional ecosystem and associated clusters

Art Boni

At some point, Rich Bendis and I should harmonize our respective lists of success factors (along with those noted by Molloy above). But, we'll leave that for another day! However, another point worth discussing here is an observation that I have made and discussed with Rich, Brian and Moira. Extensive coastal ecosystems have been developed on the East and West Coasts of the US (Boston, BioHealth Capital region, "BioHealth California" (San Francisco, Silicon Valley, LA, and San Diego). However, other regions like the mid-west (Pittsburgh, Cleveland, Columbus, Ann Arbor, Columbus, etc.) are still emerging and seeking traction. Note that these "fly-over" regions lack access to capital across the company life cycle especially beyond their earliest stages of development and capitalization by local angel groups. Also, "anchor firms" as examples. I also pointed out that these issues also exist globally.

Moira Gunn

I recall that San Diego had a similar problem in the earliest stages of its emergence, c.f. the article by Roben and Abremski in the Q1, 2021 issue on Ecosystems and Clusters. Lack of a strong VC presence there was an issue, but local and statewide economic development groups encouraged trips from the Bay Area VCs by providing space for them during their visits. So, it was a statewide economic development effort to leverage the strong Bay Area VC community.

Brian Darmody

I wonder if some mention of new applied approaches to funding health research by governments would be warranted for discussion and the implication on how that will enhance academic/industry/government health partnerships. The BARDA VC model already in existence is interesting and Biden's $6 billion ARPA-H (Health) proposal where tech managers would direct research with milestones is another initiative that probably deserves mentioning as it will move much of the federal funding to new applied arenas and away from basic research NIH has historically funded.

Interestingly, the UK is proposing a similar initiative called Advanced Research and Invention Agency (ARIA).

Peter Molloy

One of the problems I have with the network approach to biotech ecosystems as often advocated by Owen-Smith and Powell (c.f. Org. Science, 15(1), 2004) is that it is too inward facing. Born in sociological field theory, it sees the ecosystem as a network of actors, the interplay of which spins out and nurtures early-stage dedicated biotech firms (DBFs). The network is the source of value creation. It doesn't tell you what happens to these DBFs when they grow up; how do they create value? The network approach just seems to assume that somehow they go on to be commercially successful and help create a virtuous cycle that feeds back positively into the stakeholder ecosystem. That pathway to commercial success, however, is a key driver (or lack of it, a key obstacle) to any virtuous cycle that might feed back into the innovation ecosystem. That is a major problem outside the US, where the pathway to commercialization is a rocky dead-end, as per the recent paper by Gilding et al (which I co-authored) on network failure (c.f. Research Policy, 49 (2020)). The importance of the Gilding 'Network Failure' paper is that it shows that even when you have a healthy network, it can fail and be a dead-end for value creation due to its failure to tap into the pharma value chain. Innovation alone (at least as measured by network theory) is not enough to create value. To succeed, the network needs to spin out biotech firms that are able to efficiently play in the pharma value chain and effectively compete for pharma deals. Winning a share of those deals is value creation for drug development DBFs.

The other problem I have with the network model – again largely because it is inward facing – is that it places little emphasis on the investor. Yes, there's recognition that 'Risk Capital' is a stakeholder in the network, but it fails to recognize how critical it is and what happens when that risk capital is not rewarded – as is the case in Australia where the investor returns in biotech are abysmal (c.f. my paper in J. Comm. Biotech 26(1), 2021); then the capital flees to other sectors and the whole biotech network collapses. Again, I think this is as a result of the network perspective being focused on the 'system' and not recognizing the key externalities that determine its success or failure. Critically, it places little emphasis on the value chain in which drug development biotech firms operate and the pivotal role of investors.

Art Boni

In economics, a virtuous cycle (or circle) describes the chain of events in which one desirable occurrence leads to another which further promotes the first occurrence and so on resulting in a continuous process of improvement. This concept fits into the success or failure of ecosystems. I'd agree that in our definition of success, perhaps we should be more explicit about the importance of shared value amongst all partners in the value chain. Or as Peter says, to become an integral part of the pharma value chain. Only when all partners are rewarded (with their share of the "rents") will the ecosystem grow and thrive. The path to achieve this ecosystem is demonstrated in a region by the creation of one or more successful, anchor firms in the local ecosystem. This achievement really does accelerate success (as has been shown in the US) and attracts other investors and partners into the region. That's why we include the existence of anchor firms in the success factors listed in the Boni and Gunn article in the JCB Vol. 26, No. 1 (2021).

USING OBSERVATIONS TO CATALYZE SOME ALTERNATIVES FOR OPEN INNOVATION COLLABORATIONS – GLOBALLY AND NATIONALLY

Art Boni

After all of the above discussion, I reflected on what approaches might be taken as we contemplate the challenge of accelerating collaborative open innovation. What has worked previously, albeit under different conditions and constraints? In that regard, I have written articles in JCB in the last few year that highlighted four approaches taken for biopharma alliances – all span multiple regions. These (or combinations), summarized below, may be considered for creative partnering.

1) What about evolving global coalitions that expand on a version of the **Eli Lilly FIP Net** for

global partnering, i.e. a **Global Alliance FIP NET** (fully integrated pharmaceutical network) that is more focused on developing expertise to pursue solutions to broader industry issues than to individual products? The Lilly approach is described in a Master's Thesis published in 2015, authored by Raja and Sambandan titled "Open Innovation in Pharmaceutical Industry: A Case Study" https://www.diva-portal.org/smash/get/diva2:824465/FULLTEXT01.pdf.

Perhaps the Global Alliance FIP Net approach, in our context, could be called "Open Innovation on steroids", and focused on alliances to develop broad, emerging fields, such as CRISPR, regenerative medicine, neurodegenerative diseases, etc. And, and to incorporate creative cross-licensing arrangements to minimize patent disputes. Development and adoption of this idea might be accelerated by incorporating organizations like the Gates and Zuckerberg foundations, leading universities, etc.

2) Alternatively, consider a model pursued by **Pure Tech Ventures** in Boston, wherein they created an **industry alliance** that operated under the name of **Enlight Biosciences.** They formed a consortium supported by multiple global pharmaceutical companies seeking opportunities to develop. A few of the companies participating were Merck, Pfizer, Eli Lilly, J&J, Astra Zeneca, and Novo Nordisk. This alliance was not just individual product related, but broader than that in that the members had an opportunity to participate in and influence the development of multiple opportunities. The **Enlight Biosciences** and other open innovation approaches to collaborative innovation are discussed by Boni and Moehle in "Biotechnology lessons for robotics: adapting new business models to accelerate innovation", JCB, Vol. 24, No. 4, pp 37-44 (2014).

3) Another concept could be used to accelerate and increase the success rate of new ventures extending from the earliest stages of discovery and validation, thru product approval by regulatory agencies. The basic concept could be replicated by studying the **Harrington Project for Discovery and Development** conceptualized by the late David U'Prichard. This approach, launched at the University Hospitals in Cleveland, Ohio, brings together universities with accelerators (like BioMotiv) in partnership with global and national pharma partners who are not co-located. So, in theory this model is scalable globally.

4) I've been working with a colleague (Diana Joseph) who founded and heads up the Corporate Accelerator Forum – a coalition of larger corporations (cross industry) who seek to partner effectively with early stage companies via corporate accelerators. **Corporate accelerators** have evolved as an effective strategy for larger organizations to identify and work with emerging companies (and has been discussed by Diana and I in JCB previously). A new paper by Joseph and Cashin, as a mini case study on the Illumina Accelerator appears in our Vol. 26, No.2 (2021) edition and is currently in press. Illumina is clearly a world leader in developing, manufacturing, and marketing integrated systems for the analysis of genetic variation and biological function. Illumina now has accelerator operations set up in the US, UK/Cambridge, & more recently in China/Shanghai. What they have done would appear to be a great model to set up in other SE Asia areas, and should be considered as a strategy for global partnering. Also, we note that JLabs has operations in multiple locations in the US. Why not internationally?

Clearly, what we are suggesting is a bold proposal that perhaps could be tested on a limited or pilot basis with countries and regions to be determined based on their history of being able to collaborate. We would suggest Australia, New Zealand and perhaps some other emerging SE Asia countries with an interest and aspirations to develop bio clusters? In the US, adjacency to Canada and Mexico, and pre-existing trade relationships might also be a natural fit. Or to keep it parochial to the US, what about statewide or regional collaboration in the "fly over regions" of the US?

Peter Molloy

I think there is real value in creating a global alliance of locally-functioning, but globally-thinking champions for biotechnology industrialization. The partnering accelerator concept could be the missing link and a real opportunity for the productivity of non-US biotech.

I'm convinced that the majority of the issues in Australia (and with the added perspective of my 15 years working in the US biotech/pharma playground) are applicable to UK, Canada, EU and every other country/region that aspires to emulate the US success in biotech. I do think the key will be to find like-minded champions in each country or region to participate in the conversation and help build a global ex-US (or emulate US) think tank to solve our collective problems. Being in Australia, I'd suggest looking at Southeast Asia as a region to consider for building alliances with global biopharma leaders, especially those countries in SE Asia that have made long term commitments to building the industry. However, we should recognize that creating cross-over collaborations between countries alone may not yield synergy or lead

to the sought-after critical mass that is needed for sustainability. Obviously there are practical considerations as well, such as geographical and local-legal issues that confer unique characteristics and barriers to both cooperation and critical mass development in each country. However, the biggest barrier is always the overall absence of the overwhelmingly important factors that are present in the US ecosystem, as already identified.

So, we should identify those countries that fit the profile for regional innovation as noted earlier by Boni, Gunn, Bendis and Darmody.

Art Boni

At the panel discussion, I suggested that it might be worthwhile considering more extensive use of these models for regional collaborations to accelerate innovation, and include alliances across regions of the US. We often refer to the US industry collectively in terms of the US leadership in life science innovation – biopharma, MedTech, and Digital Medicine/Health. But frankly, in the US we have regions that have been emerging and growing for years. These regions, have yet to attain critical mass – even though the country as a whole is dominant. For example, a recent update on the status of Life Science PA, and their legislative agenda for that organization highlights the strength on the discovery side of the industry in the Commonwealth of Pennsylvania, with top 10 rankings in the US level of NIH funding. But, in contrast, the "industry" itself is in the early emergence stage statewide (c.f. the small number of employees per company). Philadelphia is coming along as Dennis Gross pointed out in our recent JCB issue on Ecosystems and Clusters (Vol.26). Philadelphia does seem to be getting traction in gene therapy with the new presence of Roche via their acquisition of Spark Therapeutics. So, perhaps they now have their "anchor tenant" much like Genentech in the San Francisco Bay area (and Roche's leadership there).

Pittsburgh, as illustrated by Dennis Yablonsky's article in our recent special edition on Ecosystems and Clusters is still lagging in the pursuit of transformative biopharmaceutical innovations. But, the region is making great progress in the pursuit of commercializing robotics/AI/ML innovations, and also in additive manufacturing. These digital technologies have implications for accelerating life sciences innovations in the region. I'd suggest that robots and digitization in healthcare can attract partnerships and investment capital much like the Roche presence in Philadelphia noted above. A notable observation is that the UPMC Health System, through its UPMC Enterprises unit, their commercialization arm is providing capital, expertise, and leadership to accelerate many of these digital transformations in healthcare. And, the President of that unit is a former Bay Area venture capitalist. UPMC along with Carnegie Mellon have developed a robust startup community with capacity to attract capital and partners. So, perhaps there is "light at the end of the tunnel" for this "flyover region" as the regional leadership there continues to support development of an overall innovation ecosystem that incorporates both life sciences and technology clusters. This effort started in earnest in the mid to late 1990s. Development of mature Ecosystems and Clusters have a very long development life cycle.

While this evolving discussion on the difficulty of sub-optimal regions like Australia, New Zealand, Canada and others focuses on global issues, it might be worth pointing out that while the US life science industry does indeed dominate the world, the innovation ecosystems are still largely concentrated in regions like Boston, San Francisco, San Diego and a few other regions with traction on the Eastern seaboard. Perhaps, as we discussed above, the lessons from the emergence of ecosystems globally might be extended to these "flyover regions of the US" where VC/PE funding and bio partnering as a strategy to get across growth stages is lacking. Above, we alluded to the formula for incorporating cities (regions) like Philadelphia and Pittsburgh, and perhaps other cities located in the mid-West "VC flyover region" That concept is evolving, and could provide insights for a local and national strategy in the US and most likely in other global local ecosystems as well.

CONSIDERATIONS FOR EMERGING OPPORTUNITIES IN SOUTH EAST ASIA

Art Boni

I came across and interesting article published in Genetic Engineering and Biotechnology News (GEN) from 2019. It focused on their Top 10 emerging regions in Southeast Asia for 2018, c.f. https://www.genengnews.com/a-lists/top-10-asia-biopharma-clusters-2019/. GEN ranked the regions based on public R&D spending, Patents, IPO's, and jobs.

So, it might be interesting to re-examine that list for global alliance opportunities. Of course the top 2 countries listed by GEN, **China and Japan** have historically been in many alliances and M&A arrangements with big pharma and the larger biotech companies in the US over the years. They are more natural partners in that regard; albeit on a one-off basis and not regional in a regional/global alliance. And **India** is certainly emerging recently, but not without controversy. Note especially

the activity of the Serum Institute of India in the vaccine area (see case study on SII in this volume written by Somasundaram, Soukas, Patel and Ferguson). Also refer to the article on India by Gross and Pattarkine that focused more broadly on the Indian ecosystem.

So, as we expand our discussion beyond Australia and New Zealand I'd suggest **Thailand, Singapore and Taiwan** for consideration**.** Here are a few perspectives extracted from the GEN report.

- **Thailand**: Declared its intent to "push the country's status as a global leader in bio-economy to the next level with a focus on medical robotics. And to incentive via five-year tax exemption for up to 8 years for medical robotics companies". Further, they have identified biopharma as a market for robotics. And, they are also building the county's first cancer drug production facility set to open in 2025.
- **Singapore**: "Singapore is known for its high concentration of drug developers and tools/technology developers". Singapore opened its Experimental Drug Development Centre in Biopolis", to integrate early-stage drug discovery efforts across academia, healthcare institutions, and government agencies. Their new TTC (Target Translation Consortium) is a partnership of a*Star, Duke-NUS Medical School, Lee Kong Chian School of Medicine, Nanyang Technological University, National Healthcare Group, and others. We also note that on January 1, 2018, Dr. Subra Suresh was inaugurated as the fourth President of NTU, and he is the inaugural Distinguished University Professor. He is the former President of Carnegie Mellon, a leading US university (noted for innovation, entrepreneurship and for creating spinoff companies), and before that was the Director of the US National Science Foundation. In mid-May 2021, "BioNTech announced plans to set up a regional centre and a new factory in Singapore for its vaccines, boosting its presence in Asia as a debate over patents rages and pressure grows on drug makers to raise output of COVID-19 shots". https://finance.yahoo.com/news/biontech-build-mrna-manufacturing-singapore-055603367.html
- **Taiwan:** The intent of the government is to grow biopharma and medical devices into a $32.7 billion industry by 2025, in part by developing workforce skills. ITRI and Merck have projected to train research professionals and advance new treatments with precision medicine in mind. Another priority is artificial intelligence, and to create four AI centers at universities, one of them a biotech AI center at National Cheng Kung University.

We would suggest using the criteria for successful ecosystem development discussed earlier by Boni and Gunn, and by Bendis and Darmody to screen and guide these countries as to whether their governments and cities have the necessary ingredients for participating in such global innovation endeavors vs. one-off opportunities. Molloy, Johnson and Gilding have already illustrated financial performance of the Australia biotechnology cluster and the need for a more intense examination of global partnerships to accelerate performance.

POTENTIAL NEXT STEPS ON ACCELERATING OPEN INNOVATION ALLIANCES – SUGGESTED BY THE AUTHORS, AND BY THE JCB EDITORIAL BOARD

Our Editorial Team is committed to engaging with other organizations in the US and internationally to advance the agenda outlined herein. In that regard we see some short term and long term objectives and key results (OKRs) coming out of a coalition (or "think tank") to be initiated with JCB leadership. As a framework for "leading change" let's consider John Kotter's 8 – step change model as an approach, c.f. Kotter, J. P. "Leading Change", Boston: Harvard Business School Press, 1996.

- Step One: Create a Sense of Urgency. ...
- Step Two: Form a Powerful Coalition. ...
- Step Three: Create a Vision for Change. ...
- Step Four: Communicate the Vision. ...
- Step Five: Remove Obstacles. ...
- Step Six: Create Short-Term Wins. ...
- Step Seven: Build on the Change. ...
- Step Eight: Anchor the Changes in Corporate Culture.

Specifically, it would be our intent to focus initially on Steps 1-4, by creating a small leadership team. The team could serve to articulate a sense of urgency and to act as a guiding coalition or "think tank" charged with developing consensus on a vision for change. That would include

catalyzing the initiation and development of a few pilot programs for validation and evolution of the concept (or in lean startup jargon, to develop and validate an MVP (minimum viable product) for piloting in a few test cases. As such, an objective would include identifying obstacles and or impediments needed for broader implementation in next steps (Steps 4 – 6).

At this point, we foresee the following challenges that need further study:

- Legal and governance issues for multi-country alliances and collaborations
  - Recognize that international patent rights are important for a healthy life sciences industry, c.f. Pitts, Popovian, and Winegarden article in this issue of JCB – "Temporarily" waiving biopharmaceutical patent rights (also known as "compulsory licensing"[1]) for COVID-19 vaccines is a bad idea – and a dangerous precedent".
  - Policy, regulatory, and trade/ pricing issues that affect global licensing arrangements for emerging transformative technologies.
- Trust in alliances and partnerships is essential; as it is in diverse collaborative teams even within one's own organization. This suggests that trial alliances with low risk opportunities may be needed before proceeding to a more significant and high risk opportunities. See for example a recent New York Times article on the Serum Institute of India and their recent problems with Covid-19 production and distribution. https://www.nytimes.com/2021/05/07/world/india-serum-institute-covid19.html

"THE LAST WORD" – FROM AN AUSTRALIAN PERSPECTIVE, OR EVEN FROM A US "FLY OVER" REGION

We thought it would be appropriate to reflect on this discussion and have "borrowed" the title for this last section from the US-based MSNBC talk show program segment hosted by a well-regarded journalist, Lawrence O'Donnell. So what follows is a series of observations and opinions of the principal authors of this JCB Boardroom/ Bioentrepreneurship Industry Perspectives article.

We all agree that success comes from sustained value creation for all ecosystem components. From our perspective as entrepreneurs and innovators, value is created incrementally thru the life cycle of the organization. And that occurs as a result of effective leadership that balances the opportunity, with the required resources, and with a diverse and balanced team (in effect the Timmons model of entrepreneurship). And, of course, these all evolve over the life cycle of the organization from startup to mature organization that delivers quality products to the market. We have written elsewhere about the famous HBS case by Larry Greiner titled "Evolution or Revolution as Organizations Grow" (originally published by HBS in 1972, and then validated and republished in 1998). The bottom line is that an experienced board and experienced leadership team is essential to build and guide the evolving team through its multiple stages. And, to a large extent so are experienced, connected investors and partners. Some of the needed ingredients can be "imported" or borrowed from other regions, some cannot. That is to be determined on an individual basis. For example, refer to our regional ecosystem success factors discussed earlier in this article. In our experience, leadership and resources are critical, and need to be localized and or drawn from the region. But, they can be augmented by remotely located partners.

In reality, most biotech companies are pre-commercial drug development businesses that act effectively as technology intermediaries for Big Pharma. In the Entrepreneurship Bootcamp, founded by Boni and Sammut, and run at each international BIO meeting since 2005, we refer to these as Product companies. Peter Molloy has coined the term, drug development biotechs (DDBs) – which are distinguished from platform, diagnostic and other biotechnology companies. We also often call these 'biopharma' companies, but this is a broader term that can be used to embrace the pharmaceutical business as well, as in the 'biopharma industry'. A small number of these DDBs may graduate to become Big Biotech firms, but it's a rare event – less than 1/100 in the US and none outside the US (Actelion was the sole ex-US example but was acquired by J&J). So DDBs mostly do not commercialize drugs themselves, but look for a pharma partnership or trade sale to acquire and commercialize their candidate drug (CD) pipeline. However, valuable pharma deals are a rarity outside the US. In the US, multi-billion dollar biotech-pharma deals happen regularly, and over time big pharma and big biotech have become biopharma platforms, both leveraging universities and small emerging companies to feed the product pipeline. Smaller, pre-commercial entities (DDBs) create value by building investor aspirations for that future valuable Big Pharma deal, which investors know is the only ultimate measure of the commercial value of

the DDB's pipeline. A second observation is that these VC and private equity investors are most often close to their investments – and that can be an issue in emerging regions in the US and certainly internationally. So, local VC presence is essential as noted by Boni and Gunn as well as by Bendis and Darmody.

We summarize some additional thoughts on Value Creation:

(1) **Partnerships outreach.** How does an Australian entity (or substitute the name of any other country outside US) facilitate deal-making from its distant locale, when most of the Big Pharma players are US-based or European (or at least their licensing/BD arms are based there). Non-US DDBs are at a disadvantage when it comes to getting a share of Big Pharma's attention (and credibility) simply because of geography. To compete, does a non-US DDB needs a substantial US presence? While building a US base does not help directly with building the foreign country's biotech ecosystem, it is a necessary outreach strategy to create value and it does help the local ecosystem indirectly by funneling any realized value back into that ecosystem and thereby feeding investor belief and money flow in the ecosystem.

(2) **VCs and technology quality.** In the US, VCs act as curators of technologies that can move drugs forward into clinical development and ultimately get them monetized as pharma deals or IPOs. Some may even graduate to Big Biotechs if they are not swallowed up by Big Pharma along the way. US VCs are good at the curation process and that's a major reason why US DDBs generate high returns; moreover, the investor successes from this process feed the money flow back into the local biotech ecosystem. Importantly though, the VC curation ensures that the quality of the technology that is funded in the US is consistently high. This is not the case in other markets, such as Australia, where brokers and to some extent, the stock exchange (ASX), act as curators of companies that list in order to access retail funds (in the absence of VC funding). This leads to lower quality technology and capabilities within the DDB community. The low level of funding achieved in this process also makes these companies destined to investor failure because (a) the need for constant new equity based funding (post-listing) leads to investor dilution, and (b) the limited funds raised act as a brake on the DDB's ability to drive its programs forward at a US-competitive speed. A similar situation likely applies in the UK and Canada. So these countries face a series of problems:
    (a) Lower quality technologies due to the lack of VC curation
    (b) Lack of funding to competitively drive the technologies they have
    (c) Weak investor returns due to dilutionary pressures, which leads to lack of funding

(3) **Move to the money:** Again, the answer may be for the DDB to have a base in one of the US superclusters, not just for access to new technology, talent and cluster connections, which are important, but for VC funding access. Geography is critical to most US VCs and they generally invest locally. US VCs give you technical and financial talent which are vital for building and monetizing your technology. They also act as sentinels who are on the lookout for talent and technology for you to acquire or merge with as you grow, in order to maximize value creation on the way to monetization.

(4) **Creating your first Big Biotech**: The local ecosystem will only grow to critical mass if it includes a home grown Big Biotech (one with annual sales >$1B). Examples in the US include Genentech, Amgen and Genzyme in California; and Millennium, Vertex and now Moderna in Massachusetts. This requires DDBs to migrate from their intermediary DDB role to direct commercialization roles, first becoming DDCs (drug development commercialization businesses) and then building annual sales to >US$1B. However, they can't do this in Australia, UK or Canada, because the local pharmaceutical markets are so small and unprofitable, mainly due to price controls. Once again, the answer may be to be substantially US-based, at least for commercialization.
If the simple answer is "move to the US", how does this help the local ecosystem? Are local – indeed all ex-US – ecosystems condemned to mediocrity because they are not in the US? Is there a model where sustainable local ecosystems can be created that focus only on local technology and maximize the potential of that through efficient collaboration networks, but somehow bridge to the US for VC funding,

technology enhancement and partnering/ commercialization?

(5) "**The Art of the Deal"**. In closing, we note the importance that forming and executing successful collaborations is challenging, and refer to the recent article by Boni titled "The "Art of Collaborations": Understanding the Anatomy of Transformative Transactions in Biopharma"; c.f. JCB, Vol. 25, No. 4, pp 50-56). We quote from the Abstract of that article: "This article highlights the factors that drive successful collaborations and partnerships that underlie accessing transformative technologies, and financially sharing of value created through eventual successful commercialization and incorporation into the Pharma 3.0 and then Pharma 4.0 business models". This article highlights the "softer factors" of the partnerships and collaborations that relate to the commonality of culture and vision of the partners and how they "fit" into a working, collaborative partnership and/or M&A transaction, and then into the ultimate product(s) and services that are brought to the market to create shared value. We posit that such transactions often fail because of reasons that do not involve either technology or market; but relate to these "softer" human-related factors. For illustrative purposes, we frame our discussions around several and very successful larger top tier biopharma companies that are well known for accessing external technologies as a source for transformative innovation". We highlight Roche and J&J who standout as excellent executors of successful global collaborations in our industry. More recently, we note the success of Illumina as a world leader, and how they have utilized their corporate accelerator to drive innovation nationally, and now globally.