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FINANCIAL INNOVATIONS LAB®

New Models for Financing Translational Medical Research in Singapore

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Financial Innovations Labs® bring together researchers, policymakers, and business, financial, and professional practitioners to create market-based solutions to business and public policy challenges. Using real and simulated case studies, participants consider and design alternative capital structures and then apply appropriate financial technologies to them.

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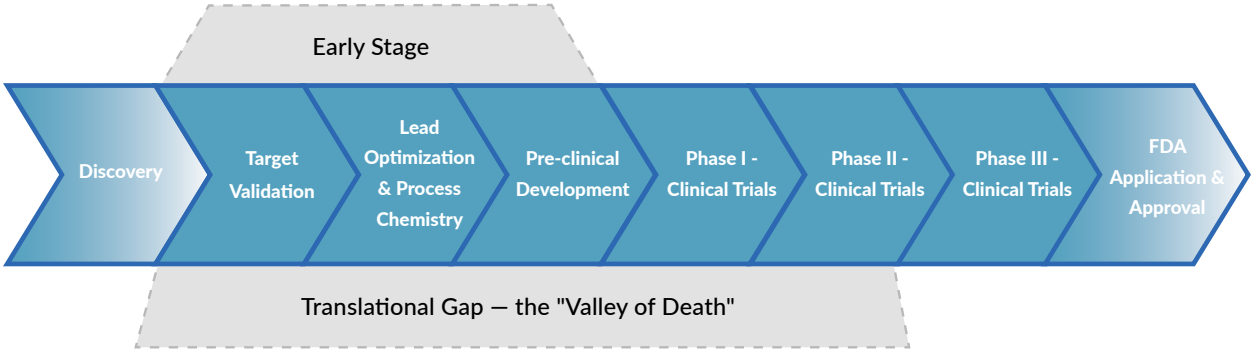
FINANCIAL INNOVATIONS LAB®

New Models for Financing Translational Medical Research in Singapore

INTRODUCTION

Medical researchers worldwide spend billions of dollars every year developing, testing, and bringing new drugs to the market. The long and arduous process of creating new drugs begins with academic and scientific research, which are largely publicly funded. The most auspicious of those findings then proceed to the critical step of translational research: the phase where scientific knowledge starts to be applied to drug development in preparation for clinical testing on humans. However, while basic science provides numerous avenues for promising ideas and expertise for all diseases, many structural, intellectual, and financial barriers have made it challenging to translate these ideas into clinical applications. These barriers range from a perpetual scarcity of funding and talent to misaligned incentives and risk appetites among researchers and investors alike. Consequently, many promising ideas in the drug development pipeline flounder once they reach the translational phase before a biotech or pharmaceutical firm is willing to move their development forward. The failure of so many ideas to make it through the translational stage is often termed the "valley of death" (see Figure 1), and it is widening across the globe.

Figure 1: The "Valley of Death" Hinders Drug Development



Source: Adapted from FasterCures, Milken Institute (2012)

Scientific drug discoveries currently face 10,000:1 odds of making it through the approval phase for commercial use.[1] Expensive human trials, investor pressure, and protracted timeframes have made traditional investors like pharmaceutical companies and life-science venture capital funds increasingly risk-averse. This leaves vast funding gaps in the early stages of drug development that create both health and economic challenges. The problem is particularly acute in Asian countries, where the biomedical manufacturing and research and development (R&D) industries are a key pillar in the national economies. This includes Singapore and most of Northeast Asia. Singapore, in particular, has struggled to cultivate a thriving translational research market, due in part to its small size and its geographic distance from larger, well-established biomedical hubs. To counteract this trend, the biomedical sector in Singapore needs to produce more promising research ventures that are geared towards commercialization.

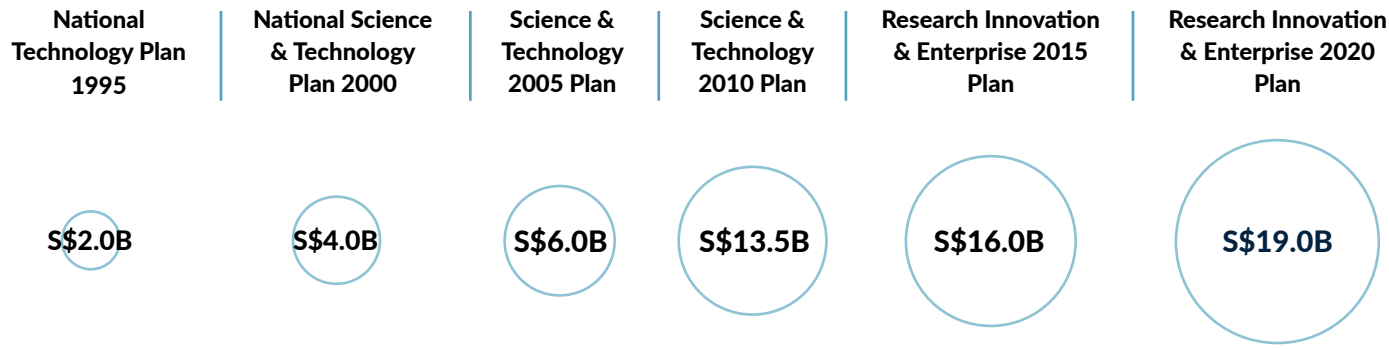
To brainstorm innovative solutions to finance and accelerate translational research in Singapore, the Milken Institute, in partnership with Duke-NUS Medical School, convened a Financial Innovations Lab® in July 2019 and a follow-up session during the Milken Institute Asia Summit in September 2019. These events brought together an active group of government leaders, investors, industry experts, corporate decision-makers, and philanthropic foundations to discuss a comprehensive range of issues and potential solutions surrounding translational research, particularly in biotech. While health-tech and med-tech startups face many of the same challenges as biotech firms, the conversations at the two brainstorming sessions mainly focused on biotechs because of their need for higher-risk investment capital and longer timelines for commercialization. Discussions included ways of attracting more and better talent, innovative funding models, financial incentives, regulations, and increased technology transfer, in relation to developments in the Singapore ecosystem. The sessions concluded with a variety of policy and financial recommendations.

ISSUES AND PERSPECTIVES

THE STATE OF BIOMEDICAL RESEARCH IN SINGAPORE

Singapore first began building its biotechnology industry in the 1980s,[2] dismissing skepticism that its small market and great distance from established biotech hubs would be a disadvantage. Singapore's government launched the Institute of Molecular and Cell Biology in 1985, with a focus on basic science and upstream research. In the early-2000s, Singapore pursued biomedical sciences as the fourth pillar of the nation's manufacturing sector, erecting the first stage of the iconic Biopolis research hub within three years of conceptualization.[3] Government funding for R&D has since increased significantly (see Figure 2) and gradually shifted towards talent attraction and development, translational clinical research, public-private and multidisciplinary collaboration, competitive funding, and commercialization and industry orientation.

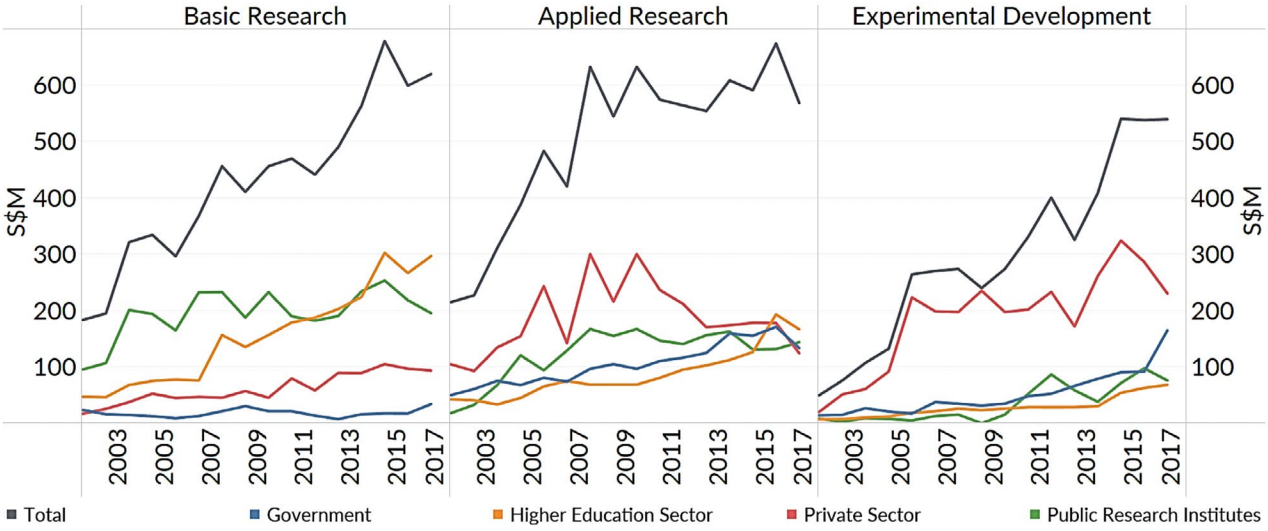
Figure 2: Planned R&D Funding in Singapore Continues to Rise



Source: National Research Foundation, Singapore (2019). Figures in SGD

Singapore's latest plan, Research, Innovation, and Enterprise (RIE) 2020, represents the government's most significant financial commitment, earmarking S$4 billion out of its S$19 billion budget for health and biomedical sciences.[4] RIE2020 further sharpens the focus on economic and health outcomes, concentrating biomedical R&D into five areas: oncology, sensory and neurological diseases, diabetes, infectious diseases, and cardiovascular diseases. In keeping with the RIE's ambitious goals, actual spending in biomedical R&D has increased significantly over the last two decades (see Figure 3). Total expenditures in basic research, applied research, and experimental development have each increased by around S$500 million since 2002. That said, R&D expenditures across all three stages have stagnated in recent years.

Figure 3: R&D Expenditures Are Soaring in All Stages of Research

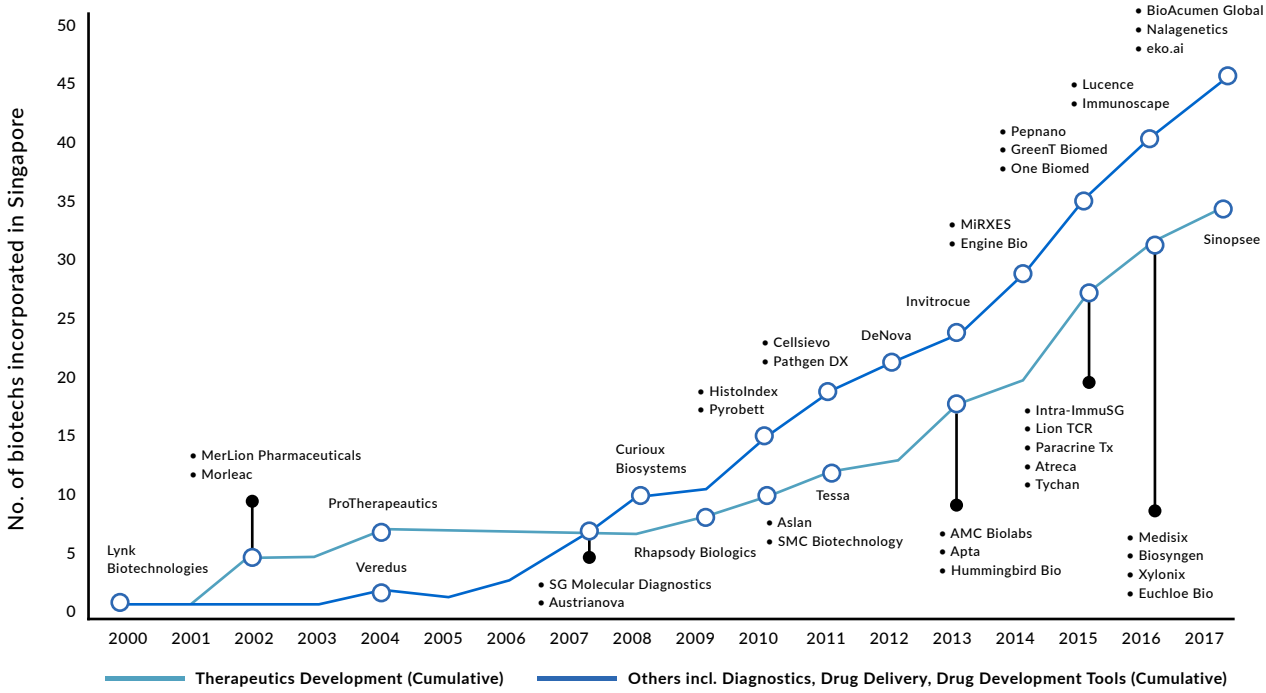


*Source: National Survey of Research & Development in Singapore, 2002 to 2017, A*STAR. Milken Institute analysis (2020). Figures for "Biomedical & Related Sciences" in SGD millions. Basic Research, Applied Research, and Experimental Development roughly correspond to the three color groups in Figure 1*

Singapore's open economy and business-friendly environment have also helped to attract talent and technology. RIE2020's 14 funding schemes[5] join a panoply of other grant programs, subsidies, and tax deductions offered by Enterprise Singapore;[6] the National Research Foundation;[7] the National Medical Research Council;[8] the Economic Development Board;[9] the Agency for Science, Technology and Research (A*STAR);[10] the Intellectual Property Office of Singapore;[11] Startup SG;[12] and the Inland Revenue Authority of Singapore.[13] On top of these economic incentives, low corruption,[14] strong compliance standards,[15] high wages, and a stable regulatory environment[16] further help draw foreign talent and investment from all over the globe.

As a result, Singapore now hosts a robust talent pool of basic scientists, promising biomedical startups, high-quality infrastructure, and support services conducive to early-stage and clinical R&D. In 2017, Singapore had more than 30 locally incorporated biotechs focusing on therapeutics development alone[17] and 79 overall (see Figure 4). These institutions have been responsible for a corresponding increase in talent. Singapore, with a population of 5.8 million, is now home to more than 2,757 full-time equivalent PhDs in biomedical and related sciences;[18] that's one doctorate-level biomedical researcher for every 2,000 people.[19]

Figure 4: Locally Incorporated Biotechs are on the Upswing



*Source: Annual Report, April 2017–March 2018, A*STAR (2018)*

The rest of Singapore's biotech ecosystem has also grown. In 2005, Duke University and the National University of Singapore partnered to create the Duke-NUS Medical School,[20] which focuses on basic and translational research. Nine years later, the fledgling medical school launched its Centre of Regulatory Excellence to "build competencies, enhance collaboration, and promote thought leadership in innovative regulatory science and policy within national regulatory agencies, industry, and academia" in the region.[21] A*STAR today has 11 biomedical research institutes and two national platforms supporting drug discovery and experimental biotherapeutics.[22] Early-stage life science funds Lightstone Ventures[23] and Esco Ventures[24] have entered this environment in the past decade, complementing larger but later-stage investors like Temasek, a global investment firm owned by the Singaporean government.[25]

Singapore's progress in the biotech field is reflected in international rankings. The city-state has consistently appeared among the top 10 in the World Intellectual Property Organization's Global Innovation Index,[27] the Bloomberg Innovation Index, and the World Economic Forum's Global Competitiveness Report.[28] In the 2016 Scientific American Worldview ranking of 54 countries in biotechnology, Singapore was second only to the US.[29] The Pugatch Consilium's 2017 Biopharmaceutical Competitiveness & Investment Survey ranked Singapore first among newcomer

markets,[30] and the Financial Times' 2019 fDi Intelligence report named the city-state as the top Biotech Location of the Future worldwide.[31] Galen Growth Asia reports that Singapore has witnessed the third-highest number of health-tech funding deals in Asia since 2018.[32,33]

Despite all these achievements, Singapore's accelerated development of its basic science pipeline highlights the difficulty in translating discoveries into cures. While Singapore holds its own in researcher density, R&D spending, and contributions to academic journals, it lags many other countries in the number of pharmaceutical patents granted. Indeed, some participants in the Financial Innovations Lab ("participants") noted that 80 percent of local biotech firms started with intellectual property (IP) originating outside Singapore.

Moreover, while funding for all stages of drug development has stayed consistent in Singapore, the costs of later-stage research tend to be much higher (see Figure 5). This is unsurprising, given the longer timeframes in clinical stages of drug development, the need to pay for patient recruitment and retainment, site overhead costs, and longer-term monitoring, all while adhering to safety standards and regulations.[34] The funding levels required for basic science are only a small fraction of the costs of clinical development and regulatory approval. Translating biomedical research into effective drugs will require significantly more funding, and, in many cases, alternative sources of capital altogether.

Figure 5: Later Stages of Drug Development Cost the Most

Stage	Timeframe	Cost	Probability of Success
Lead Identification	1 year	US $1M	50%
Target Validation	1.5 years	US $2M	50%
Lead Optimization & Process Chemistry	2-3 years	US $6M	50%
Pre-Clinical Development	1 year	US $5M	70%
Clinical Trials/FDA Application & Approval	6-8 years	US $100-200M+	12%
Total	**12-15 years**	**US $114M-214M+**	**1.05%**

Source: Industry Statistics; MIT Project Alpha (2019)

Several other barriers threaten to further impede translation and commercialization. Since its high in 2015, private sector spending has fallen in all three stages of R&D (refer to Figure 3). Part of the decline can be attributed to a mass global restructuring that saw several major pharmaceutical companies (including Novartis, Eli Lilly, Pfizer, and GlaxoSmithKline) closing research facilities in Singapore between 2010 and 2016.[35] Singapore's manufacturing output of pharmaceutical and biological products has stagnated since 2013,[36] while foreign direct investment in pharmaceutical products has fallen by nearly 75 percent since its peak in 2007.[37]

The departure of so many major pharmaceutical companies highlights the fundamental challenge Singapore faces: It is challenging to produce, attract, and retain talent, technologies, and corporations when the domestic market is small and remote from larger, well-established hubs. Government spending has mitigated the decline in experimental development for now, but new sources of financing are urgently needed to ensure the sustainability of translational biomedical research in Singapore.

THE STATE OF BIOMEDICAL RESEARCH BEYOND SINGAPORE

To foster the continued development of Singapore's biomedical sector, participants first looked to other markets for alternative models. In the US, states like Texas[38] and California[39] each sold US$3 billion in state bonds for investment in infrastructure, scholarships, and early-stage research, complementing the US$7.1 billion allocated to the National Science Foundation for the 2020 fiscal year.[40] In 2019, Texas voters overwhelmingly approved an additional US$3 billion in state bonds for cancer prevention and research.[41] These capital commitments have accelerated the development of biomedical research ecosystems in both states and produced tangible outcomes. For example, research supported by the California Institute of Regenerative Medicine led to the discovery of an effective gene therapy for severe combined immunodeficiency, a deadly immune disorder.[41] However, despite these successes, neither state's program is financially sustainable.[42,43]

On a federal level, the US National Institutes of Health (NIH) uses its NIH-Industry Partnerships program to match researchers with pharmaceutical assets.[45] This program is open to any US researcher and helps scientists test ideas for new therapeutic uses. Additionally, standardized templates created by the NIH have shortened the time it takes for industry and academic partners to negotiate legal agreements from a year to as little as three months.[46]

The UK's 2011 "Strategy for UK Life Sciences" is a comprehensive, multi-stakeholder approach to support drug development in the United Kingdom.[47] The document set out strategies to support the commercialization of academic research through public investment and greater flexibility in funding rules. It further encompassed plans to develop clinical research infrastructure that supports collaboration between

health providers and academics, encourage the adoption and diffusion of innovation in the public health system, and promote the UK as a life sciences hub. Over the subsequent 12 months, the UK received more than £1 billion in new private investment in the life sciences.[48]

China offers a different model for incentivizing drug development: subsidizing patent applications. Unfortunately, the number of companies that game the system by applying for large quantities of low-quality patents has seriously devalued the Chinese patent process. To counter the low quality of domestic patents, China also subsidizes applications by Chinese firms for patents in other countries.[49] The Chinese National Medical Products Administration also proposed in 2018 to double the period of data exclusivity for innovator biologics to 12 years, on par with the US and Europe.[50] This prevents generic drug manufacturers from using innovators' clinical trial data, thereby serving as further market protection for innovation. Additionally, Chinese regulators are accelerating drug approval by allowing pharmaceutical companies to submit their clinical results on a rolling basis, among other measures.[51] And in 2018, the Hong Kong stock exchange began allowing pre-revenue biotech and med-tech companies to list on its Main Board. As of August 2019, this has enabled eight pre-revenue firms to raise US$3 billion.[52]

At a supranational level, the European Union's "Horizon 2020" program has made €77 billion available between 2014 and 2020 to finance research and innovation in disciplines ranging from agriculture and forestry to transportation.[53] Horizon 2020's "InnovFin Infectious Diseases" program provides grants between €7.5 million and €75 million for projects to develop vaccines, drugs, and devices that have completed pre-clinical trials.[52] Horizon 2020's successor, "Horizon Europe," will authorize another €100 billion between 2021 and 2027.[55]

The private and nonprofit sectors have also come up with innovative ways to enhance biomedical R&D. GlaxoSmithKline's Accelerating Therapeutics for Opportunities in Medicine (ATOM) initiative created an open platform integrating high-performance computing, shared biological data from public and industry sources, and emerging biotechnologies.[56] ATOM aims to reduce the drug discovery timeline by five years. Pfizer established local Centers of Therapeutic Innovation at leading academic medical centers, creating entrepreneurial networks of partnerships with leading translational researchers.[57]

Public-private partnerships are also gaining traction. In Asia, Japan's Santen Pharmaceutical company launched a S$37 million partnership with the Singapore Eye Research Institute in 2017 to develop new technologies to combat ophthalmic diseases, especially those affecting Asians.[58] As a direct outcome from a Financial Innovations Lab in 2008, the Israeli government invested US$48 million to seed the creation of a US$203 million Israel-focused life science fund by the investment fund OrbiMed.[59] Four years and 17 companies later, OrbiMed closed a second Israeli

fund at US$307 million, without state support.[60] This initiative has also precipitated FutuRx, a biotech accelerator whose partners include Johnson & Johnson, Takeda Pharmaceutical, OrbiMed, and the Israeli Innovation Authority, with funding support from the Office of the Chief Scientist.[61] Separately, the Israel Innovation Authority signed a 2017 memorandum of understanding with the University of California aimed at increasing cooperation to advance global commercialization in biomedical development, among other areas.[62]

With these case studies in mind, participants set out to address Singapore's challenges in translational biomedical research, as well as design workable options to attract talent, technology, and capital. As mentioned, the fundamental challenge lies in Singapore's small market and geographic distance from other medical hubs. While the government has seen positive momentum from past policies, further steps are still needed.

SINGAPORE'S NATIONAL STRATEGY IS UNCLEAR

One of the biggest obstacles to Singapore's increased prominence in the biomedical industry is a seeming lack of consensus and clarity about the city-state's specific end goals. While the government's RIE2020 strategy helpfully highlights its priorities in the therapeutic areas and intended outcomes of biomedical research, other factors such as industry structure and target market remain less clear. Some participants felt that it was increasingly difficult to identify, and in turn, engage with the key personnel involved in national strategy formulation. They stressed that without an overarching and well-defined national strategy, it would be even harder to attract the right talent and capital from other established biomedical hubs, much less keep them in Singapore. Such churn would result in longer timeframes and inefficient usage of funds, which in turn creates higher risk and uncertainty, and potentially deters further investment. Participants agreed that Singapore's government needs to map out a realistic end goal, and then outline interim milestones, with sufficient time for talented individuals in research, business, and investment alike to drive progress.

SINGAPORE LACKS COMMERCIALIZATION EXPERTISE

Participants and many other stakeholders interviewed throughout the Lab process agreed that translational research should be driven by specialists, with the aid of entrepreneurs, venture builders, and operating partners. While the original scientists drive most translational activities in Singapore, academic researchers often lack the experience and incentives required to translate their work into commercial products. For starters, translational research has a lower frequency of publications and citations, which are key performance indicators for academics seeking tenure. Many foreign scientists have left Singapore when pushed to do translational work instead of basic science.

Moreover, basic science in Singapore has greater certainty of funding and provides stronger career stability. Participants noted that when corporate labs closed down in Singapore, many researchers chose to join public research institutions instead of starting their own biotechs or seeking out other private companies. That was because salaries in public institutions are higher, and a public sector job is more secure. Even if Singapore had more commercial startups, it would be difficult to compete with the public sector for talent.

Singapore has also encountered difficulty in attracting biotech entrepreneurs, venture builders, and operating partners to its shores. Drawing on talent from hubs like Silicon Valley, Boston, and Israel is challenging, and not only because of the significant geographical and cultural distance. For example, participants explained that US hubs are strongly associated with success and learning opportunities, which contribute irreplaceably to personal branding, experience, and network-building. Singapore's small domestic market, by contrast, offers few opportunities to develop professional networks. Hence, even highly generous expatriate packages may not draw talent from top-tier hubs. Worse, they could attract less qualified, uncommitted individuals who may subsequently leave when offered better pay elsewhere.

While public scholarships give promising locals the opportunity to study overseas and acquire knowledge in translation, the scholarships usually require them to return to Singapore before they have sufficient time to build networks or accumulate translational experience in mature markets. Without proper guidance from pharmaceutical experts and experienced investors, researchers have a difficult time fundraising and staying relevant to what is commercially viable.

SINGAPORE LACKS A ROBUST PRIVATE FUNDING MARKET

Fundraising in Singapore can also be challenging due to the limited types of financial instruments available to investors and the few domestic funding options available to promising companies. Some participants noted that virtually none of the biotechs represented at the Financial Innovations Lab were funded in Singapore, while others pointed out that Singapore's stock exchange has never listed a biotech company. Although the government awards generous tax deductions for R&D, private biomedical R&D spending is relatively low, amounting to only a quarter of gross biomedical R&D spending in 2017.[63] Additionally, the majority of business expenditures come from within the industry, unlike the US or Israel, where nonprofits provide significant contributions.[64] While the government's sizeable commitments are commendable and should be maintained, without a diverse mix of financing options, good ideas that fail to tick government checklists have nowhere else to turn.

Furthermore, application processes for public grants have many restrictions and usually take several months to over a year to complete. This deters potential investors and pharmaceutical companies, who have to report key performance indicators or returns every quarter. Domestic grant administrators and technology transfer offices can also be inexperienced. Several participants pointed to technology transfer offices in the US, which are staffed by senior professionals with extensive backgrounds. In Singapore, by contrast, staffers are often underpaid, inexperienced, and overly tied to checklists.

Participants also stressed that translational research should be market-driven to ensure that the pursuit of public health does not sacrifice commercial viability. For example, common cardiovascular morbidities impose high costs to health systems and would seem to be ripe for drug development. But they require massive trials that are too expensive for venture capital to finance. Similarly, the burden of infectious diseases is particularly high in Asia, but research in this area tends to have poor margins, thus deterring startups. Participants thus hoped that the importance of the market could be reflected in the government's next round of R&D strategy planning.

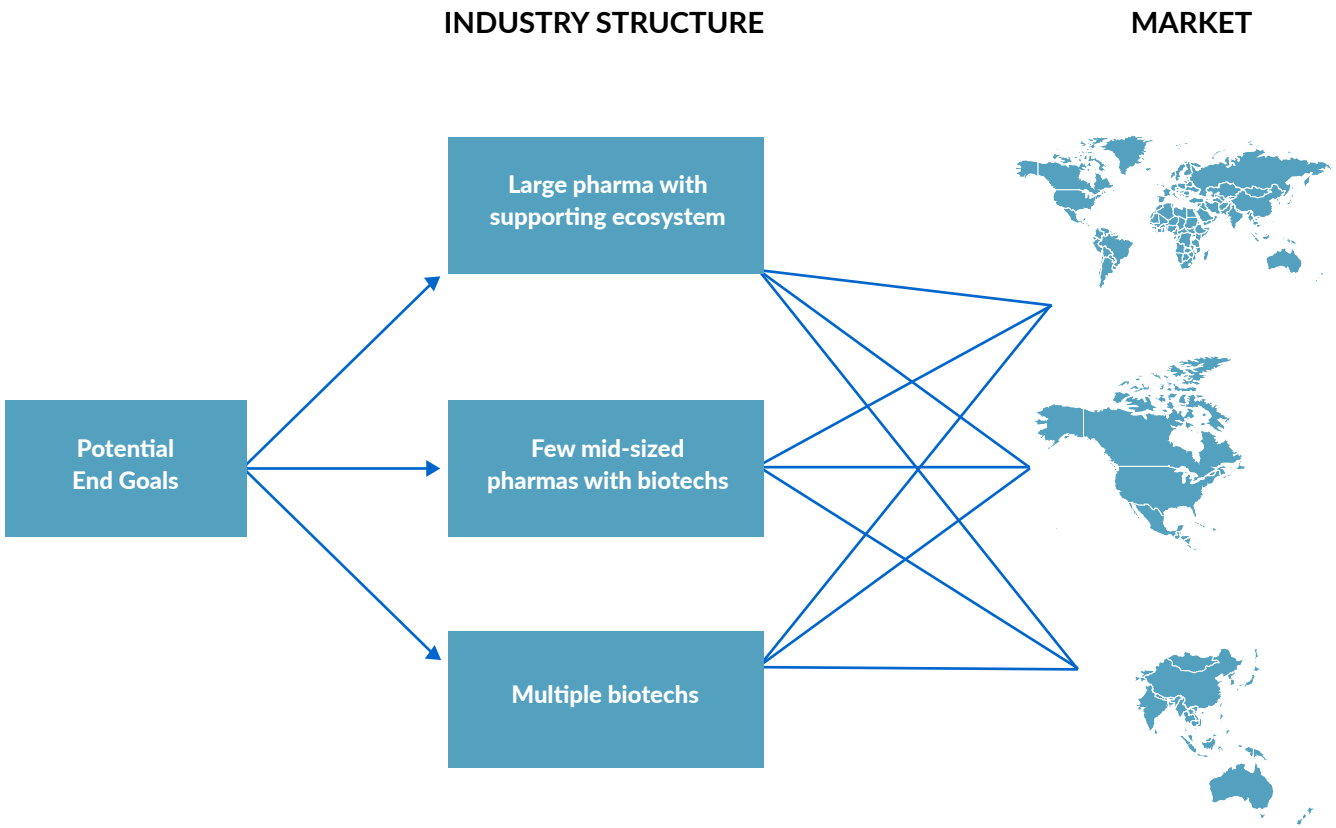
RECOMMENDATIONS

Recognizing that Singapore will always remain a small and remote market for translational research, participants identified several innovations that can leverage the nation's existing strengths and address some of its shortcomings. These recommendations cover industry development pathways and the attraction of entrepreneurs, investors, and commercialization talent, as well as innovative financing instruments. These recommendations are not mutually exclusive; on the contrary, they complement each other as parts of a comprehensive approach to develop Singapore's entire ecosystem.

SINGAPORE NEEDS TO DEVELOP A NATIONAL STRATEGY AND DEVELOPMENT PATHWAY

Participants agreed that determining a national strategy is critical to building a robust translational ecosystem for biomedical research. One key consideration is the industry structure (see Figure 6). Of the three models identified in Figure 6, Singapore is currently closest to attaining the "multiple biotechs" structure. Some participants suggested that, given its existing strengths in basic science, Singapore could anchor early-stage research, while playing a supporting role for large clinical trials in more significant markets, which it would not be able to resource itself. The Singapore Eye Research Institute's partnership with Santen Pharmaceutical serves as an example.

Figure 6: Singapore's Diverse Biomedical R&D Development Options



Source: Milken Institute (2020)

However, there are challenges to choosing the "multiple biotechs" model as a long-term goal. Most biotech startups and investors look to exit quickly through mergers and acquisitions or initial public offerings rather than continue growing organically over the long term into a large pharmaceutical company. In the last decades of the 20th century, European countries similarly tried to build early-stage biotechs to plug research gaps for large pharmaceuticals. Subsequently, European biotechs focused on quick solutions to sell to pharmaceutical firms, rather than creating companies that could scale and last. In selling their assets too soon, European biotechs ultimately struggled to improve their global competitiveness, as they sold off resources that would have helped to establish a scaling, self-sustaining startup ecosystem. While biotechs will play an increasingly important role in the research ecosystem, participants felt that Europe's experience affirms Singapore's goal to establish domestic pharmaceutical firms to complement local biotechs.

Participants further outlined the reasons for expanding Singapore's pharmaceutical industry. Firstly, pharmaceutical companies attract high-quality, later-stage talent, as well as capital and technology. Secondly, pharmaceutical firms collaborate with experienced investors to guide the scientific community toward the areas of research with the most commercial potential. Finally, because they are the ones conducting the final stages of drug trials, pharmaceutical companies would be the linchpin in creating new cures and treatments and producing economic value. Most participants acknowledged that growing or attracting a large pharmaceutical firm to anchor the R&D ecosystem should be a long-term goal for Singapore. That kind of model will take years to develop, so in the shorter term, some attendees suggested that Singapore adopt a model with a few medium-sized pharmaceuticals complementing an ecosystem of biotech companies. Other countries with such models include Japan and China.

The target market that Singapore chooses for its end products will also influence the appropriate development pathway. Focusing on the US will require personnel with a deep understanding of Food and Drug Administration regulations, the payer environment, clinical development procedures, and, more generally, epidemiology in developed countries. Most Singapore biotechs cannot afford to develop these expensive resources by themselves, so there will need to be mechanisms to share the costs. Conversely, targeting Asia will require a greater emphasis on diseases more common in Asia and the regulatory environment in half a dozen countries or more. Several participants argued that in the latter scenario, local regulators should take a more proactive stance in de-risking drug development since investments will be funding lower-profit assets. This involvement could include using Singapore's infrastructure and regulatory experience to support research and trials around the region, as well as providing purchase guarantees for low-profit, high-need areas like Asian tropical diseases. Some participants doubted that investors would be willing to fund Asia-focused biotechs, but others believed that there is good receptivity among entrepreneurs, investors, and donors alike.

Next Steps:

- Establish short- and long-term goals at the national level to further develop the biomedical research ecosystem.
- Analyze target markets to establish priorities for future funding and project development.

SINGAPORE COULD LEVERAGE ACCESS TO DATA TO ENTICE BUSINESSES AND TALENT

Several participants suggested that Singapore could carve out a niche in developing a data platform or exchange to supplement biomedical R&D. Currently, data ownership worldwide is extremely fragmented. Larger markets like Japan, South Korea, China, and Taiwan all have biobanks,[65] but Singapore is equally well-placed to become a global leader in this sphere. The city-state has numerous advantages, including its small geographical size, the ethnic diversity of patients, relatively high centralization, high penetration of wearables, quality data, and a robust tech ecosystem. In 2019, Singapore opened the world's largest whole-genome sequencing databank of Asian populations, created by researchers from local institutions after studying the genes of nearly 5,000 Singaporean volunteers.[66] Several participants noted that Singapore's robust genomic data were a draw for multinational corporations and that having genomic data, phenotypic data, and longitudinal data from wearables, all in a single place, could unlock significant potential in biomedical research.

Similarly sized markets have interesting programs underway. Israel has announced a US$287 million National Digital Health Plan to make electronic medical records from all four of its health maintenance organizations accessible to researchers.[67] Under this plan,[68] the "Mosaic" initiative aims to enroll 100,000 volunteers for their anonymized clinical, genomic, and other health information to be made available to academia and enterprises for research.[69] The increasing availability of high-quality data in Israel has further enabled new funding models, such as one in which venture capital firms and health-care providers partner to contribute funding and data, respectively, to startups in exchange for equity.[70] For example, K-Health, a New York-based startup providing personalized health information and diagnoses, chose to train its machine-learning models with data from Israel's Maccabi Health Services because US data were too siloed.[71] Given the complete and robust nature of Singapore's genomic data, and its well-developed digital ecosystem, participants felt that the government and local hospitals could structure similar incentives for foreign corporations to conduct R&D in Singapore.

Participants also suggested the government introduce a data exchange platform similar to Switzerland's Open Access program. The Swiss National Science Foundation (SNSF) has announced that all SNSF-funded research will be freely available online by 2020. By making researchers' results accessible to other researchers and the wider public, the program aims to encourage transparency, reproducibility, and collaborative innovation. Participants suggested that to incentivize data contributions, researchers could be granted early access to limited pools of data before public release.

That said, it is essential to remain aware of the risks of data sharing and Open Access, including concerns over individual privacy,[72] data governance,[73] and publication quality.[74]

Next Steps:

- Engage Singapore's government to map out a development timeline for a national biobank, using parallel markets as a guide.
- Identify health AI or big data providers that could serve as potential equity partners to Singapore's medical startups.
- Develop a standard reporting requirement for all publicly funded research, which will facilitate the consistency of data across a biobank.
- Integrate medical data to leverage as an incentive for foreign corporations to locate R&D operations in Singapore.
- Explore the viability of data exchange platforms in Singapore, while remaining aware of privacy concerns, data governance, and publication standards.

SINGAPORE COULD UNLOCK CAPITAL BY SECURITIZING ITS DRUG ASSETS

Building on the potential applications of greater data interoperability and access, participants suggested exploring ways of securitizing drug assets to attract private investment. Securitization is the practice of offering a pool of contractual assets to third-party investors as a security. Investors are repaid through the cash flow generated from the underlying assets. Mortgage-backed securities are perhaps the best-known example of asset pooling, but the film industry provides an even more relevant model. Like drug development, early-stage film production is high in risks and costs, while low on value and probability of success.[75] Both drug development and film production also operate on a "stage-gate" valuation model, where value increases over time as stages of development are completed. Securitization has been used successfully in film production to finance risky early-stage projects and thus could also be considered for drug development.

Is Film Securitization a Model for Drug Securitization?

In 1983, Silver Screen Partners pioneered the model of securitizing a portfolio of films to attract external financing. Throughout the decade, Silver Screen raised four funds totaling more than US$500 million to finance productions like *Pretty Woman* and *The Little Mermaid*, both of which went on to earn more than $200 million worldwide.[76] The securitization of film assets has since been used in various ways. In 2002, Dreamworks offered a US$1 billion deal, which relied on movies that had already wrapped on production but had yet to be released.[77] In 2011, Miramax issued a US$550 million deal on a standalone film library. The films in the portfolio included popular hits like *Pulp Fiction*, *Good Will Hunting*, and *No Country for Old Men*. The credit to back the securitization was sourced from the cash flow of existing licensing contracts, as well as new sales to television and distribution services.[78]

A major benefit of film securitization is the division of labor: Directors can focus on directing while the umbrella organization managing the pool carries out other functions like human resources, finance, and logistics. A similar situation exists in biomedical research, where it is often lamented that scientific researchers lack business acumen. Taking a page from the film industry, the biomedical research community could unlock liquidity by securitizing drug assets. Participants suggested that diversified portfolios of 20 to 50 medical assets, from different companies, countries, therapeutic areas, and stages of development, would likely be needed to mitigate risk and bring investors on board. Without a large and varied pool of assets, investors would have little reason to prefer fixed-income securitization over equity.

Additionally, for medical asset pooling to be successful in Asia, participants underscored the importance of having an investor base with a strong understanding of the region's diverse markets. Making domestic funding available early in the process would also reduce the number of later-stage assets seeking overseas financing. That, in turn, would allow for greater diversification of securitized portfolios.

Next Steps:

- Classify potential IP or medical assets that are attractive for securitization.
- Identify the market potential in Singapore to offer securitized medical assets.

SINGAPORE MUST ATTRACT A ROBUST, COMPLETE ECOSYSTEM OF INVESTORS

To create a thriving biomedical research industry, Singapore needs to develop new and creative vehicles to attract capital. A majority of participants agreed that establishing a series of early-stage or venture capital funds would be one of the best ways to do so. While some public funding contributions would be needed to kickstart these funds, most participants agreed that the funds should be sourced primarily from the private sector so that they can be truly competitive with each other.

Participants proposed attracting three funds of US$100 million each, all with strict operating guidelines and requirements. Three funds would create the opportunity for competition without overly diluting the impact of each fund, given the nascency of Asia's drug development ecosystems. After much debate, participants ultimately agreed that the funds should be divided not by sector but by funding avenues and investment philosophy, to encourage competition for deals. All three funds would have a broad, flexible life science mandate to maximize the number of startups it could invest in. However, once a fund chooses to invest in a company, it would have to adhere to a documented strategic plan, with clear targets as part of a transparent governance structure. Participants agreed that projects should be selected on a commercial basis; they also recommended that the funds prioritize investments of strategic significance to the overall region, not just on intellectual property originating in Singapore.

Given the broad investment focus of these funds, a high amount of scrutiny will fall on the investment committee and operating partners to maintain a structured process. Participants stressed that the investment committees should be independent, privately run, and, ultimately, expected to deliver a financial return. They also underscored the importance of having investment committees based in Singapore but representative of the broader regional ecosystem. These diverse and highly experienced investment committees would subsequently pass on their insights to staff who are familiar with the life sciences, building a team with more well-rounded expertise.

Participants further discussed the need for a broad range of operating partners who are ready and incentivized to join startups invested in by the funds, to support the funds and anchor invested companies in Singapore. While there is no one standard definition of an operating partner, each partner should bring a unique perspective to the conversation. An effective operating partner will serve as the point of communication between the investors and the fund's portfolio companies and will extend their knowledge from career experience into best-practice operations. In the case of biomedical research, scientists, clinicians, and business and finance professionals all provide different but equally necessary spheres of expertise. Any fund's success hinges on its ability to make the most of these collaborations.

Participants agreed that leaders should be familiar with both the US and Chinese markets, and have strong networks in each. Given the past challenge of attracting leadership talent to Singapore, operating partners must be allowed to contribute to a variety of Singapore-based organizations. Having some stake in the entire portfolio of the fund, in addition to a commitment to the startups that they are directly engaged with, gives operating partners greater confidence in moving and building their careers in Singapore. Partners then need not worry if the first enterprises prove unsuccessful because they have a capital backer that will support them continuously.

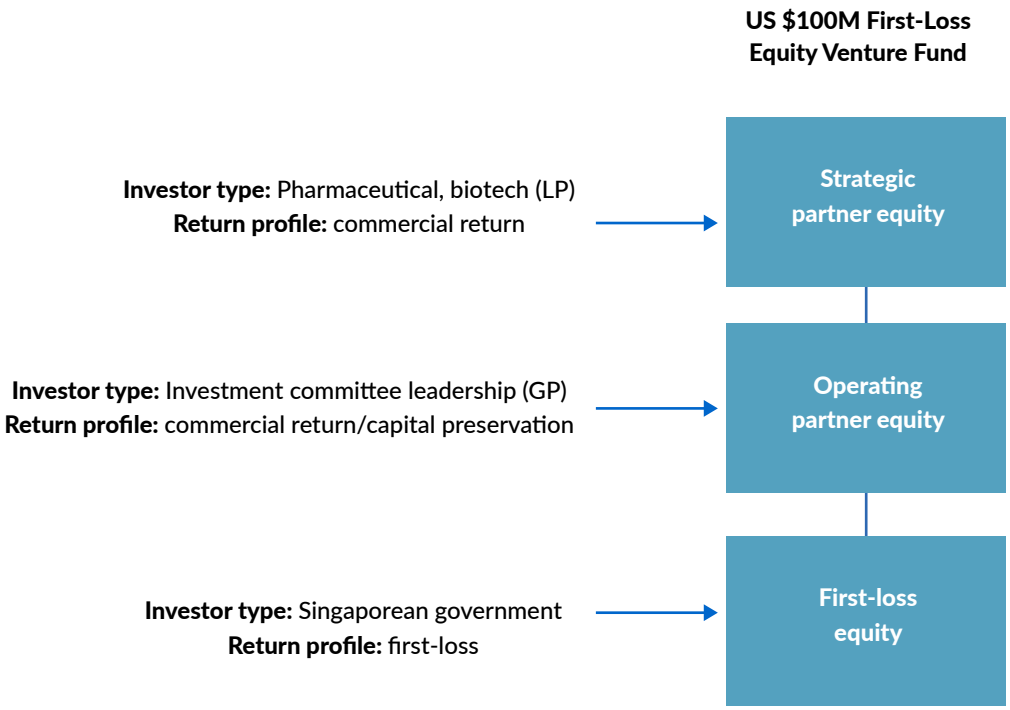
Additional financial incentives that will help Singapore's biomedical research industry reach scale include offering operating partners an equity stake in any business to which they contribute and giving senior investment committee members a stock buy-back option if the investments are successful. These will strategically serve to incentivize them to the upside.

Participants at the Lab had varying definitions of how these venture funds should evaluate success. For many biotech startups, the Holy Grail is relocation to the US for later-stage fundraising rounds, but this could conflict with government grant schemes that require firms to maintain a certain employee headcount in Singapore. Some participants predicted that even if startups do ultimately relocate, their maturation will enhance Singapore's reputation as a hub for incubating and accelerating early-stage biotechs, as was the case with Israel. When those mature biotech firms embarked on early-stage research for the next set of drug candidates, they would presumably return to Singapore. As such, participants concluded that the best measure of a venture fund's success should be its ability to raise subsequent funds and expand the funding ecosystem.

a. FIRST-LOSS EQUITY VENTURE FUND

While leadership is of the utmost importance, it is also crucial to structure the funds in a way that attracts strategic partners. Pharmaceutical companies, for example, could be helpful as limited partners (LPs) to directly guide the research direction and commercialization of venture investments. Private investors would be more attracted to these funds if the Singapore government had skin in the game. Participants discussed the option of a first-loss vehicle, with Singapore's government providing the initial equity. This type of financing would reduce the risk for subsequent investors and thus lower the barrier for co-investment from the private sector (see Figure 7). This model could be extremely effective in attracting large, institutional investors and pharmaceutical companies to the Singapore market.

Figure 7: A First-Loss Equity Venture Fund Could Attract Risk-Averse Investors



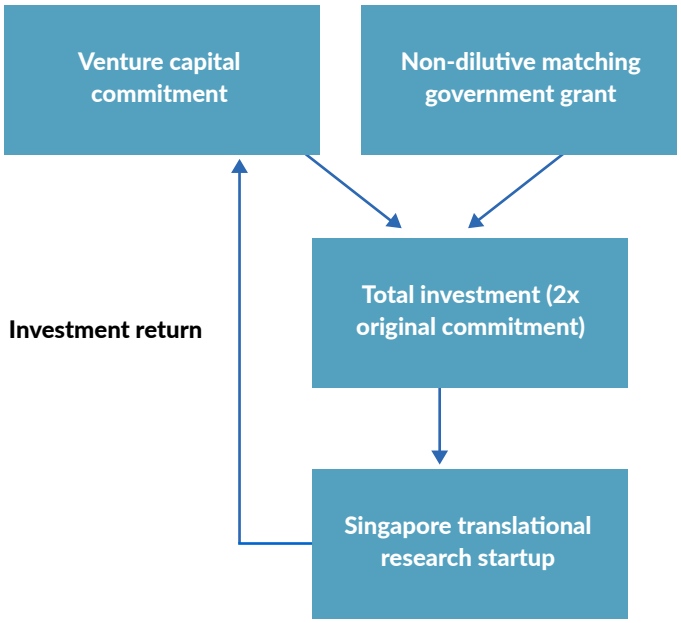
Source: Milken Institute (2020)

b. NON-DILUTIVE GRANT PROGRAM

Another way for the public sector to encourage investment in Singapore's biomedical industry is through public-private partnerships, a strategy the European Commission has employed with great success through its Innovative Medicines Initiative (IMI). Now in its second generation (known as IMI2), the initiative sets out a list of top-level priorities for medical research and invites private companies to submit ideas for attaining those goals. The EU provides half of the IMI's €3.3 billion budget; the other half comes from the European pharmaceutical industry and other private investors in the health-care field.[79] This program could serve as a model for Singapore.

A non-dilutive grant program (see Figure 8) would also encourage private investment by pairing it with government grants, doubling the return to investors without diluting their equity. Like the IMI, a non-dilutive grant program enables the public sector to influence the direction of biomedical research by making investments in those areas more attractive to investors. This model could be effectively used to further development in areas of interest at the national level for the population of Singapore or the broader region. In addition to serving regional needs, the matching grants should also align with the investments by the proposed venture capital funds.

Figure 8: Non-Dilutive Grant Programs Double the Return for Investors



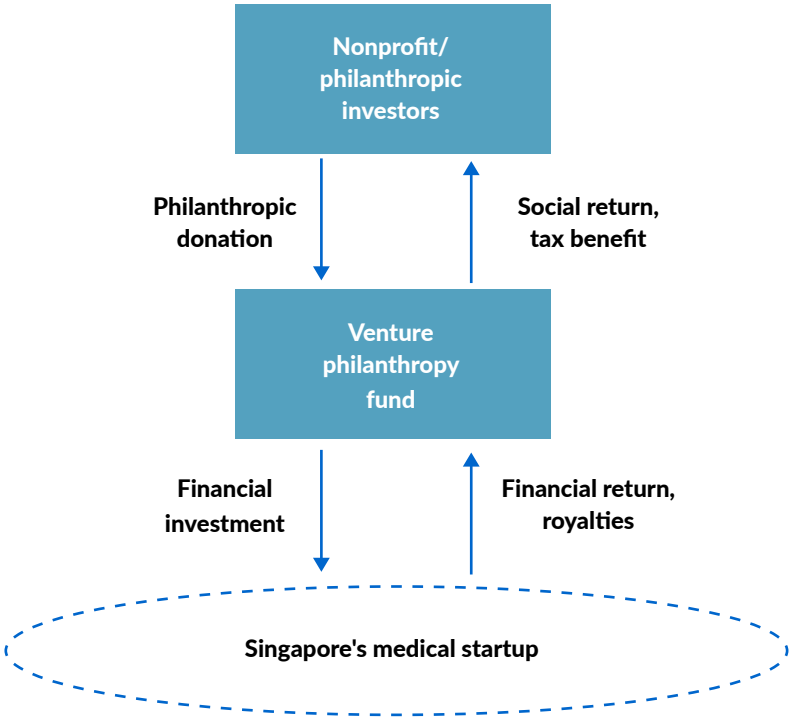
Source: Milken Institute (2020)

c. VENTURE PHILANTHROPY FUND

Participants were eager to identify funding structures that would attract alternative sources of capital, such as philanthropists and family offices, to diversify away from public funding. While Singapore is replete with family offices and philanthropic capital, the lack of flexible investment vehicles has sidelined this segment of the market. To encourage participation in translational research, participants suggested developing the kind of venture philanthropy fund commonly found in the US and Europe.

Venture philanthropy is an entrepreneurial approach that combines financial and non-financial inputs towards traditional venture capital financing to achieve charitable goals (see Figure 9).[80] Nonprofit investors are ideally positioned to invest through venture philanthropy funds because of their flexible nature and focus on patient outcomes, rather than financial return. Traditionally, in markets such as the US, venture philanthropy funds are managed by nonprofit organizations with expertise in the field of research. This structure allows investors to receive a tax benefit for their investment. These funds are often willing to take higher-risk positions over long investment time frames, with the expectation that their capital injection significantly moves a field of research forward. Venture philanthropy investments reduce risk by lowering the cost of borrowing, and in turn, attracting additional traditional capital. Given Singapore's wealth of family office capital, setting up a venture philanthropy fund with seed money from local donors could be effective in attracting significant international financing.

Figure 9: Venture Philanthropy Funds Reap Financial and Social Returns



Source: Milken Institute (2020)

The Harrington Project Blends Philanthropy and Drug Development

The Harrington Project is an exemplary model of collaboration between nonprofits and for-profit companies in drug development. It uses philanthropic funding to reduce the risk of early-stage research. The Harrington Discovery Institute is the nonprofit half of the project; it conducts annual competitions to identify scholars who have made groundbreaking medical advances.[81] Drug candidates with strong commercial potential are passed on to the for-profit arm, BioMotiv.[82] BioMotiv then collaborates with strategic industry partners to support the development and commercialization of drug discoveries across the translational valley of death. The Harrington family's initial gift of US$50 million has now attracted an additional US$330 million in philanthropic and private capital for drug development.[83] Leveraging the physician-scientist expertise at Harrington and the commercial expertise from BioMotiv and its partners, the collaboration breeds developments that can advance medical treatments.

Next Steps:

- Engage Singapore's government to review restrictions on universities and clinical research institutes accessing venture philanthropic funds.
- Identify key entrepreneurs and business leaders to test the venture fund models.
- Develop a strategic plan that includes investment and operational targets and priorities.

SINGAPORE COULD ENCOURAGE MORE COLLABORATION AND NETWORKING

All participants agreed that Singapore would benefit from more exchanges with the US, as it is the global capital for biomedical research. Establishing landing pads in top-tier hubs like Temasek's San Francisco office, for example, would allow researchers and startups to network with and market their technologies to large investors and pharmaceutical companies. Singapore could also increase networking and collaboration by revisiting its grantmaking process, which some participants said lacked flexibility in its treatment of overseas expenditures and engagement with international hubs.

As collaboration becomes ever more critical to modern innovation, a standardized system of talent development and exchanges would foster greater international cooperation, socialize researchers into multi-disciplinary research, and attract both talent and funding. Other participants suggested a government-sponsored program in which experienced entrepreneurial leaders, from a variety of industries with parallel capabilities and skillsets, take on an advisory role in young startups until they achieve certain pre-defined milestones. Government subsidies to cover the salaries of such leaders would help startups cope with wage costs.

Next Steps:

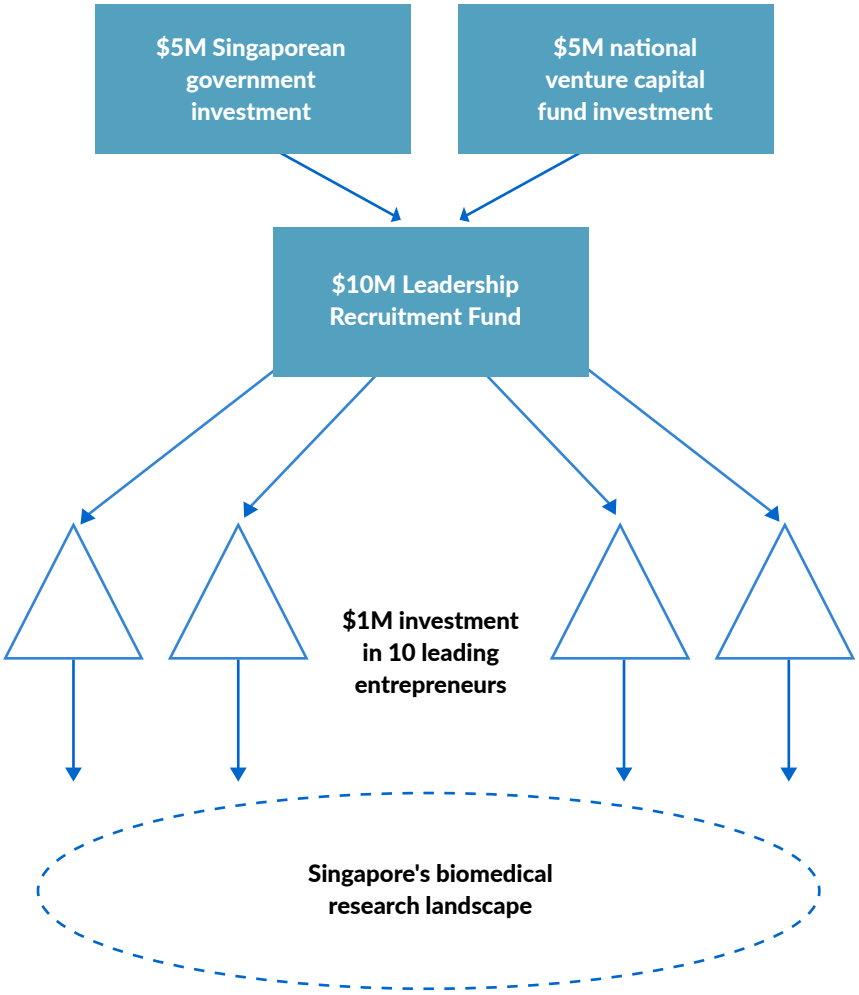
- Revisit existing restrictions on public grants and establish a pilot talent exchange program between prominent universities and research institutes.
- Establish a publicly subsidized talent transfer program to complement the work done by the private sector.

SINGAPORE COULD LAUNCH AN ACCELERATOR FUND TO ATTRACT ENTREPRENEURS

Attracting the right leadership to Singapore requires incentives that align with the overall national strategy. Participants discussed what it would take to attract experienced business professionals from established hubs to Singapore to work alongside scientists, research institutions, and universities to support business and venture creation. Participants applauded Singapore's recent increase in flexibility for its Employment Pass applications as a welcome first step.[84] However, they also noted that more could be done. Some participants referenced China's Thousand Talents Plan, a recruitment strategy to attract and retain top talent, as a model for attracting even more business and professional leaders. The Thousand Talents Plan offers generous living benefits, research incentives, and amicable working conditions in China to researchers and entrepreneurs with a strong track record of success. It even guarantees jobs for their spouses and school admissions for their children.[85] Some participants noted that with more family-friendly employment passes, it would not be difficult to draw entrepreneurs from nearer hubs, such as Israel.

Some participants suggested launching a S$10 million biotech accelerator fund to attract 10 top entrepreneurs to Singapore (see Figure 10). This fund could operate in partnership with the Tech@SG program launched in 2019, a two-year pilot program that aims to help companies grow by streamlining Employment Pass applications for foreign employees with strong tech skills.[86] Expanding on the requirements for Tech@SG, applicants to the accelerator fund must have a strong track record in fundraising, creating successful businesses, and commercialization of biotech discoveries. Each of the 10 entrepreneurs would be awarded S$1 million, in conditional stages, to incubate a certain number of Singapore-based projects within a given time frame. While $1 million is not enough to move companies to commercialization, creating such an accelerator fund ensures that key entrepreneurs will be well-placed to expand and lead biotech startups and incorporate their expertise into Singapore's biomedical research ecosystem. Participants stressed that both the government and private sector must contribute equally to this fund because having skin in the game would incentivize each party's commitment to supporting the entrepreneurs. The S$5 million from the private sector would come from the aforementioned trio of venture capital funds.

Figure 10: Leadership Recruitment Funds Accelerate Commercialization



Source: Milken Institute (2020)

Next Steps:

- Analyze best practices and lessons learned from international talent exchange programs.
- Engage business leaders and smart investment capital to market-test the concept of a Leadership Recruitment Fund.

CONCLUSION

Singapore has overcome vast odds to build a biotech industry from the ground up. The city-state's highly skilled workforce, long-term planning, government support, and pro-business environment have been essential in swiftly transforming both its economy and its basic science ecosystem. But like so many nations, Singapore has struggled to cross the translational valley of death. Singapore's small market and geographic distance from globally established medical hubs like Boston or Silicon Valley are perpetual hurdles in attracting the talent, technology, and capital necessary to complete this ecosystem. Singapore also lacks the range of financial instruments needed to attract a diverse investor base.

The Financial Innovations Lab and follow-up working session discussed ideas to entice talent and leadership to Singapore through creative funding incentives and exchange programs. To broaden investor interest, participants outlined the structure of three venture capital funds that would achieve the goals of bringing talent leadership and capital into the ecosystem. If Singapore is successful in developing its translational research ecosystem, as it has done with basic science, there could be far-reaching economic value and social benefits for Asia and beyond.

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