Submission to the Standing Committee on Science and Research Study on “Support for the Commercialization of Intellectual Property”

BioCanRx
Canada’s Immunotherapy Network
Le réseau canadien d’immunothérapie

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On behalf of BioCanR$_x$

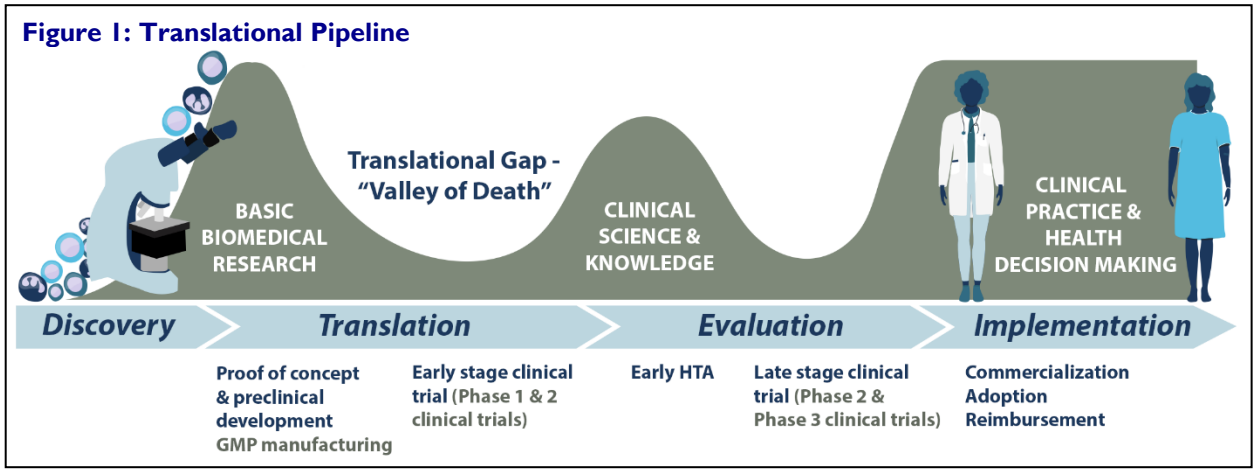
INTRODUCTION

Our ability to capitalize on Canada's health research excellence is dependent on secure and appropriate funding that supports the continuum of health research activities, from discovery to translational and clinical research and onto commercialization. Unfortunately, we are falling short on the current level of federal funding for discovery research and the nonexistence of funding mechanisms to support **translational research** – the area of research that supports the activities necessary to advance a laboratory discovery towards a clinical trial and ultimately, to improving health outcomes and commercialization. Investment in the health research continuum is inextricably linked to the overall performance of our life science ecosystem and how we compare as a country relative to our peers. The current level of federal health research funding is insufficient to ensure Canada's global competitiveness and the relative absence of translational research funding will continue to hamper our innovation potential and commercialization performance, no matter our ambitions. The commercialization of Canadian IP is dependent on overcoming the translational gap or 'valley of death'. For although IP rights are sought out by Canadian researchers via the patent system, it is their ensuing ability to 'work an invention', that is to carry out the necessary translational activities to demonstrate the usefulness of their product in early-phase clinical trials that ultimately lead to the commercialization of that IP.

THE THERAPEUTIC DEVELOPMENT "VALLEYS OF DEATH"

Presently, the term is used to define the lack of both *resources* and *expertise* in the area of product development. In the biotechnology and pharmaceutical arena, two "valleys of death" are common. The first refers to the bench-to bedside translation gap and spans the activities from lead identification and optimization to Phase II clinical trials (**see Fig. 1**). The second occurs when a technology has been validated in a clinical setting and obtains market authorization by a regulatory authority such as Health Canada or the USA FDA but is not yet approved for coverage by provincial governments or private plan payors.

Figure 1: Translational Pipeline



Addressing these "valleys of death" has become a high priority in health research, because the failure to translate research knowledge effectively into practice **is a major barrier preventing human and economic benefit from advances in biomedical sciences and our investments in early-stage research**.

The road from lead identification to market authorization and successful product launch is fraught with failure. However, the highest risk of attrition exists within the activities of the *Translational Gap*. The difficulties in bridging the first 'valley of death' are not only about science but arise largely as a result of structural issues related to funding, expertise gaps and organizational reward structures. Funding to bridge the translational gap is very challenging to obtain as venture capital and the private sector tend to be more conservative and risk-averse in their funding decisions, investing primarily in clinical research or later stages of the research continuum. The *Translational Gap* is also not supported by government health research funding sources. For example, government sources including the USA's NIH and our own CIHR, invest largely in basic research (NIH: 60%; CIHR: 64% and clinical research (NIH: 30%; CIHR: 17%, not including the recent one-time BLSS $250M Clinical Trial Fund investment). The *e*xpertise needed to carry an innovation forward through the translational gap 'valley of death' is beyond the reach and experience of those conducting government-supported basic research.

Translational research embodies a broad range of scientific, manufacturing, toxicology, regulatory and clinical disciplines. To be successful requires extensive collaboration between basic discovery scientists, toxicologists, assay developers, manufacturing process engineers, statisticians, regulatory experts and the clinical scientists who design and conduct human studies. Access to specialized facilities and the individuals within them, such as GMP biomanufacturing and advanced bioanalytics, are critical to advance a discovery from the lab to a GMP-compliant therapeutic that will be used within a clinical trial. Academic research structures contribute to the *Translational Gap* by rewarding individual success and not the collaborative effort required for translational research. Finally, the activities of translational research do not generally lend themselves to rapid publications in high-impact journals, the standard metric of success in basic research, further limiting the participation of researchers in these activities.

INTERNATIONAL EFFORTS TO ADDRESS THE TRANSLATIONAL GAP IN HEALTH RESEARCH

These pervasive structural issues have been carefully studied by government funders in the United States (USA), United Kingdom (UK) and European Union (EU) leading to the launch of specific funding initiatives and specialized centres whose mission it is to address these challenges head on. Examples of such initiatives include the US National Centre for Advancing Translational Sciences (NCATS) launched in 2011 to "shorten the journey from scientific observation to clinical intervention so that new treatments and cures for diseases can reach patients faster"; 2021 funding for NCATS was $855.5M USD. In 2008, the UK Medical Research Council (MRC) introduced a program of initiatives directed toward supporting early phase, academic-led, translational research projects to fund the continuum of translational research activities to address the findings of the 2006 review of health research. As of 2018, the UK health research funding ecosystem was overhauled to fund the translational continuum to address both the first and second valley of death (£814M BP for MRC-UK Research and Innovation (UKRI) and £1.2B for the National Institute for Health and Care Research (NIHR)). The EU's Innovative Medicines Initiative (IMI) is a €5.3 billion, 13-year initiative focused on providing funding to areas of translational research with major unmet needs. The EU also operates a translational research support initiative known as the European Advanced Translational Research Infrastructure in Medicine (EATRIS), which is similar in some aspects to NCATS to support researchers in developing their biomedical discoveries into novel translational tools.

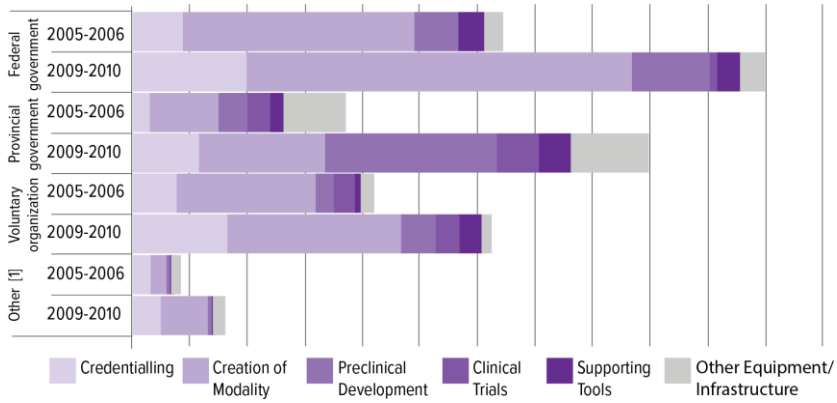
Subsequent evaluations have demonstrated the value of these investments in accelerating the process of translation and keeping "*homegrown*" discoveries within their jurisdiction while enabling these jurisdictions to rapidly respond to public health crises. As a result of these longer-term investments targeted to bridge the "*valley of death*", these jurisdictions are witnessing greater development and commercialization of novel therapeutics within their borders in addition to novel drug adoption schemes.

That Canada is not internationally competitive in the translation of biotherapeutics from the laboratory to the clinic to commercialization has been documented in numerous federal reports, acknowledged in the 2021 Biomanufacturing and Life Science Strategy and witnessed by all Canadians during the pandemic. Although we have supported pockets of excellence and innovation in biotherapeutic discovery, we lag behind the USA, the UK and the EU in our ability to translate our discoveries into clinical trials and then, commercial products. This deficiency is largely because as a country, we have not had a coherent ***investment strategy*** that links infrastructure, expertise, funding and training of HQP to carry out the critical bridging activities required to take a "good idea" all the way through to early-phase clinical testing.

LOST IN TRANSLATION – A LESSON FROM THE CANADIAN CANCER RESEARCH ECOSYSTEM

Canada remains well behind our OECD peers in the global innovation competition, including early cancer research investment, and unlike our UK, EU and USA peer countries, has not strategically invested in the support of translational research. The recent June 2022 Canadian Cancer Research Alliance (CCRA) report on Fifteen Years of Investment in Cancer Research in Canada, reported a $7.4B investment in cancer research in Canada from 2005 to 2019. In keeping with the OECD's findings regarding overall Canadian research investments relative to GDP, Canada was found to spend 'at levels well below our comparator countries' (UK and USA) in ***cancer*** research. Despite this lower investment relative to others, we also as a nation spent much *less* over the period under examination to generate a cancer research publication than the UK and USA, in effect 'getting more for our buck'. And although Canada ranks fourth in issued number of papers in cancer research (following USA/UK/Germany), we rank first in article citation frequency, indicating high average quality of the publications and of our science.

Figure 2: Investment in "Early Translational Drug Research" by Phase for Each Funding Sector, 2005-2006 and 2009-2010



The translational gap is particularly acute in oncology. Cancer cost Canadians $26.2B in 2021 alone, from combined losses of wages, taxes, out-of-pocket expenses, corporate profits, and direct healthcare costs. Yet despite the enormity of the social and economic cost, Canada spends approximately $500M/year on cancer research, most of it in early stage discovery research, amounting to about 2% of the overall annual cost of cancer. Of this**, less than 0.5% is invested in the type of translational research work carried out by BioCanR$_x$ that is necessary to launch clinical**

trials based on Canadian innovation and advance the commercialization of Canadian IP. With the exception of provincial funders (attributable almost exclusively to the Ontario Institute of Cancer Research (OICR)), Canadian funders predominantly invest in early-stage research, i.e. *Credentialing* and *Creation of Modality* as is shown in **Figure 2** above.

Although we have supported pockets of excellence and innovation in biotherapeutic discovery, we lag behind the USA, Europe and the UK in our ability to *translate our discoveries into commercial products*. As depicted in Figure 1, there is ***little to no funding*** in Canada to support stepwise preclinical to clinical translation as funders have concentrated their investments in early-stage research.. This, combined with the very high costs related to biologics development, has created a **funding and expertise gap** between traditional Government/NGO-supported research and the biotech/pharmaceutical industry that prevents the transfer of novel biotherapies out of Canadian labs to early-stage trials within Canada. Discoveries made in Canada typically see their movement up the value chain take place in the USA or elsewhere. As a result, we do not reap economic benefit from the commercialization of intellectual property arising from our cancer research investments and do not as a country benefit from early access to novel biotherapeutics via clinical trials, to the detriment of patients, their families and the Canadian taxpayer.

It is unconscionable that we do not follow through with these findings and support those organizations such as BioCanR$_x$ that are addressing the translational gap and delivering concrete results for companies and Canadians. BioCanR$_x$ investments in translational research and bridge the gap between bench to bedside directly support the **required activities for the commercialization of Canadian intellectual property (IP**).

Canada spends approximately $500M on cancer research every year, most of which is invested in early-stage research (70%).

From 2002-2022 less than 4% (30 out of 707) immunotherapy clinical trials run in Canada were based upon discoveries made in our own laboratories.

Of the 30 clinical trials based on home-grown innovation, ***43% are directly attributable to the BioCanR$_x$ translational research program.*** *This represents a substantial improvement over prior data: fewer than 1% of clinical trials in Canada were based on Canadian innovation between 2002-2015.*

About BioCanR$_x$

BioCanR$_x$ is Canada's Immunotherapy Network. We are a network of scientists, clinicians, cancer stakeholders, academic institutions, NGOs, and industry partners working together to accelerate the development of leading-edge immune oncology therapies for the benefit of patients. We invest in world-class translational research, to carry out our **Mission** of accelerating to the clinic the most promising cancer immunotherapies designed to save lives and enable a better quality of life to reach our **Vision** of turning all cancers into curable diseases. Since 2015, BioCanR$_x$ has taken a leadership position in Canada integrating, coordinating, and securing alignment of research investments, infrastructure, skills training,

patient engagement, biomanufacturing, public, not-for-profit (NFP) and private sector partnerships to advance translational research and rapidly deliver **novel, made-in-Canada immunotherapies** to Canadian cancer patients via early-stage clinical trials.

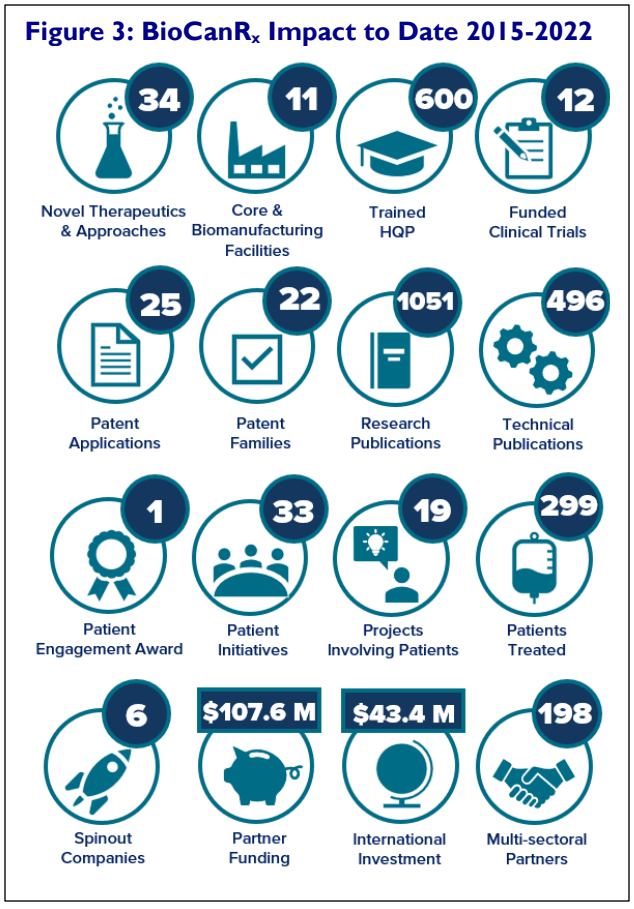
We train and develop the talent needed for a thriving Canadian health biotechnology sector, including GMP biomanufacturing, delivering a training program that has earned numerous awards for its approach to inclusion, diversity, equity and accessibility. BioCanR$_x$ has received funding from the federal government's Networks of Centres of Excellence (NCE), and support from industry, the provinces, and charities.

Partnering with academic institutions and ST& I partners, our mission-drive invests in three overarching program activities:

1) **Enabling collaborative, world-class translational cancer research** benchmarked to international efforts and accelerating the development of immunotherapies to the clinic, expanding the immunotherapy pipeline in Canada and capitalizing on our excellent early-stage investments in cancer research;
2) **Strengthening Canada's capacity to undertake world-class translational cancer research** by developing talent using an inclusive lens and facilitating access to and sustaining leading-edge facilities, GMP biomanufacturing and translational research expertise, promoting collaboration and partnerships across the STI ecosystem;
3) **Working with ST&I partners to advance commercialization in Canada and the adoption of novel therapies into our healthcare systems** for the benefit of the health and wealth of Canada.

Our approach to supporting iterative translational cancer immunotherapy development activities is **unique in Canada** and has yielded a high performing and lauded program that is providing curative therapies to Canadian cancer patients, today and moving the needle on Canada's translational gap (Figure 2) This approach is already driving transformational change in the health research ecosystem (i.e. CAR T-cell program) and **represents a shining example of what a present-day, successful implementation of the 2021 BLSS** looks like in the area of cancer research. By capturing the value of Canada's investments in early-stage cancer research and infrastructure, we are addressing an acute **health** system need critical to the well-being of Canadians, building up our translational research capacity to support **wealth creation and commercialization of IP** within the life sciences sector. The economic argument cannot be understated: the global market for cancer immunotherapy is projected to hit $350.9 billion Canadian dollars (CAD) by 2030 based on a combined annual growth rate (CAGR) of 12.6%. It is imperative that Canada captures the economic benefits of its long-term investments in early-stage

Figure 3: BioCanR$_x$ Impact to Date 2015-2022

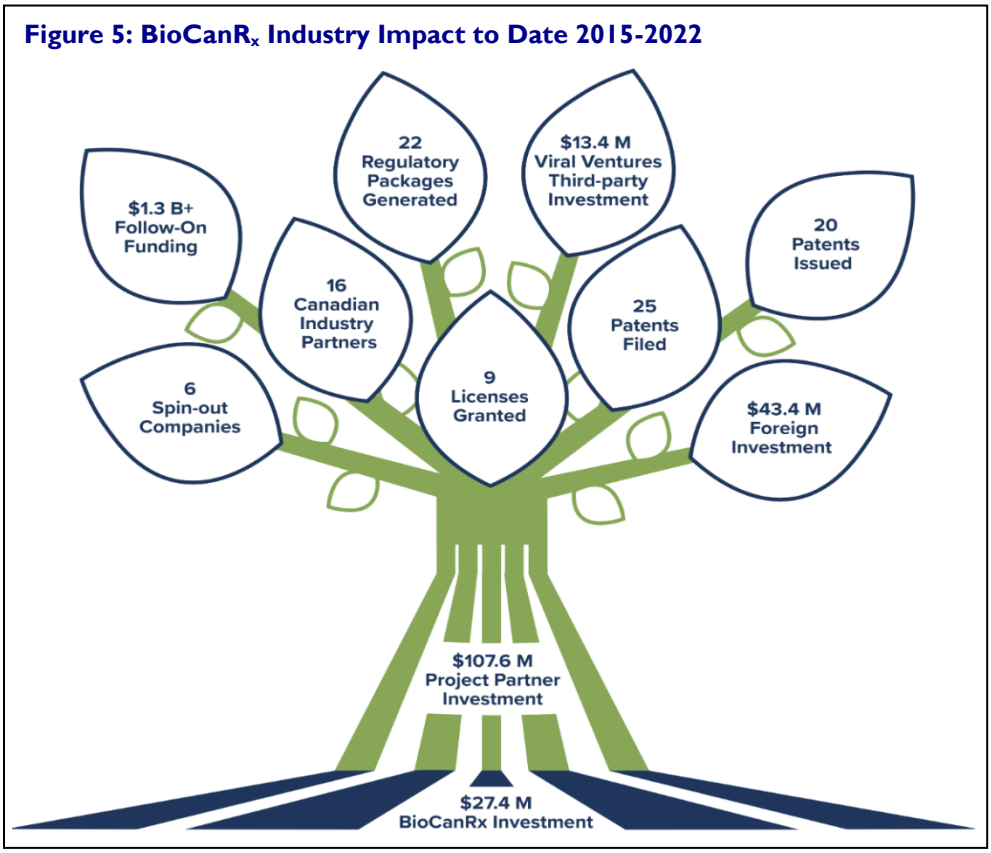


cancer research in this high growth area to support the genesis of new companies and scale existing entities to capture the enormous potential **economic benefit** for Canadians. Our impact to date demonstrates the attractiveness and pent-up demand for an integrated, efficient, and effective national translational cancer research engine in the life sciences for the development of cancer immunotherapies (**Figure 3**).

PAVING THE WAY FOR COMMERCIALIZATION OF IP

The BioCanR$_x$ translational research program accelerates the clinical development of novel immunotherapies using a staged pipeline system. This has yielded tangible results as projects have advanced along the development pipeline from pre-clinical development to clinical evaluation. As projects meet their milestones by progressing through the pipeline, they attract follow-on investment by other sector partners. The advancement of a new therapeutic approach towards the clinic has resulted in multiple commercialization outputs as shown in Figure 4, including $1.3B follow-on investment to projects and spin out companies seeded by a BioCanR$_x$ investment of $27.4M overall as of 2015.

Figure 5: BioCanR$_x$ Industry Impact to Date 2015-2022



The advancement of a new therapeutic approach towards the clinic has resulted in multiple commercialization outputs that have and will continue to maximize our long-term impact: Commercialization not only benefits BioCanR$_x$ researchers, but the entire biotechnology industry in Canada as well as the ultimate stakeholder, patients in search of better treatments.

A number of spin out companies have been created by BioCanR$_x$ researchers who acknowledged BioCanR$_x$ funding as a critical support in enabling company creation and/or growth. Entrepreneurial BioCanR$_x$

researchers also note the importance of accessing the network expertise and core facilities in advancing their asset development.

Figure 6: BioCanR$_x$ Industry Partners & Spin Out Partners (bottom row)

CONCLUSION

Underinvestment in health research is not an option – it undermines Canada's future. To ensure maximum impact in our health research investments via commercialization, Canada must take a whole of ecosystem approach and fund the entire health research continuum, including translational research. Failure to do this will further hamper Canada's ability to respond to future pandemics and our ability to capitalize on our discoveries for the benefit of Canadians. BioCanR$_x$ plays a highly unique role in the Canadian landscape to support *translation* of novel immunotherapies for the treatment of cancer as translational research is an area that Canada has not strategically developed nor invested in. Successful execution of translational projects in the development of therapeutics is highly resource intensive, requiring an extensive level of coordination, expertise and a continuum of funding. Translational research is also the only path to delivering results from our homegrown discoveries to Canadian patients and Canadian companies to commercialize our IP. BioCanR$_x$ has demonstrated this is possible, delivering results not only for our patients but for our country's innovation performance and economy.

The recent Report of the Standing Committee on Finance highlighted the importance of translational research on the topic of industry and innovation to foster economic growth through increased investments and incentives in the field of science and technology. Recommendation 143 is directly aligned to the mission and vision of BioCanR$_x$ and states:

Develop, as part of the implementation and evolution of the Biomanufacturing and Life Science Strategy, a funding strategy for mission-oriented organizations focused on translational research supporting preclinical to clinical development.

RECOMMENDATIONS

1) That as part of its study on the commercialization of IP, the Science and Research Committee examine the impact on the lack of funding for translational cancer research in Canada and the necessity of funding mission-oriented organizations focused on translational research supporting preclinical to clinical development to overcome the 'valley of death' in health research.

2) Maintain the significant momentum achieved by BioCanR$_x$ in advancing translational cancer research in Canada by providing gap funding of $12M for the period of FY2023-24 to address the March 31, 2023 funding cliff resulting from sunsetting of the Network of Centres of Excellence (NCE) program, regardless of whether we are successful in other funding avenues (i.e. Strategic Science Fund beginning April 01, 2024).

3) As part of advancing the Biomanufacturing and Life Sciences Strategy (BLSS), the Government of Canada commits to funding BioCanR$_x$, an organization with a proven track record that is currently delivering on the objectives of the Strategy, for a period of not less than five years at a level of $12M/y to ensure the continuation of its project pipeline and life-saving clinical trials using made-in-Canada immunotherapies.