



Ontario Institute for Cancer Research

Strategic Plan 2016-2021

9 November 2015

Table of Contents

Executive Summary	3
A. Introduction	9
A.1. Background	9
A.2. Progress to date	12
A.3. Highlights of OICR’s impact (2007-2015)	13
A.4. Context for the Strategic Plan 2016-2021	16
B. Strategic Plan (2016-2021)	19
B.1. Development of the strategy	19
B.2. Rationale for Strategic Plan 2016-2021	20
B.3. Transition to a new blueprint	20
B.4. Strategic Initiatives	23
B.5. Technology Programs	38
B.6. Catalyzing translation and patient impact	41
C. Achieving Results	44
C.1. Governance	44
C.2. Leadership	44
C.3. Enablers	44
C.4. Outreach and communications	45
C.5. Measuring performance	45
D. Implementation Roadmap	48
E. Conclusion	52
Appendix I: Preliminary focus and scope of TRI themes	53
Appendix II. Description of select Global Leadership in Precision Oncology initiatives	58
Appendix III: Glossary	60

Executive Summary

Context. Every hour of every day, eight people in Ontario are diagnosed with cancer and three die from the disease. It is projected that Ontario will see a 46 per cent increase in cancer patients by 2030, mainly driven by the aging of the population. Cancer currently costs Ontario more than \$1.5 billion annually and the rise in cancer cases will impose an escalating burden on the Ontario population, our healthcare system and the economy.

At the same time, owing to now deeper understanding of cancer biology, there is growing optimism that we are on the cusp of real breakthroughs against the disease. Recognizing a strategic opportunity for Ontario, the province established the Ontario Institute for Cancer Research (OICR) in 2005 to mobilize the province's cancer research strengths and catalyze the translation of clinically important knowledge, products, services and policies to improve cancer prevention, detection, diagnosis and treatment. Headquartered in Toronto's MaRS Discovery District, OICR is a collaborative translational research network that brings together and focuses scientific excellence across the province on key areas of unmet medical need for cancer patients. OICR partners with Ontario's oncology research and clinical community and the private sector to tackle projects that are complex and large in scope, facilitating transfer of knowledge, risks and costs to drive the adoption and/or commercialization of cancer innovations so that the people of Ontario and the economy benefit from promising research results and breakthroughs.

Vision

A collaborative centre of excellence in cancer research that moves Ontario to the forefront of discovery and innovation so that the people of Ontario and the economy benefit from promising research results and breakthroughs.

Mission

Partner with the Ontario oncology community to accelerate the development and implementation of clinically important knowledge, products, services and policies to improve cancer prevention, detection, diagnosis and treatment and enable patients in Ontario and worldwide to live longer and better lives.

OICR has set the following five overarching **Goals** to realize its ambitious mandate:

1. **Perform cutting-edge translational cancer research:** Undertake world-class transformative research focused on solving pressing clinical challenges to improve cancer prevention, detection, diagnosis and treatment.
2. **Mobilize Ontario research strengths around key cancer priorities:** Focus provincial expertise and capacity on collaborative, multi-disciplinary translational research activities aimed at addressing unmet clinical needs for cancer patients in Ontario and beyond.
3. **Partner with the Ontario cancer community to leverage and elevate the level and impact of cancer research in the province:** Provide access to resources, expertise, technologies and training opportunities to strengthen Ontario's translational research capacity.
4. **Drive the adoption and/or commercialization of cancer innovations in Ontario:** Collaborate with healthcare providers/agencies and private sector partners to

ensure that Ontario discoveries realize their potential to improve cancer outcomes and deliver economic benefit to Ontario.

5. **Enhance Ontario's global leadership in cancer research:** Undertake national and international initiatives where Ontario can provide leadership and unique expertise to tackle major challenges in translational cancer research.

OICR's activities are focused on three **Translational Research Priorities**:

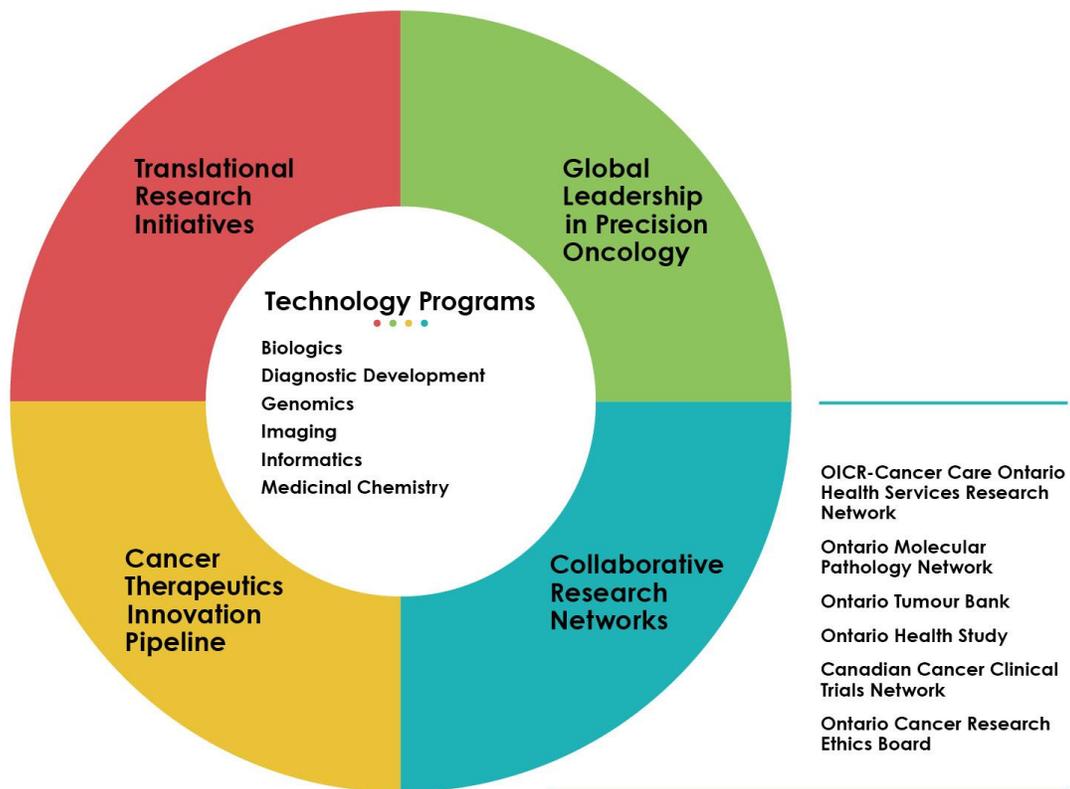
1. *Therapeutic Innovation:* Finding new ways to treat difficult cancers;
2. *Clinical Impact:* Optimizing cancer patient management and treatment decisions;
3. *Population Health:* Driving improvements in cancer prevention and care delivery.

To date, OICR's investments have supported a critical mass of leading-edge scientists, clinicians and companies addressing the growing burden of cancer. Ontario is already beginning to see a return on its investment, through innovative technologies for diagnosing and treating cancer patients, evidence-based strategies for improving healthcare delivery and cost-effectiveness, as well as economic benefits, including high-quality jobs, increasing private sector investment and a growing cluster of oncology companies taking shape in the province.

In November 2014, OICR underwent an external review by an international expert panel, which identified several areas of strength and provided specific guidance for augmenting the Institute's impact. Recommendations included increasing interactions with the Ontario oncology community and enhancing the overall capabilities of Ontario cancer research, both basic and translational. The panel also identified areas where OICR could partner to fill gaps and provide the scientific capabilities required for Ontario to excel in translational research. Subsequent discussions with researchers, clinicians and leaders of public and private organizations on how to address the recommendations and increase synergies within the Ontario oncology ecosystem have informed the development of Strategic Plan 2016-2021.

OICR's Blueprint (2016-2021). Strategic Plan 2016-2021 advances OICR's mission, goals and translational research priorities, builds on the strong foundation that has been laid and identifies opportunities where Ontario can excel in the context of the global cancer research landscape. Importantly, Strategic Plan 2016-2021 calls for a realignment of OICR's organizational blueprint to provide the integration, focus and coordination of efforts required to drive promising Ontario assets coming out of the Institute's early research efforts toward the clinic and commercial opportunity, and to provide avenues for greater engagement and partnership with Ontario cancer centres and research institutes, the private sector, government agencies, patients and other stakeholders to maximize opportunities for translating Ontario science into better cancer outcomes and economic benefit.

Accordingly, OICR's new blueprint will consist of four ambitious and collaborative **Strategic Initiatives** supported by six cutting-edge **Technology Programs** that provide expertise, resources, cutting-edge technologies and analytics:



OICR’s Blueprint (2016-2021). OICR’s research activities are focused within four Strategic Initiatives, supported by six cross-cutting Technology Programs, which collectively advance OICR’s translational research priorities of Therapeutic Innovation, Clinical Impact and Population Health.

A. Translational Research Initiatives (TRIs) will be the main translation engines of the Institute: large-scale, multi-disciplinary collaborations between laboratory and clinician scientists focused on translating Ontario assets or knowledge to address important medical needs of cancer patients. TRIs usually consist of two to five complementary projects addressing clear clinical priorities in areas that build on unique scientific strengths/ competitive advantage and critical mass of researchers and clinicians in Ontario. Proposed themes under consideration, which have already demonstrated high potential for transdisciplinary partnership and patient impact, are early breast cancer, early prostate cancer, immuno-oncology, leukemia, esophageal cancer, brain cancer and ovarian cancer. Key deliverables will include the discovery and preclinical validation of assets (targets, drug candidates, biomarkers, diagnostic and imaging probes and devices); validation of the clinical utility of assets; partnerships for further development and/or commercialization of assets; and uptake of assets by healthcare agencies or providers. The ultimate measure of TRI success will be demonstrable impact on patient outcomes and/or healthcare delivery.

B. Global Leadership in Precision Oncology will leverage Ontario’s global leadership in cancer clinical trials, genomics and Big Data to improve patient management and tailoring of interventions to individual patients. OICR will partner with cancer centres and academic institutions in Ontario to strengthen and catalyze translational cancer genomics research in the province, and will continue to lead and contribute to global precision oncology initiatives that generate the robust datasets and insights critical for guiding patient management and treatment decisions and ultimately, improving cancer outcomes. Provincial initiatives will

include partnerships with the Princess Margaret Cancer Centre (PM) and other Ontario cancer centres to establish the Ontario-wide Cancer TArgeted Nucleic acid Evaluation (OCTANE) alliance to increase next generation sequencing of cancer patients in Ontario and the establishment of the PM-OICR Translational Genomics Laboratory to develop, evaluate and translate advanced genomics/"omics" diagnostic tests. Global initiatives will include renewed commitments to the International Cancer Genome Consortium (ICGC), the Global Alliance for Genomics and Health (GA4GH) and advancing Big Data analytics to support cancer genome interpretation. While the details of the various components will be further defined in the coming months, broad indicators of success will include: (a) *translational cancer genomics in Ontario*: improved access of Ontario cancer patients to genomics testing at Ontario labs; genome-based analyses that inform clinical trials evaluating novel immune and targeted therapies; increased opportunities for genomics-based clinical research in Ontario; and greater collaboration between Ontario cancer centres; (b) *global partnerships in precision oncology*: recognition of Ontario's global leadership in cancer genomics, informatics and Big Data analytics, which attracts highly qualified personnel, clinical trials and private sector investment to the province; and translation of results from large-scale global initiatives to seed new diagnostic and therapeutic approaches and clinically-actionable guidelines that inform patient management and treatment, and ultimately improve cancer outcomes.

C. OICR's Cancer Therapeutic Innovations Pipeline strategy will address a clear gap in early oncology drug discovery, where there is limited funding available and assets are often too risky to attract private sector interest. It will capitalize on Ontario's expertise in medicinal chemistry, biologics and structural biology to advance promising discoveries into lead compounds (small molecules or biologics) that have the potential to attract partners for further development. OICR will support early stage Accelerator projects focused on target validation and high-throughput screening that deliver *in vitro* validated targets, structures, tool compounds, new pre-clinical models, new assays, novel chemistries and biologics, and new computational pharmacogenomic platforms; and Incubator projects focused on hit assessment and lead identification that yield high-quality lead compounds and biologics with demonstrated *in vivo* efficacy correlated with a pharmacodynamic biomarker that attract partnerships/investment for further development and ultimately commercialization.

D. OICR will continue to invest in five **Collaborative Research Networks** (OICR-Cancer Care Ontario Health Services Research Network; Ontario Health Study; Ontario Tumour Bank (OTB); Canadian Cancer Clinical Trials Network (3CTN); and Ontario Cancer Research Ethics Board (OCREB) that facilitate translational cancer research in Ontario, and the Institute will establish a new Ontario Molecular Pathology Network to bolster research capacity, collaboration and leadership in cancer pathology at cancer centres in Ontario. While specific indicators of success will vary across the different networks, the Collaborative Research Networks will collectively improve Ontario's ecosystem and capabilities for undertaking high-quality translational research by providing access to shared expertise, resources and enabling infrastructure.

OICR's six **Technology Programs** (Biologics, Diagnostic Development, Genomics, Imaging, Informatics and Medicinal Chemistry) will build on a strong legacy of cancer research developed during OICR's first two mandates and leverage a critical mass of principal investigators and staff scientists who deliver innovation, provide state-of-the-art technological expertise and support analytics for data interpretation. Technology Programs will contribute expertise to one or more of the Strategic Initiatives and strengthen collaboration with Ontario's scientific and clinical community to capitalize on the state-of-the-art infrastructure established by the Ministry of Research and Innovation's (MRI) investment. Support may include technical services/training related to the development of

leading-edge technologies and databases, access to OICR resources (equipment, data and samples) as well as advisory services on study design, choice of technologies, methods and data analyses. Technology Programs will be monitored on an ongoing basis for accessibility, collaboration, capacity usage, performance and user satisfaction.

In addition and closely tied to OICR's Strategic Initiatives, OICR will provide support for attracting and developing the next generation of Ontario cancer research leaders, the design and facilitation of clinical trials and commercialization of Ontario assets to yield economic benefit to Ontario:

- *Development of highly qualified personnel.* OICR will continue its Investigator Awards Program to attract and retain outstanding research and clinical investigators to Ontario. Priority will be given to the recruitment of the clinician scientists who will play an important role in the Strategic Initiatives to maximize the clinical utility of OICR-funded research, as well as young investigators who will constitute the next generation of Ontario leaders. In addition, OICR will continue supporting a number of training opportunities, including Transformative Pathology research fellowships, hosting of the Canadian Bioinformatics Workshops and training of undergraduate and graduate-level students associated with OICR-supported research projects;
- *Clinical trials.* OICR will expand its support of clinical trials to evaluate Ontario assets as part of its Strategic Initiatives and through key partnerships with industry and funding agencies. OICR will partner with Ontario clinical trials groups and facilitate trial implementation by helping to identify common hurdles across the clinical trials portfolio and address them in an effective, timely manner. Approaches will include support for trial design and planning, partnership facilitation to enable complex "omics" or imaging testing, and biostatistics training;
- *Commercialization and economic benefits.* The Fight Against Cancer Innovation Trust (FACIT), which operates as an independent business trust with OICR as its sole beneficiary, houses all of the commercial assets and related intellectual property (IP) owned by the Institute, and has become a vehicle through which Ontario oncology assets can be further developed and commercialized. OICR and FACIT will continue to accelerate the development of promising academic discoveries to a proof of concept/inflection point that will be of interest to the private sector/other partners committed to bringing health innovation and economic benefits to Ontario. With ongoing support from Ontario, OICR and FACIT project the creation of 12 more viable companies in Ontario, the attraction of investments of \$60-100M/year in Ontario companies and the creation of more than 2,000 company-related jobs over the next five years.

Achieving Results. OICR is accountable to the people of Ontario. Excellence in governance, leadership and management, an engaged workforce, high-quality and efficient operational processes, effective outreach and communications, and a robust approach to measuring the performance and impact of the Institute are essential to deliver on OICR's ambitious mandate. Management will continue to work with Ontario scientific and clinical leaders to develop and refine the structures and processes needed for the effective implementation of Strategic Plan 2016-2021, ensuring that the Institute remains nimble and able to capitalize on emerging opportunities to advance its mission, goals and strategic priorities.

In 2005, the Ontario government made a strategic investment to harness and capitalize on the substantial pockets of cancer research strength in the province to accelerate the

translation of discoveries into better patient outcomes and economic benefit. OICR has since supported the recruitment of a cadre of outstanding cancer investigators to Ontario, catalyzed high quality research around key cancer priorities, and worked to fill gaps in translational cancer research capacity in the province. With a robust pipeline of innovative assets poised to reach the clinic over the next five years, as well as important and timely initiatives being launched to foster collaboration and bolster translational research excellence within the Ontario oncology ecosystem, the people of Ontario are on the verge of realizing the transformative impact of their investment.

A. Introduction

A.1. Background

In Ontario, 40 per cent of the population will receive a diagnosis of cancer in their lifetime. Every hour of every day, eight people in Ontario are diagnosed with cancer and three die from the disease. The Canadian Cancer Society predicts that the province will see 76,000 new cancer cases and 28,500 deaths in 2015¹.

The number of new cancer cases is increasing, mainly due to aging of the population. It is projected that Ontario will see a 46 per cent increase in cancer patients by 2030. Cancer currently costs Ontario more than \$1.5 billion (direct and indirect costs) annually and the rise in cancer cases will impose an escalating burden on the Ontario population, our healthcare system and economy².

However, at the same time, owing to now deeper understanding of the biology of the disease, there is growing optimism that significant improvements will be achieved with regard to new prevention, screening and treatment strategies. Ontario boasts a vibrant cancer research community and one of the best healthcare systems in the world, which can be harnessed to devise and develop new technologies and interventions, and translate them to the clinic to improve patient outcomes. Oncology is also globally one of the leading areas of biopharmaceutical industry and private sector investment. Investment flows to jurisdictions where there is a convergence of innovators and institutions rich in research expertise and with healthcare systems that can test and apply breakthrough discoveries.

It was against this backdrop that in 2005 the Ontario government made a strategic investment to establish the **Ontario Institute for Cancer Research (OICR)** to mobilize the province's cancer research strength and drive translation of discoveries into better patient outcomes and economic benefit. Headquartered in Toronto's MaRS Discovery District, OICR is a translational research network that brings together and focuses scientific excellence across the province on key areas of unmet medical need for cancer patients (Figure 1). OICR partners with Ontario's oncology research and clinical community and the private sector to tackle projects that are complex and large in scope, facilitating transfer of knowledge, risks and costs to drive the adoption and/or commercialization of cancer innovations.

¹ Canadian Cancer Statistics 2015 (May 27, 2015), Canadian Cancer Society

² Public Health Agency of Canada, 2008



Figure 1. The OICR translational research network. Map of Ontario indicating cancer centres and major hubs where OICR's research takes place.

Vision

A collaborative centre of excellence in cancer research that moves Ontario to the forefront of discovery and innovation so that the people of Ontario and the economy benefit from promising research results and breakthroughs.

Mission

Partner with the Ontario oncology community to accelerate the development and implementation of clinically important knowledge, products, services and policies to improve cancer prevention, detection, diagnosis and treatment and enable patients in Ontario and worldwide to live longer and better lives.

Values

Excellence – We focus on quality and detail to achieve the highest standard in the work we do and the image we project, both scientifically and ethically.

Innovation – We explore new ideas and methodologies to move product and intervention concepts from the lab to the patient.

Responsiveness – We are accountable to our stakeholders and to each other in conducting our research and interacting with each other – exceeding needs and expectations.

Collaboration – We work respectfully and professionally, within our teams, cross-functionally within the Institute, and with our external partners, sharing knowledge, findings and resources, recognizing the expertise and contribution that each person brings and creating momentum collectively to achieve our goals.

Pride – We are passionate about the satisfying work that we do and the impact that it has for patients in improving prevention, early detection, diagnosis and treatment of cancer.

Goals

- 1. Perform cutting-edge translational cancer research:** Undertake world-class transformative research focused on solving pressing clinical challenges to improve cancer prevention, detection, diagnosis and treatment.
- 2. Mobilize Ontario research strengths around key cancer priorities:** Focus provincial expertise and capacity on collaborative, multi-disciplinary translational research activities aimed at addressing unmet clinical needs for cancer patients in Ontario and beyond.
- 3. Partner with the Ontario cancer community to leverage and elevate the level and impact of cancer research in the province:** Provide access to resources, expertise, technologies and training opportunities to strengthen Ontario's translational research capacity.
- 4. Drive the adoption and/or commercialization of cancer innovations in Ontario:** Collaborate with healthcare providers/agencies and private sector partners to ensure that Ontario discoveries realize their potential to improve cancer outcomes and deliver economic benefit to Ontario.
- 5. Enhance Ontario's global leadership in cancer research:** Undertake national and international initiatives where Ontario can provide leadership and unique expertise to tackle major challenges in translational cancer research.

Box 1. Translational research fosters the multidirectional integration of fundamental research, patient-oriented research and population-based research to proactively move discoveries made in the laboratory, at the patient's bedside and in the community into effective health interventions. Translational research entails the collaboration of multidisciplinary teams connecting discovery research with clinical expertise and downstream stakeholders (healthcare providers and payers as well as the private sector).

Translational Research Priorities

OICR's translational research activities are focused on three priorities to ensure maximum impact and promote collaboration between teams toward well-defined outputs:



Find new ways to treat difficult cancers.



Optimize cancer patient management and treatment decisions.



Drive improvements in cancer prevention and care delivery.

A.2. Progress to date

Strategic Plan 2007-2010

In the implementation of its first mandate (2007-2010), OICR focused on start-up activities to establish the Institute and its research programs. Infrastructure in the province was created or enhanced and 30 outstanding investigators were recruited from within Ontario as well as from several leading cancer research institutes and companies located in other Canadian provinces, the United States and Europe.

Strategic Plan 2010-2015

In the implementation of OICR's second mandate (2010-2015), the Institute fortified its scientific base to address important clinical questions impacting cancer care and accelerate translational cancer research in the province. Strategic Plan 2010-2015 articulated four objectives:

1. Facilitate the adoption of more personalized medicine for cancer.
2. Seek solutions to clinical issues that could benefit patients in the next five years:
 - i. High fatality rate of pancreatic cancer;
 - ii. Over-diagnosis of prostate cancer;
 - iii. Over-aggressive treatment of early stage breast cancer;
 - iv. Maximizing participation in population-based screening programs with a focus on colon cancer screening;
 - v. Long-term adverse effects affecting children and young adults.
3. Enhance and facilitate digitization and interpretation of cancer data.
4. Accelerate OICR's Patents to Products Program.

The Institute prioritized research themes where Ontario scientists are internationally renowned, such as cancer stem cells, novel immunotherapies, medical imaging and health services/population research, and where tremendous new global opportunities in cancer research were unfolding, such as the International Cancer Genome Consortium (ICGC). For each of these themes, OICR ensured that resources and capabilities were available in the

province to conduct the research. A disciplined approach was developed to select projects that were addressing well-defined medical needs and to monitor progress to ensure that discoveries would move along the translational research roadmap towards the clinic and the broader healthcare community (Figure 2). Strategic partnerships were formed with funding agencies, Ontario’s academic research centres, hospital and healthcare agencies and the private sector, to bring expertise and resources needed to support the development of novel diagnostics, screening approaches, therapeutics and population interventions.

Discovery	Early Translation	Late Translation	Dissemination	Adoption
<p>Discovery and pre-clinical validation of new drug targets, drug discovery assets, biomarkers, diagnostic and imaging probes and devices</p> <p>Identification of gaps and potential solutions to improve delivery of cancer prevention, screening or care</p> <p>Development of research technologies/platforms/assets</p>	<p>Last stage of pre-clinical and early clinical development (Phase 0-II) trials of drug candidates, biomarkers, diagnostics and imaging probes and devices</p> <p>Testing of new health services interventions</p> <p>Development of clinical research tools/platforms/assets</p>	<p>Late clinical development (Phase III trials, regulatory approval, or equivalent) of drugs, biomarkers, diagnostics and imaging probes and devices</p> <p>Implementation research to support dissemination and adoption</p>	<p>Dissemination, uptake, post-market evaluation (Phase IV trials or equivalent) of drugs, biomarkers, diagnostics and imaging probes and devices</p> <p>Implementation of research to understand the barriers to dissemination of new services or treatment interventions</p>	<p>Adoption of new drugs, biomarkers, diagnostics and imaging devices by healthcare providers, researchers, patients and/or the public</p> <p>Health services research to evaluate and optimize patient outcomes</p>

Figure 2. Stages of the Translational Research Roadmap. It is important to note that translation is often not a linear process; i.e., discoveries that lead to implementation in the clinic can, in turn, lead to new research questions. Consequently, a late research finding (i.e., classified in the late translation, dissemination or adoption stages) may lead back to discovery or early translation research. Creating a nimble environment that can facilitate this iterative process has been a high priority for OICR.

OICR created the Fight Against Cancer Innovation Trust (FACIT), a new business entity to enable and manage the commercial development of OICR’s and Ontario’s oncology assets, attract investment and bring economic benefits to the province. FACIT houses all of the commercial assets and related intellectual property (IP) owned by the Institute and has become a vehicle through which promising Ontario oncology assets can be further developed and commercialized.

A description of progress against the priorities outlined in the Strategic Plan 2010-2015 can be found in the [OICR Outcomes and Benefits Report \(2007-2014\)](#).

A.3. Highlights of OICR’s impact (2007-2015)

Over the past eight years, the Institute has made substantive progress towards achieving its vision of strengthening cancer research in the province, improving patient outcomes and delivering economic benefit to Ontario.

Translational research excellence in Ontario

OICR created an Investigator Awards Program to recruit and retain outstanding researchers and clinician scientists in Ontario; the 33 awardees currently supported by the program at Ontario research institutions and cancer centres have enhanced the translational cancer research capacity in the province. Together with hundreds of additional cancer researchers

involved in OICR-supported programs, they have published 2,444 peer-reviewed scientific articles (2010-2015), with a high proportion in the most influential scholarly journals in the world.

The OICR community supports the development of the next generation of cancer researchers, with more than 400 undergraduate and graduate-level trainees (MDs as well as PhDs) associated with OICR-supported research projects. In addition, the Institute supports a number of targeted training opportunities, including a biostatistics internship program supporting oncology clinical trials; Transformative Pathology fellowships supporting trainees and early career clinician scientists at institutions across the province; and by hosting of the Canadian Bioinformatics Workshops, which trains more than 200 basic and clinical researchers per year.

Box 2. *"The establishment of a major cancer research institute by the province of Ontario to accelerate the translation of scientific discovery into individual, societal and economic benefit was visionary, innovative and prescient. **Seven years into this initiative, the province has much to be proud of.**"*
International Expert Panel, 2014

OICR hosts the Ontario Cancer Research Ethics Board (OCREB) and the Canadian Cancer Clinical Trials Network (3CTN), which streamline the conduct of cancer clinical trials in the province (and nationwide) so that cancer patients gain access to investigational agents and rigorous clinical testing is completed before adoption of new treatment modalities.

OICR is also a founding partner of four Networks of Centres of Excellence (NCEs) that are advancing novel cancer diagnostic and therapeutic solutions:

	<ul style="list-style-type: none"> • Network hosted at McMaster University; • Launched in 2008 (\$28.8M award/10 years); • Supplied medical isotopes to diagnose and treat more than 10,000 cancer patients; • Launched 12 clinical trials of new imaging probes; • Developing radio-labeled agents as new diagnostic and therapeutic modalities.
	<ul style="list-style-type: none"> • Network co-hosted at Western University and Sunnybrook Hospital; • Launched in 2011 (\$13.3M award/5 years); • Spun out two cancer diagnostic imaging companies: Enhanced Medical and Focal Healthcare; • Completed system for focal liver ablation currently in clinical evaluation and in licensing discussions with industry; • Filed seven patent applications.
	<ul style="list-style-type: none"> • Network hosted at the University of Toronto; • Launched in November 2014 (\$15M award/5 years).
	<ul style="list-style-type: none"> • Network hosted at the Ottawa Hospital; • Launched in December 2014 (\$25M award/5 years).

Global leadership

OICR investments in promising areas of cancer research have helped to anchor Ontario at the leading edge of cancer genomics, Big Data and cancer stem cells, which build a new foundation for precision medicine and therapeutic discovery, and unlock new opportunities for the Ontario cancer research community. For instance, OICR launched and coordinates the ICGC, a global collaboration involving 89 project teams in 17 jurisdictions focused on comprehensively elucidating the genomic changes present in 50 tumour types/sub-types that contribute to the burden of disease in people throughout the world. In addition, OICR is a co-founder and co-host of the steering committee of the Global Alliance for Genomics and Health (GA4GH) involving 365 organizations from 35 countries working together to create a common framework of harmonized approaches to enable the responsible, voluntary and secure sharing of genomic and clinical data.

OICR co-founded the Cancer Stem Cell Consortium, which partnered with the California Institute for Regenerative Medicine and supported Ontario researchers in developing new biomarkers to guide leukemia and breast cancer treatment, as well as two drugs now in clinical trials.

OICR also supports the International Tobacco Control Policy Evaluation Project, led by Dr. Geoffrey T. Fong, a Senior OICR Investigator based at the University of Waterloo. Fong and his colleagues conduct sophisticated longitudinal cohort surveys of representative samples of tobacco users and non-users in 22 countries. These findings are used to inform tobacco control policy making in Canada and globally, leading to a reduction of cancer and other tobacco-related diseases worldwide.

Improvements in cancer care delivery and patient outcomes in Ontario

OICR has partnered with the Ministry of Health and Long-Term Care (MOHLTC), Cancer Care Ontario (CCO) and clinicians to optimize the delivery of cancer innovations in Ontario's healthcare system to maximize patient access and benefit.

In 2011, the Medical Advisory Secretariat of the MOHLTC, CCO and OICR formed a collaboration to facilitate the development of new provincial guidelines to guide treatment with cancer therapeutics recommended for use in conjunction with companion diagnostic tests that identify patients likely to benefit from treatment (i.e., precision medicine). Through this collaboration, guidelines were developed for use of the diagnostic tests: Oncotype DX for early breast cancer, KRAS for colorectal cancer, EGFR for non-small cell lung cancer and BRAF for melanoma. A recommended field study conducted by the Ontario Clinical Oncology Group (OCOG) and supported by MOHLTC subsequently showed that Oncotype DX use has allowed 22 per cent of early breast cancer patients in Ontario to avoid unnecessary chemotherapy.

In another case, to increase the rate of colorectal cancer screening in Ontario from a low 30 per cent, OICR's Health Services Research team initiated a partnership with CCO and the Institute for Clinical Evaluative Sciences (ICES) to develop and test strategies to improve participation in Ontario's ColonCancerCheck screening program. In a pilot study, when patients received letters from their family physicians indicating they were overdue for screening, participation increased by 14 per cent. A subsequent randomized controlled trial showed a further 10 per cent increase in participation when test kits were mailed directly to patients who were overdue for screening. Rollout of the intervention across the province could lead to 425 colon cancer deaths averted each year. Unexpectedly, OICR researchers found that nearly 30 per cent of patients with a positive screen did not have the required follow up colonoscopy and they are now testing strategies to address the issue.

Economic benefits for the people of Ontario

OICR and FACIT have been successful in ensuring that discoveries made in Ontario laboratories deliver economic returns to Ontario. For instance, OICR/FACIT supported the development of a novel oncolytic cancer vaccine from Ottawa and Hamilton, which is now in a Phase I/II clinical trial and has potential to become a new immunotherapy approach for the treatment of cancer. OICR/FACIT also helped develop the Cytof[®] mass cytometer from Toronto from a prototype to a commercial platform now used internationally and which has created more than 70 direct jobs in Ontario. To date, OICR/FACIT has supported the development of 23 companies that have manufactured prototypes, conducted first-in-man trials, generated sales and created 230 highly skilled jobs in Ontario (Figure 3a). Companies supported by FACIT have attracted \$169 million in investment, including more than \$144 million from the private sector (Figure 3b).

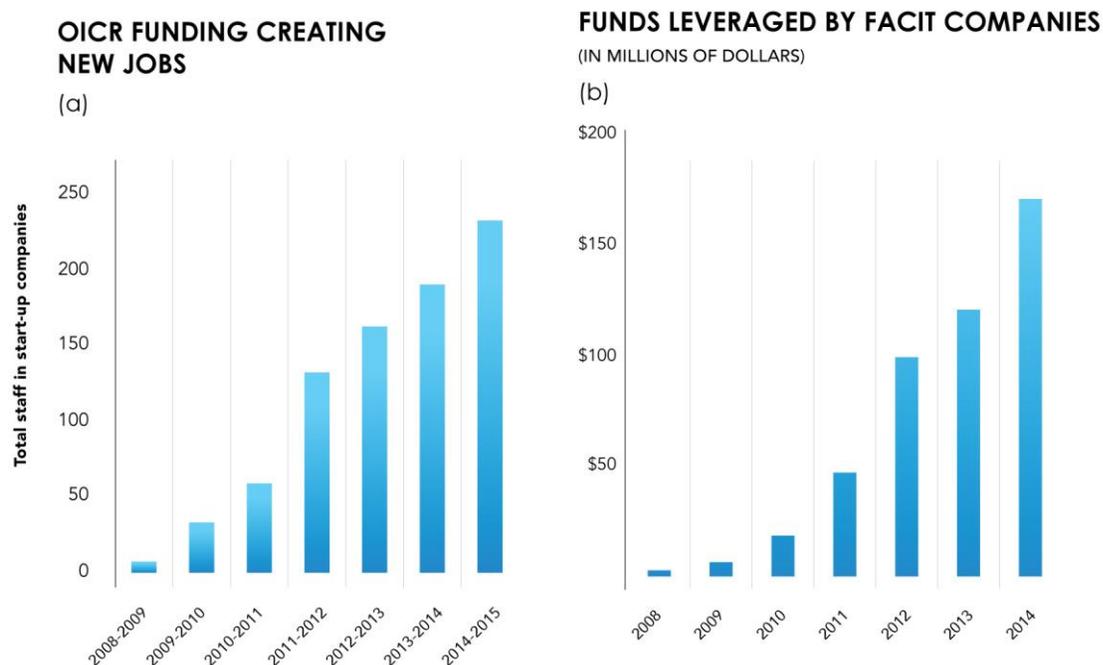


Figure 3. OICR/FACIT's economic impact. (a) Jobs created at start-up companies; (b) Cumulative funds leveraged by FACIT-supported companies

A.4. Context for the Strategic Plan 2016-2021

Strategic Plan 2016-2021 builds on the strong foundation that has been laid, while recognizing the important advances and opportunities in the global cancer research landscape over the past five years. For instance, immuno-oncology has yielded breakthroughs in treating difficult cancers, including the achievement of long-term survival for patients with metastatic melanoma and non-small cell lung cancer with checkpoint inhibitors^{3,4} and sustained remission of acute lymphoblastic leukemia through Chimeric Antigen Receptor (CAR) T Cell therapy^{5,6}. In addition, novel targeted therapies have shown

³ Ribas A, N Engl J Med 2015

⁴ Le, DT *et al.* N Engl J Med 2015; 372:2509-2520

⁵ Maude, SL *et al.* N Engl J Med 2014; 371:1507-1517

efficacy in the treatment of metastatic melanoma^{7,8,9} and non-small cell lung cancer^{10,11}. Technologies such as next generation sequencing have leapt into the clinical arena at unexpected pace and are contributing to a more rational utilization of recently approved targeted therapies. During this period, Ontario’s cancer research community, both within and beyond OICR-supported programs, has been nimble and at the forefront. It is therefore incumbent on the Institute to take stock of pre-existing activities and assets, and evaluate new opportunities where Ontario can excel.

The pipeline of assets developed within OICR-funded programs is now rich in assets including biomarkers/diagnostic tests, medical imaging devices and probes, small molecules, bio-therapeutics, immunotherapies and new drug formulations that are progressing along the translational research roadmap (Figure 4), with new discoveries continuing to emerge from preclinical research.

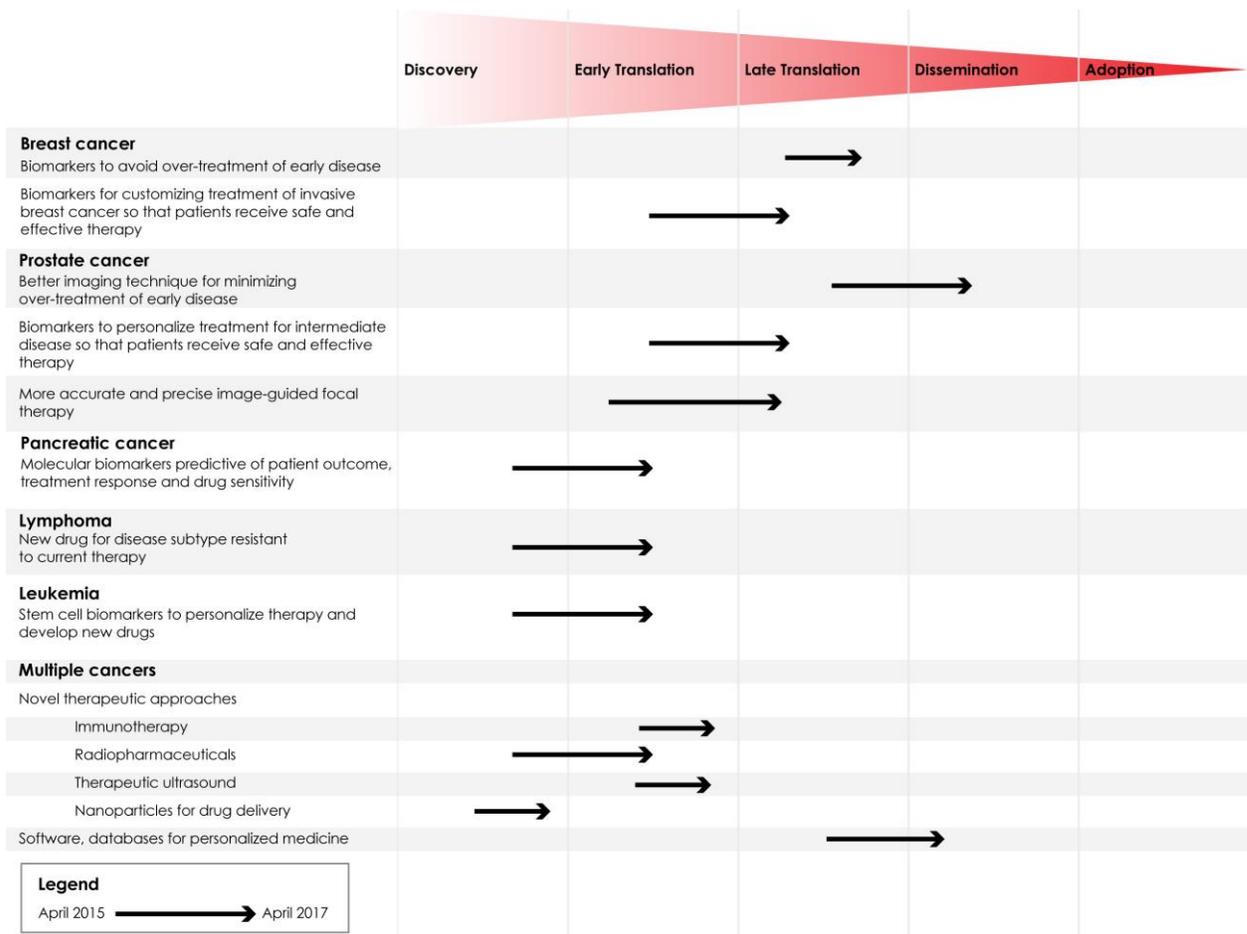
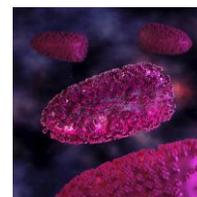
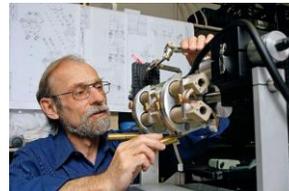


Figure 4. Select preclinical and clinical assets in OICR’s pipeline. Arrow indicates current stage of development and projected stage of development in April 2017.

⁶ Porter DL *et al.* N Engl J Med 2011; 365:725-733
⁷ Flaherty KT *et al.* N Engl J Med 2010; 363:809-819
⁸ Flaherty KT *et al.* N Engl J Med 2012; 367:1694-1703
⁹ Long GV *et al.* N Engl J Med 2014; 371:1877-1888
¹⁰ Shaw AT *et al.* N Engl J Med 2013; 368:2385-2394
¹¹ Solomon, BJ *et al.* N Engl J Med 2014; 371:2167-2177

The evaluation of the most promising assets in early clinical trials will be a critical step in obtaining tangible results that could demonstrate proof of concept and attract private sector investment. Examples of innovations expected to be tested in the clinic over the next five years and their potential impact for cancer patients include:

- *Molecular biomarkers and diagnostic imaging approaches for differentiating high-risk prostate cancer patients needing aggressive therapy and low-risk patients who should be actively monitored:* Better patient stratification would avoid over-treatment of prostate cancer, and its associated complications (e.g., infections, incontinence, sterility) and costs to the healthcare system;
- *New drug for lymphoma patients who do not respond to standard therapy:* The novel drug could potentially benefit more than 85,000 patients globally, with sales prospects of over U.S.\$1 billion;
- *Genetic test for identifying a sub-set of pancreatic cancer patients that will respond to tailored therapies:* Implementation of routine testing could identify 10 per cent of patients for whom specific treatments could increase survival from the usual 6-12 months (i.e., metastatic disease) to as much as five years;
- *Proactive strategies for decreasing the need for emergency room (ER) visits by breast cancer patients on adjuvant therapy:* Roll-out of the intervention across Ontario could improve patient outcomes and reduce ER visits and hospitalizations by one-third for these patients;
- *Oncolytic vaccines that selectively target and destroy cancer cells:* Novel approach to defeating hard to treat cancers.



Over the next five years, the Institute will continue to identify and accelerate the development of innovative concepts and technologies to fuel Ontario's translational research pipeline, focus on validating promising assets in the clinic and drive commercialization opportunities. Additional resources will be directed at addressing critical gaps in translational cancer research in Ontario.

Partnerships—with the private sector (pharma, biotech and venture capital), cancer centres, research institutes, government agencies, patients, and other stakeholders—will be critical in achieving impact for Ontario.

B. Strategic Plan (2016-2021)

B.1. Development of the strategy

In the summer and fall of 2014, OICR's President and Scientific Director and senior staff travelled to Ontario-based research institutes affiliated with universities and major cancer centres to consult with over 400 stakeholders on how OICR could further enable and catalyze translational cancer research in the province. OICR also conducted mini-retreats to seek ideas from OICR's Program Directors, its international Scientific Advisory Board (SAB) and its Board of Directors. Input was obtained from provincial partners such as CCO, Ontario's Ministry of Research and Innovation (MRI) as well as representatives of Canadian funding agencies and industry stakeholders. Dr. Nicole Onetto, OICR's Deputy Director and Chief Scientific Officer, and Dr. Craig Earle, Director of the OICR-CCO Health Services Research Program, coordinated additional meetings with clinical investigators and the leaders of clinical trial groups across the province to further refine the role that OICR could play in augmenting the capacity for high-quality clinical trials to evaluate promising cancer innovations. Finally, OICR's leaders worked with FACIT and private sector stakeholders in developing a well-orchestrated approach to commercializing potential products developed by OICR-supported scientists.

The consultation process was useful in raising provincial awareness of the translational mission of the Institute and attracted significant interest in the progress made by both OICR-supported researchers and the FACIT commercialization team. Valuable feedback was obtained regarding challenges and future opportunities for OICR and Ontario. The comments also revealed a high degree of heterogeneity among various communities, disciplines and geographic regions with regard to knowledge of the Institute's mission and expertise, as well as in the level of involvement in OICR's current projects. It became clear that better communication could lead to the identification of more/enriched translational research opportunities for the Institute. Furthermore, enhancing awareness of the Institute, its resources and the expertise of its staff could result in the engagement of more investigators interested in joining, collaborating and contributing to the OICR community.

In November 2014, OICR underwent an external review by an international expert panel. The report, released in early 2015, identified several areas of OICR strength and provided guidance for augmenting OICR's impact. The panel made specific recommendations for improvements, including that the Institute's programs based at the MaRs Centre headquarters be reconfigured to increase interactions with the external community, capitalize on the resources established by MRI's investment and enhance the overall capabilities of Ontario cancer research, both basic and translational. The panel also identified areas OICR could partner to fill gaps and provide the science capabilities required for Ontario to excel in translational research. Subsequent discussions occurred with Ontario researchers, clinicians and leaders of public and private organizations on how to address the recommendations and increase synergies within the province and across Canada in areas that include cohorts, informatics, clinical genomics, pathology and drug discovery. These consultations have been integral to addressing the recommendations of the international expert panel in the development of Strategic Plan 2016-2021.

B.2. Rationale for Strategic Plan 2016-2021

Ontario's investment in OICR has fostered the development of a cluster of cancer research excellence that has mobilized, attracted and enabled scientists, clinicians, companies and investors in the province. Strategic Plan 2016-2021 sets out the priorities and principles that will leverage the assembled critical mass to maximize opportunities to translate Ontario science into better cancer outcomes and economic benefit. To that end, Strategic Plan 2016-2021:

- Is aligned with and advances OICR's mission, goals and translational research priorities;
- Is responsive to the recommendations of the 2014 external review by the international expert panel;
- Builds on OICR's past investments, with focus on moving promising oncology assets and innovations to the clinic;
- Prioritizes research themes where Ontario scientists are internationally renowned and are uniquely positioned to significantly impact the cancer research field and translate discoveries to improve cancer patient outcomes;
- Addresses critical gaps to strengthen and enable translational cancer research in Ontario;
- Seeks to catalyze more effective collaboration with cancer centres, research institutes, government agencies, the private sector, patients, and other stakeholders to maximize the potential for innovative, translational medicine and foster the growing Ontario oncology ecosystem.

B.3. Transition to a new blueprint

OICR's blueprint during the Institute's second mandate (2010-2015) consisted of three categories of programs: Innovation, Technology and Translation (Figure 5). Investigators in each program pursued well-defined Translational Research Projects and small exploratory Catalyst Projects in alignment with the Institute's translational research priorities (i.e., Therapeutic Innovation, Clinical Impact and Population Health).

Ambitious, large-scale Translational Research Initiatives (TRIs) were subsequently established to drive collaborations across innovation, technology and translation teams and foster partnerships with the clinical community to accelerate the flow of research discoveries toward clinical testing. Two initiatives were started:

- The Improved Management of Early

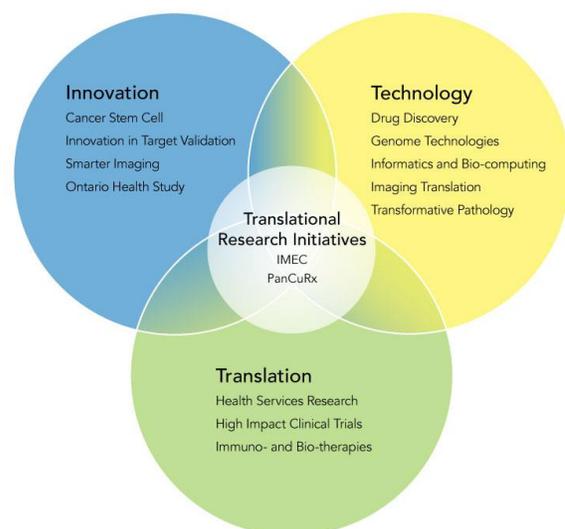


Figure 5. OICR's Blueprint (2010-2015). OICR's research activities are organized within Innovation, Technology and Translation programs. Translational Research Initiatives were established to drive collaboration across programs.

Cancer (IMEC), focused on developing new approaches to distinguish aggressive versus indolent disease for patients with early breast or prostate cancer.

- PanCuRx, focused on understanding the unique genetic and genomic features of this aggressive malignancy and developing new therapeutic approaches to address the high fatality of pancreatic ductal adenocarcinoma.

The TRI model has proven successful at bringing laboratory and clinician scientists together to address key clinical priorities and will be expanded in the future.

The 2010-2015 blueprint allowed the Institute to build significant cancer research capacity and led to many important breakthroughs (see Section A.3.). However, it has become clear that the program-based structure also created unintended silos, both among OICR teams and between the Institute and Ontario laboratories and cancer centres, particularly those not directly involved in OICR's research activities.

OICR is evolving its blueprint for 2016-2021 to better position the Institute to drive promising assets coming out of its early research efforts towards the clinic and more broadly accelerate translational cancer research in the province. The new blueprint (Figure 6) consists of four ambitious Strategic Initiatives that advance OICR's translational research priorities:

- A. Translational Research Initiatives:** Large-scale, multi-disciplinary collaborations between laboratory and clinician scientists focused on translating Ontario innovations/assets or knowledge to address important medical needs of cancer patients.
- B. Global Leadership in Precision Oncology:** Convergence of clinical genomics with big data analytics and global networks to improve patient management and tailoring of interventions to the individual patient.
- C. Cancer Therapeutic Innovations Pipeline:** A multi-institutional approach to efficiently develop cancer discoveries from Ontario laboratories into lead compounds (small molecules or biologics) that have the potential to attract partners for further development, and ultimately commercialization.
- D. Collaborative Research Networks:** Networks of experts, teams and capabilities that facilitate translational cancer research in Ontario. Includes:
 - i. OICR-Cancer Care Ontario Health Services Network
 - ii. Ontario Molecular Pathology Network
 - iii. Ontario Health Study
 - iv. Ontario Tumour Bank
 - v. Canadian Cancer Clinical Trials Network
 - vi. Ontario Cancer Research Ethics Board

The Strategic Initiatives will be supported by six cutting-edge **Technology Programs** that provide expertise, resources, cutting-edge technologies and analytics:

- i. Biologics
- ii. Diagnostic Development
- iii. Genomics
- iv. Imaging
- v. Informatics
- vi. Medicinal Chemistry

Overall, this new framework allows for greater integration, focus and coordination of Institute activities, provides an avenue for new collaborations with the Ontario cancer research and clinical community and serves as a catalyst for private sector partnerships and investment.

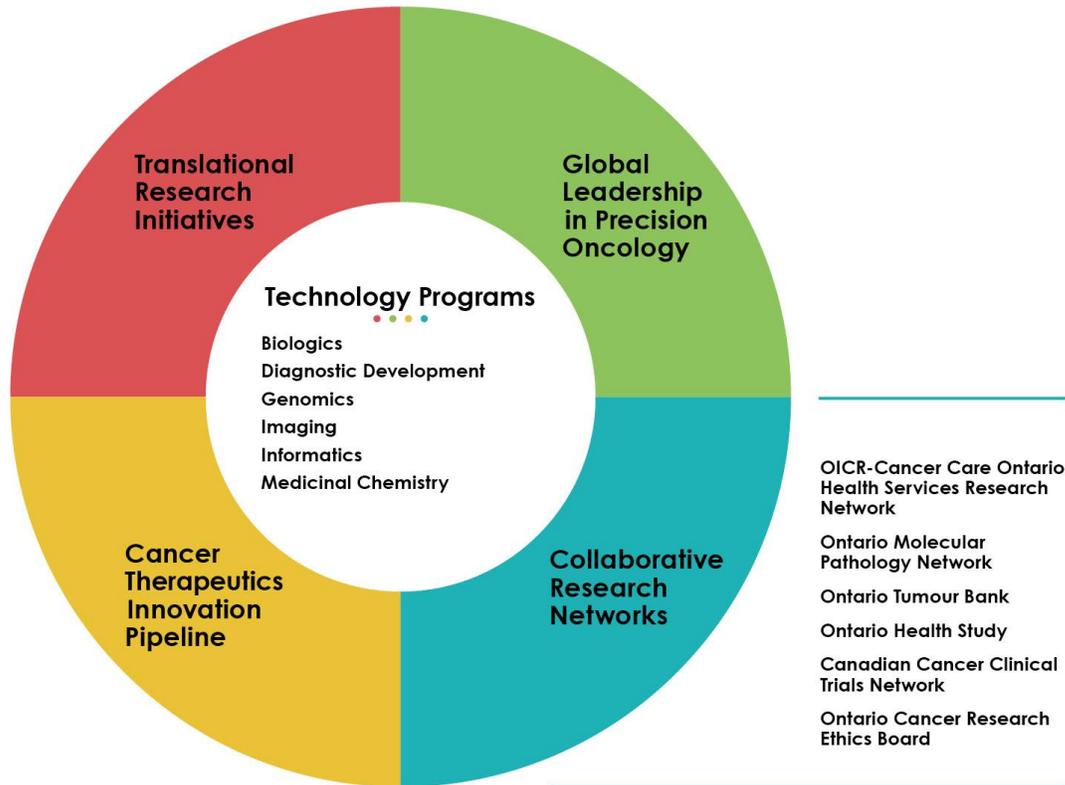


Figure 6. OICR’s Blueprint (2016-2021). OICR’s research activities are focused within four Strategic Initiatives, supported by six cross-cutting Technology Programs, which collectively advance OICR’s translational research priorities of Therapeutic Innovation, Clinical Impact, and Population Health.

The sections below outline the four Strategic Initiatives and six Technology Programs that constitute the core of OICR’s translational research strategy for 2016-2021 and investments supporting a highly-qualified cancer research workforce, clinical trials and commercialization activities that together will catalyze patient impact and economic benefits in Ontario.

B.4. Strategic Initiatives

A. Translational Research Initiatives

Goal. Translate concepts, knowledge and innovations developed in Ontario to address important medical needs of cancer patients.

Design. TRIs are the translation engines of the Institute: large-scale, multi-disciplinary collaborations between laboratory and clinician scientists focused on advancing Ontario owned/controlled assets (often developed in the context of OICR’s prior research activities) to improve cancer patient outcomes. TRI themes are selected based on clear clinical priorities in areas that build on unique scientific strengths/competitive advantages, including OICR investments in building cutting-edge Technology Programs and critical mass of researchers and clinicians in Ontario.

TRIs usually consist of two to five projects, including large research projects to evaluate and validate concepts and technologies, smaller “catalyst/blue sky” research projects, and one or more clinical trials (mandatory) that will capitalize on OICR’s investments in augmenting cancer trials in Ontario (see Section B.6.), and health services research activities (if applicable). Cohesion and complementarity of projects is critical so that clinically meaningful results are obtained with quality, speed and in a coordinated fashion. TRIs are led by research and clinician scientist co-directors supported by a management committee of principal investigators and are funded by OICR at up to \$2.5 million/year for four years (i.e., maximum of \$10 million), pending satisfactory progress/midterm review and with an expectation of additional partnered funding (Figure 7).

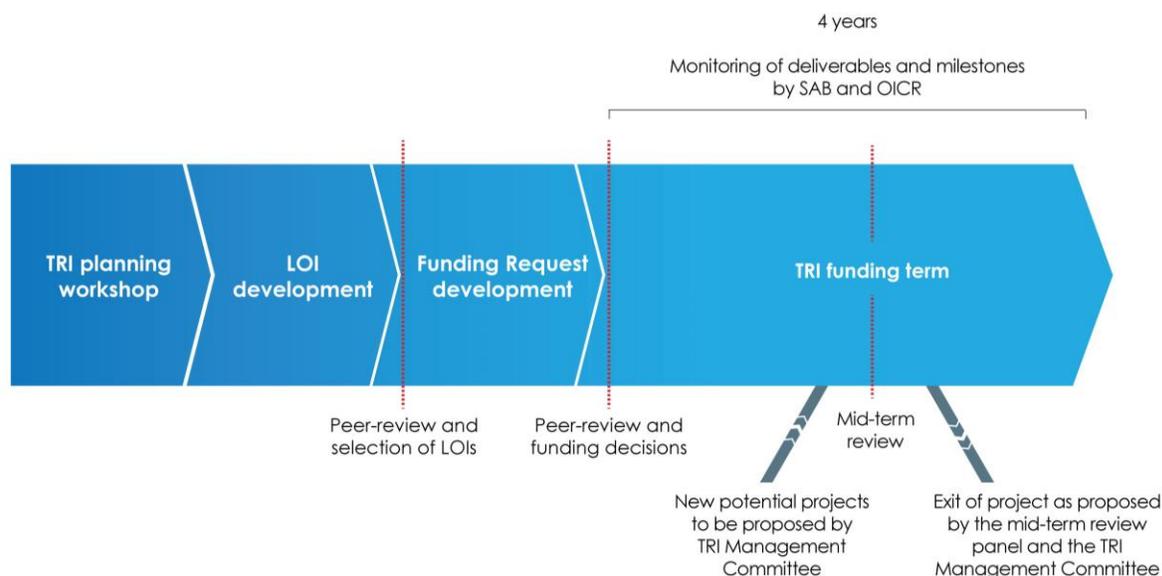


Figure 7. Process for the development, review and monitoring of Translational Research Initiatives.

In defining TRI research themes for 2016-2021, OICR reviewed pre-existing activities as well as emerging opportunities where Ontario’s cancer research community is uniquely positioned to make significant advances. The latter were identified through consultations (Section B.1.) and further explored through interactions with Ontario researchers and clinicians. Box 3 includes a list of proposed themes, which have already demonstrated high potential for transdisciplinary partnership and patient impact. OICR’s leadership has worked with Ontario leaders to define the initial focus and scope of TRI themes, as outlined in

Appendix I. Over the coming months, OICR will collaborate with Ontario research and clinical leaders to coordinate theme-based workshops that will bring together stakeholders (researchers, clinicians, funding agencies and end-users including private sector and healthcare agencies) from Ontario and beyond to further define the objectives and scope of proposed initiatives. Engagement of OICR Technology Program leaders in these workshops will be critical to promote opportunities for TRI projects to capitalize on expertise and cutting-edge technical capacities often required for internationally competitive translational research.

Box 4. Criteria for assessing TRI Proposals

- Clinical relevance
- Advances Ontario innovation or asset
- Research excellence
- Impact
- Leadership
- Expertise/capacity of the team
- Collaboration
- Likelihood of success

Workshops will explore the most promising avenues to move new concepts, biomarkers and potential therapies towards the clinic and/or other important pre-commercial milestones. Resulting TRI proposals will be evaluated by a panel of international translational research experts based on pre-defined criteria (Box 4). As the majority of OICR’s current research activities are funded until March 2017 (pending satisfactory progress), the potential renewal of existing TRIs (pancreatic, early breast and early prostate cancers) and launch of new TRIs is expected to occur thereafter. The ultimate number of TRIs launched will be dependent on budget availability.

Box 3. Proposed TRI Themes

- Pancreatic Cancer
- Early Breast Cancer
- Early Prostate Cancer
- Immuno-oncology
- Leukemia
- Esophageal Cancer
- Brain Cancer
- Ovarian Cancer

Impact. As TRIs are designed to advance high potential Ontario assets to address important medical needs of cancer patients, achievement of specific project objectives will be a key measure of success. Deliverables and milestones that represent the advancement of Ontario assets along the translational research roadmap (Figure 2) include:

- Discovery and preclinical validation of assets (targets, drug candidates, biomarkers, diagnostic and imaging probes and devices);
- Validation of the clinical utility of assets for improving cancer prevention, screening, diagnosis or treatment;
- Partnerships for further development and/or commercialization of assets;
- Uptake of assets by healthcare agencies or providers for implementation.

The ultimate, longer-term measure of TRI success will be the adoption of assets/innovations with demonstrable impact on patient outcomes and/or healthcare delivery.

B. Global Leadership in Precision Oncology

Cancer medicine is being transformed as a result of data-intensive technologies used to screen, detect, diagnose and monitor individuals before, during and after they are affected by cancer. The data captured include inherited and tumour genomes at single nucleotide resolution; high resolution anatomic, functional and molecular medical images; and administrative datasets collected by health care institutions and provincial networks. In addition to the massive size and complexity of datasets that can be generated per individual, there is an increasingly rich universe of biomedical, environmental and other data that are generated globally and can be linked to an individual. The convergence of informatics, genomics, other “omics”, epigenomics, global networking and social networks provides tremendous opportunities to improve the management of patients and the delivery of health services if clinically-useful information can be analyzed and shared with health care providers and patients in an easily interpretable form.

The major challenge facing the clinical adoption of precision medicine for cancer and other diseases is related to the difficulty in the clinical interpretation of individual (and tumour) genome sequences. At present, it is generally not possible to predict which changes in DNA sequence lead to clinical consequences, including responses to therapies. In clinical oncology, targeted therapies and novel immunotherapies that may benefit cancer patients are increasingly linked to mutational signatures that correlate with clinical outcomes such as drug sensitivities or resistance. Given the rapidly increasing arsenal of new cancer therapies, with more than 800 targeted cancer drugs under clinical investigation, it is critical to the field of precision oncology that robust data is generated to guide clinical decisions for matching therapies to mutations affecting unique patients with different tumor types. The wide variety of cancer types and the low frequencies of most cancer mutations have led to the realization that the required knowledge will only come through powerful partnerships across institutions and countries.

Goal. Leverage Ontario’s global leadership in cancer clinical trials, genomics and Big Data to improve patient management and tailoring of interventions to individual patients, bringing Ontario to the forefront of precision oncology.

Design. OICR will partner with cancer centres and academic institutions in Ontario to strengthen and catalyze translational cancer genomics research in the province and will continue to lead and participate in global precision oncology initiatives that generate the robust datasets and insights critical for guiding patient management and treatment decisions, and ultimately improving cancer outcomes. This approach is highly aligned with recommendations of the Advisory Panel on Healthcare Innovation to the Government of Canada, which recognized the importance of precision medicine and the imperative that Canada secure international leadership in contributing and applying new clinical insights to healthcare systems across the country.¹² The Panel recommended the prioritization of national and international collaboration through wide data-sharing, with due regard for privacy and security; the development of a rich talent pool; and the development and commercialization of data analytics, software and made-in-Canada precision medicine concepts to help define the future trajectory of our healthcare systems.

¹² Unleashing Innovation: Excellent Healthcare for Canada Report of the Advisory Panel on Healthcare Innovation, Health Canada (2015).

Translational cancer genomics in Ontario

Ontario clinical trials groups were early adopters of next generation sequencing (NGS) technologies in the clinical research setting. In 2011, OICR teams in genomics and bioinformatics collaborated with the Princess Margaret Cancer Centre (PM) and four additional Ontario sites (in Hamilton, London, Ottawa and Thunder Bay) in the Genomics Pathway Study, Canada's first multi-centre trial evaluating clinical genomic profiling in patients with advanced cancers to identify driver mutations that may determine a patient's response to standard or experimental targeted agents. The trial demonstrated the feasibility of rapid NGS profiling and developed the analytical pipeline and information tools for initial detection and demonstration of the clinical significance of genetic variants. Several cancer centres in the province have since implemented NGS technologies in their pathology and molecular genetics departments.

PM sees over 15,000 cancer patients per year and is a recognized leader in translational cancer research. It delivers Canada's largest clinical cancer genomics program, testing more than 1,500 patients in NGS research studies annually, and has been selected by the American Association of Cancer Research as one of seven worldwide institutions to participate in the GENIE (Genomics, Evidence, Neoplasia, Information, Exchange) program to catalyze clinical and translational research by linking clinical cancer genomic data with longitudinal clinical outcomes. Together with other Ontario cancer centre partners, PM has formed alliances with several large pharmaceutical companies, which provide preferential access to early phase clinical trials evaluating novel agents. Moreover, PM's Drug Development Program has access to a large spectrum of novel anti-cancer agents as a result of its phase I and II oncology clinical trials partnerships with the National Cancer Institute in the U.S. and pharmaceutical companies.

Capitalizing on this established cancer clinical genomics capacity and expertise, OICR will partner with PM and Ontario cancer centres to bolster translational research innovation in precision oncology through two major initiatives (see Appendix II for more detail):

1. PM and OICR will establish and support **OCTANE (Ontario-wide Cancer Targeted Nucleic acid Evaluation)** to increase NGS testing of cancer patients in Ontario and facilitate data capture and sharing (Box 5). OCTANE will develop large provincial cohorts of consented patients for initial NGS-based genomic profiling that will inform the use of approved therapies (if appropriate) and enrollment into targeted therapy and immune therapy clinical trials, and identify patients who may benefit from more advanced genomic profiling. The new Ontario Molecular Pathology Network is expected to increase the reach of OCTANE across the province. It is also envisaged that OCTANE will be a major source of samples and data for ICGMed.
2. A new **PM-OICR Translational Genomics Laboratory (TGL)** will be established at the MaRS Centre headquarters to: (1) develop and evaluate new genomics and other "omics"

Box 5. OCTANE benefits to Ontario

- Improved access of Ontario cancer patients to NGS panel-based tests;
- Expanded infrastructure for NGS panel-based testing in Ontario clinical genetic testing laboratories and province-wide registry of results;
- Increased opportunities for genomics-based clinical research in Ontario through:
 - Province-wide repository of genomically-characterized tumour tissue and blood samples;
 - Large genomically-characterized cohort that can be enrolled into specific research initiatives.

technologies for *advanced* molecular profiling of tumours, normal tissues, circulating DNA and other biospecimens obtained from cancer patients; (2) transition research-grade laboratory and computational advances into validated, robust protocols ready for rapid validation and uptake by clinical laboratories in Ontario; (3) provide a platform to Ontario clinical and basic researchers to evaluate genotype-phenotype associations and emerging genomic algorithms; (4) undertake expanded genomic analysis of subsets of patients already tested using focused panels in clinical labs (such as those enrolled in OCTANE).

OICR is currently working with PM, University Health Network (UHN) and several Ontario cancer centres to define the detailed scope, objectives and implementation models for OCTANE and TGL.

Global partnerships in precision oncology

OICR has helped to establish Ontario as a major leader in precision oncology through the launch and coordination of the ICGC and the GA4GH. Through these initiatives, OICR has created and benchmarked protocols for analyzing NGS data, developed new models for federating databases (including clouds) across countries and created legacy datasets that are fueling precision medicine research on a global scale.

1. ICGCmed: Linking Genomics to Clinical Information and Health

The first phase of ICGC, which is slated for completion in 2018, has focused on developing extensive catalogs of tumour genomic information. The proposed second phase, ICGCmed, will link genomics to clinical information and health, including lifestyle, patient history, response to therapies and underlying causes of disease, for a broad spectrum of cancers, including pre-neoplastic lesions, early cancers and metastases. The goal will be to accelerate the movement of this information into the clinic to guide prevention, early detection, diagnosis, and prognosis, and provide the information needed to match the patient's disease to the most effective combinations of therapy. As with the first phase of ICGC, a worldwide consortium will enable research advances not possible on a local scale, particularly for interpreting data from patients with rare mutations, as well as the patterns of mutation co-occurrence that shed light on underlying cancer pathways and drug response/resistance.

Box 5. ICGCmed benefits to Ontario

- Discovery of clinically important biomarkers of disease subtypes and drug response;
- International leadership in clinical genomics and Big Data;
- Attraction of new clinical trials and sponsors;
- Access to large, curated databases for clinical genome data interpretation.

OICR will support two components of ICGCmed: (1) patient accrual, data collection and analysis (target will be 1,000 patients/year over five years); and (2) data coordination and stewardship (an extension of OICR's role in the current ICGC initiative). Benefits to Ontario are highlighted in Box 5. Additional detail is provided in Appendix II.

2. Global Alliance for Genomics and Health

Realizing the potential of genomics for clinical gain requires the interpretation of vast amounts of patient data, at a scale not achievable by any one party acting alone. In 2013, OICR co-founded the GA4GH to bring together stakeholders from around the world to develop and promulgate harmonized standards (both technical and regulatory) to enable

the responsible, voluntary and secure sharing of patient genomic and clinical data¹³. GA4GH has grown to include over 368 organizations across 35 countries actively developing dozens of tools, methods, and approaches to facilitate effective, responsible data sharing, and has made important progress to unite and guide the field. Members include world leaders in healthcare, research, patient and disease advocacy, life sciences and information technology. The secretariat functions are currently hosted at OICR, the Wellcome Trust Sanger Institute and the Broad Institute. The Executive Director, Peter Goodhand and the chair of the GA4GH Steering Committee, Dr. Thomas Hudson, are based at OICR. Dr. Lillian Siu of PM is a member of the GA4GH Cancer Clinical Working Group that is aligning international cancer clinical genomics data initiatives such as GENIE.

Over the next five years, GA4GH will capitalize on its international network to continue tackling the substantial structural, technological and cultural barriers that hinder the adoption of precision medicine. OICR leaders will engage with a broad range of experts (technical, data, security, regulatory, and ethical) in Ontario, Canada and globally. The GA4GH Secretariat will continue to drive progress by the Global Alliance Steering Committee, Working Groups, coordination of members meetings, and recruitment and engagement of new members including companies such as Amazon (Seattle), Google (Mountain View), DNASTack (Toronto), and Newtopia (Toronto). By virtue of its role in GA4GH, OICR initiatives in Precision Oncology (including ICGCmed) and the Ontario Molecular Pathology Network will be at the heart of building a federated data commons that will enable research and improve precision medicine in the province of Ontario and beyond.

3. Big Data Analytics

OICR has positioned Ontario at the leading edge of cancer genome informatics. In addition to its critical role as the Data Coordination Centre for the ICGC, the Institute leads the Cancer Genome Collaboratory, a compute cloud-based cancer analysis resource, and is designing the data submission and data portal software for the new NCI Cancer Genomic Data Commons (in partnership with the University of Chicago). These activities lay the foundation for translational cancer genomics and will enable Ontario to take centre-stage in a new era of digitized medicine and precision oncology.

Over the next five years, computational biologists, software engineers, database and cloud computing architects and other experts will continue to drive the Big Data analytics that underpin the genomic medicine revolution, with specific deliverables contributing to OICR's Strategic Initiatives, including Precision Oncology, TRIs and the Ontario Molecular Pathology Network. Research activities will include:

- Developing fast, scalable databases that will allow for meaningful comparison of cancer genome datasets with other biological and clinical data, including the creation of genomic data management systems that support Clinical Laboratory Improvement Amendments (CLIA)-certified diagnostic laboratory environments at Ontario cancer centres;
- Advancing the computational identification of prognostic and predictive biomarkers in –“omics” data (e.g., DNA, RNA, methylome, etc.);
- Establishing novel diagnostic sequencing approaches that extract clinically meaningful data from personal (inherited and tumour) genomes; and

¹³ White paper: “Creating a Global Alliance to Enable Responsible Sharing of Genomic and Clinical Data” (2013) http://genomicsandhealth.org/files/public/White%20Paper%20June%203%20final_0.pdf

- Developing algorithms to analyze tumour heterogeneity in relation to biological and clinical importance.

Impact. Global Leadership in Precision Oncology is focused on both accelerating translational cancer genomics research in Ontario and bringing Ontario to the forefront of precision oncology through leadership of and contribution to global precision oncology initiatives. While specific deliverables will be further defined in the coming months as greater granularity is developed around the various components, broad indicators of success will include:

Translational cancer genomics in Ontario:

- Improved access of Ontario cancer patients to NGS panel-based tests and advanced genomics testing;
- Genome-based analyses that inform clinical trials evaluating novel immune and targeted therapies;
- Increased capacity of clinical genetics testing at Ontario labs to deliver clinical genomics testing to cancer patients;
- Increased opportunities for genomics-based clinical research in Ontario;
- Greater collaboration between Ontario cancer centres.

Global partnerships in precision oncology:

- Recognition of Ontario as a globally-leading jurisdiction in cancer genomics, informatics and Big Data analytics, which attracts highly qualified personnel, clinical trials and private sector investment to the province;
- Significant contributions to ICGCmed, GA4GH and other related global initiatives;
- Translation of results from large-scale global initiatives to seed new diagnostic and therapeutic approaches and clinically-actionable guidelines that inform cancer patient management and treatment, and ultimately improve patient outcomes.

C. Cancer Therapeutic Innovations Pipeline

Ontario has a strong tradition of basic biological research that has led to substantial contributions to the understanding of cancer and other diseases. Examples include stem cell research (Till and McCulloch), cell signaling (Pawson), cancer stem cells (Dick), developmental biology (Rossant) and many other research initiatives that offer insight into normal and disease biology, and point to targets and pathways that are relevant to new diagnostics and therapeutics being developed across a range of diseases.

Ontario previously lacked the capacity to transform promising discoveries into therapies and projects often moved elsewhere for further development as a result. Since 2000, investments from federal, provincial, philanthropic, hospital foundations and not-for-profit organizations such as the Terry Fox Research Institute, complemented by investments from OICR and its predecessor, the Ontario Cancer Research Network, have established clusters of experts and facilities generating state-of-the-art technologies, valuable cancer models, new chemical and biological tools and a better understanding of cancer pathophysiology, which have significantly bolstered early oncology drug discovery in the province. Many new therapeutic agents in discovery and development have emerged from Ontario laboratories in the past five years, including biologics (e.g., oncolytic vaccines, therapeutic antibodies), small molecule inhibitors of oncogenic targets (e.g., BCL6, PLK4), repurposed drugs for cancer indications (e.g., tigecycline for leukemia), and new formulations of drugs that can be taken orally, cross the blood-brain barrier or are better tolerated by patients. Recognition of the originality and breadth of programs in Ontario academic laboratories by venture capital and the pharmaceutical industry has resulted in investments exceeding \$100 million over the past three years and the creation of numerous start-ups.

Notwithstanding these successes, there are still several challenges in bridging the gap between discoveries made in academic laboratories and *bona fide* biopharmaceutical development. A primary issue in drug discovery is the incomplete understanding of the relevance and druggability of identified targets and pathways in normal biology and cancer pathophysiology. Another limiting factor has been access to expertise in drug discovery; this was the basis for OICR's recruitment of leaders from industry with proven track records in moving promising small molecules and biologics towards clinical candidate selection and subsequent testing in clinical trials. Collaboration and synergy between academic teams with therapeutic discovery expertise has been uneven, partly due to incomplete awareness of assets, and available expertise and facilities/resources throughout the province, which has slowed and in some cases halted the progress of promising projects. While these challenges are present in practically all jurisdictions, Ontario has the unique advantage of having created a distinct organization, OICR, to catalyze and accelerate translation in cancer research including drug discovery and development. It was therefore incumbent upon OICR to re-evaluate its strategy in therapeutic discovery to set the stage for maximizing impact in the next half-decade and beyond.

In July 2015, OICR convened Ontario experts in genomics, functional genomics, informatics, biochemistry, high-throughput screening, cancer biology, structural and computational biology, protein chemistry, medicinal chemistry, *in vitro* and *in vivo* model development, and early drug discovery to discuss opportunities to catalyze and enable early phases of cancer therapeutic development in Ontario. The points that follow summarize key principles, born out of these discussions, which will form the basis of the Ontario Cancer Therapeutic Innovations Pipeline strategy over the next five years (Figure 8).

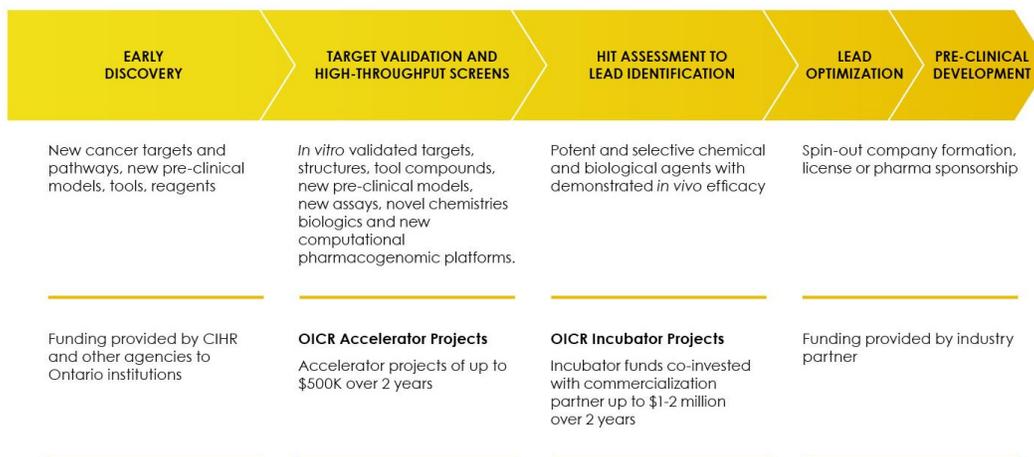


Figure 8. Ontario cancer therapeutics innovation pipeline strategy. OICR will support pre-clinical projects that develop cancer discoveries from Ontario laboratories into therapeutic lead compounds that have the potential to treat difficult cancers.

Goal. Efficiently develop cancer discoveries from Ontario laboratories into therapeutic lead compounds (small molecules or biologics) that have the potential to treat difficult cancers and have been sufficiently de-risked to attract private sector investments.

Design. OICR will support early drug development through Accelerator and Incubator projects, adopting an “Ontario-first” approach that capitalizes on the province’s exceptionally rich cancer community and outstanding drug discovery and screening infrastructure. The Institute will cast a large net to attract proposals from the community and, using peer-review, will select projects based on: (1) potential to address a well-defined clinical need; (2) strength of the target validation package; (3) originality, innovativeness and feasibility of the drug discovery approach; and (4) ability to leverage the *in vitro* and *in vivo* cancer models, including organoids and patient-derived xenografts, that represent more reliable disease models than those classically available to pharma companies.

A governance structure that brings leaders from cancer biology laboratories, high-throughput screening facilities, medicinal chemistry and biologics platforms and the private sector will be established to oversee cancer therapeutic pipeline activities. Regular networking across all projects and affiliated platforms (e.g., through biannual community meetings) will promote further collaboration between teams, and ensure that information is shared and that arising hurdles are addressed in a timely manner.

- 1. Accelerator projects: Target validation and high-throughput screening.** Early-stage projects will include high-throughput screening assay development, screens for a biologic and/or small molecule, medicinal chemistry activities, crystallography, mass spectrometry of compound interactomes/effects of compounds on target and protein networks, proof-of-principle of small molecules in pre-clinical models, bioinformatics and other computational analyses to unravel associations between molecular features and drug phenotypes and inform development of companion diagnostics. Importantly, the program will not support studies aimed at genetic proof-of-concept that a target(s) is important, but rather demonstration that hitting that target(s) with a drug-like molecule or biologic will affect cancer phenotypes (cell-based to organoid models). Accelerator project deliverables will include *in vitro* validated targets, structures, tool compounds, new pre-clinical models, new assays, novel chemistries and biologics, and new computational pharmacogenomic platforms.

Research groups leading Accelerator projects will engage early with drug discovery experts in the (1) design and development of target validation studies and therapeutic molecule generation strategies (e.g., hit and lead generation campaigns for both small and large molecules); (2) exploitation of Ontario resources (such as those available in the Structural Genomics Consortium (SGC)); and (3) planning a pre-clinical development strategy that may address issues related to manufacturing products, as well as innovative formulations for drug delivery. OICR can also provide advice (and broker collaborations) for developing assays, pharmacodynamic (PD) biomarkers, companion diagnostic tests and other patient selection tools that are now essential for successful and efficient drug development.

- 2. Incubator projects: Hit assessment and lead identification.** Second-stage funding will support rigorous analyses of small or large molecules with the aim of producing more potent and selective chemical or biological agents, characterizing their biopharmaceutical properties, demonstrating efficacy in *in vivo* models, developing a well-articulated hypothesis for the target as a treatment for the disease in the intended patient population and validating the legal freedom to operate and opportunity to generate IP.

Higher order investigations of potential lead compounds and biologics requires specialized teams that have streamlined processes for determining whether molecules possess suitable physicochemical properties to make acceptable clinical candidates. Incubator projects will be carried out in partnership between Ontario laboratories and OICR-supported Technology Programs in Medicinal Chemistry and Biologics (see Section B.5), which provide outstanding capabilities and proven expertise in advancing small molecules and biologics to stages of development that are attractive to the private sector. While OICR may be able to sustain early phase Accelerator projects from its base MRI budget, Incubator projects will ideally be co-developed with a pharmaceutical partner and/or commercial investors (including FACIT).

High-quality lead small molecules and biologics with demonstrated *in vivo* efficacy correlated with a PD biomarker are prime candidates for spin-out company formation and private sector investment. Alternatively, Lead Optimization, clinical trial application-enabling studies and early clinical studies may be pursued in partnership with biotech/pharma companies through sponsored research agreements or other mechanisms.

Partnerships: Collaboration with the broader drug discovery community and the private sector will be essential for the success of the cancer therapeutics innovation pipeline strategy. OICR will catalyze collaborations with SGC, an important global drug discovery resource based in Toronto. By nominating cancer protein targets identified through the therapeutics pipeline, 3D protein structures can be generated by SGC and chemical tools can be obtained to probe the function of such targets. The structures, tools and knowledge can be used to predict the effects of a future drug on a protein of interest, determine the target's druggability using small molecules, and guide the therapeutic strategy towards medicinal chemistry and biologics approaches. Furthermore, the SGC's network of pharma companies and international scientists can be used to catalyze downstream partnerships.

OICR will also explore collaborations with Canadian NCEs (Centre for Drug Research and Development and CQDM) given the private-public partnership models already established by these groups. OICR and FACIT will also explore creating a fund with venture capital and pharmaceutical companies to increase the number and size of Ontario projects.

Impact. OICR's Cancer Therapeutic Innovation Pipeline strategy is focused on addressing a clear gap in early oncology drug discovery, where there is limited funding available and assets are often too risky to attract private sector interest, and capitalizing on Ontario expertise in medicinal chemistry, biologics and structural biology to advance promising discoveries to a stage where they attract partners for further development.

As indicated above, project deliverables will include:

- Accelerator projects: *in vitro* validated targets, structures, tool compounds, new pre-clinical models, new assays, novel chemistries and biologics, and new computational pharmacogenomic platforms;
- Incubator projects: High-quality lead compounds and biologics with demonstrated *in vivo* efficacy correlated with a PD biomarker.

More broadly, the success of the Cancer Therapeutic Innovation Pipeline Strategic Initiative will be assessed based on:

- Attraction of partnerships/investment for further development and commercialization of drug discovery assets;
- Company creation to continue advancing assets;
- Strengthening of the Ontario ecosystem for oncology drug discovery: greater collaboration between groups, capitalizing on provincial expertise and infrastructure, and attraction of new partners.

D. Collaborative Research Networks

Goal. To strengthen and enable capacity for translational cancer research at cancer centres and academic institutions through networks of experts, teams and capabilities that link researchers and clinicians across Ontario.

Design. OICR will continue to invest in five collaborative research networks that facilitate translational cancer research in Ontario, and will establish a new molecular pathology network to bolster research capacity, collaboration and leadership in cancer pathology.

1. OICR-CCO Health Services Research Network

Ontario has a number of unique assets for health services and population research, including a large and diverse population, a single-payer universal health care system, a cancer agency focused on using evidence to drive quality improvements (i.e., CCO), outstanding health care administrative data sources, and an intellectual tradition that values health services and population research in policy decision-making. Ontario is also host to ICES, one of the world's largest population-based repositories of administrative, clinical and survey datasets.

OICR and CCO have partnered to form a network of engaged cancer health services researchers that can be drawn upon to address specific health services research priorities. Examples of projects include improving participation in colon cancer screening (described in Section A.3.) and avoiding emergency department visits for cancer patients undergoing chemotherapy (described in Section A.4.). In addition, the OICR-CCO Health Services Research Network set up 'cd-link', a data-release program that grants approved researchers at academic institutions in Ontario direct access to cancer treatment data, while respecting patient privacy, from anywhere in the province. This unique and catalytic resource allows investigators to link patient tumour characteristics with clinical and health outcomes data to enable health services research into such things as the comparative effectiveness of different patient management/treatment strategies and the optimal deployment of health resources.

Going forward, the OICR-CCO Health Services Research Network will continue to take on relevant, ambitious research projects to optimize the delivery of cancer services in Ontario. A framework has been developed based on the successful colon cancer screening collaboration to systematically evaluate and optimize new cancer programs rolled out by CCO (Figure 9), perform rapid data analysis and return to support real-time improvements with resultant benefits to patients. Examples of potential initiatives amenable to this approach are new models of care, such as family physician follow-up of cancer patients, payment reform to move towards activity-based funding in the cancer centres, and efforts to make palliative care available earlier in disease course.

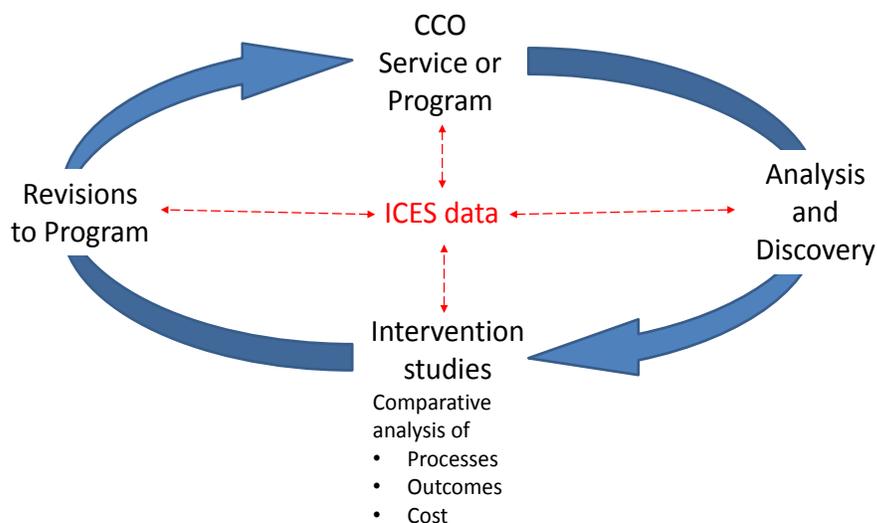


Figure 9. OICR-CCO Health Services Research Network. Framework for evaluation of new cancer programs rolled out by Cancer Care Ontario.

Impact. Project-specific deliverables and outcomes will be tracked as described in Section C.5., with the goal of driving improvements in cancer service delivery (prevention, screening and care). The ultimate impact of the OICR-CCO Health Services Research Network will be indicated by the uptake of research results and recommendations to guide evidence-based improvements in cancer service delivery that impact patient outcomes.

2. Ontario Molecular Pathology Network

The 2014 external review panel urged OICR continue to explore effective methods to ensure broader strategic engagement with Ontario’s pathology community and a joint far-sighted approach to the development of internationally competitive academic and molecular pathology expertise in the province. This capacity is critical to the development, translation and adoption of cancer innovations in the province and in particular, to take advantage of the molecular revolution in diagnostic testing and precision oncology. Recognizing that some of the barriers to academic molecular pathology relate to matters beyond the scope of OICR’s cancer research mandate (e.g., competing clinical duties, health system planning, medical school/residency training), the Institute has begun preliminary work to engage the Ontario pathology community on how OICR could bolster research capacity and leadership in cancer pathology, improve linkages with OICR and other Ontario institutions, and support the development of the next generation of research pathologists in the province.

Through consultations and a workshop with pathology leaders from hospitals and academic centres across Ontario in the summer of 2015, a consensus was built around the establishment of a molecular pathology network to support translational research and improve collaboration and sharing of information and approaches. The network would leverage OICR’s ongoing investments in pathology research, including the OICR Transformative Pathology Research Fellowship Award program, the Ontario Tumour Bank (OTB), the Diagnostic Development and Informatics programs, as well as the PM-OICR Translational Genomics Laboratory. Aligning network research activities with OICR clinical priority areas would allow for integration within TRIs and demonstrate the value of the pathologist perspective and expertise in translational research. Subsequent to the workshop, a committee of pathologists from across the province was established to develop these concepts into a proposal to be submitted to OICR, which, pending successful

international review, would support the establishment of a province-wide molecular pathology network. Efforts will be made to build partnerships that will expand the scope of activities, and reinforce capacity building and recognition of the importance of cancer pathology research.

Impact. While specific deliverables will be further defined in the coming months as greater granularity is developed around network activities, broad indicators of success will include increased participation of Ontario cancer pathologists in high-quality translational research; enhanced collaboration among cancer pathologists across the province and between pathologists and other clinical investigators; increased research training and mentorship for residents, fellows and early career pathologists; and ultimately translation of this capacity into improved diagnosis and treatment of cancer patients.

3. Ontario Health Study

The Ontario Health Study (OHS) is a member of the Canadian Partnership for Tomorrow Project (CPTP), a long-term, large cohort study that is investigating potential lifestyle, environmental, molecular and genetic causes of cancer and other chronic diseases such as diabetes, heart disease, asthma and Alzheimer's disease. More than 300,000 Canadians aged 35-69 have joined the study and nearly half of the participants have provided a biological sample. OHS has contributed 52 per cent of CPTP participants and 21 per cent of the biospecimens. These participants will be followed up for many years, with new cases of cancer and other chronic diseases identified through linkage to the Ontario Cancer Registry and other provincial health databases in partnership with ICES. The study has moved to a new stage of development; de-identified data collected on existing participants has become available to the research community to investigate the complex interplay of environmental, lifestyle and genetic factors that increase individual and community risk of common adult diseases including cancer. Together with researchers and funders of the CPTP, a common strategy will be developed to maximize the impact of the population research Technology Program that has been created.

Impact. The success of OHS will be demonstrated by its utilization by the research community to uncover novel lifestyle, environmental, molecular and genetic causes of cancer and other chronic diseases. OICR will work with researchers and funders to maximize the value and impact of OHS/CPTP.

4. Ontario Tumour Bank

The OTB was established in 2004 with the goal of providing access to high-quality biospecimens to academic and industry researchers across Ontario, Canada and beyond. It is a provincial tumour banking network with accredited laboratories across Ontario that collect tumour samples, each linked to clinical and outcome data. OTB participating sites are located in Hamilton, Kingston, London, and Ottawa. To date, OTB has collected more than 112,000 biospecimens from more than 15,000 patients, and has fulfilled 314 requests through the release of more than 33,000 sample aliquots to researchers. In a 2014 comparison of OTB with five other tumour banks in Canada, OICR was the leader with regard to the number of biospecimens released per year, the number of projects supported, external revenues and percentage of cost recovery. As a founding member of the Canadian Tissue Repository Network and through a number of keynote presentations and publications OICR has fostered development of quality standards and metrics for provincial and international biobanks that have now been adopted by the International Society for Biological and Environmental Repositories. Through the provision of high-quality annotated tissue samples OTB has contributed to several projects of the National Institutes of Health-

sponsored The Cancer Genome Atlas (TCGA) project and has, to date, been acknowledged in eight TCGA-related publications in *Nature*, *New England Journal of Medicine*, *Cell* and *Nature Genetics*.

Impact. Indicators of success will include the continued utilization of specimens for cancer research studies as well as the continued provision of high-quality service.

5. Canadian Cancer Clinical Trials Network

In partnership with other Canadian research funding agencies, OICR has consolidated its clinical trial infrastructure investments through the 3CTN. Supporting 75 Network cancer centres across Canada, including 22 sites in Ontario, 3CTN aims to increase Canada's capacity and efficiency in conducting academic cancer clinical trials, including trials testing precision oncology strategies and complex biomarker studies. Central to 3CTN's activities is the portfolio of academic, practice-changing cancer clinical trials, to which all Network sites are encouraged to recruit. The portfolio currently boasts a total of 205 trials, including 49 (24 per cent) that are led by Ontario institutions.

OICR's investment supports Ontario's participation in 3CTN in three ways: (1) hosting the national Coordinating Centre; (2) providing core funding to the Ontario sites, which has resulted in the creation of 11 highly qualified personnel positions; and (3) providing per case funding to increase Ontario patient recruitment to 3CTN portfolio trials.

Impact. Clear performance indicators such as year-over-year increased patient recruitment targets have been developed for the Network and will help OICR and its funding partners evaluate the success of 3CTN in increasing Canadian cancer clinical trials capacity and efficiency. Further to this, by reinforcing Ontario sites' clinical trials activities and recruitment, OICR-sponsored trials and correlative studies, such as those related to TRIs or Precision Oncology initiatives, will see benefits in accrual, access to biospecimens and clinical data, etc.

6. Ontario Cancer Research Ethics Board

Since 2004, OICR has been supporting OCREB, which centralizes ethics review for multi-centre cancer clinical trials in the province, ensuring that clinical research involving human subjects meets the highest standards of scientific and ethical conduct. OCREB is now the board of record for 28 of the 30 institutions in Ontario (Figure 10). OCREB's success is well documented by objective measures of quality and systems-level efficiency (see below). OICR will continue to support OCREB to facilitate the rapid implementation of academic and industry-sponsored multi-centre trials of both adult and pediatric patients.

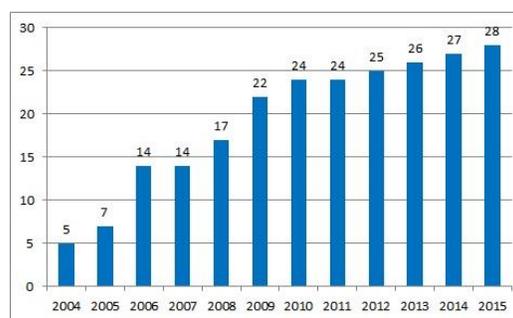


Figure 10. Number of Ontario cancer centres supported by OCREB. OCREB is the board of record for 28 out of 30 adult and pediatric centres in Ontario.

Impact. OCREB will continue to track its utility to Ontario's cancer clinical trials community using performance metrics (number of studies, time from submission to approval, etc.) and stakeholder surveys.

B.5 Technology Programs

High-impact research and innovation often requires access to state-of-the-art infrastructure consisting of research and technical experts and increasingly complex and costly equipment, including high-performance computing technologies. Teams associated with technology platforms are frequently early adopters of new technology and innovators that improve its utility, often in partnership with technology companies. The co-location of equipment and specialized teams in technology clusters can provide efficiencies that support access to the research community (through collaborative and/or service models), and training opportunities that promote interdisciplinary collaboration and foster a new generation of researchers.

OICR's six Technology Programs (Figure 6) build on a strong legacy of cancer research developed during OICR's first two mandates and leverage a critical mass of principal investigators and staff scientists that deliver innovation, provide state-of-the-art technological expertise, and support analytics for the interpretation of data. OICR's Blueprint (2016-2021) promotes greater focus of Technology Program activity on areas of OICR strategic priority and supports increased collaboration with Ontario's scientific and clinical community to leverage the resources established by MRI's investment.

The primary goal of the Technology Programs is to contribute expertise to one or more of the Institute's Strategic Initiatives. For example, the Imaging and Diagnostic Development programs will continue to provide critical intellectual and technical support to TRIs, particularly through key image-related innovations in improving the management of early breast and prostate cancer. Similarly, the Genomics and Informatics programs will be key drivers of the Precision Oncology initiatives, collaborate with the Ontario Molecular Pathology Network and the Diagnostic Development Program to support the molecular diagnostics research and data analysis, interpretation and sharing, and help to identify novel biomarkers to guide the management and treatment of cancer patients within various TRIs.

In addition, mechanisms will be implemented to ensure that the Technology Programs are accessible to Ontario researchers not directly involved with OICR Strategic Initiatives to enable cancer research in Ontario. Support may include technical services/training related to the development of leading-edge technologies and databases, access to OICR resources (equipment, data and samples) as well as advisory services on study design, choice of technologies, methods and data analyses. Details on available services and costs (if applicable, such as for reagents or technician time) will be provided on the OICR website. An outreach manager will be appointed to centralize the processing of requests, development of agreements/contracts, tracking of progress, and reporting of results.

To remain at the leading edge, Technology Programs will catalyze technology innovation, upgrade instrumentation, databases, software and other resources such as biological and chemical libraries, and seek ways to improve quality, speed and costs.

i. Biologics

The Biologics Program will leverage OICR's investments in the Innovation in Target Validation program and its predecessor, the Selective Therapies program, which enabled the recruitment, training and establishment of cutting-edge teams in the development of new antibodies to study and potentially treat cancer. Given the high importance of biological drug candidates in oncology, OICR provided seed funding to Dr. Sachdev Sidhu (recipient of an OICR Investigator Award) to establish the Toronto Recombinant Antibody Centre (TRAC)

at the University of Toronto. TRAC attracted a national award for the establishment of the Centre for Commercialization of Antibodies and Biologics (CCAB) to validate antibody candidates, test research tools, maintain antibody libraries and address issues related to the manufacture of products at the quality and scale needed for commercial success. The Biologics Program will primarily support the Cancer Therapeutic Innovations Pipeline and may also contribute to various TRI themes, including ovarian cancer.

ii. Diagnostic Development

Molecular diagnostic approaches to stratify patients and inform the use of novel therapeutics are fundamental to the realization of effective, economically viable precision oncology to improve patient outcomes. The tandem development of new therapeutics and biomarkers (i.e., companion diagnostics) is often required by regulators such as the Food and Drug Administration (FDA) in the U.S. and Health Canada, and companion diagnostics are also developed (often by academic groups) to increase the ability to predict safety and efficacy of an existing drug to improve clinical decision-making.

The development and validation of diagnostics requires the integration of histology-based practices, molecular technologies and large biospecimen collections collected in clinical trials. OICR's Diagnostic Development Program (formerly the Transformative Pathology Program) has been critically important to the establishment of OICR TRIs in early breast and prostate cancer, as well as new collaborations with Ontario clinical trials groups and researchers developing novel molecular diagnostic approaches. The program will continue to be a key resource providing cutting-edge research and value-added expertise and capabilities for biomarker validation and conversion to diagnostic assays for clinical use. The team will continue to develop novel biomarkers with a direct clinical focus, and improve and extend technology approaches to clinical diagnostic medicine. In addition to these core activities, significant effort will be devoted to further extending provincial collaborations, such as through the Ontario molecular pathology network, to enhance diagnostic development in Ontario, including:

- support for *in situ* and genomic/molecular assays from pathology biospecimens;
- access to cutting edge technologies, such as laser capture microdissection, image analysis, and molecular technologies;
- access to clinical trial tumour bank samples with associated patient data through both national and international collaborative networks, bridging the translational gap for local researchers;
- ability to produce Level 1 evidence for biomarker validation; and
- support for Health Canada and FDA submissions.

iii. Genomics

OICR's Genomics Program is evolving in light of the emergence of large-scale, low cost sequencing facilities. While the Institute's need for genome sequencing will continue to increase, a greater proportion of the more standard assays will be outsourced. The Genomics Program will continue to provide specialized expertise to support difficult projects (such as low-cellularity tumours e.g., pancreatic cancer) and targeted sequencing projects, as well as expert advice to provincial groups needing help, even in recommending third party service providers. A major new role for the Genomics Program will be to support the Translational Genomics Laboratory, a joint initiative between Princess Margaret Cancer Centre and OICR (as described in Global Leadership in Precision Oncology).

iv. Imaging

Over the past seven years, OICR's imaging activities have increased Ontario's capability to translate research into new imaging technologies and probes for cancer detection and treatment. Ablation and robotic innovations have been co-developed with imaging technologies to biopsy and treat tumours, which have been jointly evaluated in clinical trials. Networking across different Ontario centres has catalyzed effective collaboration between basic scientists and clinical researchers, which has been recognized by major national awards including the establishment of the Centre for Probe Development and Commercialization and the Centre for Imaging Technology Commercialization, as well as considerable leveraged funding and private sector partnerships.

The Imaging Program will continue to play a vital role in the conduct of TRIs, including early breast and early prostate cancers, by developing new probes and imaging tools to improve patient management in regard to diagnosis, stratification according to risk factors and determination of treatment response. Future image-guided therapies will also rely on advances in earlier detection of tumours using more sensitive imaging technologies achieved through novel imaging probes and/or combined (hybrid) imaging techniques. Improved functional characterization will be required to delineate the volume to be treated from surrounding normal tissue more accurately. These advances may allow patients to be treated earlier, when tumours are more curable.

Technology development activities will move increasingly towards image-guided intervention techniques that are used to biopsy and treat tumours with potential for improved efficacy and fewer side effects. Enhanced imaging has the potential to inform more traditional ablative approaches such as surgical techniques as well as radiation therapy. Image-guided tumour ablation systems are complex and involve the integration of advanced medical imaging systems with medical and surgical robotics, radiotherapy, guidance technology and imaging probes used to identify the tumour and its margins. Applications in development are rapidly expanding, including techniques to treat tumours in the liver, prostate, kidneys, bone and lungs.

v. Informatics

Big Data Analytics (within the Global Leadership in Precision Oncology Strategic Initiative) requires significant investment in compute hardware and its associated infrastructure. OICR is pursuing a tiered system of infrastructure that provides a range of services and economies. Firstly, OICR will continue to invest in local compute hardware and storage using the server rooms located at the MaRS Centre. This local infrastructure provides OICR with very low latency network access, which is ideal for primary analysis of genomics data generated in-house as well as work that involves sensitive Protected/Personal Health Information (PHI). Secondly, OICR will use provincial and national compute infrastructure, such as Compute Canada's SciNet and the proposed Compute Ontario facilities for projects that do not require low latency or a high degree of security. This includes algorithm development, system modeling and biomarker discovery. Lastly, OICR will make use of commercial cloud vendors when large amounts of processing power are required for specified periods of time.

Several Ontario universities and cancer centres have been building local bioinformatics capacity and have expressed interest in leveraging OICR's expertise. Tremendous opportunity exists to strengthen and amplify provincial capacity by linking groups developing new technologies to store and share data, creating software products and

discovering biomarkers that are needed for the application of precision medicine concepts in the clinical management of cancer patients. Greater collaboration and training opportunities will also enhance the development of highly qualified personnel proficient in the interpretation of cancer genomes at the highest possible standards.

vi. Medicinal Chemistry

The Medicinal Chemistry Program is composed of medicinal, analytical, computational, ADME (absorption, distribution, metabolism, and excretion) and biology experts with industry experience in developing small molecule drugs. The team collaborates with the broader scientific community in Ontario to translate discoveries made in Ontario research laboratories into new drugs, and will primarily support the Cancer Therapeutic Innovations Pipeline, as well as various TRI themes, as applicable.

The Medicinal Chemistry program team has proven expertise and capabilities in designing and optimizing compounds with drug-like properties in order to advance targets nominated by Ontario scientists. Medicinal chemists work closely and iteratively with biochemists and cell biologists to discover and optimize small molecule leads and clinical candidates. Using state-of-the-art analytical equipment, the Program provides valuable *in vitro* ADME assays, formulation support and *in vivo* exposure data to help guide efficacy and PD studies. The Program's biology core establishes biochemical and cell-based functional assays to interrogate and validate new biological targets, and discover and validate PD markers to evaluate and advance small and large molecules into clinical development.

Impact. The Technology Programs will deliver impact through their contributions to the success of the Strategic Initiatives and, more broadly, their enablement of translational cancer research in Ontario. Technology development activities within the Technology Programs will be monitored against project deliverables as described in Section C.5. Technology Programs will also be monitored on an ongoing basis for accessibility, collaboration, capacity usage, performance and user satisfaction.

B.6. Catalyzing translation and patient impact

To enable the success of the Strategic Initiatives and Technology Programs and more broadly facilitate translational cancer research excellence in Ontario, the Institute will invest in attracting and developing the next generation of Ontario cancer research leaders, clinical trials for the evaluation of promising cancer innovations and, together with FACIT, commercialization activities to yield economic benefit to the province.

a) Development of highly qualified personnel

Achievement of OICR's translational mission requires a dedicated cancer research workforce in Ontario. OICR will continue its Investigator Awards Program to attract and retain outstanding research and clinical investigators to augment Ontario's capacity to bring discoveries to cancer patients. The program is designed to provide stable recruitment and retention funding for principal investigators involved in OICR's Strategic Initiatives/ Technology Programs as well as other cancer research initiatives in the province. As of August 2015, 33 awardees are supported by the program, with 10 at OICR's headquarters in the MaRS Centre and 23 at research institutes across the province. The investigators complement a larger number of cancer researchers already based in Ontario who are also engaged in OICR research activities. Clinician scientists will play a more important role in OICR's Strategic Initiatives under the Strategic Plan for 2016-2021 to maximize the clinical utility of OICR-funded research. Recruitment of clinical investigators, as well as young

investigators, who will constitute the next generation of Ontario leaders, will be priorities for the future. OICR will work closely with partner academic institutions province-wide to identify, attract and enable promising candidates. In addition, OICR will continue supporting a number of training opportunities, including Transformative Pathology research fellowships, hosting of the Canadian Bioinformatics Workshops, and training of undergraduate and graduate-level students associated with OICR-supported research projects.

Impact. The renewed investment in the OICR Investigator Awards Program and training opportunities for students, fellows and early career scientists will strengthen cancer research capacity in the province and develop a cadre of highly qualified personnel poised to innovate and translate discoveries into better outcomes for cancer patients and economic benefits, and sustain Ontario's global leadership in cancer research. OICR will continue to monitor recruitment and retention of its investigators, as well as the effectiveness and reach of its training activities.

b) Clinical trials

OICR is currently undertaking the clinical evaluation of novel immunotherapies and imaging interventions that aim to improve outcomes for cancer patients. OICR will expand its support of clinical trials to evaluate Ontario assets as part of its Strategic Initiatives and through key partnerships with industry and funding agencies. For instance, an OICR partnership with Stand Up To Cancer Canada will support world-class teams that are initiating clinical trials for breast cancer and brain tumours.

OICR will collaborate with Ontario clinical trials groups including NCIC-CTG, OCOG and the Princess Margaret Phase I/II Consortium to evaluate Ontario assets, capitalizing on provincial clinical oncology expertise and infrastructure. OICR will facilitate trial implementation by helping to identify common hurdles across the clinical trials portfolio and address them in an effective, timely manner. Specific approaches will include:

- Support for trial design and planning, including leveraging 3CTN to match site capabilities with trial needs;
- Centralized ethics review for multi-centre cancer clinical trials in the province through OCREB;
- Facilitation of partnerships between clinical investigators and laboratories able to conduct complex "omics" or imaging testing; and
- Expansion of OICR's biostatistics training program that supplements university curriculum and provides financial assistance to biostatistician interns, graduate students and fellows placed at institutions in the province.

Impact. OICR will streamline and facilitate the evaluation of promising Ontario assets to determine clinical utility and support further development and translation to improve patient outcomes. OICR will monitor the success of its efforts at enabling the timely launch and conduct of trials, including achievement of patient accrual targets, as well as the effectiveness of its biostatistics training program at developing and placing qualified personnel at Ontario institutions.

c) Commercialization and economic benefits

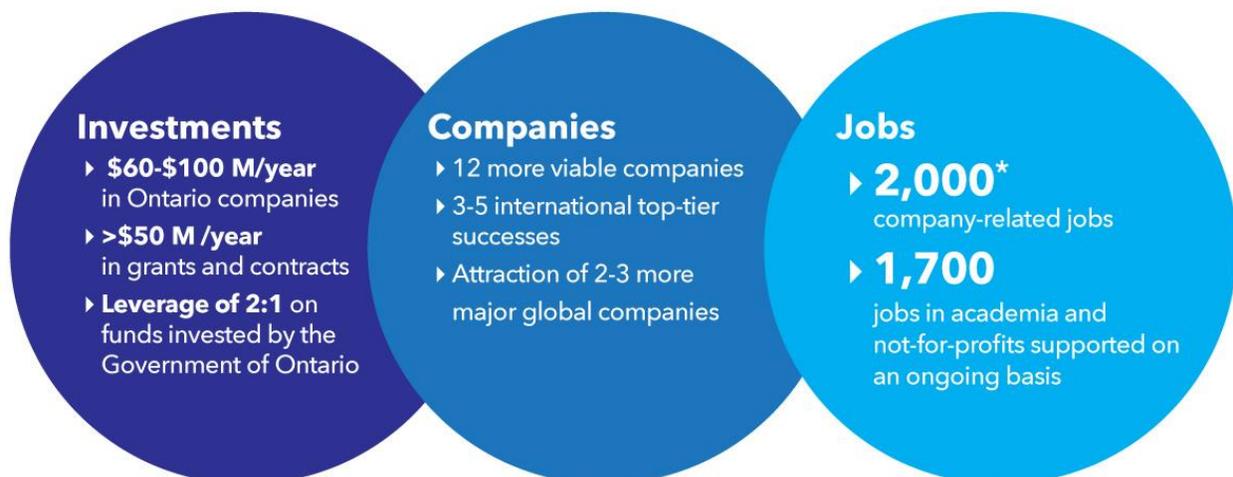
As noted in section A.2., OICR's commercialization group evolved from 2012 to 2014 into FACIT, which houses all of the Institute's commercial assets and related IP and operates as an independent business trust with OICR as its sole beneficiary. FACIT has become a strategic vehicle for transforming OICR and Ontario's oncology innovations into viable

opportunities that benefit patients, researchers, investors and the province's economy, and serves as a well-regarded point of contact for biotech and pharma firms seeking oncology investment opportunities in Ontario.

FACIT utilizes a number of approaches to achieve its broad mandate. It provides expert advice and support for cancer-related early-stage commercialization activities such as proof-of-concept, validation, creation of standard operating procedures, market analyses, IP protection and acquisition, and has collaborated effectively with other organizations to present opportunities to potential partners. Beyond the traditional technology transfer role such as out-licensing, FACIT also engages in other commercial pursuits such as company creation, startup support, and providing capital to bridge funding gaps. FACIT makes it a priority to encourage maximum participation by Ontario organizations in the development, commercialization and use of inventions arising from OICR activities, which are core elements of OICR's "Ontario First Policy."

FACIT has led discussions with private sector stakeholders that have resulted in strategic partnerships for the development and commercialization of Ontario assets (e.g. BCL6 and Marabex™) as well as investment in Ontario biotechs (e.g. Fluorinov). Mechanisms have included the creation of startup enterprises around assets, with corporate structures and funding that enable significant third party investment and high value return-on-investment potential, while retaining substantial footprint and presence within the province. As these efforts come to fruition, there is validation that FACIT's strategy of de-risking breakthrough technologies is resulting in increasingly larger investments and new jobs in Ontario.

Impact. Synergies between OICR and FACIT will continue to accelerate the development of promising academic discoveries to a proof of concept/inflection point that will be of interest to the private sector or other partners committed to bringing health innovation and economic benefits to Ontario and its citizens (see TRI and Cancer Therapeutic Innovation Pipeline sections). With ongoing support from Ontario, OICR and FACIT project to deliver the following economic impact to the province over the next five years:



* Includes Direct, Indirect and Induced jobs. Steve Morgan *et al.*, Pharmaceutical industry employment in Canada (2010). Indirect jobs refers to jobs that support the generation of goods and services by Direct employees. Induced jobs refers to jobs created by increased expenditures of employees of both the "Direct" employer and the "Indirect" employers.

C. Achieving Results

OICR is accountable to the people of Ontario. Excellence in governance, leadership and management, an engaged workforce, high-quality and efficient operational processes, effective outreach and communications, and a robust approach to measuring the performance and impact of Institute activities are essential to deliver on the OICR's ambitious mandate.

C.1. Governance

The Institute is committed to maintaining strong and effective governance at the highest level. The members of the Board of Directors bring a diverse set of skills and experience including backgrounds in science, industry, business and academia. The priorities of the Board of Directors are to provide oversight of the implementation of the Institute's strategic plan; to ensure succession planning for the renewal of the Board, the SAB and OICR's executive team; to oversee financial performance and risk management; and to assess the performance of the organization. The SAB is comprised of internationally recognized experts that provide advice to the President and Scientific Director, and to the Board. Acting on a recommendation raised by the 2014 external review panel, OICR has recruited new members that bring scientific and translational expertise to the Board. The Board has also established a new research subcommittee of the Board to provide in-depth oversight of the research strategy and performance, and to interact with the SAB on behalf of the Board.

OICR submits annual reports, operating plans and financial statements to the SAB and Board of Directors. Once approved, these are forwarded to the Ontario Ministry of Research and Innovation.

C.2. Leadership

The success of OICR will depend on the quality and commitment of its leadership and staff. OICR is led by the President and Scientific Director, supported by the Deputy Director and Chief Scientific Officer and an Executive Team.

Large-scale initiatives of the Institute will be managed by research and clinical leaders, supported by scientific management teams composed of principal investigators and stakeholder representatives (if applicable). Professional project managers will continue to be key players to assure operational and administrative coordination of these initiatives. OICR's research and clinical leaders will continue to be recognized for their scientific excellence, and will also be committed to the collaborative spirit and translational mandate of the Institute.

C.3. Enablers

The Institute's support functions (research operations, finance, human resources, facilities management, information technology, legal, communications and procurement) will deliver extraordinary customer service to staff and stakeholders by using an approach that is accessible, responsive, accountable, quality-driven and team-oriented.

Each of the Institute's teams sets goals and objectives annually, in alignment with OICR's mandate. This process focuses on continual improvement and adherence to the Institute's values of excellence, innovation, responsiveness, pride and collaboration.

Management is committed to monitoring staff engagement and satisfaction, and to adjusting human resources strategies as required. The Institute is committed to providing a safe and healthy work environment for all employees, visitors and the public, through a focus on compliance with legislative requirements, emphasis on safety, emergency response preparedness and health promotion activities.

C.4. Outreach and communications

The success of Strategic Plan 2016-2021 is predicated on working more closely with Ontario's research and clinical communities. Greater awareness of OICR's mission, priorities and activities is fundamental to the Institute's role as a catalyst for the province and will enable the identification of emerging opportunities and assets to fuel Ontario's translational cancer research pipeline. As such, renewed effort will be directed towards proactive outreach, engagement and partnership activities.

OICR will establish mechanisms (e.g., workshops/symposia, roadshows, site visits) and appoint an outreach manager to engage in two-way dialogue with Ontario institutions with the aim of promoting awareness of OICR, soliciting input and feedback on shaping Institute research activities and identifying collaboration opportunities. OICR has already begun laying the groundwork for these activities through province-wide consultations and workshops conducted to inform the development of Strategic Plan 2016-2021. In addition, OICR will better publicize information regarding the capabilities and capacity (expertise, equipment, infrastructure) of its Technology Programs to facilitate greater access to the Ontario research community; vehicles will include, among other things, a refreshed Institutional website that simplifies inquiries from investigators seeking to collaborate with OICR and a centralized point of contact for all inquiries. More broadly, OICR will engage proactively in dialogue with stakeholders in the cancer research community, including treatment providers, patients, governmental and advocacy groups, other funding agencies and the private sector to foster, strengthen and support alignment within the growing cluster of translational cancer research in the province.

Stakeholder engagement activities will be underpinned by the capacity to effectively communicate with and seek feedback from a broad and varied audience about OICR's strategic choices and capabilities. OICR is committed to open, timely and accurate communications of the Institute plans and performance, and welcomes inquiries, comments and opportunities for dialogue. When appropriate, OICR engages in proactive media relations to publicize the work and success of the Institute and its researchers. OICR will continue to seek out new opportunities and mechanisms to inform and educate the scientific community (internal and external), stakeholders and the public.

C.5. Measuring performance

OICR will measure its success in achievement of the Institute's mission of partnering with the Ontario oncology community to accelerate the development and implementation of clinically important knowledge, products, services and policies to improve cancer prevention, detection, diagnosis and treatment that deliver better outcomes for cancer patients, which is the fundamental driver of the Strategic Initiatives and Technology Programs of Strategic Plan 2016-2021. To that end, OICR will track Institutional performance broadly against its five overarching goals, and has adopted a disciplined approach to monitor progress of its research portfolio to ensure that discoveries move along the translational research roadmap towards the clinic and the broader healthcare community. The indicators described below are reflective of the anticipated Impact of the four Strategic Initiatives (Section B.4.). In addition, the Institute will continue to solicit

independent feedback on its progress and plans through periodic review by external experts.

Institutional performance

OICR will track the following key performance indicators to assess fulfillment of the Institute's five Goals and its impact:

- 1. Perform cutting-edge translational cancer research**
 - Measures of research productivity and impact: publications (total and by journal impact factor), citations;
 - Partnerships for continued development and adoption of cancer innovations arising from OICR-funded research;
 - Impact on patient outcomes/healthcare delivery.

- 2. Mobilize Ontario research strengths around key cancer priorities**
 - Engagement of Ontario cancer research and clinical community (institutions, investigators) in planning, developing and participating Strategic Initiatives;
 - Partnerships and leveraged funding secured to support Strategic Initiative and Technology Program activities;
 - Outreach activities, including scientific meetings, roadshows, public events, workshops, courses and seminars organized or partially funded by OICR;
 - Enhancement of collaboration within the Ontario oncology ecosystem as a result of engagement in OICR translational research activities.

- 3. Partner with the Ontario cancer community to leverage and elevate the level and impact of cancer research in the province.**
 - Engagement of Ontario cancer research and clinical community (institutions, investigators) in planning, developing and participating Strategic Initiatives;
 - Measures of access of investigators to Technology Programs (technologies, expertise) i.e., collaborations, responsiveness, performance, user satisfaction;
 - Increased capacity and opportunities for high quality translational cancer research at Ontario institutions, including expertise (see highly qualified personnel below), technologies/infrastructure, and networking that supports sharing of approaches, protocols, data and analysis tools;
 - Utilization of Ontario oncology resources supported by OICR, such as OTB, OCREB, 3CTN;
 - Development of highly qualified personnel: number of individuals who have enhanced knowledge, training or skills through OICR-supported research activities; training activities, symposia and other networking activities related to Technology Platforms; and investigators recruited/retained through the Investigator Awards program (including Transformative Pathology Fellowships).

- 4. Drive the adoption and/or commercialization of cancer innovations in Ontario:**
 - Number of clinical trials and patients recruited;
 - Partnerships that transfer knowledge, technologies and promising agents to organizations that will lead the subsequent stages of development and adoption;
 - Commercialization activities (through FACIT) including patents, licenses, invention disclosures, private sector investment, spin-out and job creation;
 - Contributions to evidence-based health policy, adoption of new models of care.

5. **Enhance Ontario's global leadership in cancer research.**

- Leadership of national and global initiatives;
- Significant contribution to national and global initiatives;
- Measures of research productivity and impact: publications (total and by journal impact factor), citations.

Performance of OICR's Translational Research Portfolio

OICR has developed and progressively refined its processes for monitoring the performance of its translational research portfolio to maximize the impact of its research investments. From the initial funding decisions to the oversight of research progress, OICR seeks the assistance of national and international experts to ensure scientific excellence.

Translational research portfolio management processes, which integrate best practices from academia and industry, are grouped in three categories:

1. *Funding Decisions*: based on international peer review and mid-term review.
2. *Monitoring of the Translational Research Portfolio*: based on deliverables and milestones; and
3. *Research Oversight*: through scientific advisory boards and periodic scientific, financial and IP reporting.

The Institute has established a common nomenclature that allows the qualification of the stage of research project deliverables along OICR's translational research roadmap (Figure 1). At the time of initial funding decisions, research teams provide deliverables and related milestones to track progress. Periodic monitoring of progress by OICR's management and research teams identifies potential bottlenecks and delays, and facilitates planning adjustments when needed. For large investments such as TRIs, a formal mid-point evaluation is conducted to determine whether funding should continue, be modified or discontinued. In addition, Technology Programs will be monitored on an ongoing basis for performance, capacity usage, accessibility, collaboration, and user satisfaction.

OICR's management will continue to work with Ontario scientific and clinical leaders to develop and refine the structures and processes needed for the effective implementation of Strategic Plan 2016-2021, ensuring that the Institute remains nimble and able to capitalize on emerging opportunities to advance its mandate.

D. Implementation Roadmap

A high-level, preliminary timeline for the development and launch of Strategic Initiatives and Technology Programs for Strategic Plan 2016-2021 is provided in the table below and in the chart that follows in Figure 11.

	Partners/Stakeholders	Next Steps	Proposed Timeline
Translational Research Initiatives	Researchers, clinicians, funding agencies, and end-users including private sector and healthcare agencies to participate in TRI planning workshops	<ul style="list-style-type: none"> • TRI planning workshops • Submission of LOIs • Peer-review and selection of LOIs • Submission of Funding Requests • Peer-review and funding decisions • Launch* 	<ul style="list-style-type: none"> • Nov. 2015 – Mar. 2016 • May 2016 • Jul. 2016 • Oct. 2016 • Mar. 2017 • Apr. 2017
Global Leadership in Precision Oncology	PM/UHN, Ontario cancer centres (researchers and clinicians)	1. OCTANE: <ul style="list-style-type: none"> • Planning workshops • Seed funding to establish network components including informatics systems • Submission of Funding Request • Peer-review and funding decision • Launch* 	<ul style="list-style-type: none"> • Oct. 2015 – Mar. 2016 • Apr. 2016 – Mar. 2017 • Oct. 2016 • Mar. 2017 • Apr. 2017
	PM/UHN	2. TGL: <ul style="list-style-type: none"> • Planning meetings • Recruitment of OICR Director, Cancer Genomics • Seed funding to establish network components including informatics systems • Submission of Funding Request • Peer-review and funding decision • Launch* 	<ul style="list-style-type: none"> • Oct. 2015 – Mar. 2016 • Ongoing until filled • Apr. 2016 – Mar. 2017# • Oct. 2016 • Mar. 2017 • Apr. 2017
	Global partners, Ontario cancer centres (researchers and clinicians)	3. ICGCmed: <ul style="list-style-type: none"> • Finalize ICGCmed framework • Workshop with Ontario clinical trials and pathology leaders • Identify co-funding partners 	<ul style="list-style-type: none"> • Dec. 2015 • May 2016 • Apr. 2016 – Jun. 2016

		<ul style="list-style-type: none"> • Submission of Funding Request • Peer-review and funding decision • Launch* 	<ul style="list-style-type: none"> • Oct. 2016 • Mar. 2017 • Apr. 2017
		4. GA4GH: <ul style="list-style-type: none"> • Submission of Funding Request • Peer-review and funding decision • Launch* 	<ul style="list-style-type: none"> • Oct. 2016 • Mar. 2017 • Apr. 2017
		5. Big Data Analytics: <ul style="list-style-type: none"> • Submission of Funding Request • Peer-review and funding decision • Launch* 	<ul style="list-style-type: none"> • Oct. 2016 • Mar. 2017 • Apr. 2017
Cancer Therapeutics Innovation Pipeline	Ontario academic experts in cancer biology and drug discovery; SGC; pharma/biotech companies; venture capital community; other drug discovery centres/initiatives	<ul style="list-style-type: none"> • Develop governance structure and operating model • Develop guidelines for Accelerator and Incubator project request for applications • Submission of Funding Request • Peer-review and funding decision • Launch* 	<ul style="list-style-type: none"> • Nov. 2015 – Apr. 2016 • May 2016 • Nov. 2016 • Feb. 2017 • Apr. 2017
Collaborative Research Networks	CCO, ICES, CPAC, Public Health Ontario, Ontario cancer centres and academic centres, NCIC	1. OICR-CCO Health Services Research Network: <ul style="list-style-type: none"> • Continuation of current activities • Submission of Funding Request • Peer-review and funding decision • New funding cycle begins* 2. Ontario Molecular Pathology Network: <ul style="list-style-type: none"> • Planning meetings • Submission of Funding Request • Peer-review and funding decision • Launch* 3. Ontario Health Study: <ul style="list-style-type: none"> • Bio-specimen collections, data access and linkages continuing. • OHS/CPTP sustainability strategy • Peer-review and funding decision 	<ul style="list-style-type: none"> • Oct. 2015 – Mar. 2018 • Oct. 2017 • Mar. 2018 • Apr. 2018 • Oct. 2015 – Feb. 2016 • Mar. 2016 • Jun. 2016 • Jul. 2016 • Ongoing • Jan. 2016 • Mar. 2016

		<ul style="list-style-type: none"> • Launch* 	<ul style="list-style-type: none"> • Apr. 2016
		4. Ontario Tumour Bank: <ul style="list-style-type: none"> • Continuation of current activities 	<ul style="list-style-type: none"> • Ongoing
		5. 3CTN: <ul style="list-style-type: none"> • Continuation of current activities 	<ul style="list-style-type: none"> • Ongoing
		6. OCREB: <ul style="list-style-type: none"> • Continuation of current activities 	<ul style="list-style-type: none"> • Ongoing
Technology Programs: i. Biologics ii. Diagnostic Development iii. Genomics iv. Imaging v. Informatics vi. Medicinal Chemistry	Technology Program leaders and stakeholders	<ul style="list-style-type: none"> • Contribution to Strategic Initiative planning activities and funding requests • Delineation of services that can be accessed for Ontario cancer research community • Appointment of Outreach Manager to centralize management of requests • Development of processes to support service access and collaboration • Bridge funding^ϕ • Submission of Funding Request • Peer-review and funding decision • Funding decisions and launch 	<ul style="list-style-type: none"> • Nov. 2015 – Oct. 2016 • Dec. 2015 – Jan. 2016 • Feb. 2016 – Mar. 2016 • Mar. 2016 • Apr. 2017 • Jun. 2017 • Nov. 2017 • Dec. 2017

* Pending successful review by an independent expert panel and availability of funding.

Timeline may be expedited.

^ϕ Technology Program support will be determined based on need following selection of Strategic Initiatives. Bridge funding to be provided between end of four-year budget allocations and Technology Program funding decisions.

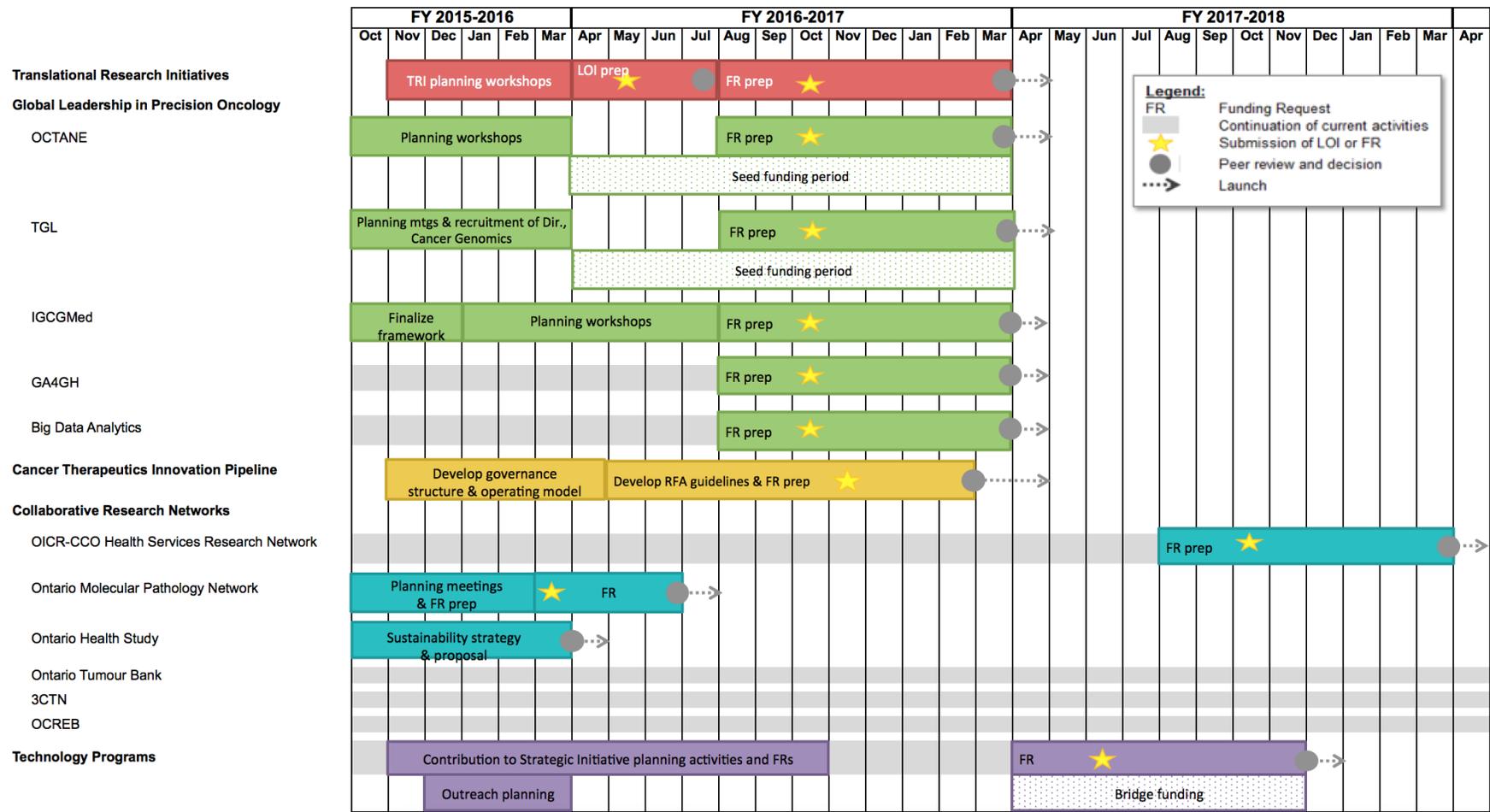


Figure 11. Summary of implementation steps for the development and launch of Strategic Initiatives and Technology Programs. Note that timelines are preliminary and only cover implementation activities from October 2015 – April 2018.

E. Conclusion

In 2005, the Ontario government made a strategic investment to harness and capitalize on the substantial cancer research excellence in the province to accelerate the translation of discoveries into better patient outcomes and economic benefit. OICR has supported a critical mass of leading-edge scientists, clinicians and companies focused on addressing the growing burden of cancer. Ontario is already beginning to see return on investment, including innovative technologies to diagnose and treat cancer patients, evidence-based strategies for improving healthcare delivery and cost-effectiveness, as well as economic benefits, including high-quality jobs, increasing private sector investment, and a growing cluster of oncology companies taking shape in the province. With a robust pipeline of innovative assets poised to reach the clinic over the next five years, as well as important and timely initiatives being launched to bolster translational cancer research capacity in the province, the people of Ontario are on the verge of realizing the transformative impact of their investment.

Appendix I: Preliminary focus and scope of TRI themes

The following descriptions of potential TRI themes identified through consultations in 2014-2015 summarize preliminary ideas proposed by Ontario researchers and clinicians. TRI objectives and plans will be further defined through workshops that engage the broader Ontario cancer research and clinical community aimed in developing detailed TRI proposals.

- **Pancreatic cancer:** The PanCuRx TRI was approved in early 2015, following an international scientific review of a proposal developed by Dr. Steven Gallinger, who is based at the University Health Network, Mount Sinai Hospital and OICR. The goal of PanCuRx is to seek solutions to the high fatality rate of pancreatic cancer by generating new knowledge about genetic and biologic subsets of disease, mechanisms of tumourigenesis and tailored treatment options.

Clinical relevance: Pancreatic Ductal Adenocarcinoma (PDAC) is the fourth leading cause of cancer death in Canada. The current five-year survival rate of 7.7 per cent is the lowest of all epithelial cancers. The major clinical challenges are: (1) PDAC metastasizes early so few patients are amenable to curative surgical resection; (2) PDAC has proved relatively resistant to systemic therapies; and (3) there has been limited benefit from the use of newer molecular targeted agents.

Ontario innovation or asset: Genomic biomarkers (1) representative of PDAC at different stages (including metastatic lesion), and (2) of resistance to systemic therapy; superior pre-clinical models (organoids and patient-derived xenografts); and Ontario's PDAC registry and clinical trial resources to facilitate testing of new therapies and biomarkers.

Approach: PanCuRx currently focuses on (1) later-stage PDAC, including locally advanced and metastatic disease, familial cases, and a range of hypoxic states and effects of microenvironment; and (2) characterizing PDAC driver genes and pathways with the aim of validating prognostic and predictive biomarkers. Greater understanding of PDAC and the factors predicting drug responsiveness/resistance will be obtained by performing detailed analysis of patients with advanced disease receiving two standard chemotherapy regimens in the context of a controlled high content clinical trial (Treatment Cohort study called COMPASS). Patients who relapse or fail to benefit from first line chemotherapy will be offered personalized second line therapies based on genomic/transcriptomic features of their tumors.

Anticipated impact: Meaningful advancements in the clinical management and treatment of PDAC patients.

- **Early breast cancer:** The goal of early breast cancer research within the current IMEC TRI is to optimize the treatment of early breast cancer guided by molecular and/or imaging biomarkers. Future objectives and approaches will be the subject of the upcoming TRI workshop.

Clinical relevance: Breast cancer is the most commonly diagnosed cancer amongst Canadian women, with a 1 in 9 lifetime risk of this disease. Across the spectrum of disease, outcomes have improved significantly over the past 20 years. However, several clinical challenges related to patient management have emerged. Breast cancer screening has resulted in a significant increase in the detection of pre-invasive ductal carcinoma *in situ* (DCIS). New approaches are needed to guide management of DCIS patients, as only a small number (approximately 5 per cent) will progress to invasive disease, while the vast majority experience excellent outcomes even if the lesions are left untreated.

In early invasive breast cancer, the challenge is to make treatment decisions that reflect the biological facets of the disease that influence prognosis. On one hand, there is a need to identify women with low risk invasive or pre-invasive breast cancer that can safely avoid overly-aggressive treatment and associated toxicity. On the other hand, there is a need to identify women with worse prognosis who are at high risk of non-response to standard chemotherapy, and thus in need of new treatment options.

Ontario innovation or asset: DCIS: A highly clinically-annotated Ontario cohort of DCIS biospecimens and molecular biomarkers that can robustly segregate patients at high risk of recurrence or progression to invasive disease from those at low risk. *Invasive breast cancer:* Biorepositories with rich collections of biospecimens collected in breast cancer trials conducted in Canada and internationally; molecular diagnostic markers for anthracycline and endocrine resistance and for identifying new drug targets; and new imaging devices and approaches (probes, pathology and image-guided therapy).

Approach: Current IMEC early breast cancer projects focus on: the identification of key molecular events in the transition from primary DCIS to invasive or non-invasive recurrence and driving treatment response and failure in patients with early invasive breast cancer; the development of new diagnostic tests that can inform treatment decisions, including response monitoring; the development of advanced imaging tools to characterize and monitor the extent of early lesions; and clinical trials to evaluate novel strategies.

Anticipated impact: DCIS: Rational stratification of patients with DCIS to reduce over-treatment, and development of biomarkers with commercial potential that could ultimately change practice guidelines for the treatment of early breast cancer. *Invasive breast cancer:* Rational stratification of women with early invasive breast cancer, development of biomarkers/treatments with commercial potential that could ultimately change treatment outcomes for women with pre-metastatic invasive breast cancer. Validation of optimal treatment of low risk women could reduce morbidity from unnecessary chemotherapy and reduce healthcare costs.

- **Early prostate cancer:** The goal of early prostate cancer research within the current IMEC TRI is to optimize the treatment of early prostate cancer guided by molecular and/or imaging biomarkers to classify indolent versus aggressive disease. Future objectives and approaches will be the subject of the upcoming TRI workshop.

Clinical relevance: Prostate-specific antigen (PSA) screening has produced a significant increase in the rate of diagnosis of prostate cancer, the most frequently diagnosed neoplasm and the third most common cancer killer among men in Ontario. Identifying patients with low risk prostate cancer that have little/no chance of progressing to invasive disease would avoid the significant morbidity associated with radical prostatectomy and other aggressive local therapies.

Ontario innovation or asset: Molecular biomarkers predictive of which intermediate risk patients will suffer relapse and which can safely be placed on active surveillance protocols; new imaging approaches (probes, pathology and image-guided biopsy and therapy); a highly clinically-annotated cohort of biospecimens; integrated cross provincial network of researchers by Prostate Cancer Canada/Movember to validate clinical diagnostic assays for early prostate cancer; and clinical capabilities to conduct complex multi-centre imaging clinical trials.

Approach: With support from OICR, Prostate Cancer Canada, Movember and the Terry Fox Research Institute, current IMEC early prostate cancer projects focus on: (1) developing biomarkers to distinguish intermediate risk prostate cancer patients that will suffer relapse from those who can safely be placed on active surveillance protocols; (2)

conducting a Phase III clinical trial to determine whether multi-parametric magnetic resonance imaging-coupled with transrectal ultrasound (TRUS)-guided biopsy to distinguish men who would benefit from aggressive treatment versus active surveillance; (3) developing imaging tools and devices for the accurate detection of prostate cancer, definition of extent of disease and characterization of potential aggressiveness; and (4) validating these new imaging tools versus pathology data to guide focal therapy in a clinical trial.

Anticipated Impact: Rational stratification of patients with indolent versus aggressive disease will optimize management, reduce morbidity and reduce healthcare costs.

- **Immuno-oncology:** Building on the success of OICR's Immuno- and Bio-Therapies (ORBiT) program, develop novel immunotherapies and enhance new immunotherapy approaches through better patient selection or rational combinations of immunotherapeutics.

Clinical relevance: Novel therapies that exploit the immune system have achieved remarkable clinical results in melanoma and other tumour types that are difficult to treat. Other immune-modalities such as those using patient-derived immune cells as well as engineered immune cells (i.e., chimeric antigen receptors) have emerged and portend improved clinical benefits.

Ontario innovation or asset: Ontario researchers supported by OICR have been successful in carrying out research from discovery of a world-first oncolytic virus vaccine platform to a Phase I/II clinical trial. Other immunotherapies, including artificial antigen-presenting cells (aAPC), human invariant chain natural killer T (iNKT) cells, adoptive cell therapy using, tumour infiltrating lymphocytes (TILs), CARs, T cell engagers and affinity matured T cell receptors (TCRs) are adding to the emerging arsenal of OICR-supported biotherapeutics.

Approach: Key areas where Ontario can play an important role include development of next generation immunotherapies; rational combination of new treatment modalities based on scientific data; and identifying subsets of patients that will derive greatest benefit from these new approaches.

Anticipated impact: Novel immune therapies to defeat hard to treat cancers. Long-term disease control in increasing proportions of patients.

- **Leukemia:** Demonstrate that monitoring stemness prognosis signatures can lead to better outcomes for leukemia patients and that targeting leukemia stem cells can lead to improved therapies. Future objectives and approaches will be the subject of the upcoming TRI workshop.

Clinical relevance: Acute myeloid leukemia (AML) survival rates are poor (approximately 30 per cent), and in the elderly, where incidence is highest, the prognosis is even more dismal (less than 10 per cent). Pediatric B-cell acute lymphoblastic leukemia (B-ALL) has high survival rates (80-90 per cent), but despite the successful treatment of ALL in children (and to a lesser extent in adults), there is significant risk of relapse that is typically fatal in children and adults who fail first-line therapies.

Ontario innovation or asset: Recognized for the discovery of cancer stem cells, Ontario leaders are at the forefront of translation pertaining to hematological malignancies; leukemic biomarkers for stratifying patients and/or individualizing treatment; stemness-based drug targets and promising pre-clinical drug candidates.

Approach: The proposed TRI would leverage Ontario expertise to define stemness biomarkers that predict survival across a wide spectrum of AML patients and translate

these into the clinic to support treatment decisions such as early transplantation for patients with poor prognosis. Ontario scientists have established that evolutionary ancestral stem and progenitor cells remain present in diagnostic blood samples indicating that complex subclonal diversity exists in these patients. By tracking clonal behavior in response to therapy in clinical samples, scientists can develop novel approaches to monitor the effectiveness of new classes of therapies that ensure that all relevant subclones are being targeted.

Anticipated impact: Clinical validation of prognostic and predictive biomarkers will lead to better stratification of patients and improved outcomes for AML patients. New drugs for high-risk ALL and clinical protocols for the rational utilization of targeted drugs.

- **Esophageal cancer:** Reduce the burden of esophageal cancer through strategies for improved screening/early detection and disease monitoring of Barrett's Esophagus.

Clinical relevance: The incidence and mortality of esophageal cancer is increasing in America and Europe. The single major risk factor for esophageal adenocarcinoma (EAC) is chronic gastroesophageal reflux disease (GERD), which frequently leads to Barrett's Esophagus (BE), a change in the lining of the esophagus that affects approximately 800,000 Canadians. Repetitive endoscopy, which is uncomfortable, limited in availability and costly, is currently the only means to evaluate GERD and to detect and monitor BE for progression to EAC. Once detected, ablative therapies are available and are generally curative for patients with high-grade dysplasia or with EAC confined to the mucosa.

Ontario innovation or asset: A simple device (swallowable encapsulated sponge) capable of sampling esophageal tissue, to which OICR has commercial rights; prognostic biomarkers to stratify EAC and esophageal squamous cell carcinoma and to characterize aggressive disease that requires intensified surveillance or ablative treatment.

Approach: Capitalize on the swallowable encapsulated sponge and genomic analyses to develop an easy to administer and cost-effective approach to screen for and monitor BE as a means of preventing progression to EAC.

Anticipated impact: A simpler, cost-effective screening and surveillance program for BE and ultimately GERD in Ontario that significantly reduces the incidence and the morbidity/mortality of esophageal cancer.

- **Brain cancer:** Develop safe and effective therapies for adult and paediatric brain tumours.

Clinical relevance: Glioblastoma (GBM) is the most common brain malignancy, with five-year survival of <10 per cent. GBM is worse in children, as most tumours are completely inoperable. The PFA subgroup of Ependymoma, comprising over 50 per cent of all patients of this childhood glial tumour, has no effective standard chemotherapy and poor prognosis. Medulloblastoma (MB), the most common malignant brain tumour in children, demands aggressive therapy to effect cure, but mortality remains high in certain molecular subgroups, and the quality of life of survivors is often very poor due to damage to the brain during therapy.

Ontario innovation or asset: World-leading, well-annotated, patient outcome-linked biobank consisting of 1,500 human MB and 500 ependymomas. Ontario scientists have made seminal discoveries in understanding clonal diversity, stemness properties of cancer cell populations associated with treatment resistance and tumour relapse, as well as the identification of driver mutations for GBM, MB and other brain tumours, and have developed expertise in the development and manufacture of viral, immune and radiation based therapies that attack brain malignancies. The molecular classification system being used worldwide in clinical trials for children with medulloblastoma and

ependymoma was developed with large contributions from researchers in Ontario, and routine molecular diagnostics are now available to children in Ontario with medulloblastoma.

Approach: Use integrative genomic and functional analysis to define how brain tumour cellular and genetic heterogeneity leads to disease progression and resistance to therapy, and develop novel therapeutic approaches for children and adults.

Anticipated impact: Curative therapies for brain tumours in children and adults, and improved the quality of life for survivors.

- **Ovarian cancer:** Develop novel therapeutic approaches for the management of platinum-resistant ovarian cancer.

Clinical relevance: Ovarian cancer is the most lethal gynaecological malignancy, with no strategies available for early detection or screening. At least 75 per cent of the patients with advanced disease relapse and die from platinum-resistant disease.

Ontario innovation or asset: Ontario teams have made progress in the development of potential drug candidates and innovative biomarkers to impact the management of platinum-resistant ovarian cancer and to ultimately introduce new treatment strategies; unique collection of well-annotated ovarian cancer patient-derived xenografts.

Approach: Pre-clinical and clinical evaluation of new classes of biologics to treat ovarian cancer. Characterize novel biomarkers such as changes in the kinome profiles in patient-derived tumours subsequent to platinum therapy to guide rational utilization of available targeted therapies and interferon-based signatures to guide the use of immune therapies.

Anticipated impact: More rational utilization of targeted therapies and new immunotherapies for treating platinum resistant ovarian cancer.

Appendix II. Description of select Global Leadership in Precision Oncology initiatives

This following section supplements the abridged descriptions provided in Section B.4.

OCTANE

PM and OICR will establish and support OCTANE (Ontario-wide Cancer TArgeted Nucleic acid Evaluation), a province-wide alliance that will build on the success of IMPACT (Integrated Molecular Profiling in Advanced Cancers Trial) and COMPACT (Community Oncology Molecular Profiling in Advanced Cancers Trial) clinical trials at PM to increase NGS testing of cancer patients in Ontario. OCTANE will create large provincial cohorts of consented patients to enter initial genomic profiling and co-ordinate the development of informatics tools to capture and share associated clinical data. Patient cohorts will facilitate targeted therapy and immune therapy clinical trials in the province, and identify patient subsets for more advanced genomic profiling. OCTANE will offer NGS-based sequencing through established College of American Pathologists (CAP)/Clinical Laboratory Improvement Amendments (CLIA)/Ontario Laboratory Accreditation (OLA) labs at Princess Margaret Cancer Centre (PM)/University Health Network (UHN) and other cancer centre-based labs as they become available. All patients will be asked to provide consent for data-sharing with other cancer researchers, and will include a provision for review of patient health records through patient charts or administrative databases (i.e., Cancer Care Ontario New Drug Funding Program, Provincial Cancer Registry, etc.) to obtain additional information about time on therapy and survival. The OCTANE study will aim to ramp-up to 5,000 patients per year, and ultimately increase to 10,000 patients annually. The establishment of the Ontario Molecular Pathology Network (see D. Collaborative Research Networks) is expected to increase the reach of OCTANE across the province. It is also envisaged that OCTANE will be a major source of samples and data for the ICGCmed program described below. OICR is currently working with PM and several Ontario cancer centres on defining the detailed scope and objectives for OCTANE and planning for implementation.

PM-OICR Translational Genomics Laboratory (TGL)

A new PM-OICR Translational Genomics Laboratory (TGL) will be established to develop and evaluate new genomics and other “omics” technologies for *advanced* molecular profiling of tumours, normal tissues, circulating DNA and other biospecimens obtained from cancer patients. The mandate of the TGL will be to transition research-grade laboratory and computational advances into validated, robust protocols ready for rapid validation and uptake by clinical laboratories in Ontario. In this translational capacity, the TGL will interface directly with existing PM/UHN CAP/CLIA labs that have established and implemented standard panel NGS tests suitable for initial standard of care. The TGL will also provide a platform to Ontario clinical and basic researchers for evaluating genotype-phenotype associations and emerging genomic algorithms. This patient-centered research activity will include expanded genomic analysis of subsets of patients already tested using focused panels in clinical labs (such as those enrolled in OCTANE), and who may benefit from additional, in-depth genome analyses. OICR, PM and UHN are currently actively planning the operational details for the establishment of the TGL, which will be located within the Genomics Technology Program space at the MaRS Centre headquarters.

ICGCmed

The first phase of ICGC, which is slated for completion in 2018, has focused on developing extensive catalogs of tumour genomic information. International cancer and genomics

researchers and funding agencies from North America, Europe, Asia and Australia are currently discussing ICGCmed, a second phase that will link genomics to clinical information and health, including lifestyle, patient history, response to therapies and underlying causes of cancer. The goal will be to accelerate the movement of this information into the clinic to guide prevention, early detection, diagnosis, and prognosis, and provide the information needed to match the patient's disease to the most effective combinations of therapy. Globally, the number of patients involved in ICGCmed projects will exceed 250,000 over the next decade. Investments will support a range of projects of varying size, which in aggregate will analyze over 5,000 genomes per member project, and will tackle a broad spectrum of cancers, including pre-neoplastic lesions, early cancers and metastases. This will lead to the discovery of new therapeutic targets, improved prioritization of existing therapies, more precise disease definitions and improved strategies to manage drug resistance.

OICR will support two components:

1. *Patient accrual, data collection and analysis:* OICR will bring Ontario clinical trials leaders to brainstorm on a collaborative project (or mixture of projects) that would contribute to ICGCmed (~ 1,000 tumours/year over five years). Patients will be drawn primarily from OCTANE but also from additional highly-informative clinical trials, such as small trials studying patients with exceptional response to therapy and other extreme phenotypes, basket trials used to match mutation profiles in cancer patients to one or more targeted agents, and large randomized trials of experimental therapies. Clinically relevant patient specimens will also be sourced from provincial resources such as the Ontario Tumour Bank. Analyses will primarily consist of whole genomes, transcriptomes and methylomes. Long-term outcomes will be collected in order to enrich the knowledge of how mutations are linked with the disease types and therapeutic outcomes, which will be key to informing future clinical interpretation of cancer genome data and patient management.
2. *Data coordination and stewardship:* OICR's informatics program will serve as the Data Coordination Centre of ICGCmed (as it is doing presently for ICGC). The ICGCmed Data Coordination Centre will build the capacity to handle data from 250,000 cancer donors over a 10-year period. Distributed cloud computing linked facilities around the world will be required both to achieve the economies of scale¹⁴ and to ensure that primary datasets are stored in jurisdictions approved by international project members.

As with the first phase of ICGC, a worldwide consortium for ICGCmed will enable research advances that are insurmountable on a local scale, particularly for interpreting data from patients with rare mutations, as well as the patterns of mutation co-occurrence that shed light on underlying cancer pathways and drug response/resistance. Because of the heterogeneity within many forms of cancer, pooling large numbers of samples associated with clinical information such as medical history, response to therapy and outcomes is the only way to have sufficient statistical power to study the cancers and propose new paradigms, new drug targeting approaches and offer better treatment to patients. Collaboration will also enable benchmarking exercises and sharing of technology, which will improve analyses. While some cancers are more prevalent in some regions and will be the focus of study in particular countries, all cancers occur in all countries and an international consortium will help amass and distribute useful knowledge beyond geographical borders.

¹⁴ Stein L *et al.* Nature (July 2015) 523:149-151

Appendix III: Glossary

3CTN	Canadian Cancer Clinical Trials Network
aAPC	Artificial Antigen Presenting Cells
ADME	absorption, distribution, metabolism and excretion
ALL	acute lymphoblastic leukemia
AML	acute myeloid leukemia
BE	Barrett's Esophagus
CAP	Biotherapeutics for Cancer Treatment
CAR	Chimeric Antigen Receptor
CBW	Canadian Bioinformatics Workshops
CCAB	Centre for the Commercialization of Antibodies and Biologics
CCO	Cancer Care Ontario
CDRD	Centre for Drug Research and Development
CIMTEC	Centre for Imaging Technology Commercialization
CLIA	Clinical Laboratory Improvement Amendments
COMPACT	Community Oncology Molecular Profiling in Advanced Cancers Trial
CPAC	Canadian Partnership Against Cancer
CPDC	Centre for Probe Development and Commercialization
CPTP	Canadian Partnership for Tomorrow Project
CTA	Clinical Trial Application
DCIS	Ductal Carcinoma <i>in situ</i>
EAC	Esophageal Adenocarcinoma
FACIT	Fight Against Cancer Innovation Trust
FDA	Food and Drug Administration
FR	Funding Request
GA4GH	Global Alliance for Genomics and Health
GB	Glioblastoma
GENIE	Genomics, Evidence, Neoplasia, Information, Exchange
GERD	Gastroesophageal Reflux Disease
ICES	Institute for Clinical Evaluative Sciences
ICGC	International Cancer Genome Consortium
IMEC	Improved Management of Early Cancer
IMPACT	Integrated Molecular Profiling in Advanced Cancers Trial
iNKT	Invariant Chain Natural Killer T
IP	intellectual property
LOI	Letter of Intent
MB	Medulloblastoma
MOHLTC	Ministry of Health and Long-term Care
MRI	Ministry of Research and Innovation
NCE	Networks of Centres of Excellence
NGS	next generation sequencing
OCOG	Ontario Clinical Oncology Group
OCREB	Ontario Cancer Research Ethics Board
OCTANE	Ontario-wide Cancer TArgeted Nucleic acid Evaluation
OHRI	Ottawa Hospital Research Institute
OHS	Ontario Health Study
OLA	Ontario Laboratory Accreditation
OICR	Ontario Institute for Cancer Research
ORBiT	Immuno- and Bio-therapies
OTB	Ontario Tumour Bank
PD	pharmacodynamic
PDAC	pancreatic ductal adenocarcinoma

PM.....Princess Margaret Cancer Centre
PSA Prostate-specific Antigen
SAB Scientific Advisory Board
SGC..... Structural Genomics Consortium
TCGA..... The Cancer Genome Atlas
TCR T Cell Receptor
TGL Translational Genomics Laboratory
TIL Tumour Infiltrating Lymphocyte
TRAC Toronto Recombinant Antibody Centre
TRI.....Translational Research Initiative
TRUSTransrectal Ultrasound
UHN University Health Network