OICR
Ontario Institute
for Cancer Research

HEALTH

RESEARCH

ECONOMY

Cancer solved together

OICR Strategic Plan 2021-2026

Contents

1 Executive summary

Context. Nearly one in two people in Ontario will receive a diagnosis of cancer in their lifetime and one in four people are expected to die from the disease, which is now the leading cause of death in the province. The province is expected to see 91,000+ new cancer cases and 30,000+ cancer-related deaths in 2020. In addition to the terrible toll of cancer on patients, families, and society, the disease exerts a significant burden on our health system and economy, with direct Ontario healthcare costs currently totalling more than $2.6 billion annually.

Why is cancer so difficult to diagnose and treat?

- Cancer is not one disease
- Every patient's cancer is different at the molecular level
- Tumours are heterogeneous, so even parts of the same tumour can be different
- Cancer evolves to be more complex over time and can become resistant to treatment
- Rare cancer stem cells, present in the tumour from day one, can resist treatment and allow a seemingly eliminated tumour to regrow
- Cancer can suppress the immune system, keeping the body from recognizing or destroying tumours
- New approaches to treatment are complex because they are individualized to each patient, which is termed **precision medicine**

Cancer results from the accumulation of changes in the genetic material (DNA) of a cell, which results in abnormal, uncontrolled growth. Although some people are born with genetic mutations that predispose them to cancer, the inevitable accumulation of genetic changes over time causes cancer incidence to increase with age. Ontario is projected to see a 25 per cent increase in cancer patients over the next ten years, driven primarily by the aging of the population, which will impose even greater burden on our health system and the economy.

Fortunately, investment in cancer research has resulted in major advances that have helped drive cancer mortality rates down for many cancers. Our understanding of how cancers develop and progress is now growing at a rapid pace and yielding new insights capable of transforming patient outcomes. For instance, recent studies led by the **Ontario Institute for Cancer Research (OICR)** and our collaborators have established that cancer-causing mutations arise years, even decades, before malignancies are detected, significantly broadening the window for the detection and elimination of cancerous cells before the disease can take hold. With the burden of cancer growing in the coming years, there has never been a better time to strengthen our healthcare system by capitalizing on research.

OICR was established in 2005 to mobilize and reinforce Ontario research excellence in the fight against cancer, realize the local economic value of cancer discoveries, and make Ontario a major global address for cancer research and innovation. As **Ontario's facilitator of translational cancer research**, OICR brings together researchers, clinicians, patients and caregivers, health system partners, industry and funders to drive solutions to cancer needs and accelerate the advancement of discoveries to improve cancer prevention, detection, diagnosis and treatment.

VISION

Cancer solved together

MISSION

Partner with the oncology community to translate cancer research discoveries, transforming cancer care to benefit patients, and strengthening the Ontario economy

VALUES

Excellence | Innovation | Collaboration
Impact | Responsibility | Community

OICR invests resources in three areas:

- Strengthening Ontario's capacity to undertake world-class cancer research;
- Driving collaborative, translational cancer research;

- Working with partners to facilitate the advancement, commercialization and adoption of cancer innovations into clinical practice.

As shown in **Figure 1**, OICR's research portfolio is grouped under three integrated Themes:

1. **Adaptive Oncology**: Developing knowledge and approaches to detect and monitor cancer over its life cycle in order to enable precise and proactive clinical management.
2. **Clinical Translation**: Advancing Ontario cancer discoveries through early clinical validation, partnering with industry and the health system for downstream development and implementation of new treatments, diagnostics and biomarkers, thus fostering precision medicine for cancer patients.
3. **Therapeutic Innovation**: Validating novel cancer drug targets and advancing selective therapeutic candidates towards clinical development.

Figure 1: OICR's Research Themes and Enablers

In addition, OICR enables world-class translational cancer research in Ontario through:

1. **Talent Mobilization** activities focused on recruiting, developing, and engaging outstanding Ontario cancer researchers and clinician-scientists.
2. The **Collaborative Research Resources**, which provide access to cutting-edge research tools, assays, databases, expertise, resources and infrastructure.
3. Our partnership with **FACIT**, which invests in and builds local companies to accelerate commercialization of Ontario cancer discoveries to patients, attracts investment and industry partners, and creates and retains private sector jobs in Ontario. The scale of OICR's investment in FACIT facilitates commercialization by addressing a critical gap not filled by any other entity of higher learning and research in Ontario.

Ultimately these investments aim to improve Ontario's **research system**, reinforcing Ontario's position at the forefront of cancer research and innovation, with discoveries translated and adopted by the **health system** to improve cancer prevention, patient survival and quality of life, and strengthen the local innovation **economy**.

> "OICR is a world-class research institute that has built on existing cancer research strengths in the province and fostered the commercialization of new therapies and innovations that benefit people in Ontario, Canada, and worldwide."
>
> *2020 OICR External Review Report*

Achievements and impact to date. OICR's investments over the past 15 years have nurtured a collaborative, world-class cancer research system that is working together to solve cancer, and realize the value of homegrown innovation for the people of Ontario. We have established a critical mass of outstanding scientists, clinicians and trainees at our facilities in the MaRS Discovery District and at universities, cancer centres and research institutes across Ontario. We have filled critical capacity gaps so that Ontario has the talent, collaborations,

technologies and infrastructure in place to conduct world-class cancer research and translation. We have led major global cancer genomics and Big Data initiatives that have resulted in seminal insights into cancer development that are driving precision medicine and therapeutic discovery, and we have mobilized provincial research strengths to address cancer priorities, realizing significant benefits for Ontario. For instance, our long-term investment in pancreatic cancer, a deadly cancer with a five-year net survival of only 8 per cent, has resulted in ground-breaking understanding of the disease and novel treatment strategies, tailored to individual patients, which are now being tested in clinical trials in Ontario, across Canada and around the world. Altogether, we have supported clinical trials that have provided more than 22,000 patients with access to new cancer innovations.

Our investments have yielded a rich pipeline of discoveries poised for translation. These include novel molecular biomarkers, diagnostics and imaging systems to make cancer detection more precise and less invasive; artificial intelligence-based systems to guide the selection of therapies for individual patients; and a rich portfolio of innovative therapeutic assets, including a first-in-class drug candidate for leukemia that has been partnered with local industry and is in preparation for clinical testing. We have worked with Ontario Health (Cancer Care Ontario) to develop evidence-based strategies for improving healthcare delivery, including approaches to increase participation in lifesaving colorectal cancer screening, and a safe, cost-effective model for delivering follow-up care to breast cancer survivors through their primary care physicians instead of at cancer centres, which serves as a model for the deployment of broader cancer service closer to home.

In partnership with FACIT, we have supported the innovations behind the creation of 27 start-up companies, support 1,000+ highly skilled jobs each year, and attract $3 for cancer research and innovation for every Ministry dollar invested. FACIT investments in Ontario start-ups have attracted $1.2B in additional financing, allowing them to take root and scale in the province.

Strategic Priorities for 2021-2026. OICR undertook a highly consultative strategic planning process that engaged the cancer research and clinical communities, patients and caregivers, health system and industry partners, and global thought leaders on the future of oncology and strategic opportunities for Ontario leadership and impact. In March 2020, OICR underwent an external review by an international expert panel, which assessed the Institute's achievements and impacts, its structures and operations, and its emerging strategy. The panel was impressed with OICR's accomplishments, validated our critical role in the cancer research system, and provided valuable recommendations that have informed the priorities and principles articulated in this strategic plan.

Strategic Plan 2021-2026 seeks to capitalize on Ontario strengths and successes to develop solutions to stem the growing health and economic burden of cancer on society. Our emphasis on earlier cancer detection offers the best opportunity to stop cancer before it can take hold, grow more complex and spread (**Figure 2**). The **overarching focus** of Strategic Plan 2021-2026 is to **develop the knowledge and tools to implement next generation cancer precision medicine in Ontario, where cancer patients are diagnosed as early as possible, treated precisely and definitively, and monitored proactively to detect and resolve recurrence, dramatically transforming survival and quality of life.**

Next generation precision medicine requires a number of advanced tools:

1. **Diagnostics** capable of detecting early cancers with high sensitivity and specificity.
2. An arsenal of safe and effective **treatments**.
3. **Clinical decision-support tools** for selecting the most suitable treatment course for each patient, based on the analysis of biomarkers associated with treatment responses and clinical outcomes of large numbers of cancer patients.

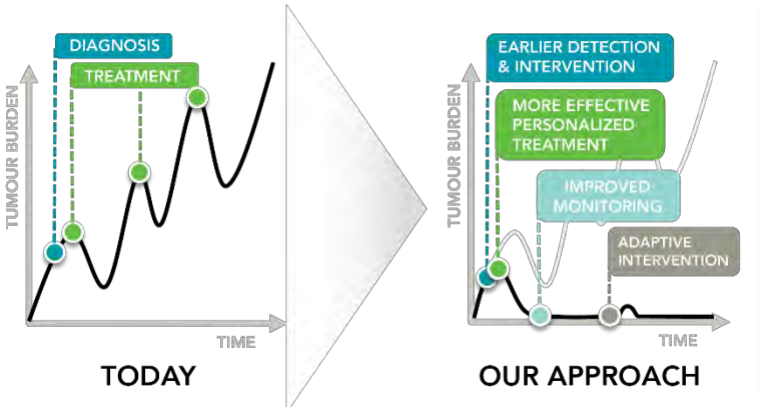


Figure 2: The importance of early detection, personalized treatment and ongoing disease monitoring in decreasing tumour burden and improving patient outcomes.

4. Sensitive, precise, minimally-invasive **monitoring tools** and analytical approaches for detecting trace amounts of tumour recurrence in cancer survivors to intervene before the cancer spreads.

Developing these tools and translating them into clinical practice requires an integrated translational research pathway that links discovery to patient impact. OICR's investments over the past 15 years have established and reinforced the foundational components of this pathway, in partnership with Ontario's research and clinical communities, FACIT and Ontario Health (Cancer Care Ontario). As outlined below and summarized in **Table 1**, OICR's investments for 2021-2026 will strengthen, speed and scale this pathway to turn insights in cancer development into precision medicine innovations that are implemented into Ontario's heath system to transform patient outcomes.

2021-2026 Goals

1. ***Advance early detection and intervention research*** to understand the earliest events in cancer development and how tumours evolve to become more complex and harder to treat. This knowledge will inform the development of **tools for early detection, intervention** and **monitoring for recurrence**. We will capitalize on unique Ontario research platforms to track cancer development over time, including the Ontario Health Study and a registry of patients and families who carry genetic susceptibility to cancer, which will be developed by the new Ontario Hereditary Cancer Research Network. We will also bring together a network of clinicians and scientists to drive an innovative translational research platform where novel therapies will be tested in newly-diagnosed and recurrent cancer patients prior to surgery through Window of Opportunity and neo-adjuvant clinical trials. Findings from these studies will provide deep molecular understanding of how these therapies fight cancer, and will help identify patients likely to benefit from these therapies in the future.

2. ***Reinforce Ontario's global leadership in data sharing and analytics***, exploiting Big Data to determine the clinical and molecular features that predict an individual patient's response to therapy, forming the basis for the **clinical decision-support tools** to drive next generation precision medicine. We will establish the Ontario Hereditary Cancer Research Network Registry of patients and families with hereditary cancer syndromes. This will be integrated with the new Ontario Health Data Platform and will serve as a template on which to build other integrative health research platforms. We will also apply Ontario's world-renowned artificial intelligence (AI) expertise to analyzing medical images, which has potential to revolutionize cancer diagnostics.

3. ***Expand a robust Ontario pipeline of novel cancer therapeutics*** with potential to transform cancer **treatment**. We will build up our drug discovery pipeline, which is currently advancing 10 first-in-class/best-in-class Ontario therapeutic assets towards clinical development, providing more investment opportunities for FACIT and entrepreneurship opportunities for the research community. We will also work towards greater integration of provincial capabilities and resources in a new Drug Discovery Community that will advance promising drug candidates, attract industry partners and enable local commercialization.

4. ***Drive the translation and commercialization of cancer innovations in Ontario*** so that safe and cost-effective precision medicine tools can be **adopted into clinical practice to transform patient survival and quality of life**. We will establish a Clinical Translation Pathway to develop and test practice-changing diagnostics, clinical decision-making tools and therapeutics in clinical trials, especially in the pre-surgical setting described above. This pathway will be fueled by innovations emerging from OICR-supported research, and from research institutions across the province. We will also link this pathway to our drug discovery efforts through new pharmacogenomic screens of residual tumours from our therapeutic trials. FACIT will continue to lead the commercialization of these tools, identifying projects with high commercial potential and facilitating early commercial planning, seeding new Ontario start-ups and attracting investment and industry partners, enabling Ontario to compete in the growing precision medicine market. We will also work with existing large clinical trials groups in Ontario to ensure there is a receptor for developing promising assets in increasingly large and complex clinical trials. OICR is committed to strengthening our partnership with Ontario Health (Cancer Care Ontario) to ensure there is a pathway to systematically evaluate and implement cancer innovations into the health system so patients can benefit.

5. ***Strengthen and sustain Ontario capacity for translational cancer research*** to drive the scientific breakthroughs that will fuel cancer innovation. Our success as an organization is tightly tethered to the value we place on collaboration. All of the above components will be enabled through the recruitment, development and networking of research talent and expertise, targeted investment in collaborative research platforms and infrastructure, and critical partnerships with Ontario cancer centres, universities and research institutes, patients and caregivers, the private sector and government.

Table 1: 2021-2026 Goals and Investments (tactics), mapped to their respective Research Themes and Enablers

1. Advance early detection and intervention research Execute a focused, multi-disciplinary strategy for early cancer detection and intervention, developing and validating tools to address patient and health system needs.	
	Research on early cancer detection, tumour heterogeneity and evolution to inform tools for early cancer diagnosis, treatment selection, and monitoring for early recurrence
	Ontario Health Study and Ontario Hereditary Cancer Research Network to study early events in cancer initiation and develop approaches for early detection, precise intervention and monitoring
	Window of Opportunity trials and other pre-surgical trials to test interventions in newly diagnosed and recurrent patients amenable to surgery to identify new biomarkers for precision medicine
2. Reinforce Ontario's global leadership in data sharing and analytics Advance national and international data sharing efforts to identify new cancer biomarkers and pathways informing the development of next generation cancer diagnostics, clinical decision-support tools and therapies.	

- ICGC-ARGO (International Cancer Genome Consortium-Accelerating Research in Genomic Oncology) Big Data coordination, harmonization, sharing and analysis
- Ontario Hereditary Cancer Research Network Registry of hereditary cancer patients and carriers

3. Expand a robust Ontario pipeline of novel cancer therapeutics

Partner with the Ontario research community and FACIT to strengthen and advance a provincial pipeline of promising oncology assets that attract investment in successful commercial ventures.

- Enhancement of Therapeutic Innovation, fueling and advancing a first-in-class/best-in-class drug pipeline into clinical development and patient testing
- Building towards a Drug Discovery Community leveraging expertise and resources across the province to strengthen the Therapeutic Innovation pipeline

4. Drive the translation and commercialization of cancer innovations in Ontario

Collaborate with healthcare agencies/providers, FACIT and private sector partners to advance Ontario discoveries to cancer patients and deliver economic benefit to Ontario.

- Clinical Translation Pathway to develop and validate practice-changing diagnostics, clinical decision-making tools and therapeutics
- Implementation science research and partnership with Ontario Health (Cancer Care Ontario) to promote health system adoption of cancer care innovations
- Sustaining FACIT's commercialization entity to translate innovations to patients and market

5. Strengthen and sustain Ontario capacity for translational cancer research

Support and develop Ontario research talent and provide access to world-class technology platform, resources and infrastructure to address provincial needs and maintain Ontario research leadership.

- Renewed Investigator Awards program, OICR Scientific College and Rising Stars in Cancer Research Network to recruit, develop and engage Ontario talent
- Broadened access to leading-edge technologies, resources and clinical trials infrastructure for world-class cancer research and translation

Achieving results. OICR is accountable to the people of Ontario. In implementing Strategic Plan 2021-2026, OICR is committed to:

1. Emphasizing excellence in translational research funding decisions and oversight, including assessing potential value to the health system and commercial opportunity.
2. Integrating patient perspective and insight across our priorities, programs and processes.
3. Embracing concepts of equity, diversity and inclusion in our research design, practice, personnel support mechanisms and training.
4. Ensuring that all data arising from OICR-funded projects is made available to the research community in a timely fashion (whenever possible).

5. Engaging regularly with Ontario researchers, clinicians, patients, research institute leaders, government, health system partners, funders and industry to exchange knowledge, maintain the currency of our strategy and facilitate collaborations and partnerships.
6. Delivering high-quality, efficient operational processes to support strategic plan execution.

We will continue to work with Ontario cancer research and clinical communities and Ontario Health (Cancer Care Ontario) to develop and refine the structures and processes needed for the effective implementation of Strategic Plan 2021-2026, ensuring that the Institute remains nimble and able to capitalize on emerging opportunities to advance our mission.

Impact. Ontario's COVID-19 research response has highlighted the value of collaboration, coordination, data sharing and speed of discovery and translation—all attributes that OICR has been building within the cancer community. We will further entrench these capabilities across the province, capitalizing on Ontario's world-class science and ingenuity to develop solutions to stem the growing burden of cancer on society and drive economic growth. In partnership with FACIT, we will deliver the following outcomes and impacts to Ontario:

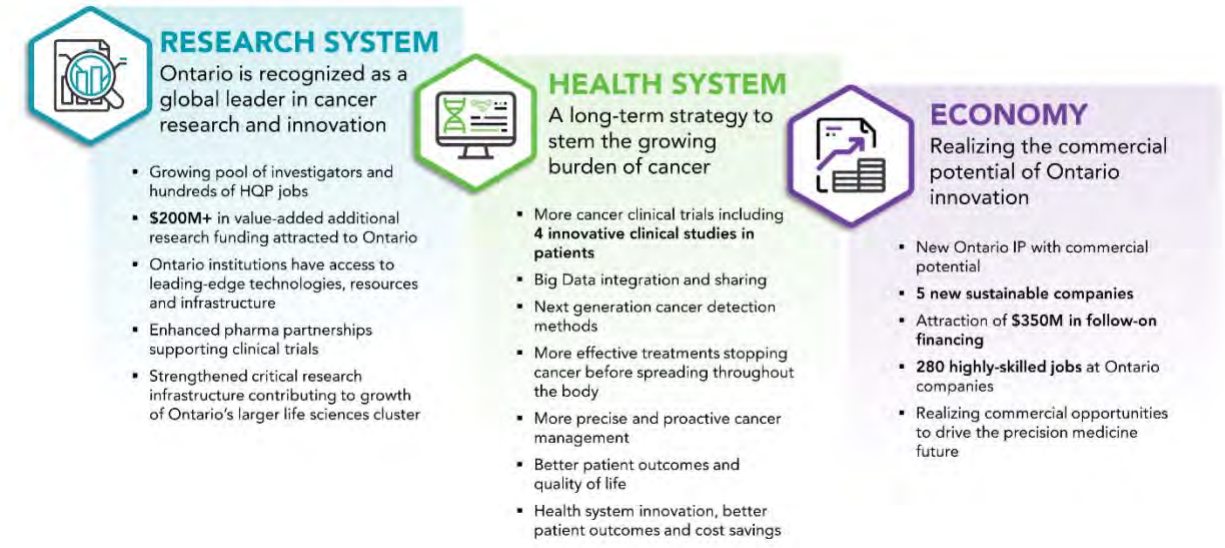


Figure 3: Expected five year outcomes and impacts.

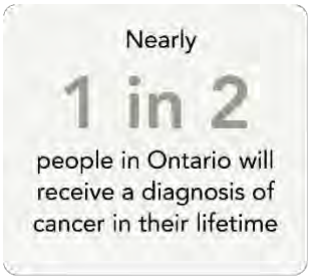
Strategic Plan 2021-2026 articulates an ambitious strategy to usher in next generation precision medicine approaches that can help transform the trajectory of cancer in Ontario. The impact of these approaches on individual cancer patients will be profound. It will equip patients and their clinicians with a personalized, proactive cancer management plan that includes safer, more effective and less invasive testing and treatment to fight their disease and return to living healthy and productive lives. Working together with researchers, clinicians, patients, government, health system partners, industry and collaborators around the world, we will help make this vision a reality for cancer patients and ensure the health and economic benefits of cancer research are fully realized for all Ontarians.

2 Introduction

2.1 The health and economic challenge of cancer in Ontario

Nearly one in two people in Ontario will receive a diagnosis of cancer in their lifetime and one in four people are expected to die from the disease, which is now the leading cause of death in the province.[i] The province is expected to see 91,000+ new cancer cases and 30,000+ deaths in 2020. In addition to the tremendous toll of cancer on patients, families, and society, the disease exerts a significant burden on our health system and economy. Direct Ontario health system costs related to cancer total more than $2.6 billion annually.[ii]

Cancer results from the accumulation of changes in the genetic material (DNA) of a cell, which results in abnormal, uncontrolled growth. Although some people are born with genetic mutations that predispose them to cancer, the inevitable accumulation of genetic changes over time causes cancer incidence to increase with age. Ontario is projected to see a 25 per increase in cancer patients over the next ten years, due primarily to the aging of the population[iii], which will impose even greater burden on our health system and the economy.



Ontario Health (Cancer Care Ontario), 2020.

Ongoing investment in cancer research has resulted in major advances, including new approaches for prevention, diagnosis and treatment that have helped drive cancer mortality rates down for many cancers. More than 500,000 people in Ontario diagnosed with cancer over the last 30 years are alive today largely as a result of cancer research and a strong cancer care system coordinated by Ontario Health (Cancer Care Ontario), which emphasizes evidence-based, person-centred care.[iv] Ontario has the highest rate of cancer survivorship in Canada, ranking third for 5-year survival in a study of 21 jurisdictions across seven countries.[v] Moreover, our understanding of how cancers develop and progress is now growing at a rapid pace and yielding new insights capable of transforming patient outcomes. For instance, recent studies led by the **Ontario Institute for Cancer Research (OICR)** and our collaborators have established that cancer-causing mutations arise years, even decades, before malignancies are detected, significantly broadening the window for the detection and elimination of cancerous cells before the disease can take hold.

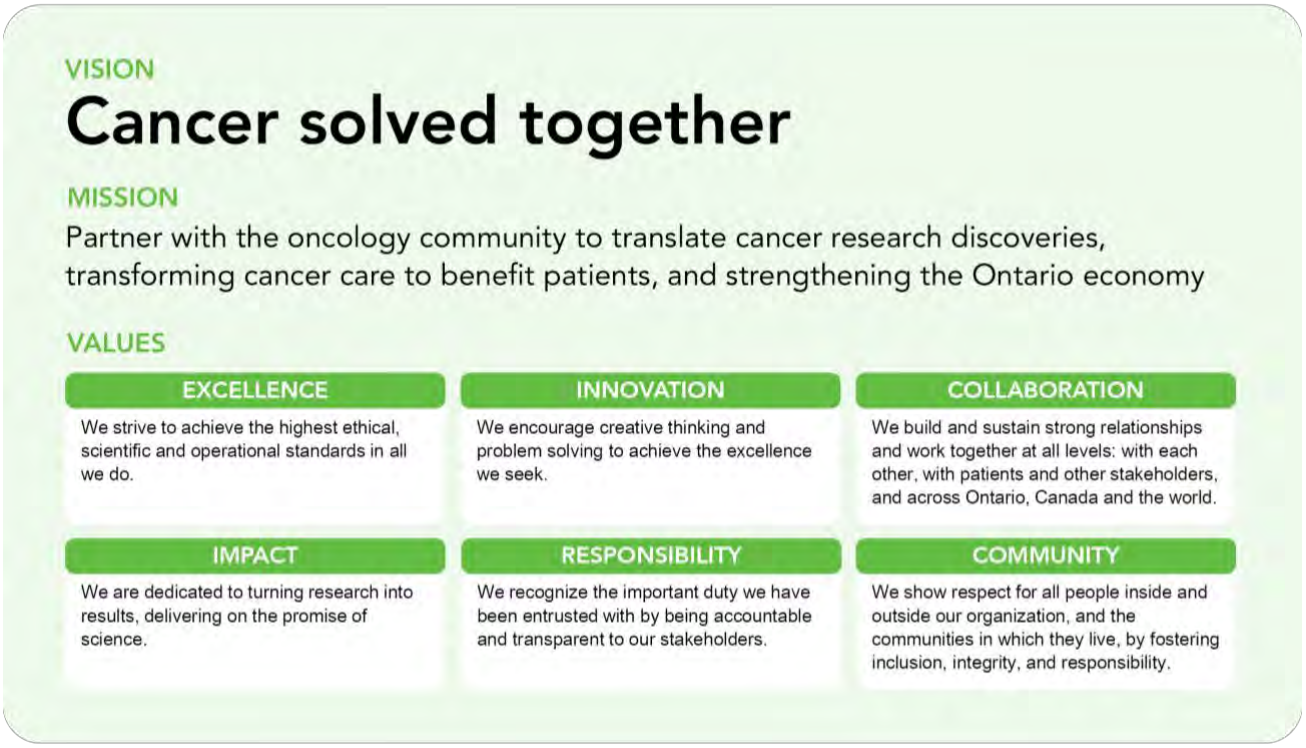
With the burden of cancer growing in the coming years, there has never been a better time to strengthen our healthcare system by capitalizing on research.

Ontario has a rich history of cancer research excellence, with many seminal discoveries that have transformed the understanding of disease biology and pioneered new therapeutic approaches. However, historically Ontario has struggled to translate and commercialize this research locally to further benefit patients and the provincial economy.

In 2002, the Ontario government under the Honorable Mike Harris and the Honorable Ernie Eves recognized that a concentrated effort was needed in the fight against cancer. The **Ontario Institute for Cancer Research (OICR)** was established in 2005 to mobilize and reinforce Ontario research excellence in the fight against cancer, realize the local economic value of cancer discoveries and make Ontario a major global address for cancer research and innovation.

2.2 OICR's mandate and role in the Ontario oncology ecosystem

With core funding from Ontario's Ministry of Colleges and Universities (MCU), OICR is the province's **facilitator of translational cancer research**, bringing together researchers, clinicians, patients and caregivers, health system partners, industry and funders to drive solutions to cancer needs and accelerate the advancement of discoveries to improve cancer prevention, detection, diagnosis and treatment.



OICR invests its resources in three areas:

- **Strengthening Ontario's capacity to undertake world-class cancer research** by recruiting and developing talent; providing access to leading-edge technology and data sharing platforms and research resources; promoting collaboration across the oncology ecosystem; and advancing provincial, national and global cancer research priorities.
- **Driving collaborative, translational cancer research** by advancing discoveries to the clinic and promoting the adoption of innovations into practice, and by mobilizing Ontario talent around research areas with high potential to transform cancer care and patient survival.
- **Working with partners to facilitate the advancement, commercialization and adoption of cancer innovations into clinical practice** so that patients benefit from research breakthroughs.

Ultimately these investments aim to improve Ontario's:

Research system, such that Ontario is at the forefront of cancer research and innovation, with universities, hospitals and institutes working together to tackle patient and health system priorities.

Health system, such that research informs strategies for cancer prevention, detection and intervention, and cost-effective cancer innovations are adopted into care to improve patient survival and quality of life.

Economy, such that Ontario is home to a robust ecosystem for commercializing cancer research discoveries.

OICR currently supports research at its facilities in the MaRS Discovery District and in 18 communities across Ontario, including eight universities, 25 hospitals and 16 institutes.[vi] On an annual basis, more than 1,700 highly qualified personnel contribute to OICR research projects.

2.3 Research Themes and Enablers

OICR's research portfolio is grouped under three integrated Themes (Figure 1), with specific Programs and projects led by investigators at OICR and at universities, hospitals and institutes across Ontario:

1. **Adaptive Oncology**: Developing knowledge and approaches to detect and monitor cancer over its life cycle in order to enable precise and proactive clinical management.
2. **Clinical Translation**: Advancing Ontario cancer discoveries through early clinical validation, partnering with industry and the health system for downstream development and implementation of new treatments, diagnostics and biomarkers, thus fostering precision medicine for cancer patients.
3. **Therapeutic Innovation**: Validating novel cancer drug targets and advancing selective therapeutic candidates towards clinical development.

Figure 1: OICR's Research Themes and Enablers

In addition to collaborative research conducted under these Themes, OICR enables world-class translational cancer research in Ontario through:

1. **Talent Mobilization** activities focused on recruiting, developing, and engaging outstanding Ontario cancer researchers and clinician-scientists.
2. The **Collaborative Research Resources**, which provide access to cutting-edge research tools, assays, databases, expertise, resources and infrastructure.
3. Our partnership with **FACIT**, which invests in and builds local companies to accelerate commercialization of Ontario cancer discoveries to patients, attracts investment and industry partners, and creates and retains private sector jobs in Ontario. The scale of OICR's investment in FACIT facilitates commercialization by addressing a critical gap not filled by any other entity of higher learning and research in Ontario.

2.4 Highlights of OICR's impact

> "OICR is a world-class research institute that has built on existing cancer research strengths in the province and fostered the commercialization of new therapies and innovations that benefit people in Ontario, Canada, and worldwide."
>
> *2020 OICR External Review Report*

Achievements against the goals set out in Strategic Plan 2016-2021, and the positive impact of OICR's activities on Ontario's research system, on its patients and the health system, and on the economy are detailed in the 2016-2021 Outcomes and Benefits Report. Major outcomes and impacts are outlined below.

Promising breakthroughs

OICR's investment in cancer research excellence has yielded a rich pipeline of discoveries poised for translation, with potential to significantly improve cancer care. These include:

- Ten novel first-in-class and/or best-in-class drug discovery projects and assets in development (Section 5.3);
- A rapid, low-cost method of identifying aggressive pancreatic cancer, allowing patients with this highly fatal disease to quickly move from diagnosis to treatment;
- A deep learning system that can accurately determine the tissue of origin of primary and metastatic cancers, informing therapy choice for difficult-to-classify tumours;
- A new blood-based, highly sensitive early cancer detection technology measuring abnormal DNA methylation from cancer cells, which has the potential to revolutionize cancer detection;
- A new radiotherapy technology shown to boost five-year survival for patients with oligometastatic cancer to 46 per cent compared to 24 per cent with standard of care in a Phase II clinical trial. Phase III trials are currently underway to confirm the overall survival benefits and to identify biomarkers to predict which patients are likely to benefit from this technology;
- A novel molecular biomarker – currently being evaluated in international trials – to identify acute myeloid leukemia patients with more resistant disease that could benefit from aggressive therapy and follow-up;
- Two novel molecular biomarkers – now undergoing validation of clinical utility and cost-effectiveness – for differentiating high-risk early prostate cancer patients needing aggressive therapy from low-risk patients who should be actively monitored, which could avoid the over-treatment of prostate cancer and its associated complications (e.g., infections, incontinence, sterility) and costs to the healthcare system;
- A new prostate cancer imaging probe and associated imaging methods – now in clinical trials – that can pinpoint prostate cancers more accurately and classify their severity better than the current gold standard;
- A safer radiotherapeutic with improved selectivity and specificity over standard of care – now in clinical trials – for the targeted treatment of chemotherapy-resistant cancers;

- A new 3D ultrasound system for guiding needle placement during the treatment of gynecological cancers – now in clinical testing – that ensures that radiation is delivered accurately while minimizing uterine perforation and other complications;
- Protocols and software to help bring novel handheld nanopore long-read sequencing into cancer research and care, greatly increasing the speed and decreasing health system costs for cancer detection. Earlier versions of this open-source software were used to track Ebola and Zika virus outbreaks in the field; the current software is helping to trace COVID-19 cases.

Accelerating the path to patients

OICR partners with cancer centres, patients, industry and Cancer Care Ontario/Ontario Health to translate validated, evidence-based cancer innovations into patient care.

- Since 2014, more than 22,600 Canadians (more than 13,600 from Ontario) have accessed new cancer interventions through academic cancer clinical trials facilitated by the Canadian Cancer Clinical Trials Network, coordinated and supported by OICR.[vii] This represents a 74 per cent increase in patient accrual to adult cancer trials in Canada and a 164 per cent increase in Ontario;[viii]
- 3,500+ cancer patients at seven Ontario cancer centres have accessed next generation DNA sequencing of their tumours (via the OCTANE study) to inform their treatment or facilitate their enrollment into precision medicine trials. The initiative recently received support from Roche to expand recruitment to 500 additional patients at five community hospitals in Ontario;[ix]

- 300+ pancreatic cancer patients have benefited from personalized medicine to identify tailored treatment options for this highly lethal disease (via the COMPASS trial).[x] External funding has allowed the trial to expand in Ontario, and to open across Canada and Israel. A new landmark neo-adjuvant trial (NeoPancONE) was recently initiated to evaluate a potentially curative treatment strategy for operable pancreatic cancer.
- Demonstrated that sending letters from family doctors indicating that patients were overdue for colorectal cancer screening improved screening rates by 10 per cent.[xi] These findings were implemented by Cancer Care Ontario and by 2017, 62 per cent of eligible Ontarians were up to date with their screening versus 27 per cent of the eligible population in 2008."[xii, xiii]
- Demonstrated that delivering follow-up care for breast cancer survivors through their primary care physicians compared to care on-site at cancer centres resulted in fewer hospitalizations and cancer clinic visits, similar or better patient outcomes, and an average health system cost savings of $4,257 per patient. The methodology and findings are poised to inform Cancer Care Ontario/Ontario Health policy on transitioning care to community providers system-wide.
- Since 2012, trained nearly 250 Prevention Practitioners across Canada to implement evidence-based techniques for the prevention and screening of cancer, diabetes and cardiovascular disease in family care practices through the BETTER Program, supported by OICR's Investigator Awards program. BETTER improved chronic disease prevention and screening by 37 per cent in participating clinics.

- Findings from the International Tobacco Control Policy Evaluation Project–the first and largest international cohort study of tobacco use, co-founded and led by an OICR Investigator Award holder–have informed, supported and demonstrated the impact of bans on smoking in cars with children, the 2011-12 revision to Canada's pictoral health warnings, and Canada's recent plain packaging regulations.
- Completed a practise-changing trial (PRECISE) assessing the use of MRI-based imaging for early prostate cancer detection, replacing needless and potentially harmful prostate biopsies, which is being evaluated for health system adoption by Cancer Care Ontario/Ontario Health;
- Developed a unique prostate biopsy system, licensed to Eigen and in use around the globe, which combines 3D ultrasound data with non-invasive MRI data to detect prostate cancer with higher accuracy and fewer complications than the current standard of care;
- Developed robotic techniques for liver cancer ablation that use ultrasound image-guidance rather than computed tomography guidance, reducing the radiation dose to the patient and improving the availability of the therapy. This technology has been licensed to Perfint Healthcare, integrated with Perfint's ultrasound technology and used in clinics worldwide.

Driving innovation ecosystem growth and economic impacts

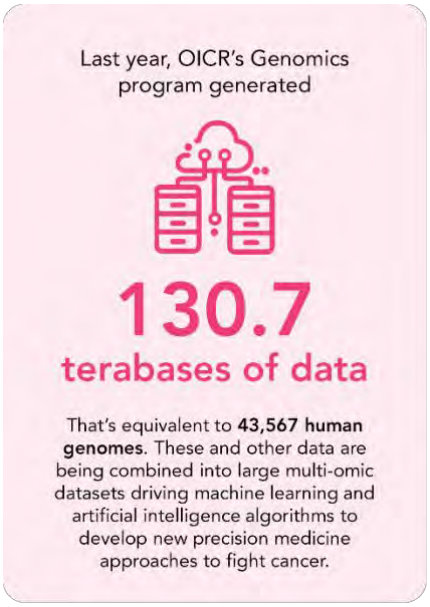
OICR partners with FACIT to commercialize cancer discoveries. FACIT provides seed capital, builds sustainable and scalable companies and jobs in Ontario, provides access to industry expertise, business management and networks needed for commercialization, and attracts investors and partners.

- OICR and FACIT have supported the innovations behind the creation of 27 start-up companies. Together, OICR, FACIT and resulting start-ups support 1,000+ highly skilled jobs in STEM fields on an annual basis;[xiv]
- Every dollar invested in OICR and FACIT operations creates $1.82 in economic output;[xv]
- Every Ministry dollar received attracts an additional $3 from private sector and public funders to the province;[xvi]
- In 2008, an OICR-supported collaboration between investigators in Toronto, Ottawa and Hamilton led to the development of a novel oncolytic viral immunotherapy, which, with FACIT management, investment, operations and business support, was spun out into Ottawa-based Turnstone Biologics. Turnstone partnered with Abbvie in the largest partnership in an oncolytic field (2017), and with Takeda (2019), attracting $330M+ to date, with 37 direct jobs created and three clinical trials underway.
- OICR's Drug Discovery team discovered and led the development of a new first-in-class drug candidate targeting WDR5 for leukemia and other cancers based on a probe molecule developed in collaboration with the Structural Genomics Consortium. In 2016, FACIT spun out and invested in Propellon Therapeutics to commercialize the discovery, which attracted a partnership valued at up to $1B USD with OICR-FACIT founded Triphase Accelerator and the global pharmaceutical company Celgene. The deal represents one of the largest oncology licensing transactions for a preclinical asset in Canadian history, and the largest biotech asset transaction worldwide for academia/not-for-profit organizations. The asset is now entering Investigational New Drug (IND)-enabling studies in preparation for clinical testing.

- In 2008, OICR supported the establishment of the Centre for Probe Development and Commercialization (CPDC) and has provided ongoing research support. Since 2015, FACIT has supported and invested in CPDC spinout Fusion Pharmaceuticals, a Hamilton-based clinical-stage company developing next generation radiopharmaceuticals, which recently completed Ontario's largest biotech IPO, with a market capitalization of over $500 million.

Anchoring Ontario at the forefront of cancer research and innovation

OICR's leadership of large-scale global cancer genomics and Big Data generation, integration, analysis and sharing have enabled ground-breaking discoveries into cancer development that are driving precision medicine and therapeutic discovery.



- Led the International Cancer Genome Consortium (ICGC), a 10-year global Big Data effort (completed in 2019) to gather, catalogue and share patterns of genomic variation in 24,000+ donors across 38 tumour types and 47 jurisdictions. The project, which includes contributions from The Cancer Genome Atlas (TCGA) project in the US, identified multiple new cancer genes and pathways, including targets for immunotherapy, other targeted therapies and prognostic biomarkers;
- Led ~700 global researchers in the PanCancer Analysis of Whole Genomes project, which analyzed more than 2,600 tumours from the ICGC dataset. Major insights, published in 23 papers appearing in *Nature* and affiliated journals include:
    - Most cancers result from changes in a small number of common biological pathways, which can inform the use of targeted therapies across different tumour types;
    - About half of tumours have cancer-causing mutations in the 'dark matter' between genes, unlocking new diagnostic and treatment strategies;
    - The earliest genetic changes that lead to cancer can occur decades before diagnosis, opening up a much greater opportunity for early detection.
- Now providing scientific leadership and hosting the Data Coordination Centre for ICGC-ARGO (Accelerating Research in Genomic Oncology), the next phase of ICGC, which aims to analyze biospecimens and link multi-omic and clinical data from 100,000+ cancer patients to facilitate machine learning of clinically relevant patterns to speed the development of new treatments;
- Co-founded and host of the Global Alliance for Genomics and Health (GA4GH), which has mobilized 500+ members across 90 countries to co-develop technical standards and policy frameworks, including the internationally-accepted Framework for Responsible Sharing of Genomic and Health-Related Data, and has created several harmonized approaches that are supporting all major international genomics initiatives, including the Terry Fox Research Institute Marathon of Hope Cancer Centre program Canadian data sharing initiative.

3 Context for Strategic Plan 2021-2026

3.1 Strategic planning process

OICR kicked off an extensive, highly consultative strategic planning process with its Board of Directors (Board) in September 2018. We engaged the cancer research and clinical communities, our advisory committees, patients and caregivers, health system and industry partners, and global thought leaders on the future of oncology and strategic opportunities for Ontario leadership and impact. In March 2020, OICR underwent an external review by an international expert panel, which assessed the Institute's achievements and impacts, our structures and operations, and our emerging strategy. The panel was impressed with OICR's accomplishments, validated our critical role in the cancer research system, and provided valuable recommendations to inform our priorities and principles for 2021-2026. An outline of major strategic planning activities and findings can be found in **Appendix A**.

3.2 Ontario landscape

As Ontario's facilitator of cancer research, OICR's investments seek to leverage and reinforce provincial strengths and address critical gaps in translational cancer research capacity, ensuring that the province has the world-class talent, collaborations, technologies and infrastructure in place to realize the value of Ontario innovation. **Table 1** summarizes current strengths and gaps in Ontario's oncology ecosystem, which form the basis for the priorities outlined in this strategic plan.

Table 1: Snapshot of current translational cancer research capacity at OICR and Ontario Institutions.

	STRENGTHS	GAPS
People	▪ Many established scientific leaders ▪ Motivated clinician-scientists at several centres	▪ Recruitment and retention of young investigators ▪ Gaps in mid-level investigators and succession in key areas of strength
Technologies	▪ Imaging, genomics, computational biology, Big Data software systems, artificial intelligence/machine learning, epigenetics, medicinal chemistry, bioengineering, organoid models, immunology, stem cells	▪ Access to bioinformatics/data science expertise, pipelines ▪ Awareness of technologies at OICR and other centres ▪ Proteomics (emerging area)
Infrastructure	▪ Robust biobanks, unique cohorts, big data infrastructure, extensive and linkable health administrative datasets	▪ Access to tissues and datasets ▪ Data linkage across multi-disciplinary datasets and disparate systems ▪ Pathways for adoption of innovations into the health system
Disease Areas	▪ Include prostate, breast, leukemia, brain, pancreatic, lung, ovarian cancers; heritable cancers; pediatric cancers	▪ Linkage of research to health system priorities ▪ Addressing needs of Indigenous and other underserved populations
Therapeutics	▪ Image-guided interventions, radiation therapy, oncolytic virus vaccines, small molecules	▪ Access to and integration of drug discovery expertise ▪ Biologics (emerging area)

Clinical Trials	▪ Clinical trials networks and supporting infrastructure ▪ Imaging trials, companion animal comparative trials	▪ Recruitment in remote communities, some smaller centres; ▪ Window of Opportunity trials ▪ Access to pharma drugs
Commercializ-ation	▪ FACIT ▪ Recent investments at some centres in entrepreneurship training, start ups ▪ Recent commercial successes from Ontario IP	▪ Access to commercialization support and investment capital for commercialization in Ontario, including retention of IP in Ontario after initial investment ▪ Experienced biotech leaders ▪ Local commercial receptors

3.3 Environmental scan

The following provides a snapshot of the current state and future outlook of cancer care and research.

Cancer care is becoming earlier, less invasive, and more precise. Despite tremendous medical advances, cancer is still often detected late, when the burden of disease is high and patient outcomes are poor. However, recent studies, including those led by OICR and collaborators, have established that cancer-causing mutations arise years, even decades, before malignancies are detected, significantly broadening the window for the detection and elimination of cancerous cells before the disease can take hold. Studies have shown that treatment costs for early-diagnosed cancer patients are two to four times lower than those diagnosed with advanced-stage disease.[xvii,xviii]

Why is cancer so difficult to diagnose and treat?

- Cancer is not one disease
- Every patient's cancer is different at the molecular level
- Tumours are heterogeneous, so even parts of the same tumour can be different
- Cancer evolves to be more complex over time and can become resistant to treatment
- Rare cancer stem cells, present in the tumour from day one, can resist treatment and allow a seemingly eliminated tumour to regrow
- Cancer can suppress the immune system, keeping the body from recognizing or destroying tumours
- New approaches to treatment are complex because they are individualized to each patient, which is termed **precision medicine**

When cancer is left untreated, it evolves to become more complex and often spreads. Detecting cancer earlier, before this complexity arises, and developing personalized treatment plans for patients that anticipate and prevent tumour evolution are key to stopping cancer. Big Data drives these approaches. Collaborations across disciplines, sectors and geographies are helping to tackle this problem on a much larger scale.

We now know that cancer is not one disease, but rather manifests as distinct disease subsets based on unique molecular characteristics of patient tumours, and that these subsets grow and respond differently to treatment. This understanding has given rise to precision (or personalized) medicine approaches, which aim to provide the best possible treatment to each patient, and minimize unnecessary interventions and associated side effects and costs. To implement precision medicine, we need biomarkers/diagnostics that predict therapeutic response in patient subsets and profile patients and their tumours over time. The integration of novel molecular approaches and advanced imaging with conventional pathology is giving rise to exciting new diagnostic capability, and artificial intelligence/machine learning (AI/ML) systems that leverage Big Data sets are even beginning to outperform pathologists in some diagnoses. Liquid biopsy, in which cancer is detected from tumour fragments in a patient's blood or other fluids, is expected to replace traditional biopsies, which will greatly facilitate cancer screening and monitoring. Although Ontario has made significant headway in these areas, the lack of models for the assessment and reimbursement of novel cancer diagnostics is hindering their adoption into the health system to inform treatment.

The development of novel cancer therapies remains a key industry focus, accounting for ~30 per cent of pharma's product pipeline.[xix] Promising treatment approaches include immunotherapy (to activate the body's immune system to destroy cancer), molecular and biologic therapies targeting mutated pathways that lead to cancer growth and spread, next generation radiation therapy, and image-guided interventions. Many treatment modes have been shown to ultimately activate (or inhibit) anti-cancer immune responses, such that combining approaches offers opportunity to maximize a patient's immune response to their cancer, as well as mitigate therapy resistance. In addition, the use of neoadjuvant therapy to shrink tumours prior to surgery is showing great promise in eliminating disease burden, especially in newly diagnosed cancers, and the global oncology community is beginning to shift focus into this cancer space.

Patients are increasingly engaged and empowered in directing cancer care and research. Patients have more access to personal health data than ever before, as well as to information found online/via social media, and are embracing technology (mobile apps, wearable biosensors, telehealth) for remote care, disease monitoring and to facilitate their cancer journey. Patients are also playing a more active and impactful role in cancer research, from sharing lived experience through to co-design and co-leadership of research projects. At the same time, accessing and navigating cancer care and clinical trials remains heavily impacted by geography and social determinants of health, particularly among remote, Indigenous and underserved populations.

Big Data and computational tools are greatly accelerating the power and pace of cancer research. Mining large datasets (including molecular, clinical, environmental and social data) through AI/ML approaches is critical to understanding cancer development and informing precision medicine. It is not hard to imagine a future where every patient encounter is viewed as a research opportunity, with the data gathered leveraged to inform health policy in a Learning Health System model. New computational tools on the horizon, including classical-quantum hybrid formats and full quantum computing, will offer increased strength and speed for analyzing large multi-dimensional, multi-factorial datasets. However, challenges associated with data quantity, quality and ensuring privacy necessitate systems for integrating and exploiting disparate datasets safely, responsibly and transparently to capitalize on the potential of Big Data to drive precision medicine.

Funding for cancer research in Canada is on the decline. Overall cancer research investment in Canada declined by 18.9 per cent from 2011-2016,[xx] reflecting decreased funding at both federal and provincial levels, as well as in the health research charity sector, which has undergone consolidation and is experiencing historical loss in revenue during the COVID-19 pandemic[xxi]. Similarly, cancer centres, which rely on revenue from cancer clinical trials to underwrite research costs, have been deeply impacted by the pandemic[xxii]. The impending surge in cancer cases underscores the urgent need for sustaining cancer research momentum, scaling translational models that have successfully advanced cancer discoveries to patients, and reinvesting returns to seed further innovation.

4 Overarching priorities for 2021-2026

Strategic Plan 2021-2026 seeks to capitalize on Ontario strengths and successes to develop solutions to stem the growing health and economic burden of cancer on society. Our emphasis on earlier cancer detection offers the best opportunity to stop cancer before it can take hold, grow more complex and spread (**Figure 2**).

The **overarching focus** of Strategic Plan 2021-2026 is to **develop the knowledge and tools to implement next generation cancer precision medicine in Ontario, where cancer patients are**

diagnosed as early as possible, treated precisely and definitively, and monitored proactively to detect and resolve recurrence, dramatically transforming survival and quality of life.

Next generation precision medicine requires a number of advanced tools:

1. **Diagnostics** capable of detecting early cancers with high sensitivity and specificity;
2. An arsenal of safe and effective **treatments**;
3. **Clinical decision-support tools** for selecting the most suitable treatment course for each patient, based on the analysis of biomarkers associated with treatment responses and clinical outcomes of large numbers of cancer patients;
4. Sensitive, precise, minimally-invasive **monitoring tools** and analytical approaches for detecting trace amounts of tumour recurrence in cancer survivors to intervene before the cancer spreads.

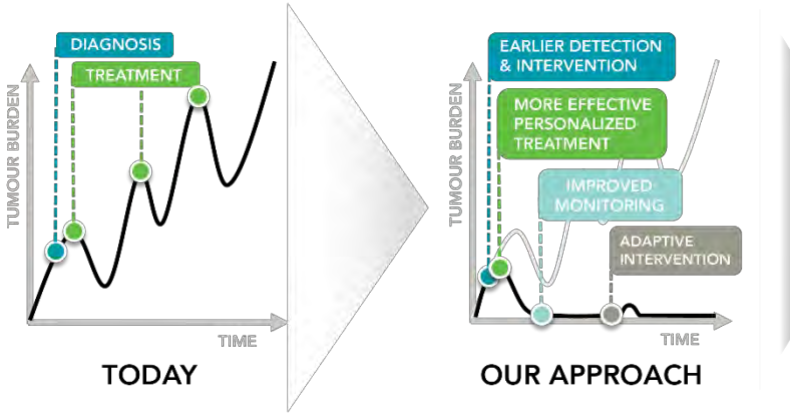


Figure 2: The importance of early detection, personalized treatment and ongoing disease monitoring in decreasing tumour burden and improving patient outcomes.

Developing these tools and translating them into clinical practice requires an integrated translational research pathway that links discovery to patient impact. OICR's investments over the past 15 years have established and reinforced the foundational components of this pathway, in partnership with Ontario's research and clinical communities, FACIT and Ontario Health (Cancer Care Ontario). As outlined below and summarized in **Table 1**, OICR's investments for 2021-2026 will strengthen, speed and scale this pathway to turn insights in cancer development into precision medicine innovations that are implemented into Ontario's heath system to transform patient outcomes.

2021-2026 Goals

1. ***Advance early detection and intervention research*** to understand the earliest events in cancer development and how tumours evolve to become more complex and harder to treat. This knowledge will inform the development of **tools for early detection, intervention** and **monitoring for recurrence**. We will capitalize on unique Ontario research platforms to track cancer development over time, including the Ontario Health Study and a registry of patients and families who carry genetic susceptibility to cancer, which will be developed by the new Ontario Hereditary Cancer Research Network. We will also bring together a network of clinicians and scientists to drive an innovative translational research platform where novel therapies will be tested in newly-diagnosed and recurrent cancer patients prior to surgery through Window of Opportunity and neo-adjuvant clinical trials. Findings from these studies will provide deep molecular understanding of how these therapies fight cancer, and will help identify patients likely to benefit from these therapies in the future.

2. ***Reinforce Ontario's global leadership in data sharing and analytics***, exploiting Big Data to determine the clinical and molecular features that predict an individual patient's response to therapy, forming the basis for the **clinical decision-support tools** to drive next generation precision medicine. We will establish the Ontario Hereditary Cancer Research Network Registry

of patients and families with hereditary cancer syndromes. This will be integrated with the new Ontario Health Data Platform and will serve as a template on which to build other integrative health research platforms. We will also apply Ontario's world-renowned artificial intelligence (AI) expertise to analyzing medical images, which has potential to revolutionize cancer diagnostics.

3. ***Expand a robust Ontario pipeline of novel cancer therapeutics*** with potential to transform cancer **treatment**. We will build up our drug discovery pipeline, which is currently advancing 10 first-in-class/best-in-class Ontario therapeutic assets towards clinical development, providing more investment opportunities for FACIT and entrepreneurship opportunities for the research community. We will also work towards greater integration of provincial capabilities and resources in a new Drug Discovery Community that will advance promising drug candidates, attract industry partners and drive local commercialization.

4. ***Drive the translation and commercialization of cancer innovations in Ontario*** so that safe and cost-effective precision medicine tools can be adopted into **clinical practice to transform patient survival and quality of life**. We will establish a Clinical Translation Pathway to develop and test practice-changing diagnostics, clinical decision-making tools and therapeutics in clinical trials, especially in the pre-surgical setting described above. This pathway will be fueled by innovations emerging from OICR-supported research, and from research institutions across the province. We will also link this pathway to our drug discovery efforts through new pharmacogenomic screens of residual tumours from our therapeutic trials. FACIT will continue to lead the commercialization of these tools, identifying projects with high commercial potential and facilitating early commercial planning, seeding new Ontario start-ups and attracting investment and industry partners, enabling Ontario to compete in the growing precision medicine market. We will also work with existing large clinical trials groups in Ontario to ensure there is a receptor for developing promising assets in increasingly large and complex clinical trials. OICR is committed to strengthening our partnership with Cancer Care Ontario/Ontario Health to ensure there is a pathway to systematically evaluate and implement cancer innovations into the health system so patients can benefit.

5. ***Strengthen and sustain Ontario capacity for translational cancer research*** to drive the scientific breakthroughs that will fuel cancer innovation. Our success as an organization is tightly tethered to the value we place on collaboration. All of the above components will be enabled through the recruitment, development and networking of research talent and expertise, targeted investment in collaborative research platforms and infrastructure, and critical partnerships with Ontario cancer centres, universities and research institutes, patients and caregivers, the private sector and government.

Table 1: 2021-2026 Goals and Investments (tactics), mapped to their respective Research Themes and Enablers

1. Advance early detection and intervention research Execute a focused, multi-disciplinary strategy for early cancer detection and intervention, developing and validating tools to address patient and health system needs.	
Research on early cancer detection, tumour heterogeneity and evolution to inform tools for early cancer diagnosis, treatment selection, and monitoring for early recurrence	
Ontario Health Study and Ontario Hereditary Cancer Research Network to study early events in cancer initiation and develop approaches for early detection, precise intervention and monitoring	

- Window of Opportunity trials and other pre-surgical trials to test interventions in newly diagnosed and recurrent patients amenable to surgery to identify new biomarkers for precision medicine

2. Reinforce Ontario's global leadership in data sharing and analytics

Advance national and international data sharing efforts to identify new cancer biomarkers and pathways informing the development of next generation cancer diagnostics, clinical decision-support tools and therapies.

- ICGC-ARGO (International Cancer Genome Consortium-Accelerating Research in Genomic Oncology) Big Data coordination, harmonization, sharing and analysis
- Ontario Hereditary Cancer Research Network Registry of hereditary cancer patients and carriers

3. Expand a robust Ontario pipeline of novel cancer therapeutics

Partner with the Ontario research community and FACIT to strengthen and advance a provincial pipeline of promising oncology assets that attract investment in successful commercial ventures.

- Enhancement of Therapeutic Innovation, fueling and advancing a first-in-class/best-in-class drug pipeline into clinical development and patient testing
- Building towards a Drug Discovery Community leveraging expertise and resources across the province to strengthen the Therapeutic Innovation pipeline

4. Drive the translation and commercialization of cancer innovations in Ontario

Collaborate with healthcare agencies/providers, FACIT and private sector partners to advance Ontario discoveries to cancer patients and deliver economic benefit to Ontario.

- Clinical Translation Pathway to develop and validate practice-changing diagnostics, clinical decision-making tools and therapeutics
- Implementation science research and partnership with Ontario Health (Cancer Care Ontario) to promote health system adoption of cancer care innovations
- Sustaining FACIT's commercialization entity to translate innovations to patients and market and grow jobs

5. Strengthen and sustain Ontario capacity for translational cancer research

Support and develop Ontario research talent and provide access to world-class technology platform, resources and infrastructure to address provincial needs and maintain Ontario research leadership.

- Renewed Investigator Awards program, OICR Scientific College and Rising Stars in Cancer Research Network to recruit, develop and engage Ontario talent
- Broadened access to leading-edge technologies, resources and clinical trials infrastructure for world-class cancer research and translation

Our impact will be achieved through partnerships across the Ontario oncology ecosystem:

- **Cancer centres, universities and research institutes**: to advance cancer research priorities, leverage capacity and expertise, seed collaboration and share knowledge;
- **Patients and caregivers**: to advise on and partner in our research priorities;
- **FACIT**: to drive research commercialization and attract industry partners and investors;
- **Government of Ontario**: The Ministry of Health (Cancer Care Ontario/Ontario Health) to inform on unmet cancer care needs/priorities and facilitate the ultimate implementation of research innovations into the healthcare system; the Ministry of Colleges and Universities and Ministry of Economic Development, Job Creation and Trade to ensure our work continues to deliver value to Ontario's research system and helps drive the innovation economy.

5 Thematic priorities for 2021-2026

The following section outlines the directional shifts and new initiatives under Adaptive Oncology, Clinical Translation and Therapeutic Innovation Research Themes.

5.1 Adaptive Oncology

Challenge. Cancer is a mercurial adversary which constantly adapts and evolves in response to the patient's immune defenses and applied treatments. It does this through a process of mutation, natural selection and evolution which over time selects for cancer cells that are stronger, more aggressive, and resistant to therapy (**Figure 3**). Cancers are known to evolve resistance to all types of therapy, including cytotoxic chemotherapy, targeted therapies, immunotherapy, radiation therapy and surgery.

Our current paradigm of cancer management leaves us flying blind with respect to tumour evolution. The key changes that determine a tumour's response to therapy are at the molecular (DNA, RNA, and protein) level, but only a minority of cancers are subjected to molecular analysis. Of these, few receive the type of comprehensive molecular characterization needed to understand the genetic complexity of a tumour and predict which therapeutics it is most likely to respond to. Furthermore, because cancer is a moving target, tumours need to be repeatedly sampled across time in order to understand how they are evolving and to inform strategies for treating them effectively in more rational and informed ways.

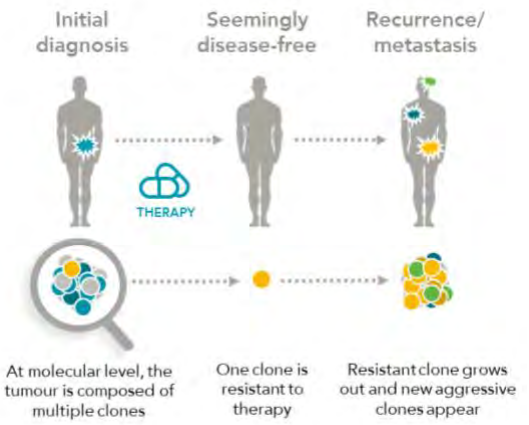


Figure 3: Cancers often recur because of tumour evolution.

Goal. Adaptive Oncology (AO) seeks to develop diagnostic tools that provide a comprehensive portrait of the tumour at the time that the patient first presents to the medical system, to update this portrait throughout the course of treatment, and to use the information to guide clinical decision making. These tools are leveraged with data integration platforms that allow comparison of large numbers of cancer patients to each other, with artificial intelligence/machine learning and other Big Data tools used to extract novel associations between molecular changes and clinical behaviour. The ultimate goal is to provide physicians with the diagnostic and decision-support tools needed to monitor the trajectory of a tumour's evolution, interpret its significance, develop a therapeutic plan that anticipates how the tumour will respond to therapy, and be able to modify the plan in a real-time fashion to adapt to changes in the tumour's characteristics.

Design. AO is comprised of five technology-oriented Programs, four service-oriented Resources, and four knowledge-exchange Networks (**Tables 3**, **4** and **5**). The Programs develop new tools and techniques, and support research within the OICR Research Themes and with the Ontario cancer research community via the Collaborative Research Resources (Section 6.2). The Resources provide key infrastructural services, such as high-performance computing, while the Networks play an important role in knowledge mobilization and dissemination. Ministry funding contributes roughly 50 per cent of AO's research budget, with the remainder supported by government, indirect charitable foundation support and industry grants. Guidance is provided by the Adaptive Oncology Scientific Advisory Committee (AO-SAC). AO's main areas of research and development and the role that the Programs, Resources and Networks play in advancing them are outlined below.

Adaptive Oncology in Action

To better understand the vision of the future driving the mission of Adaptive Oncology (AO), consider a patient today who was a past smoker diagnosed with early lung cancer that could have been caught earlier if improved screening and detection methods were available. She receives standard surgery shortly after diagnosis to remove the tumour with or without a period of chemotherapy afterwards. The surgery is successful, but two years later, a follow-up exam reveals recurrence of the tumour in her lung, which has also spread to her spine and brain. The lung tumour is removed and undergoes laboratory testing, which reveals a gene mutation that is associated with too much production of a protein called EGFR, a receptor on the tumour's cells that drives proliferation. Fortunately, there is a drug that can be used to reduce the expression of EGFR and the patient does well on this treatment for six months with a partial response. After six months, she complains of additional symptoms and imaging reveals there is more evidence of tumour spread to additional parts of her body. The patient is given chemotherapy, but the disease is too far advanced, and sadly the patient dies three years after her initial diagnosis.

The same patient could be managed quite differently through an AO approach, linked cohesively to OICR's Clinical Translation and Therapeutic Innovation Themes. AO researchers would exploit new technologies to better understand the unique characteristics of her tumour to better anticipate its evolution. The patient could participate in an innovative neo-adjuvant trial (i.e., a trial that aims to shrink the tumour before it's removed), supported by OICR's Clinical Translation Theme, which starts with a biopsy of the tumour, where it is found that EGFR is over-produced. After treatment, the patient undergoes surgery to remove the remaining residual tumour. During the trial the patient has regular blood samples collected (liquid biopsies) so that her oncologist can determine how much tumour DNA is circulating around her body at a given time, which could signify cancer recurrence or metastasis. The blood samples show a fall of tumour DNA to undetectable levels within a month following therapy and surgery, providing relief for the patient and her family. However, about one year later, well before she has any symptoms of recurrence, tumour DNA again appears in a blood sample. Further analysis of the liquid biopsy by OICR's Genomics program indicates that the tumour has acquired a new mutation driving resistance to standard therapies. This finding is verified by analysis of a sample taken of her tumour after the neo-adjuvant therapy in the clinical trial she participated in. This molecular finding allows the patient to be eligible to enroll in an Ontario-based trial of an experimental therapy. She participates in a new drug combination trial that is successful for her particular type of lung cancer, her recurrent tumours disappear on imaging scans, and her tumour DNA levels drop to zero in subsequent liquid biopsies. Five years later, the patient remains alive with no evidence of disease. Interestingly, further study of her tumour after neo-adjuvant therapy finds an alteration in a new signaling pathway, which stimulates a new drug discovery project supported by OICR's Therapeutic Innovation Theme. Thus, the patient participates in an interlinked research process greatly benefitting her as well as driving new innovation.

Table 3: AO Technology Programs.

Genomics	Next generation sequencing technology development and services in an IQMH/CAP/CLIA[xxiii]-certified environment. Advanced technologies offered include liquid biopsy, sequencing, and long-read sequencing via the Oxford Nanopore.

Diagnostic Development	Discovery and validation of molecular biomarkers and translation into robust diagnostic assays that can be applied in the clinical laboratory for clinical trials and validation of new precision medicine approaches.
Imaging	Development and provision of imaging technologies ranging from cancer-specific imaging probes to robotic systems for precise real-time 3D ultrasound-guided and MRI-guided tumour sampling procedures.
Genome Informatics	Development and deployment of software systems for collecting, harmonizing and sharing large cancer datasets via the cloud.
Computational Biology	Utilization of datasets from all the above technologies for the development and application of algorithms for cancer genome analysis, biomarker discovery, cancer pathway discovery, data integration and tumour evolution.

AO research areas

1. Detecting early cancers

Overview. Early cancers are genetically simpler, have not yet spread, and are less likely to have developed defenses against the host immune system and therapeutics. However, too many cancers only become clinically evident at later stages of development when they are much harder to treat. AO researchers working in this area seek to understand how cancers arise and to develop technologies to detect early-stage tumours.

Approach. Multiple ongoing and planned projects address early cancer detection. These include:

Non-invasive cancer detection with liquid biopsies. The Genomics program, working hand-in-hand with Computational Biology, is developing liquid biopsy technologies for detecting traces of tumour DNA in the circulating blood of patients with early cancers. A particularly promising technique called cfMeDIP, developed in collaboration with researchers at University Health Network (UHN) and now being commercialized with an industry partner, is able to simultaneously detect the presence of a likely cancer and identify the tumour site. This technique is being applied retrospectively to blood samples collected from healthy participants in the Ontario Health Study who later went on to develop cancers. Preliminary results show that circulating DNA from these cancers was present prior to diagnosis, demonstrating the feasibility of screening for cancers prospectively in at-risk individuals.

Table 4: AO Resources.

Ontario Tumour Bank (OTB)	Acquisition, storage and distribution of cancer-related biospecimens for research contributed by Ontario cancer centres, including bespoke specimen collection and derivation. The OTB will sunset under Strategic Plan 2021-26.
Canadian Data Integration Centre	A consultancy service that provides wet and dry lab support for advanced genomics and bioinformatics studies.
ICGC Data Portal and the Cancer Genome Collaboratory	Provide community researchers with access to the holdings of the International Cancer Genome Consortium project (>22,000 tumour genomes) in a secure compute environment.

Algorithms to Flag Mammography Patients Who Need Additional Screening. Annual mammography is an effective way to catch and treat breast cancers early. However, mammograms miss about 50 per cent of cancers in the densest breasts.[xxiv] The Imaging program is using radiomic and ML techniques to identify which mammograms have a high likelihood of missing early tumours, and are incorporating these algorithms into a decision-support system that will recommend such patients for additional screening through other means such as positron-emission mammography, which is being developed within AO and through FACIT's investment in Radialis, a start-up company in Thunder Bay.

Table 5: AO Knowledge Exchange Networks.

Global Alliance for Genomics in Health (GA4GH)	An international standards-making body that provides protocols for responsibly sharing human genomics and clinical data, co-founded by and hosted at OICR.
Ontario Molecular Pathology Network (OMPRN)	A network that provides research, training and networking opportunities to pathologists and trainees, providing the skills needed to bring molecular techniques into the pathology laboratory and spearhead the coming transition to precision medicine for cancer.
Ontario Hereditary Cancer Research Network (OHCRN)	A new (2021) Ontario-wide initiative to develop protocols, registries, cohorts and other resources for evaluating patients and families carrying germline mutations that increase their risk of cancer.

The Ontario Hereditary Cancer Research Network (OHCRN, new activity). Hereditary Cancer Syndromes (HCS), caused by inherited mutations in cancer causing genes, comprise 10 per cent of all cancer cases.[xxv] There are more than 8,000 cases of HCS-associated cancers every year in Ontario. Knowledge gained from studying HCS patients and their families have provided key insights into our understanding of cancer genomics. Because HCS carriers have a high risk of developing cancers at an early age, they are eligible for many clinical trials, and are ideal populations for studying cancer development and for testing potential strategies for cancer screening, detection and prevention.

AO will establish the OHCRN to foster collaboration among HCS researchers through training and networking events, mentorship opportunities, collaborative funding opportunities, and the development of shared infrastructure. The flagship deliverable from this project will be an Ontario-wide HCS registry that allows clinical and molecular information on consenting HCS patients and their families to be shared across the province. This registry will help patients and their clinicians find eligible clinical trials, and support OHCRN research projects to develop new strategies to identify, evaluate and monitor individuals at high risk for developing cancer, which can be evaluated in Clinical Translation-sponsored trials.

2. Monitoring tumour heterogeneity and evolution

Overview. By the time most tumours are detected, they consist of multiple populations (clones) with distinct genomic identities, a phenomenon known as 'tumour heterogeneity'. Over time, clones evolve and expand in response to internal and environmental pressures, with some becoming resistant to cancer therapies and dominating relapsed tumours.

Approach. As described below, multiple projects are studying the biology of tumour heterogeneity and developing technologies for monitoring its evolution. The techniques and decision-support algorithms developed can then be tested in clinical trials supported under the Clinical Translation Theme.

Heterogeneity in Time. Using liquid biopsy techniques such as cfMeDIP developed by the Genomics program and collaborators, the Diagnostic Development and Computational Biology Programs are following changes in tumour DNA over time in the blood samples of cancer patients undergoing therapy, in the hope that the direction and rate of change will predict the tumour's response to therapy or can be used as an early indicator of tumour recurrence. If successful, this research will lead to the development of an entirely new class of time-based biomarkers for cancer management.

Precision Robotics for Tumour Sampling and Therapeutics. To exploit our advancing knowledge of molecular differences within the same tumour (termed spatial heterogeneity), we require systems that allow us to precisely target a defined section of the tumour to sample it for molecular analysis, or to inject it with a matching therapeutic. The Imaging program develops advanced devices that combine robotics with multi-modal imaging techniques that together allow a radiologist to superimpose real-time ultrasound imaging data on a 3D reconstruction of the tumour from MRI or computed tomography. Computer-guided robotic systems can then precisely guide biopsy needles, radioactive seeds, or chemotherapy agents into selected regions of the tumour while avoiding damage to healthy tissues. The work has resulted in numerous commercial products (see Section 2.4) and will be applied to preclinical studies of tumour heterogeneity and evolution, and potentially in clinical trials supported by the Clinical Translation Theme.

3. Integrating and sharing multi-omics Big Data sets

Overview. The rapid advancement of molecular 'omics and radiomics (which uses algorithms to extract a large number of quantitative features from medical images) have created an acute need for computer systems that can generate, capture, organize and share these large datasets and link them to clinical data. By integrating across large numbers of patients and their clinical outcomes, researchers can apply AI/ML techniques and other analytic methods to determine which clinical and molecular features predict an individual patient's response to therapy.

Approach. The Genome Informatics group is a unique team of software engineers, bioinformaticians and computer scientists who work collaboratively with wet and dry lab researchers to create compelling web and cloud-based systems for responsibly exchanging 'omic, imaging and clinical data.

The *ICGC and ICGC-ARGO Data Coordinating Centres* coordinate the data collection, harmonization and publication of data from >24,000 cancer patients, with an ultimate target of 100,000 patients by 2030. A unique feature of the international ICGC-ARGO project is its aim to collect detailed treatment and response data from patients enrolled in therapeutic clinical trials, which will allow researchers to identify biomarkers for precision medicine. Data from these projects are available from a web-based research portal built at OICR that has won accolades for its design and usability, as well as in the cloud-based Cancer Genome Collaboratory described in **Table 4**.

Recent advances in radiomics and the application of artificial intelligence to digital imaging are poised to revolutionize cancer diagnostics. Machine learning researchers have demonstrated that AI systems can accurately identify cancers in both radiological imaging studies and in scanned pathology images, and that these systems can achieve the same accuracy as human radiologists and pathologists. AI systems do not become fatigued or distracted, and can discern subtle quantitative patterns not apparent to human perception. Under Strategic Plan 2021-2026, AO's Imaging program will increase its activities in the areas of radiomics and AI-based feature recognition and image classification by

sponsoring training activities and workshops, and by promoting collaborations among biomedical imaging and AI researchers through its recently established *Machine Learning for Medical Imaging Consortium*. This effort will be supported by: (1) awarding up to two Investigator Awards to early- to mid-career researchers working in quantitative imaging; and (2) establishing joint research initiatives with AI researchers and advanced imaging instrument developers. Also in support of this effort, AO will provide the means to generate and share large imaging datasets for the purposes of training and testing machine-learning models.

Defining success. The Adaptive Oncology Theme will develop insights into cancer's "playbook" so that clinicians can anticipate and counter the twists and turns of cancer evolution. The Theme will deliver new molecular and imaging technologies for early cancer detection and monitoring, precision hybrid imaging systems for sampling tumour tissues and administering spatially targeted therapeutics, and decision-support software for administering the right therapy to the right patient at the right time.

Key metrics to track success (see **Appendix D**) will include:

- Number and impact of publications;
- Number of invention disclosures, patent applications and awards;
- Amount of leveraged research funding attracted;
- Number of persons with enhanced knowledge, training or skills;
- Number and impact of collaborations across Research Themes and with the community;
- Development, release and utilization of new infrastructure and resources, such as the OHCRN Registry;
- Number of AO research discoveries tested in Clinical Translation-sponsored trials.

5.2 Clinical Translation

Challenge. There are well-described challenges in mobilizing new knowledge generated by scientific research into practical applications that are adopted into clinical practice (**Figure 4**). Basic or 'discovery' science is highly creative with unpredictable findings, whereas research that is conducted with patients must be de-risked and more deliberate. The goal of translational research is to bridge the two 'valleys of death' between the laboratory bench or workstation and the patient's bedside. Translational research is complex. Success depends on the engagement of many partners, including the health system, health regulators and in some cases the private sector, as well as scientists, clinicians, and especially patients and their families.

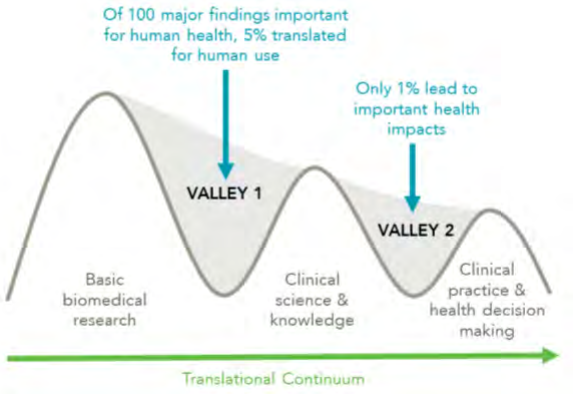


Figure 4: Valleys of death addressed by translational research. Copyright University of Pittsburgh 2000. Reis et al., Clin Transl Sci, 2008.

Goal. The Clinical Translation (CT) Theme is the translational engine of the Institute, advancing discoveries from the Adaptive Oncology and Therapeutic Innovation Themes, and from scientists across the province into clinical testing. Its goal is to advance Ontario cancer discoveries through early clinical validation, partnering with patients, industry and the health system for downstream development and implementation. The Theme's focus is to support earlier and more effective detection and intervention in hard to treat cancers through innovative biomarker-focused clinical trials that drive scientific knowledge and lead to the rapid advancement of new approaches.

Clinical Translation in Action

To understand Clinical Translation's (CT) vision for the future, first consider a patient today who has just received a diagnosis of pancreatic cancer. This is devastating news and likely the worst day in this person's life. Treatment options for pancreatic cancer are limited to a small number of chemotherapies, with radiation and surgery also available to a subset of patients. Pancreas cancers tend to recur and spread, and the result is that pancreatic cancer is today the third largest cause of cancer death in Canada, with a five-year net survival of a mere eight per cent.

Through the CT Theme, however, this patient could be enrolled in a clinical trial providing them with new treatment options based on understanding of the unique molecular characteristics of their cancer.

Thanks to preclinical research studies supported by OICR, scientists now know there are five major subtypes of pancreatic cancer, based on the molecular tags or 'biomarkers' expressed in the tumour. Further laboratory work revealed that a particular biomarker, GATA6, acts as a signpost being expressed at higher and lower levels, and may predict whether a patient will, or will not, respond to chemotherapy. Our pancreas cancer patient can be given a new clinical trial option: to be treated before their surgery with early chemotherapy (called 'neo-adjuvant' therapy, meaning it is given to shrink the tumour before it is removed), then receive surgery, and then another round of chemotherapy (called 'adjuvant' therapy, meaning it is given in addition to surgical treatment) to kill any residual cancer cells and reduce the likelihood of recurrence. Samples of the patient's tumour would be taken at different stages and sent back to the laboratory so that additional studies could be done to determine levels of GATA6 and other biomarkers of treatment response. Researchers can also study the tumour cells in a laboratory setting to determine the ability of a large number of chemotherapy drugs to kill the cancer cells. In this way, the right treatment can be matched to an individual patient's tumour. This finetunes the best treatment for the individual patient, ideally resulting in longer survival and a better quality of life. Every patient in the clinical trial would be carefully followed to see how they respond to treatment and how well they recover so that clinicians and scientists can understand which future patients will benefit from a particular treatment and which will not. This reduces unnecessary or ineffective treatment and leads to changes in what oncologists in Ontario and around the world deliver as standard care for their pancreatic cancer patients with particular biomarkers.

Design. Clinical Translation consists of three Research Initiatives and three Platforms and Networks.

Research Initiatives

1. Clinical Translation Pathway

Overview. OICR will establish a Clinical Translation Pathway (CTP) to progressively move scientific ideas from preclinical investigation through to early clinical testing. The CTP represents the evolution of OICR's previous Translational Research Initiatives (TRIs) and support for stand-alone clinical trials. Its design addresses shortcomings in the TRI model, including the need for a clearer path to translational application; failure to initiate or execute on planned clinical trials proposed at program outset; limited collaboration amongst teams and with other OICR research programs to capitalize on cross-cutting molecular themes and new cancer drug discovery opportunities; insufficient flexibility to accommodate new projects and investigators; and limited opportunity for career development of early career investigators.

Approach. The CTP will embrace multi-centre collaborative science, with opportunities to promote new collaborations across research areas and disciplines to spark innovation, harnessing the expertise of scientists, clinicians, patients and industry partners. The following principles will be adopted:

- Focus on early detection and intervention of untreated cancers with poor patient outcomes in the adult or pediatric settings;
- Bring together clinical and scientific expertise and build on Ontario's proven strengths;
- Evaluate and fund preclinical and clinical research projects separately;
- Support early phase clinical trials, focusing on biomarker-rich pre-surgical window of opportunity and neo-adjuvant Phase I and Phase II trials;

- Increase connectivity to Adaptive Oncology and Therapeutic Innovation programs, networks and resources for biomarker analysis and investigation of novel therapeutic targets;
- Integrate implementation science questions within the scope of funding opportunities;
- Provide funding to explore novel collaborations between programs and disciplines.

The CTP will consist of three funding streams: Clinical Acceleration Team Awards (CATA), pre-CATA projects and Convergence Projects (**Figure 5**).

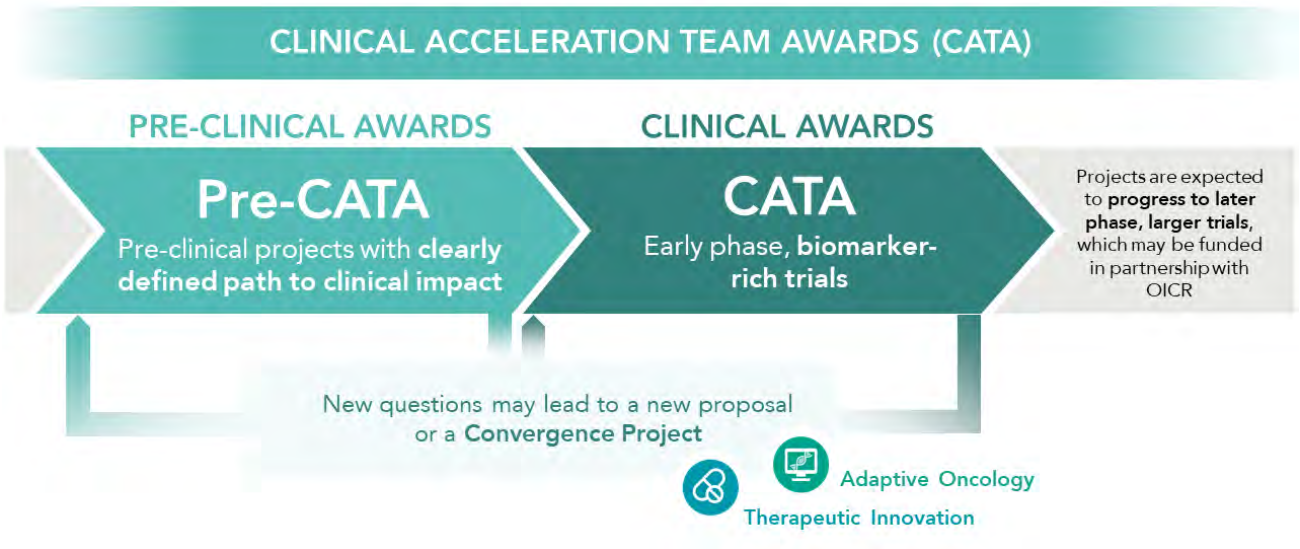


Figure 5: Overview of the Clinical Translation Pathway.

An open Request for Applications (RFA) will be issued for projects that fit within the pre-CATA, CATA or Convergence Project models. Scientific and clinical teams that include multi-institutional collaborators and both senior and early career investigators will be encouraged. The Clinical Translation Scientific Advisory Committee (CT-SAC) will provide independent scientific guidance to the CTP, overseeing application peer review, monitoring project progress against defined deliverables and advising on opportunities to increase program impact. **Appendix B** provides more detail on the scope of trials that will be emphasized.

In addition to the open CTP RFA, *OICR will make a strategic investment in pancreatic cancer research*. OICR has had a strategic focus on improving the understanding and treatment of pancreatic cancer since its founding. Pancreatic cancer is the third leading cause of cancer death in Ontario and Canada, with a five-year net survival of 8 per cent.[xxvi] OICR committed to cataloguing genomic abnormalities associated with pancreas tumours within the ICGC Project, and the PanCuRx TRI evolved from that work, focused on linking genomic analysis of pancreas adenocarcinomas from individual patients with tailored therapeutic approaches. Identification of such biomarkers of treatment response have led to additional clinical trials testing chemotherapy administered before and after surgery to improve patient outcomes. This progression of increasingly patient-centric research translating genomic findings through to clinical testing of new treatment strategies in a very poor outcome disease epitomizes the purpose of the new CTP and the need for long-term research investments to change clinical practice.

2. Window of Opportunity (WOO) Network

Overview. As treatments become more precisely targeted to the molecular characteristics of a patient's tumour, a deep understanding of the biology associated with these characteristics is needed to inform which patients are likely to benefit from novel therapies. "Window of Opportunity" (WOO) refers to the period of time between a patient's cancer diagnosis and their cancer surgery. WOO trials allow the brief evaluation of novel therapeutics, which have previously demonstrated safety requirements in Phase I-II trials, in healthier patients (newly diagnosed or those with recurrent tumours amenable to surgery) to study their effects on tumour biology. Biopsies taken before, during and after this short therapeutic window allow for comprehensive analysis of the mechanism of action of the therapeutic(s) and possible mechanisms that may later lead to tumour relapse. Application of these insights will lead to identification of new biomarkers that will inform more precise patient diagnostics and treatments, including identifying patients likely to respond to the treatment when administered over a longer time interval prior to surgery, as well as in the advanced cancer setting. Although short WOO trials do not have therapeutic intent, the findings can be later tested in therapeutic neo-adjuvant trials.

Pharmaceutical and radiotherapeutic companies are increasingly embracing the idea of detecting and treating cancer earlier and need more academic alliances to study the mechanisms of action of drugs in their development pipelines. OICR is currently piloting a WOO trial in breast cancer in collaboration with Glaxo SmithKline (GSK) to test the effects of a new epigenetic modulator drug.

Approach. OICR will establish a bedside-to-bench WOO clinical trials network that will position Ontario as a world leader in this rapidly growing field of oncology. It will bring together clinical groups across Ontario to test and analyze new treatments/combinations of treatments, including therapeutic imaging, in newly diagnosed and recurrent patients amenable to surgery. The Network will integrate and build on OICR strengths, link clinical (surgeons, clinical oncologists, radiation oncologists, pathologists) and lab collaborators across the province, provide opportunities for training clinician-scientists in precision medicine approaches and tools, and attract industry partners to provide access to novel therapies and/or approved agents that can be applied in new ways (**Figure 6**).

The WOO network will have an initial scientific focus on immunomodulation - how therapeutic approaches modulate the ability of a patient to mount an effective immune response against their cancer - which is critical to make immunotherapy more effective, less toxic and more durable.

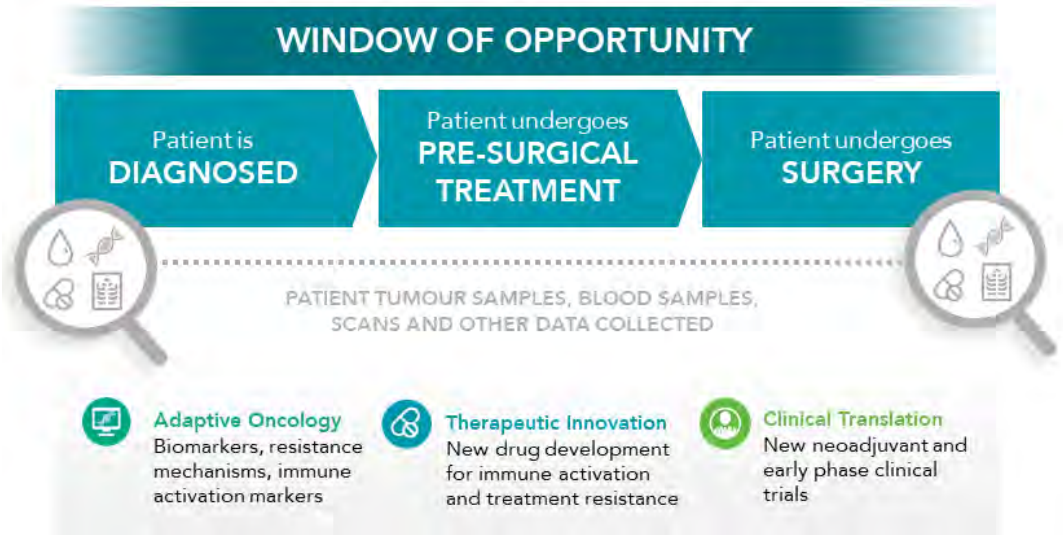


Figure 6: Overview schematic of the WOO concept.

The WOO network will be co-led by an OICR scientist and a surgical-oncologist and overseen by a steering committee of clinicians, scientists and a patient advisor. The network will:

1. Engage a provincial community of clinicians, scientists and patients interested in WOO trials.
2. Develop ideas for impactful new WOO trials in immunomodulation.
3. Provide resources for common protocols, patient engagement, standardized analysis.
4. Drive common analytical and data sharing platforms for OICR-supported WOO trials.
5. Provide a single expert body for engaging pharma partners.

Core laboratory support will be offered through AO technology programs. There may be an opportunity to partner with existing clinical trials groups and the Canadian Cancer Clinical Trials Network to facilitate patient enrollment. A province-wide request will be issued for WOO trial ideas and involvement to generate trial concepts, connect people and ideas, and improve upon them. Trial proposals will be submitted to the CT-SAC for independent peer review and funding recommendation to OICR leadership and Board.

3. Implementation science

Overview. Implementation science is an area of health services research focused on generating evidence to improve healthcare practices and policies that benefit patients, caregivers and the population. It results in real system change and policy shifts through an evidence base and political processes. Examples of implementation science include the collection of real-world evidence of therapeutic or diagnostic effectiveness from clinical practice; policy change to approve the use of novel diagnostic tools in cancer care; changes in system delivery to reduce health inequities; and health technology assessment and implementation.

Implementation science is based on the ideal of a Learning Health System (LHS) in which clinical experience, research and real-world data are linked dynamically and every patient interaction is an opportunity to improve the health system and health outcomes. Recent advancements towards an LHS model in Ontario include the formation of the consolidated Ontario Health agency and investment in the new Ontario Health Data Platform.

Approach. Implementation science will be highlighted within the CTP as an area of research in scope for funding so that health systems research questions can be addressed early and proactively when developing new clinical trials and potential practice-changing paradigms. Importantly, OICR will also continue and strengthen our partnership with Ontario Health (Cancer Care Ontario) to develop a pathway to systematically evaluate and implement more cancer care innovations into the health system (Ontario Pathway Towards Innovation in Cancer Care (OPTICC)).

Research Platforms and Networks

1. Ontario Health Study (OHS) and the Canadian Partnership for Tomorrow's Health Project

OHS is a research platform consisting of 225,000 Ontarians who have committed to contribute personal data over their lifetimes for studying how lifestyle, genetics and the environment affect people's health, including cancer susceptibility.

OICR has provided 10 years of support to initiate and build OHS, the largest regional cohort of the national Canadian Partnership for Tomorrow's Health (CanPath) study, Canada's premier population study of 350,000 participants. CanPath is based at the University of Toronto's Dalla Lana School of Public Health (DLSPH) and has independent national governance, operational, scientific and

sustainability committee. OICR hosts all of the CanPath data, including OHS data, and CanPath's National Scientific Director is also a Senior Principal Investigator at OICR. CanPath currently receives financial and in-kind support from eleven organizations, both national and provincial bodies, including OICR. OICR will continue to support all operations and provide some research support to OHS, and provide scientific and data management leadership to CanPath.

There is tremendous opportunity to leverage OHS/CanPath data with OICR's focus on early stage cancer, including studying genetic, environmental and lifestyle risks of cancer to identify novel disease prevention interventions, as well as the evolution of cancer over time in order to develop innovative ways to detect and treat cancer earlier. In this way, OHS/CanPath is a powerful data platform linking Clinical Translation, Adaptive Oncology and Therapeutic Innovation priorities. CanPath is a member cohort of the International Hundred Thousand Cohort Consortium (IHCC), a global network of population cohorts promoting translational research through cross-cohort data linkage. CanPath has also played a role in national COVID-19 surveillance and tracking initiatives.

CanPath includes about 8,000 self-identified Indigenous participants, most of whom are living in urban settings (approximately one third have contributed biological samples). The CanPath leadership, including OICR, are committed to developing partnerships with Indigenous communities to understand their needs in personalized health. Working with the Waakebiness-Bryce Institute for Indigenous Health at DLSPH, an Indigenous health strategy will be co-developed with Indigenous participants for data linkage and genomic investigation of participant contributions that respects their unique cultural contexts and health priorities. There is also a strategic intent to explore new Indigenous participant recruitment to the cohort.

2. Canadian Cancer Clinical Trials Network (3CTN)

3CTN is a pan-Canadian network established in 2014 to improve patient accrual to academic cancer clinical trials. As a national initiative with a consortium of eight funders and four collaborating organizations, 3CTN has independent governance, operational and advisory committees. OICR hosts and supports the Coordinating Centre, which is the operational and communications hub of the network, and supports Ontario sites. The Network's current four-year strategic plan renewal covers the period beginning in fiscal year 2018-19 and extending through fiscal year 2021-22.

3CTN's goal of increasing effectiveness and impact of academic clinical trials ties into OICR's priorities to increase translational impact through support of clinical testing. In the coming years, 3CTN will have a strategic emphasis on supporting pediatric clinical trials and implementing a new framework to support greater remote access to clinical trials.

3. Ontario Cancer Research Ethics Board (OCREB)

OCREB currently serves as a research ethics board (REB) to 27 of 28 Ontario institutions that conduct oncology clinical trials, streamlining the review process, minimizing redundancy, ensuring harmonization and consistency, and saving the time and cost of having a study reviewed by REBs at every study site.

OCREB operations are supported by OICR in a partial cost-recovery model, with some operational support subcontracted to Clinical Trials Ontario. In 2021-2026, OCREB will have a greater emphasis on inclusion of pediatric clinical trials in its portfolio and will continue to participate in efforts to nationalize cancer REB reviews. OCREB will also revise its performance metrics to address questions of clinical trial efficiency and effectiveness. It is expected that OCREB will be critical in supporting the

design and review of trials within the CTP, particularly the WOO Network which will require multi-centre collaboration for rapid accrual in many cases.

Defining success. The Clinical Translation Theme will result in a dynamic translational pathway in which scientific findings progress from preclinical studies to innovative clinical trials, further seeding new convergent ideas and collaborations that will result in new treatments, changes in how care is provided for cancer patients and increased understanding of how to detect, diagnose and treat cancer earlier. Our work with Ontario Health (Cancer Care Ontario) together with oncology system stakeholders is expected to result in a defined pathway to systematically evaluate and implement cancer innovations into the Ontario health system, and progress towards a Learning Health System model, in which research and clinical data are increasingly linked and data from individual patient interactions are utilized to improve care.

Key metrics to track success (see **Appendix D**) will include:

- Number and impact of publications;
- Number of invention disclosures, patent applications and awards;
- Amount of leveraged research funding attracted;
- Number of persons with enhanced knowledge, training or skills;
- Number and impact of collaborations across Research Themes and with the community;
- Measures of increased collaboration and partnership with the pharmaceutical industry;
- Number of novel clinical trials supported;
- Measures of increased, timely access to clinical trials for Ontario cancer patients;
- Number of collaborative projects supported that involve Adaptive Oncology and/or Therapeutic Innovation investigators;
- Evidence of health system and/or policy change in Ontario;
- Number of new diagnostics developed and implemented to select patients for therapy;
- Number of research studies in which patient partners are engaged in program design and delivery, and impact of this engagement.

5.3 Therapeutic Innovation

Challenge. Ontario researchers have recognized strengths in identifying and validating pathways that are important for cancer growth and spread. However, mounting a drug discovery campaign against biological targets in these pathways requires substantial resources and scientific expertise often found exclusively within biotech and pharma companies, such that academic discoveries are often published and then picked up by industry to develop into cancer therapies. Starting in 2008, OICR built in-house drug discovery expertise to translate Ontario discoveries into therapeutic candidates, generating valuable intellectual property (IP) and local commercialization opportunities. This has resulted in a large portfolio of promising advanced therapeutic assets, as well as new discoveries poised to feed the pipeline. Additional resources and expertise from across the community are now needed to capitalize on these opportunities to develop novel therapies for cancer patients and realize more economic benefit for the people of Ontario.

Goal. The goal of Therapeutic Innovation (TI) is to prosecute novel, validated cancer drug targets and advance selective therapeutic candidates through to clinical development, collaborating with FACIT to ensure that these assets possess a competitive target product profile to attract further investment, licensing opportunities and/or pharma partnerships leading to clinical trial testing, regulatory review and ultimately, market approval as a cancer medicine.

Therapeutic Innovation in Action

To understand Therapeutic Innovation's vision for the future, consider a potential scenario where members of OICR's Adaptive Oncology and Clinical Translation teams are leading a pre-surgical clinical trial (e.g., a Window of Opportunity Trial) for a new drug for leukemia. Working together, they identify a new pathway that is reducing the effectiveness of the drug being tested, causing patients to become resistant to the treatment.

OICR's Drug Discovery Program is brought in to develop a drug targeting the newly discovered pathway that can be used in combination with existing therapies to effectively treat leukemia. Through the CTIP program, the joint team is able to discover and optimize compounds that block the target, kill resistant leukemia cells, and demonstrate in vivo efficacy in unique mouse models developed locally. With these encouraging results, FACIT decides to invest in the program and creates an Ontario spinoff company to advance the asset into clinical studies. This asset is partnered with the local clinical accelerator Triphase that quickly brings the potential drug into clinical trials that are conducted in Ontario. Clinicians across the province are now able to refer other leukemia patients to the clinical trials conducted with this innovative therapy.

The preliminary results from the clinical trials are encouraging and demonstrate the safety of the drug. These exciting results attract the attention of a large pharmaceutical company that licenses the asset and further invests in the start-up company to develop the compound in Canada, advancing it into Phase 2 proof of concept clinical studies. Thus, patients in Ontario receive access to a promising new therapy, while the spinoff company creates new jobs, attracts international investment and brings other economic benefits to the province.

Design. TI consists of the Drug Discovery program and the Cancer Therapeutics Innovation Pipeline (CTIP). There are currently 10 promising assets advancing through the TI pipeline (**Figure 7**).

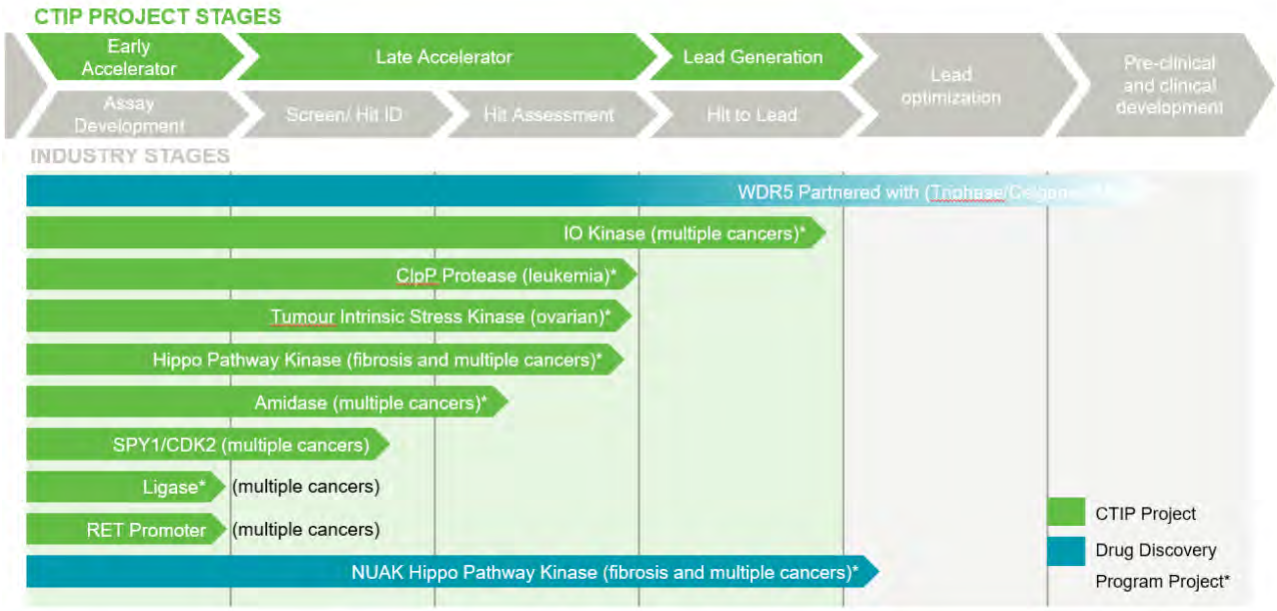


Figure 7: Therapeutic Innovation pipeline (combined CTIP and Drug Discovery assets in development) as of August 2020. The Drug Discovery program is currently leading or participating in 70% of the CTIP portfolio, indicated by an asterisk, and continues to support the development of WDR5 and back up compounds via partnership with Triphase/Celgene/BMS. Note: Top arrow refers to CTIP phase designation and below this arrow are the corresponding standard industry stages.

1. Drug Discovery program

Overview. The Drug Discovery program aims to: (1) identify, validate and prioritize therapeutic targets that have first-in-class or best-in-class potential from OICR's programs and Ontario labs; (2) identify lead compounds and preclinical candidates for prioritized cancer targets that possess a competitive

target product profile to attract investment; and (3) bridge the gap between academia and industry by providing pharmaceutical drug discovery expertise in an academic environment.

Approach. The Drug Discovery program is comprised of more than 30 researchers with extensive pharma/biotech drug discovery experience and expertise spanning the entire drug discovery process from target identification and validation to clinical candidate selection. The program combines a unique mix of biology and analytical, computational and medicinal chemistry expertise with the state-of-the-art infrastructure necessary to successfully advance drug discovery projects.

The success of the Drug Discovery program is exemplified by a landmark deal with Triphase/Celgene for a first-in-class epigenetic drug targeting WDR5 (on-going) and a partnership with Janssen on the BCL6 target (terminated at late lead optimization). These partnerships were enabled by FACIT, including seed funding, company creation and partnership negotiations. In addition, Drug Discovery provides collaborative research resources to the Ontario research community (>25 requests annually).

Increased base funding will be allocated to the Drug Discovery program under Strategic Plan 2021-2026 to ensure that it is properly resourced to develop promising assets, address growing community demand, and enable the development of the Drug Discovery Community model described below. OICR will pilot the exchange of staff scientists and trainees between the Drug Discovery program and Ontario labs to facilitate mutual learning, and will work in conjunction with FACIT to engage with the Ontario research community to scout for new cancer drug targets, provide advice to drug discovery researchers, and identify commercialization opportunities.

2. Cancer Therapeutics Innovation Pipeline (CTIP)

Overview. CTIP is a competitive program open to investigators at Ontario academic institutions, small biotechs or start-up companies to identify and advance novel, selective lead molecules (small molecules or biologics) capable of attracting partnerships and investment for further preclinical and clinical development.

Approach. CTIP will continue to fund proposals at three stages of drug discovery: Early Accelerator, Late Accelerator and Lead Generation (**Figure 8**). A project can enter at any stage and can advance across stages as deliverables are met based on a go/no go decision aligned with industry standards. Projects may include collaboration with the Drug Discovery program and may access preclinical models from CT and biomarker support from AO. Expert and strict stage-gated strategic and scientific review is provided by the Therapeutics Pipeline Advisory Committee (TPAC).

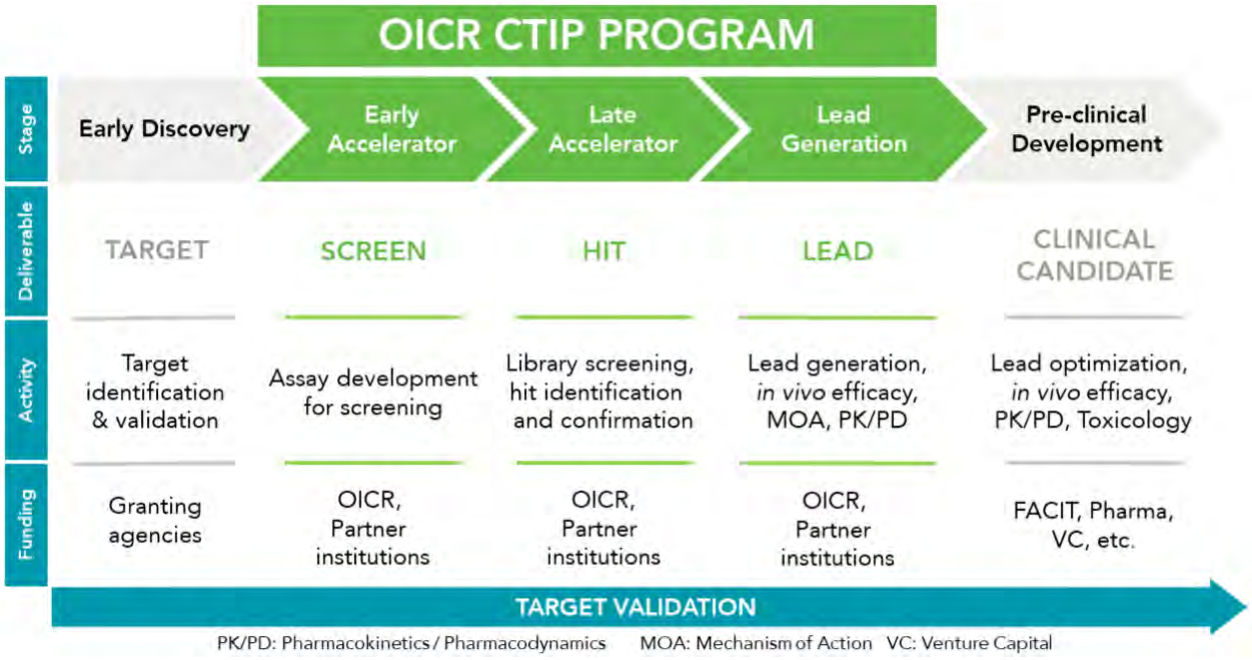


Figure 8: Overview of the Cancer Therapeutics Innovation Pipeline. Investigators with a validated target apply to the Early Accelerator stage to develop an assay to screen for molecules that modulate the target and advance to Late Accelerator to conduct a screen, while biologists on the team establish additional assays (biochemical and cell based) to help evaluate the resulting hits. Hits are prioritized and optimized by medicinal chemists to advance the project to Lead Generation, where a robust testing cascade is used to demonstrate the compounds' mechanism of action and specificity in cells. The compounds' metabolic properties are also assessed and optimized to ensure that their pharmacokinetic profile supports in vivo animal studies. A lead is declared if the team establishes efficacy in an appropriate animal model, at which point FACIT has the option to further invest in the project to advance it into lead optimization and eventually, selection of a molecule for clinical testing.

Currently in its third year of funding, CTIP is advancing 10 promising first-in-class and/or best-in-class projects in its pipeline (**Figure 7**). Under Strategic Plan 2021-2026, additional resources will be allocated to grow and develop the pipeline, source new targets, enable deep target validation across the pipeline, and strengthen the IP position around leading assets to attract external funding and partners for downstream development. The following principles will be applied to optimize CTIP:

1. Greater flexibility in the funding and timing of Late Accelerator and Lead Generation projects to better support the development of high-quality assets and attract co-development partners.
2. Raising the bar for project entry to industry standards and increased vigilance around the competitive landscape across the CTIP portfolio to ensure clear market pull.
3. Expanded community engagement to encourage investigators from across the province, including from smaller cancer centres and universities, to submit new proposals and work with them together with input from TPAC to develop strong submissions.
4. Better networking of drug discovery groups across the province to leverage expertise and resources .

A longer-term goal of Therapeutic Innovation is to scale the CTIP program by partnering with Ontario cancer centres and universities to form a **Drug Discovery Community (DDC)** that leverages joint resources to advance the most promising assets. To support this vision, OICR will increase engagement activities that bring together the Ontario cancer drug discovery community, including workshops/symposia to share knowledge, build collaboration, and identify promising assets for

development. In addition, the OICR will also provide access to training and educational resources on topics such as intellectual property identification, management and protection; the drug discovery process; target validation; and industry requirements. Where possible, OICR will also facilitate hands-on training through lab rotations and exchanges.

Defining success. The TI Theme will result in the development and advancement of a robust portfolio of promising first-in-class or best-in-class Ontario assets that attract follow-on investment from FACIT and other partners for downstream development and clinical testing. We will also make measurable progress towards the establishment of the DDC model, where pooled resources and expertise are leveraged to scale the breadth and impact of Ontario drug discovery efforts, driving local commercialization of Ontario IP and associated economic benefit.

Key metrics to track success (see **Appendix D**) will include:

- Number of invention disclosures and patent applications;
- Number of projects/assets that advance through the TI pipeline, attract further investment;
- Number of partnerships, licenses and start-ups;
- Amount of private sector investment in the TI pipeline and partnered assets;
- Number of persons with enhanced knowledge, training or skills;
- Number and impact of collaborations across Research Themes and with the community;
- Progress in developing a larger unified drug discovery-development model through the DDC.

5.4 Integration across Research Themes

The Clinical Translation Pathway bridges AO and TI research (**Figure 9**), enabling a bedside to bench and back model to fuel the research pipeline and validate promising discoveries. It will:

- Allow for the preclinical and clinical validation of discoveries arising from AO and TI research;
- Facilitate the application of WOO trial findings to inform new biomarker development in AO;
- Leverage AO technology and data sharing platforms to support CTP projects, including CAP/IQMH-certified Imaging and Genomics platforms for diagnostic-grade testing of patients in CATA trials;
- Enable biomarkers, novel targets, preclinical models and knowledge gained from clinical trials to inform new and existing TI projects;
- Integrate implementation science research with AO projects to facilitate the development of innovations for adoption into the health system;
- Integrate new concepts from across the portfolio through the Convergence projects in the CTP.

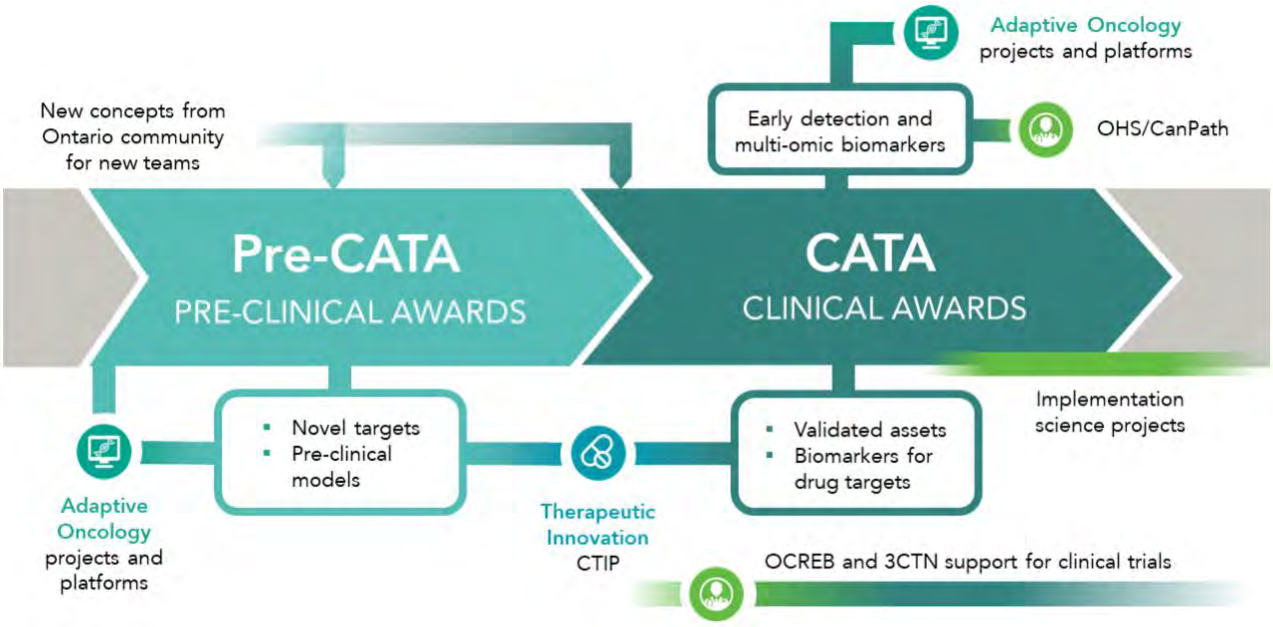


Figure 9: The Clinical Translation Pathway integrates research across OICR's Research Themes.

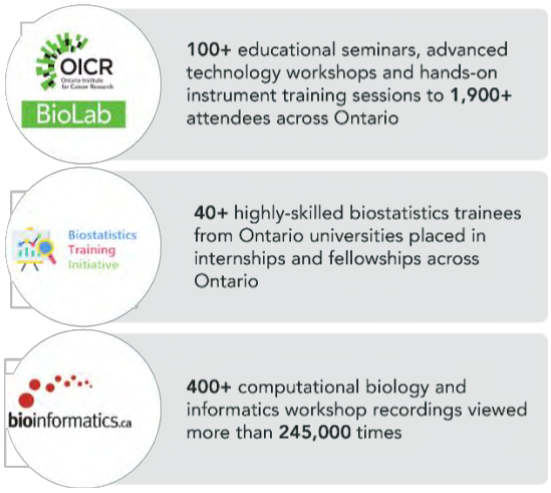
In addition, AO-TI interactions will be fostered through:

- Recruitment of a new investigator with expertise in drug target selection, systems biology, and response biomarker development;
- Systems biology initiatives to mine drug sensitivity/resistance data to find novel drug synergy and/or additive activities will be supported through CTIP; and
- Integration of AO expertise into CTIP projects to help identify biomarkers for targets of interest.

6 Enablers

6.1 Talent Mobilization

Since its inception, OICR has invested in developing a critical mass of world-class researchers in Ontario to drive the discovery and translation of cancer innovations. The primary vehicles have been the Investigator Awards (IA) program, focused on attracting and retaining outstanding scientists and clinician-scientists to the province; training opportunities within research labs across the province; and targeted training initiatives including advanced laboratory methods and emerging technologies, bioinformatics, biostatistics and molecular pathology. Strategic Plan 2021-2026 brings these efforts together under a coherent strategy for talent mobilization, which embraces concepts of equity, diversity and inclusion (EDI), and is focused on developing and supporting the next generation of cancer researchers, and strengthening engagement with investigators and trainees across Ontario to build and benefit from a more connected and collaborative cancer research community.



1. Investigator Awards

The current IA program consists of three categories of Investigators (Levels I, II, Senior) and two categories of clinician-scientists (Levels I and II). Funding supports salary and/or research, as determined by host institutions, in five-year terms (six years for initial appointments of Investigator Level I and Clinician-Scientists) that are renewable based on successful evaluation by academic tenure-like review panels. As of July 31, 2020, OICR is supporting 30 OICR Investigator Awardees (22 Investigators and eight Clinician-Scientists) across 10 institutions, including nine MDs.

The IA program will evolve under Strategic Plan 2021-2026 to address emerging challenges that are hampering its sustainability and impact. These are: (1) the recruitment of early and mid-career investigators is impeded by unrestricted commitments to senior-level investigators due to an absence of term limits (assuming continued successful review); (2) recent awards have lacked explicit principles for integration with OICR priorities, as well as for gender, diversity and geographic distribution; and (3) inconsistent connectivity of IA holders to OICR misses an opportunity to leverage their expertise and strengthen connections with Ontario cancer research institutions to improve the Institute's impact.

Approach. The renewed IA program will focus on the recruitment and retention of early and mid-career investigators to build the next generation of world-leading translational cancer researchers, which has become increasingly critical as institutions navigate the impacts of the COVID-19 pandemic. Recruitment will align with OICR priorities and mentorship goals, addressing gaps in expertise or reinforcing areas of Ontario strength. The following changes will be implemented:

1. Term limits will be introduced to free up funding for new awards. OICR will partner with host institutions to plan for sustainable career paths following award terms.
2. Criteria for award term renewal will be updated to include enhanced standards.
3. Senior investigators will be recruited by exception to address local expertise gaps and/or for leadership succession.
4. Co-funding models will be sought with host institutions to the greatest extent possible.
5. IA opportunities will be communicated with greater transparency.
6. Equity, diversity and inclusion will be considerations in appointments.
7. IAs will have formal affiliation with OICR programs/PIs and participate in the Scientific College.
8. Mid-career and Senior Investigators will be asked to participate in the mentorship of Early Career Investigators and to identify collaborative opportunities for convergent research.

2. OICR appointments and Scientific College

OICR grants Associate (status-only) appointments to investigators at external research institutions who are highly engaged in one or more OICR research project and are active members of the OICR community, and Affiliate (status-only) appointments to exceptional investigators at external research institutions who share scientific focus with OICR and collaborate with OICR investigators in support of Institute research priorities. As of August 2020, there are nine OICR Associates and two Affiliates.

Under Strategic Plan 2021-2026, OICR appointments will be expanded, in alignment with OICR priorities and EDI principles. In addition, the Institute will establish the *OICR Scientific College* to better connect and leverage OICR-associated investigators at Ontario universities, cancer centres and research institutes. The College will include OICR Investigators (internal investigators, and those receiving an IA award), Associates and Affiliates, and scientists participating in OICR-funded research projects. Activities will include targeted annual meetings, speaker's series, and mentorship opportunities for new and early career investigators and trainees.

3. Building the next generation of innovators

Since 2016, OICR has supported 500 graduate and undergraduate students across the province through hands-on learning opportunities. OICR will continue to develop the next generation of cancer researchers by growing the number of trainee opportunities within OICR's Research Themes, providing mentorship opportunities through the OICR Scientific College, and promoting career development through the recently established the *Rising Stars in Cancer Research Network*, a pan-Ontario network to promote cancer research performed by trainees (undergraduate, graduate and medical students and postdoctoral fellows) at Ontario academic institutions. The Network's goals include promoting trainee research, and providing networking, mentorship and professional development activities, including in IP education and entrepreneurship.

Defining success. Investments in Talent Mobilization will result in a growing cadre of world-class investigators and Highly Qualified Personnel (HQP) recruited/retained and developed in Ontario, who are highly engaged in advancing OICR and Ontario cancer research priorities, and reflect the diversity of Ontario talent.

Key metrics to track success (see **Appendix D**) will include:

- Number of Investigators recruited/retained, by career-stage;
- Number of persons with enhanced knowledge, training or skills;
- Number and impact of OICR-supported scientific meetings, events, workshops, courses and seminars, and number of attendees
- Measures of equity, diversity and inclusion (to be determined based on EDI policy);
- Number of jobs created/supported through OICR research funding.

6.2 Collaborative Research Resources

OICR established the Collaborative Research Resources (CRR) to broaden access to OICR technology infrastructure, expertise and resources for the Ontario cancer research community through cost sharing arrangements structured as collaborations or as fee-for-service projects. In the last half of fiscal year 2019-2020 alone, more than 286 projects were conducted, giving rise to a range of outputs, including 98 shared assets, research tools or resources, 98 instances of leveraged funding, 90 training opportunities, 63 contributions to clinical studies, 37 publications, seven contributions to clinical or educational guidelines, two contributions to policy, and five health services-related improvements. Drawing on feedback from the 2020 External Review, under Strategic Plan 2021-2026, the technology programs and resources under CRR will strengthen their business plans, including objectives, outreach plans and metrics to monitor performance and community needs on an ongoing basis.

Defining success. The Collaborative Research Resources will continue to ensure that Ontario institutions have access to leading-edge technologies, resources and infrastructure to conduct world-class cancer research and translation.

Key metrics to track success (see **Appendix D**) will include:

- Utilization of OICR technologies, services and resources;

- Number and impact of collaborations with the Ontario cancer research community.

6.3 FACIT

OICR created FACIT[xxvii] to deliver Ontario First commercialization to realize the value of made-in-Ontario IP. FACIT operates as an independent corporation. OICR invests in FACIT to further facilitate OICR's purposes of initiating, supporting, and stimulating the translation of cancer research into treatments, programs, technologies, and therapies for the benefit of persons diagnosed with cancer or who are at risk of having or developing cancer.

FACIT invests in and builds local companies to develop Ontario cancer innovations, manages IP assets and associated value-generating strategies, attracts investment and industry partners, and creates and retains private sector jobs in Ontario. OICR works to foster an environment that enables FACIT's activities and helps to sustain its operations. OICR's investment in FACIT drives an "Ontario First" translational model ensuring that made-in-Ontario ideas become made-in-Ontario solutions. This model integrates outstanding Ontario science, healthcare market pull, early commercial planning, seed capital, expert IP management, and industry experience to de-risk promising discoveries and drive value creation in Ontario, better positioning them to ultimately reach the market and patients. In this way, OICR and FACIT address a critical gap not filled by any other entity of higher learning and research in Ontario.

FACIT's award-winning commercialization model has anchored competitive biotech companies and innovations to the province by providing Ontario First seed capital, executive management, corporate and market guidance, and access to an industry/investor network. By enabling Ontario to compete with incumbent markets for IP development, the differentiated OICR-FACIT translational model has increased the value of Ontario's best oncology innovations, attracted additional investment from the private sector, and derived local value from IP. Examples of this model's success are provided under Section 2.4 (*Driving innovation ecosystem growth and economic impacts*). OICR's and FACIT's success in research translation and commercialization, respectively, has produced a promising pipeline of high-quality oncology innovations that is ripe for advancement. A snapshot of FACIT's current asset portfolio, included in **Appendix C**, illustrates a breadth of innovation types, as well as several investments that have advanced with support from FACIT's early-stage Prospects funding to equity-based Compass Rose funding. FACIT is committed to capitalizing on these opportunities, attracting the next generation of innovations for its asset portfolio, and securing new and impactful investment and industry partnerships.

Under Strategic Plan 2021-2026, OICR will continue its investment in FACIT to enable commercialization efforts and benefits to Ontario's life sciences ecosystem. This includes an optimized alignment of FACIT activities with the technology and research strengths of OICR to develop commercialization frameworks for diagnostics and data science and informatics tools as well as working with OICR to investigate the possibility of new revenue streams by commoditizing some of OICR's technology platforms in genomics, informatics, and drug discovery. FACIT will also work with other venture capital entities in Ontario to collaborate on investments and share information and knowledge to further drive the development of Ontario-based IP and ensure assets are optimally capitalized to develop and stay in the province. In addition, FACIT will work with OICR's Drug Discovery program to engage and educate the Ontario research community in identifying and developing the best oncology drug assets that have a pathway towards commercialization.

The high-level goals for FACIT during 2021 to 2026 are captured in the following five priorities to sustain its commercialization operations for Ontario. The model will be positioned as a key receptor

capable of scaling impact as provincially catalyzed investment capital begins to match the increasing strategic importance of IP.

CORE: Strengthen FACIT's commercial foundation to accelerate innovation outcomes and manage growth in the existing portfolio of Ontario IP and assets.

As a general reflection of overall enterprise growth, and consistent with potential growth within the biotechnology market, assets under FACIT's management have increased by ten-fold over the last five years. This commercialization success has led to the need for FACIT to continue dedicating resources to manage its existing portfolio of assets.

FACIT's funding/investment programs require more than just capital alone to achieve innovation outcomes. Thus, a suite of services and management processes will also be employed to foster a greater likelihood of successful returns. This includes tapping into a broad array of knowledge experts in areas of strategic importance to help mitigate many of the challenges faced by FACIT's commercialization initiatives.

FACIT will also ensure that efficient OICR and FACIT corporate and tax structures are in place and maximum residual capital is available to re-invest in Ontario innovations. For example, as FACIT builds on successes, its achievements are expected to be accompanied by a sporadic influx of financial gains. Historically, most Canadian health commercialization initiatives have had minimal infrastructure requirements for management of financial returns, and these were not in place when FACIT started. Tools that will be employed to manage tax planning will help ensure that FACIT's corporate structure can optimize the capital available to FACIT to re-invest in Ontario's breakthrough technologies and better position FACIT to continue to attract third party investment partners as well as the momentum of economic development. These considerations are critical for the further support and stability of FACIT's investment programs since investments in biotech and life sciences/healthcare continue to be speculative with an uncertain timing of financial returns. These and other critical Core activities requiring a certain operating expense are needed to maintain FACIT as a leading seed investment vehicle for Ontario First commercialization and a ready receptor of investment capital from a variety of public and private partners.

FUEL & SCALE UP: Bolster investment pipeline through bridging promising innovations to the next value inflection point; address seed gap and enhance investment portfolio by applying venture principles to commercialization.

FACIT provides essential funding and commercial support to improve translation for Ontario start-ups and researchers developing cancer-related technologies. Although a broader and deeper funding program will be needed to allow FACIT to retain influence over later stage investments in the future, FACIT's current seed funding programs – the Prospects Oncology Fund and the Compass Rose Oncology Fund – remain essential sources of commercialization funds to address the seed stage gap and prevent the export of promising innovations.

FACIT will continue to champion the Ontario First mission by ensuring strong new ventures are adequately capitalized to establish roots in the province and grow and compete on the international stage. This involves FACIT continuing its work in identifying cutting edge oncology assets for the

Prospects Fund and Compass Rose investment vehicles as best it can with the pool of available investment capital balanced with the need to continue to support its current portfolio of assets.

In addition to financial capital, FACIT will continue to deliver other critical drivers of a healthy innovation ecosystem by facilitating access to technical expertise and providing professional management to new start-ups. These and other non-financial commercial supports for FACIT's portfolio of assets, alongside its financial investments, will continue to be one of FACIT's unique means of servicing the Ontario marketplace and keys to its success.

DIVERSIFY: Expand commercialization support and facilitate technology transfer across all oncology innovation verticals.

FACIT has realized the need to cast a wider net in the diversity of its investment activities to address the breadth of new assets developed at OICR and across the province, including diagnostics, predictive biomarkers to drive precision clinical management of cancer patients, and the development and commercialization of data analysis and other informatics tools. In addition, opportunities exist to commoditize technology platforms, such as next-generation sequencing and software tools developed at OICR. In the ensuing years, FACIT will put additional effort into identifying new opportunities in these asset classes augmenting its established and growing portfolio of investment in therapeutics and devices. FACIT will take a highly selective approach in deciding which new assets to support given the limited amount of liquid capital available as it continues to support its existing assets (many of which are yet to deliver financial returns) as well as the need to critically define the market appetite and pathway to patient impact of any new IP. FACIT will endeavor to share with stakeholders the importance of Ontario First incentives and capital to allow for investment into more diverse assets that may have longer pathways to realize innovation outcomes.

EVOLVE: Leverage successful commercialization venture model and explore alternative funding sources and collaboration with other seed venture investment groups to reinforce FACIT and fill the seed gap in Ontario.

Growing biotechnology companies create local jobs, industry experience, and talent as part of commercialization and is contingent upon having greater access to local capital and availability of talent for company management and access to resources. FACIT, as well as the overall Ontario seed stage venture capital investment community has come to the realization that more coordination and collaboration of resources, intelligence, subject matter expertise, and in some cases pooled investing, is needed to further drive the local life sciences innovation ecosystem. In addition, public-private partnerships that invest, retain, and develop assets concurrently in a hybrid, community-supported model can further drive the risk-reward capital pool for Ontario life sciences. To augment its commercial reach and impact, FACIT will engage with other seed stage investment groups and work with the Ontario government in securing a larger pool of investment capital for life science commercialization that can also be channeled into further investment in oncology-based assets. FACIT will endeavour to collaborate with select partners in seeding high-value oncology assets that require a larger initial capital contribution that promise to have significant therapeutic and financial impact for Ontario. This will include leveraging expertise and resources in a reciprocal fashion to further FACIT's capabilities and impact, as needed. Lastly, FACIT will work with OICR to explore the possibility of developing commercialization models arising out of select technology cores to generate additional revenue streams for the future.

ENGAGE: Promote market pull innovation development and entrepreneurial culture across Ontario to expand deal flow and drive the local ecosystem.

The goal of building a culture of entrepreneurship/commercialization in Ontario is critical to the Province's ability to attract and drive partnerships, commercialize products, drive innovation and create a basis for sustainable differentiation in the market. A challenge in this regard has been bridging the different mindsets of industry and academia. These differences in approach include structuring scientific experiments to answer questions related to product needs rather than investigating scientific concepts in a more open-ended manner or working with teams that have predefined project goals rather than exploratory research valued by traditional funding agencies. As part of its long-term goals to impact Ontario, FACIT will continue the establishment of a culture of entrepreneurship among its partners around the province and by doing so will be recognized as an outward-facing community leader for Ontario commercialization of life sciences and healthcare innovations.

FACIT will also work on driving the recommendations coming out of the report by the Expert Panel on IP to the Ontario Government entitled *"Intellectual Property in Ontario's Innovation Ecosystem*" to generate more disruptive IP in Ontario (Canada overall), educate and train our post-secondary sector researchers on "IP savviness" and build an entrepreneurship mindset beyond the traditional academic confines. FACIT is committed to engaging key Ontario government stakeholders to develop a central long-term comprehensive and coordinated strategy to arrive at the most effective solutions for Ontario. Leveraging FACIT's proven Ontario First commercialization expertise will meet the goals for IP strategy in Ontario and realize the benefits of local health research for the people of Ontario.

Overall, OICR intends to be more deliberate in fostering research programs that have ultimate commercial potential. This includes working with FACIT to enhance CTIP, and leveraging Triphase, where appropriate, to validate therapeutic candidates in the clinic. OICR will engage FACIT more broadly in providing a "commercialization/industry lens" to assess funding applications to help identify projects with high potential to lead to new IP and downstream investment while meeting clinical translational needs for patients. OICR leadership will assist FACIT in working with other seed capital entities to generate co-investment opportunities, where appropriate.

Defining success. Commercialization through FACIT will help develop and realize the local value of Ontario IP, including attracting partnerships for asset development and validation, and the creation of sustainable Ontario companies that attract private sector investment and create local jobs.

Key metrics to track success will include:

- Number of invention disclosures, patent applications and awards;
- Number and impact of partnerships for IP development and validation, including number of innovative human trials or studies providing patients with access to promising new interventions or diagnostics;
- Number of licenses executed;
- Number of sustainable start-ups created, and number of companies seeded and/or enabled through application of FACIT commercialization expertise;
- Number of jobs created at Ontario companies;
- Amount of private sector investment in Ontario companies;
- Cumulative value returned to shareholders from FACIT-funded projects.

7 Achieving results

7.1 Operations

OICR is accountable to the people of Ontario. The Institute prepares an annual business/operating plan, approved by its Board and submitted to MCU, which outlines annual objectives and activities to be carried out to deliver on the priorities set out in its strategic plan. The following summarizes the structures and principles underpinning the execution of Strategic Plan 2021-2026.

Governance, leadership and advisory structures. OICR is led by its President and Scientific Director and Executive team and governed by a volunteer skills-based Board. An institutional Scientific Advisory Board advises OICR leadership and the Board on overall scientific strategy. OICR's three Research Themes are each led by Heads and advised by Scientific Advisory Committees (SACs). Programs, networks and resources within the Themes are led by scientists and clinician-scientists, based at OICR and/or at Ontario universities and cancer centres according to where the expertise and capabilities lie.

Research portfolio*.* In implementing Strategic Plan 2021-2026, OICR is committed to:

1. *Emphasizing excellence in translational potential in funding decisions and oversight:* All research programs, projects, networks and resources (whether funded at OICR or at external institutions) are adjudicated by independent, external peer-review in accordance with criteria defined in RFAs, with funding decisions approved by the OICR Board. Progress towards deliverables is reviewed at least annually by thematic SACs or equivalent[xxviii] who may recommend changes to research activities and budget. Investigator Awards renewals are reviewed by the Investigator Awards Retention and Promotion Committee, which makes recommendations on continued funding to the OICR Board. All research programs, projects, networks, resources and IAs report annually[xxix] on key performance indicators in accordance with OICR's agreement with MCU.
2. *Embracing concepts of equity, diversity and inclusion (EDI):* OICR will develop an EDI policy and processes for its implementation in our research design, practice, personnel support mechanisms and training.
3. *Integrating patient perspective and insight*: OICR will build a closer relationship with patients, caregivers and family members to integrate their voice and priorities throughout the organization. In addition to the patient and caregiver representatives already in place on the OICR Board, a council of patients and caregivers will be appointed to advise the organization on patient partnership. A Patient Partnerships Lead has been recruited to lead this important work, which will include the development of a community of patients and patient organizations, the inclusion of patient advisors on research steering/advisory committees and on key projects, and the creation of patient-focused educational resources.
4. *Data sharing:* All data arising from OICR-funded projects will be made available to the research community in a timely fashion, except when premature disclosure would interfere with IP protection, commercialization efforts, or contractual agreements with collaborative parties.

Engagement and communications. OICR engages with a range of stakeholders, including researchers, clinicians, patients, research institute leaders, government, health system partners, funders and industry to exchange knowledge, maintain the currency of its strategy and facilitate collaborations and partnerships. Under Strategic Plan 2021-2026, OICR will initiate more regular

interactions with Ontario institutions, including hosting more regular site visits, more virtual events, meetings and seminars accessible across the province, using OICR's communications platforms to promote research findings from smaller institutes and young researchers, and integrating more patient perspectives into OICR communications.

Corporate Services. The Institute's support functions (finance, human resources, risk and compliance, privacy, facilities management, lab support and operations, information security and information technology, legal, procurement and health and safety) will continue to support OICR's strategic goals through the delivery of professional, high-quality programs and services to staff and stakeholders through an approach that is accessible, responsive, accountable, customer focused and team-oriented. Corporate Services proactively re-evaluates its processes and systems. For instance, information technology and security are evaluated and enhanced regularly, including yearly third-party assessment of its systems. Moving forward, increased attention will be afforded to staff career development and the mental health of employees (especially in light of workplace changes associated with the COVID-19 pandemic). In addition, enhanced development for investigators will be instituted to improve their leadership and group dynamic skills with their trainees and peers.

7.2 Implementation roadmap

OICR intends to provide up to six months of supplemental funding to research projects funded through Strategic Plan 2016-2021 that have experienced delays due to the COVID-19 pandemic (COVID funding), and up to 12 months of bridge funding to programs, networks and resources that will continue under Strategic Plan 2021-2026. Bridge funding allows these components to develop robust research and business plans commensurate with their funding envelopes, which will be finalized after the 2021-2026 budget allocation is finalized with MCU. Funding of new projects and continuing or new programs, networks and resources will follow immediately after the COVID and bridge funding periods.

A high level, preliminary timeline for the development and launch of programs, projects, networks and resources in support of Strategic Plan 2021-2026 is provided in **Figure 10** below:

Figure 10: Summary of Implementation Plan. (*OICR will solicit Funding Requests from 3CTN, BTI, OCREB, and OHS however reviews are expected to be conducted by their respective boards/committees with recommendations returned to OICR.) Timelines for Convergence Awards to be determined as projects advance and opportunities for collaboration arise.

We will continue to work with Ontario cancer research and clinical communities and Ontario Health (Cancer Care Ontario) to develop and refine the structures and processes needed for the effective implementation of Strategic Plan 2021-2026, ensuring that the Institute remains nimble and able to capitalize on emerging opportunities to advance our mission.

8 Impact

Strategic Plan 2021-2026 articulates an ambitious strategy to stem the growing burden of cancer, ushering in next generation precision medicine approaches that can help transform the trajectory of cancer in Ontario. The impact of these approaches on individual cancer patients will be profound. It will equip patients and their clinicians with a personalized, proactive cancer management plan that includes safer, more effective and less invasive testing and treatment to fight their disease and return to living healthy and productive lives. Working together with researchers, clinicians, patients, government, health system partners, industry and collaborators around the world, we will help make this vision a reality for cancer patients and ensure the health and economic benefits of cancer research are fully realized for all Ontarians.

OICR's logic model (**Appendix D**) depicts how the Institute's investments will deliver outputs and outcomes that will ultimately drive research, health and economic benefits for Ontario over the next five years. These include:

Research system:
Ontario is recognized as a global leader in cancer research and innovation

- Growing pool of outstanding investigators and hundreds of highly qualified personnel (HQP) recruited/retained and developed at institutions across Ontario;
- Big Data integration and sharing across Ontario, linked to national and global initiatives, driving precision medicine research and translation;
- Ontario institutions have access to leading-edge technologies, resources and infrastructure to conduct world-class cancer research and translation;
- Research networks developed to share expertise, standardize approaches and undertake collaborative research;
- Innovative tools developed and disseminated to drive patient partnership in cancer research;
- **$200M+** in value-added additional research funding attracted to Ontario **($120M+ by end of 2023-24)**;
- Enhanced pharma partnerships supporting clinical trials;
- Strengthened critical cancer research infrastructure across the province, contributing to Ontario's larger life sciences cluster's research and impact.

Health system:
A long-term strategy to stem the coming surge in cancer cases

- More cancer clinical trials in Ontario, including **4 first in human trials** providing patients with access to promising new interventions **(2 first in human trials by end of 2023-24)**;
- An increasing number of clinical studies in the early cancer detection and intervention space, testing next generation cancer detection modalities and more effective treatments for newly diagnosed cancer to prevent progression to advanced disease, stopping cancer in its tracks;
- Precise and proactive cancer management, resulting in better patient outcomes and quality of life, and health system cost savings;
- A pathway to systematically evaluate and implement cancer innovations into the Ontario health system, allowing cancer patients to realize the benefits of cancer research;
- Progress towards a Learning Health System model, in which research and clinical data are increasingly linked and data from individual patient interactions are utilized to improve care.

Economy:
Realizing the commercial potential of Ontario innovation

- Generation of new Ontario IP with commercial potential, including drug candidates, diagnostics, prototypes, software, and tools;
- **5 new sustainable companies will be created** that achieve third party follow-on financing **(2 new sustainable companies will be created by end of 2023-24)**;
- **Attraction of an additional $350M in follow-on financing** to FACIT's asset portfolio to further advance Ontario innovations **(an additional $140 million attracted by end of 2023-24);**

- **In addition to supporting and creating jobs at OICR and OICR-affiliated institutes, 280 highly skilled jobs at Ontario companies/start-ups will be created for the next generation of scientists and entrepreneurs (115 jobs by end of 2023-24).** By cultivating HQP jobs in the biotech sector, associated start-ups are better positioned to be sustainable and scaled. Success with these start-ups can lead to strong economic growth opportunities, including additional expansion of skilled jobs to more than 10,000 in the province.

9 Appendix A: Strategic planning process

OICR kicked off an extensive, highly-consultative strategic planning process with its Board in September 2018. Key activities included:

- A review of existing research programs to assess performance and identify opportunities for greater impact;
- A strategic foresight exercise aimed at defining the potential impact of cancer in 2040 and resulting implications for OICR's strategic priorities;
- Visits to 16 Ontario cancer centres and universities to understand priorities, gaps and opportunities for collaboration, with follow up sessions to discuss and help shape emerging OICR priorities;
- A survey of OICR and FACIT's partners and collaborators to assess the value we bring and opportunities for augmenting impact;
- Strategic discussions with the OICR Board, Scientific Advisory Board and thematic Scientific Advisory Councils;
- Think tanks with cancer researchers and clinicians, FACIT, Ontario Health (Cancer Care Ontario), disease charities, patients, caregivers and other stakeholders to flesh out potential opportunities;
- A series of staff surveys, coffee hours and strategic planning workshops;
- A patient partnership workshop that resulted in tangible recommendations for how OICR could better integrate the patient/caregiver perspective in Institute priorities, programs and operations;
- Coordination with the Canadian Cancer Research Alliance visioning exercise to leverage consultation and survey data and enable alignment with other funders of cancer research; and
- A refresh of OICR's enterprise risk universe to understand and assess key organizational risks in order to inform how opportunities are prioritized and implemented.

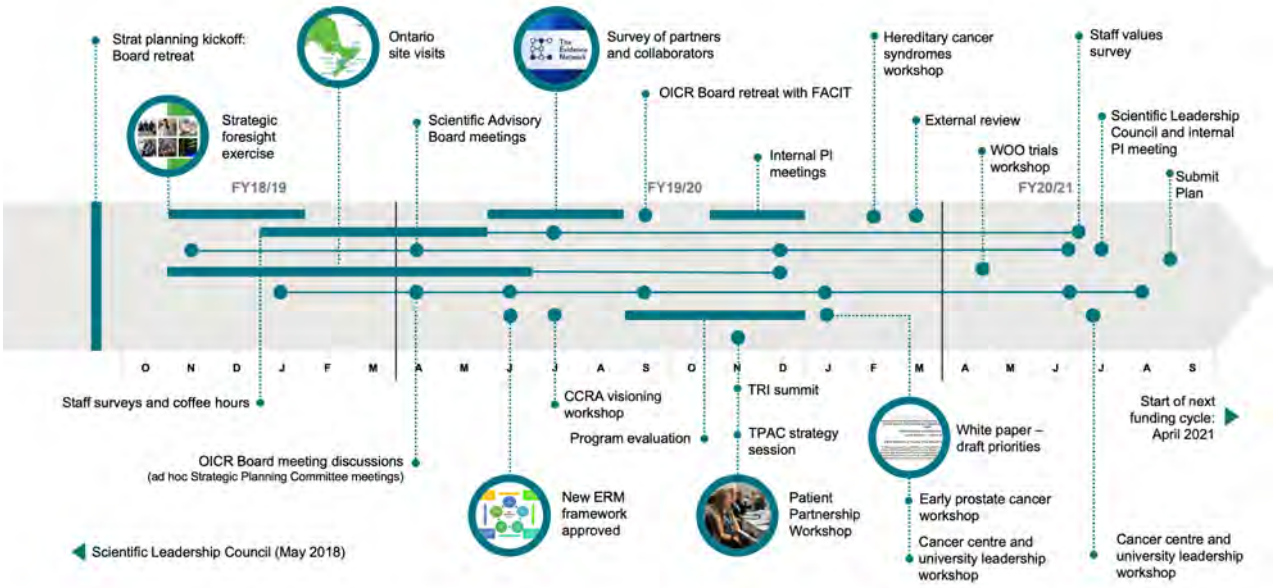


Figure 11: Summary of the strategic planning process.

Key takeaways from the consultations with Ontario stakeholders and advisors:

- Remaining at the cutting-edge of research technologies and approaches is critical for Ontario's global leadership in translational cancer research—this should be addressed by appropriately balancing investments in strengthening technology platforms at the MaRS centre, and reinforcing unique strengths at specific centres;
- Ontario has the best chance of improving cancer patient outcomes by working together – leveraging resources, collaborating across disciplines and across centres/regions, and sharing data in a safe and responsible way;
- Up front partnership with patients, clinicians and health system decision-makers remains critical to ensure that cancer research is aimed at unmet clinical needs and to facilitate the implementation of resulting innovations into care;
- Many centres are looking for additional support with commercialization and in fostering an entrepreneurial culture, which are important drivers of economic development for the province;
- Ontario needs to invest in the next generation of scientists and clinician-scientists through innovative training, recruitment and retention models;
- As the world moves into Big Data, there is a unique opportunity for OICR/Ontario to further our leadership in data sharing and informatics by building up AI/ML;
- Ontario cancer centres face distinct challenges due to regional context (e.g., demographics, linkage to a medical school, maturity of research institute, institutional investments, access to resources, etc.); creative collaborations are needed, including better networking between centres to share expertise and scale successful models.

The information gathered from these discussions were synthesized into an Ontario cancer research landscape document, which included an assessment of context and trends, strengths, gaps and opportunities, which form the basis for the priorities in Strategic Plan 2021-2026.

Many translational research opportunities were considered, discussed and refined through consultations with stakeholders across the province. The Institute has prioritized the opportunities where the Institute can make a unique contribution as an essential partner to the Ontario oncology ecosystem, by:

- Addressing unmet clinical need in areas aligned with Ontario research strength;
- Addressing critical gaps in Ontario translational research capacity (people, infrastructure, technology, networking) across the province;
- Further strengthening an area of Ontario global leadership or has high potential to develop into an area of global leadership for the province.

On a portfolio level, the strategic plan seeks to balance opportunities likely to yield nearer and longer-term measurable impact (health and economic), maintaining a moderate level of risk.

A key milestone in this process was the 2020 External Review of the Institute, in which an expert panel assessed OICR's current performance, impact and operations, as well as draft priorities for 2021-2026, and provided recommendations that have informed the finalization of this strategic plan.

10 Appendix B: Clinical trial emphasis in the Clinical Translation Pathway

The Clinical Translation Pathway will emphasize the funding of three types of clinical trials:

1) **Solid tumours amenable to complete or partial surgical resection upon initial diagnosis:** Early-stage trials using short or longer-duration pre-surgical interventions testing specific drugs, biologics, radiation therapy, alone or in combinations, coupled with comprehensive biomarker analysis of tumours and blood. Promising therapeutic results can lead to later stage trials (e.g., larger randomized trials) with the aim of changing clinical practice, which can be championed by other clinical trial consortia, such as Canadian Cancer Trials Group. As described below, pre-surgical window of opportunity trials and neo-adjuvant trials linked to biomarker analysis will be ke foci. In some studies, patients can be followed after surgery to test new imaging modalities (e.g., PET tracers) and liquid biopsy technologies developed through the Adaptive Oncology Theme with the aim of detecting early recurrence or renewed progression of disease. This, together with the molecular analysis and other *in vitro* investigations on the initial resected tumour, can inform clinicians on secondary therapies to deal with relapse or renewed disease progression, possibly in a more effective way.

2) **Primary-diagnosed solid tumours and blood cancers that are not amenable to upfront surgery** (e.g., certain brain cancers and leukemias): Innovative new drug, radiation and/or biologics can be tested in early phase exploratory trials linked to comprehensive biomarker assessment. These new therapies can be tested for various durations before current standard-of-care to assess effectiveness and/or combined with standard-of-care. In each case, the analysis of patient samples (tumour biopsies, blood) need to be specific primary or secondary endpoints. As above, some studies can opt to follow patients more long-term to test cancer imaging modalities or biomarkers (e.g., liquid biopsies) to track and detect recurrence or further progression of disease.

3) **Validation of diagnostics and biomarker tests for patient selection to improve clinical practice and clinical decision-making for early stage cancers:** There is a need for improved tests to help guide clinicians in this setting (e.g., early stage prostate cancer) to make more informed decisions using newer multi-omic tools to avoid invasive and toxic therapies when not needed or to avoid under-treatment. For example, in these trials on early-stage cancers, new biomarkers, biomarker combinations, and imaging technologies (or combinations thereof) can be validated as patient selection tools for more aggressive therapeutic intervention in higher-risk patients or watch and wait (surveillance) in lower-risk patients. The goal will be to perform trials leading to changes in clinical management that the health system (Ontario Health (Cancer Care Ontario)) would consider implementing.

11 Appendix C: FACIT's Asset Portfolio

Innovation Type	FACIT-funded assets through the Prospects Oncology Fund		FACIT-funded assets through the Compass Rose Oncology Fund	
Therapeutics	TALON PHARMACEUTICALS	Potassium channel antagonists	triPHASE	Local accelerator/receptor to expedite proof-of-concept and development of pre-IND cancer therapies
	Queens	CYP26 inhibitors for the treatment of leukemia and myeloma	FLUORINOV	FV162 Oral Proteasome Inhibitor
	DALRIADA	DT-1 class of small molecules with selective cancer cell-killing activity due to a unique "cloaking" mechanism	TURNSTONE BIOLOGICS	New class of targeted viral immunotherapies to fight cancer
	The Ottawa Hospital Research Institute	Cell-targeted amiR-containing exosomes that deliver sustained and amplified viral-mediated cell killing for pancreatic cancer	Fusion	Next-gen radiotherapeutics
	Notch THERAPEUTICS	Universally compatible source for the next generation of CAR-T therapies		WDR5 inhibitors for leukemia and solid tumours
	OICR	Cyclic and heterocyclic hydrazone-based linkers for antibody-drug-conjugates (ADC)		
	OICR	Programme targeting multiple members of the WD40 repeat domain (WDR) family with small molecules		
	UNIVERSITY OF TORONTO	Split Intein-Mediated Protein Ligation (SIMPL): a unique and disruptive system for detecting PPIs in real time		
	P² Pappas Pharma	Ganglioside-based cancer vaccine		
IT platforms	ZILIOMICS	Informatics platform enabling actionable clinical decision via interpretation and translation of tumor genomic sequences	ZILIOMICS	Informatics platform enabling actionable clinical decision via interpretation and translation of tumor genomic sequences
	16BIT	Breast cancer screening AI algorithm to pre-screen benign mammograms	PRIVACY ANALYTICS	Software that unlocks vast potential of health data without compromising individual privacy
	DNASTACK	AI platform to enable public/private data sharing networks, genotype-phenotype associations, patient match/recruitment	DNASTACK	AI platform to enable public/private data sharing networks, genotype-phenotype associations, patient match/recruitment
	bridge7	Scaling clinical expertise with AI to automate and improve the delivery of cancer care		
	Replica Analytics	Modeling software to create synthetic data based on real clinical datasets		
Med tech	Radialis Medical	Solid-state PEM system that produces higher resolution images and reduces radiotracer dose compared to PEM	HARMONIC MEDICAL	An ultrasound system to both detect and treat tumours for the relief of pain without surgery
	Nanology Labs	Nano-theranostic platform that enhances MRI contrast signal in the tumor as well as radiation therapy efficacy	Nanology Labs	Nano-theranostic platform that enhances MRI contrast signal in the tumor as well as radiation therapy efficacy
	XPAN	Less invasive access port to maximize laparoscopic surgical oncology	XPAN	Less invasive access port to maximize laparoscopic surgical oncology
		Multi-spectral X-ray imagers that improve the quality and accuracy of chest X-rays, & reduce demand for CT diagnostics		
	POLUMIROS INC.	Soft tissue filler for breast cancer patients - cosmetically superior, minimally-invasive cost-effective solution		
Diagnostics	OICR	Diagnostic gene test to predict which patients benefit from anthracycline chemotherapy	CELLULAR ANALYTICS	Microfluidic circulating tumour cell (CTC) capture platform and lung cancer biomarker chip
	Sunnybrook	Algorithm to predict breast cancer patient response to neoadjuvant chemotherapy		

Figure 12: FACIT's Asset Portfolio, current as of August 2020.

12 Appendix D: Measuring our Impact

OICR's logic model (**Table 6**) depicts how the Institute's investments under Strategic Plan 2021-2026 will deliver outputs and outcomes that will ultimately result in improvements to Ontario's cancer research, health and economic systems. While it takes an average of 17 years for research evidence to reach clinical practice,[xxx] OICR is on track to realize meaningful gains stemming from the advancement of discoveries in its current pipeline and sourcing promising innovations from across Ontario for further development. Outputs, such as publications, additional research funding and early clinical findings and select outcomes from this logic model will serve as inputs for future activities.

Table 6: OICR Logic Model for 2021-2026.

Inputs	Activities	Outputs (1-3 years)	Outcomes (3-15 years)	Impacts (15+)
People **Funding** **Technology, resources, Big Data** **Partner** **Promising research discoveries**	**Strengthen Ontario's capacity for translational cancer research** • Support and develop the next generation of cancer researchers • Enable access to leading edge technologies, resources, Big Data • Engage ecosystem stakeholders to identify research priorities, seed collaboration and share research results **Drive translational cancer research** • Conduct collaborative research • Lead, advise and contribute to the success of national and international cancer organizations/initiatives **Develop and commercialize IP (partnership with FACIT)** • Early commercial planning, strategy & IP management • Ontario First seed investments, de-risking assets for private sector • Create, manage & scale Ontario start-ups.	**Strengthened capacity for translational cancer research in Ontario** • Cadre of world-class investigators and Highly Qualified Personnel (HQP) recruited/retained and developed • Research community has access to leading-edge technologies, resources • New research funding to Ontario • Collaborations and partnerships to advance research priorities • New resources developed and shared to drive patient partnership in cancer research **Knowledge created and shared** • Findings that move the cancer field forward • Big Data developed, integrated and shared to drive precision medicine • IP generated: drug candidates, diagnostics, clinical decision-making tools, research tools • Clinical guidelines, health policies developed to support the implementation of innovations • Ontario contribution to national and global cancer research initiatives **IP developed and commercialized** • Partnerships for IP development, validation • Ontario companies created/seeded/enabled • Private sector investment in Ontario companies • Ontario jobs created	**Research system** • Ontario is recognized as a global leader in cancer research and innovation • Growing pool of outstanding Ontario investigators and HQP • Growing cancer research investment in Ontario • Increased cancer clinical trials in Ontario, including WOO and neoadjuvant trials • Patients are increasingly partnering in Ontario cancer research **Health System** • Patients access novel diagnostics, interventions via clinical trials in Ontario • Pathway established to systematically evaluate and implement cancer innovations into the health system • Precision medicine, driven by multi-parameter diagnosis, is standard of care for a growing proportion of cancers • Progress towards a learning health system model, in which research and clinical data are increasingly linked and data from individual patient interactions are utilized to improve care **Economy** • Growing ecosystem of sustainable Ontario start-ups/receptors, jobs and investment • Cultivation of skilled talent, entrepreneurs & management • Ontario realizes the value of homegrown IP	**Research system** • Ontario is at the forefront of cancer research and innovation, with universities, hospitals and institutes working together and leveraging integrated Big Data to tackle patient and health system priorities. • Ontario cancer research success leveraged across the life sciences sector, contributing to a larger cluster of research activity and impact **Health system** • Improved cancer prevention • Majority of cancers detected, treated and resolved early • Increased cancer patient survival and quality of life • Access to cost-effective cancer innovations across Ontario **Economy** • Robust ecosystem to commercialize research discoveries and harness the value of these made-in-Ontario ideas

OICR will work with MCU and its Board to prioritize and finalize a suite of indicators to track progress towards the achievement of Institute priorities against the goals set out in Strategic Plan 2021-2026. We will aim to establish targets by the end of Q1 2021-22, in consideration of baseline performance data, benchmarking of peer organizations and final confirmation of our funding. Potential indicators have been mapped to the logic model in **Table 7**. Program-specific metrics will roll up into Institute-level metrics.

Table 7: Draft OICR Logic Model indicators for 2021-2026.

Outputs (1-3 years)	Outcomes (3-15 years)	Impacts (15+)

Strengthened capacity for translational cancer research in Ontario
 	
• # of persons with enhanced knowledge, training or skills
• # of investigators recruited/retained by career-stage (early, mid or senior)
• *Measures of equity, diversity and inclusion (TBD)*
• # of jobs created/supported through OICR research funding
• Utilization of OICR technologies, services and resources
• # and impact of collaborations (provincial, national and international) and across OICR Research Themes
• $ secured and impact of partnerships that advance common priorities
• $ leveraged by OICR-supported investigators (internal and externally-based)
• Case studies of OICR contribution to the advancement of cancer research ecosystem priorities
 	
Knowledge created and shared
 	
• # and impact of publications (citation-based indicators)
• *Metric around Big Data collection, integration and sharing (TBD)*
• # new assets created by type
• Open source assets disseminated and used
• # of health policies created, cited
• # of clinical guidelines created/updated, cited
• # of scientific meetings, public events/outreach, workshops, courses and seminars organized or partially-funded by OICR (and # of attendees)
• # of media hits and social media interactions
	Research system:
	
	• Case studies of OICR's impact on accelerating, promoting and facilitating translation
	• # and impact of stakeholders collaborating through OICR support
	• $ cancer research investment in Ontario (CCRA data)
	• # of cancer clinical trials in Ontario, including early cancer (WOO and neo-adjuvant) trials
	• # of patients recruited to OICR or FACIT-supported trials
	• *Patient engagement (TBD)*
	
	Health system:
	
	• Pathway established to systematically evaluate and implement cancer innovations into the health system
	• Case studies of OICR's impact on:
	  ○ Improved patient access to novel interventions
	  ○ Adoption of health policies, clinical guidelines into practice to enhance prevention or patient care
	• *Metric on access to personalized medicine (TBD)*
	• *Metric on progress towards a learning health system (TBD)*
	
	Economy:
	
	• Upward trending:
	  ○ # of sustainable start-ups that achieve 3rd party financing
	  ○ # Ontario jobs created
	  ○ Amount of private sector investment in Ontario companies
	  ○ # of firms still active after 3, 5 years & # employees
	  ○ $ invested in Ontario by partners attracted by FACIT
		Research system:
		
		• Greater attraction of world-class HQP, global collaborations and investment in Ontario cancer research compared to 2005 baseline (prior to OICR) and across the life sciences sector
		
		Health system:
		
		• Decreased cancer incidence
		• Most cancers detected, treated and resolved at an early stage
		• Increased patient survival
		• Decreased cancer morbidity
		• Cost-effective cancer innovations adopted into care
		
		Economy:
		
		• Growing ecosystem of Ontario oncology companies, jobs and investment

IP developed and commercialized • # of invention disclosures • # of patent applications and awards • # and impact of partnerships for IP development and validation • # of licenses executed • # of start-ups created • # of companies seeded/enabled • # of jobs created at Ontario companies • $ of private sector investment in Ontario companies • Cumulative value returned to shareholders from FACIT-funded projects		

13 Glossary

3D	Three-dimensional
3CTN	Canadian Cancer Clinical Trials Network
AI	Artificial Intelligence
AO	Adaptive Oncology
ARGO	Accelerating Research in Genomic Oncology
BCL6	B-Cell Lymphoma 6 Protein
BETTER	Building on Existing Tools to Improve Chronic Disease Prevention
CanPath	Canadian Partnership for Tomorrow's Health
CAP	College of American Pathologists
CATA	Clinical Acceleration Team Awards
CCO	Cancer Care Ontario
CCRA	Canadian Cancer Research Alliance
cfMeDIP	Cell-free Methylated DNA Immunoprecipitation
CLIA	Clinical Laboratory Improvement Amendments
COMPASS	Comprehensive Molecular Characterization of Advanced Ductal Pancreas Adenocarcinoma for Better Treatment Selection: A Prospective Study
CPDC	Centre for Probe Development and Commercialization
CRR	Collaborative Research Resources
CT	Clinical Translation
CTIP	Cancer Therapeutics Innovation Pipeline
CTP	Clinical Translation Pathway
DDC	Drug Discovery Community
DLSPH	Dalla Lana School of Public Health
DNA	Deoxyribonucleic acid
EDI	Equity, Diversity and Inclusion
EIR	Executives in Residence
GA4GH	Global Alliance for Genomics and Health
GSK	Glaxo SmithKline
HCS	Hereditary Cancer Syndrome
HQP	Highly Qualified Personnel
IA	Investigator Award
ICGC	International Cancer Genome Consortium
IHCC	International Hundred Thousand Cohort Consortium
IND	Investigational New Drug
IP	Intellectual Property
IQMH	Institute for Quality Management in Healthcare
IT	Information Technology
LOI	Letter of Intent
LHS	Learning Health System
MCU	Ministry of Colleges and Universities
MD	Medical Doctorate
ML	Machine Learning
MRI	Magnetic Resonance Imaging
OCREB	Ontario Cancer Research Ethics Board
OCTANE	Ontario Cancer Targeted Nucleic Acid Evaluation
OHCRN	Ontario Hereditary Cancer Research Network
OHS	Ontario Health Study
OICR	Ontario Institute for Cancer Research
OMPRN	Ontario Molecular Pathology Research Network
OPTICC	Ontario Pathway to Innovation in Cancer Care
OTB	Ontario Tumour Bank
PEM	Positron Emission Mammography

PET	Positron Emission Tomography
PK	Pharmacokinetics
PM	Princess Margaret Cancer Centre
REB	Research Ethics Board
RFA	Request for Applications
RNA	Ribonucleic acid
RNA-seq	Ribonucleic acid sequencing
SAB	Scientific Advisory Board
SAC	Scientific Advisory Committee
STEM	Science, Technology, Engineering and Math
TBD	To be determined
TCGA	The Cancer Genome Atlas
TI	Therapeutic Innovation
TIAP	Toronto Innovation Acceleration Partners
TPAC	Therapeutics Pipeline Advisory Committee
TRI	Translational Research Initiative
UHN	University Health Network
US	United States
USD	United States Dollars
VC	Venture Capital
WOO	Window of Opportunity

[i] Cancer Care Ontario,2020. Ontario Cancer Statistics 2020.
[ii] de Oliveira, C., et al.., 2018.
[iii] Cancer Care Ontario, 2020.
[iv] Cancer Care Ontario, 2018.
[v] De, P., 2019. and Arnold, M., 2019.
[vi] Organizations receiving OICR funding directly or through 3CTN, 2016-2020.
[vii] Based on trial recruitment of adult patients at participating Network sites in comparison to baseline pre-3CTN data from 2011-2013.
[viii] Fiscal year reporting period: April 1, 2019 - March 31, 2020.
[ix] Accrual data spans August 2016 through March 2020.
[x] COMPASS trial accrual data as of January 2020.
[xi] Tinmouth J., et al., 2014. https://onlinelibrary.wiley.com/doi/full/10.1002/ijc.29191
[xii] Cancer Care Ontario, 2017. https://www.cancercareontario.ca/en/screening-performance-report-2016
[xiii] Cancer Care Ontario, 2012. https://www.cancercareontario.ca/sites/ccocancercare/files/assets/OCSPAnnualReport2010.pdf
[xiv] Start-up companies since 2004-05.
[xv] Represents the average annual economic impacts of OICR and FACIT MaRS-based operating expenditures based on financial data from 2010-2018 applied to Statistics Canada's 2015 Input-Output model.
[xvi] The ratio of OICR and FACIT leveraged funding to OICR's base funding amount was 2.93 in 2018-19.
[xvii] World Health Organization: Early cancer diagnosis saves lives, cuts treatment costs, 3 Feb 2017.
[xviii] Kakushadze, Z., et al., Data 2017, 2, 30;
[xix] McKinsey Cancer Centre: The next wave of innovation in oncology. September 2016.
[xx] Canadian Cancer Research Alliance (March 2019). Cancer Research Investment in Canada, 2016.
[xxi] https://www.cbc.ca/news/health/health-charities-1.5651328
[xxii] https://ipolitics.ca/2020/03/31/with-clinical-trials-halted-funding-drop-uhn-fears-layoffs-among-researchers-working-on-covid-19/
[xxiii] Accreditations: Institute for Quality Management in Healthcare (IQMH), College of American Pathologists (CAP), Clinical Laboratory Improvement Amendments (CLIA)
[xxiv] https://densebreastscanada.ca/

[xxv] npj Genomic Medicine (2016) 1, 15006; doi:10.1038/npjgenmed.2015.6; published online 13 January 2016.
[xxvi] Brenner DR, Weir HK, Demers AA, Ellison LF, Louzado C, Shaw A, Turner D, Woods RR, Smith LM. Projected estimates of cancer in Canada in 2020, CMAJ. 2020;192:E199-205.
[xxvii] OICR established FACIT as an independent business trust (the "Trust"), to further accelerate efforts in commercialization and support its not-for-profit status. The Trust housed all the commercial assets and related commercial activities, and was the vehicle through which OICR's IP and assets were further developed and commercialized. As a result of FACIT's commercialization successes, and based on financial and legal advice, the Trust incorporated FACIT Inc. in 2018 as a wholly-owned subsidiary. The business of the Trust was subsequently transferred to the corporation, including the IP transferred from OICR and related commercial assets. The Trust owns all of the issued and outstanding shares of FACIT Inc. and OICR remains the sole beneficiary of the Trust.
[xxviii] Programs that are part of broader collaborative efforts (3CTN, OCREB, GA4GH, CanPath) include independent committees that monitor progress.
[xxix] The Collaborative Research Resources report semi-annually to OICR leadership on collaborations or services provided to the research community.
[xxx] Balas and Bohen, 2000.

Ontario Institute for Cancer Research
MaRS Centre
661 University Avenue, Suite 510
Toronto, Ontario
Canada, M5G 0A3

Telephone: +1-416-977-7599
Toll-free number: +1-866-678-6427

info@oicr.on.ca
@oicr_news
@oicrpics
www.oicr.on.ca

Ontario

Funding provided by the Government of Ontario.